About IKP Centre for Technologies in Public Health

IKP Centre for Technologies in Public Health (ICTPH) is a research centre that aims to improve the health of poor populations by focusing on designing, developing and delivering innovative solutions in healthcare concerning India and the developing world through an inclusive process that scientifically integrates knowledge of factors influencing health and diseases in India, regular evaluation and impact assessment of existing health systems and integration of appropriate technology for optimal health care delivery. ICTPH aims to learn, discover and apply relevant innovative solutions for health care leading to improved health for the people of India and other developing countries and to integrate technological advances with delivery of affordable, accountable and accessible health care. ICTPH has prioritized the diseases of its interest as malaria, tuberculosis, reproductive health, diarrhoeal diseases and diabetes.

IKP Centre for Technologies in Public Health is structured as an autonomous centre within ICICI Knowledge Park (IKP), a not-for-profit Research Park in Hyderabad, India focusing on Life Sciences.

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Foreword

The IKP Centre for Technologies in Public Health (ICTPH) aims to identify the most important evidence gaps in the current knowledge that India and developing countries have about health technologies. ICTPH has prioritized the diseases of its interest as malaria, tuberculosis, reproductive health, diarrhoeal diseases and diabetes. Pertinent to Diabetes, ICTPH is interested in the current status of the burden of the problem of diabetes and its consequent complications within the Indian and the developing world context, management strategies extending the range of preventive, curative and therapeutic interventions including rehabilitation with a focus on determining gaps in knowledge as well as potential areas for improvement. The report will be utilized by ICTPH to explore potential product development and/or development of product diffusion and scale up strategies. We welcome comments and suggestions from our readers.

Reports on strategies for tuberculosis, reproductive health, diarrhoeal diseases and malaria are also available as a part of our Working Paper Series.

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Executive Summary

ICTPH (ICICI Centre for Technologies in Public Health) is interested in the current status of the burden of the problem of diabetes and its consequent complications within the Indian and the developing world context, management strategies extending the range of preventive, curative and therapeutic interventions including rehabilitation with a focus on determining gaps in knowledge as well as potential areas for improvement.

Diabetes is a metabolic disease characterized by hyperglycemia (high circulating blood glucose) resulting from defects in insulin secretion, insulin action, or both. Diabetes takes three major forms; Type 1 diabetes due to absolute insulin deficiency, Type 2 diabetes, the major form, characterized by insulin resistance and third type of diabetes, gestational diabetes recognized during pregnancy. The World Health Organization (WHO) estimated that there were 135 million diabetics in 1995 and this number would increase to 350 million by the year 2030 with India emerging as the diabetic capital in the world with around 40.9 million diabetics currently and expected to rise to 69.9 million by 2025.

Diabetes-Related Mortality and Disability are a huge problem in many countries and so is the economic burden of diabetes. While the risk factors for diabetes vary by disease type, interventions against diabetes include those for preventing the disease, those for detecting the disease in its asymptomatic stage, and those for managing the disease to reduce its complications. Data are sparse on community- or population-based strategies for preventing diabetes along with other chronic diseases such as CVD (Cardio-Vascular Diseases). The benefits of early detection of type 2 diabetes through screening are not clearly documented, nor are the choice of the appropriate screening test established but still the value of doing this is justified as it has a bearing on the long term consequences of diabetes and its associated mortality and morbidity.

Evidence does exist of managing type 2 diabetes with the availability of medications and it requires a multidisciplinary team approach. People with diabetes play a central role in managing their disease and diabetes education is an integral part of diabetes care. Venous plasma glucose is the standard method for measuring and reporting glucose concentrations in blood and the Oral Glucose Tolerance Test (OGTT) is still retained as a diagnostic test/gold standard for diabetes mellitus and Glycated Hemoglobin (HbA1c) which reflects average plasma glucose over the previous 2–3 months in a single measure is the test for monitoring control status. Urine glucose monitoring is a viable, cost-effective way of monitoring diabetes control,

especially when the cost of blood glucose monitoring makes it inaccessible or when people do not wish to perform blood testing. Insulins are now available in different molecular forms, some because of species differences and some by design through molecular engineering. Modern highly purified animal insulins are safe, effective and reasonably reproducible in their actions. Human insulins, prepared usually by genetic engineering, are similar to highly purified pork insulins. Insulin is an essential drug according to the World Health Organization (WHO) but it is not yet universally accessible to all those who need it in the majority of the world's countries.

Simple, practical, non-invasive and inexpensive methods are needed to identify individuals at high risk for IGT (Impaired Glucose Tolerance) and diabetes and to limit the proportion of the population requiring diagnostic glucose tolerance tests and there is a need for non-invasive testing in diabetes. Few options are under different stages of clinical trials.

The research agenda in diabetes extends through the prevention, epidemiological, economics, operational and basic research areas. ICTPH has a role by itself or through appropriate collaborations and partnerships to extend its activities in the field of diabetes in all the above research areas.

A. Methodology used for Health Technology Assessment of Diabetes

The main purpose of the study was to identify the most important evidence gaps in the current knowledge about health technologies in diabetes so as to assist ICTPH to develop strategic directions and plans to address them. To identify these important knowledge gaps, ICTPH used a variety of complementary methods:

- Direct consultation of people and organizations
- Extracting research recommendations from high quality systematic reviews
- Horizon scanning

Direct Consultation

These have included electronic communication, and conference attendance.

Systematic reviews

Completed reviews in the Cochrane Library, which includes reviews from the Health Technology Assessment program were systematically scanned for research recommendations. Primary, secondary and tertiary information sources were also scanned by extensive searching of specialist and general medical literature and selected Internet sites.

Horizon scanning

Suggestions from this source identify important technologies that are likely to be available within the next 1-3 years. These might be new technologies, or a change in indication or use of an existing technology. To be considered important, at least one of the following characteristics was thought to be true:

- A significant health benefit if the technology diffuses widely
- A major cost impact if the technology is widely diffused because of unit costs and/or patient numbers and/or service re-organization, retraining or other requirements
- The speed of diffusion will be rapid

- Likely to have significant ethical, social, legal or patient-related issues with regards to the use of the technology.
- Significant affect on the current guidelines and clinical guidance on the adoption of the technology.

B. Diabetes – An Introduction

B.1 Nature and Distribution of Diabetes

Diabetes is a metabolic disease characterized by hyperglycemia (high circulating blood glucose) resulting from defects in insulin secretion, insulin action, or both. The current WHO diagnostic criteria for diabetes is – fasting plasma glucose ≥ 7.0mmol/l (126mg/dl) or 2–h plasma glucose ≥ 11.1mmol/l (200mg/dl). Despite the limitations with the data from which the diagnostic criteria for diabetes are derived, the current criteria distinguish a group with significantly increased premature mortality and increased risk of micro-vascular and cardiovascular complications. The fasting plasma glucose cut-point for Impaired Fasting Glucose (IFG) is 6.1mmol/l [1].

B.2 Classification of Diabetes

Diabetes takes three major forms. Type 1 diabetes results from destruction of the beta cells in the pancreas, leading to absolute insulin deficiency. It usually occurs in children and young adults and requires insulin treatment. Type 2 diabetes, which accounts for approximately 85 to

95 percent of all diagnosed cases, is usually characterized by insulin resistance in which target tissues do not use insulin properly. A third type of diabetes, gestational diabetes, is first recognized during pregnancy. Other rare types of diabetes include those caused by genetic conditions (for example, maturity-onset diabetes of youths), surgery, drug use, malnutrition, infections, and other illnesses[1-3].

B.3 The Burden of Diabetes

Diabetes affects persons of all ages and races. The disease reduces both a person's quality of life & life expectancy and imposes a large economic burden on the health care system and on families. Over the past decade it has been obvious that the prevalence of type 2 diabetes is increasing rapidly. Diabetes mellitus is one of the main threats to human health in the 21st century. The prevalence of diabetes ranges from nearly 0 per cent in New Guinea to 50 per cent in the Pima Indians. The past two decades have seen an explosive increase in the number of people diagnosed with diabetes world-wide. The World Health Organization (WHO) estimated that there were 135 million diabetics in 1995 and this number would increase to 350 million by the year 2030[1-4]. This is double the current number. Equally alarming and less well known is the fact that, of these people, only around one half are known to have the condition. This has been shown repeatedly in epidemiological surveys. An added concern is that half of those who do present with type 2 diabetes clinically already have signs of the complications of the disorder. It has not yet been proven that earlier detection will improve the outcome of people with type 2 diabetes, but it seems logical to suggest that it may help. The implication of this is that people need to be screened for diabetes on a regular basis. There is still uncertainty whether this should be done on a population-wide basis or just for those people who can be shown to have a high risk. It is also uncertain at what age the screening programs should be introduced, if at all.

B.4 Diabetes in India

India leads the world today with the largest number of diabetics in any given country. In the 1970s, the prevalence of diabetes among urban Indians was reported to be 2.1 per cent and this has now risen to 12.1 per cent[5,6]. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "diabetes capital of the world". According to the Diabetes Atlas 2006 published by the International Diabetes Federation[5], the number of people with diabetes in India currently around 40.9 million is expected to rise to 69.9 million by 2025 unless urgent preventive steps are taken. Moreover, there is an equally

large pool of individuals with impaired glucose tolerance (IGT), many of whom will develop type 2 diabetes mellitus in the future. With a high genetic predisposition and the high susceptibility to the environmental insults, the Indian population faces a high risk for diabetes and its associated complications. Diabetes can affect nearly every organ system in the body. The so called "Asian Indian Phenotype" refers to certain unique clinical and biochemical abnormalities in Indians which include increased insulin resistance, greater abdominal adiposity *i.e.*, higher waist circumference despite lower body mass index, lower adiponectin and higher high sensitive C-reactive protein levels[7-9]. This phenotype makes Asian Indians more prone to diabetes and premature coronary artery disease. At least a part of this is due to genetic factors. However, the primary driver of the epidemic of diabetes is the rapid epidemiological transition associated with changes in dietary patterns and decreased physical activity as evident from the higher prevalence of diabetes in the urban population. Even though the prevalence of micro-vascular complications of diabetes like retinopathy and nephropathy are comparatively lower in Indians, the prevalence of premature coronary artery disease is much higher in Indians compared to other ethnic groups. The most disturbing trend is the shift in age of onset of diabetes to a younger age in the recent years. This could have long lasting adverse effects on nation's health and economy. Early identification of at-risk individuals using simple screening tools like the Indian Diabetes Risk Score (IDRS) and appropriate lifestyle intervention would greatly help in preventing or postponing the onset of diabetes and thus reducing the burden on the community and the nation as a whole[10-13].

A random multistage cross-sectional population survey was undertaken to determine the prevalence of Diabetes Mellitus (DM) and impaired glucose tolerance (IGT) in subjects aged 25 years and above in India in 2004. The study was carried out in 77 centers (40 urban and 37 rural). 18,363 (9008 males and 9355 females) subjects were studied. Blood samples were taken after a fast of 10-12 h and 2 h after 75 g of oral glucose. Subjects were categorized as having IGT or DM using the World Health Organization (WHO) (1999) criteria. The standardized prevalence rate for DM in the total Indian, urban and rural populations were 4.3, 5.9 and 2.7%, respectively. The corresponding IGT rates in the three populations were 5.2, 6.3 and 3.7%, respectively. The urban prevalence of DM and IGT was significantly greater than in the rural population ($P < 0.001$ in both instances). The prevalence of DM was significantly, more than that of IGT ($P < 0.001$) within both the rural and urban populations[14].

B.5 Secular Trends and Projections

In 2003, the worldwide prevalence of diabetes was estimated at 5.1 percent among people age 20 to 79. The prevalence of diabetes was higher in developed countries than in developing countries. In the developing world, the prevalence was highest in Europe and Central Asia and lowest in Sub-Saharan Africa. Some of these variations may reflect differences in the age structures and level of urbanization of the various populations. By 2025, the worldwide prevalence is projected to be 6.3 percent, a 24 percent increase compared with 2003. The largest increase in prevalence by 2025 is expected to be in East Asia and the Pacific, and the smallest in Sub-Saharan Africa. In terms of those affected, the biggest increase in the developing countries is projected to take place among adults of working age. In 2003, 194 million people worldwide ages 20 to 79 had diabetes, and by 2025, this number is projected to increase to 333 million, a 72 percent increase. The developing world accounted for 141 million people with diabetes (72.5 percent of the world total) in 2003. During the same period, the number of people with diabetes is projected to double in three of the six developing regions: the Middle East and North Africa, South Asia, and Sub-Saharan Africa [15].

B.6 Diabetes-Related Mortality and Disability

The death rate of men with diabetes is 1.9 times than the rate for men without diabetes, and the rate for women with diabetes is 2.6 times than for women without diabetes. Premature mortality caused by diabetes results in an estimated 12 to 14 years of life lost. Cardiovascular Disease is the leading cause of death in those with diabetes in developed countries. The World Health Organization (WHO) estimates that, in 2001, 959,000 deaths worldwide were caused by diabetes, accounting for 1.6 percent of all deaths, and approximately 3 percent of all deaths caused by non-communicable diseases. More recent estimates by WHO suggest that the actual number may be triple than this estimate and that about two-thirds of these deaths occur in developing countries. Within the developing regions, most deaths caused by diabetes occurred in East Asia and the Pacific and the fewest in Sub-Saharan Africa. Diabetes-related complications include micro-vascular diseases (for example, retinopathy, blindness, nephropathy, and kidney failure) and macro-vascular diseases (coronary heart disease, stroke, peripheral vascular disease, and lower-extremity amputation). Those complications result in disability. The World Health Organization estimated that, in 2001, diabetes resulted in 19,996,000 disability-adjusted life years (DALYs) worldwide. More than 80 percent of the DALYs resulting from diabetes were in developing countries. East Asia and the Pacific had the largest burden, the Middle East and North Africa had the smallest burden. DALYs resulting from

diabetes increased by 250 percent worldwide from 1990 to 2001 and by 266 percent for low- and middle-income countries [16-21].

B.7 Economic Burden of Diabetes

Diabetes imposes large economic burdens on national health care systems and affects both national economies, individuals and their families. Direct medical costs include resources used to treat the disease. Indirect costs include lost productivity caused by morbidity, disability, and premature mortality. Intangible costs refer to the reduced quality of life for people with diabetes brought about by stress, pain, and anxiety. Good data on the direct medical costs of diabetes are not available for most developing countries. In developing countries, the indirect costs of diabetes are at least as high, or even higher, than the direct medical costs. Because the largest predicted rise in the number of people with diabetes in the next three decades will be among those in the economically productive ages of 20 to 64, the future indirect costs of diabetes will be even larger than they are now. Diabetes lowers people's quality of life in many ways, including their physical and social functioning and their perceived physical and mental well-being[22-25].

B.8 Risk Factors for Diabetes

Risk factors for diabetes vary by disease type.

Type 1 Diabetes

Type 1 diabetes is most likely a polygenic disease and a number of potential environmental risk factors have been implicated – including dietary factors; breastfeeding; initiation of bovinemilk; infectious agents (for example, enterovirus, rotavirus, and rubella); chemicals; and toxins – but the results have been inconclusive.

Type 2 Diabetes

The risk for type 2 diabetes is higher in monozygotic twins and people with a family history of diabetes. This finding strongly suggests that genetic determinants play a role, but so far few genes have been associated with type 2 diabetes. Environmental factors include prenatal factors, obesity, physical inactivity, dietary and socioeconomic factors. Exposure to diabetes in utero increases the risk of developing type 2 diabetes in early adulthood. Disproportionate

growth and low birth weight increase the risk of developing diabetes and insulin resistance. In the postnatal environment, breastfeeding protects against the development of obesity, insulin resistance, and diabetes. The strongest and most consistent risk factors for diabetes and insulin resistance among different populations are obesity and weight gain: for each unit increase in body mass index, the risk of diabetes increases by 12 percent. The distribution of fat around the trunk region, or central obesity, is also a strong risk factor for diabetes. Diabetes risk may be reduced by increasing physical activity. Conversely, a sedentary lifestyle and physical inactivity are associated with increased risks of developing diabetes. Some studies report a positive relationship between dietary fat and diabetes, but specific types of fats and carbohydrates may be more important than total fat or carbohydrate intake. Polyunsaturated fats and long-chain omega-3 fatty acids found in fish oils may reduce the risk of diabetes, and saturated fats and trans-fatty acids may increase the risk of diabetes. Sugar-sweetened beverages are associated with an increased risk of diabetes. High intakes of dietary fiber and of vegetables may reduce the risk of diabetes. Increased affluence and westernization have been associated with an increase in the prevalence of diabetes in many indigenous populations and in developing economies. Conversely, in developed countries, those in lower socioeconomic groups have a higher risk of obesity and consequently of type 2 diabetes. Surrogates for socioeconomic status, such as level of education attained and income are inversely associated with diabetes in high-income countries[26-46].

C. Interventions and Delivery Modes against Diabetes

Interventions against diabetes include those for preventing the disease, those for detecting the disease in its asymptomatic stage, and those for managing the disease to reduce its complications.

C.1 Preventing Type 1 Diabetes

Not enough scientific evidence is available to indicate that type 1 diabetes can be prevented, although various interventions have been explored. Examples of tested interventions include eliminating or delaying exposure to bovine protein and using insulin or nicotinamide for people at high risk of developing the disease.

C.2 Preventing Type 2 Diabetes

Four major trials – in China, Finland, Sweden, and the United States – have demonstrated that intensive lifestyle interventions involving a combination of diet and physical activity can delay or prevent diabetes among people at high risk [47-50]. In the largest randomized, controlled trial to date, the Diabetes Prevention Program, the goals of the intensive lifestyle intervention were weight loss of 7 percent of baseline bodyweight through a low-calorie diet and moderate physical activity for at least 150 minutes per week. After 2.8 years of follow-up, the average weight loss was 4.5 kilograms for those in the lifestyle intervention group and less than 0.3

kilograms for those in the placebo group. The lifestyle intervention reduced the incidence of diabetes by 58 percent. Pharmacological studies of diabetes prevention have been reviewed and in summary, a variety of specific medications have been tested (for example, metformin, acarbose, orlistat, troglitazone, angiotensin-converting enzyme [ACE] inhibitors, statins, estrogens, and progestins) and have been found to lower diabetes incidence, but the expense, side effects, and cumulative years of drug intervention are practical concerns. Except for the Diabetes Prevention Program no trial of medication intervention has directly compared the effectiveness of a drug to that of lifestyle modification[51].

C.3 Issues related to Diabetes Prevention

Data are sparse on community- or population-based strategies for preventing diabetes along with other chronic diseases such as CVD. Available studies on preventing type 2 diabetes have used clinic-based approaches targeted at high-risk groups, and researchers generally agree that type 2 diabetes can be prevented or its onset delayed. Pending applying this into practice, however, deserves answers to many unanswered questions, like – Who would benefit from diabetes prevention? How can those who may benefit be identified? What are the costs and cost-effectiveness of diabetes prevention at a population level? What or how could we generate relevant evidence on diabetes prevention and management from developing countries, in line with the priorities and approaches of the countries?

C.4 Screening for People with Diabetes or Pre-Diabetes

The benefits of early detection of type 2 diabetes through screening are not clearly documented, nor are the choice of the appropriate screening test established. Questionnaires used alone tend to work poorly; biochemical tests alone or in combination with assessment of risk factors are a better alternative[52].

C.5 Conclusions & Recommendations of WHO for Screening Type 2 Diabetes

Conclusions

- The issue of screening for type 2 diabetes is important both in terms of individual health, day-to-day clinical practice and public health policy.
- There is currently no direct evidence as to whether individuals will or will not benefit from the early detection of type 2 diabetes through screening.
- Despite this lack of direct evidence, early detection through screening is already taking place both by inviting individuals from the general population to come forward for screening and, opportunistically, when individuals perceived to be at high risk of developing diabetes attend for health care (usually primary health care) for other reasons.

- These activities present opportunities for collecting observational data which, although no substitute for direct RCT (Randomized Controlled Trials) evidence, can provide important, circumstantial evidence about efficiency, costs and impact.

- There is direct evidence that the incidence of diabetes can be reduced in people at high risk of the future development of type 2 diabetes who may be identified as a result of activities directed towards diabetes detection.

- If screening can be shown to be beneficial, the most important epidemiological considerations determining whether to screen in any given population will be (1) the prevalence of undiagnosed type 2 diabetes in that population and (2) the degree to which type 2 diabetes is associated with risk of cardiovascular disease, diabetes specific complications and other important health outcomes in that population.

- The most important health systems considerations will be its capacity (1) to carry out the screening (2) to provide effective health care for those who screen positive (3) to address the psycho-social needs of those who undergo screening and (4) to implement effective prevention in those who, though not confirmed to have diabetes at the time, are at high risk of its future development.

- The most important population considerations will be (1) the acceptability of the screening program to those invited to attend (2) the extent to which any lack of acceptability reduces uptake (3) the psychosocial impact of each screening outcome positive and negative, 'true' and 'false' and (4) the ability of those found to be at risk of future development of diabetes to modify these risk.

- The most important economic considerations are (1) the cost of early detection to the health system and to the individual (2) the extra costs of treatment following early detection and (3) the relative cost effectiveness of early detection compared with that of improving the care of clinically detected (as opposed to screen detected) cases.

- The most appropriate protocol for screening for undiagnosed type 2 diabetes in a particular setting should consider (1) the sensitivity and specificity of the screening methods available (2) the number of people who will need to be screened (3) the number of people who will need subsequent diagnostic testing (4) resource implications and (5) costs.

- Screening for type 2 diabetes is a dynamic topic in which new evidence will become available and further considerations will arise over time.

Recommendations

- Health authorities and professional organizations should formulate policies concerning screening for type 2 diabetes even if the policy is that screening is not currently to be advocated. In formulating that policy, the benefits and costs to the individual and their well-being are of paramount importance.

- There is an urgent need for direct RCT evidence on the effects of early detection of type 2 diabetes through screening. Such evidence should include health outcomes related to diabetes, cardiovascular disease, psychosocial outcomes and economic considerations for individuals, health systems and the wider society. Although RCTs directed to answering these questions may be costly and logistically difficult, there is, in the current state of knowledge, no ethical reason why they should not be undertaken.

- Since the results of such RCTs will not be available for some time (if ever), there is also an urgent need to develop a framework (or model) which would permit countries to evaluate the cost-effectiveness of earlier detection of diabetes compared to other preventive and therapeutic interventions.

- Testing apparently unaffected individuals at increased risk of having diabetes when these individuals attend for health care for other reasons (sometimes called 'opportunistic screening') may be justified provided (1) the reasons for testing are adequately explained to the individual (2) the health system has the capacity for the clinical management of those who screen positive (3) methods with adequate sensitivity and specificity are available (4) the psycho-social needs of those who screen positive and those who screen negative can be met and (5) the health system can implement effective preventive strategies for those confirmed to be at high risk for the development of diabetes. There is no evidence to justify haphazard screening.

- If such opportunistic screening is advocated then this should be carried out according to a policy which should (1) be clear and relevant in its aims and objectives (2) be based as far as possible on sound evidence (3) take into account the epidemiology of

type 2 diabetes and related cardiovascular disease risk in the population and (4) be sensitive to competing local health priorities.

- The choice of the method or methods for screening will depend on the resources available, the acceptability of the methods in the population being screened and the levels of sensitivity, specificity etc. that are required. Methods of screening which might be regarded as unacceptable in high resource settings (e.g. testing for urinary glucose) may be suitable in low resource settings.

- Where screening is already taking place, formal evaluation should be integral to these activities. The results of such evaluations could contribute to the general assessment of the value of early detection and should be used in the modification or curtailment of the activities being evaluated.

- Given the dynamic nature of this topic, policies for screening for type 2 diabetes must be reviewed from time to time as new evidence accumulates[52].

D. Managing Diabetes

High-quality evidence exists for the efficacy of several current treatments in reducing morbidity and mortality in people with diabetes. In addition, few previous studies found positive effects for short follow-up (less than six months) of self-management training on knowledge, frequency, and accuracy of self-monitoring of blood glucose; self-reported dietary habits; and glycemic control. Effects on lipids, physical activity, weight, and blood pressure varied[53].

A wide range of treatment options are available for type 2 diabetes, each with distinct modes of action[54-55].

- α-glucosidase inhibitors (e.g. acarbose) delay digestion and absorption of carbohydrates.
- Sulfonylureas and meglitinides stimulate insulin release from the pancreas.
- Biguanides (e.g. metformin) suppress liver glucose output, enhance insulin sensitivity in the liver and stimulate insulin-mediated glucose disposal – they do not stimulate insulin secretion.
- Thiazolidinediones (e.g. rosiglitazone, pioglitazone) decrease insulin resistance in fat, muscle and the liver.

E. Cost-Effectiveness of Interventions and Priorities

Type 2 diabetes is a complex disorder – effective management requires broad expertise. A multidisciplinary team combines the experience of diabetologists, cardiologists, nurse

specialists, dieticians, podiatrists and other specialists, and places the individual at the center of the team. A multidisciplinary team approach has also demonstrated better glycemic control, fewer complications and hospitalizations, improved patient quality of life and lower annual costs compared with standard primary care[23].

Most of the interventions to prevent and treat diabetes and its complications significantly affect the use of health services. The limitations of clinical trials include their failure in most cases to capture the entire intervention effect over a lifetime and to include all segments of a population to whom the intervention may apply. Evaluating the cost-effectiveness of interventions often requires the use of computer simulation models, but data availability, technical complexity, and resource needs present a significant barrier to constructing such models for developing countries. Furthermore, data on interventions are often available only from developed countries, and these data are often extrapolated to developing countries.

Estimating the Cost-Effectiveness of Interventions in Developing Countries is one of the priorities worth pursuing currently. Estimates for developing countries applying the Mulligan and others' framework (2003) to estimate the costs of intervention and diabetes care in each developing region was developed. The estimates included costs and effectiveneness for three health service indexes, including hospital bed days, outpatient and inpatient services, and laboratory tests and procedures and then combining it as one overall index for diabetes care in accordance with the share of each component in developing countries and interventions ranked in terms of their priorities[56-59].

Level 1 Interventions

Glycemic control in a population with poor control (hemoglobin A1c greater than 9 percent or another measure of glucose control in situations where HbA1c tests may be unaffordable) is cost saving because the reduction in medical care costs associated with both short-term and long-term complications is greater than the cost of intervention. Glycemic control for people with type 1 diabetes involves insulin use and, for people with type 2 diabetes, depending on the stage and severity of the disease, consists of diet and physical activity, oral glucose-lowering agents, and insulin. Patient education is an essential component of these interventions to encourage patients to comply with medication regimes and to change to and maintain healthy lifestyles. Glucose is generally poorly controlled in people with both type 1 and type 2 diabetes, mostly because of lack of access to insulin and other diabetes supplies in developing countries. A survey conducted by the International Diabetes Federation in 1997

showed that no country in Africa had 100 percent accessibility to insulin. Ensuring adequate access to insulin should be an important priority for developing countries.

Blood pressure control for people with diabetes and hypertension reduces the incidence of both microvascular and macrovascular diseases. Major medication interventions include an ACE inhibitor, thiazide diuretics, or a beta blocker. Blood pressure control is cost saving mainly because of its large health benefits and relatively low intervention costs. Because many blood pressure medications are generic drugs, the costs are much lower in developing countries. In addition, the prevalence of people with poor control of blood pressure may be high in developing countries. Complications related to foot problems are common among diabetics in developing countries. For example, in India, 43 percent of diabetes patients had foot-related complications. Interventions for foot care are low tech and require little capital. Interventions for foot care in developing countries should include educational programs for patients and professionals (for example, on foot hygiene, treatment of calluses, awareness of functional infections, and care for skin injuries); access to appropriate footwear; and multidisciplinary clinics. All three interventions could be cost saving, mainly because the cost of the interventions is low and the interventions can reduce the risk of foot ulceration and amputation, which are costly. Applying these interventions for high risk patients, such as those with at least one previous foot ulcer or amputation, would yield even larger savings[56,57,60,61].

Level 2 Interventions

Interventions in this category represent good value for money but may present some difficulties in terms of feasibility. Preconception care among women of reproductive age includes patient education and intensive glucose management. This intervention reduces short-term hospital costs for both mothers and infants and improves birth outcomes. However, the intervention may not be feasible in some developing countries because of the resources needed for the intervention and the difficulty of reaching the target population. The potential population eligible for a lifestyle intervention (those with impaired glucose tolerance or impaired fasting glucose) is large in developing countries. The International Diabetes Federation estimates that the prevalence of impaired glucose tolerance was at least as high as the prevalence of diabetes in all regions. The expertise required for the intervention, such as dietitians and exercise physiologists, and the capacity of health care systems to handle the large populations eligible for the intervention may present a barrier to implementing the intervention in many developing countries. People with diabetes are at higher risk of complications from influenza and pneumococcal infections than those without diabetes.

Influenza vaccinations are a relatively cost effective intervention, mainly because of the low intervention cost. However, the level of adoption for the intervention would depend on a country's ability to deliver the intervention to the targeted population. The detection of proliferative diabetic retinopathy and macular edema by dilated eye examination followed by appropriate laser photocoagulation therapy prevents blindness. Annual screening and treatment programs for diabetic retinopathy cost US $700 or less per QALY (Quality Adjusted Life Year) gained in developing countries. The intervention is more cost-effective among older people, those who require insulin, or those with poor glucose control. In addition, screening less frequently, such as every two years, may be more cost-effective than screening every year. Eye complications among people with diabetes are common in developing countries; for example, 39 percent of people with diabetes in India had eye-related complications. Although laser treatment is an effective intervention, such treatment may not be available in many developing countries or may be extremely costly.

ACE inhibitors can lower the blood pressure of those with hypertension and delay the onset or prevent further progression of renal disease for those with diabetes. Compared with screening for microalbuminuria and treating only those who have the condition, offering ACE inhibitors to all people with diabetes was more cost-effective. This intervention was more cost-effective among younger people and was sensitive to the cost of drug. Thus, lowering the cost of the medication is a key factor for the success of this intervention in developing countries. Smoking cessation includes both counseling and using medication such as a nicotine patch. Smoking cessation appears to be the least cost-effective among the level 2 interventions. However, the benefits of smoking cessation may be underestimated because the calculations only took the reduced risk of CVD into account. Adding the health benefits derived from preventing cancer and pulmonary diseases would improve the cost-effectiveness of smoking cessation. Considering the high prevalence of smoking in developing countries, smoking cessation should be a high-priority intervention, but the availability of the nicotine patch may be a barrier to implementing this intervention in developing countries[56, 61-64].

Level 3 Interventions

Compared with the level 1 and 2 interventions, those in this category are even less feasible. In general, depending on the cost-effectiveness and feasibility, these interventions may not always be justifiable for all people in developing countries, given the limited health care resources.

However, these interventions may be reasonable for selected subpopulation groups, such as those who can afford them. Metformin therapy for preventing type 2 diabetes among people at high risk, such as those with prediabetes, is feasible because the drug is affordable in many developing countries; however, the intervention may not be good value for money. Cholesterol control intervention for people with diabetes falls into the same category. The cost-effectiveness of both these interventions would improve if the costs of the drug could be lowered.

The aim of intensive glucose control is to lower the glucose level of a person with diabetes to a level close to that of a person without diabetes. Implementing this intervention is a lower priority, mainly because of its relatively low cost-effectiveness in the context of the limited health care resources in developing countries. Although the U.K. Prospective Diabetes Study clearly demonstrates that lowering glucose levels can prevent or delay long-term diabetes complications[65], the marginal return on very intensive glucose control in developing countries was relatively small.

Screening for undiagnosed diabetes is a low-priority intervention mainly because of its relatively high cost per QALY. However, screening for undiagnosed diabetes can be a worthwhile intervention for subpopulation groups, such as those that have a high prevalence of undiagnosed diabetes. In addition, screening for undiagnosed diabetes may be a worthwhile intervention for patients with risk factors for other chronic diseases, such as hypertension, high lipid profiles, and prediabetes. Annual screening for microalbuminuria was a low-priority intervention because screening added costs with no significant benefits. Treating all persons with diabetes with ACE inhibitors was a better treatment option than screening for microalbuminuria and treating only those who have the condition[66].

E.1 Cost-Effectiveness of a Polypill to Prevent CVD

A meta-analysis estimated that a hypothetical polypill could reduce the risk of CVD by 80 percent among all people over 55 or people with diabetes of any age. This hypothetical pill is a combination of three half-dose antihypertensive medications – aspirin, statin, and folic acid. Currently, neither is it available for use, nor have estimates of its benefits and adverse effects been confirmed in a formal, randomized, controlled trial. The idea is thus still theoretical. The cost-effectiveness of this hypothetical pill was, however, simulated using a computer model of people with newly diagnosed diabetes in the United States, and the assessment found that a polypill intervention would cost US $11,000 per QALY gained. The intervention would be cost

saving if such a pill cost US $1.28 or less per day. It is estimated that the cost-effectiveness ratio of the polypill ranged from US $560 to US $1,280 per QALY gained for developing country regions. A barrier to this intervention, in addition to the feasibility of producing such pill, is that its benefits and side effects would still have to be established in a randomized clinical trial[67-68].

E.2 Cost-Effectiveness of Diabetes Education

People with diabetes play a central role in managing their disease. Thus, diabetes education is an integral part of diabetes care. The goal of diabetes education is to support the efforts of people with diabetes to understand the nature of their illness and its treatment; to identify emergency health problems at early, reversible stages; to adhere to self-care practices; and to make necessary changes to their health habits. Health providers can deliver diabetes education programs in various settings. Evaluating the effectiveness of health education is challenging because of the difficulty of separating out its effect from that of other interventions. Training in diabetes self-management reduces medical costs for diabetes care in developing countries in the short term. A multicenter intervention study in 10 Latin American countries demonstrated that an education program could reduce the cost of drugs by 62 percent, and another program in Argentina found a reduction in diabetes-related costs of 38 percent. Because the costs of education programs are generally low, the intervention may be cost-effective. Training patients to better manage their diabetes is also feasible because of its low technical complexity, low capital requirements, and cultural acceptability. Thus, diabetes education should be a high-priority intervention for all developing regions[56-57,61].

F. Treatment

The quality of diabetes care generally remains suboptimal worldwide, regardless of a particular country's level of development, health care system, or population[69-74]. The Diabcare-Asia project was conducted in the late 1990s. Results from India, Singapore, and Taiwan (China) found that in 1998, 32 to 50 percent of the diabetic population had poor glycemic control (equivalent to HbA1c - 8 percent), 43 to 67 percent had high cholesterol (greater than 5.2 millimoles per deciliter), and 47 to 54 percent had an abnormal level of triglyceride (greater than 1.7 millimoles per deciliter). There is now recommended guidelines for care of those with diabetes especially Type 2. These include:

Standard care

Standard care is evidence-based care which is cost-effective in most nations with a well developed service base, and with health-care funding systems consuming a significant part of national wealth. Standard care should be available to all people with diabetes and the aim of any health-care system should be to achieve this level of care. However, in recognition of the considerable variations in resources throughout the world, other levels of care are described which acknowledge low and high resource situations.

Minimal care

Minimal care is the lowest level of care that anyone with diabetes should receive. It acknowledges that standard medical resources and fully-trained health professionals are often unavailable in poorly funded health-care systems. Nevertheless this level of care aims to achieve with limited and cost-effective resources a high proportion of what can be achieved by Standard care. Only low cost or high cost effectiveness interventions are included at this level.

Comprehensive care

Comprehensive care includes the most up-to-date and complete range of health technologies that can be offered to people with diabetes, with the aim of achieving best possible outcomes. However the evidence-base supporting the use of some of these expensive or new technologies is relatively weak[75].

F.1 Quality of Diabetes Care

Small, single-site studies indicate that several interventions to improve quality of care at the patient, provider, or system levels are promising. A systematic review found that multifaceted professional interventions may enhance providers' performance in managing diabetes care; that organizational interventions involving regularly contacting and tracking patients by means of computerized tracking systems or through nurses can also improve diabetes management; that patient-oriented interventions can improve patients' outcomes; and that nurses can play an important role in patient-oriented interventions by educating patients and facilitating patients' adherence to treatment regimes. Interventions that could modify providers' behavior include education as part of more complex interventions that also focus on systems and on the organization of practices—for example, feedback on performance, reminder systems, consensus development, and clinical practice guidelines. Potential systemic interventions include the use

of continuous quality improvement techniques; feedback on performance; physician incentives for quality; nurses to provide diabetes care (which is typically provided by physicians); computerized reminder systems for providers, alone or in combination with a performance feedback program; patient-tracking or other reminder systems to improve regular follow-up; dedicated blocks of time set aside for diabetes patients in primary care practices; team care; electronic medical record systems; and other methods, such as telephone and mailing reminders, chart stickers, and flow sheets to prompt both providers and patients. Interventions that empower patients can be successful components of diabetes programs. A systems-oriented approach using manual or computerized systems that remind patients to make follow-up appointments and that prompt staff members to generate reminder cards for patients can improve compliance with follow-up and enhance efficiency of office practices. In addition, comprehensive implementation of multiple risk factor interventions in real-life settings has been shown to reduce vascular events by more than 50 percent among people with diabetes[76-80].

G. Tests for Diabetes Mellitus and Impaired Glucose Tolerance

Venous plasma glucose is the standard method for measuring and reporting glucose concentrations in blood. However in recognition of the widespread use of capillary sampling, especially in under-resourced countries, conversion values for capillary plasma glucose are provided for post-load glucose values. Fasting values for venous and capillary plasma glucose are identical. Glucose should be measured immediately after collection by near-patient testing, or if a blood sample is collected, plasma should be immediately separated, or the sample should be collected into a container with glycolytic inhibitors and placed in ice-water until separated prior to analysis.

The oral glucose tolerance test (OGTT) is still retained as a diagnostic test/gold standard for the following reasons:

- Fasting plasma glucose alone fails to diagnose approximately 30% of cases of previously undiagnosed diabetes,
- OGTT is the only means of identifying people with IGT (Impaired Glucose Tolerance),
- OGTT is frequently needed to confirm or exclude an abnormality of glucose tolerance in asymptomatic people.

An OGTT should be used in individuals with fasting plasma glucose 6.1– 6.9mmol/l (110–125mg/dl) to determine glucose tolerance status. Currently HbA1c is not considered a suitable diagnostic test for diabetes or intermediate hyperglycemia as yet.

Measurement of glucose in blood remains the mainstay of testing for glucose tolerance status. There are a number of important considerations which can influence this measurement which require careful attention in order to ensure an accurate result. Most portable devices measure the glucose concentration directly in the plasma component of the blood by filtering out the red blood cells. The signal is then calibrated to produce a readout either as blood or plasma glucose. Laboratory measures normally now use separated plasma, with determination of the amount or concentration of glucose in a fixed volume. Only devices which measure out a fixed volume of blood, and then determine the glucose within that volume, measure true whole blood glucose concentration. As glycolysis inhibitors take time to penetrate into red blood cells, only immediate separation of plasma will avoid some lowering of glucose levels in the sample, though rapid cooling can reduce this loss. Accordingly modern recommendations are

for laboratory plasma measurements on appropriately handled samples, and matched calibration of portable devices. Glucose measured in plasma is approximately 11% higher than glucose measured in whole blood. However this difference is dependent on haematocrit, increasing to 15% at a haematocrit of 0.55 and decreasing to 8% at a haematocrit of 0.30. For this and other reasons the conversion of whole blood glucose to plasma glucose is problematic and the previously published WHO conversion tables may be inaccurate in some situations. It should also be noted that many portable glucose measuring devices are still calibrated to whole blood despite the International Federation of Clinical Chemistry (IFCC) recommendation that all glucose measuring devices report in plasma values. Measurement differences may also arise depending on the site of collection of the blood sample. Venous and capillary samples will give the same result in the fasting state but in the non-fasting state capillary will give higher results than venous samples[81-86].

Glycated Hemoglobin (HbA1c) reflects average plasma glucose over the previous 2–3 months in a single measure which can be performed at any time of the day and does not require any special preparation such as fasting. These properties have made it the gold standard for assessing glycaemic control in people with diabetes and have resulted in its consideration as an option for assessing glucose tolerance in people without diagnosed diabetes. Overall the performance of HbA1c has been similar to that of fasting or 2–h plasma glucose but the actual HbA1c threshold value has differed between studies. These favourable aspects of HbA1c need to be balanced against the reality that HbA1c measurement is not widely available in many countries throughout the world. Furthermore there are aspects of its measurement which are problematic. Although in reference laboratories the precision of HbA1c measurement is similar to that of plasma glucose, global consistency remains a problem. Furthermore the HbA1c result is influenced by several factors including anaemia, abnormalities of haemoglobin, pregnancy and uraemia. Some of these factors may be a bigger problem in under-resourced countries due to a higher prevalence of anaemia and of haemoglobinopathies. The precise effect of these factors on the HbA1c result varies with the laboratory method used. Taking all of these considerations into account, it is concluded that the role of HbA1c in the diagnosis of diabetes and intermediate hyperglycaemia is not established and that it could not be recommended as a diagnostic test at this time[87-91].

G.1 The Role of Urine Glucose Monitoring

Diabetes is a complex disorder that requires vigilant monitoring on a long-term continuous basis by the person with diabetes and their family to achieve optimal control in an effort to avoid

the serious complications of diabetes. Blood glucose self monitoring and urine glucose self monitoring are the two primary methods used by the person with diabetes to monitor their diabetes control, and where appropriate make treatment adjustments. The recommended frequency of testing varies, depending on the type of diabetes and the particular circumstances.

The IDF (International Diabetes Federation) position on urine glucose monitoring is that:

- Urine glucose monitoring is not a substitute for blood glucose monitoring, but rather an alternative or complement which can provide very valuable information where blood glucose monitoring is not accessible, affordable, or desired.
- Urine glucose monitoring should continue to be available throughout the world.
- Education about its role and appropriate use should be part of essential education about diabetes for health care professionals and governments.
- It can be used separately to, or in conjunction with, blood glucose monitoring in particular circumstances and settings.
- It should continue to be included on the World Health Organization Essential Drugs List.
- The major promotion by industry of blood glucose monitoring should not result in the appropriate role of urine glucose monitoring being underestimated.
- As long as results are interpreted correctly, and limitations understood, it provides valuable information in persons with type 2 diabetes treated by diet and/or tablets, in people with type 2 who use insulin, and in people with type 1 diabetes, who cannot afford blood glucose testing or who, for other reasons, may not use it.
- Because it is significantly cheaper than blood glucose monitoring, it has a very important role to play in settings where blood glucose monitoring is not accessible due to cost, or where blood glucose monitoring can only be done relatively infrequently. This occurs in some situations in both developing and developed countries.
- Its use should be determined by the individual health care professional in conjunction with the person with diabetes, taking into account all the circumstances.

Advantages/disadvantages and roles

Urine testing is easy to perform by simply passing urine onto a test strip, or using reagent compounds; does not require a meter with associated maintenance and battery replacement needs; does not require lancets with the associated safety and disposal issues; is not complicated by issues relating to the withdrawal of old and introduction of new meter models and strips and confusion and wastage caused by the often large number of models available. It is therefore a more appropriate technology for many settings. Before the advent of blood glucose monitoring in the 1970s, urine glucose monitoring was universally used, with many people able to maintain good control. Blood glucose monitoring has now replaced urine monitoring in most resource-rich settings. However, insistence on blood glucose monitoring in economically disadvantaged settings could result in no monitoring at all, which would be a major loss compared to the very important information available from urine glucose monitoring. The withdrawal of visually readable blood glucose strips has made blood monitoring even more inaccessible to people with low incomes. The continuing availability of urine glucose testing is a critical issue in such circumstances, even beyond the time when cheaper blood glucose strips may become available. Studies in some economically developed countries indicate that significant percentages of the population cannot afford to purchase diabetes supplies on an ongoing basis. Urine glucose monitoring is a viable option in such circumstances, with occasional blood glucose measurements to help ensure acceptable control.

Interpretation

The limitations and proper interpretation of urine glucose test results need to be understood. These include that urine testing gives the results since the last time urine was voided. If the urine is free of glucose, it is an indication that the blood glucose level is below the renal threshold, which can vary, but is usually accepted as corresponding to a blood glucose level of 10 mmol/l (180 mg/dl). Results also do not distinguish between moderately raised and grossly elevated blood glucose levels. A particular concern is that a negative test does not distinguish between normoglycaemia and hypoglycaemia. In pregnancy, urine testing is less reliable because the renal threshold for glucose can drop significantly. Some strips also allow for the measurement of urine ketone and protein levels. Urine ketone measurement is particularly useful in the early recognition and management of diabetic ketoacidosis.

Summary

- Urine glucose monitoring is a viable, cost-effective way of monitoring diabetes control, especially when the cost of blood glucose monitoring makes it inaccessible or when people do not wish to perform blood testing. However, it is particularly helpful in persons at low risk of hypoglycaemia and whose blood glucose levels are not too high and generally stable.

- Occasional blood glucose measurements should be made to help monitor acceptable control. Increasingly, emphasis is being given to blood glucose monitoring, for example through advertising, without commensurate publicity being given to the valuable role of urine glucose monitoring.

- This lack of information may result in health care professionals, people with diabetes and governments downgrading or becoming increasingly unaware of the importance and usefulness of urine glucose monitoring in appropriate circumstances, in both developing country and some developed country settings[92-96].

H. Animal, Human and Analogue Insulins & Facts[97]

Insulins are now available in different molecular forms, some because of species differences and some by design through molecular engineering. Modern highly purified animal insulins are safe, effective and reasonably reproducible in their actions. Human insulins, prepared usually by genetic engineering, are similar to highly purified pork insulins. Concerns that hypoglycaemia problems are greater with human insulins have not been substantiated by research. There is no overwhelming evidence to prefer one species of insulin over another and

patients should not be changed from one species of insulin to another without reason. Genetically modified insulin analogues may provide advantages in patients with problematic hypoglycaemia but they are expensive and there are no long term safety data. Early animal insulins were effective but had imperfect absorption profiles. There were also concerns about their ability to induce an immune response (immunogenicity), which increased the variability of their action profiles. The highly purified "mono-component" insulins reduced the immunogenicity, resulting in faster, shorter actions. Disappointingly, the immunogenicity of human insulin is similar to that of highly purified pork insulin, to which it is clinically equivalent. Highly purified animal insulins are effective agents to treat diabetes. Human insulin is at least as good as highly purified pork insulin. In many parts of the world, beef insulin provides access to a low cost insulin. While their prices remain lower, highly purified pork and to a lesser extent beef insulins are entirely acceptable and there is no reason to convert. Human insulin has the theoretical advantage that it can be synthesized in limitless quantities at relatively low cost. All insulins have slightly different properties and patients should not be changed from one to another insulin type unless there is a clear advantage. No insulin type will suit every patient and it is important that variety is maintained in order to find the insulin that suits each patient best. More recently, genetically modified insulins are being introduced in which the human insulin gene is deliberately altered to confer some specific desirable properties, including a more reproducible action profile. Rapidly acting analogues give better post-prandial (after meal) glucose control and contribute less to nocturnal hypoglycaemia than earlier short acting insulins. New "background or basal" insulins have flatter action profiles and are less prone to cause hypoglycaemia in the night. These insulins are more costly and it is important to recognize that they have not delivered overall improvements in glucose control in large studies. They may have different properties from human insulin and animal insulins and are likely to prove most beneficial in intensified therapy, when good control cannot be achieved without problematic hypoglycaemia.

All insulin therapy is associated with the risk of hypoglycaemia, sometimes severe. There is no evidence that this is worse with human rather than animal insulins. Concerns have been raised in some countries that human insulin use was associated with a different and higher risk of hypoglycaemia. The evidence for this has remained anecdotal, despite serious attempts to document it and find a mechanism. Patients with problematic hypoglycaemia need careful monitoring. Their insulin regimen should be prescribed with knowledge of the expected actions of the insulins involved. Insulin regimens should take into account risk factors such as exercise, alcohol ingestion and illness and these should be clear to the patient. Problematic

hypoglycaemia can generally be treated effectively without changing insulin species although patient choices should be respected. Despite the lack of scientific evidence, some patients do better on specific insulin types and some older insulins may have individual benefits in some settings.

Conclusion

- People with insulin deficient diabetes require adequate and secure supplies of safe and affordable insulins.
- Genetic engineering, currently used to make human insulin, should be able to deliver this, as its production capacity is theoretically limitless.
- Animal insulins remain a perfectly acceptable alternative and indeed some patients prefer them.
- Newer insulins offer potential advantages but until these are proven to deliver real long-term benefits safely and affordably, it seems appropriate to use them in patients experiencing specific problems that a specific analogue might reasonably be expected to address.

I. Issues related to Insulin, Test Strips and Other Diabetes Supplies[97-98]

Insulin is an essential drug according to the World Health Organization (WHO) but it is not yet universally accessible to all those who need it in the majority of the world's countries. Most people with diabetes who live in countries where insulin is not subsidized and cannot afford to buy this life-saving drug. Test strips and other diabetes supplies, such as blood glucose monitoring equipment and oral drugs, are also often too expensive for many people with

diabetes. However, the lack of access to insulin, test strips and other diabetes supplies is not just a question of supply and demand or affordability. Problems of distribution, storage, transportation, withdrawal of animal insulin and taxation combined with traditions and beliefs, limited or inappropriate access to healthcare, lack of diabetes education, and appropriate nutrition are also factors that perpetuate the lack of insulin and diabetes supplies for those who require it to survive. The problem is made worse in many developing countries by the lack of good epidemiological data on diabetes and adequate healthcare facilities. In addition, the epidemic of obesity in many countries compounds the problems faced by people with diabetes. Difficulties accessing diabetes care are common to millions of people with diabetes around the world. A study carried out in 2002 showed that in 40% of the countries that were surveyed, people with diabetes did not have uninterrupted access to insulin; some developing countries reported that access to insulin was assured less than 25% of the time. A more recent study carried out in 2006 indicates that the situation has not improved: only 20% of the surveyed countries were able to ensure constant access to insulin. Irregular access or total lack of access to insulin and diabetes supplies can result in very serious consequences for people with diabetes; in many cases death. Various factors contribute to reduced access to diabetes care in many parts of the world. Among these is the lack of an effective support network to provide information and assistance to people with diabetes. Organizations representing people with diabetes play a key role in improving the daily lives of those living with the condition; but in many countries these groups lack the means to carry out their work effectively.

To address this situation, the International Diabetes Federation (IDF) Task Force developed the Association Twinning Initiative (ATI), which encourages IDF Member Associations in developed countries to partner with selected Associations in developing regions. The aim is to initiate and implement projects to improve access to insulin and diabetes care in these areas.

Emergency situations provoked by natural disasters and civil unrest can impact heavily on the lives of people with diabetes – such was the case in South-East Asia following the tsunami in 2004, and in Lebanon as a result of the military conflict this year. The delivery of healthcare is often disrupted or blocked entirely, placing people's lives at risk. The Task Force works to ensure availability of insulin and diabetes supplies in emergency situations and, in recent years, has been active in monitoring and responding to requests for assistance following a number of crises around the world.

I.1 Insulin Availability & Rapid Assessment Protocol for Insulin Access Surveys[99-101]

It is alarming that more than 80 years after the discovery of insulin, many people around the world die every day because they cannot access the drug. In order to identify regions where action is required, it is essential that the different levels of access to diabetes supplies are assessed. Over the years, the IDF Task Force has carried out four surveys on access to insulin, which have served to inform its actions and activities. The results of each new survey indicated that the major obstacles that had been identified in previous studies continued to prevent many people with diabetes from obtaining essential life-saving medication. The valuable information obtained from these surveys supports the work of the Task Force in providing information on insulin and diabetes monitoring equipment. One of its most notable achievements is the International Colour Code for Human Insulin Preparations, which was developed in collaboration with a variety of partners, including the major insulin manufacturers. A universal colour code means that similar preparations of insulin have the same colour on the label regardless of manufacturer, and that this is standardized worldwide. Such a colour code helps to reduce confusion and uncertainty for people with diabetes who have to buy insulin abroad or from a different source. Following an IDF initiative, major insulin manufacturers have agreed on a universal colour code for human insulin preparations. All parties are now actively working together to produce a colour code for insulin analogues.

The Task Force works closely with a number of partners who share its objectives and are committed to finding solutions to the problems surrounding access to diabetes care. These include Rotary International, which supports children with diabetes in many countries; IFL (Insulin For Life, www.insulinforlife.org), which distributes emergency diabetes supplies in situations of acute need; and the International Insulin Foundation (IIF), which works to improve access to insulin in developing countries. The Task Force also includes representatives of the principal manufacturers of insulin, test strips and other diabetes supplies. The diabetes epidemic continues to grow; in future years, it is set to impact hardest upon the populations of low- and middle-income countries. It is therefore increasingly important that adequate diabetes care be made available to everyone. The global diabetes community must expect nothing less than the universal availability of insulin, test strips and other diabetes supplies for those who depend upon them to survive.

The most recent survey, carried out in 2002, extended coverage to the access and availability of diabetes supplies including urine test strips, blood glucose meters and blood glucose test

strips. The survey reconfirmed the wide variation in prices of insulin and diabetes supplies which an IDF survey of diabetes associations in 1999 had found. The 1999 survey found, for example, that the price of a 10-ml vial of U100 animal insulin varied from USD 10 to USD 47 in

Table 1: Information for diabetes clinics in developing countries that are considering introducing HbA1c testing. The options listed have a relatively low outlay, and may be cost-effective in low volume settings (e.g. 200 tests per month), and offer point-of-care testing (i.e. results on the spot)

countries where there were no state subsidies for this essential drug.

The 2002 survey also found, among other things, that:

- Many people in economically developing countries do not appear able to access insulin because they cannot afford it.
- Animal insulin is considerably cheaper in those countries where both human and animal insulin are available.
- In many countries, insulin in vial form is significantly cheaper than the same type of insulin in pen-fill cartridge form.
- Blood glucose test strips appear to be even less accessible than insulin for the same reason of affordability.
- Urine test strips are significantly more accessible because they are much more affordable. They provide a viable testing method in the absence of affordable glucose testing. There seems to be evidence that the use of urine test strips may be decreasing without a commensurate increase in the use of blood glucose test strips, i.e. increasing numbers may not be testing at all.

COMPANY NAME	ADDRESS	PRODUCT
Bayer	Bayer HealthCare LLC Diagnostic Division 511 Benedict Avenue Tarrytown, NY 10591 USA Tel: +1 914 631 8000 Fax: +1 914 524 2132 info@labnews.de www.bayerdiag.com	***DCA – 2000*** ➢ Machine Cost: Approximately $3,000 ➢ Cost per test: $8-9 ➢ Results in 6 minutes ➢ Technical Complexity: simple specimen preparation ➢ Most common usage: Diabetes clinics, low or medium volume ➢ Portable ➢ Cartridge shelf-life: 15 months (refrigerated); 3 months (room temperature)
Bio-rad Laboratories	Bio-Rad Laboratories 1000 Alfred Nobel Drive Hercules, CA 94547 USA Tel: +1 510 724 7000 Fax: +1 510 741 5817 Isg_websupport@bio-rad.com www.bio-rad.com	***Micromat II**** ➢ Machine cost: $600-900 ➢ Cost per test: approximately $8 ➢ Results in 5 minutes ➢ Technical complexity: requires some specimen preparation ➢ Most common usage: doctor's surgeries low volume ➢ Portable ➢ Shelf-life: 16 months (refrigerated); 1 month (room temperature)
Metrika	Metrika, Inc. 510 Oakmead Parkway Sunnyvale, CA 94085 USA A1cNowMail@metrika.com www.metrika.com	***A1c Now In View*** ➢ Disposable single kits, around the size of a pager (10 tests per box for physician use, 2 tests per box for patient use) ➢ Cost per test: approximately $11-12 ➢ Result in 5 minutes ➢ Technical complexity: requires some specimen preparation. New all in one sampler available from 2006 ➢ Most common usage: home testing, can also be used in clinic setting, volume variable ➢ Shelf-life: 6 months at room temperature, refrigeration preferable

* Also marketed by Cholostech Corporation (www.cholostech.com) as Cholostech GDX
Source: www.idf.org

- Taxes are still a significant factor affecting the price of insulin, and other diabetes supplies in a large number of countries even though WHO essential drugs guidelines state that there should be no taxes on insulin.

The Task Force also collaborates with the International Insulin Foundation (IIF), a non-profit organization, to seek ways of improving access to insulin, the equipment for its delivery and the education for its use for people with type 1 diabetes, their families and carers in developing countries. The IIF in collaboration with local partners carries out an in-depth assessment of the health system looking at different aspects of the country's organization of

medical supplies and care using a protocol it has developed. This protocol, the Rapid Assessment Protocol for Insulin Access (RAPIA), draws on the principles of Rapid Assessment Protocols (RAP) which have been developed and implemented in several different areas, including infectious diseases, drug abuse and nutrition, for the purpose of applying preventive and therapeutic interventions.

The RAPIA is carried out by interviewing key stakeholders at different geographical and organizational levels and is aimed at getting these people's perspectives on the problems that people with diabetes face accessing insulin and proper diabetes care. Any necessary background documents are also collected.

The information gathered by the RAPIA relates to:

- Health service structure and functioning - drug procurement, diabetes management
- Diabetes policies
- Reported and observed practice for management of patients with type 1 diabetes
- Availability of insulin, syringes and monitoring equipment
- Existence of distribution networks for insulin
- Insulin supply-related knowledge and attitudes amongst people with diabetes and their carers.

Once all this information is collected the IIF writes a report on the situation and proposes a series of recommendations to help improve the situation. The IIF has carried out this assessment in Mozambique and Zambia, where it is currently working with the respective Ministries of Health and diabetes associations to improve the well-being of people with diabetes in these countries.

J. Prevention of Diabetes & its Complications: The Role of Non-Invasive Methods

Simple, practical, non-invasive and inexpensive methods are needed to identify individuals at high risk for IGT and diabetes and to limit the proportion of the population requiring diagnostic glucose tolerance tests. Agencies and Organizations working on diabetes recommend the use

of brief patient questionnaires to help healthcare professionals to quickly identify people who may be at a higher risk and who need to have their level of risk further investigated. This type of questionnaire could also be used by individuals for self-assessment.

The Finnish Type 2 Diabetes Risk Assessment Form[102] developed in 2001 is an example of an effective patient questionnaire and should be used as the basis for developing national questionnaires which take into account local factors. It has eight scored questions, with the total test score providing a measure of the probability of developing type 2 diabetes over the following 10 years. The reverse of the form contains brief advice on what the respondent can do to lower their risk of developing the disease, and whether they should seek advice or have clinical examinations. The test takes only a couple of minutes to complete and can be done on the internet, in pharmacies or at various public campaign events.

Similarly the Indian Diabetes Risk Score (IDRS)[103] from a geographical cohort with urban and rural components of Chennai called IDRS with two modifiable risk factors (waist circumference and physical inactivity) and two non-modifiable risk factors (age and family history of diabetes), has provided an non-invasive and inexpensive method to identify those with high risk for diabetes and unidentified diabetics in Indian populations.

The IDRS has a sensitivity of 72.5% and specificity of 60.1% and is derived based on the largest population based study on diabetes in India Chennai Urban Rural Epidemiological Study (CURES). The advantage of IDRS is its simplicity, low cost and is easily applicable for mass screening programmes. IDRS should be tested in other population based studies in India both rural and urban. Prospective follow up studies on non-diabetic subjects with high-risk score are needed to assess the predictive nature of IDRS. IDRS may be predictive of metabolic syndrome and cardiovascular disease as three of the factors [age, physical activity and

waist circumference] are risk factors for both metabolic syndrome and cardiovascular disease. In resource poor settings where questionnaires are not available or impractical, measurement of waist girth gives a simple prescreening tool allowing those at highest risk to be identified.

Step 1: Identification of those who may be at Higher Risk

The current consensus recommends that all individuals at high risk of developing type 2 diabetes be identified through opportunistic screening by doctors, nurses, pharmacists and through self-screening. In any population, individuals at high risk can be easily identified through a simple, practical and non-invasive questionnaire[102-104], such as the Finnish Type 2

Diabetes Risk Assessment Form/Indian Diabetes Risk Score, which focuses on risk factors such as age, waist circumference, physical activity, family history, cardiovascular history, gestational history and drug history.

Step 2: Measurement of Risk[52]

Individuals at high risk should then have their plasma glucose levels measured by a health professional. This will not only detect cases of IFG (Impaired Fasting Glucose) or IGT (Impaired Glucose Tolerance), but also cases of undiagnosed diabetes. The presence of IGT and IFG give a considerably increased risk of developing type 2 diabetes. Interventions targeted at such individuals therefore provide an opportunity to delay or prevent the onset of type 2 diabetes. Other diabetic risk factors that should also be assessed at this stage include the presence of increased waist circumference; high blood pressure; family history of diabetes; raised triglycerides; or a pre-existing cardiovascular disease. The presence of any of these factors will increase a person's risk of developing diabetes.

Step 3: Intervention to Prevent the Development of type 2 Diabetes[52]

There is substantial evidence that lifestyle changes (achieving a healthy body weight and moderate physical activity) can help prevent the development of type 2 diabetes and should be the initial intervention for all people at risk.

Obesity, particularly abdominal obesity, is central to the development of type 2 diabetes and related disorders. Weight loss improves insulin resistance, hyperglycaemia and dyslipidaemia in the short term, and reduces hypertension. Overweight and obese people should therefore be encouraged to achieve and maintain a healthy body weight. A structured approach such as that taken during the Diabetes Prevention Program (DPP) can produce long-term weight loss of 5-7% of baseline body weight. Increased physical activity is particularly important in maintaining weight loss. Regular physical activity also improves insulin sensitivity; reduces plasma levels of insulin in people with hyperinsulinaemia; improves dyslipidaemia and lowers blood pressure. Moreover, physical activity increases metabolically active muscle tissue and improves general cardiovascular health. Increased physical activity also reduces the risk of type 2 diabetes.

IDF recommends a goal of at least 30 minutes of moderate physical activity (e.g. brisk walking, swimming, cycling, dancing) on most days of the week. Regular walking for at least 30 minutes per day reduces diabetes risk by 35-40%. This can comprise several bouts of activity adding up to 30 minutes. Some people, including those with a high level of risk of developing diabetes

who cannot change lifestyle sufficiently, will also require pharmacotherapy. However, they should be encouraged to still maintain lifestyle changes, as they will continue to deliver long-term health benefits. IDF recommends that when lifestyle intervention alone has not achieved the desired weight loss, and/or improved glucose tolerance goals, as set by the health-care provider, metformin in the dose of 250 - 850 mg two times daily (depending on tolerance) should be considered as a diabetes prevention strategy (particularly in those aged less than 60 years with a BMI (Body Mass Index) greater than 30 (greater than 27 in certain ethnic populations) and a FPG (Fasting Plasma Glucose) of 110 mg/dl) who do not have any contraindications.

J.1 New Definition helps Identify Children at Risk of Metabolic Syndrome[105-109]

The IDF has launched a new definition to identify children and adolescents at increased risk of developing type 2 diabetes and cardiovascular disease in later life. The metabolic syndrome is a cluster of the most dangerous risk factors for type 2 diabetes and cardiovascular disease. Its early identification is very important to facilitate preventive action. This first simple, unified definition from the IDF for children and adolescents is consistent with that available for adults. Intrauterine events for the unborn child and factors during early development years predispose a child to disorders such as obesity, pre-diabetes, and metabolic syndrome. At the same time, urbanization, unhealthy diet and sedentary lifestyle are increasing the risks for the coming generations.

The new definition is simple and easy to apply in clinical practice. Waist measurement is the main component. Percentiles, rather than absolute values of waist circumference have been used to compensate for variation in child development and ethnic origin.

The definition is divided according to age-groups: age 6 to 10; 10 to 16; and 16 or older. IDF suggests that the metabolic syndrome should not be diagnosed in children younger than 10, but that a strong message for weight reduction should be delivered for those with abdominal obesity.

For children age 10 or older, metabolic syndrome can be diagnosed with abdominal obesity (using waist circumference percentiles) and the presence of two or more other clinical features (elevated triglycerides, low HDL-cholesterol, high blood pressure, increased plasma glucose). Although some of these as well as body size and proportions change with age and development,

in the absence of contemporary definitive data, the criteria adhere to the absolute values in IDF's adult definition. The exception is that one (rather than a sex-specific) cut-off is used for HDL. For children older than 16, the IDF adult criteria can be used.

J.2 Diabetes Education[110-117]

Diabetes is increasing at an alarming rate globally. It is a complex, chronic condition that affects all areas of a person's life and that requires high quality care. To this end, diabetes education is of critical importance and should be considered an integral part of diabetes prevention and care. Unfortunately this is not the case in many countries of the world where diabetes education is, at best, in its infancy or non-existent. The combination of lack of access to quality medical management and diabetes education leads to poor clinical outcomes, reduced quality of life and high health-related costs due to service utilization and the costs of treatment.

WHO and IDF's position is that:

- All people with diabetes, no matter where they live, have the right to learn about their disease.
- Healthcare professionals must be educated to be responsible for prevention and provision of diabetes care.
- People at risk and the wider public must know the risk and learn about prevention.
- Health ministries have to ensure they have a comprehensive diabetes education strategic plan integrated into their National Diabetes Programme.

Education is a key component in the prevention and treatment of diabetes and should be directed to three audiences: the individual and those affected by the disease, healthcare providers and the community at-large. Today, although many people are aware of the value of education, findings of a survey similar barriers in the provision of education: financial, limited access, lack of knowledge and education resources.

As the world incidence of diabetes grows efforts to promote self-management education, training for providers and public awareness are critical in reducing the humanistic and economic burden caused by the disease. For people affected by diabetes, self-management

education training is important since people with diabetes and their families provide 95% of their care themselves. Without appropriate education people cannot make the complex daily medical decisions required for good health, quality of life and survival. The goal of diabetes self-management training is to support the efforts of people with diabetes to:

- Understand the nature of their illness and its treatment
- Identify emerging health problems in early, reversible stages
- Adhere to self-care practices
- Make needed changes in their health habits

Diabetes self-management training assists people in dealing with the emotional and physical demands of their disease, given their unique socio-economic and cultural circumstances.

Healthcare providers must be active participants in facilitating quality diabetes self-management education and care and to motivate their patients to undertake the demanding daily regimen associated with diabetes care. It is also considered best practice for diabetes education and care to be provided by an integrated multi-disciplinary team including, at a minimum, the person with diabetes, a nurse, a dietitian and physician who are skilled in diabetes management, and possibly a pharmacist and a behavioral scientist. All of them need to be educated on the provision of quality care and prevention methods. It is recognized that in many countries healthcare providers are facing numerous barriers, such as:

- Too many patients for the number of healthcare professionals who have specific training
- A lack of access to and availability of education programs for health professionals and their patients
- A wide variation in standards for diabetes education within and between countries

More broadly, the public must be made aware of the serious health consequences of diabetes. Educating the public in the provision and support of prevention strategies and quality care is key in the spirit of improving community health.

In this connection, IDF recommends that for the prevention and treatment of diabetes to be successful through education initiatives, governments, local, national and international health associations must organize efforts to promote the training, exploration of technological methods to enhance education, financial support, access and public awareness of diabetes education. IDF recommends that governments in particular address the burden of diabetes needs on three levels:

- Central governmental level where the burden of the disease needs to be recognised and the importance of diabetes education acknowledged, promulgated, funded and delivered according to the IDF Standards for Diabetes Education.

- Health professional training directed at medical and non-medical health professionals. Diabetes education should be included in medical schools and postgraduate curricula. It should also be directed at non-medical health professionals and be implemented based on the IDF International Curriculum for Health Professional Education.

- Local policies and procedures developed to support the delivery of evidence-based diabetes education.

K. Non-invasive Testing for Diabetes – Options[118-122]

Conventional diabetes screening methods such as the FPG and the OGTT are inconvenient and often perform poorly. Diagnosis of diabetes typically does not occur until 7-9 years post onset when 50% of patients have one or more irreversible complications. The FPG requires a fasting blood sample; and the OGTT test requires fasting, ingestion of a glucose load, and multiple blood samples. Due to poor sensitivity the FPG misses up to 60% of the people, and the OGTT suffers from poor reproducibility with a Coefficient of Variation of up to 18%. These deficiencies can lead to false-negative or inconsistent results and add to the undiagnosed problem.

A one-minute experimental diabetes screening system that uses light to detect diabetes-related biomarkers found in skin regardless of color is under clinical trails at the moment. Previously reported studies of a prototype of the portable desktop system have shown it outperforms both the fasting plasma glucose (FPG) test and the A1C test as a rapid and non-invasive screen for pre-diabetes and type 2 diabetes. The investigational device, not yet approved for use in the United States, is being designed for use at physician-supervised point-

of-care locations. Known as Scout DS(TM), manufactured by VeraLight Inc. of Albuquerque, New Mexico, the simple-to-use device weighs about 10 pounds and does not require the patient to fast or provide a blood sample. Using light directed onto a small area of an individual's forearm the device is able to detect abnormal concentrations of advanced glycation endproducts (AGEs), which correlate well with diabetes and pre-diabetes and are associated with the disease's serious complications. The medical device is slated for U.S. market introduction in the second half of 2008. The Scout DS prototype is currently undergoing a large-scale pivotal trial in the United States. A calibration trial of 1,700 subjects at risk for type 2 diabetes has completed data collection at eight U.S. sites. This phase of the trial is designed to assure its ability to predict abnormal glucose tolerance in a wide range of individuals. In August 2007, the system will be undergoing further testing at 20 U.S. sites in 5,400 subjects at risk for type 2 diabetes. In all cases, Scout DS is being compared to the gold standard Oral Glucose Tolerance Test (OGTT) as the reference method.

K.1 Diabetes Odometer

Analogous to a "diabetes odometer," AGEs are a sensitive metric for the cumulative damage the body endures due to the effects of abnormally high blood sugar and oxidative stress. AGEs harm the proteins that make up the blood vessels, connective tissue, and are thought to be major factors in aging and age-related chronic diseases. According to medical experts, non-invasive skin detection of AGEs could replace the FPG test as the medical workhorse for screening people suspected of having diabetes.

K.2 Glucowatch G2 Biographer

Glucowatch G2 Biographer is a continuous glucose monitoring device that is worn like a watch with auto sensors that does non-invasive glucose testing through the skin. This glucowatch provides glucose readings for as frequently as 10 minutes at a time for as long as 13 hours at a time. Glucowatch G2 Biographer is intended to supplement not replace traditional finger stick tests. In fact, glucowatch is calibrated with a finger stick test. Using that diabetes test as a measure, the Glucowatch G2 Biographer will monitor the ups and downs of blood sugar levels. Pre-set warnings can be put in place to warn you when blood sugar levels are too high or too low.

K.3 Blood Glucose Meters

These are used extensively to monitor blood glucose levels in individuals with diabetes mellitus. In addition, the BD Logic® (Becton, Dickinson and Co., Franklin Lakes, NJ) and FreeStyle® (Abbott Diabetes Care, Alameda, CA) meters are used to transmit data directly to insulin pumps for calculation of insulin doses and to calibrate continuous glucose sensors. Thus, the accuracy of these meters is especially important.

K.4 Pulmonary Insulin Delivery[123]

Since the discovery and use of insulin in the early 1920s investigators have continually sought to deliver it by the pulmonary route. Publications appearing through every decade from the 1920s onward, has published attempts to deliver insulin by inhalation. Yet, multiple problems confounded the development of the pulmonary route. These included low bioavailability, highly variable nonreproducible delivery, irritation, and cumbersome delivery devices. Some attempts used "absorption enhancers," some of which had their own problems. Then, in the late 1990s,

a number of advances in both device design and pharmaceutical formulation led to various development programs for inhaled insulin preparations. Some of these have fallen by the wayside, while others have stalled because of an increasingly crowded landscape. Still others are waiting in the wings and may yet emerge. Here is an overview of four programs that are farthest along in clinical development. One of these, the Exubera® Pulmonary Insulin Delivery System (Pfizer Pharmaceuticals, New York, NY; and Nektar Therapeutics, San Carlos, CA), was approved by the U.S. Food and Drug Administration in 2006 for use in adults with both

type 1 and type 2 diabetes. Two others, the AIR® Inhaled Insulin System (Eli Lilly and Co., Indianapolis, IN; and Alkermes Inc., Cambridge, MA) and the AERx® Insulin Diabetes Management System (Novo-Nordisk A/S, Bagsvërd, Denmark; and Aradigm Corp., Hayward, CA), are in Phase III clinical trials. All three of these provide prandial insulin with initial availability similar to rapid-acting insulin analogues, but with slightly longer duration of effect. The fourth, also in Phase III trials, is Technosphere® Insulin (MannKind Corp., Valencia, CA), which is a super-rapid-acting insulin that happens to be inhaled, and has an action profile quite different from the others.

L. Research and Development agenda [22, 124, 125]

The following subsections discuss the major issues for research and development.

Prevention Research

- Well-designed community-based studies of primary prevention for type 2 diabetes are needed, especially as part of multifactorial interventions, in developing countries.
- Research is also needed into safer and cheaper drugs to prevent diabetes when lifestyle intervention either is not feasible or has failed.
- There is a need to know the long-term effects of diabetes prevention on CVD and other outcomes. More effective and cheaper ways to prevent the major complications of diabetes are also needed.
- Other areas also deserving research include noninvasive methods for monitoring blood glucose and more effective and efficient ways of screening for pre-diabetes, diabetes, and early diabetes complications.
- Evidence of the benefits of diabetes education on outcomes is lacking, and organized research to assess effective components of diabetes education and their impact on control of risk factors and long-term outcomes should be a priority.

Epidemiological and Economics Research

- Data on trends in and the effects of risk factors for diabetes in developing countries — obesity; birth-weight; physical inactivity; television viewing; dietary factors; fast foods; socioeconomic factors; and effects of urbanization, industrialization, globalization, and stress – are needed.
- Low-cost ways to obtain such data in a standardized manner may be worth considering.
- More data are also needed on the costs of diabetes, the impact of the disease on quality of life, and the cost-effectiveness of various interventions in the context of developing countries.

Health Systems and Operational Research

- Greater emphasis on translation research is needed including well designed and standardized studies of quality of care and outcomes.

- Research aimed at understanding system-level complexity and finding ways to deliver chronic disease care that takes such complexity into account is also a priority.

- Simulation models suitable for assessing cost-effectiveness and for forecasting the burden in developing countries are needed.

- Operational research aimed at understanding the tradeoffs and the best mix of resource allocation for diabetes and chronic disease care in developing countries is also needed.

Basic Research

- Further strategic unraveling of the genetic basis of type 2 diabetes and gene-environment interactions may help explain the diabetes epidemic and provide better understanding of the patho-physiology of the disease.

- Understanding the role of prenatal influences, especially in developing countries, may offer productive opportunities for interventions.

- Because of the increasing occurrence of type 2 diabetes in children, as well as the role of obesity in accelerating the onset of type 1 diabetes, further research into the typology and classification of diabetes is vital.

- The rapid industrialization and economic development being experienced by several developing countries may make research into the role of socioeconomic factors, urban stress, and lifestyle factors on the causation of diabetes productive.

M. Summary IKMC 06[126] – Diabetes & Non-Communicable Diseases

Technology can be used at any stage in the natural course of the disease to manage diabetes - from primordial prevention to tertiary care management. At the tertiary level, the focus is on

early diagnosis and management of systemic complications of diabetes. Secondary level prevention aims at preventing the onset of complications through diet, exercise, oral medications/insulin and education. Innovative technology solutions can be developed to deliver insulin better. Insulin pumps that program insulin delivery are available and useful but are expensive. Insulin inhalers are becoming available. Technology developments and innovations need not always be instrument oriented. An Indian Diabetes Risk Score has been developed using epidemiological data that provides a non invasive tool as a first line screening to identify persons at risk for diabetes. The emphasis is on the need for an integrated approach extending from prevention to rehabilitation in addressing the emerging health challenges of the NCDs. The implication of the role of multiple factors in the development of NCDs is enough evidence to address the NCDs through an integrated approach. The measures to address these challenges is a combination of education for awareness generation, policy related measure and inculcated healthy living habits. An integrated approach should allow for earlier detection, self referrals, measures for opportunistic disease screening and minimise missed opportunities for detection as and where possible. The role of integrated management like treating hypertension with diabetes mellitus is more effective and complements each other. There is need for more institutions and resources to carry out operational and action research in the field of NCDs. Controlling diabetes needs education and health promotion, screening for diabetes, and appropriate management. Training for human resources, and technology solutions like telemedicine may be needed to supplement ongoing efforts. Low cost insulin availability is the key to the Indian diabetes context. Injections will continue to remain the most affordable method for insulin administration for time to come. Lower cost injection devices like pens and pumps will also become available in the near future in India. Non-invasive insulin delivery is a reality; this includes inhaled, buccal and in future probably oral routes. These technologies will have to mature considerably to be price competitive with injectable insulins.

N. Potential Directions for ICTPH

Following up on the assessment report presented above and the deliberations on management of diabetes and its complications in the International Knowledge Millennium Conference 2006, the potential directions with respect to diabetes that ICTPH can pursue include:

- Further validation of the Indian Diabetes Risk Score in different parts of India at the community level as a non-invasive tool in first line screening to identify persons at risk for diabetes as well as for diabetes control.

- Assist in the development of a registry system for diabetes and its complications within the national context similar to the diabetes atlas that is available internationally.

- Support collaborative research for noninvasive methods of monitoring blood glucose and more effective and efficient ways of screening for pre-diabetes, diabetes, and early diabetes complications.

- Support studies that look at gene-environment interactions that may help explain the diabetes epidemic and provide better understanding of the patho-physiology of the disease including the role of prenatal influences, especially in developing countries, and type 2 diabetes in children,

- Ensuring adequate access to insulin and necessary diabetes supplies like testing strips and monitoring kits should be an important priority for India and developing countries. Furthering studies comparing human and animal insulins as well reviewing the non-invasive methods of insulin delivery to be explored at an appropriate time.

- Health economic studies on comprehensive integrated disease management for non-communicable diseases including diabetes from the societal perspective.

O. Abbreviations

ACE	Angiotensin – Converting Enzyme
AGE	Advanced Glycation Endproducts
ATI	Association Twinning Initiative
BMI	Body Mass Index
CURES	Chennai Urban Epidemiological Study
CVD	Cardio Vascular Diseases
DM	Diabetes Mellitus
DPP	Diabetes Prevention Program
FPG	Fasting Plasma Glucose
IDRS	Indian Diabetes Risk Score
IDF	International Diabetes Federation
IFG	Impaired Fasting Glucose
IFL	Insulin For Life
IFCC	International Federation of Clinical Chemistry
IIF	International Insulin Foundation
IGT	Impaired Glucose Tolerance
IKMC	International Knowledge Millennium Conference
OGTT	Oral Glucose Tolerance Test
QALY	Quality Adjusted Life Years
RAP	Rapid Assessment Protocols
RAPIA	Rapid Assessment Protocol for Insulin Access
RCT	Randomized Controlled Trials
NCD	Non-Communicable Disease
WHO	World Health Organization

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