DIABETES MELLITUS

from epidemiology to health policy

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DIABETES MELLITUS

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DIABETES MELLITUS
van epidemiologie naar gezondheidsbeleid

Proefschrift

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Voor Helina, Suzanne, Corné en Lotte
Voor mijn ouders

CONTENTS

CHAPTER 1

Introduction

EPIDEMIOLOGY AND HEALTH POLICY

This thesis deals with the interrelationship between epidemiology and health policy. According to Rothman (1), the clearest of many definitions of epidemiology that have been proposed has been attributed to Anderson, who defined epidemiology as "the science of disease occurrence" (2). The primary task of epidemiological research is to quantify the occurrence of illness in order to evaluate hypotheses about the causation of illness and its sequelae, and to relate disease occurrence to characteristics of people and their environment.

Health policy in the broadest sense relates to the actions of government, doctors and other players who aim to maintain and improve the state of health of individuals and the population. More specifically, a distinction can be made between policy designed for health care and for prevention. Health care involves the organisation of diagnostics, treatment, nursing and care ('cure and care'). Broadly speaking, it covers activities directed at people who already have health problems. Prevention focuses on measures and activities with the purpose of averting health problems. It may involve collective measures to prevent specific diseases (vaccination programmes, screening programmes), measures to promote health (health information and education), and measures to improve safety (health protection, for example regulations on the safety of food)(3).

Although the physicist Kelvin emphasized the importance of measurement in science, his words also apply to the importance of epidemiology for health policy: "*I often say that when you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely, in your thoughts, advanced to the stage of Science, whatever the matter may be*" (4). Despite the fact that the choices that need to be made in health policy are social or political in nature, the availability of data from epidemiological research to express "it" (i.e. health problems) in numbers should actually play a crucial role in underpinning decision-making.

The interrelationship between epidemiology and health policy is presented in Figure 1. It summarizes the policy cycle which consists of four steps (5). As Figure 1 shows, epidemiology has two functions in the policy cycle:

1. to provide data which can be used in the *preparation of new policy*, and
2. to provide data which can be used to *evaluate current policy*.

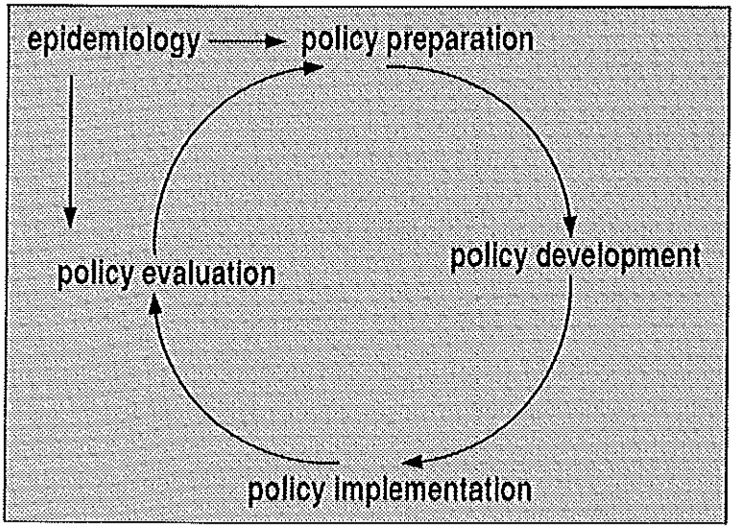

Figure 1: The cycle of health policy and the place of epidemiology in it.
Source: adapted from Nota Gezondheidsbeleid, 1991 (5).

HEALTH POLICY AND HEALTH STATUS

The way health policy can influence health status can be illustrated by the conceptual model devised when drawing up the document entitled 'Public Health Status and Forecasts: the health status of the Dutch population over the period 1950-2010' (3). This model, which will be extended in the next issue of the document due in 1997 (6), has the following functions:

1. to provide a structure for the development of ideas;
2. to define boundaries;
3. to offer a structure for orderly handling of the subject matter;
4. to serve as a basis for producing a formal model in mathematical terms.

The conceptual model contains elements of previously published models (7-10) and is shown in its basic form in Figure 2. The model shows that health status is defined by determinants and that it results in health care utilisation. Health status and the ensuing health care utilisation (and costs) play a part in giving direction to health policy. By means of prevention and/or health care, this policy aims to influence health status through the determinants of health. This dynamic process is affected by autonomous demographic, sociocultural, economic and technological developments.

The structure of the conceptual model, which is discussed in more detail in the 'Public Health Status and Forecasts' document, is essentially static. It describes a pattern of effects in a qualitative sense. In fact we are interested in the dynamics of the system: we want to know how the health status and the resultant burden on care facilities have *changed* over time as a consequence of all those different influences. This is of great importance for making *future projections*. Preparing policy and setting priorities not only require information about the current situation but also about past and expected future developments.

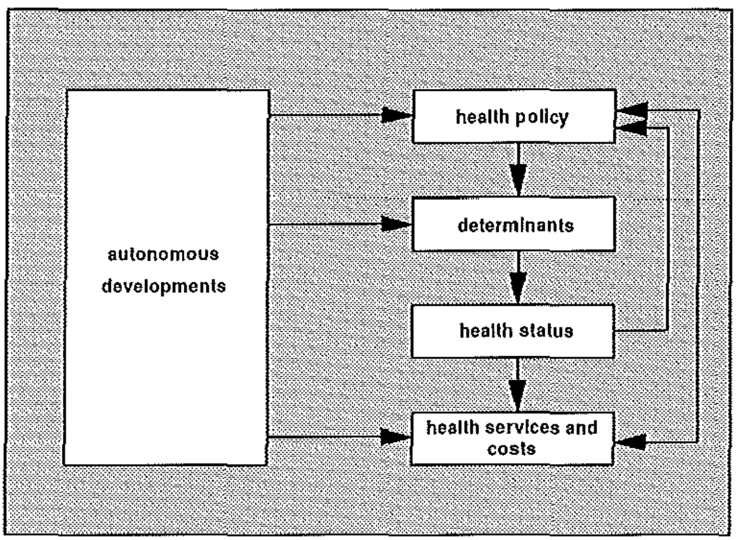

Figure 2: A conceptual model for public health.
Source: Ruwaard et al., 1995 (6).

THE CHOICE FOR DIABETES MELLITUS

The inspiration for choosing diabetes mellitus as the theme of this thesis came from the scenario project entitled 'The future burden of chronic diseases for Dutch society: scenarios for diabetes mellitus, chronic non-specific lung diseases and rheumatoid arthritis 1990-2005' (11-15). This project started in 1988 and was performed on behalf of the Steering Committee on Future Health Scenarios (a body set up in 1983 by the State Secretary of the Ministry of Welfare, Health and Cultural Affairs) in order to give an overview of anticipated future developments in the field of public health and health care. Scenario projects had already been carried out for cardiovascular diseases (16), cancer (17), accidents and traumas (18) and for ageing (19) and medical technology (20).

Chronic diseases have been selected as the subject of a separate scenario study because these diseases represent the major public health problem of our age, in the same way as infectious diseases afflicted our society in the last century. Chronic diseases may be defined in various ways; generally these cover diseases from which people suffer continuously or intermittently over a period of years. Due to their severity they involve long-term disabilities and handicaps which impose a lasting burden on the health care system (15,21-23).

Chronic diseases are many and varied, which makes it impossible to lump them all together. One of the first questions that therefore needs to be answered in conducting a study on chronic diseases is to define which diseases are to be regarded as chronic, and which of these are to be included in the study. Since scenario studies had already been conducted for cardiovascular diseases and cancer, which account for the main part of total mortality, it was clear that attention should also be directed towards a number of chronic diseases that are less important in terms of mortality but which by contrast contribute considerably to morbidity.

At the request of the Steering Committee, the TNO Institute for Prevention and Health (formerly TNO Institute for Preventive Health Care) carried out a pilot study in order to make a considered choice. On the basis of three criteria - occurrence, average duration and severity/intensity of care - researchers at this institute recommended that scenario studies be set up in the field of diabetes mellitus and chronic non-specific lung disease. As a third disorder, the choice was narrowed down to rheumatoid arthritis or multiple sclerosis (24,25). The Steering Committee ultimately chose rheumatoid arthritis because of its more frequent occurrence.

The 'Chronic Diseases' scenario study posed two sets of questions:

1. What are the likely trends in the number of patients, the number and severity of complications, the quality of life and the degree of care/self-care in response to changes in determinants (risk factors), developments in medical technology,

changes in the structure of care and treatment, and demographic and sociocultural developments; and what implications will this have in terms of the demands made on health care over the next ten to fifteen years?
2. What means do the government or other organizations and groups in society have to influence these developments and what possible effect might these have?

Given the rapid rate of change in this field and the large degree of uncertainty that must be taken into account, it became clear that it would not be possible to make considered judgments for a period of more than ten to fifteen years. For this reason the scenarios have not been taken beyond the year 2005.

This thesis is restricted to diabetes mellitus and deals only with developments in the occurrence of the disease. After finishing the scenario study for diabetes, research projects were started that provided insight into trends in the occurrence of diabetes mellitus. Results from the scenario study and in particular from the consecutive research activities are presented in this thesis.

AIM OF THE STUDY

The overall objective of the studies described in this thesis is to elucidate the occurrence of diabetes mellitus in the Netherlands and its development over time. As diabetes mellitus is a major cause of prolonged ill health and premature mortality which requires a substantial amount of health care, the implications of the changing occurrence for health policy are raised as well. More specifically, the study aims to answer four main questions:

1. what is the occurrence of diabetes mellitus?
2. has the occurrence of diabetes mellitus changed in recent years?
3. what are possible future developments in the occurrence of diabetes mellitus?
4. what are the likely implications of these developments for health policy?

STRUCTURE OF THE THESIS

The four questions that need to be answered serve as a guideline for the structure of this thesis. The *points of departure* are dealt with in Chapter 2, which gives a general description of the disease and the concepts employed. It also substantiates the choices that need to be made to ensure that the most suitable sources are used for incidence, prevalence, remission and mortality data. These choices are based on the available information at the time the scenario project was conducted (the first question in the thesis).

The second question is dealt with in Chapters 3 and 4, which focus on *changes* in the occurrence over a ten-year period. Chapter 3 describes the changes in the incidence of insulin-dependent diabetes mellitus among children under 20 years of age. The findings are based on the first (1978-1980) and second (1988-1990) nation-wide retrospective studies covering the total Dutch population. Chapter 4 addresses the assessment of possible changes in the incidence of diabetes mellitus in all age groups in the Netherlands in the period 1980-1983 and 1990-1992. It describes the results of a large registration network of sentinel stations (the Dutch Sentinel Practice Network) consisting of about 1% of the Dutch population.

Possible *future developments* are presented in Chapters 5 and 6 (the third question). In Chapter 5 projections of the number of patients are based on the information provided by the scenario project (background study). In addition, we updated the projections in Chapter 6 by using the 'trend' data from Chapters 3 and 4.

Finally, Chapter 7 addresses the fourth question by paying attention to the possible implications of these findings for *health policy*. The general discussion (Chapter 8) is followed by a summary.

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CHAPTER 2

Diabetes mellitus: points of departure

'General description of the disease' (first section) is based on the manuscript:
Dirk Ruwaard, Edith J.M. Feskens. Diabetes mellitus. In: Ruwaard D. Kramers PGN (red.) Volksgezondheid Toekomst Verkenning. De gezondheidstoestand van de Nederlandse bevolking in de periode 1950-2010. Rijksinstituut voor Volksgezondheid en Milieuhygiëne. Den Haag: Sdu Uitgeverij, 1993 pp. 303-308.

'Concepts and approach' (second section) and 'Current knowledge of incidence, prevalence, remission and mortality' (third section) are based on the report:
Steering Committee on Future Health Scenarios. Chronic diseases in the year 2005. Volume 1, Scenarios on diabetes mellitus 1990-2005. Dordrecht/Boston/London: Kluwer Academic Publishers, 1991.

ABSTRACT

This chapter describes the principles underlying this thesis. As the subject is diabetes mellitus, it starts by providing a general description of the disease. The (changes in) diagnostic criteria and classification, its symptoms and course, and the determinants are briefly reviewed.

Secondly, the conceptual model employed and the stepwise approach selected to answer the questions which are dealt with in this thesis are the subjects of the section 'Concepts and approach'. There are two major prerequisites for constructing sound future projections for health policy purposes: the transcription of the conceptual model into a dynamic (mathematical) model and the availability of data.

Finally, the section 'Current knowledge of incidence, prevalence, remission and mortality' focuses on the availability of epidemiological data on the occurrence of diabetes mellitus. It substantiates the choices made to ensure that the most suitable sources were used for incidence, prevalence, remission and mortality (available at the time we conducted the scenario study). There are two reasons why this information is included in 'the points of departure'. It is not only the first step in the stepwise approach (performing a background study to gain insight into the occurrence of diabetes). In addition, the scenario study also revealed a lack of recent representative data. This observation was the starting-point for further research activities to provide insight into trends in the occurrence of diabetes.

GENERAL DESCRIPTION OF THE DISEASE

Diagnostic criteria and classification

Diabetes mellitus is a chronic metabolic disorder. It is associated with excessive levels of blood glucose, on which the diagnosis is based. In 1985 the World Health Organization (WHO) defined cutoff values above which diabetes mellitus is regarded as being present (1). These values for diabetes mellitus (and for impaired glucose tolerance and normal glucose tolerance) according to the oral glucose tolerance test (OGTT) are presented in Table 1. The glucose values differ, depending on the glucose load (fasting or 2 hrs after a 75 g glucose load), where the blood sample is taken (i.e. from a capillary or vein) and whether the glucose level is measured in whole blood or in plasma.

Table 1: Diagnostic values for the oral glucose tolerance test.

	Glucose concentration, mmol/litre			
	Whole blood		Plasma	
	Venous	Capillary	Venous	Capillary
Diabetes mellitus				
Fasting value	≥ 6.7	≥ 6.7	≥ 7.8	≥ 7.8
2 hrs value[a]	≥10.0	≥11.1	≥11.1	≥12.2
Impaired glucose tolerance				
Fasting value	< 6.7	< 6.7	< 7.8	< 7.8
2 hrs value[a]	6.7-10.0	7.8-11.1	7.8-11.1	8.9-12.2
Normal glucose tolerance				
Fasting value	< 6.7	< 6.7	< 7.8	< 7.8
2 hrs value[a]	< 6.7	< 7.8	< 7.8	< 8.9

a: two hours after a 75 g glucose load under standardized conditions.
Source: World Health Organization, 1985 (1).

The OGTT is often used in epidemiological research (or during pregnancy). However, in clinical practice the diagnosis diabetes is usually based on the presence of the classic diabetic symptoms (polyuria, hunger, thirst, weight loss, tiredness, dizziness, drowsiness or, in extremis, coma) combined with a single abnormal blood glucose level or on two abnormal levels without complaints measured on different occasions. An abnormal level is defined as a capillary blood glucose fasting value equal to or exceeding 6.7 mmol/litre (although a fasting state is difficult to prove) and/or a randomly measured capillary blood glucose value equal to or exceeding 11.1 mmol/litre. If the blood glucose levels are inconclusive, an OGTT is recommended. Instead, a high carbohydrate breakfast test is often used in everyday practice.

The above-mentioned 1985 cutoff values used to diagnose diabetes mellitus were adapted from the 1980 criteria (2). In 1980 the cutoff values were rounded to the nearest mmol/litre, whereas in 1985 they were rounded to the nearest tenth of a mmol/litre. The first time the WHO published diagnostic criteria was in 1965 (3). Depending on age, the diagnosis could be established two hours after a 50 g or 100 g glucose load in the case of a blood glucose value equal to or exceeding 7.2 or 7.8 mmol/litre measured in venous whole blood or capillary whole blood, respectively. If these criteria are compared with the current ones (established in 1985), the former are less strict: the diagnosis 'diabetes mellitus' based on the WHO 1965 criteria is assumed to correspond roughly to the diagnosis 'diabetes mellitus including impaired glucose tolerance' according to the WHO 1985 criteria (4,5). When interpreting trend data on the occurrence of diabetes, it is essential to be aware of these changes in diagnostic criteria.

There are various forms of diabetes mellitus. The classification of diabetes mellitus and associated categories of glucose intolerance adopted by the WHO in 1985 is given in Table 2. The two most common forms are insulin-dependent diabetes mellitus (IDDM) and non-insulin-dependent diabetes mellitus (NIDDM). IDDM represents about 10-20% and NIDDM about 80-90% of all diabetic patients (6,7).

Instead of IDDM and NIDDM the older terms type I and type II diabetes are still widely used. Although IDDM and NIDDM are clinically descriptive subclasses and type I and type II represent different pathogenetic mechanisms, IDDM and type I diabetes on the one hand and NIDDM and type II diabetes on the other were regarded as completely synonymous (i.e. carrying no etiological or pathogenetic implications)(1). In clinical practice and for research purposes the pragmatic assumption is sometimes made that diabetes diagnosed before the age of 20-30 will be mainly IDDM and above 20-30 years mainly NIDDM (amongst others, 8).

Recently, the classification presented in Table 2 has been disputed. As a result of increasing knowledge about the different causes of diabetes, it seems likely that further refinement or revision of the classification will soon be possible. Therefore, it is no longer recommended to use the terms IDDM and NIDDM as synonymous with type I and type II diabetes, respectively (9). For instance, some patients clinically diagnosed as NIDDM appeared to have type I diabetes according to the pathogenetic process (Latent Autoimmune Diabetes in Adults; LADA)(10). In addition, it has long been observed that NIDDM can also be subdivided into several forms. One subtype of NIDDM in adolescence and in young adults shows a strong autosomal dominant inheritance pattern (11). The term maturity-onset diabetes of the young (MODY) is used to describe this subtype, which in itself is genetically heterogeneous (12-15).

Table 2: Classification of diabetes mellitus and associated categories of glucose intolerance.

A. Clinical classes

Diabetes mellitus (DM)
- Insulin-dependent diabetes mellitus (IDDM)
- Non-insulin-dependent diabetes mellitus (NIDDM)
  (a) Non-obese
  (b) Obese
- Malnutrition-related diabetes mellitus (MRDM)
- Other types of diabetes associated with certain conditions and syndromes:
  (1) pancreatic disease; (2) disease of hormonal etiology; (3) drug-induced or chemical-induced conditions; (4) abnormalities of insulin or its receptors; (5) certain genetic syndromes; (6) miscellaneous.

Impaired glucose tolerance (IGT)
(a) Non-obese
(b) Obese
(c) Associated with certain conditions and syndromes

Gestational diabetes mellitus (GDM)

B. Statistical risk classes (subjects with normal glucose tolerance but a substantially increased risk of developing diabetes)

Previous abnormality of glucose tolerance

Potential abnormality of glucose tolerance

Source: World Health Organization, 1985 (1).

Symptoms and course

Patients suffering from the metabolic disorder diabetes mellitus often exhibit symptoms such as frequent urination, heavy eating and drinking, weight loss, tiredness and dizziness. In particular in IDDM, coma - caused by acidification and excessive blood glucose levels combined with dehydration - can sometimes be the first sign of the presence of the disease. Over time, multiple chronic complications may occur, resulting from damage to large and small blood vessels and nervous tissue. This can lead to complications such as myocardial infarction, stroke, circulation disorders in the legs, blindness, kidney diseases and loss of sensitivity and/or pain in the limbs (see Table 3). The epidemiological aspects of the acute and chronic complications of both IDDM and NIDDM are reviewed in the scenario report (16).

In patients with NIDDM, chronic complications may also be found at the time of diagnosis, or the complications may actually be the reason for suspecting the presence of diabetes (8,17-20). This is partly due to the fact that a large number of NIDDM patients (at least 50%) are not known to be carrying the disease and are therefore as yet undiagnosed (5,21-24). The occurrence of the symptoms and complications can severely reduce life expectancy and the quality of life (not only in physical terms but also as regards mental and social consequences) and is responsible for a substantial degree of health care utilisation in Dutch society. In the Netherlands the health care costs related to diabetes are estimated to be about 1% of total health care costs. However, this underestimates the real costs, as it only represents the costs incurred when diabetes is the primary diagnosis (16).

Table 3: Acute and chronic complications arising from diabetes mellitus.

acute complications:	ketoacidosis/ketoacidotic coma hyperosmolar non-ketoacidotic coma hypoglycaemia/hypoglycaemic coma
chronic complications:	coronary heart disease cerebrovascular accident peripheral vascular disease diabetic foot neuropathy nephropathy retinopathy

Determinants

IDDM arises in genetically susceptible individuals who are exposed to putative environmental or exogenous triggers that may activate immunological mechanisms, leading to a progressive loss of pancreatic islet beta cells (25-27). The excessive glucose concentration stems from a lack of the hormone insulin (insulin deficiency), which is produced by the beta cells. The immunological and inflammatory mechanisms concerned have not yet been clearly defined. It is an insidious process which may occur over many years. During the 'pre-diabetic' stage of the evolution of the disease, individuals can often be recognized by the presence of immunological markers and a decline in pancreatic beta-cell function (28). Studies carried out on healthy children in the Dutch population have shown that in the presence of certain immunological markers, 50% of the children concerned develop IDDM within eight years (29).

The fact that *hereditary factors* play a role is apparent from studies of identical twins, which demonstrate a higher concordance rate for IDDM in monozygotic twins (25-40%) than in dizygotic twins (5-10%) (30-32). In addition, the overall risk of IDDM among whites in the United States of America is 0.2-0.4%, while the risk in siblings of probands with IDDM is about 5% and in the offspring of diabetic parents 2-3% (if the mother has the disease) and 5-6% (if the father has the disease)(32). The major genetic predisposition is conferred by genes located on the short arm of chromosome 6, either within or in close approximation to the major histocompatibility complex (33,34).

Viruses, such as mumps, rubella and coxsackie, are suspected exogenous determinants (35). It is thought that incidence peaks noted by some observers in autumn and early winter could be explained by the presence of viruses (36). In addition, there are indications that *diet* may also play a role. For example, breast-feeding could have a protective effect, while a high level of consumption of protein-rich foods and carbohydrates or nitrosamine-containing foods could increase the risk of IDDM (37-39). However, a recently published meta-analysis of 17 case-control studies showed that the increased risk of IDDM associated with early infant diet exposures is small and may be explained by methodological shortcomings (40). Quantification of the relative contribution of the different determinants has so far not been possible.

Primarily, IDDM and NIDDM are clinically descriptive subclasses of diabetes. Whereas IDDM appears to be the result of an auto-immune disease process (i.e. a type I pathogenetic process), the etiology and pathogenesis of NIDDM is heterogenous.

Many patients with NIDDM and individuals with an impaired glucose tolerance (IGT) exhibit insulin resistance and hyperinsulinaemia in association with dyslipoproteinaemia, central obesity and hypertension. This cluster of cardiovascular determinants has been described by a number of names such as 'syndrome X' or 'Reaven syndrome' (41), the chronic metabolic syndrome, and the insulin resistance syndrome (42). The extent to which this cluster of determinants represents a single disease process is still unclear (43). Persons with a history of IGT and gestational diabetes are at increased risk of developing NIDDM. The rate of progression from IGT to NIDDM is about 2-3% per year in studies carried out in the UK and the USA, and the incidence of NIDDM in women with gestational diabetes is about 3-5% per year (44,45).[1]

Whereas IDDM is most commonly encountered at a younger age (< 20-30 years), NIDDM is a form of diabetes particularly associated with advancing age. Apart from *age*, *heredity* is currently considered as an important risk factor associated with NIDDM, apparently playing an even greater role than it does in IDDM. In the case of identical twins, a concordance rate of 95-100% for NIDDM can be found (30). The risk of developing NIDDM in individuals where one or both parents have NIDDM is almost three times as great as in those whose parents are free of the disease (47).

Irrespective of the presence or absence of the disease in the family, *overweight* increases the risk of the occurrence of NIDDM by a factor of two to three (48). There are indications that people must be overweight for some time before it becomes a risk factor for diabetes (49,50). Also the *distribution of fat* around the body is an important factor. Abdominally localised body fat (a 'paunch') imposes an additional risk (51).

It has been demonstrated that *physical inactivity* promotes the development of NIDDM (44,47). The composition of the *diet* is also a risk factor. In line with the 'Guidelines for a healthy diet' published by the Netherlands Nutrition Council in 1986 (52), the consumption of high-fibre foods and unsaturated fatty acids at the expense of foods rich in saturated fatty acids is encouraged to prevent NIDDM (48). To what extent *alcohol use* and *smoking* are independent determinants for NIDDM is still unclear. The results of several studies on alcohol use (53-58) as well as smoking (56-61) are contradictory. Table 4 summarizes the relative risks of established determinants for NIDDM.

[1] In addition, there are indications that 10-20% of NIDDM is the result of an auto-immune disease process as found in IDDM (Latent Auto-immune Diabetes in Adults) and that 2-4% is the result of specific gene mutations (46).

Table 4: Relative risks of established determinants for NIDDM.

Determinant	Indicator	RR	Reference
Endogenous:			
genetic factors	1 or 2 parents with diabetes	2.9	47
body weight	BMI >25kg/m^2	2.5	48
	waist/hip ratio >1	2.5	51
Exogenous:			
physical activity	energy expenditure <2,000 kcal/week	1.7	47
nutrition	Guidelines for a healthy diet	0.7	48

BMI: Body Mass Index (weight (kg)/height^2 (m))
Note: for the risk of NIDDM in those with IGT and gestational diabetes, see text.

CONCEPTS AND APPROACH

The ultimate question to be addressed in this thesis is: what are the likely implications of future developments in the occurrence of diabetes mellitus for health policy (Chapter 7)? Future developments may be explored in various ways. In the Netherlands the scenario method has been applied extensively in recent years. By drawing a distinction between likely developments on the one hand and the potential for influencing these developments on the other, an attempt has been made to provide a structure for the wide range of future possibilities.

In a scenario study, a number of possible images of the future are drawn up with the aid of scenarios. In general, a scenario can be defined as follows: "*A scenario describes how the present situation for a part of society may be changed into a particular image of the future by means of a series of possible developments. The aim in doing so is to obtain greater insight into the underlying mechanisms and the ways in which these can be influenced*" (62).

A distinction is often drawn between exploratory and strategic scenarios. A strategic scenario takes a particular (desired) image of the future and explores the various strategic paths in which this might be achieved. In an exploratory scenario the future is studied by examining a number of different possible images of the future. In this thesis the future is confined to exploratory scenarios with regard to the occurrence of diabetes until 2005 (Chapters 5 and 6).

The two major prerequisites for constructing sound future projections for health policy purposes are: (1) the transcription of the conceptual model into a dynamic (mathematical) model and (2) the availability of epidemiological trend data.

From a conceptual to a mathematical model

The conceptual model shown in Figure 1 describes the interrelationships between the epidemiological concepts incidence, prevalence, remission and mortality or life expectancy. Table 5 summarizes the definitions used.

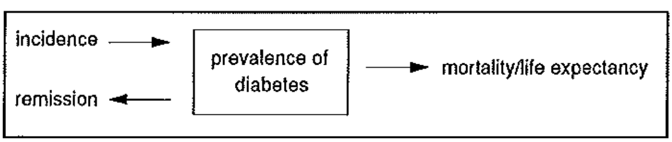

Figure 1: Prevalence of diabetes mellitus as a result of incidence, remission and mortality/life expectancy.

Figure 1 indicates that the number of patients with diabetes mellitus (prevalence) is the net result of an inflow and outflow of patients. The inflow is equal to the incidence, while the outflow is the sum of remission and mortality. These concepts can be interrelated by using such a conceptual model, which describes the pattern of effects in a qualitative sense. But what we are ultimately interested in is the dynamics of the system: we want to quantify the number of diabetic patients projected for the period up to 2005, taking into account several influences, some of which may be disease specific (e.g. changes in exposure to risk factors) while others are autonomous (e.g. demographic developments). The more we know about potential developments, the more relevant it is to reshape the conceptual model into a dynamic model in which the relationships between the concepts as defined in Table 5 are presented in formal mathematical terms (Chapters 5 and 6).

Table 5: Definitions of concepts used in relation to diabetes mellitus.

prevalence:	the number of diagnosed diabetic patients at a moment in time in a defined population (e.g. expressed per 10,000 persons)
incidence:	the number of newly-diagnosed diabetic patients per unit of time in a defined population (e.g. expressed per 10,000 persons per year)
remission:	the chance of recovery from diabetes mellitus per unit of time (e.g. per year)
mortality:	the risk of patients with diabetes mellitus dying per unit of time (e.g. per year)
life expectancy:	the number of years before dying from age at onset of diabetes mellitus

Availability of data

To judge what sources will be used to obtain the necessary data to make projections, every scenario study begins with a background study resulting in a description of the *present* situation (see next section in this chapter). In addition, this background study is also designed to identify gaps in information needed to make accurate projections.

One of the problems arising from the background study for diabetes was the lack of information on *trends* in the occurrence of diabetes representative for the Dutch population. Therefore, additional studies were conducted to deal with this problem (Chapters 3 and 4).

In scenario studies extra information is often collected by means of a Delphi study to identify the factors that will determine *future* developments. A systematic inventory of future expectations is compiled by means of repeated rounds of questionnaires sent to experts with interim anonymous feedback reports. While a Delphi study provides the building blocks for future scenarios, these blocks then need to be combined in an acceptable manner. In order to check for consistency - which is an indispensable element - a workshop was convened to bring together some of the participants in the Delphi study. The results of the Delphi study and the workshop provided information for Chapters 5 and 6 of this thesis. The stepwise approach used to answer the questions in this thesis is summarized in Table 6.

Table 6: Stepwise approach.

Step	Question to be answered	Chapter
1. Background study	What is the occurrence of diabetes mellitus?	2[a]
2. Two 'trend' studies	Has the occurrence changed in recent years?	3 and 4
3. Drawing up scenarios[b]	What are possible future developments?	5 and 6
4. Interpretation	What are the likely implications for health policy?	7

a: see next section in this chapter.
b: with the aid of a mathematical model and additional information from the Delphi Study.

CURRENT KNOWLEDGE OF INCIDENCE, PREVALENCE, REMISSION AND MORTALITY

The background study provided a description of current knowledge about the occurrence, i.e. the incidence, prevalence, remission and mortality of diabetes mellitus in the Netherlands. The findings were also compared with other countries. The study was completed in May 1989 and is briefly reviewed in this section with respect to the occurrence of diabetes mellitus in the Netherlands. The results have been described in detail in previous publications (16,63).

In 1988 a search revealed that the *incidence and/or prevalence* of diabetes mellitus in the Netherlands in the period 1971-1987 had been studied in 18 surveys. In terms of the method of data collection the surveys can be divided into four categories:

1. morbidity registration by general practitioners (9 surveys);
2. questionnaire forming part of population survey (6 surveys);
3. questionnaire submitted to internists and paediatricians (1 survey);
4. screening survey for glucose tolerance in general practice (2 surveys).

As we were particularly interested in the burden on health care in the Netherlands, the following basic principles were applied to choose the most appropriate sources: the data should represent clinically-known patients and not those as yet undiagnosed, and they should be representative for the Dutch population as a whole in terms of age, gender, degree of urbanization and geographical variation. The incidence among 0-19 year-olds was most reliably represented by the questionnaire survey conducted among all Dutch paediatricians and internists in the period 1978-1980 (64,65). The Dutch Sentinel Practice Network, which represents about one percent of the Dutch population as a whole, was used to estimate the incidence from age 20 onwards (recorded in the period 1980-1983) and the prevalence for all age groups (recorded in 1980)(66). Due to the lack of gender-specific figures in the Sentinel Practice Network, additional information about the sex ratios as identified in the continuous morbidity registration of the Nijmegen University General Practitioners Institute was used (63).

Table 7 presents the incidence, expressed as an annual average, and the prevalence according to age and gender. The table reveals that both the incidence and prevalence increase with age and that the prevalence is higher among women than among men. The table also shows the absolute number of patients with diabetes mellitus, calculated on the basis of the size and composition of the population in 1980 (67). The number of clinically-known diabetic patients appeared to be 191,000 in 1980, which corresponded to a prevalence of 1.35% of the population. The annual number of newly-diagnosed patients amounted to 17,300, which corresponded to an incidence of 0.12% in 1980.

Table 7: Incidence and prevalence of diabetes mellitus per 10,000 inhabitants and the absolute number of patients with diabetes mellitus in the Netherlands according to age and sex in 1980.

Age	Incidence		Prevalence		Absolute number	
	men	women	men	women	men	women
0- 4	0.7	0.6	2	2	88	84
5- 9	1.2	1.0	2	2	108	104
10-14	1.4	1.5	7	14	431	833
15-19	1.2	0.9	7	21	440	1,276
20-24	1.4	1.6	10	31	605	1,797
25-34	3.3	2.7	25	25	3,048	2,838
35-44	7.0	6.5	46	64	4,107	5,317
45-54	20.8	18.7	131	127	9,859	9,537
55-64	26.1	26.1	280	342	17,615	23,378
≥ 65	49.9	52.7	599	728	40,104	69,385
Total[a]	11.3	13.2	109	161	76,375	114,549

a: the total figures for the incidence and prevalence have been standardized by age on the basis of the size and composition of the population in 1980 (67).
Source: Steering Committee on Future Health Scenarios (16).

The interpretation of these incidence and prevalence figures is subject to a number of problems:

1. The incidence and prevalence figures relate to all forms of diabetes mellitus. It may be assumed that by far the largest contribution is made by IDDM (10-20%) and especially NIDDM (80-90%)(6,7).
2. The data do not permit a classification into IDDM and NIDDM over the entire age range. Nor do the other surveys allow any distinction to be made in this respect. Only the survey among paediatricians and internists provides information on the incidence of IDDM < 20 years (64,65).
3. A comparison with the other surveys indicates a certain degree of dispersion in the estimates, which needs to be taken into account when making projections.
4. Depending on the quality of the registration, underreporting needs to be taken into account (i.e. the degree of meticulousness with which general practitioners in fact record patients diagnosed as having diabetes mellitus).
5. The morbidity patterns registered in general practice specifically reflect the health problems presented by those who make an appeal to the health care system. As the general practitioner operates as a 'gatekeeper' in the Netherlands, most problems (e.g. diabetes) will be detected. However, people living in institutions for a long time (e.g. nursing homes) and relying on institutional doctors will be missed. This may result in an underestimation of the incidence and prevalence when diabetes is relatively more prominent among such people.
6. A large American survey (1976-1980) among 20-74 year-olds indicated that only 50% of all patients with diabetes mellitus were diagnosed as such (21). When our search was conducted, there were indications to suggest that there is a high prevalence of undiagnosed glucose metabolism disorders among individuals aged over 65 years in the Netherlands as well (22). Recently, this was confirmed by several other studies (5,23,24).

The extent to which *remission* (in addition to mortality) makes a significant contribution to the outflow of the diabetic population is unknown. Nor is it clear to what extent reported cases of remission are due to misclassification (e.g. instances in which it later turns out that a patient has been diagnosed as having diabetes mellitus on the basis of inadequate data). In so far as remission takes place this will be confined to NIDDM. It is possible for overweight patients with NIDDM to achieve an improvement - i.e. a drop - in the blood glucose level by losing weight. Despite the remission, these 'patients' will remain under a certain degree of medical supervision. For this reason, it has been decided in this study to assume that no remission takes place.

Assuming no remission, the outflow from the diabetic population will be wholly determined by *mortality*. In the Netherlands, statistics on the causes of death are compiled by Statistics Netherlands (formerly the Central Bureau of Statistics). On the basis of the International Classification of Diseases, both the underlying (primary) cause of death and other diseases that could have contributed towards death (i.e. secondary causes) are recorded. The sum of diabetes mellitus as primary and secondary cause of death can give an impression of mortality. There is however need for caution. On the one hand, death certificates are mainly concerned with the primary cause of death. On the other hand, multi-morbidity - especially at a later age - can mean that chronic diseases (including diabetes mellitus) are not sufficiently registered as secondary causes of death.

When this background study was carried out, no other studies had been conducted in the Netherlands to examine the underreporting of diabetes mellitus as primary and secondary cause of death. Studies in other countries revealed that in the case of deceased patients with diabetes mellitus, the disease was not mentioned at all on the death certificate in between 25-77% of all cases (68). Recently, it has become evident that in the Netherlands only about 50% of all registered cases of diabetes on the death certificates were coded in the statistics with diabetes specified as cause of death (69).

Another means of determining the outflow from the diabetic population resulting from mortality is based on the reduction of life expectancy of patients with diabetes mellitus in relation to the total population. A number of surveys in other countries have indicated that the younger the age at which diabetes mellitus is diagnosed the greater the reduction of life expectancy will be. This is shown in Figure 2 (70).

In this respect it should be noted that:
1. The spread in reduction of life expectancy falls the later the age at which diabetes mellitus is diagnosed.
2. No distinction can be made between IDDM and NIDDM.
3. Whether or not men and women with diabetes mellitus suffer the same reduction of life expectancy is disputed (74).

For the purposes of making future projections, it has been decided that the reduction of life expectancy as identified in studies from other countries provides a more reliable measure of the outflow from the diabetic population than the Dutch cause of death statistics. Besides, data on life expectancy provide additional information compared with mortality data, because the duration of diabetes is also included.

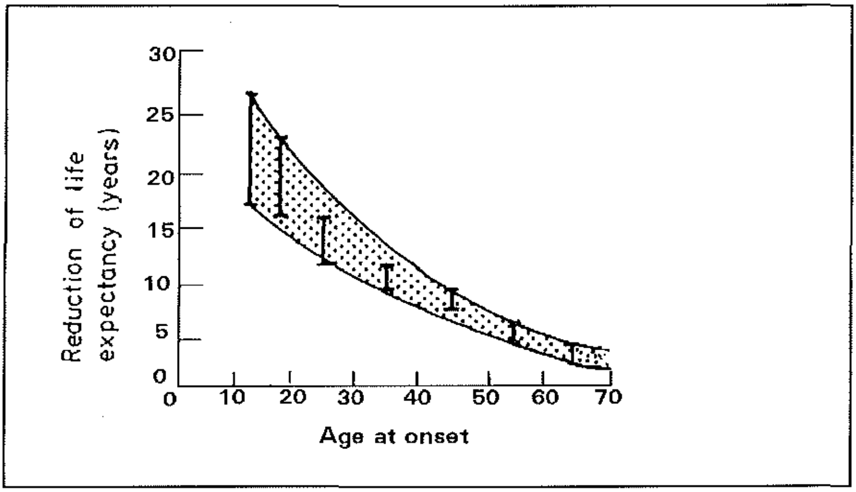

Figure 2: Reduction of life expectancy among patients with diabetes mellitus according to age at onset.

Note: the shaded area in Figure 2 is the area between the highest and lowest estimates.

Source: the data come from Marks & Krall (71), Goodkin (72), and Panzram (73), adapted by Van der Veen (70).

According to this background study as a first step to answering the questions that are addressed in this thesis, it was decided in conclusion:

- to choose the questionnaire survey conducted among all Dutch paediatricians and internists to estimate the incidence among 0-19 year-olds (recorded in the period 1978-1980)(64,65);
- to choose the continuous morbidity registration of the Dutch Sentinel Practice Network to estimate the incidence from age 20 onwards (recorded in 1980-1983) and the prevalence for all age groups (recorded in 1980)(66);
- to assume that no remission takes place;
- to choose the reduction of life expectancy as identified in studies from other countries instead of Dutch mortality statistics (70-73).

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CHAPTER 3

Increasing incidence of type I diabetes in the Netherlands: the second nation-wide study among children under 20 years of age

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ABSTRACT

Objective - A nation-wide retrospective study was conducted to assess the incidence of type I diabetes in the Netherlands among children <20 years of age in 1988-1990. The first study with a similar design covered 1978-1980.

Research design and methods - The capture-recapture census method was chosen for analysis of the data. A questionnaire was sent to all Dutch paediatricians and internists, and for the ascertainment, a similar questionnaire was sent out separately to members of the Dutch Diabetes Association, which is the national patient association.

Results - The average achieved ascertainment rate was 81%. The ascertainment-adjusted annual incidence was 13.2/100,000 for 0-19 year-old children, indicating an increase of 23% compared with the 1978-1980 survey; for 0-14 year-olds, the increase amounted to 17%.

Conclusions - This study suggests a sustained increase of type I diabetes in the Netherlands because the cumulative incidence studied previously in the 1960-1970 birth cohorts of male army conscripts 18 years of age was also found to rise. In contrast to Northern European countries, an increase in incidence for the age category 0-4 years could not be found.

INTRODUCTION

During the past decades, an increase in incidence of type I diabetes has been found in several countries (1-6). A study amongst the 1960-1970 birth cohorts of 18 year-old male army conscripts revealed that the incidence of type I diabetes is also rising in the Netherlands (7). Our study offers an opportunity to assess recent changes in incidence of type I diabetes in the Netherlands in both sexes because this second nation-wide study covering 1988-1990 had a design similar to the previous 1978-1980 study (8).

RESEARCH DESIGN AND METHODS

A questionnaire was sent in January 1991 to all paediatricians and internists to obtain data on children <20 years of age newly diagnosed with type I diabetes during the years 1988, 1989, or 1990. The questionnaire requested information on the child's initials, gender, date of birth, date of first insulin injection, and residence at that time.

As in the first study (8), the national Dutch Diabetes Association (DDA) was selected as a secondary source for validation. In April 1991, the DDA mailed a questionnaire to all members registered since 1988 and born since 1968. Registration and reporting by the specialists and DDA have not changed since the first study.

The ascertainment rate was defined as the proportion of responding patients from the DDA who also were reported by the specialists. The method used to estimate the incidence and its confidence intervals (CIs) is based on the capture-recapture census described by Hook et al. (9). The same formulas have been used to recalculate the incidence figures for 1978-1980. Changes in incidence estimates per 100,000/year were considered significant when the CIs did not overlap. For the 0-19 and 0-14 year-olds, the incidence rates were standardized to the age (5-year intervals) and sex distribution of the population during 1978-1980.

RESULTS

On 1 November 1991, 100% and 87% of the paediatricians and internists, respectively, did respond. The paediatricians reported 840 youngsters and the internists reported 329 youngsters 0-19 years of age in whom insulin treatment was initiated in 1988-1990. Of the DDA questionnaires received, 799 met the criteria. From the 1,169 patients reported by the specialists, 643 (55%) were also responding members of the DDA. Of the 156 DDA members not reported by the specialists, 36 were treated by non-responding specialists, 117 were treated by responding specialists who failed to report, and 3 were under treatment by doctors who were missing on the mailing list (two general practitioners and one paediatrician abroad).

No significant differences were found in ascertainment rates according to sex, month of first insulin injection, year of first insulin injection, and province of residence at that time (two-way χ^2 test; $P<0.05$). Ascertainment by paediatricians (91%) was significantly higher than by internists (54%), and consequently, the overall decrease in ascertainment rate with age was significant (Table 1).

Table 1: Cases of type I diabetes reported by specialists and members of the DDA according to type of specialist, age starting on insulin, and rate of ascertainment.

	Cases of type I diabetes (n)			Rate of ascertainment (%)	Significance of difference in ascertainment rate
	Specialists	DDA members	Both sources		
Type of specialist					
Paediatrician	840	570	520	91	$P<0.001$
Internist	329	227	123	54	
Age starting on insulin (years)					
0- 4	160	110	99	90	$P<0.001$
5- 9	292	204	181	89	
10-14	436	290	256	88	
15-19	281	195	107	55	

Note: The sum of DDA members according to type of specialist (797) is not equal to the sum of members according to age starting on insulin (799) because two members were treated by general practitioners.

The ascertainment-adjusted incidence rate was 13.2/100,000 (95% CI 12.7-13.7) per year for 0-19 years-olds and 12.4/100,000 (95% CI 12.1-12.7) per year for 0-14 year-olds. For boys as well as girls, the ascertainment-adjusted incidence increased with the first three 5-year age categories, after which a decline was observed in the age category 15-19 years (Table 2).

Table 2: Ascertainment-adjusted 3-year incidence of type 1 diabetes and the annual incidence per 100,000 according to age and sex.

Age (years)	Ascertainment-adjusted number (1988-1990)	Mean population over the 3 years	Ascertainment-adjusted incidence per 100,000/year	95% CI
Boys				
0- 4	96	470,081	6.8	6.3- 7.2
5- 9	159	453,269	11.7	11.0-12.4
10-14	259	465,841	18.5	17.9-19.1
15-19	287	578,051	16.6	14.3-18.9
Girls				
0- 4	83	450,499	6.1	5.9- 6.3
5- 9	173	433,872	13.3	12.9-13.7
10-14	235	444,098	17.7	16.9-18.4
15-19	221	554,671	13.3	11.5-15.1

When comparing our data with the ascertainment-adjusted annual incidence rates for 1978-1980 (10.9/100,000 (95% CI 10.5-11.4) for 0-19 year-olds; 11.1/100,000 (95% CI 10.7-11.5) for 0-14 year-olds), a significant increase of 21 and 12% was apparent for the age-ranges 0-19 and 0-14 years, respectively. The standardized ascertainment-adjusted incidence in 1988-1990 was 13.5/100,000 (95% CI 13.0-14.0) per year for 0-19 year-olds and 12.9/100,000 (95% CI 12.6-13.2) per year for 0-14 year-olds, indicating an even larger increase of 23 and nearly 17%, respectively. Table 3 shows the ascertainment-adjusted incidence rates for both periods according to age. With the exception of the age category 0-4 years, the incidence increased significantly.

Table 3: Ascertainment-adjusted annual incidence of type I diabetes per 100,000 with its CIs according to age in 1978-1980 and 1988-1990.

	1978-1980		1988-1990	
Age (years)	Incidence per 100,000/year	95% CI	Incidence per 100,000/year	95% CI
0- 4	6.8	6.6- 7.1	6.4	6.2- 6.7
5- 9	11.0	10.3-11.6	12.4	12.0-12.7
10-14	14.3	13.4-15.3	18.1	17.6-18.6
15-19	10.4	9.3-11.6	15.0	13.5-16.5

CONCLUSIONS

This study is the first one in which the change in incidence over time has been estimated by the capture-recapture census method (9). Comparing the standardized results of this study (1988-1990) with the first nation-wide study (1978-1980), a significant increase in incidence of type I diabetes was found of 23 and 17% for the age-ranges 0-19 and 0-14 years, respectively. This increase could not be attributed to factors leading to a spurious rise, such as improvement of diagnosis, changes in case definition, or declining disease-specific mortality (10). Especially in the 0-14 year age category with high ascertainment rates, the increase could not be attributed to underreporting.

Drykoningen et al. (7) studied the cumulative incidence of type I diabetes in male army conscripts 18 years of age in the Netherlands over a 10-year period. A significant nonlinear increase in the birth cohorts of 1960-1970 was found (on the average 4.4% with each annual birth cohort). Although the cumulative incidences for birth cohorts are not directly comparable to the incidences found in the current study, both studies suggest a sustained significant increase in incidence of type I diabetes in the Netherlands.

The Diabetes Epidemiology Research International Group reported an annual increase in incidence ranging from 10.1% in New Zealand to 2.8% in Norway (3). Although the rise established in our study is lower than in those countries, it is a substantial increase. In our study the absence of increase in the 0-4 year-olds is striking. This contrasts with the findings in Sweden and Finland (4,5). In Leicestershire the most prominent increase could even be found in the youngest age categories (3). In both our studies a north-south gradient was not present in our small but densely populated country.

The causes of the increasing incidence, as observed in several countries, are unknown. It is unlikely that it can be attributed to changes in genetic susceptibility (11,12). Although etiologically important factors in the environment have not been identified with certainty, observed differences in incidence over time and between countries may be helpful in the search for environmental determinants of type I diabetes.

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CHAPTER 4

Is the incidence of diabetes increasing in all age groups in the Netherlands? Results of the second study in the Dutch Sentinel Practice Network

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ABSTRACT

Objective - To assess possible changes in the incidence of diabetes in all age groups in the Netherlands during a 10-year period (1980-1983/1990-1992).

Research design and methods - Since 1970, a network of sentinel stations (the Dutch Sentinel Practice Network) consisting of about 1% of the Dutch population has been in operation to gain insight into the morbidity patterns of the Dutch population as recorded by general practitioners. One of the items recorded from 1990 to 1992 was the incidence of diabetes. The first study with a similar design that registered the incidence of diabetes was conducted from 1980 to 1983.

Results - The overall incidence of diabetes increased significantly by 12.1% in the period between the two studies. This overall increase can largely be attributed to a statistically significant increase in the age group 45-64 years (30.5%). Although not statistically significant, the 36% increase of diabetes in the age group 0-19 years is in accordance with the increase of type I diabetes based on the first and second nation-wide retrospective studies covering the total Dutch population.

Conclusions - There is a marked increase in the incidence of diabetes in the age group 45-64 years. This selective increase is probably not due to a real rise caused by changes in exposure to risk factors but to an earlier recognition of symptoms and signs of diabetes followed by blood glucose measurements and/or to more intensive case finding in general practice.

INTRODUCTION

In recent decades, an increase in the incidence of type I (insulin-dependent) diabetes has been found in several countries (1-6). A study among the 1960-1970 birth cohorts of 18 year-old male army conscripts (7) and a comparison of the first (1978-1980) and second (1988-1990) nation-wide retrospective studies (1988-1990) among individuals <20 years of age (8,9) revealed that the incidence of type I diabetes is also rising in the Netherlands.

Whether the incidence of diabetes is also increasing for those >19 years of age in the Netherlands is not known. One of the results of a Delphi investigation that we conducted in 1989-1990 among 33 experts on diabetes in the Netherlands indicated an average expected increase in incidence of 8% for the period 1980-2005 (10,11). The study presented here offers an opportunity to assess empirically based changes in the incidence of diabetes, especially for those >19 years of age, during a 10-year period (1980-1983/1990-1992).

RESEARCH DESIGN AND METHODS

In the Netherlands, general practices are a useful source for gaining insight into the morbidity patterns of the population. In the Dutch health care system, everyone has their own general practitioner, who operates as a 'gatekeeper'. This implies that health problems will first be presented to the general practitioner and that no patient will visit a specialist without being referred by his or her general practitioner. In addition, the specialist informs the general practitioner about clinical or policlinical findings (such as diagnosis and laboratory results). However, it should be emphasized that the morbidity patterns registered in general practice specifically reflect the health problems presented by those who make an appeal to the health care system.

Since 1970, a network of sentinel stations (the Dutch Sentinel Practice Network) has been in operation to gain insight into the morbidity patterns of the Dutch population as recorded by general practitioners (12). This network has been designed to be as representative for the Dutch population as possible (for age, sex and degree of urbanization) and covers about 1% of the population. It was realized when recruiting the 'spotter' physicians that there could be no question of a random sample of Dutch general practitioners; an expressly positive attitude on the part of the participating physicians was called for, plus an intention to participate for a number of years. Primarily physicians that had participated in the forerunner of this network (the first Dutch National Morbidity Survey), which consisted of 50 general practitioners (12), were involved. In addition, interested general practitioners who applied themselves or were recommended by others were selected, taking into account the criteria that the network should be representative for the Dutch population and cover 1% of the total. The same criteria were used when a general practitioner left the network and had to be replaced by another. To determine how representative the study sample is compared with the total Dutch population, a census is performed every 2 years. Since 1970, the network has consisted of 60-65 general practitioners working in about 45 sentinel stations.

A committee decides annually which items will be recorded on a registration form that has to be filled in by the general practitioner and sent to the Central Project Bureau once a week. At this bureau, the forms are checked, and in the case of uncertainties, the general practitioner is contacted. One of the items recorded in 1990-1992 by 63 general practitioners (43 sentinel stations) was the incidence of diabetes, which is defined as the number of patients newly diagnosed during that period per 1,000 person-years according to the diagnostic criteria formulated in 1985 by the World Health Organization (WHO) (13). The overall denominator (expressed in person-years) represents the sum of the separate denominators per sentinel station. To estimate the denominator per sentinel station during the period 1990-1992, the number of people present in that station (according to the census of 1991) was multiplied by the registration period (mostly the full period of 3 years, in one station 2 years, and in another station half a year). For every recorded patient, a supplementary questionnaire was filled in to collect information about the diagnostic approach, the treatment given, and the complications present at age of onset.

The first time the incidence of diabetes was recorded in the Dutch Sentinel Practice Network was in the period 1980-1983 (62 general practitioners working in 46 sentinel stations). To estimate the denominator, the censuses of 1979, 1981 and 1983 were used. At that time, the WHO criteria of 1980 (14) were used instead of the 1985 criteria (13). Depending on the circumstances in which the blood glucose value was measured (whole blood/plasma, venous/capillary, fasting/2 h after a 75-g glucose load), the diagnostic cutoff levels according to the 1980 and 1985 criteria differ 0.0-0.3 mmol/l from each other. For instance, according to the 1985 criteria, the diagnostic fasting cutoff value measured in capillary whole blood amounted to ≥6.7 mmol/l, while this value was ≥7.0 mmol/l using the 1980 criteria. On the other hand, the diagnostic cutoff value in capillary whole blood 2 h after a 75-g oral glucose load was ≥11.1 and ≥11.0 mmol/l, applying the 1985 and 1980 criteria, respectively. As we recorded the glucose values in our second study (1990-1992) and retrospectively traced the glucose values of the incident cases (who were still alive) in our first study (1980-1983), it became possible to detect spurious changes in the incidence caused by differences in diagnostic criteria. It appeared that only one newly diagnosed patient (out of 654) in the second study (based on 1985 criteria) would not have been diagnosed using the 1980 criteria (a thirsty 61 year-old woman with a fasting blood glucose of 6.9 mmol/l), while all newly diagnosed patients in the first study (based on 1980 criteria) would have been diagnosed according to the 1985 criteria.

To correct for changes in incidence caused by demographic developments, all data was standardized (by 5-year age groups and sex) to the Dutch population of 1990. Because the first study did not distinguish between men and women, we pooled these figures in the second study. This was also done with the subsequent age groups >65 years. Changes in incidence were then calculated for the age groups 0-19, 20-44, 45-64, and >64 years. Statistical significance was tested with the *z* test to compare two proportions ($P<0.05$). In addition, the 95% CIs of the differences in incidence were estimated using the normal approximation for the binomial distribution.

RESULTS

Table 1 shows the incidence of diabetes. Note that the incidence increases up to 80 years of age, after which a decline can be seen. This applies to men as well as to women. A significant difference between men and women according to age group (*z* test; $P<0.05$) could not be found. However, the absolute number of newly diagnosed diabetic patients is the largest in the age group 45-65 years.

Table 2 presents the changes in incidence by comparing our recent study in the sentinel network (1990-1992) with the former one (1980-1983). The figures indicate that the overall incidence of diabetes increased significantly by >12% over a period of 10 years. This overall increase can largely be attributed to a significant increase in the age group 45-64 years. For the other age groups, the increase is not significant, although the relative increase is most prominent in the youngest age group.

Table 1: Estimated incidence (per 1,000 person-years) and total number of newly diagnosed patients with diabetes in the Netherlands in 1990 according to the Dutch Sentinel Practice Network.

	Men				Women				Total			
	1	2	3	4	1	2	3	4	1	2	3	4
Age group (years)												
0-19	10	52.236	0.2 (0.1-0.4)	372	8	50.411	0.2 (0.1-0.3)	296	18	102.647	0.2 (0.1-0.3)	668
20-44	45	89.192	0.5 (0.4-0.7)	1.605	25	88.029	0.3 (0.2-0.4)	868	70	177.221	0.4 (0.3-0.5)	2.473
45-64	132	46.255	2.9 (2.4-3.4)	4.443	143	47.336	3.0 (2.5-3.5)	4.710	275	93.591	3.0 (2.6-3.3)	9.153
65-79	110	19.438	5.7 (4.6-6.8)	3.597	121	24.922	4.9 (4.0-5.7)	4.152	231	44.360	5.2 (4.5-5.9)	7.749
≥80	23	4.186	5.5 (3.5-8.2)	732	37	8.735	4.2 (3.0-5.8)	1.270	60	12.921	4.6 (3.5-6.0)	2.002
Total	320	211.307	1.5 (1.3-1.6)	10.749	334	219.433	1.5 (1.3-1.7)	11.295	654	430.740	1.5 (1.4-1.6)	22.044

Data are 1) observed number of newly diagnosed patients in the Sentinel Practice Network in the period 1990-1992; 2) total number of person-years in the Sentinel Practice Network (1990-1992); 3) estimated incidence per 1.000 person-years, standardized to the Dutch population in 1990 (95% CI); 4) estimated total number of newly diagnosed patients in the Netherlands in 1990.

Table 2: Estimated incidence of diabetes per 1,000 person-years in 1980-1983 and in 1990-1992, standardized to the Dutch population in 1990.

	1980-1983	1990-1992	Absolute increase (95% CI)	Increase (%)
Age group (years)				
0-19	0.13	0.17	0.05 (-0.03-0.13)	35.9
20-44	0.41	0.43	0.01 (-0.09-0.12)	3.4
45-64	2.26	2.95	0.69 (0.25-1.13)	30.5
≥65	5.15	5.16	0.01 (-0.80-0.82)	0.3
Total	1.33	1.49	0.16 (0.01-0.31)	12.1

CONCLUSIONS

To obtain incidence estimates that are less prone to chance, a rather large population size is needed. The Dutch Sentinel Practice Network, consisting of more than 140,000 people, has the largest denominator of all Dutch continuous morbidity registrations in primary care. The others contain 50,000 people or fewer (15-18). Nevertheless, we recorded the incidence in a 3-year period to increase the denominator even more.

To correct for an undercount of cases, the capture-recapture census method is recommended in the literature, using an independent secondary source for ascertainment (19). Even though a secondary source for validation is lacking, the incidence figures found in the Dutch Sentinel Practice Network are likely to be reliable. The network has been in operation for a long period of time, and the general practitioners who participate in it are not only highly motivated but also experienced in recording health problems. Most general practitioners have been participating for many years; about 66% of the general practitioners are still involved after a 10-year period. Besides, in the Dutch health care system, general practitioners play a central role because they operate as gatekeepers. In spite of the fact that diabetic patients are diagnosed or treated by a specialist, the general practitioner is informed by the specialist and is therefore able to record health problems detected by the specialist. According to the results of the supplementary questionnaire from our recent study (1990-1992), 17.9% of all newly diagnosed patients were recorded in this way. Nevertheless, just a few cases might have been missed at the end of the recording period because of a delay in transferring information. However, the same applies to the previous study.

On the other hand, when the incidence figures from the Dutch Sentinel Practice Network are compared with those from the relatively small samples of other continuous morbidity registrations in primary care, the incidence in the sentinel network is 1.5- to 2-fold lower (15-18). Discrepancies in the objectives, design, definition of the numerator (such as diagnostic criteria), extent and definition of the denominator, and length of the recording period are assumed to be responsible for the differences (20). For example, the Dutch Sentinel Practice Network is specially designed to obtain incidence and prevalence figures in primary practice, while other registrations focus more on recording medical consumption, or include uncertain diagnoses.

This study is the first in the Netherlands to assess possible changes in the incidence of diabetes for all age groups based on a rather large denominator. When the results of this study were compared with the former study with a similar design, it appeared that the relative increase (nearly 36%) was greatest in the age group 0-19 years. However, the number of cases in this younger age group is too few to obtain statistically significant changes, despite the fact that the sentinel network covers about 1% of all Dutch inhabitants and that in both studies several years were used to estimate the average annual incidence. Nevertheless, the change in incidence of diabetes in the age group 0-19 years is indicative of an important increase. This finding is in line with the 23% increase of type I diabetes based on the first (1978-1980) and second (1988-1990) nation-wide retrospective studies involving all paediatricians and internists and covering the total Dutch population (8,9). The causes of this increasing incidence, observed in several countries (1-9), are unknown.

It is striking that above 20 years of age, a statistically significant increase in the incidence is only found in the age group 45-64 years. As stated earlier, this rise is probably not the result of changes in diagnostic criteria. Besides, it seems unlikely that changes in exposure to risk factors, especially for type II (non-insulin-dependent) diabetes, are responsible for this 30.5% age-specific increase. Three large screening projects on cardiovascular risk factors in which height and weight were measured indicated that in the period 1974-1991 there was no change in the mean BMI (kg/m^2) or marked increase in the age-adjusted prevalence of obesity (BMI ≥ 30 kg/m^2) in the Dutch population (21,22). Data from the last screening project among 36,000 men and women aged 20-59 years showed a stable BMI in the period 1987-1991, with a slight significant increase in obesity of 0.3% per year for men. The mean prevalence of obesity amounted to 7.4% for men and 9.0% for women, respectively (22). A marked change in the prevalence of physical inactivity in the period 1987-1991 was not observed either (22).

Recently, general practitioners have become very aware of diabetes as a public health problem. In 1988, the Dutch College of General Practitioners published its 'Standard Diabetes Type II' (23). This standard contains guidelines on the diagnosis, treatment, and support of non-insulin-using type II patients. One of the recommendations is to examine every person with an impaired glucose tolerance annually. In 1988-1990 the Steering Committee on Future Health Scenarios emphasized the phenomenon of underreporting diabetes and the importance of the disease as a major and growing cause of prolonged ill health and premature mortality (10). The Steering Committee brought to the attention of medical practitioners the results of the second National Health and Nutrition Examination Survey (NHANES II, 1976-1980) carried out in the U.S. It was found that diagnosed patients in the age range 20-74 years represent only 50% of all patients with diabetes (24). Recently, it appeared that in the Netherlands, many individuals also suffer from undiagnosed disturbances in glucose metabolism (25-27). In a cross-sectional study among 2,472 persons aged 50-74 years in the Dutch town of Hoorn, the prevalence of previously diagnosed diabetes was 4.2%, while diabetes was newly diagnosed in 4.8% by means of an oral glucose tolerance test (27). The Hoorn Study findings are in line with those from the NHANES: roughly 50% of patients with diabetes were undiagnosed. In accordance with pronouncements in the literature (28,29), the Steering Committee is cautious about the establishment and administration of large screening programmes for type II diabetes. It was recommended instead to explore the possibilities of case finding in general practice among people >50 years of age with obesity and/or a positive family history of type II diabetes and/or the existence of complications that might be attributable to diabetes. These developments may have influenced the general practitioners' diagnostic behaviour and might be responsible for the increase found in the age group 45-64 years, because this group is of special interest with respect to case-finding activities in general practice.

To verify this hypothesis, a questionnaire was sent to the general practitioners who participated during both recording periods. It was confirmed that for this age group there is a tendency to measure blood glucose in those who make an appeal to the health care system for other health problems (case finding). On the other hand, the general practitioners observed that people are better able to recognize symptoms associated with diabetes, whereas a greater alertness on the part of the general practitioner leading to earlier recognition may also be of importance. In addition, blood glucose measurements to confirm the diagnosis conducted by the general practitioner when symptoms are found are common nowadays (replacing the less sensitive measurements of glucose in the urine used in the past).

To underpin these observations quantitatively, it is valuable to compare the use of diagnostic tests and the presence of symptoms in newly diagnosed patients over time. An increase in case-finding activities will be accompanied by a decline in the existence of initial symptoms. However, when an increase in case-finding activities as well as an increase in early recognition of symptoms and signs is evident, the results will be difficult to interpret. Unfortunately, because valid additional information was not available from the former study, it is difficult to establish changes in the diagnostic approach. The recent study indicated that in addition to glucose measurements to establish the diagnosis, 65.4% of the cases also initially presented symptoms and signs associated with diabetes.

Our findings illustrate that to interpret trend data, one must be aware of different kinds of developments that not only are confined to etiological factors per se, but also take into account changes in health care practice. This is necessary not only to interpret time trends in the incidence (and prevalence) of type II diabetes found within one study, but also to make comparisons between studies and countries. The ideal solution for disentangling real trends from trends due to changes in the proportion of diagnosed and undiagnosed patients is to link periodic or continuous morbidity registrations (physician-diagnosed cases) both in time and on an individual level with intermittently performed population-based (screening) surveys. It is worthwhile to explore the most cost-effective ways to achieve this ideal.

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CHAPTER 5

Forecasting the number of diabetic patients in the Netherlands in 2005

Published as:
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ABSTRACT

Objectives - There is evidence from past decades that the number of diabetic patients has increased independently of changes in demography. A static model that takes into account only demographic changes is therefore unable to forecast the expected number of diabetic patients correctly.

Methods - We developed a dynamic model in which actual incidence, prevalence and life expectancy data are used and alternative assumptions about future trends in these parameters can be incorporated.

Results - This dynamic model forecasts higher numbers of diabetic patients than the less sophisticated static model. According to the dynamic model, a 46% increase in the number of diabetic patients in the Netherlands can be expected, from 244,000 in 1990 to 355,000 in 2005 (about 2.5% annually). The static model forecasts a 22% increase.

Conclusions - Diabetes mellitus will become a more serious public health problem than can be expected from demographic changes only. In planning future health care, monitoring of trends in incidence, prevalence, remission, and mortality or life expectancy is a necessary prerequisite.

INTRODUCTION

In planning future health care for an aging Western population, one of the main problems is the number of patients with chronic diseases expected in the next few decades. Diabetes mellitus is a major and growing cause of prolonged ill health and premature mortality that affects tens of millions of people in countries at all levels of development (1). Therefore, diabetes mellitus was selected as a case study for further investigation in the Netherlands (2,3).

The results of two prognostic models (static and dynamic) for computing the number of patients with diabetes mellitus expected in the Netherlands in 2005 are presented. The static model takes into account only actual prevalence data and demographic changes. The dynamic model also makes use of information about actual incidence as well as life expectancy data. The dynamic model was developed because there is evidence that in past decades type I (insulin-dependent) as well as type II (non-insulin-dependent) diabetes mellitus increased independently of demographic changes (4-8), which makes the static model inadequate.

With a historic simulation procedure, it was possible to compute prevalence figures and compare them with actual prevalences. This procedure can be considered a validation of the dynamic model. Varying the actual incidence, prevalence, and life expectancy data on diabetic patients made it possible to test the sensitivity of the dynamic model in forecasting the number of diabetic patients in 2005 (sensitivity analysis).

To our knowledge this is the first study that uses more than demographic changes to compute the number of diabetic patients expected.

METHODS

Description of the two models

Two distinct models are used to compute the number of patients expected in the year 2005. The first is called a 'static' or 'equilibrium' model. In this model the assumption is made that the age and sex-specific prevalence of diabetes mellitus will remain constant over time. Apart from the prevalence, the only parameter of importance is demography (changing quantity and composition of the Dutch population until 2005). A simple multiplication of the age and sex-specific prevalence by the population estimates at a certain moment yields the expected number of diabetic patients. This model makes it possible to determine the influence of demographic changes on the number of patients expected.

The second model is called a 'dynamic' or 'disequilibrium' model. In this model the age and sex-specific prevalence is not presumed in advance to be stable over time. Extra data are needed on the age and sex-specific influx of new patients into and the age and sex-specific efflux of known patients out of the pool of diabetic patients. The incidence represents the influx. The efflux is the sum of diabetic patients who die and the diabetic patients who recover from the disease. In our model, data on the reduction of life expectancy from the moment diabetes mellitus is diagnosed, instead of mortality figures from death certificates, are used to define the efflux. Data based on death certificates are considered to be unreliable. On 25% to 77% of the death certificates of patients with diabetes mellitus, this disease is not mentioned at all (9). Recovery from diabetes mellitus is not unlikely, but often temporary and medical care in terms of blood glucose and weight control is still recommended. Therefore the assumption is made that recovery does not occur.

In the dynamic model two variants are used. In the first variant the incidence remains constant over time; in the second variant a regular age and sex-specific increase in incidence is taken into account. In both variants the reduction of life expectancy is kept constant over time, because in the literature there is no evidence that life expectancy has changed substantially for the majority of the patients (type II patients). The impact of improved survival, of type I patients only, on the projections would be limited. First, type I patients represent only 10% to 20% of all patients. Second, because of demographic changes in the period from 1980 to 2005 (i.e., the aging of the Dutch population), the absolute numbers of type II patients will strongly increase, while the proportion of type I patients will decrease. For a more detailed description of the models, see Appendix A and Hoogenveen et al. (10).

To start the dynamic model we had to estimate the age and sex-specific distribution of the diabetic patients over the years of remaining life expectancy in the first year of the simulation period. A more detailed description of this precalculation procedure is given in Appendix B.

Data used

As baseline for computing the number of diabetic patients expected in 2005, the year 1980 was selected. The most reliable and representative data for the Netherlands stem from periods around this year. The age and sex-specific prevalence in 1980 is presented in Figure 1. It represents known diabetic patients registered in 1980 in a Dutch sentinel network of general practitioners, distributed all over the country and covering about 160,000 inhabitants of all ages (1.2% of the Dutch population)(11). The incidence in 1980 is presented in Figure 2. The incidence for age categories older than 19 years was recorded in the period from 1980 through 1983; the data were obtained from the same study as the prevalence figures (11). Although the sentinel network was covering about 160,000 inhabitants and 4 years were used to estimate the average annual incidence, the incidence of diabetes mellitus in the younger age categories is too small to obtain reliable figures. For the age categories from birth through 19 years, therefore, we used the nation-wide retrospective study of children younger than 20 years, which registered all new type I diabetic patients in the period 1978 through 1980 (12). The method chosen was a questionnaire distributed to all Dutch paediatricians and internists. To correct for undercount of cases, the same questionnaire was given separately to members of the Dutch Diabetes Association, employing the capture-recapture census method for calculating the ascertainment-corrected incidence figures (13). Because diabetes in persons from birth through 19 years of age is almost entirely type I diabetes, the ascertainment-corrected annual incidence is presumed to represent all diabetic patients. Although ascertainment did not take place in the Dutch Sentinel Practice Network, prevalence and incidence figures are likely to be reliable because in the Netherlands every person has a general practitioner who records the patient's health problems, whether the patient will be treated by the general practitioner or by another doctor. Nevertheless, it is possible that newly diagnosed patients who will be treated by a specialist have not yet been recorded by the general practitioner. In that case the recorded incidence will be underestimated only slightly, because nearly 70% of all patients will be diagnosed by the general practitioner (11).

The reduction of life expectancy for diabetic patients is presented in Figure 3 (14). These data, which have been used in the dynamic model, are taken from three longitudinal studies of diabetic patients (15-17). Comparing these data and mortality data of the Dutch population from the Central Bureau of Statistics, we estimated the reduction of life expectancy for diabetic patients at onset to be 20% to 35%, depending on age at onset. For patients whose age at onset was in the category birth through 19 years and for those older than 79 years, the reduction of life expectancy was 30% to 35%; for patient aged

20 through 79 years the reduction of life expectancy was 20% to 30%, decreasing with age.

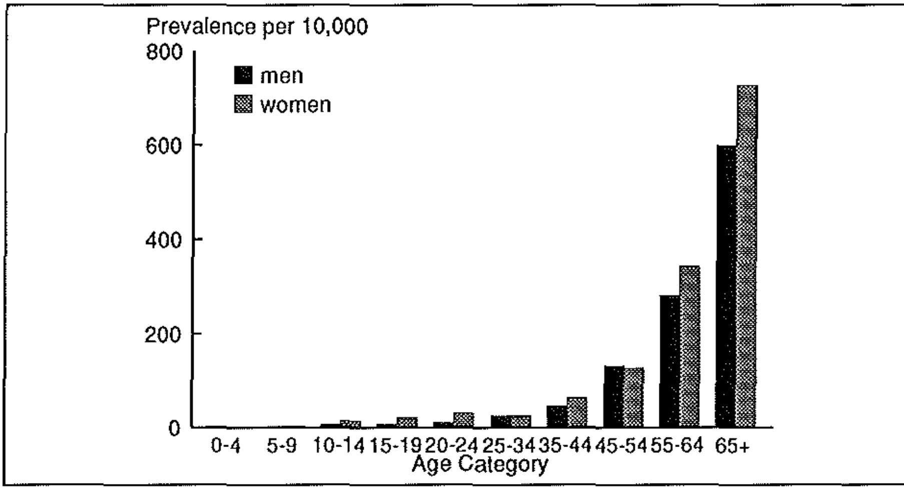

Figure 1: Prevalence of diabetes mellitus per 10,000 inhabitants in the Netherlands in 1980, by age and sex.

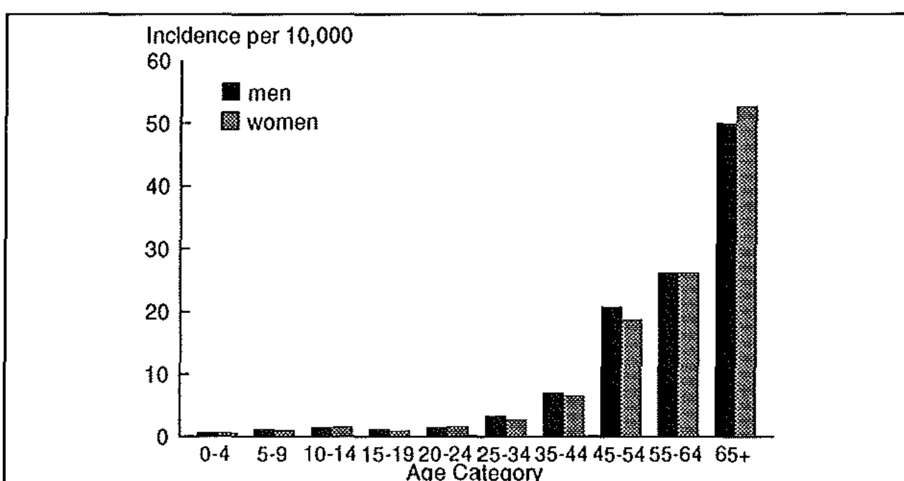

Figure 2: Incidence of diabetes mellitus per 10,000 inhabitants in the Netherlands in 1980, by age and sex.

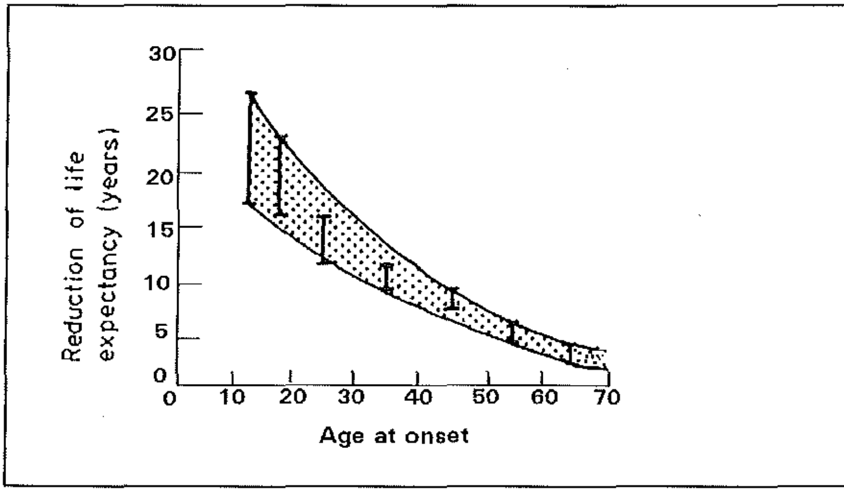

Figure 3: Reduction of life expectancy for diabetic patients, by age at onset.
Note: The shaded area indicates the region between the highest and lowest estimates.
Source: Reprinted with permission from van der Veen (14). Copyright 1988, The MacMillan Press Ltd.

An expected increase in incidence of 8% is assumed for the period 1980 through 2005 in the second variant of the dynamic model. This assumption is based on the average increase expected by 33 experts on diabetes mellitus in the Netherlands, one of the results of a Delphi investigation (18). The demographic data come from the Dutch Central Bureau of Statistics. The assumptions of the middle variant of the Central Bureau of Statistics population forecasts are used to estimate the future number of inhabitants in the Netherlands (19).

Historic validation and sensitivity analysis

Two validation procedures were performed to analyze the stability of the model, that is, whether the data on incidence, prevalence, and reduction of life expectancy due to diabetes mellitus and the assumption of no remission result in a state of relative equilibrium of the dynamic model. The first validation procedure was a historic simulation of the prevalence between 1955 (specific demographic data before 1955 are lacking) and 1980, assuming time-independent relative incidence and reduction of life expectancy to forecast the 1980 absolute prevalence. We compared the calculated prevalence with the 1980 data. This historic simulation also made it possible to subdivide the prevalence for those older than 64 years into the more specific age categories 65 through 79 years and 80 years and older. The actual data gave just one prevalence for all those older than 64 years.

The second validation procedure was a sensitivity analysis. We analyzed the impact on the forecast prevalence in 2005 of variations in some main model parameters (i.e., the 1980 prevalence, incidence and reduction of life expectancy data for diabetic patients). For the incidence and prevalence, two variants were used: a 5% increase and a 5% decrease in each age and sex-specific category compared with the actual data for 1980. For the reduction of life expectancy, a 25% increase and 25% decrease were used. Also, one variant with a linear increase in incidence with age for those older than 64 years was used. For this age category the available empirical data yielded just one value for the incidence for men and one for women. These values were used in the dynamic models but may not be in accord with reality. The literature provides evidence that the incidence increases with age for those older than 64 years (20). Therefore, in one variant a linear increase in incidence with age was assumed for those older than 64 years.

RESULTS

Expected number of patients predicted by the two models

The static model predicted an increase from 191,000 patients (1.35% of the population) in 1980 to 268,000 (1.65% of the population) in 2005, an increase of nearly 41%. Growth and aging of the Dutch population are responsible for increases of 15% and 25%, respectively. The dynamic model resulted in an increase to 339,000 patients (2.1% of the population) in 2005, that is, a total increase of 78% between 1980 and 2005. The extra increase of 37% over the prediction of the static model is the result of the disequilibrium between the influx and efflux of patients. The incidence exceeds the mortality. The second variant of the dynamic model resulted in an increase to 355,000 patients (2.2% of the population) in 2005, that is, an additional increase from 78% to 86%. In this variant the influx exceeds the efflux of patients even more.

The absolute increase in the number of diabetic patients in the period 1980 through 2005 according to the two models is presented in Figure 4. The estimated number of patients in 1990 predicted by the static model is 220,000 (1.5% of the population), compared with

242,000 (1.6% of the population) and 244,000 (1.6% of the population) predicted by the first and second variants of the dynamic model, respectively.

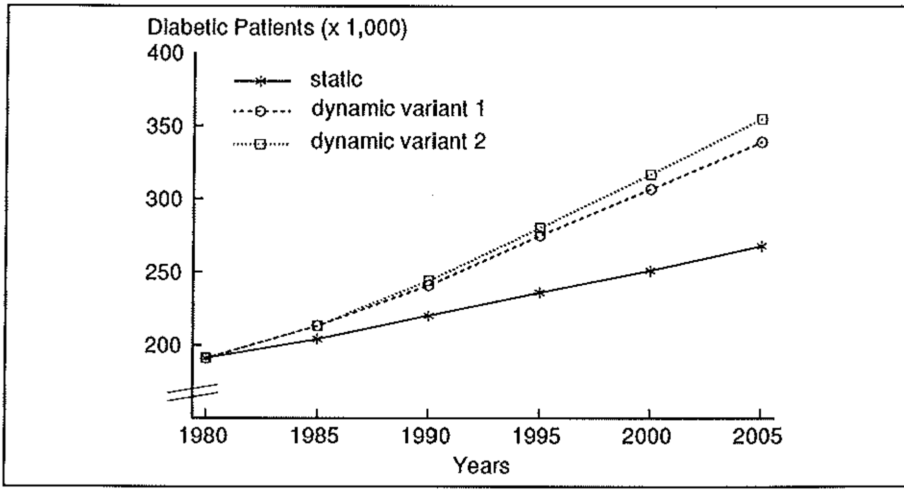

Figure 4: Expected increase in the number of diabetic patients in the Netherlands between 1980 and 2005, according to the static model and variant 1 and 2 of the dynamic model.

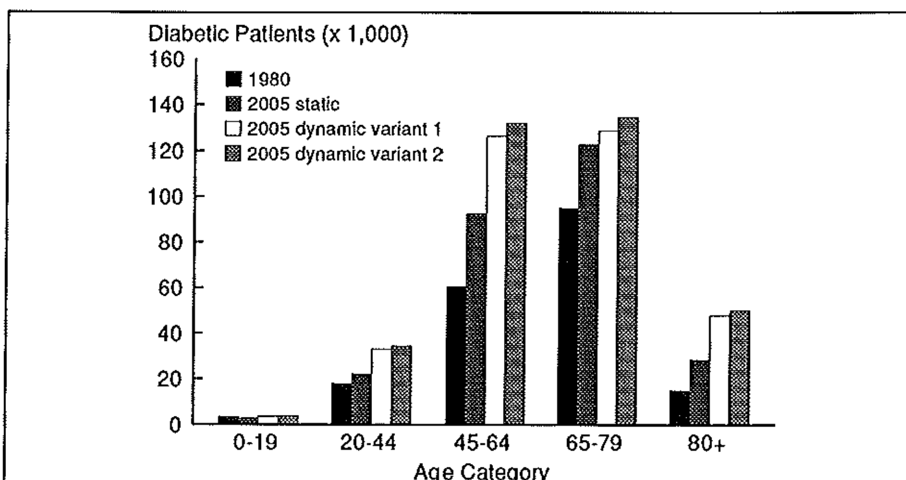

Figure 5: Age-specific prevalence for diabetes mellitus in 1980 and 2005, according to the static model and variant 1 and 2 of the dynamic model.

Age-specific analysis reveals that the expected absolute rise in the period 1980 through 2005 is most prominent in the age category 45 through 64 years (Figure 5). This applies to men as well as to women. Relatively, the most pronounced increase was found for the age category 80 years and older (in the dynamic model the number of patients in this category in 2005 is about 3.0 to 3.5 times the number in 1980, for both men and women).

Historic validation and sensitivity analysis

The historic simulation showed a 10% higher prevalence in 1980 than the empirical numbers. This difference is statistically significant ($P<.001$). The calculations also showed that the prevalence for the oldest category (80+ years) in 1980 (2.8% for men, 5.8% for women) was lower than that for the 65 through 79 year-old category (6.6% for men, 7.7% for women).

Table 1: Projected percentage changes[a] in the number of patients in 2005, according to the dynamic model.

Age and sex-specific change	Change in the number of diabetic patients in 2005		
	Men	Women	Total
Prevalence			
+5	+0.2	+0.4	+0.3
-5	-0.2	-0.4	-0.3
Incidence			
+5	+4.8	+4.6	+4.7
-5	-4.8	-4.6	-4.7
Life expectancy			
+25	+2.3	+11.0	+7.1
-25	-9.0	-3.7	-6.1

a: as a result of variation in age and sex-specific prevalence, incidence, and life expectance in 1980.

The results of the sensitivity analysis for the dynamic model (first variant) are presented in Table 1. A 5% change in the age and sex-specific prevalence in 1980 changes the total number of patients in 2005 by less than 1%. For the incidence, a 5% change in each age and sex-specific category results in a similar 5% change in the total number of patients in 2005. When the reduction of life expectancy is changed by 25%, the total number of patients in 2005 changes by 6% to 7%. For men, a decrease in life expectancy influenced the results more than an increase; for women, the opposite applied. If instead of one value for all those older than 64 years, a linear increase in incidence is used, a decrease of 9,000 patients (2.7%) is found in 2005 (not presented in Table 1).

DISCUSSION

Two models were used to compute the projected number of diabetic patients: a static and a dynamic model. The static model forecasts 268,000 patients in 2005; the dynamic model (second variant) 355,000. These estimates include all classes of diabetes mellitus (1). Type II diabetes represents about 80% to 90% and type I diabetes about 10% to 20% of all diabetic patients (21,22).

Of the two models, the dynamic model is considered to be the more valid. For the static or equilibrium model, the assumption was made that the age and sex-specific prevalence remains constant over time. This type of model for chronic diseases can be used only if the age and sex- specific incidence and life expectancy of diabetic patients are constant during a long period. For diabetes this is unlikely, because an increasing incidence has been reported in the literature (4-8). Our historic simulation procedure supports this observation. It appeared that the forecasted prevalence for 1980 was about 10% higher than the actual registered prevalence in 1980.

In the dynamic or disequilibrium model, it appeared that the influx of new patients was higher than the efflux of known patients, particularly in the second variant, in which an increasing incidence was assumed. There is no reason to assume that the past increase in incidence, as reported in the literature, has stopped. Furthermore, there are no indications of a significant change in life expectancy for the majority of the diabetic population (type II patients). Therefore, this parameter was kept constant. Consequently, the second variant, which resulted in a total increase of 86%, is viewed as the more valid. On the other hand, it is quite obvious that the increase in incidence contributes relatively little to this total increase in the number of diabetic patients in 2005 (8%). In contrast, changes in demography (static model) and the disequilibrium between influx and efflux in the first variant of the dynamic model caused increases of 41% and 37%, respectively.

As stated earlier, the dynamic model was validated by a historic simulation procedure. This procedure resulted in a lcwer prevalence for those persons aged 80 years and older in 1980 than for persons aged 65 through 79 years. This finding may be a consequence of the use of just one incidence for those older than 64 years. Empirical age-specific incidence data for those older than 64 years were nonexistent. Therefore we might have underestimated the incidence for those aged 80 years and older and, as a consequence, we may have underestimated the prevalence for this age category in 1980. In the second place, the estimated number of patients dying in this age category may be too high (the reduction of life expectancy has been overestimated), thereby underestimating the prevalence for those aged 80 years and older in 1980. On the other hand, the lower prevalence in the oldest age category has been confirmed by several empirical studies (8,23-25).

The sensitivity analysis revealed that the dynamic model is most sensitive to variations in incidence and is relatively insensitive to variations in prevalence. (This applies to all diseases characterized by a prevalence that increases with age.) The majority of the diabetic patients in 1980 were older than 64 years of age and most of them will not survive until 2005; almost all of the diabetic patients in 2005 will represent incident patients diagnosed in the period 1980 through 2005. The validity of the prevalence and incidence data used is considered in the Methods section.

The dynamic model was moderately sensitive to changes in life expectancy for diabetic patients. It is striking that for men a decrease in life expectancy influenced the results more than an increase. For women the opposite applied. This is probably due to the cutoff point: the year 2005. The explanation may be that the age of onset of diabetes is relatively lower for men than for women (Figure 2). Men diagnosed at the age of 45 years in 1980 will still be alive in 2005 if life expectancy remains unchanged or increases, but they may be dead in the event of an extra reduction of life expectancy. On the other hand, women diagnosed at the age of 65 years in 1980 will probably be dead in 2005 if life expectancy remains unchanged or decreases, but they may be alive in the event of an increase in life expectancy.

When a linearly increasing incidence for those older than 64 years of age was used, instead of one incidence, the predicted number of patients in 2005 decreased by 9,000 (2.7%). The explanation is simple. First, a higher incidence in the oldest category results in a shorter duration of the disease. Those in the oldest category will die earlier. In the second place, the countervailing lower incidence for the age category 65 through 79 years, which is a larger group (denominator), will result in a larger absolute decrease in the number of diabetic patients.

The results presented in this paper relate only to the number of patients diagnosed. In the second National Health and Nutrition Examination Survey (1976-1980) in the United States, it was found that diagnosed patients represent only 50% of all diabetic patients (26). Also, in the Netherlands it appears that many individuals suffer from undiagnosed disturbances in glucose metabolism (27-29). Preliminary results of a cross-sectional study in the Netherlands of 2,800 persons aged 50 through 74 years revealed that the prevalence of previously diagnosed diabetes was 4.8%. Diabetes was newly diagnosed by means of a glucose tolerance test in 5.3%.[29] Assuming that those results (roughly 50% undiagnosed patients) apply to the whole Dutch population and that all hitherto undiagnosed cases are diagnosed in 2005, an extra 355,000 diabetic patients can be expected in 2005. On the other hand, it is not unlikely that these patients represent a subcategory needing less intensive medical care.

Successful planning of future health care for diabetic patients depends on the availability of valid epidemiological data on trends in the incidence, prevalence, remission, and mortality or life expectancy for patients with this condition. Both the diabetes study of the Dutch Sentinel Practice Network and the registry of type I diabetes by all Dutch paediatricians and internists will be repeated - the former in the period 1990 through 1992, the latter retrospectively for the period 1988 through 1990. Therefore it will be possible to partly validate the models. Although the present computations concern diabetes mellitus in the Dutch population, the method is also relevant for other chronic diseases and other countries. The main restriction is the availability of valid data. It is therefore highly recommended that registries for diabetes mellitus and other chronic diseases be started and/or improved.

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APPENDIX A - Static and dynamic models for computing the number of patients expected in the future.

	Static model	Dynamic model
Purpose:	Estimating changes in absolute prevalence numbers due to demographic changes	Estimating changes in absolute prevalence numbers due to demographic and epidemiologic changes
Definition:	Equilibrium: time-independent age and sex-specific relative prevalence figures	Disequilibrium: time-dependent age and sex-specific relative prevalence figures
Assumptions (age and sex specifically):	Influx equals efflux	(a) no remission (both variants) (b) time-independent reduction of life expectancy (both variants) (c) time-independent relative incidence figures (first variant) (d) time-dependent relative incidence figures (second variant)
Formulas:	(1),(2)	(3)-(6)

The static model projects actual relative prevalence figures on future population numbers.

Formulas:

$$prev_{yr,s,a} = POP_{yr,s,a} \cdot PREVFR_{1980,s,a} \quad (1)$$

$$prev_{yr} = \Sigma_{s,a}\ prev_{yr,s,a} \quad (2)$$

where yr = time moment, s = sex, a = age, prev = absolute prevalence numbers, POP = absolute population numbers, and PREVFR = relative prevalence figures. Names in capitals are data, names in lowercase letters are model results. The interpretation of the formulas is as follows:

(1) The absolute prevalence number in each age and sex category in a certain year is the product of the time-independent relative prevalence figure and the time-dependent population number in that specific category.
(2) The total prevalence number in a certain year is the sum of all age and sex-specific prevalence numbers in that year.

The dynamic model is a Markov model. The Markov assumption is that the future behaviour of an individual depends only on his or her actual state, not on his or her (disease) history. The main states being distinguished are health status - and, if being a patient, remaining life expectancy - and age and sex.

Formulas:

$$rle_{yr,s,a} = le_{yr,s,a} - LERED_{yr,s,a} \quad (3)$$

$$inc_{yr,s,a} = POP_{yr,s,a} \cdot INCFR_{yr,s,a} \quad (4)$$

$$prev_{yr+1,s,d} = prev_{yr,s,d+1} + \Sigma_a\ inc_{yr,s,a} \cdot (\ d = rle_{yr,s,a}) \quad (5)$$

$$prev_{yr,s,0} = 0 \quad (6)$$

where (see also above): rle = remaining life expectancy, le = normal life expectancy, LERED = reduction of life expectancy on age at onset, inc = absolute incidence numbers, INCFR = relative incidence figures, and d = remaining life expectancy. The interpretation of the formulas is as follows:

(3) The remaining life expectancy is the difference between the normal and the reduction of life expectancy.
(4) The absolute incidence number in each age and sex category in a certain year is the product of the time-independent relative incidence figure and the time-dependent population number in that specific category.
(5) The absolute prevalence number at the end of each year is the sum of the prevalence number at the start of the year and the incidence number during the year. The remaining life expectancy of the prevalent cases who survive decreases with 1 year.
(6) Patients die when their remaining life expectancy is zero.

APPENDIX B - Procedure for estimating age and sex-specific distribution of patients over years of remaining life expectancy.

To start the Markovian dynamic model, we had to estimate the age and sex-specific distribution of the prevalence numbers over the remaining life expectancy in the first year of the simulation period (1980). We made two assumptions for this precalculation procedure. First, the absolute incidence number decreases with a constant multiplicative factor back in time. We had to make this assumption because of the lack of specific demographic data for the years before 1955. Second, the remaining life expectancy on the age at onset of diabetes is constant over time. The main formulas of this precalculation are as follows:

$$inc_{1980,s,a} = POP_{1980,s,a} \cdot INCFR_{1980,s,a} \quad (1)$$

$$inc_{yr,s,a} = 0.98 \cdot inc_{yr+1,s,a} \quad (2)$$

$$prev_{1980,s,a,d} = \Sigma_{yr<1980,a^*} inc_{yr,s,a^*} \cdot (rle_{1980,s,a^*} > [1980\text{-}yr]) \cdot$$

$$(a\text{-}a^* = 1980\text{-}yr) \cdot (rle_{1980,s,a^*}\text{-}d = 1980\text{-}yr) \quad (3)$$

$$prev_{1980,s,d} = \Sigma_a \{prev_{1980,s,a,d} \cdot PREVFR_{1980,s,a} \cdot POP_{1980,s,a}/\Sigma_d prev_{1980,s,a,d}\} \quad (4)$$

where (see also Appendix A): a = age in the year of prevalence (1980), a* = age in the year of incidence. The interpretation of the formulas is as follows:

(1) The absolute incidence number in each age and sex category in 1980 is the product of the relative incidence figure in 1980 and the population number in that specific category in 1980.
(2) The absolute incidence number in each age and sex category in a certain year before 1980 is the absolute incidence number in that specific category in the next year multiplied by 0.98.
(3) The absolute prevalence number in 1980 is the sum of the incidence numbers during the years before 1980 that are still alive in 1980. The three multiplicative factors show the three conditions on the incidence numbers: survival to 1980, aging from age a* in the year of incidence to age a in 1980, and reduction of the life expectancy on the age at onset equal to the difference between the year of incidence and 1980.
(4) The calculated prevalence numbers are scaled so that the age and sex-specific numbers agree with the 1980 data. A sensitivity analysis showed that the prognostic model results (Appendix A) are not sensitive to the exact implementation of the precalculation procedure, that is, the choice of the multiplicative factor in equation (2), when the simulation period is about 25 years. A 5% change in this multiplicative factor changes the total number of patients in 2005 by less than 1%.

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CHAPTER 6

Forecasting the number of diabetic patients in the Netherlands in 2005: an update

Submitted as:

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ABSTRACT

Objectives - To partly validate and update our forecasts of the number of diabetic patients in the Netherlands during the period 1980-2005 with new and more detailed data.

Methods - Two studies that recorded the prevalence and incidence of diabetes around 1980 were repeated around 1990, using a similar design. The actual prevalence in 1990 was compared with that in 1980 and with the estimated prevalences for 1990 according to our previous forecasts. The actual prevalence and incidence figures from around 1990 were used to compute several variants for the expected number of patients until 2005.

Results - A decline of 11% in the number of patients was observed between 1980 and 1990. Compared with the estimated prevalences for 1990, the actual prevalence in 1990 (1.1%) was 23-30% lower. The incidence increased by 12% between 1980 and 1990. The update yielded an increase in the number of patients in the period 1990-2005 of 23-127%, depending on the variant chosen.

Conclusions - Between 1980 and 1990, the prevalence decreased whereas the incidence increased, resulting in an increase in the number of diabetic patients in the foreseeable future. Diabetes mellitus is a growing public health problem and therefore important in planning future health care.

INTRODUCTION

During the past century, developed countries world-wide have experienced a considerable increase in life expectancy. It was noticed that a reduction in fatal communicable diseases was accompanied by an increase in non-communicable diseases. This epidemiologic transition changed diabetes from a rare disease into a disease that is now recognised as a major global public health problem. Diabetes mellitus is expected to become even more important as developing countries get more westernized (1).

Crude estimates indicate that well over 100 million people are affected by diabetes mellitus around the world (2). As it often results in substantial morbidity and mortality, the disease has a significant health and socio-economic impact. The proportion of estimated total health care costs related to diabetes is 3.6% in the United States of America and 4-5% in the United Kingdom (3). Besides, recent data suggest that in the United States of America the costs of diabetes care are rising rapidly (4-6).

The recognition of diabetes as a major public health problem and the notion that it will become even more prominent in the future makes the disease important in terms of planning future health care. From this point of view, one of the first questions that needs to be answered is how the occurrence of diabetes is likely to develop in the foreseeable future.

In order to answer that question we constructed a static and a dynamic model in which incidence, prevalence, and life expectancy data can be used and alternative assumptions about future trends in these parameters can be incorporated. In 1993, we published forecasts of the number of diabetic patients in the Netherlands for the period 1980-2005, based on incidence and prevalence data from two studies conducted around 1980 (7). As both studies were repeated around 1990, it became possible to partly validate the previous model results and to update the forecasts for the period up to 2005.

METHODS

Description of the two models

In our previous forecasting study, two distinct models were used to compute the number of patients expected in the period 1980-2005. The first is called a 'static' or 'equilibrium' model. In this model the assumption is made that the age and sex-specific prevalence of diabetes mellitus will remain constant over time. Apart from the prevalence, the only parameter of importance is demography (the changing quantity and composition of the Dutch population until 2005). A simple multiplication of the age and sex-specific prevalence by the population estimates at a certain moment in time thus yields the expected number of diabetic patients. This model makes it possible to determine the influence of demographic changes on the number of patients expected.

The second model is called a 'dynamic' or 'disequilibrium' model. In this model the age and sex-specific prevalence is not presumed to be stable over time. Additional data on the age and sex-specific influx of new patients into and efflux of known patients out of the pool of diabetic patients are needed. The incidence represents the influx. The efflux is the sum of diabetic patients who die or who recover from their disease. The models have been described in more detail in a previous publication (7).

Data used in the previous forecasting study

In our previous forecasting study, the prevalence represented known diabetic patients registered in 1980 in the Dutch Sentinel Practice Network of general practitioners, distributed all over the country and covering about 1% of the Dutch population (8). The incidence for age categories older than 19 years was recorded in the same sentinel network (1980-1983), whereas for the age category 0-19 years the nation-wide retrospective study (1978-1980) among all children aged under 20 years was used (9). The demographic data corresponded to the data from Statistics Netherlands (10), and life expectancy data were adapted from three longitudinal studies among diabetic patients (11). Although recovery is likely, it is said to be mostly temporary, whereas medical care in terms of blood glucose and body weight control is still recommended. Therefore the assumption was made that recovery does not occur.

In addition to the forecasts based on the static model, two variants were used in the dynamic model. In the first one the incidence remained constant over time, while in the second one a regular age and sex-specific increase in the incidence of 8% for the period 1980-2005 (i.e. 0.3 % per year) is taken into account. This increase was expected by 33 experts on diabetes mellitus in the Netherlands according to the Delphi investigation we conducted (12). In order to start the dynamic model, we had to estimate the (age and sex-specific) years of remaining life expectancy among the prevalent cases in the first year of the simulation period, as the data on life expectancy are related to the reduction of life expectancy by age at onset (i.e. amongst incident cases). A more detailed description of this precalculation procedure is available in a previous publication (7).

Data used in the present study

Employing a similar design, the Dutch Sentinel Practice Network recorded the clinically known diabetic patients in order to estimate the prevalence in 1990 (see Figure 1). All those who consulted the general practitioner in 1990-1991 and who were diagnosed with diabetes before 1 January 1990 were recorded as prevalent cases, irrespective of the reason for consultation. In addition to the first study, a supplementary questionnaire was filled in for each recorded patient by the general practitioner to gather information about the diagnostic approach, the treatment given and the presence of complications. In order to avoid missing cases because of this extra workload, it was decided to register the prevalent cases for two years (1990-1991) instead of one (1980) as in the former study.

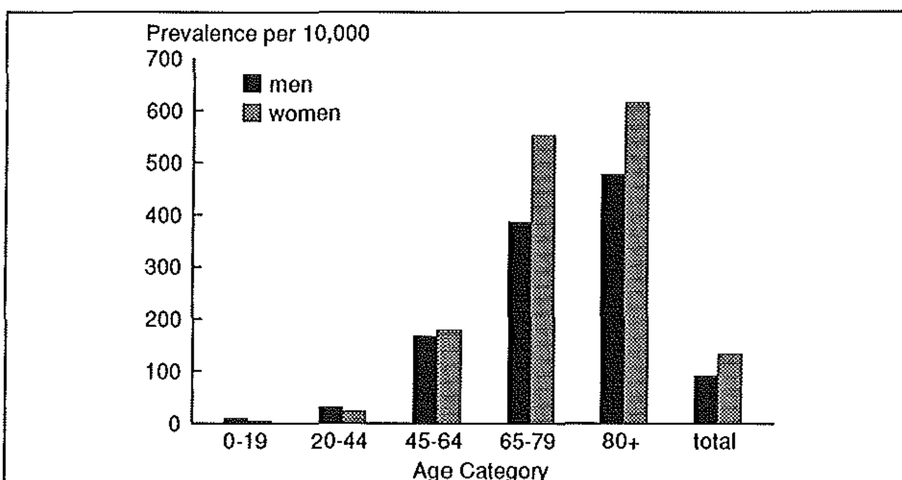

Figure 1: Prevalence of diabetes mellitus per 10,000 inhabitants in the Netherlands in 1990, by age and sex.

Regarding the incidence, new data were obtained in a way similar to both former studies. For the age category 0-19 the nation-wide retrospective study among all those under 20 was repeated for the period 1988-1990 (13). For those over 19, the same Dutch Sentinel Practice Network was used, which again recorded the incidence of diabetes in the period 1990-1992 (14). Figure 2 shows the incidence according to age and sex around 1990 based on these studies.

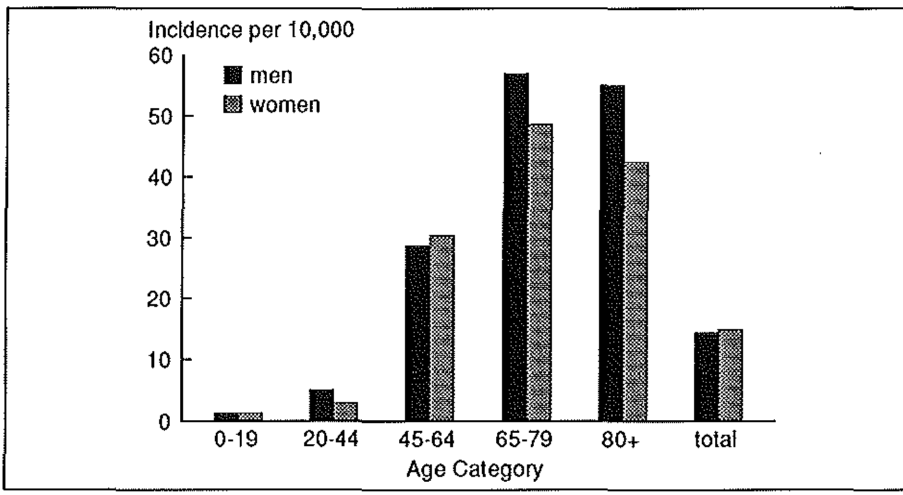

Figure 2: Incidence of diabetes mellitus per 10,000 inhabitants in the Netherlands in 1990, by age and sex.

Table 1 presents the 10-year changes in prevalence and incidence according to age. To adjust for changes caused by demographic developments, all data was standardized (by 5-year age category and sex) to the Dutch population of 1990. Because the first study in the Dutch Sentinel Practice Network did not distinguish between men and women (at that time we obtained sex-specific figures by extrapolating age-specific sex differences from another Dutch registry in general practice (15)), we pooled these figures in the present study. This was also done with the age categories above 65 years. Changes in prevalence and incidence were then calculated for the age categories 0-19, 20-44, 45-64 and over 64. Statistical significance was tested with the z-test to compare two proportions ($P<0.05$). In addition, the 95 percent confidence intervals (CI) of the differences (in prevalence and incidence, respectively) were estimated using the normal approximation for the binomial distribution. The method used to estimate the incidence and the differences for the age category 0-19 years with its confidence limits is based on the capture-recapture census as described by Hook et al. (16).

Table 1: Age-specific changes (per 10,000) in prevalence and incidence over a ten-year period (between around 1980 and 1990), standardized to the Dutch population of 1990.

Age	Prevalence decline (95% CI)		Incidence increase (95% CI)	
0-19	1.4	(-2.1- 4.8)	0.2	(0.2- 0.3)
20-44	10.3	(4.1- 16.6)	0.1	(-0.9- 1.2)
45-64	49.1	(27.3- 70.9)	6.9	(2.5-11.3)
65+	178.4	(126.9- 229.8)	0.1	(-8.0- 8.2)
Total	37.7	(29.6- 45.7)	1.6	(0.1- 3.0)

Validation and update

With the availability of new empirically based data, it became possible to partly validate the previous model results and to update the forecasts for the period up to 2005.

The actual prevalence in 1990 was compared with that in 1980 and with the estimated prevalences in 1990 (as a result of the static model and the two variants of the dynamic model according to our previous forecasting study). The actual incidence changes were compared with the assumptions made in the two variants of the dynamic model according to the previous study (i.e. no increase and an increase of 0.3% per year, respectively).

We updated the model for the period 1990-2005. In agreement with our previous forecasting study, the model-technical characteristics as well as the data on demography, life expectancy and recovery were kept identical in this 'update'. However, the new prevalence and incidence figures from around 1990 were used. In addition to the forecast based on the static model (adopted as the basic scenario), three variants were computed according to the dynamic model. The first and second variants correspond with the two variants used in our previous forecasting study (i.e. a constant incidence and a regular age and sex-specific increase in the incidence of 0.3 % per year for the period 1990-2005, respectively). In addition, in a third variant the actual age-specific incidence increase found in the ten-year period was assumed to continue regularly (yearly) during the period 1990-2005.

RESULTS

The number of prevalent cases in 1990 amounted to 170,000 diabetic patients (1.1%). This represents a decline of 11% since 1980 (191,000). However, the previous forecasting model estimated 220,000, 242,000 and 244,000 diabetic patients in 1990 according to the static model and the two variants of the dynamic model, respectively. The actual prevalence in 1990 was 23-30% lower compared with the estimated prevalences. Standardized to the Dutch population of 1990, there was no significant change in the age category 0-19 years, in contrast to the age categories 20-44, 45-64 and 65+ which yielded relative declines of 29%, 23% and 27%, respectively (see also Table 1).

A constant incidence and an expected increase of 8% (i.e. a yearly increase of 0.3% per age category) in the period 1980-2005 were assumed in the first and second variants of the dynamic model in our previous forecasting study. Empirically, between around 1980 and 1990 an overall significant incidence increase of 1.6 per 10,000 (i.e. 12%) was found (see Table 1). This overall increase can largely be attributed to a statistically significant increase in the age category 45-64 years (31%). However, the increase was also significant for the youngest age category (23%). Although the actual increase is based on two points in time without information about the period in between, this increase corresponds to a calculated annual rise of 1.1%, which is higher than the increase assumed in the second variant of the previous forecasting study (0.3%).

According to the static model, the 'update' of the forecast for the period 1990-2005 resulted in an increase from 170,000 patients in 1990 to 208,000 patients in 2005 (i.e. 23%), whereas the former static model predicted an increase from 191,000 in 1980 to 220,000 in 1990 and 268,000 in 2005 (i.e. 22% in the period 1990-2005). In this 'update', the consecutive three dynamic variants showed an increase to 346,000 (104%), 353,000 (108%) and 385,000 (127%) diabetic patients, respectively. The first and second dynamic variants of the previous forecasting study resulted in 339,000 and 355,000 patients. This is in accordance with the findings of both corresponding variants in the 'update', although the input parameters (starting incidence and prevalence data) were different (see Table 2).

Table 2: Expected number of diabetic patients in the Netherlands in 2005 according to the previous forecasting study and the present 'update'.

Variants	Assumptions regarding the actual prevalence and incidence figures[a]	Number of diabetic patients in 2005	
		Previous study[b]	Present 'update'[c]
Static model:	age and sex-specific prevalence constant	268,000	208,000
Dynamic model:			
- variant 1	age and sex-specific incidence constant	339,000	346,000
- variant 2	age and sex-specific increase in incidence of 0.3% per year	355,000	353,000
- variant 3	sustained increase in incidence of 1.1% per year (age-dependent) in 1990-2005 based on the actual increase in 1980-1990 (see Table 1)	-	385,000

a: In the previous forecasting study and the present 'update' the model-technical characteristics as well as the data on demography, life expectancy and recovery were identical. Source: Ruwaard et al. (7).

b: Based on actual prevalence and incidence figures from around 1980. The number of patients in 1980 amounted to 191,000. Source: Ruwaard et al. (7).

c: Based on actual prevalence and incidence figures from around 1990 (see Figure 1 and 2). The number of patients in 1990 amounted to 170,000.

Age-specific analysis revealed that the expected absolute and relative increase in the number of patients in the period 1990-2005 is most prominent in the age category 45-64 years (Figure 3). This applies to men as well as to women. In the dynamic model the number of patients for this age category in 2005 is about 2.6-3.2 times that of 1990 (depending on the variant chosen).

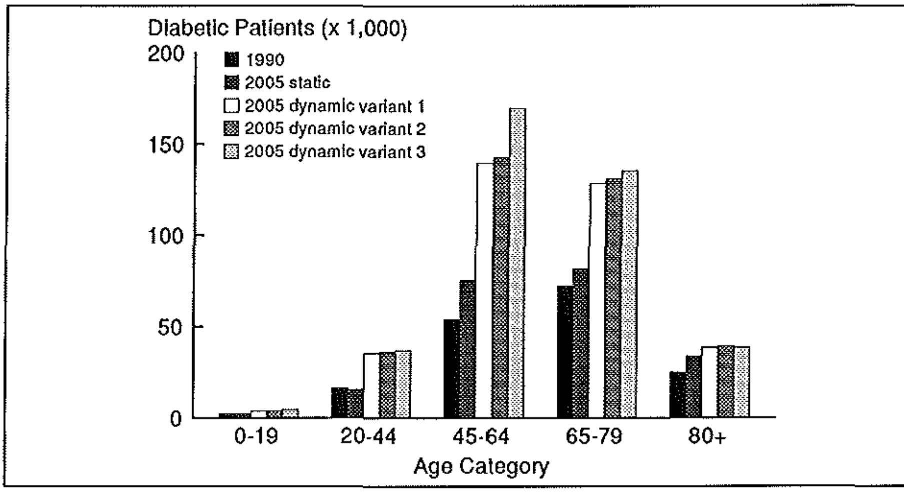

Figure 3: Age-specific prevalence of diabetes mellitus in 1990 and 2005, according to the static model and three variants of the dynamic model.

DISCUSSION

The objective of this study was two-fold: (1) to validate the previous model results and (2) to update the forecasts for the period up to 2005. The number of diabetic patients decreased from 191,000 in 1980 to 170,000 in 1990, while the previous study predicted an increase. This considerable discrepancy could not be explained by changes in the design of the Dutch Sentinel Practice Network. The network has been in operation since 1970 and the general practitioners who participate in it are not only highly motivated but also experienced in recording health problems. Most general practitioners have been participating for many years and about 66% of them are still involved after a ten year period (17). Unfortunately, the opportunity to correct for an undercount of cases by using an independent secondary source, as described by Bishop et al. (18) and by LaPorte et al. (19), was not available in the Dutch Sentinel Practice Network for both recording periods. On the other hand, in the most recent study all prevalent cases were recorded over a two-year period and the general practitioner received reviews of the patients recorded in order to avoid missing cases. Nevertheless a decrease in prevalence was found.

If the decline in prevalence is real then a decrease in incidence or in life expectancy or a considerable chance of recovery (or a combination of these) seem to be conceivable explanations. However, no decrease in incidence was found between around 1980 and 1990; rather there was an increase (13,14). A decrease in life expectancy as an explanation of the fall in prevalence during this period is not credible either, as there are no indications to support this. On the contrary, there is more reason to believe that life expectancy is on the increase, because deaths from cardiovascular diseases (an important cause of death among diabetic patients) are declining in the Netherlands (20,21). However, studies in England and Wales indicate that diabetic patients are not experiencing the same fall in cardiovascular mortality as that experienced by the general population (22).

In our previous forecasting study, the assumption was made that recovery does not occur. However, several recent studies in which an audit of diabetic care in general practice took place (23-27), indicated that a considerable number of previously-diagnosed diabetic patients did not meet the diagnostic criteria for diabetes formulated in 1985 by the World Health Organization (28). For instance, in the Continuous Morbidity Registration Nijmegen in the Netherlands, a total number of 427 patients were registered between 1967 and 1989 as newly-diagnosed diabetic patients by their general practitioner. In 111 cases (26%) the diagnosis could not be confirmed according to the 1985 WHO criteria (27). Cromme also established in Dutch general practice that in nearly 27% of the previously-diagnosed diabetic patients aged over 64 years and treated with diet or oral hypoglycaemic drugs, the diagnosis could not be reconfirmed with an oral glucose tolerance test when applying the 1985 WHO criteria. It were patients put on diet in particular, who were responsible for this considerable change (80%)(25). In addition, in a population-based survey of glucose intolerance among 2 468 subjects aged 50-74 years living in the Dutch town Hoorn, the diagnosis could not be reconfirmed in about 15% of all self-reported previously-known cases, reducing the prevalence in this group from 4.2% to 3.6%. The cases in whom the diagnosis could not be confirmed all used diet only and represented 57% of the total diet-treated group (29).

In order to find out whether these observations also contribute to the observed decrease in prevalence in the Dutch Sentinel Practice Network, we performed a questionnaire survey among the general practitioners. It appeared that from those who remembered their diagnostic behaviour (78%), the majority (62%) diagnosed diabetes less frequently after 1980 than before 1980. Of the general practitioners, 24% rechecked all known prevalent cases registered in 1980 resulting partly in 'recovery', whereas the prevalent cases in 1990 were all diagnosed according to the 1985 criteria. Because both in our recent and former study in the Dutch Sentinel Practice Network the way of treatment was recorded, we were able to check whether a decline in diet therapy could also be found. From those treated with diet or oral hypoglycaemic drugs, 43% and 25% used diet in 1980 and 1990, respectively.

The audit of diabetic care in general practice apparently resulted in a clearance of the diabetic register, in particular with regard to those treated with diet only. This clearance may be the result of a real recovery (e.g. by means of changes in lifestyle with consequent loss of weight) or may be due to changing diagnostic criteria. Although it is not possible to quantify the separate contributions of these possible causes, the effect of the changes in diagnostic criteria may have been largely responsible for the observed decrease in prevalence. The first time the World Health Organization (WHO) formulated diagnostic criteria was in 1965 (30), with subsequent revisions in 1980 (31) and 1985 (28). Although the 1980 and 1985 criteria do not differ much from each other, the diagnosis 'diabetes mellitus' based on the 1965 criteria is supposed to correspond roughly to the diagnosis 'diabetes mellitus including impaired glucose tolerance' according to the 1985 criteria (32,33). As many people in the Netherlands have impaired glucose tolerance (25,33-35), the changes in diagnostic criteria may have important consequences where the diabetic register contains a considerable number of these people. This kind of effect can be excluded for the observed change in incidence between 1980-1983 and 1990-1992, as the incidence figures in both studies are based on the 1980 and 1985 criteria, respectively (14).

The second objective of this study was to update the forecasts for the period up to 2005. As the 1990 prevalence was lower and the incidence higher compared with the 1980 data, the dynamic model is preferable to the static model to compute the expected number of patients (i.e. assuming no constant age and/or sex-specific prevalence in the period 1990-2005). The sharper increase in the number of patients in the first variant of the dynamic model in this 'update' reflects the greater discrepancy (disequilibrium) between the starting prevalence and incidence figures in 1990 compared to the 1980 figures used in our previous study, resulting in a quite similar number of patients in 2005 (see Table 2).

This first variant of the dynamic model assumes the 1990 age and sex-specific incidence to be constant over the period 1990-2005. However, there are no indications that the increase in incidence for type 1 diabetes found in the age category 0-19 years will stop, although the etiology remains obscure (13,36). The marked increase in incidence in the age category 45-64 is probably not caused by a real rise due to changes in exposure to risk factors, but due to an earlier recognition of symptoms and signs of diabetes followed by blood glucose measurements and/or to more intensive case finding in general practice (14). This is plausible because in line with the findings in the United States of America (37), it appeared that many individuals in the Netherlands also have undiagnosed diabetes (25,33-35). It is uncertain whether activities in general practice relating to diabetic care will continue at the 1990 level or will be further intensified. On the other hand, a continuous increase in incidence as a result of these activities is precluded because eventually most subclinical cases will have been diagnosed. Hence, the third variant may result in an overestimation over the years.

In view of the existence of a considerable number of undiagnosed diabetic patients (not only confined to the 45-64 year age category), the real number of known diabetic patients in the future very much depends on the policy for detecting the undiagnosed patients (e.g. by case finding or population-based mass screening programmes)(37). According to both most recently conducted population-based surveys of glucose intolerance in the Netherlands (around 1990) at least 50% of all diabetic patients aged 50 years and older are currently undiagnosed (34,35). Assuming that this is also applicable to those aged 20-49 (37), and all subclinical patients will have been diagnosed by 2005, then the estimate could be double that of the first variant, i.e. 700,000 patients. This seems unlikely however, because so far there is insufficient evidence that widespread population screening is cost-effective (38-40).

In addition, two other factors need to be mentioned that might influence the expected number of patients. Firstly, as a result of the changes in diagnostic criteria for diabetes, the life expectancy that is used in both forecasting studies is probably too optimistic because the data stem from three longitudinal studies conducted before 1980 (41-43). According to Panzram, mortality studies on diabetic populations initiated in the sixties and seventies have included a considerable percentage of patients with impaired glucose tolerance (44), who are expected to have a more favourable life expectancy. On the other hand, as already mentioned, the decline in death from cardiovascular diseases (an important cause of death among diabetic patients) in the Netherlands might also be beneficial to diabetic patients (20,21). Secondly, recent data indicate that the prevalence of obesity has been increasing among the Dutch population in the late eighties and early nineties with as a possible consequence a real increase in the incidence of diabetes over the years (45).

In order to successfully plan future health care for diabetic patients, one of the questions that needs to be answered is what the expected number of patients will be in the foreseeable future. Therefore, a model and valid epidemiological data on trends in the incidence, prevalence, recovery, and life expectancy are essential. In addition, awareness of possible developments in health care (such as changes in diagnostic criteria and case finding activities) and of changes in exposure to risk factors is also a necessary prerequisite to obtain reliable forecasts.

In conclusion, the number of known diabetic patients recorded in the Dutch Sentinel Practice Network decreased by 11% between 1980 and 1990. This is probably due to a clearance of the diabetic register in general practice. The incidence increased by about 12% between 1980 and 1990. All projections forecasted an increase in the number of known diabetic patients in the period 1990-2005 (23%-127%, depending on the variant chosen). However, the real extent of increase will very much depend on the policy for detecting undiagnosed patients. As diabetes is a disease with a major and increasing health and socio-economic impact, it is strongly recommended to update the projections on a regular basis as new figures (preferably validated by a secondary source) become available.

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CHAPTER 7

Changing occurrence of diabetes mellitus and implications for health policy: from a global to a national perspective

Submitted as:
Dirk Ruwaard[1], Edith J.M. Feskens[1], Harry Verkleij[1], Anton F. Casparie[2], Daan Kromhout.[1,3] Changing occurrence of diabetes mellitus and implications for health policy: from a global to a national perspective.

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ABSTRACT

The recognition of diabetes as a major public health problem and the notion that numbers of patients are expected to increase world-wide make the disease important for health policy and raise questions concerning the possibilities for influencing the expected increase by means of prevention, and the possible consequences for health care. Based on the current knowledge, as published in the international literature, an attempt has been made to answer these questions and to address the health policy implications of the findings at the national level.

Up to now, primary prevention of insulin-dependent diabetes mellitus (IDDM) has been confined to research without practical implications. To identify the determinants of IDDM, an important contribution can be made at the national level by joining the international network of childhood diabetes registries. Determinants of non-insulin-dependent diabetes mellitus (NIDDM) have been identified by epidemiological studies (overweight, physical inactivity and unhealthy diet), but there are few empirically-based published studies that have examined the effect of interventions on these determinants. Because there are many similarities between both diseases, the experience gained from the prevention of cardiovascular diseases can serve as an example for primary preventive strategies for NIDDM at a national level. As at least 50% of all patients are undiagnosed, a national strategy based on knowledge gained internationally is needed to formulate policy for detecting those individuals in a community and/or clinical setting. As the number of diabetic patients is expected to increase while increasing financial constraints are being placed on health care, more cost-effective ways to treat diabetic patients and to reduce the complications associated with the disease will need to be found.

In order to gain insight into the changing burden of diabetes and to determine the feasibility and effectiveness of intervention strategies, the disease needs to be monitored. Data from a national coordinated monitoring system (with several subsystems) can provide the input for health models designed to forecast future developments, which may be a valuable tool for underpinning health policy decisions.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder that represents a major public health problem. Over time, multiple chronic complications may occur, such as cardiovascular diseases (myocardial infarction, stroke), circulation disorders in the legs, blindness, kidney diseases and loss of sensitivity and/or pain in the limbs. As a consequence, both quality of life and life expectancy are reduced. Diabetes mellitus is therefore responsible for a substantial degree of health care utilisation (1).

During recent decades a great deal of effort has been expended to prevent and control diabetes mellitus at various levels. At a global level, this effort resulted in the landmark resolution on the *Prevention and Control of Diabetes* adopted in 1989 by the World Health Assembly (2). At the European level, the meeting organized by the World Health Organization (WHO) Regional Office for Europe and the European Office of the International Diabetes Federation (IDF) in 1989, with representatives of government health departments, patients' organizations and diabetes experts from all European countries, resulted in the *St Vincent Declaration Action Programme* (3). This programme, which provided the first official initiative to develop plans and policies for the improvement of diabetes care, was adopted by the WHO Regional Committee for Europe in 1991 (4). At the national and regional level, a number of professional and lay organizations have joined forces and WHO has published guidelines for the development and implementation of national diabetes programmes (5,6). Finally, at the patients' level, daily care provided by professionals reflects that effort. It is encouraging that many organizations and individuals are somehow involved in activities with the ultimate goal of preventing and controlling diabetes.

Despite all these efforts it is a source of concern that diabetes is a growing public health problem world-wide. Based on 250 prevalence studies recently conducted in various populations, McCarty and Zimmet roughly estimated that the global number of diabetic patients will increase from 110.4 million in 1994 to 239.3 million in 2010 (7). They emphasized that this result should be interpreted as a general indicator of diabetes frequency and will need to be revised as new and better data become available. Diabetes is also a growing public health problem in the Netherlands. Independent of demographic changes, it appeared that in the period between 1980-1990 the overall incidence increased by 12%. Age-specifically, the increase for those < 20 years and for those 45-64 years amounted to 23% and 31%, respectively (8,9). Moreover, it is expected that in the period 1990-2005 the number of known diabetic patients will increase by at least 23% as a result of demographic changes. Also, taking into account the initial imbalance between incidence and mortality which will become even greater if the observed increase in incidence of 12% continues during the period 1990-2005, an increase by 127% can be expected (10).

The recognition of diabetes as a major and growing public health problem raises questions concerning the possibilities for influencing the expected increase in the number of patients by means of prevention, and the possible consequences of the expected increase in terms of the burden on health care.

METHODS

Prevention and health care: definitions used

In health policy, a distinction is often made between primary, secondary and tertiary prevention on the basis of the natural history of a disease. In the literature, the definitions used to describe the various forms of prevention are not always identical. With respect to the prevention of diabetes we used the following definitions (11). *Primary prevention* covers activities aimed at preventing a disease from occurring (i.e. reducing the incidence) in susceptible individuals or populations through modification of environmental and behavioural risk factors/determinants, or specific intervention for susceptible individuals. *Secondary prevention* involves activities aimed at early detection of as yet undiagnosed cases of diabetes followed by treatment with the aim of reversing the condition and/or halting its progression. When a disease has already been diagnosed, any action to prevent it from getting worse or leading to disablement is a form of *tertiary prevention*. In this manuscript the term *health care* is used to address this tertiary form of prevention, to distinguish it from both other forms that may have a major influence on the number of patients. Figure 1 presents the definitions used here in relation to diabetes mellitus schematically.

It should be realised that primary prevention, secondary prevention and health care are closely related. During the natural course of a disease there is often a gradual transition from the healthy to the unhealthy or diseased state. To make a clear distinction between primary and secondary prevention for diabetes, blood glucose cutoffs above which diabetes is regarded as being present can be used (1). Preventive activities aimed at those who do not meet these criteria are basically primary preventive activities. In addition, there is also a close relationship between secondary prevention and health care. The result of secondary preventive activities will lead to an increased burden on health care, at least initially.

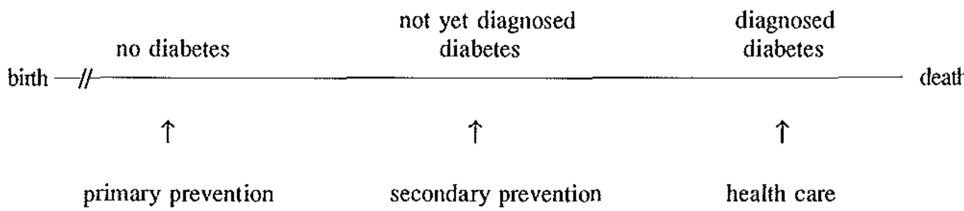

Figure 1: Schematic presentation of primary prevention, secondary prevention, and health care related to diabetes mellitus.
Source: adapted from Taylor et al., 1993 (12) according to the definitions used by WHO (11).
Note: this is not a linear time axis.

Approach

The observed and expected increase in the number of diabetic patients raises the question what the options are and what the policy is or might be to influence this increase by means of primary and/or secondary prevention. Knowledge about the epidemiology of diabetes (i.e. its determinants) is essential for effective implementation of preventive measures. A useful paradigm for developing a public health strategy for prevention consists of three phases: evidence from observational epidemiological studies (cross-sectional and prospective), evidence from intervention trials and finally, public health action (13). According to these phases, the meaning of primary and secondary prevention has been addressed for the two most common forms of diabetes, i.e. insulin-dependent diabetes mellitus (IDDM) and non-insulin-dependent diabetes mellitus (NIDDM)[1], by reviewing the current state of knowledge as published in the international literature. In this perspective, an attempt has been made to view the consequences of the changing number of patients for health care. Finally, the implications of these findings for health policy at a national level are discussed.

[1] IDDM represents about 10-20% and NIDDM about 80-90% of all diabetic patients (14,15).

PREVENTION AND IDDM

Determinants of IDDM

IDDM arises in genetically susceptible individuals who are exposed to putative environmental or exogenous triggers that may activate immunological mechanisms, leading to a progressive loss of pancreatic islet beta cells (16-18). The excessive glucose concentration stems from a lack of the hormone insulin (insulin deficiency), which is produced by the beta cells. The immunological and inflammatory mechanisms concerned have not yet been clearly defined. It is an insidious process which may occur over many years. During the 'pre-diabetic' stage of the evolution of the disease, individuals can often be recognized by the presence of immunological markers and a decline in pancreatic beta-cell function (19). Studies carried out on healthy children in the Dutch population have shown that in the presence of certain immunological markers, 50% of the children concerned develop IDDM within eight years (20).

The fact that *hereditary factors* play a role is apparent from studies of identical twins, which demonstrate a higher concordance rate for IDDM in monozygotic twins (25-40%) than in dizygotic twins (5-10%) (21-23). In addition, the overall risk of IDDM among whites in the United States of America is 0.2-0.4%, while the risk in siblings of probands with IDDM is about 5% and in the offspring of diabetic parents 2-3% (if the mother has the disease) and 5-6% (if the father has the disease)(23). The major genetic predisposition is conferred by genes located on the short arm of chromosome 6, either within or in close approximation to the major histocompatibility complex (24,25).

Viruses, such as mumps, rubella and coxsackie, are suspected exogenous determinants (26). It is thought that incidence peaks noted by some observers in autumn and early winter could be explained by the presence of viruses (27). In addition, there are indications that *diet* may also play a role. For example, breast-feeding could have a protective effect, while a high level of consumption of protein-rich foods and carbohydrates or nitrosamine-containing foods could increase the risk of IDDM (28-30). However, a recently published meta-analysis of 17 case-control studies showed that the increased risk of IDDM associated with early infant diet exposures is small and may be explained by methodological shortcomings (31). Quantification of the relative contribution of the different determinants has so far not been possible.

Primary prevention of IDDM

According to the determinants of IDDM, two ways of primary prevention can be distinguished: (1) by reducing exposure to the determinants and (2) by means of active intervention in the 'pre-diabetic' stage with pharmacological agents.

The results of genetic and epidemiological studies showed that at least 60% of IDDM world-wide is environmentally determined and thus potentially avoidable (32). However, as mentioned above, the determinants of IDDM are far from clear. The importance of cow's milk as an environmental trigger is the subject of research in a multinational, prospective, double-blinded trial in North America and Europe (33). In this Trial to Reduce the Genetically at Risk (TRIGR) about 5,400 newborn first-degree relatives of IDDM patients with high-risk genes will receive either a standard cow's milk baby formula or breast-feeding/non-antigenic protein hydrolysate until 6 months of age with a follow-up of 10 years to detect IDDM.

The second way requires active intervention in the 'pre-diabetic stage' in order to halt or reverse the auto-immune disease process. In particular two multinational, prospective, intervention trials should be mentioned. Firstly, the European Nicotinamide Diabetes Intervention Trial (ENDIT). In this trial conducted in Europe and North America, an estimated number of over 400 first-degree relatives of IDDM patients with high titres of islet cell antibodies will be randomly allocated to either a nicotinamide (free radical scavenger)-treated group or a placebo-treated group. In a second trial, the Diabetes Prevention Trial-Type I (DPT-I), over 800 relatives of IDDM patients with prediabetes according to immunological and metabolic markers will receive insulin in order to allow beta-cell rest and to encourage the development of antigen tolerance or will receive a placebo (33). In addition, several immune intervention studies in vitro, in animals and in high-risk persons or in newly diagnosed IDDM patients have been performed or are under consideration (34).

Currently, many questions remain unanswered as regards the most appropriate intervention to prevent diabetes as well as the individuals who should be targeted (on the basis of family history, genetic markers, immunological risk markers and/or metabolic risk markers). To identify individuals in any of the stages of prediabetes, massive screening efforts are required. However, not all individuals will eventually develop diabetes. For instance, first-degree relatives are at a 10-fold increased risk of developing IDDM, while the majority (95-97%) will not develop the disease (23). Besides, 85-90% of IDDM patients do not have a first-degree relative with IDDM. It will be some years before the results of ongoing trials become available, and newly emerging prevention strategies have still to be tested in large-scale, long-term and well planned clinical trials (11).

Secondary prevention of IDDM

The meaning of secondary prevention, as we defined it, might be of less importance in IDDM than in NIDDM. Once the disease becomes manifest with declining insulin production and increasing hyperglycaemia, symptoms develop rapidly and most cases come to medical attention in a period of days or weeks. Therefore, screening at this later stage is unnecessary as it would be impractical and as there is no sustained benefit in achieving diagnosis a few days early (35,36). The available experience with immunosuppressive therapy or nicotinamide therapy administered shortly after clinical diagnosis indicates that improvement of beta-cell function is not sufficient or longlasting. The onset of intervention comes too late in many cases, as 80-90% of the beta-cell mass are already destroyed at onset of the disease (34).

PREVENTION AND NIDDM

Determinants of NIDDM

Primarily, IDDM and NIDDM are clinically descriptive subclasses of diabetes. Whereas IDDM appears to be the result of an auto-immune disease process (i.e. a type I pathogenetic process), the etiology and pathogenesis of NIDDM is heterogenous.

Many patients with NIDDM and individuals with an impaired glucose tolerance (IGT) exhibit insulin resistance and hyperinsulinaemia in association with dyslipoproteinaemia, central obesity and hypertension. This cluster of cardiovascular determinants has been described by a number of names such as 'syndrome X' or 'Reaven syndrome' (37), the chronic metabolic syndrome, and the insulin resistance syndrome (38). The extent to which this cluster of determinants represents a single disease process is still unclear (39). Persons with a history of IGT and gestational diabetes are at increased risk of developing NIDDM. The rate of progression from IGT to NIDDM is about 2-3% per year in studies carried out in the UK and the USA, and the incidence of NIDDM in women with gestational diabetes is about 3-5% per year (40,41).[2]

Whereas IDDM is most commonly encountered at a younger age (< 20-30 years), NIDDM is a form of diabetes particularly associated with advancing age. Apart from *age*, *heredity* is currently considered as an important risk factor associated with NIDDM, apparently playing an even greater role than it does in IDDM. In the case of identical twins, a concordance rate of 95-100% for NIDDM can be found (21). The risk of developing NIDDM in individuals where one or both parents have NIDDM is almost three times as great as in those whose parents are free of the disease (43).

Irrespective of the presence or absence of the disease in the family, *overweight* increases the risk of the occurrence of NIDDM by a factor of two to three (44). There are indications that people must be overweight for some time before it becomes a risk factor for diabetes (45,46). Also the *distribution of fat* around the body is an important factor. Abdominally localised body fat (a 'paunch') imposes an additional risk (47).

Table 1: Relative risks of established determinants for NIDDM.

Determinant	Indicator	RR	Reference
Endogenous:			
genetic factors	1 or 2 parents with diabetes	2.9	43
body weight	BMI >25kg/m^2	2.5	44
	waist/hip ratio >1	2.5	47
Exogenous:			
physical activity	energy expenditure <2,000 kcal/week	1.7	43
nutrition	Guidelines for a healthy diet	0.7	44

BMI: Body Mass Index (weight (kg)/height^2 (m))
Note: for the risk of NIDDM in those with IGT and gestational diabetes, see text.

[2] In addition, there are indications that 10-20% of NIDDM is the result of an auto-immune disease process as found in IDDM (Latent Auto-immune Diabetes in Adults) and that 2-4% is the result of specific gene mutations (42).

It has been demonstrated that *physical inactivity* promotes the development of NIDDM (40,43). The composition of the *diet* is also a risk factor. In line with the 'Guidelines for a healthy diet' published by the Netherlands Nutrition Council in 1986 (48), the consumption of high-fibre foods and unsaturated fatty acids at the expense of foods rich in saturated fatty acids is encouraged to prevent NIDDM (44). To what extent *alcohol use* and *smoking* are independent determinants for NIDDM is still unclear. The results of several studies on alcohol use (49-54) as well as smoking (52-57) are contradictory. Table 1 summarizes the relative risks of established determinants for NIDDM.

Primary prevention of NIDDM

As with IDDM, two ways of primary prevention can be distinguished: (1) by reducing exposure to the determinants and (2) by means of pharmacological intervention in those with IGT (which can be viewed as a 'pre-diabetic' stage).

As overweight, physical inactivity and the composition of the diet are established determinants, behavioural interventions such as restricting caloric intake, reducing dietary saturated fat and increasing physical activity may be beneficial in diabetes prevention. These measures are probably most usefully applied to high-risk individuals (those with a positive family history, with elements of the chronic metabolic syndrome, with a history of gestational glucose disturbances, changing from traditional to Westernized lifestyles, from rural to urban societies or from active to sedentary lifestyles). In addition to the high-risk approach, a population-wide approach which aims to modify lifestyles by introducing health education programmes is strongly recommended in societies susceptible to NIDDM (41).

Based on the results of 11 cohort studies on overweight and the incidence of NIDDM, it can be estimated theoretically that prevention of overweight as indicated by BMI $\geq$25 kg/m^2 could result in a reduction of 10-60% of the incidence of NIDDM, with an intermediate value of about 30% (44). As regards physical activity, it has been estimated that 25% of NIDDM in the USA can be attributed to physical inactivity (58). As the majority of NIDDM cases appear to be lifestyle related, it is potentially preventable through the pursuit of a healthy way of life. In order to prove this, intervention studies are needed.

No large-scale studies have yet been published that prove that a healthy lifestyle intervention can prevent NIDDM (42). The feasibility of behavioral interventions for the prevention of NIDDM has been demonstrated in Malmö, Sweden, in a study of two groups of middle aged men with IGT (59). Those in the treated group (n=161) were given physical training and advised to reduce sugar and fat, increase complex carbohydrate and fibre in the diet, and lose weight if they were overweight. The treated group showed a significant weight loss, most of which was maintained for 5 years, whereas the reference group did not (n=56). After 5 years, 11% of the treated persons and 21% of the reference group had developed diabetes according to the WHO criteria. This study demonstrated the feasibility of a 5-year diet exercise programme. However, the effect of treatment remains uncertain because those involved were not assigned randomly to the treated or reference group. Fortunately, the preliminary results of a successful diet and exercise intervention have recently been reported (60). A total of 530 subjects with IGT were randomized into four groups; a control group without intervention, a diet-only intervention group, an exercise-only intervention group and a group receiving diet and exercise treatment. The cumulative incidences after a follow-up of 6 years were 15.7%, 10,0%, 8.3% and 9.6% in those four groups, respectively. The results indicate that diet and/or exercise intervention treatment are effective methods for reducing the incidence of NIDDM.

It should be realised that these positive results are based on a trial among people with IGT. Hopefully, these results will be confirmed in other intervention studies and also apply to such high-risk groups outside of a trial or even in the general population. However, it is well known that (sustained) weight reduction is hard to achieve. Despite activities to promote health in the general population (regarding weight control, physical activity and healthy diet) it is a matter of concern that an increase in the mean BMI and the prevalence of obesity (BMI $\geq 30 kg/m^2$) has been observed in the Netherlands in the late eighties and early nineties, and for a longer period in several other countries (61).

The second way of primary prevention is by means of oral antidiabetic drugs normally used in the treatment of NIDDM. As these drugs are known to stimulate insulin secretion and/or insulin action and/or to inhibit intestinal glucose absorption, the potential for preventing NIDDM in IGT subjects had been studied in three randomised trials (62-64). Unfortunately, the summary cumulative incidence rate ratio (active drug/placebo) was 0.9 (95% CI: 0.6-1.5) suggesting that the active treatment had little or no effect (65).

Secondary prevention of NIDDM

Several secondary preventive activities can be distinguished, such as community screening and case finding (i.e. clinical screening). Community screening involves the application of a screening test to individuals in the population or a part of it in order to determine whether a certain disease might be present, prior to the appearance of clinical signs or symptoms (66). Although case finding also targets asymptomatic persons, it focuses on individuals rather than the population. A person who consults a physician for a certain health problem will also be examined for the presence of other diseases if that person is thought to be at increased risk. In addition, such individuals might also be detected by routine examinations (67,68).

In the Netherlands there appeared to be a highly age-specific increase in the incidence of diabetes (31%) for those aged 45-64 between 1980-1990, which is probably due to earlier recognition of the signs and symptoms of diabetes and more intensive case finding in general practice (9). This is plausible because several Dutch studies revealed that many individuals have undiagnosed disturbances in their glucose metabolism (69-72). In line with findings in the United States of America (73), roughly 50% of all diabetic patients are undiagnosed.

In accordance with pronouncements in the literature (74), the Dutch Steering Committee on Future Health Scenarios was cautious about the establishment and administration of large community screening programmes for NIDDM (75). In 1990 the Committee recommended instead to explore the possibilities of case finding in general practice among persons above 50 years of age with obesity and/or a positive family history of NIDDM and/or the existence of complications that might be attributable to diabetes.

Opinions on the value of mass screening have changed frequently over recent decades. In the sixties and seventies it was widely recommended. In 1978 the Diabetes Screening Workshop in Atlanta, Georgia, proclaimed that screening to detect diabetes should not be encouraged, except during pregnancy. Evidence of benefits did not outweigh the evidence of adverse effects, whereas the cost of screening was not justified (76). Are there now more valid reasons for mass screening to detect NIDDM?

To decide whether screening programmes in general are worthwhile, a number of criteria have been formulated, which can be summarized as follows: the disease should be an important health problem; there should be an accepted treatment and an agreed policy on who to treat as patients; there is a recognizable latent or early symptomatic stage of the disease and the prognosis should be better if the disease is diagnosed and treated early, as opposed to late or never; an appropriate screening test which is acceptable to the population should be available; facilities for diagnosis, treatment and follow-up should be available and the costs should be justified by the benefits, and finally; the screening programme should be a continuing process and not a 'one-off' exercise (77).

It is established that NIDDM represents a major clinical and public health problem for which there is an accepted treatment with an agreed policy on who should be considered as patients according to the WHO criteria (1). As stated earlier, roughly 50% of all diabetic patients are undiagnosed. It appeared that the onset of NIDDM may occur 9-12 years before clinical diagnosis (78). Besides, there is a great deal of evidence that micro and macrovascular complications begin to develop before clinical diagnosis. For instance, diabetic retinopathy is estimated to become evident approximately 7 years before diagnosis of NIDDM (78). Retinopathy and nephropathy appeared to be present in 10-29% and 10-37% of clinically-diagnosed NIDDM patients, respectively (78-85). In general terms, macrovascular disease and macrovascular determinants are as frequent in undiagnosed NIDDM as in established NIDDM and twice as high as in non-diabetic individuals; they are even present before the real onset of diabetes, namely in the stage of impaired glucose tolerance (86-90). Moreover, it was observed that the adverse effect of diabetes on coronary heart disease is enhanced disproportionately when macrovascular disease determinants (i.e. risk factors) are present (91,92).

Finally, it has been demonstrated that mortality in individuals with undiagnosed NIDDM is at least as frequent as in those with established NIDDM and significantly higher than in non-diabetic individuals. In the 11-year follow-up of the Paris Prospective Study, mortality was 23%, 20% and 9% in undiagnosed diabetic persons, established diabetic patients and in non-diabetic individuals, respectively (93), and in the 15-year follow-up of the Whitehall Study, the mortality rate per 1000 person-years was 40, 27 and 12, respectively (94). The higher mortality in the undiagnosed compared with established patients may be due to a lack of treatment or insufficient treatment of associated determinants, such as hypertension and dyslipidaemia, as the majority of patients died of macrovascular disease. For instance, it appeared from the Hoorn Study in the Netherlands that 14% of all established NIDDM patients with hypertension were untreated, while in those cases which remained undiagnosed the proportion was 31% (90). It is therefore indisputable and also in line with the criteria for screening, that NIDDM is characterized by a preclinical period with the presence of both micro and macrovascular complications and an increased risk of morbidity and mortality.

There was less agreement regarding the criterion that the prognosis is better if the disease is diagnosed and treated early than rather late or never (74). The difference of opinion focused primarily on the glucose hypothesis, i.e. whether it is possible or not to decrease the risk of the development and progression of diabetic complications by lowering blood glucose concentrations. In the meantime, two randomized clinical trials have clearly demonstrated that intensive treatment improves glycaemic control and decreases the incidence rates and rates of progression of *microvascular* complications in IDDM patients (95,96). Although these trials are restricted to IDDM patients, it is widely believed that the results support the hypothesis that hyperglycaemia is causally related to these complications (97-102). In that case, lowering glycaemia in NIDDM patients will also be beneficial.

Nevertheless, some investigators are still cautious about applying the results of the IDDM trials to NIDDM. The impact of the side effects of the intensive therapies based on oral medication or insulin necessary to achieve normoglycaemia in patients with NIDDM (such as hypoglycaemia, weight gain, increased risk of cardiovascular events) is unknown (103). However, there are indications that intensive therapy may be accompanied by a very low rate of severe hypoglycaemia and without significant weight gain (104). Besides, available clinical trials have not so far confirmed the fear that insulin increases the risk of macrovascular events in individuals with NIDDM (105-108). Therefore, the most important research question relating to metabolic control in NIDDM is now whether glucose control prevents or delays *macrovascular* disease in patients with NIDDM (109). Hopefully the Veterans Affairs Cooperative Study (104) and the UK Prospective Diabetes Study (110) on glycaemic control and complications in NIDDM will shed more light on this crucial issue.

On the other hand, it would be unfortunate to restrict the discussion of screening for NIDDM to the benefits and side effects of glycaemic control only. As mentioned earlier, micro and macrovascular complications and several determinants are already evident in the preclinical period. Evidence strongly indicates that early detection of NIDDM and intervention with diet, weight control, exercise and treatment for hypertension and dyslipidaemia will improve the prognosis in NIDDM (99). In addition, earlier detection of complications, such as retinopathy, followed by adequate treatment (coagulation therapy) will certainly improve the quality of life by preventing blindness.

This approach will help focus the discussion more on questions such as who, where, when, and how to screen for NIDDM (depending on the distribution of the prevalence in the population and available resources) rather than waiting for evidence to decide whether mass screening for NIDDM would be beneficial. Harris and Modan (99) conclude that screening for NIDDM is an important measure for promoting health. In community screening programmes where considerations of cost and efficiency are important, restricting screening to individuals who are obese and/or hypertensive might be considered. In the clinical setting, it is important to incorporate periodic screening for diabetes into routine follow-up of at-risk patients (i.e. case finding). In addition, Knowler believes screening is clearly indicated for asymptomatic individuals with conditions often associated with diabetes, such as micro and macrovascular complications and their determinants, for whom diagnosis and treatment of diabetes would help in the management of these complications (100).

The available screening tests for NIDDM include questionnaires, biochemical screening tests and a combination of both. The validity of these tests (sensitivity, specificity, positive predictive value) has been reviewed by Engelgau et al. (111). However, the proper choice for a certain test or combination of tests will depend on the selected approach (community screening or case finding) and the available resources. The use of a risk-assessment questionnaire seems reasonable. In the community setting, a capillary glucose measurement is easily performed and can produce reasonably good results when adjusted for the postprandial period and age of the person being screened. Screening for urine glucose, fasting glucose, and glycosylated hemoglobin tend to lack sensitivity. In the clinical setting, postprandial venous glucose adjusted for the postprandial period and age may be reasonable. Harris and Modan endorse the OGTT (a single 2-hr post-challenge glucose measurement) as the primary screening method because the complexity of this test is more than balanced by its sensitivity, specificity and positive predictive value (99).

In conclusion, up to now there is insufficient evidence to indicate the value of mass screening of asymptomatic individuals. However, several organizations have made recommendations for community screening among high risk groups or in a clinical setting (11,35,36,112-114), although the performance of the strategies has yet to be quantitatively evaluated. Operational research is needed to define more clearly the question as to who should be screened, when, where, and how screening should be carried out and the effectiveness of such screening programmes, taking into account the available resources. The results of that research will provide insight into possible consequences as regards the burden on health care (see also below).

CONSEQUENCES FOR HEALTH CARE

Health care for diabetes encompasses a broad spectrum of activities (ranging from glucose control by diet and antidiabetic medication with appropriate education to detection of determinants and complications followed by adequate treatment) provided by a range of health care professionals, such as the general practitioner, the internist, the paediatrician, the diabetic nurse, the dietician, the podotherapist, and the ophthalmologist.

All these activities place a heavy burden on health care and health care costs. The proportion of estimated total health care cost related to diabetes is 3.6% in the United States of America and 4-5% in the United Kingdom (115). Recent data suggest that in the United States of America the costs of diabetes care are rising rapidly (116-118). In the Netherlands the health care costs for diabetes are estimated to be about 1% (119,120) of total health care costs. However, this estimate only represents the costs incurred when diabetes is the primary diagnosis. As diabetes mellitus is often involved in other health problems (micro and macrovascular diseases), this figure underestimates the real health care costs (121,122), and taking this into account, the health care costs in hospitals attributable to diabetes are about twice as high in the Netherlands (123).

The expected increase in the number of patients makes the disease important not only for prevention but also for planning future health care and allocating health care costs. At first sight, it seems plausible that an increase in the number of patients will increase the burden on health care and costs by an equivalent amount. However, results from empirically-based studies do not confirm this. For instance, in the Netherlands it appeared that between 1980 and 1991 the number and duration of hospital admissions due to IDDM among those < 20 years decreased more than 30% and nearly 55%, respectively (124), while an increase in incidence of 23% was noted in the same period (8). Apparently, there is a shift from costly in-patient to relative inexpensive out-patient care, probably due to improved care, diabetes education and self-management. Therefore, these kinds of health care developments as well as the policy of reducing budgets and capacity and increased productivity need to be taken into account and may be responsible for changes in the burden on certain health care provisions and health care costs (125-129).

As stated earlier, the real extent of the increase in diabetic patients expected over the next decades will very much depend on the policy for detecting undiagnosed individuals. This raises the question whether these earlier diagnosed patients have a different health status that needs more or less health care than those not detected by screening. Determinants for complications as well as the prevalence of macrovascular complications in undiagnosed NIDDM are very common and are as frequent as in diagnosed NIDDM. However, some of these patients may already be receiving medical attention because of these determinants and complications without being aware of the existence of diabetes. Hence, the burden on health care will not increase as much as expected. If the detected patients are treated adequately as early as possible, it is believed that their health status will be less impaired in the long run compared with patients who were diagnosed and treated several years after the age at onset. As a consequence the burden on diabetes health care may eventually decrease.

In conclusion, it is not easy to foresee what the burden on health care will be in the near future as a result of changes in the occurrence of diabetes. It is very likely that the number of patients will increase, irrespective of developments in the field of primary prevention. However, in addition to the number of patients, changes in the health status (as a result of possible secondary preventive and health care activities) as well as developments in health care (such as a shift from in-patient to out-patient treatment, the policy of reducing budgets and capacity, and increased productivity) will influence the burden on health care and the concomitant costs for diabetes.

IMPLICATIONS FOR HEALTH POLICY AT THE NATIONAL LEVEL

The recognition of diabetes as a major public health problem and the notion that IDDM and NIDDM will become even more prominent in the future makes the disease important for health policy. World-wide, a great deal of research focused on finding tools for preventing and controlling diabetes. What are the implications of the results of this research for health policy at the national level?

Two ways to prevent IDDM from occurring have been described: (1) by reducing exposure to the determinants and (2) by means of active intervention in the 'pre-diabetic' stage with pharmacological agents. Up to now, primary prevention of IDDM is still confined to research without practical implications. Some large multinational trials are under way. Although it seems likely that pharmacological interventions may contribute to the prevention of IDDM in the future, epidemiological studies designed to search for determinants need to be encouraged. At the national level, an important contribution can be made by joining the international network of childhood diabetes registries (WHO Multinational Project for Childhood Diabetes (WHO DIAMOND))

(130). Observed differences in incidence over time and between countries will be helpful in the search for environmental determinants for IDDM.

As regards the two ways of primary prevention for NIDDM, there is some cause for optimism. In contrast to IDDM, determinants for NIDDM have been identified by epidemiological studies. Unfortunately, few empirically-based studies have been published that examine the effect of interventions on the established determinants with regard to the development of NIDDM. Therefore, additional clinical trials are needed to test this possibility. Meanwhile, the experience gained from the prevention of cardiovascular diseases can serve as an example for primary preventive strategies for NIDDM (131). In line with the recommendations of the WHO (132), the Dutch National Diabetes Platform encourages an integrated approach to the primary prevention of NIDDM (by means of health promotion related to lifestyle), together with other non-communicable diseases with common determinants, such as cardiovascular diseases (133). Whether pharmacological interventions can prevent NIDDM is unknown. The results from the few trials that have been performed are not encouraging.

Internationally, several organizations have made recommendations for community screening among high risk groups or in the clinical setting to detect as yet undiagnosed patients with NIDDM (11,35,36,112-114). It is unlikely that universal guidelines on secondary preventive strategies will be established because the distribution of high risk groups, the resources available, and the existing health care structures differ from country to country. It is therefore strongly recommended that a national strategy be established, based on knowledge gained internationally. The implementation has to be taken place in such a way that the results can be evaluated in order to define more clearly the who, when, where, and how of screening and the effectiveness of screening programmes in a community and/or clinical setting. The development of all kinds of different local programmes to detect diabetic patients without proper evaluation of costs and health benefits, should be avoided.

Although it is not easy to foresee what the burden on health care will be in the near future, it is very likely that the number of patients will increase while financial constraints in health care are becoming increasingly evident. Therefore, considerable efforts will be needed to find more cost-effective ways to treat diabetic patients and to reduce the complications associated with the disease. It is encouraging that representatives from all European countries have agreed on the five-year 'St Vincent' targets for reducing complications caused by diabetes (3). To evaluate progress towards these targets, it is necessary to assess the current situation and to follow the rate at which complications develop. Unfortunately, reliable data are still lacking in most countries, including the Netherlands.

It is quite clear that several kinds of developments have influenced and will continue to influence the disease, possibly with important consequences. In order to gain accurate and up to date insight into the relative importance of these developments for the necessary health care facilities and costs, and to determine the feasibility and effectiveness of intervention strategies, it is essential to improve or start monitoring of the disease.[3] Although activities in this field have started in several European countries (136), including the Netherlands (137,138), there is a need for central coordination at the national level to set up a coherent monitoring system based on those sub-systems that already exist and new ones that need to be developed. As diabetes is often accompanied by other diseases (comorbidity), an integrated approach to monitoring activities is recommended. Data from such a monitoring system can provide the input for health models designed to forecast future developments, which may be a valuable tool for underpinning health policy decisions (139-147).

A great deal of effort from all parties involved in reducing the heavy burden of diabetes is needed to make well-considered decisions with the help of monitoring and modelling. For the Netherlands, a key role can be played by the Netherlands Diabetes Federation, in which the parties involved in diabetes care and research have joined together in 1995 (148). Just as the results of world-wide research activities as well as efforts from WHO have been of great help for the development and implementation of national programmes to prevent and control diabetes, experience gained at the national level may be helpful to other countries wishing to combat the global threat of diabetes.

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[3] Health monitoring is defined here as the continuous collection, analysis, interpretation and dissemination of data on individuals or groups to detect the occurrence of certain events and their putative causes for the purposes of planning and evaluating of interventions (adapted from Foege et al., 1976 (134), and Thacker et al.,1988 (135)).

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CHAPTER 8

General discussion

In this thesis the occurrence of diabetes mellitus in the Netherlands, the changes in recent years and possiblė future developments have been described. Based on the current knowledge published in the international literature, the likely implications of these developments for health policy at a national level have been addressed. Following a brief recapitulation of the main finding as presented in Chapters 2-7, this chapter focuses on some methodological considerations regarding the validity of the selected sources (to assess the occurrence of diabetes), the trend data, and the future projections. In this light, the importance of monitoring diabetes as well as the health status of the population in general will be discussed in order to improve the availability and use of epidemiological data for health policy purposes. Finally, conclusions will be drawn.

MAIN FINDINGS

The incidence among 0-19 year-olds was based on a questionnaire survey conducted among all Dutch paediatricians and internists, while the Dutch Sentinel Practice Network was used to estimate the incidence from age 20 onwards and the prevalence for all age groups. As both studies were conducted around 1980 and repeated around 1990, changes over a ten-year period could be obtained. It appeared that the overall incidence of diabetes mellitus had increased significantly. Age-specifically, this increase could be attributed to a statistically significant increase in the age groups 0-19 and 45-64 years, respectively. Although the causes for the increase in the youngest age group are unknown, the increase in the older age group is probably due to earlier recognition of the signs and symptoms of diabetes followed by blood glucose measurements and/or to more intensive case finding in general practice. However, the prevalence of diabetes for those 20 years and older had decreased significantly during the same period. Apparently, the audit of diabetic care in general practice may have resulted in a clearance of the diabetic register which in particular may be the result of changing diagnostic criteria.

Two forecasting studies examined the possible future developments in the occurrence of diabetes mellitus until 2005. The first study forecasted the number of patients during the period 1980-2005 based on the incidence and prevalence data from around 1980, whereas in the second study the data from around 1990 were used for the period 1990-2005. Both studies revealed that the number of diabetic patients will increase considerably. However, in view of the existence of a considerable number of undiagnosed diabetic patients (at least 50%), the real number of known diabetic patients in the future very much depends on the policy for detecting these patients (e.g. by case finding or population-based screening programmes).

The recognition of diabetes as a major public health problem and the notion that it will become even more prominent in the future makes the disease important for health policy. Up to now, primary prevention of IDDM has been confined to research without practical implications. To identify the determinants of IDDM, an important contribution can be made at the national level by joining the international network of childhood diabetes registries. Determinants of NIDDM have been identified by epidemiological studies (overweight, physical inactivity and unhealthy diet), but there are few empirically-based published studies that have examined the effect of interventions on these determinants. Because there are many similarities between both diseases, the experience gained from the prevention of cardiovascular diseases can serve as an example for primary preventive strategies for NIDDM at a national level. As at least 50% of all patients are undiagnosed, a national strategy based on knowledge gained internationally is needed to formulate policy for detecting those individuals in a community and/or clinical setting. As the number of diabetic patients is expected to increase while increasing financial constraints are being placed on health care, more cost-effective ways to treat diabetic patients and to reduce the complications associated with the disease will need to be found. In order to gain insight into the changing burden of diabetes and to determine the feasibility and effectiveness of intervention strategies, the disease needs to be monitored.

METHODOLOGICAL CONSIDERATIONS

The validity of the selected sources for assessing incidence, prevalence, remission and mortality

Incidence and prevalence

Two surveys were chosen from 18 wherein the incidence and/or prevalence of diabetes mellitus had been examined during the period 1971-1987 (Chapter 2). Both have since been repeated, which made it possible to observe changes over time. As we were particularly interested in the burden on health care in the Netherlands, the following basic principles were applied to choose the most appropriate sources: the data should represent clinically-known patients and not those as yet undiagnosed, and they should be representative for the Dutch population as a whole in terms of age, gender, degree of urbanization and geographical variation.

The incidence among 0-19 year-olds was assessed twice retrospectively (in 1978-1980 and in 1988-1990) by a *questionnaire survey conducted among all Dutch paediatricians and internists* (Chapters 2 and 3). To obtain incidence estimates that are less prone to chance, the survey was not only nation-wide but also lasted three years. To correct for an undercount of cases, the Dutch Diabetes Association was used as a secondary source for ascertainment. The overall rate of ascertainment (defined as the proportion of responding patients from the Dutch Diabetes Association who were also reported by the specialists) was 88% and 81% in the two studies, respectively. However, age-specific analysis revealed that the rate of ascertainment was relatively low for the age category 15-19 (79% and 55% in the first and second survey, respectively) in contrast with the age category 0-14 years (89% and 90%). Apparently, the primary source (the specialists) used to assess the incidence for those aged 15-19 years was rather poor and a substantial correction of incidence is needed because of ascertainment bias. As the majority of all patients aged 15-19 had been recorded by internists and the rate of ascertainment for internists was worse than that of paediatricians (a total of 75% and 94% in the first versus a total of 54% and 91% in the second study, respectively), the internists in particular seemed to be less reliable as a primary source. Therefore, the application of the capture-recapture census method by using a secondary source for ascertainment is strongly recommended in these kinds of studies (1-4).

The incidence (especially from age 20 onwards) and the prevalence of clinically-known diabetes were also assessed twice (around 1980 and 1990) in the *Dutch Sentinel Practice Network* (Chapters 2, 4 and 6). In the Netherlands, general practices are a very useful source for gaining insight into the morbidity patterns of the population. In the Dutch health care system everyone has their own general practitioner, who operates as a 'gatekeeper'. This implies that health problems will first be presented to the general practitioner and that no patient will visit a specialist without being referred by his or her general practitioner. In addition, the specialist informs the general practitioner about clinical or policlinical findings (such as diagnosis and laboratory results). However, it should be emphasized that the morbidity patterns registered in general practice specifically reflect the health problems presented by those who make an appeal to the health care system. Hence, those who have undiagnosed diabetes will be missed and people living in institutions for a long time (e.g. nursing homes) and relying on institutional doctors will also be missed. This may result in an underestimation of the incidence and prevalence when diabetes is relatively more prominent among such people.

To obtain valid incidence estimates which are less prone to chance, a sufficiently large population is needed. The Dutch Sentinel Practice Network, consisting of about 1% of the Dutch population, has the largest denominator of all Dutch continuous morbidity registrations in primary care. Nevertheless, the incidence has been recorded for several years in both periods to increase the denominator even more. Although the incidence data found in the Dutch Sentinel Practice Network are likely to be reliable (the network has been in operation for a long period of time and the general practitioners who participate in it are not only highly motivated but also experienced in recording health problems), a few cases might have been missed at the end of the recording period because of a delay in transferring information from the specialist to the general practitioner.

In contrast with the nation-wide retrospective study to assess the incidence among 0-19 year-olds, a secondary source for validating the incidence and prevalence in the Dutch Sentinel Practice Network was lacking. To make use of the Dutch Diabetes Association as a secondary source would be problematic. The Sentinel Practice Network represents only 1% of the total population instead of 100% in the nation-wide retrospective study, and the majority of the members of the Dutch Diabetes Association represent young IDDM patients while in general practice most patients suffer from NIDDM. It would be more efficient to send a questionnaire to all those belonging to the general practices to gain information about self-reported incidence and prevalence. However, a basic premise of the capture-recapture census method is that the secondary source must be independent of the first one. This is not possible as the general practitioners would need to be involved in such an activity at the same time as they were recording the patients. A third possibility that has been considered is to make use of prescription data from pharmacies. As a nation-wide central drug database of pharmacy dispensing histories is not available in the Netherlands (5), the Sentinel Stations are distributed all over the country, and several pharmacies are involved per station, we rejected this option. However, if such a nation-wide central database were available and valid, it would be very cost-effective to validate morbidity registers in cases of diseases for which drug prescription is applicable. Such a central database could even be used as the primary source. With regard to diabetes, this applies to IDDM patients using insulin and NIDDM patients using insulin or oral hypoglycaemic drugs, but not to NIDDM patients treated with diet only. Based on the results of the second study in the Dutch Sentinel Practice Network, approximately 20% of all prevalent patients were treated with diet only.

When the most recently obtained incidence (1990-1992) and prevalence data (1990) from the Dutch Sentinel Practice Network are compared with those obtained from other studies conducted in general practice among all ages around 1990, the incidence as well as the prevalence is low in the Practice Network (Table 1).

Table 1: Incidence and prevalence of diabetes mellitus (per 1,000 for all ages) according to studies conducted in general practice around 1990.

Study	Period	Population[a]	Location	Incidence[b]	Prevalence[b]	Source
DSPN[c]	1990-92	140,000	Netherlands	1.5	11.3	thesis
RNH-Limburg	1994	63,000	Limburg	1.9	24.9	6
CMR-Nijmegen	1987-91	12,000	Nijmegen	2.2	19.4[d]	7
Transition Project[e]	1985-88	41,000	Neth./Antilles	2.4	11.2	8,9
National Survey[f]	1987-88	83,000	Netherlands	3.5	-	10
sub-project NS	1988	24,000	S-E Netherlands	-	12.3[g]	11
Reenders	1987-88	42,000	Hoogeveen	-	14.5	12
Verhoeven	1987	12,000	Heerde	-	19.0	13

a: rounded numbers.
b: except for the sub-project of the National Survey and Reenders, all incidence and prevalence figures are standardized to the Dutch population of 1990.
c: Dutch Sentinel Practice Network.
d: Continuous Morbidity Registration Nijmegen; prevalence is the mean of the known cases recorded per year during the period 1987-1991.
e: recording period per general practice is one year.
f: 332,000 persons were followed for 3 months.
g: sub-project of the National Survey; prevalence is 7.0 when patients are removed who did not meet the criteria for diabetes or for whom the diagnosis was not clear.

In general, it is known that differences in morbidity rates between studies conducted in general practices can be ascribed to discrepancies in the objectives, the design, the definition of the numerator (such as diagnostic criteria), the extent and definition of the denominator and the length of the recording period (14). For instance: the Dutch Sentinel Practice Network is specially designed to obtain incidence and prevalence figures in primary practice, while other registrations focus more on recording medical consumption and/or include uncertain diagnoses. Despite the fact that most studies are too small to obtain reliable incidence data for diabetes, some factors may be particularly responsible for the observed differences in the incidence and prevalence of diabetes. The general practitioner's behaviour for detecting as yet undiagnosed diabetic patients may be of great influence on the recorded incidences, as over 50% of all patients have undiagnosed diabetes (15-18). Another important factor that may exert considerable influence on the recorded prevalences is the number of false positive cases. In some studies, an audit of diabetic care even resulted in a clearance of the diabetic register by around 25% (15,19)(see also under the heading 'Remission' below).

As a consequence, a high detection rate for undiagnosed patients by means of case finding in a general practice in which an audit did not take place will result in a much higher prevalence compared with the prevalence assessed in a general practice which has been audited and has a low detection rate for undiagnosed patients. Unfortunately, these kinds of developments could not be disentangled quantitatively in the Dutch Sentinel Practice Network. As the contribution of these influencing factors may vary between different studies (and even within one study on different occasions), it is very difficult to validate the results of one study with those of others without having quantitative information about these influencing factors (see also the section on 'Trend data' below).

Remission

At the time we conducted the background study (Chapter 2), it was decided to assume that no remission takes place. Information about the chance of remission was lacking and in so far as real remission takes place (e.g. by means of losing weight) these 'patients' will remain under a certain degree of medical supervision. However, recent studies indicate that as a result of an audit in general practice a considerable number of diabetic patients do not meet the 1985 WHO criteria for diabetes mellitus (Chapter 6). This clearance of the diabetic register may be the result of a real recovery (e.g. by means of changing lifestyle with loss of weight) or may be due to changing diagnostic criteria. Although it is not possible to quantify the separate contributions of these possible factors, the effect of changing diagnostic criteria may have been largely responsible for the observed decrease in prevalence in the Dutch Sentinel Practice Network (see the section on 'Trend data' below).

Mortality

For the purposes of making future projections, it was decided that the reduction of life expectancy as identified in studies from other countries provides a more reliable measure of the outflow from the diabetic population than the Dutch causes of death statistics (Chapter 2). Besides, data on life expectancy provides additional information when compared with mortality data, because the duration of diabetes is also included. However, it is not clear to what extent these life expectancy data also apply to the

Dutch diabetes population. In addition, as a result of the changes in diagnostic criteria for diabetes, the life expectancy that is used is probably too optimistic because the data stem from three longitudinal studies conducted before 1980 (20-22). According to Panzram, mortality studies on diabetic populations initiated in the sixties and seventies have included a considerable percentage of patients with impaired glucose tolerance (23), who are expected to have a more favourable life expectancy. On the other hand, the decline in death from cardiovascular diseases (an important cause of death among diabetic patients) in the Netherlands (24,25) might also have benefitted to diabetic patients in terms of life expectancy.

Trend data

In order to gain insight into possible changes in the occurrence of diabetes mellitus, both the survey among all Dutch paediatricians and internists as well as the survey in the Dutch Sentinel Practice Network have been repeated with a similar design 10 years later. However, it should be understood that neither survey recorded data on a continuous basis, which means that two points in time are compared whereas data regarding the period in between are lacking. It is therefore not possible to conclude that the incidence of IDDM among the age category 0-19 is rising continuously. However, from combining the incidence studies with the previous study that reported the increase of IDDM in the 1960-1970 birth cohorts of 18 year-old male army conscripts, a sustained increase of IDDM in the Netherlands is suspected (26).

The same uncertainty applies to the significant increase in incidence observed in the age category 45-64 when comparing the first (1980-1983) and second study (1990-1992) in the Dutch Sentinel Practice Network. It cannot be ruled out that the increase in incidence may have started in the late eighties or early nineties. In fact, this seems rather plausible, as the level of incidence very much depends on the behaviour of the general practitioners for detecting the undiagnosed persons. Recently, general practitioners have become very aware of diabetes mellitus as a public health problem for several reasons:

1. in 1988 the Dutch College of General Practitioners published its standard for diabetes mellitus type II (i.e. NIDDM)(27);
2. in 1988-1990 the Steering Committee on Future Health Scenarios emphasized the phenomenon of underreporting diabetes mellitus and the importance of the disease as a major and growing cause of prolonged ill health and premature mortality and recommended exploring the possibilities of case finding in general practice among

people over 50 with obesity and/or a positive family history of NIDDM and/or the existence of complications that might be attributable to diabetes (28);
3. since the early nineties evidence from several Dutch studies has been accumulating that many individuals in the Netherlands also have undiagnosed disturbances in glucose metabolism (15-18,29), and in view of these reasons;
4. the study by itself may have influenced the general practitioners' behaviour with regard to detecting as yet undiagnosed patients, although this does not guarantee a sustained behavioural change.

To interpret the decreased prevalence observed between 1980 and 1990 numerous developments need to be taken into account that influence incidence, life expectancy and remission. Changes in exposure to determinants for diabetes, changes in diagnostic criteria or the accuracy of confirming the diagnosis as well as changes in policies for detecting as yet undiagnosed patients may have influenced the incidence. Changes in diagnostic criteria as well as improvements in health care may have influenced life expectancy, whereas changes in diagnostic criteria as well as an audit in general practice may have influenced the extent of recovery. Unfortunately, these different kinds of developments could not be disentangled quantitatively in the Dutch Sentinel Practice Network (see also under the heading 'Incidence and prevalence' above).

Future projections

It is beyond dispute that valid data are needed to make future projections. However, as mentioned earlier, there is variation in the incidence and prevalence data when comparing different studies and reliable Dutch mortality data are lacking. This should be kept in mind when interpreting the future projections. They do not predict the number of patients in the true meaning of prediction, but explore possible future developments according to the assumptions made.

Historic validation and sensitivity analysis
Two validation procedures have been performed to analyze the stability of the dynamic model (Chapter 5). That is, whether the data on incidence, prevalence and reduction of life expectancy due to diabetes mellitus and the assumption of no remission result in a state of relative equilibrium of the dynamic model.

The first validation procedure was a historic simulation of the number of prevalent cases between 1955 (specific demographic data before 1955 are lacking) and 1980, assuming time-independent (i.e. constant) relative incidence and reduction of life expectancy to forecast the 1980 absolute numbers. We compared the calculated prevalent number of cases with the 1980 data. The historic simulation showed a 10% higher prevalence in 1980 than the empirical numbers. This difference is statistically significant and seems plausible; the incidence in 1980-1983 which has been used throughout the whole simulation period may be too high, as an increase in incidence has been reported in the literature (26,30-33). Real trend data on incidence, life expectancy and remission are needed to validate the model characteristics, but these data are lacking.

The second validation procedure was a sensitivity analysis. We analyzed the impact on the forecasted prevalent number of cases in 2005 of variations in some main model parameters, i.e. the 1980 prevalence, incidence or reduction of life expectancy data for diabetic patients (Chapter 5). The sensitivity analysis revealed that the dynamic model is most sensitive to variations in incidence and moderately sensitive to variations in life expectancy. The dynamic model was relatively insensitive to variations in prevalence. This is obvious as all prevalent patients at the onset will have died in the long run. This finding has been confirmed in the forecasting 'update' study (Chapter 6). Despite a lower starting prevalence in 1990 in the 'update' study, the number of diabetic patients in 2005 is in accordance with the findings of both corresponding variants in the first forecasting study as a result of a higher starting incidence in 1990. This implies that in particular the incidence data (as well as the life expectancy data) needs to be valid to make future projections. The validity of these data has been discussed earlier (see the section on 'The validity of the selected sources....' above).

Limitations of the dynamic model used

The dynamic model used focuses on making future projections regarding the number of diabetic patients. However, this is only a first step towards a useful model for health policy purposes. Extensions of the model are necessary in two directions. Firstly, determinants for diabetes need to be incorporated to simulate possible effects on the incidence of diabetes. Secondly, disease stages with their characteristics (such as concomitant exposure to determinants and complications) need to be incorporated to simulate the 'natural' course of diabetes and the possible effects of clinical interventions to enhance quality of life and life expectancy. The outcomes of such an extended model may be of great help in planning future health care, as it not only takes into account the number of patients anticipated, but also takes account of their health status.

So far, the proposed extensions of the model are limited to diabetes as a major public health problem per se. However, diabetes mellitus cannot be regarded separately, because it shares common determinants with other diseases such as coronary heart disease (e.g. unhealthy diet, physical inactivity and overweight) whereas diabetes itself is accompanied by determinants (such as hyperglycaemia, hypertension, dyslipoproteinaemia and overweight) for macrovascular diseases, such as coronary heart disease, cerebrovascular accidents and peripheral vascular disease and for microvascular diseases (such as nephropathy and retinopathy, including neuropathy). Therefore, an integrated approach is needed to judge the benefits of interventions when there are competing causes of morbidity and mortality. Work has started on developing such a model. However, up to now the most important limitation has been the lack of valid data.

FROM EPIDEMIOLOGY TO HEALTH POLICY

As described in the Introduction of this thesis, epidemiology has two main functions in the policy cycle:

1. to provide data which can be used in the *preparation of new policy*, and;
2. to provide data which can be used to *evaluate current policy* (see Figure 1 in Chapter 1).

Despite the fact that the choices that need to be made in health policy are social or political in nature, the availability of data from epidemiological research should actually play a crucial role in underpinning decision-making. In addition, a mathematical model in which the data can be incorporated may serve as an important tool for predicting possible future developments and assessing the effects of health interventions.

Health policy is defined here as the actions of government, doctors and other players who aim to maintain and improve the state of health of individuals and the population. This ultimate goal can be subdivided according to the form of intervention. A widely used distinction is that of primary and secondary prevention and health care which is known as tertiary prevention (see Chapter 7 for definitions). As not everyone working in the field of prevention and health care will be involved in all these activities it should be realized that in order to make the data useful for health policy purposes they should be made available to those responsible for the different kinds of intervention. For instance, health care providers will be more interested in the health status of their patients in order to control the quality of care or to evaluate health care interventions, while community workers will focus more on the health status of the total population and group interventions. Besides, health care planners will be more interested in possible changes in the need for health care.

Diabetes mellitus: from epidemiology to health policy

The results of this thesis indicate that diabetes mellitus is a growing public health problem in the Netherlands. It appeared that in the period between 1980 and 1990 the overall incidence increased significantly for IDDM as well as for NIDDM. Besides, it is expected that in the period 1990-2005 the number of known diabetic patients will increase considerably. These epidemiological findings raise questions for health policy concerning the possibilities for influencing the expected increase in the number of patients by means of prevention, and the possible consequences of the expected increase in terms of the burden on health care. Answers to these questions are presented in Chapter 7.

With regard to health care policy, it is worth mentioning that representatives of government health departments and patients' organizations from all European countries met with diabetes experts under the aegis of the WHO Regional Office for Europe and the International Diabetes Federation European Region in St Vincent, Italy in 1989. They unanimously agreed on general goals and five-year targets aimed at creating conditions in which a significant reduction in this heavy burden on health can be achieved (34). With respect to complications, the five-year targets are:
1. to reduce new blindness due to diabetes by one third or more;
2. to reduce new end-stage diabetic renal failure by at least one third;
3. to reduce by one half the rate of limb amputation for diabetic gangrene;
4. to cut morbidity and mortality from coronary heart disease in diabetic patients by vigorous programmes of risk factor reduction and;
5. to achieve pregnancy outcomes in diabetic women that approximates that of non-diabetic women.

However, to evaluate progress towards the targets of the St Vincent Declaration, it is necessary to assess the current situation and to follow the natural course of the disease and the rate at which complications develop. Unfortunately, reliable data are still lacking.

Because of the lack of valid data, it was decided for this thesis to restrict the subject to the occurrence of diabetes in the Netherlands and its developments over time. The dynamic model used focuses on future projections regarding the number of diabetic patients. However, this is only a first step if it is to be useful for health policy purposes. Monitoring the disease in its different aspects is urgently needed to make proper decisions and to evaluate the effect of policy decisions and interventions (see below).

Monitoring diabetes mellitus

It is quite clear that several kinds of developments have influenced and will continue to influence diabetes mellitus, possibly with major consequences. However, in order to gain accurate and up to date insight into the relative importance of these developments for the necessary health care facilities and costs, and to determine the feasibility and effectiveness of intervention strategies, it is essential to improve or start monitoring of the disease. Health monitoring is defined here as the continuous collection, analysis, interpretation and dissemination of data on individuals or groups to detect the occurrence of certain events and their putative causes for the purposes of planning (i.e. policy preparation with subsequent policy development and implementation) and evaluating of interventions (35,36)(see Figure 1 in Chapter 1).

To ensure that the data gathered is brought to the attention of those responsible for making health policy decisions, the different aspects to be monitored can be subdivided chronologically according to the various forms of health policy interventions, i.e. primary prevention, secondary prevention, and health care (see Figure 1 in Chapter 7). For instance, monitoring determinants and disease incidence are related to primary prevention, whereas monitoring the ratio diagnosed/undiagnosed diabetes is related to secondary prevention and monitoring complications is related to health care. To disentangle the influence of several kinds of developments, a coherent monitoring system (with several subsystems) needs to be set up, which links outcome-specific data with prevention and control programmes. Attention should not only be paid to sustaining or improving current monitoring of the incidence, prevalence and mortality of diabetes, but also to setting up new monitoring systems to gain insight into the changing consequences of the disease for health status (such as the existence of complications). A few elements (or subsystems) that need to be considered as essential components of such a coherent monitoring system for diabetes are briefly summarized below.

Monitoring determinants for diabetes mellitus

In order to gain insight into possible future changes in the incidence of diseases, monitoring determinants in the population may be very helpful. With regard to NIDDM, it is essential to monitor changes in weight, physical activity and the composition of the diet. An example of such a monitoring system is the project 'Monitoring Risk Factors and Health in the Netherlands', in which a combined health interview survey and a health examination survey is conducted annually among 5,000 persons aged 20-59 (37). For those under 20, the 'Child Health Monitoring System' which is also conducted annually among 5,000 individuals in the Netherlands, is a useful source in this respect (38). Unfortunately, such a monitoring system for those above 60 years of age is lacking. Monitoring the entire age range including an interview survey combined with a health examination survey would be of great value.

However, it should be realized that additional information (such as the relative risk and time-lag) from national and international epidemiological research is needed to transcribe the impact of changes in 'exposure' to these determinants on the incidence of NIDDM for modelling purposes. Examples of such population-based cohort studies in the Netherlands are the Hoorn Study (17,39) and the Rotterdam Study (40). In addition to these cohort studies, follow-up studies linked to current monitoring systems are also useful for obtaining additional longitudinal-based information (41).

Monitoring the incidence and prevalence of diabetes mellitus

To obtain reliable incidence figures that are not prone to chance, the incidence of IDDM among youngsters needs to be examined in the Netherlands at a national level. Sample surveys would be less appropriate because of their lack of statistical power. Both incidentally performed retrospective studies among all paediatricians and internists have been replaced since 1993 by a continuous prospective registry among all Dutch paediatricians to assess the incidence of IDDM among children (42). This registry will eventually also provide the prevalence data (cumulative incidence), as the disease is chronic and mortality is low (and can be corrected for). Joining the international network of childhood diabetes registries (WHO Multinational Project for Childhood Diabetes (WHO DIAMOND)) is worthwhile (43). Observed differences in incidence over time and between countries may be helpful in the search for environmental determinants for IDDM.

In the Netherlands, but also in other comparable countries, the incidence of diabetes above 14 or 19 years can best be recorded by the general practitioner. General practices here provide a very useful source for gaining insight into the morbidity patterns of the population for reasons which have been mentioned earlier (see the section 'The validity of the selected sources....'). Attention should be paid to the sample size. In our two studies of general practice several years were combined to assess the incidence more reliably. In order to disentangle the causes of possible changes in incidence in general practice, it is recommended to record the reason for encounter when the diagnosis of diabetes is made (such as symptoms, case finding or routine examination). However, it should be emphasized that the morbidity patterns registered in general practice specifically reflect the health problems presented by those who make an appeal to the health care system. In order to find out the changing diagnosed/undiagnosed ratio, part of a continuous morbidity registration (physician-diagnosed cases) should be linked both in time and on an individual level with intermittently performed population-based (screening) surveys. In addition, it is recommended to audit the register intermittently to find out whether or not patients 'recovered' from their disease. The prevalence can be assessed intermittently, but eventually the prevalence can be derived from the cumulative incidence minus those who recovered from diabetes and those who died.

The importance of a secondary source for ascertainment to correct for an undercount of cases and the significance of using a central drug database as a primary source to assess the occurrence of diabetes has been discussed earlier (see the section 'The validity of the selected sources....').

Monitoring the course of diabetes mellitus

In order to judge whether certain targets (such as those agreed on in the St Vincent Declaration with regard to reduction in complications) will be achieved by means of adequate health care, it is necessary to be informed about the existence of complications among diabetic patients and their appearance over time. From this perspective it should be mentioned that the changing occurrence of complications may not only be dependent on the health care provided. Besides, it is likely that the effects of activities in the field of secondary prevention will not be confined to changes in the number of patients, but that the health status of the patient may also alter (see Chapter 7). Hence, monitoring characteristics of the diabetic population, such as the mode of treatment, the glucose levels, and the complication status is necessary.

Although this information can be obtained from a relative small number of patients involved in population-based cohort studies (such as the Hoorn Study (39) and the Rotterdam Study (40)), the Dutch National Diabetes Platform started a project with the aim of exploring the possibilities for setting up a longitudinal and standardized diabetes monitoring system in the Netherlands (44,45), with the WHO/IDF-Diabcare basic information sheet as its point of departure (34,46). According to this sheet, data such as therapy, glucose levels, the presence of determinants, symptoms and complications need to be gathered. Such a registry, linked with a registry to monitor the occurrence of diabetes, will be of great value to guard and improve the quality of care and will offer possibilities for research activities (intervention and evaluation studies). Activities aimed at gathering data at a local level, sending them to a central node for analysis, and providing feedback have been started at both a European and a national level (47).

Monitoring death and diabetes mellitus

As mentioned earlier, the national mortality statistics are not suitable for assessing mortality among diabetic patients. For that purpose we decided in our study that the reduction of life expectancy as identified in studies from other countries provides a more reliable measure of the outflow from the diabetic population. As life expectancy is not expected to be stable over time and may vary between countries, such studies are still needed at a national level. However, national data from causes of death statistics could provide the necessary information if a 'multiple-cause' encoding procedure were to be introduced. This implies that the presence or absence of diabetes should be recorded on all death certificates, as has also been recommended for monitoring the targets of the St Vincent Declaration Action Programme for Europe (34).

Although some activities in the field of monitoring diabetes have been started in the Netherlands, there is a need for central coordination to set up a coherent monitoring system based on several (sub)systems which already exist and others which need to be developed. A key role can be played by the Netherlands Diabetes Federation, in which the parties involved in diabetes care and research have joined together in 1995 (48).

From diabetes to an integrated approach: monitoring health in the population

For several reasons diabetes has to be put in a broader perspective. Diabetes shares common determinants with other diseases and is itself a determinant for other diseases. Taking into account these interrelationships, the effect of interventions can be estimated more accurately. For instance, losing weight in overweight individuals is not only beneficial for diabetes but also for coronary heart disease. Therefore the total public health effect will be underestimated if the outcome (decrease in incidence) is confined to diabetes.

However, it should be realized that overweight is just one determinant for both diseases, with the consequence that by decreasing weight the onset of disease may only be postponed. As life expectancy is likely to increase because of preventive activities, people will be exposed to other diseases which might otherwise not have occurred. Hence, the phenomenon of competing morbidity and mortality also needs to be taken into account (49). Therefore, not only the effect of certain interventions for a specific disease itself, but also for related diseases as well as for diseases which are not primarily related, need to be taken into account in order to make well-considered decisions. The epidemiological transition clearly showed a rapid fall in infectious diseases with an increase in life expectancy unmasking chronic diseases (50). Therefore, a so-called 'episystems' approach which investigates the processes and patterns of several diseases instead of one could lead to important insights and will certainly be important for forecasting future diseases in populations (51,52). This approach was also the reason that in successive monitoring projects in the Netherlands, the number of determinants and the number of chronic diseases to be monitored have been increased (37).

In addition, diabetes needs also to be put in a broader perspective from a financial point of view. In recent years it has become increasingly evident that financial constraints dictate choices in health policy. The crucial question is then how and in what areas the greatest health gain (i.e. to live lives which are as long and as healthy as possible) can be achieved with the available resources. This ultimate aim of health policy distinguishes two elements: extending life expectancy ('adding years to life') and improving the quality of life or health expectancy ('adding life to years'). The relationship between life expectancy and health expectancy can be illustrated with the help of Figure 1.

This Figure presents a survival curve (calculated for Dutch males for 1990) in which the fraction of the relevant birth cohort still alive is given at each age (the outer curve). The inner curve ('health curve') gives the percentage of the cohort which is in good health at each age; the difference between the curves (the shaded area) gives the hypothetical percentage which is in poor health. For females the survival curve lies further to the right, since women live on average more than 6 years longer than men (in 1990 the life expectancy of males and females was 73.8 and 80.1 years, respectively). On the other hand, the inner curve probably does not vary significantly from that for males. The benefit that females have with respect to total life expectancy is thus spent primarily in ill-health (53). When life expectancy is extended, the survival curve becomes more rectangular (compression of mortality), whereas narrowing of the shaded area between the curves results in a compression of morbidity.

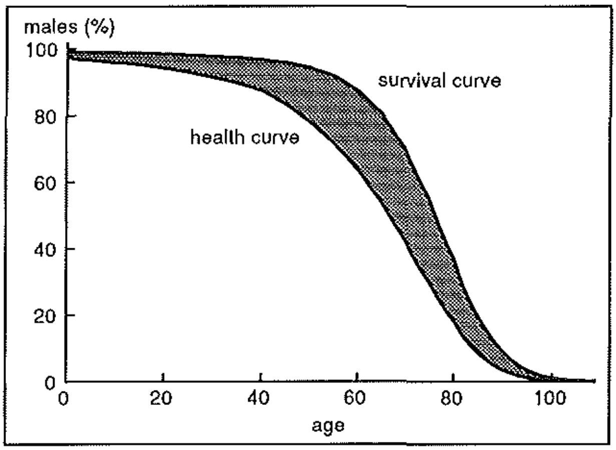

Figure 1: Survival curve in 1990 (calculated) and 'health curve' (hypothetical) for Dutch males according to age.
Source: Ruwaard et al., 1993 (53); adapted from Manton and Soldo, 1985 (54).

From this perspective, four questions are relevant for health policy to make well-considered decisions from an integrative viewpoint:

1. Which specific health problems largely determine life expectancy (survival curve) and the unhealthy period within it (shaded area)?
2. Which determinants are responsible for these health problems?
3. What are the expectations in this regard in the years ahead?
4. What are the possibilities for improving both life expectancy and the unhealthy period?

In order to answer these questions a great deal of information is needed. An attempt to do so for Dutch society has been made in the project 'Public Health Status and Forecasts. The health status of the Dutch population over the period 1950-2010'. The basic conceptual model of this project is illustrated in Chapter 1 (Figure 2). In Figures 2 and 3 below the basic model is shown in more detail for the indicators of health status and for the determinants, respectively. A more detailed description of these elaborated submodels with their different layers is given in a report on this project (53).

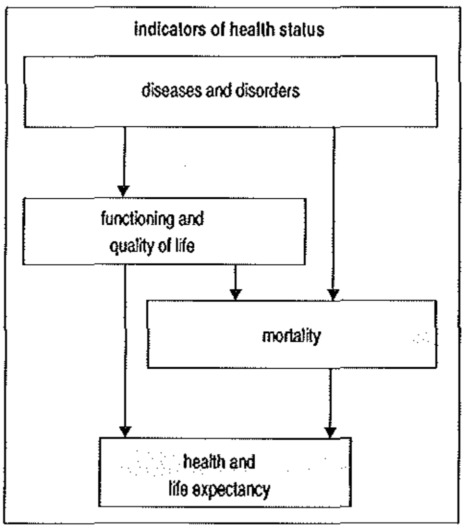

Figure 2: The conceptual model elaborated for the indicators of health status.
Source: Ruwaard et al., 1993 (53).

A large number of experts contributed to this project in order to quantify health problems and health risks by using all kinds of existing health monitoring (including surveillance) and health information systems. Ultimately, these contributions have been used as building blocks to integrate the material (i.e. looking at 'things in context') in order to answer the questions listed above and to be helpful for health policy purposes. It appeared that despite the fact that a great deal of information is available in the field of public health in the Netherlands, there are also particular shortcomings.

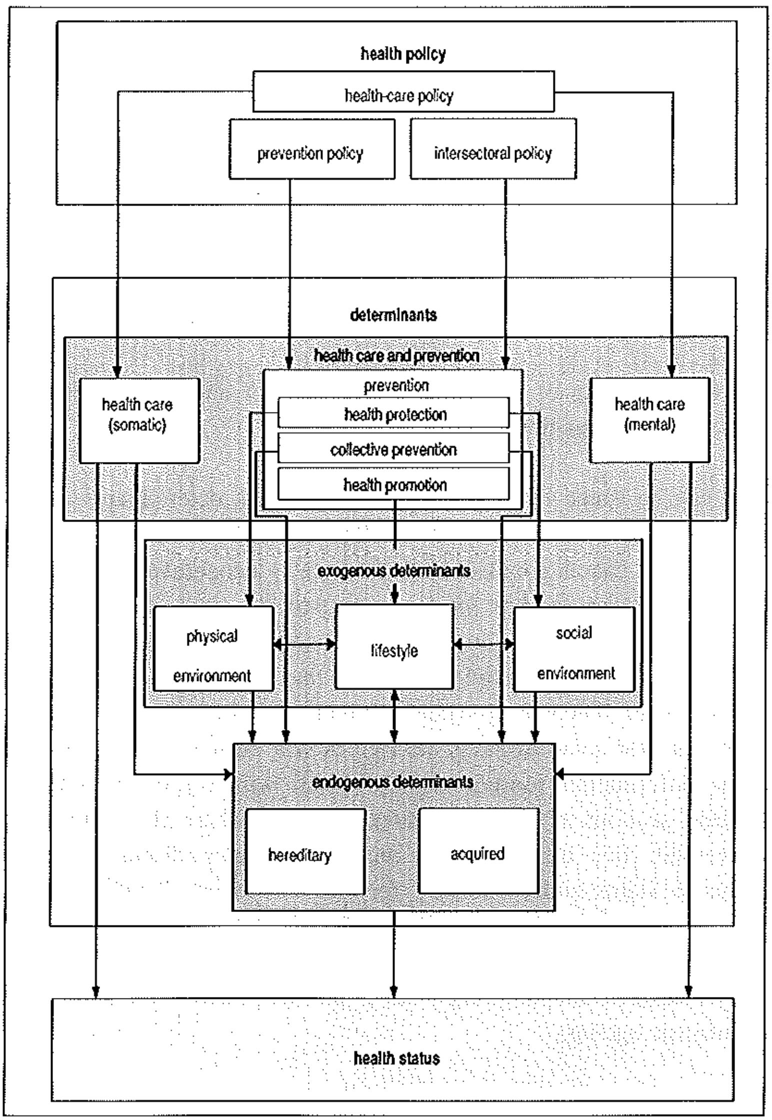

Figure 3: The conceptual model elaborated for the determinants.
Source: Ruwaard et al., 1993 (53).

On the basis of the questions raised and the conceptual model used, five levels of information needs can be distinguished. These levels differ in that they require more and more *coherent use of data*, which means that increasing demands are made on the quality and structure of data. The levels are:

1. *recording the situation at a specific point in time for individual* indicators of health status and determinants;
2. *recording trends over time for individual* indicators of health status and determinants (comparability of data over time);
3. *simultaneously recording series of different* indicators or determinants (direct comparison and assessment of combinations);
4. *describing relationships* between various indicators, between indicators and determinants, and between various determinants (linking different layers of the conceptual model);
5. *making forecasts* with the help of modelling (integration of data both within and between the layers and also over time).

With regard to (1) it can be stated that, for most indicators and determinants, data is available on the current situation. This information often falls short, however, as far as its representativeness of the Dutch population as a whole is concerned. Data on the incidence and prevalence of diseases has for the most part not been collected at the population level. Exceptions are the data on IDDM and cancer. The data for incidence and prevalence has mostly been approximated on the basis of data obtained from general practitioners or other 'encounter' records, which only contain the *presented morbidity*. This means that for some diseases the figures will be underestimations (e.g for NIDDM). Various information sources also fall short with respect to both the youngest and the oldest sections of the population, and also where the residents of institutions are concerned. For the indicators and determinants discussed in the document 'Public Health Status and Forecasts', for various reasons insufficient data was available. This is the case, for example, with mental disorders and their determinants. A number of determinants were also dealt with as a broad group, because of a lack of an easily measured unit (e.g. exposure to physical factors, the state of the immune system, or intrinsic ageing).

As far as (2) is concerned, quantitative data on *trends over time for individual indicators and determinants* is only available for mortality over the whole period 1950-1990. For certain indicators and determinants, information is indeed available over a shorter period. This trend data comes from regional sources more often than data used to describe the situation at a specific point in time. The reason for this situation is the limited number of monitoring systems which have been in operation for a fairly long time. Recently, an increase in regularly repeated or continuously recorded data has been noticed. Where monitoring has taken place, the data collected has sometimes proved to be of limited use because of changes in the definitions and measuring instruments used. Such changes may be prompted by new insights, which does not alter the fact that, for the sake of continuity, efforts must be made towards standardisation and the comparability of procedures and definitions over time.

With regard to (3), *comparison* of data on individual indicators or determinants certainly appears to be possible where only a single source is involved, for example general practitioners' records, surveys, or specific investigations in which several indicators and/or determinants are measured simultaneously. In this way, the occurrence of combinations of indicators and determinants at the personal level can also be investigated. It often proves difficult to compare data from different sources because of (sometimes minor) differences in the design of the study or the definitions used.

As regards (4), information on *relationships* between diseases and their determinants does not generally come from recording systems but from cohort studies aimed at identifying the causes of diseases. There is still a considerable lack of clarity here, for example with respect to the determinants of many chronic, non-life threatening disorders of a somatic or mental nature. There is also too little data available on the consequences of diseases and disorders for functioning and the quality of life in the somatic, psychological or social sense ('impact'), and likewise on the non-disease specific relationships between determinants and quality of life. This means that the link between the occurrence of diseases and the significance of these for the 'unhealthy years of life' can hardly be made. Only for the indicators 'invalidity' and 'sickness leave' and, to a limited extent, for self-rated health is any insight into the share of underlying (groups of) diseases obtained from records and surveys.

Finally, as regards (5): through *modelling* of all the types of data mentioned (incidence/ prevalence of diseases and disorders, quality of life, mortality, past trends, trends in the determinants concerned, and interrelationships), this document essentially strives to make *forecasts* by estimating expected changes in health status and the effect on these of possible interventions. A modest start has been made with this in the project 'Public Health Status and Forecasts'. It will be clear that all the shortcomings in the areas discussed earlier accumulate here and reinforce each other.

To sum up, it may be said that the ideal monitoring system for providing information for a forecast should have the following features:
- determinants and indicators of health status are recorded for all layers of the conceptual model;
- recording takes place in a nationally representative way, which also offers insight into the distribution over various sections of the population;
- the recording of data is regularly repeated over time;
- linking of individual data is attempted as far as possible.

As long as the wide-scale standardized application of smart cards in health care remains a dream for the future (55,56), a significant step towards achieving a more appropriate health information system may be accomplished by improving the links between existing health interview surveys, epidemiological monitoring programmes, general practitioners' records, nation-wide health care and insurance systems, and statistics on causes of death.[1] However, it would be disappointing if privacy legislation would hinder research activities and the optimal use of data in order to get insight into the possibilities to improve life expectancy and the unhealthy part of it (57).

A stepwise approach for tuning monitoring and information systems in order to answer the above-mentioned questions is urgently needed. After it has been decided what kind of information is necessary (58, amongst others), an extensive inventory of the existing monitoring and information systems needs to be available (59). Validation of these systems according to the five levels of information requirements is important to judge whether they are appropriate or need to be adapted.

As a general practitioner operates as a 'gatekeeper' in the Netherlands, general practice is potentially a very useful source for gaining insight into the morbidity patterns of the population. A continuous morbidity registration of sufficient power in general practices distributed all over the country, combined with intermittent health interviews and health examination surveys and linked with other nation-wide health care and insurance systems would be of great value. This would substantially meet the requirements of an ideal monitoring and information system mentioned above. For instance, this will provide information on a continuous or regular basis about the Dutch population in

[1] In most cases the information needed to provide a firm basis for aetiological relationships and to enable model simulations of developments over time to be made cannot be obtained from registration systems; here, cohort studies are needed, which involve the follow-up of groups of people over time. In addition to these cohort studies, follow-up studies linked to current monitoring systems are also useful for obtaining additional longitudinal-based information.

terms of comorbidity as well as self-perceived health while the physician-based health status is also known. The flexibility of the system required to anticipate current health policy issues can be guaranteed by surveys performed intermittently. The National Information Network of Primary Care which is currently being developed, may be used for that purpose (60). As regards NIDDM, the essential elements to be monitored, as mentioned earlier, can be incorporated in this approach. Although such a core system would be of great value, other systems will still be necessary (e.g. registry for IDDM (42) and cancer (61). However, possibilities for harmonising these systems need to be considered.

To be successful in setting up a coherent monitoring and information system that will be useful for health policy, special attention should be paid to the following issues:
- All parties involved (i.e. the data suppliers as well as the users) need to be convinced of the necessity of such an approach. Thacker and Stroup stated that the major barriers to a successful comprehensive, nation-wide, integrated public health surveillance and information system are a lack of appreciation for the value of high-quality provisional surveillance data and a weak societal commitment to public health (62).
- Major prerequisites if the system is to be useful are that it (1) is flexible and offers an infrastructure for incorporating new important health policy questions and (2) reports all requested findings to those involved in making health policy decisions in a timely manner. Therefore, a well-organized method of data collection, central analysis as well as dissemination of the results by telecommunication systems are all necessary. An example of such a surveillance system is the recently developed Infectious Diseases Surveillance Information System (ISIS) for the Netherlands at the National Institute of Public Health and the Environment (63).
- As regards data collection, standardized measuring methods for each data element are essential to facilitate analysis and comparison with data collected in other systems. Although additional assurances of confidentiality and privacy considerations will be required, the ability to link data to other systems will be of great value for an integrative approach.

The principles and practice of public health surveillance and health information systems in the United States are described in detail in the literature (36,62,64).

It should be realized that a great deal of effort from all parties involved is needed to answer the crucial question as to how and in what areas the greatest health gain (i.e. to live lives which are as long and as healthy as possible) can be achieved with the available resources. A prerequisite is the existence of a coherent monitoring and information system. This implies national cooperation and the willingness to cut across disease boundaries. International exchange of experiences in this field (e.g with the Centers for Disease Control (36,62,64), and the World Health Organization (65,66)) is strongly recommended. Outside the direct area of health, such as in the field of environmental outlooks (67,68) and weather forecasts (69), exchange of experience regarding monitoring and forecasting at a local, national and international level can also be beneficial.

CONCLUSION

The results described in this thesis indicate that a considerable increase in the number of diagnosed diabetic patients can be expected. This notion makes the disease important for health policy. For several reasons (e.g. regarding the validity and availability of data, and possible developments in preventive and health care policy) it is not easy to foresee what the exact number of patients and the concomitant burden on health care and costs in the near future will be. In order to make more accurate forecasts and to support policy preparation as well as policy evaluation, the disease and its determinants need to be monitored.

However, it would be inappropriate to confine monitoring to diabetes alone, as changes in the occurrence or course of diabetes may influence other related and even unrelated diseases (competing morbidity and mortality). In addition, the available resources are limited and need to be allocated where the greatest health gain can be achieved. This also applies to resources for monitoring. Therefore, an integrated approach to setting up a coherent monitoring and information system is strongly recommended.

Data from such a monitoring and information system can provide the input for health models designed to forecast future developments, which may be a valuable tool that can be used to underpin health policy decisions. However, a great deal of effort is required from all parties involved to make well-considered decisions backed up by sound monitoring and accurate health modelling.

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SUMMARY

This thesis deals with the interrelationship between epidemiology and health policy as regards diabetes mellitus (Chapter 1). Diabetes mellitus has been selected because this chronic metabolic disorder represents a major public health problem. Over time, multiple chronic complications may occur, such as myocardial infarction, stroke, circulation disorders in the legs, blindness, kidney diseases, and loss of sensitivity and/or pain in the limbs. As a consequence, both quality of life and life expectancy are reduced. Diabetes mellitus is responsible for a substantial degree of health care utilisation. The objectives of the studies described in this thesis are to investigate the occurrence of diabetes mellitus in the Netherlands, the changes that have taken place in recent years as well as possible future developments. In addition, the implications of these epidemiological developments for health policy have been addressed.

The points of departure are dealt with in Chapter 2, which gives a general description of the disease and the concepts used. In a **background study**, which was completed in 1989, an inventory was made of the available data regarding incidence, prevalence, remission, and mortality of diabetes in the Netherlands. The *incidence and/or prevalence* of diabetes mellitus had been estimated in 18 surveys during the period 1971-1987. As we were particularly interested in the burden on health care in the Netherlands, the following basic principles were applied to choose the most appropriate sources: the data should represent clinically-known patients and not those as yet undiagnosed, and they should be representative for the Dutch population as a whole in terms of age, gender, degree of urbanization and geographical variation. The incidence among 0-19 year-olds was based on a questionnaire survey conducted among all Dutch paediatricians and internists in the period 1978-1980. The Dutch Sentinel Practice Network, which represents about one percent of the Dutch population, was used to estimate the incidence from age 20 onwards (recorded in the period 1980-1983) and the prevalence for all age groups (recorded in 1980). The annual number of newly-diagnosed patients amounted to 17,300, which corresponded to an incidence of 0.12% in 1980. The number of clinically-known diabetic patients appeared to be 191,000 in 1980, which corresponded to a prevalence of 1.35% of the population. Both the incidence and prevalence increased with age.

Reliable information on *remission* and *mortality* among diabetic patients in the Netherlands was not available. As regards remission, it was assumed that no recovery takes place. Despite the possibility of remission, the assumption was made that these 'patients' will remain under a certain degree of medical supervision. Reduction of life

expectancy as observed in studies from other countries was chosen to assess the outflow of diabetic patients as an alternative to mortality statistics for diabetes. From these studies it appeared that the younger the age at which diabetes is diagnosed the greater the reduction of life expectancy will be.

The two studies that examined the incidence around 1980 were repeated around 1990 using a similar design (**two 'trend' studies**). Comparing the results of the first (1978-1980) and second (1988-1990) nation-wide retrospective studies among children under 20 years of age, it appeared that the incidence had increased by 23% (Chapter 3). This suggests a sustained increase of insulin-dependent diabetes mellitus (IDDM) in the Netherlands, as it was found that the cumulative incidence previously studied in the 1960-1970 birth cohorts of male army conscripts at 18 years of age had also risen. The causes of the increasing incidence of IDDM, also observed in several other countries, are unknown.

Comparing the results from the first (1980-1983) and second (1990-1992) incidence studies in the Dutch Sentinel Practice Network, it appeared that the overall incidence of diabetes mellitus increased by about 12% (Chapter 4). This overall increase can largely be attributed to a statistically significant increase in the 45-64 age group (31%). This selective increase of non-insulin-dependent diabetes mellitus (NIDDM) is probably not caused by a real rise due to changes in exposure to determinants. It is more likely that the increase is due to earlier recognition of the signs and symptoms of diabetes followed by blood glucose measurements and/or to more intensive case finding in general practice. Although not statistically significant, the 36% increase of diabetes mellitus in the 0-19 age group is in accordance with the increase of IDDM based on the first and second retrospective studies covering the total Dutch population.

When age and gender-specific prevalences are not stable over time, a static model that only takes into account demographic changes is unable to correctly forecast the expected number of diabetic patients. We therefore developed a dynamic model in which actual incidence, prevalence, and life expectancy data are used and in which alternative assumptions about future trends in these parameters can be incorporated. **Two forecasting studies** examined possible future developments in the occurrence of diabetes mellitus. The first study (Chapter 5) estimated the number of patients during the period 1980-2005, based on the information provided by the background study described in Chapter 2. In the second study (Chapter 6), the forecasts were updated for the period 1990-2005 by using the incidence data from around 1990 based on the two 'trend' studies described in Chapters 3 and 4. Furthermore, new prevalence data were used, as the prevalence study of diabetes in the Dutch Sentinel Practice Network was repeated in 1990. It appeared that the prevalence of diabetes for those 20 years and older had decreased significantly between 1980 and 1990. A decrease of 11% (from 191,000 to 170,000 diabetic patients) was observed. Apparently, the audit of diabetic care in general practice may have resulted in a clearance of the diabetic register which in particular may be the result of changing diagnostic criteria.

Although the input parameters (starting incidence and prevalence data) were different in each of the forecasting studies, the number of diabetic patients to be expected in 2005 were quite similar, amounting to 340,000-355,000 (2.1-2.2% of the total population). This increase is in particular the result of an imbalance between the incidence and life expectancy data (a higher inflow and lower outflow, respectively). This imbalance was even greater in the second forecasting study because of a higher incidence at baseline. Therefore the initial lower prevalence resulted in a similar number of diabetic patients in 2005 to that found in the first forecasting study. Assuming that the *increase* in incidence as observed in the 'trend' studies continues during the period 1990-2005, the estimated number of patients in 2005 will rise even further to 385,000. However, in view of the existence of a considerable number of currently undiagnosed diabetic patients, the real number of known diabetic patients in the future will probably be substantially higher (see below).

The recognition of diabetes as a major and growing public health problem raises questions concerning the possibilities for influencing the expected increase by means of prevention, and the possible consequences for health care. Based on the current knowledge published in the international literature, an attempt has been made to answer these questions and to address the **health policy implications** of the findings at the national level (Chapter 7). Up to now, primary prevention of IDDM has been confined to research without practical implications. To identify the determinants of IDDM, an important contribution can be made at the national level by joining the international network of childhood diabetes registries. Determinants of NIDDM have been identified by epidemiological studies (overweight, physical inactivity and unhealthy diet), but there are few empirically-based published studies that have examined the effect of interventions on these determinants. Because there are many similarities between both diseases, the experience gained from the prevention of cardiovascular diseases can serve as an example for primary preventive strategies for NIDDM at a national level.

Epidemiological studies suggest that at least 50% of all NIDDM patients may be undiagnosed. The implications for secondary prevention have been discussed. Up to now there is insufficient evidence for mass screening of asymptomatic individuals with diabetes. Operational research is needed to define more clearly the different aspects of screening and the effectiveness of screening in a community or clinical setting. It is unlikely that universal guidelines on secondary preventive strategies will be established because the distribution of high risk groups, the resources available, and the existing health care structures differ from country to country. It is therefore strongly recommended that a national strategy be established, based on knowledge gained internationally.

It is not easy to foresee what the burden on health care will be in the near future as a result of changes in the occurrence of diabetes. It is very likely that the number of patients will increase, irrespective of developments in the field of primary prevention. However, in addition to the number of patients, changes in the health status (as a result of possible secondary preventive and health care activities) as well as developments in health care (such as a shift from in-patient to out-patient treatment, the policy of reducing budgets and capacity, and increased productivity) will influence the future burden on health care and the concomitant costs for diabetes. As the number of diabetic patients is expected to increase while financial constraints in health care become increasingly tighter, considerable efforts will need to be made to find more cost-effective ways to treat diabetic patients and to reduce the complications associated with the disease.

In the general discussion (Chapter 8) some methodological issues regarding the validity of the selected sources for assessing the occurrence of diabetes, the 'trend' data, and the future projections, have been addressed. It is indisputable that valid data are needed to make future projections. However, for various reasons there is a discrepancy between the incidence and between the prevalence data when comparing different Dutch studies, and reliable mortality data on diabetes are lacking. In addition, it should be realised that neither study described in this thesis recorded data on a continuous basis - they only compared two points in time. Data regarding the period in between are lacking, which might produce a less reliable estimate of the trend over the whole period. When interpreting the future projections, it should be borne in mind that they do not predict the number of patients in the true meaning of prediction. The projections explore possible future developments according to the assumptions made. In this light, the importance of monitoring diabetes as well as the health status of the population in general has been discussed in order to improve the availability and use of epidemiological data for health policy purposes.

In conclusion, the results described in this thesis indicate that diabetes mellitus is a serious and growing public health problem. The disease is therefore important for health policy. For several reasons (e.g. regarding the validity and availability of data, possible developments in preventive and health care policy), it is not easy to foresee what the exact number of patients and the concomitant burden on health care and costs in the near future will be. In order to make more accurate forecasts and to support policy preparation as well as policy evaluation, the disease and its determinants need to be monitored. However, it would be inappropriate to confine monitoring to diabetes alone, as diabetes shares common determinants with other diseases and is itself a determinant for other diseases (such as cardiovascular diseases). Changes in the occurrence and course of diabetes may thus influence other related and even unrelated diseases (competing morbidity and mortality). Therefore, an integrated approach to setting up a coherent monitoring and information system is strongly recommended. A significant step towards achieving a more appropriate health information system may be accomplished by improving the links between existing health interview surveys, epidemiological monitoring programmes, general practitioners' records, nation-wide health care and insurance systems, and statistics on causes of death. Data from such a monitoring and information system can provide the input for health models designed to forecast future developments, which may be a valuable tool that can be used to underpin health policy decisions.

SAMENVATTING

Dit proefschrift stelt de interactie aan de orde tussen epidemiologie en gezondheidsbeleid aan de hand van diabetes mellitus (hoofdstuk 1). Diabetes is gekozen omdat deze chronische stofwisselingsziekte een belangrijk volksgezondheidsprobleem vormt. Op den duur kunnen bij diabetespatiënten meerdere chronische complicaties optreden, zoals het hartinfarct, beroerte, circulatiestoornissen in de benen, blindheid, nierziekten, gevoelsstoornissen en/of pijn in de ledematen. Als gevolg hiervan nemen de kwaliteit van leven en de levensverwachting af. De ziekte vereist dan ook de nodige aandacht van de gezondheidszorg. De doelstellingen van de in dit proefschrift beschreven onderzoeken zijn het bestuderen van het voorkomen van diabetes mellitus in Nederland, de veranderingen hierin in de afgelopen jaren alsmede de mogelijke toekomstige ontwikkelingen. Tevens zijn de implicaties van deze epidemiologische ontwikkelingen voor het gezondheidsbeleid beschreven.

De uitgangspunten staan vermeld in hoofdstuk 2. Dit hoofdstuk geeft een algemene beschrijving van de ziekte en de gehanteerde concepten en definities. Een **achtergrondstudie**, die in mei 1989 werd afgesloten, gaf inzicht in de beschikbare informatie over de incidentie, prevalentie, herstel en sterfte aan diabetes in Nederland. De *incidentie en/of prevalentie* was in 18 onderzoeken bestudeerd in de periode 1971-1987. Aangezien we in het bijzonder geïnteresseerd waren in het beslag op de gezondheidszorg in Nederland, werden de volgende uitgangspunten gehanteerd om tot een selectie van de meest geschikte bronnen te komen; de cijfers over het voorkomen van diabetes dienen betrekking te hebben op de klinisch gediagnostiseerde patiënten en niet op degenen die ongediagnostiseerd zijn, en de cijfers dienen representatief te zijn voor de totale Nederlandse bevolking naar leeftijd, geslacht, urbanisatiegraad en geografische spreiding. De incidentie onder 0-19 jarigen werd gebaseerd op een vragenlijst-onderzoek onder alle Nederlandse kinderartsen en internisten in de periode 1978-1980. De Continue Morbiditeits Registratie Peilstations Nederland, die circa een procent van de Nederlandse bevolking vertegenwoordigt, werd geselecteerd om de incidentie vanaf 20 jaar (gemeten in de periode 1980-1983) en de prevalentie voor alle leeftijden (gemeten in 1980) te schatten. Het jaarlijks aantal gediagnostiseerde diabetespatiënten bedroeg 17.300, hetgeen overeenkomt met een incidentie van 0,12% in 1980. Het aantal klinisch bekende patiënten bedroeg 191.000 in 1980, hetgeen overeenkomt met een prevalentie van 1,35% van de bevolking. Zowel de incidentie als prevalentie stijgen met de leeftijd.

Betrouwbare informatie over *herstel* en *sterfte* bij patiënten met diabetes zijn niet beschikbaar in Nederland. Ondanks de mogelijkheid van herstel is aangenomen dat dit niet optreedt, omdat deze 'patiënten' over het algemeen toch onder medische controle blijven. De reductie in levensverwachting, zoals gevonden in buitenlandse onderzoeken, is gekozen om de uitstroom van diabetespatiënten te bepalen als alternatief voor gegevens afkomstig van de sterftestatistiek. Uit deze onderzoeken bleek dat hoe jonger de diagnose diabetes wordt gesteld, des te groter de reductie in levensverwachting.

De twee onderzoeken die de incidentie bepaalden rond 1980 zijn rond 1990 herhaald met eenzelfde opzet (**twee 'trend' onderzoeken**). Bij vergelijking van de resultaten van het eerste (1978-1980) en tweede (1988-1990) landelijke retrospectieve onderzoek onder kinderen tot 20 jaar, blijkt dat de incidentie met 23% is gestegen (hoofdstuk 3). Dit suggereert een blijvende toename in insuline-afhankelijke diabetes mellitus (IADM) in Nederland, aangezien de cumulatieve incidentie in de 1960-1970 geboorten-cohorten van mannelijke 18-jarige dienstplichtigen ook bleek te stijgen. De oorzaken van de stijgende incidentie van IADM, die ook in verschillende andere landen is gevonden, zijn niet bekend.

Uit vergelijking van de resultaten van het eerste (1980-1983) en tweede (1990-1992) incidentie-onderzoek van de Peilstations Nederland blijkt dat de incidentie van diabetes met 12% is gestegen (hoofdstuk 4). Deze totale toename is in belangrijke mate het gevolg van een significante toename in de leeftijdsgroep 45-64 jaar (31%). Deze selectieve toename van niet-insuline-afhankelijke diabetes mellitus (NIADM) is waarschijnlijk niet veroorzaakt door een verhoogde blootstelling aan determinanten (risicofactoren). Het is waarschijnlijker dat deze toename het gevolg is van een eerdere herkenning van klachten en kenmerken passend bij de ziekte gevolgd door bloedglucose bepalingen en/of intensievere case finding in de huisartspraktijk. Alhoewel niet statistisch significant, de 36% toename van diabetes in de leeftijdsgroep 0-19 jaar is in overeenstemming met de toename van IADM gebaseerd op de bevindingen uit het eerste en tweede landelijke retrospectieve onderzoek.

Als de leeftijd- en geslachtspecifieke prevalenties niet constant zijn in de tijd, is een statisch model, dat alleen veranderingen in demografie in rekening brengt, niet geschikt om het toekomstig aantal patiënten met diabetes mellitus te berekenen. Daarom ontwikkelden we een dynamisch model waarin de feitelijke gegevens over de incidentie, prevalentie en levensverwachting zijn gebruikt en alternatieve aannames over toekomstige trends in deze parameters kunnen worden verwerkt. **Twee scenario-studies** onderzochten mogelijke toekomstige ontwikkelingen in het voorkomen van diabetes mellitus. De eerste studie (hoofdstuk 5) berekende het aantal patiënten voor de periode 1980-2005, gebaseerd op de informatie uit de achtergrondstudie beschreven in hoofdstuk 2. In de tweede studie (hoofdstuk 6) zijn deze berekeningen bijgesteld voor de periode 1990-2005 met gebruik van de incidenties rond 1990, zoals gevonden in de twee 'trend' onderzoeken die zijn beschreven in hoofdstuk 3 en 4. Tevens zijn nieuwe gegevens over de prevalentie gebruikt, aangezien in de Peilstations Nederland de prevalentie opnieuw is onderzocht in 1990. Hieruit bleek dat de prevalentie van diabetes vanaf 20 jaar significant is gedaald tussen 1980-1990. We constateerden een daling van 11% (van 191.000 naar 170.000 diabetespatiënten). Veranderde diagnose-criteria zijn mogelijk in belangrijke mate verantwoordelijk voor een opschoning van het diabetesbestand in de huisartspraktijk.

Alhoewel de invoergegevens (start incidentie en prevalentie) verschillend zijn in elk van de scenariostudies, is het aantal te verwachten patiënten met diabetes in 2005 vergelijkbaar en wordt geschat op 340.000-355.000 (2.1%-2.2% van de totale bevolking). Deze toename is in het bijzonder het gevolg van het niet in evenwicht zijn van de incidentie en de levensverwachting (respectievelijk een hogere instroom en een lagere uitstroom). Dit speelt een nog grotere rol in de tweede studie vanwege een hogere incidentie bij aanvang. Daarom resulteert de initiële lagere prevalentie in de tweede studie in een vergelijkbaar aantal diabetespatiënten in 2005 als in de eerste studie. Als de *stijging* in incidentie zoals gevonden in beide 'trend' onderzoeken zich voortzet in de periode 1990-2005, dan zal het aantal te verwachten patiënten in 2005 zelfs stijgen tot 385.000. Indien echter rekening gehouden wordt met het gegeven dat een aanzienlijk aantal diabetespatiënten momenteel niet als zodanig gediagnostiseerd is, zal het werkelijke aantal bekende patiënten in de toekomst waarschijnlijk aanzienlijk hoger zijn (zie hierna).

De herkenning van diabetes mellitus als een belangrijk en toenemend volksgezondheidsprobleem roept vragen op wat de mogelijkheden zijn om de te verwachten toename te beïnvloeden door middel van preventie en wat de mogelijke consequenties zijn voor de gezondheidszorg. Gebaseerd op de huidige kennis zoals gepubliceerd in de internationale literatuur, is getracht deze vragen te beantwoorden en de **implicaties voor het gezondheidsbeleid** op nationaal niveau te adresseren (hoofdstuk 7). Tot nu toe blijkt primaire preventie van IADM zich te beperken tot onderzoek, vooralsnog zonder toepassing in de dagelijkse praktijk. Om de determinanten van IADM op te sporen kan op nationaal niveau een belangrijke bijdrage geleverd worden door zich aan te sluiten bij het internationale netwerk van diabetesregistraties voor kinderen. Determinanten van NIADM zijn opgespoord in epidemiologisch onderzoek (overgewicht, lichamelijke inactiviteit en ongezonde voeding), maar er zijn slechts weinig onderzoeken gepubliceerd die het effect van interventies op deze determinanten beschrijven. Aangezien er vele raakvlakken zijn tussen beide ziekten, kan de ervaring die is verkregen met de preventie van hart- en vaatziekten als een voorbeeld dienen voor primaire preventie-strategieën voor NIADM op nationaal niveau.

Epidemiologische onderzoeken wijzen uit dat tenminste 50% van alle patiënten met NIADM als zodanig niet gediagnostiseerd is. De implicaties voor secundaire preventie zijn besproken. Tot nu toe is er onvoldoende bewijs dat massale screening in de bevolking van asymptomatische personen met diabetes rechtvaardigt. Toegepast onderzoek is noodzakelijk om meer inzicht te krijgen in de verschillende aspecten van screening en de effectiviteit van screening in bevolkingsonderzoek of klinische praktijk. Het is onwaarschijnlijk dat universele richtlijnen voor secundaire preventie-strategieën zullen worden vastgesteld, omdat de verdeling naar risicogroepen, de beschikbare middelen en de bestaande zorgstructuren van land tot land verschillen. Een nationale strategie op basis van internationaal verworven kennis is daarom sterk aan te bevelen.

Het is niet eenvoudig te voorzien wat in de nabije toekomst het beslag op de gezondheidszorg zal zijn als een gevolg van de veranderingen in het voorkomen van diabetes mellitus. Het is zeer waarschijnlijk dat het aantal patiënten zal toenemen, onafhankelijk van ontwikkelingen op het terrein van primaire preventie. Tevens zullen veranderingen in de gezondheidstoestand (als gevolg van mogelijk activiteiten op het terrein van secundaire preventie en therapeutische mogelijkheden) alsmede ontwikkelingen in de gezondheidszorg (zoals een verschuiving van klinische naar poliklinische zorg, bezuinigingen en verhoogde produktiviteit) de toekomstige last op de gezondheidszorg en de daaruit voortkomende kosten voor diabetes beïnvloeden. De te verwachten toename van het aantal patiënten met diabetes onder omstandigheden van verminderde beschikbaarheid van financiële middelen in de gezondheidszorg, impliceert dat belangrijke inspanningen geleverd moeten worden om de diabetespatiënten effectiever te behandelen en complicaties te voorkomen.

In de algemene discussie (hoofdstuk 8) is aandacht besteed aan enkele methodologische aspecten van de onderzoeken, zoals de validiteit van de geselecteerde bronnen voor het bepalen van het voorkomen van diabetes, de 'trend' gegevens en de toekomstprojecties. Het staat buiten kijf dat betrouwbare gegevens nodig zijn om toekomstprojecties uit te voeren. Echter, vanwege uiteenlopende redenen zijn er discrepanties waar te nemen tussen incidentie- en prevalentiegegevens van verschillende Nederlandse onderzoeken. Ook ontbreken betrouwbare sterftecijfers voor diabetes in Nederland. Daarnaast dient men zich te realiseren dat de beschreven 'trend' onderzoeken slechts twee punten in de tijd met elkaar vergelijken. Gegevens over de tussenliggende periode ontbreken. Hierdoor wordt een minder betrouwbare trendschatting over de hele periode verkregen. Bij het interpreteren van de toekomstprojecties dient men zich ervan bewust te zijn dat zij niet het toekomstig aantal patiënten voorspellen maar slechts een indicatie geven. De projecties exploreren mogelijke toekomstige ontwikkelingen gegeven de aannames. In deze context is het belang van monitoring van diabetes en van de gezondheidstoestand in het algemeen bediscussieerd om de beschikbaarheid en het gebruik van epidemiologische gegevens voor het gezondheidsbeleid te verbeteren.

Concluderend kan gesteld worden dat de in dit proefschrift beschreven resultaten aangegeven dat diabetes mellitus een belangrijk en in omvang toenemend volksgezondheidsprobleem is. De ziekte is dan ook van belang voor het gezondheidsbeleid. Om uiteenlopende redenen (zoals de validiteit en beschikbaarheid van gegevens, mogelijke ontwikkelingen in het preventie- en gezondheidszorgbeleid) is het niet eenvoudig om te voorzien wat het exacte aantal patiënten en het beslag op de gezondheidszorg en de kosten in de nabije toekomst zullen zijn. Om meer onderbouwde toekomstprojecties te maken en de voorbereiding en evaluatie van gezondheidsbeleid te ondersteunen, dienen de ziekte en de determinanten ervan 'gemonitored' te worden. Het is echter onvoldoende om monitoring te beperken tot diabetes alleen, omdat diabetes gemeenschappelijke determinanten heeft met andere ziekten en zelf ook een determinant is voor andere ziekten (zoals hart- en vaatziekten). Veranderingen in het voorkomen en het beloop van diabetes kunnen dus van invloed zijn op andere gerelateerde en zelfs niet gerelateerde ziekten (vervangende en concurrerende morbiditeit en mortaliteit). Het verdient dan ook sterke aanbeveling om een coherent monitoring- en informatiesysteem op te zetten. Een belangrijke stap hiertoe kan gezet worden door koppeling te bewerkstelligen tussen bestaande gezondheidsenquêtes, epidemiologische monitoring programma's, huisartsen-registratiesystemen, landelijke zorg- en verzekeringssystemen en doodsoorzaken-statistieken. Gegevens van zo'n monitoring- en informatiesysteem kunnen gebruikt worden voor gezondheidsmodellen die ontworpen zijn om toekomstige ontwikkelingen te verkennen, en daarmee belangrijk gereedschap leveren om beslissingen in het gezondheidsbeleid te ondersteunen.

DANKWOORD

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ABOUT THE AUTHOR

Dirk Ruwaard was born on August 17th, 1960 in Katwijk aan Zee, the Netherlands. After completing secondary school (Atheneum at the Pieter Groen College in Katwijk aan Zee) in 1978, he studied Mathematics and Physics in Delft for one year. He started to study Medicine in September 1979 at Leiden University Medical School, the Netherlands. He obtained his medical degree cum laude in September 1986. Subsequently, he worked at the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, in Amsterdam, and as an army conscript. In February 1988 he started research at the Institute of Social Medicine, at the Medical Faculty of the University of Leiden (Head: Prof D. Kromhout), on the project 'The future burden of chronic diseases for Dutch society: scenarios for diabetes mellitus, chronic non-specific lung diseases and rheumatoid arthritis 1990-2005'. Since 1989 this project has been carried out at the National Institute of Public Health and the Environment (RIVM) in Bilthoven, the Netherlands. This project was the starting-point for the further research activities described in this thesis. In 1988 and 1989 he attended the Summer Course in Epidemiology at the Leiden/Erasmus Rotterdam University Medical Schools and the Summer Program in Epidemiology (focusing on epidemiology, health risk assessment and health services reseach) at the Department of Epidemiology of the Johns Hopkins University School of Hygiene and Public Health in Baltimore, USA, respectively. From 1991-1993 he specialized in Social Medicine at the TNO Institute for Prevention and Health, Leiden. In 1992 he became head of the Public Health Analysis Branch within the Department for Public Health Forecasting, and project leader of the project 'Public Health Status and Forecasts' at RIVM. In January 1996 he was appointed deputy head of the Department for Public Health Forecasting. Furthermore, he is a member of a number of committees and societies in the field of public health research.