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THE SOCIETAL IMPACT OF DIABETES MELLITUS AND DIABETES CARE

Methodology

by

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FOREWORD

The present Working Paper is one in a series of three papers (WP 2005:4; WP 2005:5; WP 2005:6) on the societal impact of diabetes mellitus and diabetes care in Bangladesh. The work was initiated by Novo Nordisk A/S, Corporate Health Partnerships and conducted of a team consisting of the four authors. An external evaluation was made by an invited Critical Board. The team received a number of valuable suggestions from the board, and most of these are included. Still, the content of the final reports is the responsibility of the authors alone. The project was financed by Novo Nordisk A/S.Two reports on type 1 and type 2 by the authors are available on request from Novo Nordisk A/S when published.

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Timetable for main phases of the project:

Calendar year 2002: Initial planning and preparation of project protocols
Development of epidemiological model data and cost structure

Calendar year 2003: Using empirical data sets for validation and supplementary analyses
First reporting of results

Calendar year 2004: Final analyses and reporting

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EXECUTIVE SUMMARY

Diabetes mellitus, with its two main types; Type 1 diabetes and Type 2 diabetes, represents a global health problem due to increasing prevalence and associated risk of devastating complications such as gangrene, blindness, kidney failure as well as premature morbidity and mortality due to heart and vascular diseases. Access to optimal treatment differs between societies. This prompts for health economics appraisals of the societal impact of diabetes and the treatment of diabetes.

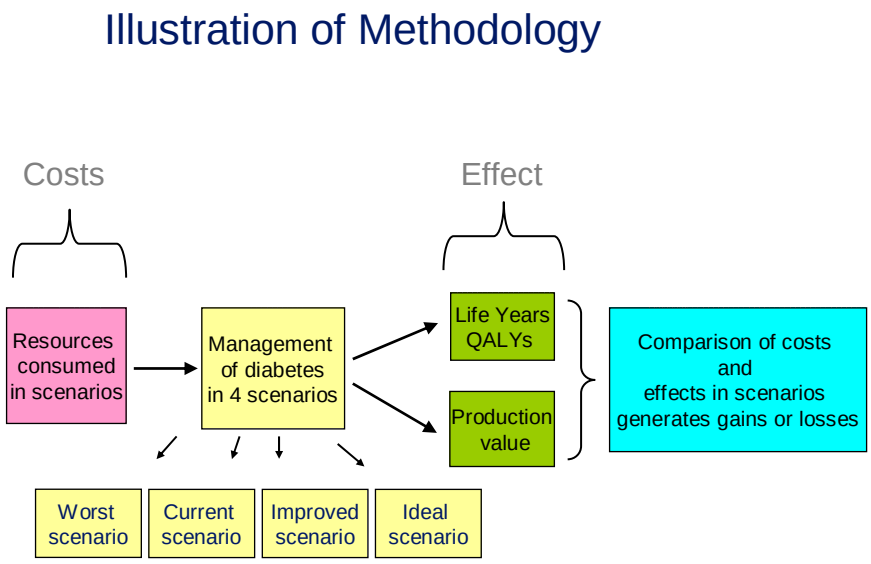
The project presented here includes a range of studies focusing on various aspects of the societal impact of diabetes and its treatment in different societies. This first report presents methodologies and considerations of relevance for the project.

In terms of epidemiological design and methods, focus of the studies is on patient populations in a given society, as experienced in the calendar year 2001. Based on epidemiological modelling, validated and supplemented by empirical data whenever possible, a range of different hypothetical scenarios has been established. From epidemiological modelling four contrasting scenarios have been established: The "Current" scenario, representing the real situation for T1D in Denmark; the "Worst" scenario, representing the hypothetical situation that insulin has never been available; the scenario "Improved", representing a situation believed to represent realistically possible improvements in diabetes care; and, the "Ideal" scenario, representing the hypothetical variant of the "Improved" scenario in which T1D is not associated with any excessive risk of complications and mortality. Each scenario is characterised by assumptions concerning current and previous access to treatment of diabetes. For each scenario, a cost structure comprising healthcare costs, non-healthcare costs, informal care-givers´ time and patients´ time is quantified. Effects and benefits are expressed by means of gains in patient-years, quality of life-adjusted patient-years and gains in production value, when the scenarios are contrasted with the scenario reflecting the current situation for the year 2001. An overview of the strategy of analysis is presented in fig. 1.

The methodology applied generally rests on the notion that we are operating in a perfectly competitive market economy. To the extent that market economies are not in full operation as may be the case in developing countries, appropriate adjustments to the standard theoretical framework are discussed.

In the first place, studies have been carried out for a developed nation using Denmark as an example. Subsequently, comparative studies are reported for a developing nation using Bangladesh as an example.

Fig. 1. Strategy of analysis



WHY THIS PROJECT?

The application of health economics methodology to the field of diabetes has been reviewed recently (1). Furthermore, chapter four in the new Diabetes Atlas (2) contains updated estimates of the economic impact of diabetes, globally as well as regionally. Finally, a substantial investment is ongoing concerning the development of computer models that simulate clinical courses and associated costs for patients profiled according to specified risk factors (for example, the Mt. Hood initiative (3)). Therefore, it is pertinent to ask: Why this new project?

It appears that most of the literature and data available on the economic impact of diabetes represent cost-of-illness studies only and frequently confined to direct healthcare costs. Such information is of no particular value when priorities and allocation of resources must be made. As a novelty, we wish to assess current scenarios with alternative scenarios, thereby facilitating decision-making in the healthcare sector. We also focus on the current situation (representing a one-year calendar window) in a society, with its dynamic population of patients with differing disease history, complication status and age. This is in contrast to the simulation models performed as part of the Mt. Hood initiative (3) in which the focus is on the future of an individual patient. Therefore, we cannot immediately make use of the Mt. Hood models for the purpose of the present project.

We believe that the results of this project will stimulate criticism and discussion, and by doing so providing the basis for further refinement and improvements in related future activities. Furthermore, by means of the project it will become evident which kind of basic data related to the clinical characteristics of patients and the cost components of diabetes care that are necessary in order to perform proper health economics evaluations in diabetes care.

1. INTRODUCTION

Most people would agree that access to healthcare services is a precondition for societal prosperity. From an economic point of view the relevant question arises: can the costs associated with any increase in healthcare spending be justified by the corresponding increase in health and derived benefits? Among such benefits are the utility of living longer and/or in a better health condition, production value and subsequent change in the demand for healthcare.

Diabetes mellitus, representing a spectrum of diseases and conditions with the common characteristic of abnormal glucose metabolism, can be considered a major global health problem. The main types of diabetes comprise Type 1 diabetes (characterised by an absolute deficiency in the endogenous insulin production) and Type 2 diabetes (characterised by insulin resistance and relative insulin deficiency), of which Type 2 diabetes is by far the most prevailing diabetes type. Recent estimates suggest that currently almost 200 millions subjects suffer from diabetes worldwide. A substantial proportion of the patients are un-diagnosed at this point in time. The global prevalence of diabetes is expected to rise to some 333 millions subjects by the year 2025 (2). Diabetes mellitus, diagnosed or un-diagnosed, is associated with the risk of devastating complications such as gangrene, blindness, kidney failure as well as premature morbidity and mortality due to heart and vascular diseases.

In countries where access to healthcare is available, the care of people with diabetes also entails significant costs to the healthcare system. Hospitalisation and treatment of late complications (e.g. blindness, kidney disease, amputations and heart related problems) due to poorly treated diabetes are the main cost drivers. It is estimated that the annual direct healthcare costs of diabetes worldwide for people aged 20-79 years, currently is in the range of 153 to 286 billions dollars. These figures are expected to rise to an estimate between 213 and 396 billions dollars by the year 2025, accounting for between 7% and 13% of total healthcare spending in most countries, and up to 40% in a population with particularly high prevalence of diabetes (2).

Insulin has been available for the treatment of diabetes mellitus for some 75 years. Also, peroral drugs for the treatment of particularly Type 2 diabetes and medications for preventing and controlling associated diseases and complications have been available for decades. Together with a constant improvement in the knowledge of how to prevent and manage the complications of diabetes this has had a huge impact on the survival of people with diabetes and, in particular, the quality of life of people with diabetes. Despite this, diabetes is still a serious disease even in countries where treatment is available. Furthermore, lifestyle-induced health problems combined with ageing of populations in the developed world and improved general living standards and survival in the developing world are producing more, not less people with diabetes.

For the individual untreated diabetes means that the ability to produce and consume or the quality of life, and the ability to prosper as a person, are potentially limited depending on the severity of the person's diabetes and whether there are complications. From a societal

perspective, a potential contribution from a productive person to the welfare of the household and the rest of society is lost.

In contrast, optimal treatment for diabetes has positive effects on human health and, consequently, people with diabetes can live an almost normal life with a reduction in their otherwise high risk of disability and premature death. Access to treatment for diabetes also positively impacts the patients´ quality of life and their financial situation through improved productivity. Their intellectual and emotional capacity and that of their families are no longer primarily focused on worries about health but rather on more positive, forward-looking and productive activities.

Based on these considerations, we asked the following question: What are the advantages to a society of ensuring access to diabetes treatment and diabetes care, and what are the costs? Similarly, one may ask what the potential benefits are – and at which costs if treatment of diabetes in a given society was improved to a level without diabetes-associated excess mortality and morbidity. To answer these questions Novo Nordisk has introduced a demonstration project that helps examine various aspects of the current societal costs and benefits of diabetes care.

In a developed society this question may seem less relevant as there is already a long history of treating patients with diabetes. Thus, a more relevant question would relate to issues of improving or altering the existing pattern and extent of treatment. This is of high relevance to a developing society with scarce resources and no systematic treatment of diabetes mellitus. For health policy makers in such countries a pertinent question is whether they should introduce and upgrade treatment of diabetes in the publicly provided or supported healthcare services. To answer such a question, a health economic evaluation might be of relevance along with an analysis of the budgetary consequences. One way to approach such analysis would be first to establish a model of costs and benefits, based on a developed country with a fully developed treatment programme, and then consider how the analysis could be adjusted to a developing country. Secondly, it would also be possible to assess data requirements for the analysis for a developing country from the initial analysis.

This first report presents considerations of methodology of relevance for the project. Subsequent reports in this series deal with the specific studies performed as integral part of the project.

2. EPIDEMIOLOGICAL PRINCIPLES

Basic epidemiological considerations

Epidemiological methods play important roles in diabetes care and research. Descriptive *incidence* studies are fundamental for the monitoring of changing risk over time and provide clues to hypotheses of the aetiology of diabetes to be further explored and tested in case-control studies. Information on the *mortality and incidence of complications* provides the basis for establishing the prognosis in diabetes and assessing needs for improvements in diabetes care. *Prevalence rates* (or correctly prevalence proportions) provide information on the size of the patient population and are therefore particularly useful in setting priorities and allocating resources in healthcare.

The epidemiology of diabetes is changing constantly. For both Type 1 diabetes and Type 2 diabetes increasing numbers of patients have been reported from many different countries, most pronounced for Type 2 diabetes (2). The risk of developing the diabetes-associated complications, notably retinopathy, nephropathy and macro vascular morbidity, is correlated with the level of long-term glycaemic control. The morbidity for people with diabetes will, together with mortality from diabetes, change in the future as improved facilities for treatment and control will be available to an increasing number of patients. Under these circumstances any "snapshot" picture of the prevalence, incidence and mortality in diabetes must be interpreted with caution and should be accompanied by the establishment of modelling techniques that provide for a continuous monitoring of trends in these measures.

Prevalence is estimated as the number of people with diabetes (with/without complications) living at a given point of time. If the population base (i.e. the total population in which the prevalent patients live and from which all new cases origin) is administratively and demographically well-defined, prevalence proportions are estimable.

Incidence represents the number of new cases developed during a time-unit. If the population base is well-defined, incidence rates are obtained by division with the relevant number of person-years at risk in the population base. If the population base is undefined, only incidence in absolute numbers is estimable, representing the number of new registrations per time-unit.

Morbidity (the number of new complications) and *mortality* are estimated by the number of events during a time-unit divided by the relevant number of person-years at risk for this event. These person-years are obtained from the relevant components of the prevalence population with reference to the midpoint of the respective periods.

Methods and concepts of relevance for the project

The project concerns an appraisal of *currently prevailing* health economic situation of diabetes in various societies with general reference to the calendar year 2001. In epidemiological terms, this is equivalent with observing the *dynamic* population of patients with diabetes within a *time-window* representing the calendar year 2001. Then, *the*

fundamental epidemiological measure of relevance is the number of patient-years (life-years) experienced by people with diabetes in the society concerned during the calendar year 2001. Cost components and events will be expressed per patient-year, stratified by age, complication status and diabetes type (as described below), and the health economic evaluations will be performed using estimated patient-years in the contrasting scenarios (as also described below).

Ideally, the number of patient-years experienced in the dynamic population of people with diabetes is obtained as the integral of population size (prevalence) over time - here the calendar year 2001. This requires, however, access to day-to-day information on the actual prevalence, and such data are not available. Therefore, we will use estimated point prevalence for estimating number of patient-years by appropriate interpolations. For a chronic disease like diabetes this is judged fully acceptable since changes in prevalence over a period of one year will only be modest and is supposed to be of linear nature.

Classification by diabetes type and complication status

The project will perform analyses separately for the two main types of diabetes, Type 1 diabetes (T1D) and Type 2 diabetes (T2D).

Both the costs of treating diabetes and the mortality and quality of life are strongly associated with the presence of long-term (chronic) complications of diabetes. Limitations in the availability of valid epidemiological data make it necessary to adopt a pragmatic approach. Therefore, attempts will be made in the present project to divide the prevalence population (stratified by age groups) of patients with diabetes into three categories by complication status, as indicated in Table 1.

Table 1. Classification of patients by three states of complication

Complication status	**Patient profile of complications**
State 0: No signs of chronic complications; No impairment in daily living function	No signs of complications present
State 1: Signs of minor/early chronic complications; No or only minor (insignificant) impairment in daily living function	Retinopathy, not including proliferate retinopathy; *and/or* Microalbuminuria; *and/or* Light neuropathy without open ulceration;
State 2: Presence of chronic complications, with significant impairment in daily living function	Overt nephropathy, incl. end stage renal disease; *and/or* Proliferate retinopathy and/or blindness; *and/or* History of stroke and/or myocardial infarction; *and/or* History of amputation (regardless of level)

Scenario building

Health economic evaluations of the kind employed in this project are founded on comparisons between contrasting scenarios. Therefore, we have established a range of standard scenarios for the societies under study. Each scenario is related to a given year (2001) and outlines a specific situation with an array of patient-years and corresponding estimated costs, for a situation specified according to current and previous availabilities of treatment in diabetes.

The central scenario represents the "Current" situation, i.e. with estimated number of patient-years and corresponding costs, as believed to represent a realistic situational analysis for the year 2001 in the society concerned. Alternative scenarios will be established from epidemiological modelling under specified assumptions concerning current and previous availabilities of treatment in diabetes. In this respect it must be stressed that the patient population in the "Current" scenario has obtained its size and age composition as a consequence of access to diabetes treatment and care during decades prior to year 2001. Therefore, a comparison of patient-years experienced under competing scenarios reflects the cumulative effect of access to treatment over previous decades and cannot be interpreted as an isolated effect of treating diabetes during the year 2001.

The scenarios of interest may be characterised as follows:

"Worst" scenario
This scenario is supposed to reflect the situation concerning diabetes in the society concerned as if treatment for diabetes incl. insulin treatment had never been available. The scenario is based on estimates of patient-years experienced during the calendar year 2001 under this assumption. This scenario is relatively easily established for T1D because of the essential need of access to insulin treatment. Since it is too difficult to establish this scenario for T2D in a developed nation like Denmark, we have maintained it only for developing countries, here Bangladesh, where the worst case is not so far away from the current situation.

"Current" scenario
This scenario is supposed to reflect the current situation concerning diabetes (specified for diabetes type) in the society concerned. The scenario represents the key reference scenario and is based on estimates of patient-years actually experienced during the calendar year 2001.
The medical items and related costs in this scenario are specified separately for each of the subsequent studies since these items will vary by country and type of diabetes.

"Improved" scenario
This scenario has been established to investigate the consequences of possible and realistic improvements in diabetes care (with implications for the number of patient-years and corresponding distributions by age group and complication status). This scenario follows the same demographical model as the "Current" scenario however with the change that effectively over the last decades further improved diabetes treatment and access to diabetes care have been in force. The specific definition of the "Improved" scenario varies by diabetes type and society and is outlined separately for each of the studies comprising this project. The scenario is based on estimates of patient-years experienced during the calendar year 2001 under such assumptions.

The "Improved" scenario incorporates a further item termed improved organization of diabetes care: The required reorganization of diabetes care involves multiple structural and procedural changes in the health care system in order to move from a model of acute care to focusing on chronic care and to adopt a person centred consultation rather than a disease-centred care model.

The process for enabling this change depends to a large extent on effective changes in the collaboration of the health care sector. DAWN (Diabetes, Awareness, Wishes and Needs) (4) is a study of the psycho social aspects of diabetes care and is used in the improved scenario to reflect the necessary changes. The DAWN call to action for improved diabetes care is facilitated globally by Novo Nordisk in collaboration with IDF (International Diabetes Federation).
The key focus areas for improved diabetes care in the DAWN call to action are:

- Enhance communication between people with the condition and their healthcare professionals
- Improve communication and coordination among all healthcare professional groups
- Promote effective self-management
- Removal of patient and healthcare professional barriers to effective therapy
- Enable improved psychosocial support for people with the condition

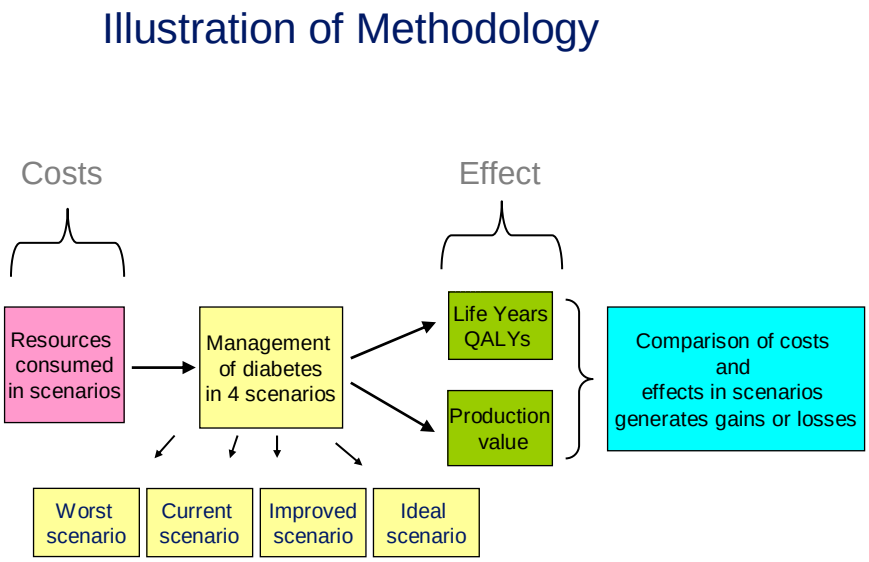
"Ideal" scenario
This scenario represents a hypothetical variant of the "Improved" scenario. In the "Ideal" scenario it is assumed that organization and efforts in diabetes care, as specified in the "Improved" scenario, result in a situation where diabetes incurs no excess mortality nor any excess morbidity. Accordingly, all patients in the "Ideal" scenario are assigned to the category with no complications. Thus, under this scenario the epidemiological model uses longevity in the general population to obtain the hypothetical number of patient-years (all falling in the class of no complications). The number of patient-years estimated for the year 2001 under this scenario is adjusted for the mortality level in the general population concerned.

It may seem unrealistic to introduce the "Ideal" scenario with the currently available treatment modalities and ways of organizing diabetes care. However, the "Ideal" scenario may serve a purpose by representing the extreme upper range of effects and benefits and by providing a framework for a health economic appraisal of any new, and more effective, treatment modality that might be introduced in the future.

Strategy of analysis

Fig. 1 illustrates the strategy of analysis for each scenario. Inputs are resources, valued in monetary terms (costs), and outputs are either gained life years, gained quality adjusted life years or gained production value.

Fig. 1. Strategy of analysis



3. PRINCIPLES OF HEALTH ECONOMICS

Basic principles and considerations

Basically, health economics is about applying economic theory and methods to issues in health and the healthcare sector. One of the specific areas of health economics is economic evaluation in healthcare. This topic deals with the problem of how to allocate scarce resources in such a way that the benefits – measured in one way or another - from using these resources are maximised.

An (health) economic evaluation can be performed from different perspectives. The societal perspective includes all costs and benefits, no matter who bears the costs and who receives the benefits. It is, however, possible to take a more narrow view and make a calculation for, e.g. the patients alone or patients and their families disregarding the costs and benefits to others who may be affected. Other types of analyses focus on the public sector alone and disregard the patients. Such analyses are often carried out as fiscal analyses (another name is budget impact analysis) in contrast to economic analyses. While economic analyses on the cost side are based on calculation of the cost of using scarce resources – be they valued at the market or not - fiscal analyses are budget analyses based on expenditure from and receipts to a public authority (e.g., state, county or municipality) or a heath insurance fund. It should be noted that only a societal perspective represents an appropriate basis for priority setting if suboptimal decision making is to be avoided.

The societal perspective seems preferable as it includes all consequences for anybody who is affected, in contrast to other approaches. It is possible, of course, to present an analysis based on both the societal and a more narrow approach.

Ideally, measurements of costs are based on the opportunity cost concept: what is the value of using a resource in the best alternative use? If a market value is available, and the market is functioning as approximately a perfect market (entailing that products are sold until the point where marginal benefits equal marginal costs), the market value of a scarce resource represents the opportunity cost, i.e. benefits foregone. If no market value is available, an imputed value has to be found as an approximation (e.g. the value of household production).

It is worth noticing that expenditures are not necessarily identical to costs. Budget impact analyses are based on expenditures rather than costs. In the case where a payment is made for using a resource (e.g., salary payment) the two concepts can be considered as identical. It is, however, possible to think of payments without a corresponding cost. For instance, the payments of sick leave benefits or pensions are regarded as transfers of purchasing power, and there are no corresponding costs (except the cost of administering the payment).

In welfare economics the ultimate aim is to maximise individual utility. Utility is a concept that is assumed to depend on the degree, to which individual preferences are fulfilled, e.g. preferences for consumption and (good) health. In contrast to a welfare economic paradigm

is the so-called extra-welfare economic paradigm (5) which does not measure effect in terms of utility, but rather in terms of factors that are assumed to influence utility such as e.g., health. Within this paradigm the ultimate aim may be formulated as to maximise the number of healthy years in a population from an intervention.

Traditional welfare economics is based on the view that if the necessary conditions for a market to function are fulfilled, then the market will lead to the most efficient allocation of resources. This is a situation where it is not possible to improve the situation for one person without worsening it for another. The situation is not necessarily the most preferred one from a societal point of view however, as it can exist along with any distribution of income among individuals, and the resulting distribution may not be acceptable. Several other problems arise in this connection as there are a number of conditions for the perfect market to function, that will not be fulfilled in the real world, in particular in the market for healthcare, where a number of market failures exist. Consequently, most societies have chosen to substitute the self-regulation forces of the market - "the invisible hand" - with a "visible hand" in the market for healthcare. This implies that decisions as to allocation of resources to healthcare and specific healthcare activities must be decided explicitly.

To assist such decisions, various types of (health) economic evaluations are available. In order to make a full economic evaluation, a comparison should be made between at least two alternatives, and both costs and consequences should be included. The basic types of (health) economic evaluation are: cost-minimisation, cost-effectiveness, cost-utility and cost-benefit analysis.

Cost-minimisation: A method of comparing the costs of alternative forms of treatment that is assumed to have an equivalent medical effect in order to find the least expensive way of achieving the outcome.
Cost effectiveness: A method of comparing alternative treatments in which cost and consequence vary. The outcomes of alternative treatments are measured in the same non- monetary units (e.g. life years gained) (Cost per patient year)
Cost-Utility: A special form of cost effectiveness analysis in which the cost per unit of utility (QALY's) is used as outcome measure (Cost per QALY).
Cost-benefit analysis: A method where all costs incurred and the resulting benefits are expressed in monetary units and a net monetary gain/loss ratio or cost/benefit ratio is computed.
Cost consequence analysis: A variant of cost effectiveness analysis in which the components of costs and consequences (health outcomes) of alternative programs are listed without attempting to aggregate these results into cost effectiveness ratios or cost utility ratios.
(Kielhorn A, Graf von der Schulenburg J-M. *The Health Economics Handbook,* Adis International 2000.)

As cost and consequences of alternatives are presented, such analyses can be used as input in a priority setting process. It is not implied that policies should be guided totally by the results of such analyses, as there may exist other relevant issues – such as distributional concerns.

Another kind of analysis is the cost-of-illness study that is characterised by calculating the total cost of a given illness. Traditionally, a taxonomy of costs (direct, indirect and intangible costs) has been used in making such calculations. While direct costs refer to cost of diagnosing, treating and caring, indirect costs refer to loss of productivity due to sickness absence or premature death, and intangible costs are costs associated with anxiety and suffering. As the calculations only will give one figure – the cost – as opposed to the types of economic evaluation mentioned above, this type of analysis is not readily applicable for priority settings. In economic evaluation rather than asking what the costs of diabetes are, we ask what the costs of intervening against the disease are and what are the gains?

While the taxonomy used in cost-of-illness studies has been widely used in health economic evaluations, we follow the recommendations by Drummond et al. (1997) (6) and avoid using them, in particular because the term 'indirect cost' is used by the accounting profession to denote overhead costs, which may create confusion. Moreover, intangible costs are not costs in the sense that they represent use of scarce resources. Rather, these items are – when used in an evaluation - related to the consequences of an intervention, either the process or the end result.

Having obtained a measure of each cost item, an equally important question is who are paying these costs. Use of healthcare is often deductible or associated with a co-payment so the patient is paying a share of the total costs while the rest is paid for by the insurer or from a public healthcare budget. The private versus public costs depends on the national health cost reimbursement and benefit systems and differ between countries. In determining public health budgets it is necessary to foresee how much the healthcare sector will require from collected taxes.

The approach in the present study

The epidemiological basis for the present evaluation is patient-years, derived from prevalence data, in contrast to incidence data, as we look at a time window of one calendar year. Consequently, we are not measuring life time cost or benefits on individual basis. The same approach was taken recently by the American Diabetes Association (7).

The present project rests on a health economic evaluation in the sense that costs and consequences of current treatment of diabetes are compared with hypothetical alternative scenarios. We use three approaches to measuring benefits.

The first approach is a cost-effectiveness approach where we use *patient-years gained (or lost)* on the benefit side and compare with total costs in various contrasting scenarios. As a principle, a societal approach - which includes both the patients and the rest of society - would require that all costs of subsistence per gained year of living should be accounted for including gains and losses in general consumption, related and unrelated health care costs and production value. In the present analyses we include only diabetes related health care costs, and exclude general consumption as well as production value changes in the cost effectiveness analyses and cost utility analyses. The issue is touched upon in the discussion section.

The second approach is a cost-utility approach, which is identical to the foregoing approach on the cost side. On the benefit side, we use *quality adjusted life-years* (QALYs) rather than

merely patient-years gained. The approach involves weighting life-years with some preference-based weights (as explained below), so the quality of the gained life-years is accounted for.

Third and finally, we use the cost-benefit approach. From a welfare economic point of view benefits should be measured as the utility based evaluation stating the consequences of an intervention – what is the population willing to sacrifice to have access to the treatment program? We take, however, a more narrow approach as we measure benefits in terms of the value of productive gains. This is the traditional human capital approach. Treatment is viewed as an investment in human capital, and the pay-off is measured in terms of productivity gains - and hence contribution to GDP. The human capital approach has been used as the sole basis for valuing health improvements.

Apart from the reservation about the narrow character of the human capital approach mentioned above, there are practical problems involved in using it (6). In theory we are measuring the value of gained productive time due to an intervention, and we equalise this value with earnings on the labour market. However, the labour market is often imperfect, so the wage rate does not necessarily reflect the value of added productive time. Moreover, not all healthy time gained is used to earn a wage, but used for production in the household. Consequently a so-called shadow price has to be found. This can be done either as the opportunity costs of time (what could be earned in the labour market) or as replacement costs (how much would it cost to replace a homemaker). ADA (7) has more or less arbitrarily assumed that the value of homemaking for someone who is working in the labour market is 20% of the wage while it is 40% of a corresponding wage for someone who is not working on the labour market. In the present study we have included the value of homemaking for those between 15-65 but not participating in the labour market as a separate item fixed at an arbitrarily value of 50% of the average labour market wage used to value the productive gains. We have chosen not to include a value of time for people that are not in the productive ages. This issue is touched upon in the discussion section.

Further We assume that the probability of a treated patient without any impediments to have a job is equal to the percentage of the total number of people who are actively participating on the labour market. The special implications of diabetes for people in the workforces are taken into account through reduced productivity for people in complications group 1 compared to the productivity if those in complication group 0. People in complication group 2 are not assumed to be able to work in the labour market or in the household.

We have chosen to carry out an economic evaluation of costs and effects of treatment of diabetes as seen from both a societal perspective and from the private and public perspective. By ensuring that both the public and the private costs are included a comparison between countries is facilitated, and it enables us to present a comprehensive 'holistic' picture of society's costs of diabetes rather than just focusing on the budgetary implications of the disease.

General considerations on costs, effects and gains

There are several types of costs involved in the care and management of diabetes for both the individual and the healthcare system. Survival may involve need of treatment for later complications. These types of disease related health care costs are included in the present analysis, as we have chosen a one-year window, and thereby included patients who may be at all possible stages in the life-course of their illness. With regard to **costs** we follow the US Panel (8) and distinguish between costs of using:

- *Health Care resources:* Routine doctor visits, insulin, peroral and other medicines, blood glucose monitoring, patient education, hospital treatment of acute and chronic complications and physiotherapy. These cost items range from the relatively low cost items (primary care consultations and hospital out-patient episodes) to very high cost items (long hospital in-patient stays for the treatment of complications)

- *Non-healthcare resources:* Use of nursing homes and disability assistance in formal care.

- *Patient time:* The time of patients used for check-up visits and admissions

- *Informal care-givers' time:* The time of relatives supporting and taking care of the patient. This includes time used by family members to assist a patient visiting a doctor or a hospital. The time consumption of parents with dependent children or relatives to elderly persons with diabetes are in particular impacted by this category

Concerning **effects** we use three approaches

- (patient) life-years gained (or lost),

- quality of life-adjusted life-years gained (or lost)

- patients' productivity gains (or losses) measured in monetary units

The three approaches should be seen as alternative ways of expressing the effects rather than additive measures. Patients´ productivity gains and (quality adjusted) life-years may be interpreted as complementary measures of effect if the quality-of-life measure does not encompass valuation of production gains/losses. It is generally uncertain whether such considerations have been included in valuations of health states. Hence, one should be wary of possible double counting

Measurement of effects in terms of health improvements

Health improvements are measured in terms of patient life-years gained with further quality-adjustment of patient life-years.

Health state improvements attributable to the current availability of treatment ("Current" scenario) against the alternative of no treatment ("Worst" scenario) can be measured in terms of gained patient life years. Similarly, potential further improvements in health state (obtained if improved or maximally efficient treatment would be available) may be estimated from the hypothetical scenarios "Improved" and "Ideal"; here, gains will be expressed in positive values. These results are calculated by estimating the difference in patient-years between the relevant contrasting scenarios. As these gained years are not lived in perfect health, they are quality adjusted. The use of quality of life adjustments to a given set of health states is a way of integrating a quality and a quantity measure into one numeric measure.

Finally, the national economic base and the private financial situation are impacted through the gained contribution to production from improved survival, although not necessarily in perfect health, but with the risk of complications, disability and premature retirement.

Quality adjusted patient-years

The purpose of developing QALYs (quality adjusted patient life years) as a consolidated measure of quantity (patient-years) and quality (the value of patient-years), is to find a common reference point to compare e.g. the effect of different medical interventions. Applying those measures means that it is possible to compare which option that creates most QALYs in overall terms and in some cases cost per QALY. It should be underlined that cost per QALY is not the only input when choosing treatment option; there may be other relevant arguments for prioritising (e.g. an option with higher cost/QALY may be prioritised because one group of patients are considered to have a greater need for treatment than another group).

When a medical therapy has an effect in terms of prolonging life, the average extra length of life is estimated. The next step is to describe the value of the extra patient-years gained from the intervention. To do this a generic quality of life questionnaire is needed. One such questionnaire is the EQ-5D.

EQ-5D is a measure of health status for use in evaluating health and healthcare. It provides a simple descriptive profile and generates a single index value for heath status on which full health is assigned a value of 1 and death a value of 0. EQ-5D has been specially designed to complement other quality of life measures such as the SF-36, NHP, SIP and disease-specific measures.

EQ-5D self-classifier (commonly referred to as page 2): describes health status according to 5 dimensions. Each dimension is divided into 3 levels.

MOBILITY
I have no problems with walking about
I have some problems with walking about
I am confined to bed

SELF-CARE
I have no problems with self-care
I have some problems washing or dressing myself

I am unable to wash or dress myself

USUAL ACTIVITIES (e.g. work, study, housework family or leisure activities)
I have no problems with performing my usual activities
I have some problems with performing my usual activities
I am unable to perform my usual activities

PAIN/DISCOMFORT
I have no pain or discomfort
I have moderate pain or discomfort
I have extreme pain or discomfort

ANXIETY/DEPRESSION
I am not anxious or depressed
I am moderately anxious or depressed
I am extremely anxious or depressed

By combining different levels from each dimension, EQ-5D defines a total of 243 health states. These may be converted to a score using "**sets of values**" derived from general population samples. Each possible set of values may be transformed by a regression analysis to a scale ranging from 0 to 1, following the empirically derived equation suggested by Greiner et al. (9)

For the present study, we have asked a group of eight experienced Danish diabetes nurses to review a number of typical health states related to diabetes and translate these health states using the EQ-5D questionnaires. Subsequently, each scoring has been transformed to an index value following the suggestion by Greiner et al (9), as reviewed above. For each patient case, the mean of the individual nurses' values was used.

According to these results we have used the Quality of Life-coefficients of 0.95, 0.85 and 0.65 for patient-years experienced in complication states 0, 1 and 2, respectively. These values have been used irrespectively of age grouping.

When the extra patient-years gained from an intervention is quality adjusted, it simply means that the e.g. 2 extra patient-years gained, are adjusted according to what level of quality the 2 patient-years are lived in. So if the 2 extra patient-years are lived in a state of some anxiety, pain and with self care and mobility problems, they may be estimated to have a value of 0.656 on a scale with 1= one year in full health and 0= death. This then means that the QALY gained from the intervention in question, is 1,312 QALY (2 years x 0.656 quality of life = 1,312 QALY).

We have used the same QoL assumptions in Bangladesh as in Denmark thereby implicitly assumed that parameters of life quality can be transferred between cultures and social systems that are fundamentally different. This issue is further dealt with in the discussions section.

The economic conditions in a developing country

This study has as one of its focus areas to describe how investments in health impact the socio economic situation in a developed economy as well as in a developing economy. Most economic theory is developed on the basis of how developed market economies work. To analyze the workings of the economic mechanisms in a developing country we have adjusted the framework to fit that situation.

The economic relations in a developing country are quite different from a well developed industrialised, market-based economy. A substantial part of production is not fully registered in monetary terms. One reason is that the institutional framework for registering production activities, for instance a universal income tax system, does not exist. Another reason is that a large part of the basic production and consumption activities takes place in a barter economy without monetary transactions and, finally, the household sector plays an important economic role. In order to neither over- nor underestimate the socio-economic consequence of healthcare improvements, two different strategies for calculating production value changes are applied; a narrow concept based on production registered as GDP and a broader concept in which the value of household production and other production in the informal sector is included.

To take account of such characteristics of the economy in a developing country we distinguish between the:

- formal and informal production sectors
- workforce and unemployment
- productivity and income levels of formal and informal workers
- cash income and barter economy
- distribution and valuation of time for working and nursing (distinguishing between formal and informal caregivers).

Access to healthcare is characterised by

- urbanisation/rural areas
- physical access to healthcare
- financial affordability

Still, the methods used in valuation of costs are basically the same as in the report on Denmark and as described in the remainder of this report.

The formal and informal sector of economic activity

Two different economic sectors are assumed to exist side by side: The formal sector based on monetary flows where people are working for wage income, and an informal sector based on barter and household production. Besides household production such as subsistence farming and care-giving the large informal sector includes trading and small-scale production. A large part of the average consumption is based on production from the informal sector and is therefore not registered as contributing to GDP. It is assumed that the formal sector is equivalent to the economic activity registered as GDP.

The informal sector is primarily based on household production that is essential for the survival and basic needs of the family. An estimate of the size of the formal versus the informal sector is made by looking at the age distribution of the population (population below 15, between 15 and 65, and above 65), and combining this with the official figures for the workforce and for unemployment. The classical way of looking at the workforce can be problematic in a developing country because people above 65 years and some children between 10 and 15 years are probably part of the workforce. In contrast some of the richest 10% are non-productive because domestic servants do all the housework.

We assume that the real workforce includes the majority of those above 65 years who are physically able to work (all in complication group 0) and a share of those below 15 years (10% of those in complication group 0). In our model the special characteristics of diabetes are taken into account through reduced productivity for people in complications group 1 compared to the productivity if those in complication group 0. People in complication group 2 are not assumed to be able to work.

Although official registered unemployment figures exist in developing countries, often there is no general unemployment benefit or general old-age pension. Consequently, survival demands some kind of productive activity of the unemployed and old aged people with no other income.

Level of income

It is assumed that the productivity in the informal sector is lower compared to the formal sector. This is justified by an assumption that the best educated people work in the formal sector. Therefore the average income level in the formal sector has been set equal to the GDP per capita while the income in the informal sector is 2/3 of that level. The average income in the informal sector (i.a. the shadow price) is higher than the 50 % of the income in the formal sector used in the Danish part of our study and the 40% used in the ADA study (7) to measure the value of production in the informal sector. Although arbitrarily chosen it reflects the assumption that the informal sector in a developing country is an important production sector not just in household production but also in areas that compete with the formal sector although at a lower efficiency. The issue of shadow prices is further discussed in the discussion section. We have chosen to use GDP pr capita as the measure of average income to ensure that the estimate of the production value is on the low side. A sensitivity using a higher level of income than GDP pr capita for valuation of production value is presented in the specific analyses of both type 1 and type 2 in Bangladesh.

To make the results more comparable with international data and, in particular, healthcare costs in the developed world, selected prices and results are also shown in PPP. All price data and results in this study, which are not explicitly denominated PPP are in local price levels.

Access to healthcare

A differentiation is made between those that can afford to pay for healthcare and those that receive free healthcare. Only a fraction of the population in the developing world can afford to pay for health care. The rest of the population cannot afford to pay for healthcare and only receive treatment if there is a free (public or private) healthcare centre.

Informal nursing

An important non-healthcare cost is informal care-giving. There are almost no formal nursing facilities in Bangladesh to take care of people in complication group 2. This places a large burden on relatives (informal care-givers) to care of people with high levels of complications, disabilities and dying patients. Especially low income, informal care-givers are assumed to be burdened as they provide nursing for people who cannot afford to pay for healthcare, thus assumed to be in a highly disabled state. A key element in the *Improved scenario* compared to the *Current* is the reduction of non-healthcare resources as the number of people in need of nursing is reduced. This has important implications for the time resources released for essential household production in the informal sector.

Relation between healthcare improvements and economic growth

Studies show that there is a relation between improved health and economic growth. There is a growing consensus that investments in health pay off in terms of improved economic activity, which again leads to greater ability to fund health care systems.
The WHO (10) has estimated that each 5 years' improvement in life expectancy is associated with a increase in economic growth of about 0.3-0.5% per year provided that other growth factors are equal. We have used these results to calculate the size of the increase in GDP which could be achieved in Bangladesh as a consequence of the increased survival in the *Improved scenario*. Since diabetes is a chronic disease added life-years amongst these patients will not entail the same level of productivity gains as for persons whose life-expectancy is prolonged in a state of perfect health. In our model the specific characteristics of diabetes are taken into account through differentiated productivity for people in complications group 1 compared to complication group 0. People in complication group 2 are assumed not to be able to work in the labour market or in the household.

4. DISCUSSION: ISSUES OF CONTROVERSY

About productivity gains and losses

A major effect of treating diabetes patients is gain in patient-years that may be valued by various methods. A derived effect may be a cost in terms of use of time by informal care-givers. It is generally accepted that individuals' time - whether work time or leisure time, or used in paid work or non-paid work - has an opportunity cost. Still, practical details on how to account for these costs in economic evaluations are controversial (11).

Literature on methods on economic evaluations in healthcare, e.g. Drummond et al. (6), recommends the inclusion of productivity costs and gains when the societal perspective is used. The approach is controversial, however, when applied to cost-effectiveness analysis where a calculation is made of the net cost per unit of outcome measured in physical terms. It has been argued by Gerard and Mooney (12) that because outcome measures in health economic evaluations are a health category, the opportunity cost of gained health is health forgone, not consumption. In response, Koopmanshap and Rutten (13) have argued that budgets are arbitrary divisions in the allocation of resources, so productivity changes should be included. At this point of time, the issue seems unsettled.

A related argument concerns the inclusion of productivity gains or costs in cost-utility analyses. When calculating the QALYs gained we move from a traditional welfare economic approach, based on individual utility maximisation, to a so-called extra welfarist approach (5) where the implicit or explicit aim is to maximise the number of QALYs gained in a population. If we follow this route and focus more on aggregate health in society rather than individual utility, the productivity costs or gains can be seen as non-health effects. As the maximand 'health gains' are used under the extra welfarist approach, one may argue that there is no place for productivity costs or gains in health economic evaluations. This point of view has been challenged in the literature, however (11).

Valuation of productivity gains and losses

One issue is whether or not to include time gained or forgone in health economic evaluations. Another issue is the principles of valuation of time when included. Basically three approaches have been applied in the literature.

1) The human capital approach uses the present value of an increased stream of lifetime income. The approach has been used in cost-benefit analyses to value the benefit side, and income gains has been used as the only benefit. It is, however, not based on the principles of welfare economics as it takes a more narrow approach and implicitly assumes that income is the only source of welfare and that the aim is to maximise the gross national product. Moreover, unpaid working time or leisure time is not valued. In principle, time used outside the labour market has an opportunity cost as the time is limited, and there are alternative uses of the time. Assuming that a choice exists between paid work and leisure time, the opportunity cost of working time is forgone leisure, which can be valued at the

margin as wage net of taxes on income. Likewise, the change in time for household production should be valued as the net wage, provided that there is a real choice between allocation time to employment or household production and leisure time.

An alternative approach is to include the value of time in household production estimated by the cost of buying these services on the market. Thus, the gross wage rate of individuals in paid work of the same type would be the relevant value of time. It has been argued that this would be an upper bound as the household production is probably less efficient (11b). In contrast, loss of productive time due to sickness absence from work should be valued by gross wage rate (as in the present study) as the opportunity cost is the loss of production.

2) A modified version of the human capital approach is the friction cost approach, suggested by Koopmanshap et al. (14). In their approach it is argued that cost of lost production is simply the time it takes to replace a worker, provided that there exist some unemployment. The opportunity cost of absence from work due to sickness, invalidity or death is then identical to the production loss during the time span it takes to substitute a worker with another. Thus, they assume that the long term cost of absence is zero when unemployment exists (and there is a negligible productivity loss). Lost productivity is thus much lower compared to the human capital approach. When applied to production gains, it would be lower compared to the remaining lifetime earning. This approach is also controversial and debated in the literature. But, if applied in the present study, the productivity gains would almost disappear.

One of the problems with this way of reasoning is that the same kind of logic might be applied on the cost side of healthcare implying that the opportunity cost of using healthcare personnel may be negligible when unemployment exists among healthcare personnel. We have chosen to concur with the human capital approach and assume that the probability of a treated patient without any impediments to have a job is equal to the percentage of the total number of people who are actively participating on the labour market.

3) The US panel (15) suggested the valuation of the effect of a disease on productivity through a QALY measure. The panel was concerned that monetary valuation of changes in productivity, in particular in case of changed mortality, would result in double counting. The panel wished to keep the monetary valuation of all effects that were on resources, separated from the valuation of effects that could be considered to be directly associated with individual health (11). This point of view is also controversial, however, and has been discussed in the literature. We have chosen, when relevant, to present both the QALY gain and productivity gain, but we also underline that these two measures should not be seen as independent measures that could be added, but rather as two aspects of the gains.

An important contribution by the panel was a listing of several components of productivity costs, and they stressed that change in mortality or morbidity would affect various areas of the economy through change in productivity. They take the point of view of loss due to health, while we take the opposite view – gains due to treatment. It can be inferred from their reasoning that both health gain and the effect of gain (in work time and in leisure time) on sick individuals are valued through QALYs. This notion does not, however, reflect the scenario in countries such as Denmark where people are to some extent compensated for loss in net income caused by illness. If people are largely compensated disutility associated with loss of income will not be reflected in valuations of health states.

External effects are valued through personal income taxes; effect on persons who change employment is the net income. In future work, we may refine the calculations by using these components of overall productivity effects due to illness. In the present work we have not divided productivity changes into categories, but presented total societal production gains/losses due to changes in health.

The QALY gain

How a QALY should be perceived is still a controversial issue. To some, it is considered as purely health related quality of life, that is, utility derived from health per se. To others, it would include the utility derived from consumption while being healthier. The interpretation depends on how the QALY-instrument has been constructed, especially the kind of questions that were asked the panel in connection with obtaining QALY weights. In Meltzer's model (16), no distinction is made between utility of health per se and consumption. This implies either that utility of consumption is neglected, or that consumption is considered a part of the utility of living longer and/or in better health. When increased production – and consequently also increased wages and consumption – is presented along with QALY gains in the same table, there is a risk of double counting if these are considered independent gains. One has to be aware of this in the interpretation of the findings in the present study, so the presentation of patient-years and/or QALYs along with productive gains should rather be seen as alternative ways of presenting beneficial effects of treatment.

Adoption of QALYs to diabetes care in Bangladesh

We use the same QoL assumptions in Bangladesh as in Denmark for the simple reason that we do not have any specific parameters for a developing country. The consequence of that is that implicitly we assume that parameters of life quality can be transferred between cultures and social systems that are fundamentally different. On the other hand it has been argued that quality of life (QoL) has different values depending on other circumstantial factors e.g. if people are starving their QoL is of secondary interest. It may very well be true; nevertheless, if the person is starving it will have an impact on his or her QoL, i.e. the quality of their lives will change according to their actual life situation. This means that it seems reasonable and sound even in a developing country to consider the effect a treatment (like the availability of insulin) has on the QoL of persons.

Net productivity value and consumption

Another issue regarding the socio economic value of production is whether consumption should be deducted from the production value or not.

The individual cost of consumption can also be interpreted as the willingness to pay to maintain ones own life. The net production value (gross production value minus the consumption) is a measure of the value to society of an individual person alive.

In Pearce and Howarth (17) and in COWI (18) the net production loss (production minus consumption) used as measure of the price of a statistical life is discussed. As pointed out by

Pearce and Howarth (17) if the cost of consumption is subtracted from the gross production value the final link to the original idea of socio economic cost benefit analysis is cut. A rigorous application of this approach would lead to a low or zero value of an older person because the person already has reach the pension age and even negative value because the person is consuming more than he is producing for the rest of his life.

By including internal as well as the external value of life elderly people are clearly discriminate against because they do not have a production value. This is also the implication of the human capital approach. The question then becomes whether it is regarded as un-ethical to save the life of a 20 year old persons instead of an 80 year old person from a rational perspective that the first one still can contribute to the societal economy. In a country like Bangladesh where funds are extremely scarce this is of course a political reality when prioritisation is made.

In this study the CEA and CUA analyses do not include the external value of one more person alive. In the narrow CBA we have only focused on the gross contribution to society,

Future costs

A related issue is the question of including future costs. The project follows a conventional approach in health economic evaluation which includes only future costs related to the specific illness - in this case diabetes. The approach is controversial, however, and it has been criticised by, e.g. Garber and Phelps (19) and Meltzer (16) because it may give a too optimistic estimate of the contributions from patients as the risk of disease increases with age.

Meltzer demonstrates that a cost-effectiveness analysis is consistent with lifetime utility maximisation only if it includes all future medical and non-medical expenditures. The more or less arbitrary distinction between "related" and "unrelated" costs becomes irrelevant. For example, "a hamburger eaten or cholesterol level checked 20 years after someone's life is saved by a given medical intervention should be counted as a cost of that intervention. If the intervention had never taken place, those resources would have been available for other uses." (16b).

A consequence of the traditional approach is that both absolute and relative cost-effectiveness of medical interventions will be altered compared to this ideal. Especially, the cost-effectiveness of interventions that extend life compared to improving the quality of life will be overstated by the traditional approach. In older populations, the traditional approach is biased in favour of interventions which extend the length of life rather than improves the quality of life. We have assumed in the present study that over life time, the average individual's production and consumption will be even. As can be inferred from the arguments above, this approach may give a too optimistic estimate of the contributions from diabetes patients as the health risks associated with the disease increases with age.

Net expenditures in the suggested approach by Meltzer (16) and others are calculated as the additional costs of consumption and medical care, net of earnings. The approach implies that the net cost is smaller the higher is the income of a patient or patient group. This involves an ethical problem that was considered eliminated in the traditional approach to cost-effectiveness analysis. This has not been dealt with in the present study.

Previous costs: prevention

As described in this report the focus of the study is a one year time window. As a consequence an issue of interpretation may arise if the cost and effect of certain measures take place with a time lag. This leads to a distinction between measures that result in an immediate impact on survival and quality of life (treatment) while another part of the measures results in a reduced number of future complications etc (prevention). Including costs related to prevention measures in the analysis would require that such costs where treated as costs related to a previous period and should therefore be discounted.

Diabetes management covers exercise, diet and medication and the issues of differentiation between preventive costs and treatment costs is not clear cut. Prevention could be defined as preventing people from going from a state of impaired glucose tolerance to a state of diagnosed diabetes. Alternatively it could be defined as "preventing a person with well controlled diabetes without complications from getting complications". The distinction is somewhat arbitrary, but we find it essential to take it into consideration in the study. As our study does not include screening or diagnosis of unknown diabetes patients the second definition is the most relevant for us.

Neither insulin, nor oral anti-diabetic drugs or other health care items in this study can be characterised as prevention. There is no cost included under hospitalisation that is for prevention. Insulin, oral anti diabetic medication and monitoring as well as routine diabetes control is also regarded as treatment. Home monitoring is included as a tool to ensure proper insulin treatment and routine diabetes control (included eye doctors as well as other specialist) are important elements in proper treatment. Physiotherapy is included primarily as treatment for people with serious foot problems. The only cost item that to some extent may be characterised as prevention in our study is "medication with other drugs". A distinction is made between medication to patients in complication group 2 and to patients in complication groups 0 and 1. Patients in complication group 2 have already had some form of stroke or cardiovascular event and the medication is part of treatment of the event, while among the patients in group 0 and 1 the medication can be characterised as prevention of events that otherwise would transfer the patient to complication group 2.

To take account of this, costs related to "medication with other drugs" than insulin and peroral medication for people without complications (in complication group 0 and 1), is categorised as an investment in prevention. This analysis is only relevant for Denmark as no measures taken in Bangladesh can be regarded as investments in prevention.

The costs related to prevention measures in this study are of minor importance and we have therefore chosen not to discount prevention costs in the core analyses. The impact of excluding these cost are shown to be negligible in a sensitivity analysis.

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