

The challenge of poorly controlled diabetes mellitus

P Home

SUMMARY

Diabetes is a growing healthcare challenge worldwide, with significant socioeconomic implications in industrialised and developing nations. Epidemiological studies indicate that diabetes is likely to reach epidemic proportions within the next few decades. A considerable proportion of people either have impaired glucose tolerance with a significant risk of development of diabetes, or have undiagnosed Type 2 diabetes. Many are poorly controlled on existing therapies, with significant implications for patients' quality of life and for healthcare expenditure. Pivotal to reducing the risk of morbidity and the development of complications and mortality is the normalisation of both fasting and postprandial blood glucose levels. Various healthcare initiatives address the attainment of this treatment goal; however, there is still a need for better disease management in both Type 1 and Type 2 diabetes.

Key-words: Prevalence · Review · Treatment · Type 1 Diabetes · Type 2 Diabetes.

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Diabetes Metab 2003,29,101-9

RÉSUMÉ

Le défi du diabète mal contrôlé

Le diabète constitue un défi croissant de santé dans le monde, avec des retombées socioéconomiques significatives dans les nations industrialisées ou en développement. Les données épidémiologiques indiquent que le diabète atteindra probablement des proportions épidémiques dans les toutes prochaines décennies. Une part considérable d'individus présentent soit une intolérance au glucose avec un risque significatif de développer un diabète, soit un diabète de type 2 méconnu. Nombreux sont mal contrôlés par les traitements existants, avec des implications significatives sur la qualité de vie des patients et sur les dépenses de santé. La normalisation tant de la glycémie à jeun que des valeurs glycémiques postprandiales joue un rôle pivot dans la réduction des risques de morbidité, du développement des complications et de la mortalité. Plusieurs approches de soins visent à atteindre cet objectif; cependant, le besoin d'une meilleure prise en charge persiste, tant pour le diabète de type 1 que pour le diabète de type 2.

Mots-clés : Prévalence · Revue · Traitement · Diabète de type 1 · Diabète de type 2.

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Received: ; revised: December 10, 2002

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Diabetes mellitus is a significant global health-care challenge, both in industrialised and developing nations. Estimates of future prevalence indicate that diabetes is reaching epidemic proportions worldwide, with between 5 and 10% of the world population affected. This review highlights the scale of the problem and some of the actions being taken to address it. MEDLINE searches for all English-language epidemiologic, prevalence and socioeconomic studies, healthcare initiatives and treatment guidelines published between January 1990 and September 2001 were undertaken. Studies selected for detailed review assessed the effects of glycaemic control on complications, comorbidities and mortalities in Type 1 and Type 2 diabetes, preferably by randomised, double-blind, placebo-controlled, multinational trials. Guidelines for the diagnosis and treatment of diabetes and its complications were also identified.

Potential benefits of intervention

Diabetes is usually associated with macrovascular and microvascular complications, which are a significant cause of comorbidity and mortality in people with diabetes. Macrovascular complications include ischaemic heart disease (IHD), peripheral vascular disease, and stroke [1, 2]. As in the general population there is considerable variation in the prevalence of IHD; however, people with diabetes have a 2- to 8-fold increase in cardiovascular mortality compared with people who do not have diabetes in the same population [3]. Comorbidities such as hypertension and diabetes-associated dyslipidaemia significantly amplify the risk of IHD [4-6]. People with diabetes have approximately twice the prevalence of hypertension compared with non-diabetic patients [3]. In the UK Prospective Diabetes Study (UKPDS), nearly 40% of subjects were defined as hypertensive on entry (receiving antihypertensive treatment or with a mean systolic blood pressure ≥ 160 mmHg and/or a mean diastolic blood pressure ≥ 90 mmHg) [7] and in the Multiple Risk Factor Intervention Trial (MRFIT), mean blood pressure was significantly higher in the subset of men with diabetes [8].

Microvascular complications of diabetes, such as peripheral neuropathy, diabetic retinopathy and diabetic nephropathy, are directly related to poor glycaemic control [9, 10]. People with diabetes are 17 times more prone to kidney disease, with diabetic nephropathy being the most common complication [11]. Diabetic nephropathy may eventually lead to end-stage renal disease and thus significant mortality.

Approximately 30-40% of people with diabetes develop retinopathy, and diabetes is the most common cause of blindness in the working years of life in developed countries [12]. However, peripheral neuropathy is probably the most common complication, present in approximately 40% of patients with diabetes and leading to limb amputation in conjunction with peripheral vascular disease in many [11].

These data underline the significant health risks associated with diabetes and the clear need for effective intervention. The benefits of tight blood glucose control (more intensive therapy) are well documented in a number of long-term, large-scale trials. In particular, the incidence of macro- and microvascular disease has been shown to be significantly decreased [9, 10, 13-15] with a concomitant improvement in quality of life [16-18]. While the short-term costs of more intensive therapy in the Diabetes Control and Complications Trial (DCCT) were higher than for conventional therapy [19], the impact of tight blood glucose control on the long-term costs of diabetes was found to be highly favourable in a cost-benefit model [16]. Implementing modern rather than traditional therapy in a population with Type 1 diabetes in the USA (120,000 people who met DCCT enrolment criteria) would result in a gain of 920,000 years of sight, 691,000 years free from end-stage renal disease, 678,000 years free from lower limb amputation, and 611,000 years of life at an additional cost of US\$4.0 billion over the lifetime of the population. The incremental cost per life-year gained was estimated to be US\$28,661 within the range accepted to be cost-effective. Gains in cost-effectiveness in terms of both additional life-years and quality-adjusted life-years are also found in people with Type 2 diabetes [20]. An incidence-based simulation model of Type 2 diabetes has also reported that maintaining normoglycaemia results in a decrease in diabetic comorbidity, with an associated increase in patient life expectancy of 1.39 years.

Cost models demonstrate that overall medical care charges increase significantly for every 1.0% increase above an HbA_{1c} of 7.0% [21], whereas a sustained reduction in HbA_{1c} can produce significant cost savings within 1-2 years of improvement [22]. The reasons for these short-term savings are unclear, but may be related to reduced symptom burden and greater functionality. In the long term the high costs of treating hyperglycaemia may be offset by a reduction in the costs of treating diabetic complications [20, 23]. For instance, in the Kumamoto study, the use of more intensive insulin therapy increased primary treatment costs by 30%, but resulted in a 50% reduction in the costs associated with complications [24]. Similar cost offsets were reported for intensive blood glucose control in the UKPDS [25].

To what extent can endpoints be changed?

Results from the DCCT and UKPDS show that normalisation of blood glucose levels is pivotal in reducing the risk of morbidity, the development of complications, and mortality in both Type 1 and Type 2 diabetes. In Type 1 diabetes, obtaining tight blood glucose control with insulin therapy remains a key challenge, while in Type 2 diabetes hyperglycaemia has to be managed in tandem with other

cardiovascular risk factors (chiefly hypertension, dyslipidaemia and smoking).

In Type 1 diabetes, the DCCT established that intensive management (using enhanced patient education in the context of intensive insulin therapy — three or more injections/day or by external pump) to achieve near normal blood glucose levels reduced microvascular complications such as retinopathy (76% reduction), neuropathy (60% reduction) and nephropathy (50% reduction) [9].

The UKPDS suggested that tighter blood glucose control in people with Type 2 diabetes also reduces the morbidity and mortality associated with macrovascular and microvascular complications [10, 15]. After 10 years' intensive treatment, the risk for any diabetes-related endpoint was 12% lower than in the conventional group (95% CI, 1-21%, $p = 0.029$). This was mainly due to a 25% reduction in microvascular endpoints.

Control of postprandial hyperglycaemia (PPHG) was associated with a significant reduction in the rate of myocardial infarction and mortality in the Diabetes Intervention Study [14]. Because people with Type 2 diabetes spend approximately 50% of their time in the postprandial state, the possible contribution of PPHG to overall poor glycaemic control should not be underestimated [14, 26, 27]. Plasma glucose levels measured in the early and extended post-lunch period (2 and 5 h postprandial, respectively) in people with Type 2 diabetes are found to correlate better with glycosylated haemoglobin (HbA_{1c}) than with fasting plasma glucose [28]. HbA_{1c} levels therefore provide a reliable index of overall long-term glycaemic control, since measurement of HbA_{1c} takes into account blood glucose control around the clock, consistent with the observation that HbA_{1c} is a better predictor of neuropathy progression than fasting plasma glucose [29].

Why are we not more successful in achieving targets?

Community-based studies in the USA have shown that mean fasting plasma glucose is generally as high as >180 mg/dL (>10.0 mmol/L) in people with diabetes, compared with approximately 85 mg/dL (4.5 mmol/L) in those without diabetes [30]. Data from the UKPDS and other studies in Type 2 diabetes also indicate the extent to which people with Type 2 diabetes fail to maintain effective blood glucose control. Appropriate target levels of fasting plasma glucose have been recommended as <126 mg/dL (<7.0 mmol/L) in the prevention of microvascular disease and <108 mg/dL (<6.0 mmol/L) for reducing the risk of major vessel disease [31]. In the UKPDS, 94% of subjects had fasting plasma glucose levels ≥ 7.0 mmol/L (≥ 126 mg/dL) on entry to the study and HbA_{1c} levels were approximately 9.0%.

There are a number of possible reasons why blood glucose control remains poor. Firstly, evidence suggests that

treatment habits among both clinicians and people with diabetes change too slowly to stay in line with research findings. Secondly, there is a continued lack of training facilities for healthcare professionals in many countries. Thirdly, in Type 2 diabetes there is a seemingly inevitable decline in insulin secretory function, meaning that doctors and patients are always chasing deteriorating blood glucose control, with an unwelcome increase in burden of tablet consumption or the escalatory dose of insulin. In a Norwegian study of patients with established Type 2 diabetes of more than 2 years' duration, mean HbA_{1c} at study entry was $>9.0\%$, and during the course of 1 year's treatment, over 60% of patients on oral agents switched to insulin therapy due to an $HbA_{1c} > 10.0\%$, a level regarded as much too high a threshold by many [32]. Fourthly, the burden of insulin injections and tablet load reduce concordance with injected insulin regimens, and indeed up to one-quarter of people have been reported to have a psychological problem with insulin injection [33]. Finally, the view still persists with some professionals that Type 2 diabetes is 'mild diabetes' and that patients should not be overly concerned.

The burden of diabetes

Epidemiological burden

Global incidence and prevalence

According to a 1997 estimate [12], 120 million people have Type 2 diabetes (approximately 2% of the world population) and an additional 4 million have Type 1 diabetes. Type 2 diabetes accounts for more than 85% of all cases of diabetes in developed countries and almost all cases in developing countries. It appears to be epidemic (affecting a high and increasing proportion of the population) in many parts of the world, and represents a serious and growing global health challenge primarily as a result of increased obesity, ageing populations, increasing urbanisation and a more sedentary lifestyle [34, 35]. However, data from many parts of the world with high and increasing prevalence (Asia, Latin America, China) are not broadly based, and so this estimate is likely to be markedly low.

There is considerable variation in the relative distribution of the two major forms of diabetes (Types 1 and 2) between ethnic groups and communities [12]. Type 1 diabetes is one of the most common childhood diseases in developed European countries and the incidence has increased dramatically in some newly prosperous countries [12, 36]. Susceptibility to Type 1 diabetes varies somewhat by ethnic origin, as evidenced by the low genetic susceptibility in indigenous Japanese populations. The incidence of Type 1 diabetes ranges from 0.5/100,000 children per year in China to over 35/100,000 children per year in Finland [12].

The prevalence of Type 2 diabetes differs markedly between communities, even within ethnic groups, and the degree to which the population assumes a more urbanised,

sedentary lifestyle is a major contributing factor. The US National Health and Nutrition Examination Surveys III (NHANES III) revealed that the prevalence of diagnosed Type 2 diabetes in the adult US population in non-Hispanic blacks and Mexican-Americans was 1.6 and 1.9 times that in non-Hispanic whites, respectively [37].

Expected growth

By 2010, one estimate of the worldwide prevalence of diabetes is that it will reach 215 million, although newer data from a number of countries suggest this figure will be reached much sooner [12, 36]. King *et al.* [36] predicted a rise in global diabetes prevalence to 5.4% of the world population by the year 2025 (a 27% increase in developed countries and a 48% increase in developing countries).

The incidence of Type 2 diabetes in particular is expected to increase considerably as developing countries become more Westernised in terms of availability of healthcare and modernisation of existing resources, as well as a result of substantial improvements in diabetes surveillance and screening. Growth is projected to be greatest in Asia and Africa, where diabetes could become 2-3 times more common than it is today [12]. By 2025, more than 75% of people with diabetes will be from developing countries, compared with 62% in 1995 [36]. Although there are far fewer reports of the incidence of Type 1 diabetes in developing countries, the prevalence of Type 1 diabetes is also likely to increase worldwide due to the increased longevity of people with diabetes (resulting from better diagnosis, increased insulin availability and technical advances in risk factor control and management of complications). The countries with the greatest numbers of people with diabetes are India, China and the USA, and this is likely to remain so by the year 2025 [36]. Global estimates and projections of diabetes (total) are presented in *Table I*.

Table I
Estimates and projections of diabetes – 2000 to 2025 (figures in millions).

	2000 [12, 36]	2010 [12]	2025 [36]
Worldwide	147-154	221	299
Africa	9	14	—
Asia	85	132	—
Europe	27	33	—
France	2.0	3.0	
Germany	3.5	4.5	
UK	2.1	3.1	
Latin America	16-18	23	39
North America	14-15	18	22

Underdiagnosis

There is a general acknowledgement that the figures above seriously underestimate the true prevalence of diabetes. Underdiagnosis of Type 1 diabetes is often thought not to be an issue since there is an absolute requirement for exogenous insulin, but where medical facilities are poor, children may simply die of 'gastroenteritis' or, in Africa, 'AIDS'. However, there is evidence (reviewed in reference 38) that 5-30% of people with Type 2 diabetes have some of the clinical and immunological features of Type 1 diabetes, such as islet cell antibodies (ICAs) and/or insulin autoantibodies, and/or autoantibodies to glutamic acid decarboxylase (GAD). Such antibody-positive people have variously been described as having 'latent autoimmune diabetes in adults (LADA)', 'latent Type 1 diabetes', 'progressive insulin-dependent diabetes mellitus (PIDDM)', 'Type 1½ diabetes', or even 'Type 3 diabetes' [38]. Animal studies, and some studies in people with Type 1 diabetes, suggest that exogenous insulin may slow the progressive deterioration of islet β -cell function where pancreatic damage is due to an autoimmune process [39-41].

There is significant late diagnosis of Type 2 diabetes, largely as a result of the progressive nature of the disease, compounded by a lack of awareness about diabetes in the general population [42]. Type 2 diabetes is frequently insidious in onset, with a significant proportion of people likely to remain undiagnosed for several years before symptoms appear, or a complication leads to diagnosis, accounting for the high percentage of people already showing complications as discussed above [10, 43, 44]. NHANES III found the prevalence of undiagnosed Type 2 diabetes to be 2.7% of the population (5.4 million people) in the US using American Diabetes Association (ADA) criteria and 6.3% using World Health Organisation (WHO) criteria (1988-1994 figures) [37]. The higher prevalence noted with the WHO criteria is due to the identification of more people as having diabetes when the 2-h oral glucose tolerance test (OGTT) glucose criterion is included.

Recently, both the ADA and WHO revised their diagnostic criteria for diabetes [45, 46] by recommending the lowering of the diagnostic value of the fasting plasma glucose concentration to ≥ 7.0 mmol/L (≥ 126 mg/dL) from the previous level of ≥ 7.8 mmol/L (≥ 140 mg/dL). This was partly in recognition of the fact that, even at 7.0 mmol/L, patients have a substantially increased risk of microvascular disease mainly because a number of studies suggest that this level relates best to the 2-h oral OGTT cut-off. This lowering of the threshold will lead to a further increase in the number of people diagnosed with diabetes and, indeed, recent papers suggest a further lowering of the fasting, but not 2-h OGTT cut-off, criterion is indicated [47].

Socioeconomic and healthcare burden of diabetes

In addition to the considerable impact on affected individuals, diabetes and its complications result in substantial expenditure by healthcare systems [18, 48-50]. Diabetes is a significant burden, not only to payers (in terms of costs of initial therapy, treatment to targets, complications), but also to employers (work absenteeism), and patients/families in both the short and long term [17, 18].

Diabetes is a leading cause of mortality and the number of deaths for which diabetes is the underlying cause is steadily increasing. In 1990, diabetes was ranked the 16th-leading cause of death worldwide and accounted for 0.6 million deaths. However, this figure was a marked underestimation since, although diabetes can cause mortality directly, most deaths are due to indirect causes, in particular cardiovascular disease, recorded as the end-stage health event. Adjustment for the heightened risk of death from other causes resulted in 2.8 million deaths being attributable to diabetes in 1990 [51]. Mortality studies suggest a 50% 10-year life expectancy for people with diabetes, with 60-70% of deaths related to diabetes [27, 52-55]. Thus, with the prevalence of diabetes now reaching 200 million, around 13 million people per annum will be dying from diabetes-related complications.

The total health burden attributable to diabetes rose from the 29th to the 14th most important cause worldwide after taking into account not only the directly attributable burden, but also its role as a risk factor for death and disability for other conditions. Moreover, incorporation of attributable burden into DALY (disability-adjusted life years) estimates raised diabetes from 14th to 2nd rank in developed countries, beaten only by ischaemic heart disease itself [56].

A global estimate of the costs associated with managing diabetes is difficult because, in poorer countries, healthcare expenditure is not monitored and treatment is not always available. Estimates from 1990 suggest that the annual per capita healthcare cost ranges from US\$11 in China to \$1,860 in the USA [50]. In industrialised countries, the healthcare costs for people with diabetes are between 2 and 4 times higher than the cost for the general population. Consistent with this, studies suggest that one-seventh of the total US dollar expenditure on healthcare in the USA was spent on the care of people with diabetes, and in 1997 the US medical expenditure attributable to diabetes was US \$98.2 billion [18].

Direct economic costs of diabetes are those generated by the resources used in managing the condition and its complications (acute and long term), including all drugs, consultations, education, monitoring, referrals to other specialities and admissions. In the USA, treatment for diabetes and acute metabolic complications accounted for US\$7.7 billion in 1997 [18]. Other costs included direct hospital care (US\$27.5 billion), physician visits (US\$3.2 billion) and nursing home care (US\$5.5 billion). Indirect economic costs

address the potential resources that are lost as a consequence of the disease, taking into account the societal costs of morbidity, disability and premature mortality. The indirect costs of diabetes in 1997 in the USA were absenteeism (US\$1.4 billion), permanent disability (US\$32.5 billion) and mortality (US\$17.0 billion).

Personal burden of diabetes

People with Type 2 diabetes are not only hyperglycaemic, but are frequently also hypertensive, dyslipidaemic and obese. The risk of cardiovascular disease increases substantially when such risk factors coexist, making lifestyle modifications and early and rigorous treatment of hypertension essential. The ADA [57] has estimated that 75-80% of adults with diabetes die as a result of IHD, cerebrovascular disease and/or peripheral vascular disease. In personal terms, therefore, a diagnosis of Type 2 diabetes suggests a need for continuing attention to control of blood glucose, blood pressure and blood lipids through medication, diet and exercise. People with Type 1 diabetes, and increasingly those with Type 2 diabetes, have the additional burden of subcutaneous insulin injections, self-monitoring and care of their insulin supplies and equipment.

Initiatives from government and other healthcare organisations

The substantial and increasing socioeconomic burden of diabetes and the realisation that effective interventions are available have prompted healthcare communities around the world to scrutinise their care provision and delivery, with the common aim of setting national and international standards, addressing deficiencies, removing inequalities and promoting future investment and research. In general, the initiatives recommend the implementation of national management strategies for diabetes, improved education for people affected with diabetes, health professionals and the general public, equal access to medication and supplies, and support for research to advance the knowledge of diabetes management.

Europe

A 'landmark' event in Europe was the St Vincent Declaration of 1989, endorsed by governments in this WHO region, and which included achievable targets for the reduction of long-term diabetes complications (blindness, renal failure, limb amputations and cardiovascular disease). While its 5-year goals were certainly not all met in all countries, the St Vincent Declaration has acted as a catalyst for pan-European national initiatives (*Tab II*).

The St Vincent Declaration Action Programme [58] resulted from collaboration between the European offices of the WHO, the International Diabetes Federation (IDF), and professional, government, healthcare and payer organisations. As part of the Action Programme, the IDF (European

Table II

Example objectives and recommendations of government and healthcare initiatives.

Region	Initiative	Objectives
Europe	St Vincent Declaration	— Improve quality of life and quality of care
	IDF (Europe)	— Maximise implementation of guidelines
	National Service Framework (UK)	— Guarantee local and national standards of care — Improve access to specialist services — Optimise education for patients and healthcare professionals
USA	NDEP	— Increase public awareness of the seriousness of diabetes — Improve the understanding and knowledge of healthcare providers — Promote responsible self-management — Healthcare policies
	DQIP	— Assess clinical performance measures (eg, HbA _{1c} , lipid testing measurements, surveillance for complications) to permit comparison between healthcare providers — Assess measures related to patient education, health status, patient satisfaction, access to healthcare
	HCQA/HEDIS	— Monitor quality of health plans — Measure quality of diabetes care
Rest of the World	Declaration of the Americas (PAHO/IDF)	— Improve public recognition of diabetes and develop national organisations to promote public awareness — Develop national strategies — Develop integrated healthcare models to ensure communication of information at all relevant levels — Allocate adequate resources and sustain supply of affordable medications — Empower people with diabetes and healthcare professionals and promote partnerships
	Western Pacific Declaration on Diabetes (WHO/IDF)	— Recognise economic burden — Establish diabetes as a priority — Develop and implement national prevention programs — Work towards universal access to quality care — Encourage strategic alliances — Recognise and promote the importance of diabetes education — Integrate diabetes activities with those of other noncommunicable diseases — Address problems of discrimination against people with diabetes — Encourage research

Region) developed comprehensive guidelines for the management of Type 1 and Type 2 diabetes, and for the management of cardiovascular risk in people with Type 2 diabetes [31, 59, 60]. In the UK, a National Service Framework (NSF) for diabetes is currently in development. Following publication of the new National Standards for Diabetes Care in 2001, work is progressing on the delivery strategy, which is due to be implemented from 2003.

USA

For many years, the ADA has published guidelines for the management of diabetes based on the results of clinical

trials and expert opinion. These are continually updated and have recently been revised in light of the results of the DCCT and the UKPDS clinical trials. In an effort to encourage the setting of a national standard for the care of people with diabetes, a number of US government agencies have collaborated with the ADA.

National Diabetes Education Program (NDEP)

The NDEP is a joint initiative sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health, and the Division of Diabetes Translation of the Centers for Disease Con-

trol and Prevention in the USA [61], and has the overall aim of reducing the burden of diabetes in the USA. The NDEP has four main objectives (*Tab II*), which have given rise to development of program partnerships, development and dissemination of educational tools and resources, dissemination of knowledge-based guidelines, and the promotion of policies/activities to improve quality and access to diabetes care.

Diabetes Quality Improvement Program (DQIP)

The DQIP began as a coalition of a number of patient, professional, and healthcare organisations with the aim of improving the outcomes of care for the > 3.5 million patients with diabetes covered by the public health system in the USA. In the year 2000, DQIP measures were incorporated into the Health Plan Employer Data and Information Set (HEDIS) of the National Commission of Quality Assurance (NCQA) (*Tab II*). Continuing these initiatives, the ADA instigated the Provider Recognition Program (PRP). By the end of 2000, more than 1,200 physicians (caring for an estimated 500,000 people with diabetes) had achieved recognition.

Rest of the world

Declaration of the Americas

It was estimated in 1996 that over 25% of the world population with diabetes lived in North or South America. Growing recognition of the burden of diabetes in these continents led to a pan-American initiative launched in the same spirit as the St Vincent Declaration some years previously. With considerable overlap with the US NDEP initiative, the Declaration of the Americas on Diabetes stipulated 10 main aims that are summarised in *Table II*.

Western Pacific Declaration on Diabetes

An important part of the WHO Prevention and Control of Noncommunicable Diseases initiative was the signing of the Western Pacific Declaration on Diabetes in June 2000 [62], developed under the joint leadership of the WHO and the IDF. The Declaration aims to integrate eight strategies as part of a healthy lifestyle initiative for the prevention of all noncommunicable diseases. Implementation activities in the Western Pacific area are currently the subject of a major co-operative activity between the respective regional offices of WHO and IDF.

Conclusion

Diabetes represents an increasing global health challenge with significant socioeconomic implications, and a large percentage of people with diabetes are undiagnosed or poorly controlled on existing therapies. Goals of management include achieving targets for fasting and postprandial blood glucose levels, blood lipid profiles and blood pressure, for the prevention of complications. A number of national and international initiatives have been launched to reduce the bur-

den of diabetes, but implementation of stated objectives remains a challenge. In both Type 1 and Type 2 diabetes, there is substantial room for improvement in management approaches, including advances in detection, monitoring, education and therapies.

References

1. Panzram G. Mortality and survival in type 2 (non-insulin-dependent) diabetes mellitus. *Diabetologia*, 1987, 30, 123-31.
2. Kannel WB, McGee DL. Diabetes and cardiovascular risk factors: the Framingham study. *Circulation*, 1979, 59, 8-13.
3. Tuomilehto J, Rastenyte D. Epidemiology of macrovascular disease and hypertension in diabetes mellitus. In: Alberti K, Zimmet P, De Fronzo R, Keen H, eds. "International Textbook of Diabetes Mellitus" (2nd Edn.), Chichester: J. Wiley, 1997, 1559-83.
4. Epstein M. Diabetes and hypertension: the bad companions. *J Hypertens*, 1997, 15, S55-S62.
5. Clark CM. The burden of chronic hyperglycemia. *Diabetes Care*, 1998, 21, C32-4.
6. Turner RC, Millns H, Neil HA, *et al*. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS 23). *BMJ*, 1998, 316, 823-8.
7. Hypertension in Diabetes Study (HDS). Prevalence of hypertension in newly presenting type 2 diabetic patients and the association with risk factors for cardiovascular and diabetic complications. *J Hypertens*, 1993, 11, 309-17.
8. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-year cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care*, 1993, 16, 434-44.
9. Diabetes Control and Complications Trial (DCCT) Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*, 1993, 329, 977-86.
10. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. *Lancet*, 1998, 352, 837-53.
11. World Health Organization (WHO). Prevention of diabetes mellitus: report of a WHO study group. Geneva: World Health Organization, 1994.
12. Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabet Med*, 1997, 14, S7-85.
13. Ohkubo Y, Kishikawa H, Araki E, *et al*. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin dependent diabetes mellitus: a randomized, prospective 6 year study. *Diabetes Res Clin Pract*, 1995, 28, 103-17.
14. Hanefeld M, Fischer S, Julius U, *et al*. Risk factors for myocardial infarction and death in newly detected NIDDM: the Diabetes Intervention Study, 11-year follow-up. *Diabetologia*, 1996, 39, 1577-83.
15. Adler AI, Neil HA, Manley SE, Holman RR, Turner RC. Hyperglycemia and hyperinsulinemia at diagnosis of diabetes and their association with subsequent cardiovascular disease in the United Kingdom Prospective Diabetes Study (UKPDS 47). *Am Heart J*, 1999, 138, S353-9.
16. Diabetes Control and Complications Trial (DCCT) Research Group. Lifetime benefits and costs of intensive therapy as practiced in the diabetes control and complications trial. *JAMA*, 1996, 276, 1409-15.

17. Testa MA, Simonson DC. Health economic benefits and quality of life during improved glycemic control in patients with type 2 diabetes mellitus: a randomized, controlled, double-blind trial. *JAMA*, 1998, 280, 1490-6.
18. American Diabetes Association (ADA). Economic consequences of diabetes mellitus in the US in 1997. *Diabetes Care*, 1998, 21, 296-309.
19. Diabetes Control and Complications Trial (DCCT) Research Group. Resource utilization and costs of care in the diabetes control and complications trial. *Diabetes Care*, 1995, 18, 1468-78.
20. Phillips CJ. The economic implications of implementing evidence-based diabetic treatment strategies. *Int J Clin Pract*, 1998, 52, 181-7.
21. Gilmer TP, O'Connor PJ, Manning WG, Rush WA. The cost to health plans of poor glycemic control. *Diabetes Care*, 1997, 20, 1847-53.
22. Wagner EH, Sandhu N, Newton KM, McCulloch DK, Ramsey SD, Grothaus LC. Effect of improved glycemic control on health care costs and utilization. *JAMA*, 2001, 285, 182-9.
23. Eastman RC, Dong F, Javitt JC, *et al.* Model of complications of NIDDM. *Diabetes Care*, 1997, 20, 735-44.
24. Wake N, Hisashige A, Katayama T, *et al.* Cost-effectiveness of intensive insulin therapy for type 2 diabetes: a 10-year follow-up of the Kumamoto study. *Diabetes Res Clin Pract*, 2000, 48, 201-10.
25. Gray A, Raikou M, McGuire A, *et al.* Cost effectiveness of an intensive blood glucose control policy in patients with type 2 diabetes: economic analysis alongside randomised controlled trial (UKPDS 41). United Kingdom Prospective Diabetes Study Group. *BMJ*, 2000, 320, 1373-8.
26. Kuusisto J, Mykkänen L, Pyörälä K, Laakso M. NIDDM and its metabolic control predict coronary heart disease in elderly subjects. *Diabetes*, 1994, 43, 960-7.
27. Standl E, Balletshofer B, Dahl B, *et al.* Predictors of 10-year macrovascular and overall mortality in patients with NIDDM: the Munich General Practitioner Project. *Diabetologia*, 1996, 39, 1540-5.
28. Avignon A, Radauceanu A, Monnier L. Nonfasting plasma glucose is a better marker of diabetic control than fasting plasma glucose in type 2 diabetes. *Diabetes Care*, 1997, 20, 1822-6.
29. Dyck PJ, Davies JL, Wilson DM, Service FJ, Melton LJ 3rd, O'Brien PC. Risk factors for severity of diabetic polyneuropathy: intensive longitudinal assessment of the Rochester Diabetic Neuropathy Study cohort. *Diabetes Care*, 1999, 22, 1479-86.
30. Harris MI. Diabetes in America: epidemiology and scope of the problem. *Diabetes Care*, 1998, 21, C11-4.
31. European Diabetes Policy Group. Guidelines for diabetes care: a desk-top guide to Type 2 diabetes mellitus. Brussels: International Diabetes Federation (Europe), 1999.
32. Birkeland KI, Rishaug U, Hanssen KF, Vaaler S. NIDDM: a rapid progressive disease. Results from a long-term, randomised, comparative study of insulin or sulphonylurea treatment. *Diabetologia*, 1996, 39, 1629-33.
33. Zambanini A, Newson RB, Maisey M, Feher MD. Injection related anxiety in insulin-treated diabetes. *Diabetes Res Clin Pract*, 1999, 46, 239-46.
34. Zimmet PZ, McCarty PJ, de Courten MP. The global epidemiology of non-insulin-dependent diabetes mellitus and the metabolic syndrome. *J Diabetes Complications*, 1997, 11, 60-8.
35. Rosenbloom AL, Joe JR, Young RS, Winter WE. Emerging epidemic of type 2 diabetes in youth. *Diabetes Care*, 1999, 22, 345-54.
36. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care*, 1998, 21, 1414-31.
37. Harris MI, Flegal KM, Cowie CC, *et al.* Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. *Diabetes Care*, 1998, 21, 518-24.
38. Juneja R, Palmer JP. Type 1½ diabetes: myth or reality? Autoimmunity, 1999, 29, 65-83.
39. Diabetes Control and Complications Trial (DCCT) Research Group. Effects of intensive therapy on residual β -cell function in patients with type 1 diabetes in the Diabetes Control and Complications Trial. *Ann Intern Med*, 1998, 128, 517-23.
40. Krarup T, Madsbad S. Effect of two periods with intensified insulin treatment on B-cell function during the first 18 months of type 1 (insulin-dependent) diabetes mellitus. *Diabetes Metab*, 1986, 12, 256-60.
41. Madsbad S, Krarup T, Regeur L, Faber OK, Binder C. Effect of strict blood glucose control on residual beta-cell function in insulin-dependent diabetics. *Diabetologia*, 1981, 20, 530-4.
42. Harris MI, Eastman RC. Early detection of undiagnosed diabetes mellitus: a US perspective. *Diabetes Metab Res Rev*, 2000, 16, 230-6.
43. UK Prospective Diabetes Study (UKPDS) Group. Complications in newly diagnosed type 2 diabetic patients and their association with different clinical and biochemical risk factors. *Diabetes Res*, 1990, 13, 1-11.
44. Harris MI, Klein R, Welborn TA, Knudman MW. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. *Diabetes Care*, 1992, 15, 815-9.
45. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*, 1997, 20, 1183-97.
46. Alberti KGMM, Zimmet PZ, for the WHO Consultation. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Geneva: World Health Organization, 1999.
47. Rodriguez-Moran M, Guerrero-Romero F. Fasting plasma glucose diagnostic criterion, proposed by the American Diabetes Association, has low sensitivity for diagnoses of diabetes in Mexican population. *J Diabetes Complications*, 2001, 15, 171-3.
48. Krosnick A. Economic impact of type II diabetes mellitus. *Prim Care*, 1988, 15, 423-32.
49. Huse DM, Oster G, Killen AR, Lacey MJ, Colditz GA. The economic costs of non-insulin dependent diabetes mellitus. *JAMA*, 1989, 262, 2708-13.
50. Jönsson B. The economic impact of diabetes. *Diabetes Care*, 1998, 21, C7-10.
51. Murray CL, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet*, 1997, 349, 1269-76.
52. Brun E, Nelson RG, Bennett PH, *et al.* Verona Diabetes Study. Diabetes duration and cause-specific mortality in the Verona Diabetes Study. *Diabetes Care*, 2000, 23, 1119-23.
53. Swerdlow AJ, Jones ME. Mortality during 25 years of follow-up of a cohort with diabetes. *Int J Epidemiol*, 1996, 25, 1250-61.
54. Moss SE, Klein R, Klein BE. Cause-specific mortality in a population-based study of diabetes. *Am J Public Health*, 1991, 81, 1158-62.
55. Wong JS, Pearson DW, Murchison LE, Williams MJ, Narayan V. Mortality in diabetes mellitus; experience of a geographically defined population. *Diabet Med*, 1991, 8, 135-9.
56. Murray CL, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet*, 1997b, 349, 1436-42.
57. American Diabetes Association (ADA). Detection and management of lipid disorders in diabetes. *Diabetes Care*, 1993, 16, 828-33.
58. Krans HMJ, Keen H, Porta M, Steahr Johansen K, eds. Diabetes care and research in Europe: the St Vincent Declaration action programme, 2nd Edn. Copenhagen: World Health Organization, Regional Office for Europe, 1995.

59. European Arterial Risk Factor Policy Group. A strategy for arterial risk factor management in type 2 (non-insulin-dependent) diabetes mellitus. Brussels: International Diabetes Federation (Europe), 1997.
60. European Diabetes Policy Group. Guidelines for diabetes care: a desktop guide to Type 1 (insulin-dependent) diabetes mellitus. Brussels: International Diabetes Federation (Europe), 1998.
61. Clark CM. Reducing the burden of diabetes: the National Diabetes Education Program. *Diabetes Care*, 1998, 21, C30-1.
62. World Health Organization (WHO). Prevention and control of non-communicable diseases. Regional Office for the Western Pacific, Geneva: WHO, 2000.