The prevalence of diabetes mellitus in the Netherlands

A quantitative review

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The prevalence of diabetes above the age of 30 years in The Netherlands was estimated and the influence of methodological variables on the reported prevalence rates was quantified. Fifteen Dutch studies performed since 1970 were entered in logistic regression models with the presence or absence of known diabetes above the age of 30 years as a dependent variable. In order to quantify the variability among studies, the study methodology and population characteristics were chosen as independent variables. The age-standardized prevalence of known diabetes varied between the studies. The total prevalence of known diabetes above the age of 30 years in 1993 can be estimated at 2.7% on the basis of the cases reported by general practitioners and at 3.2% based on self-reported cases in surveys. The prevalence according to age increased by 7.1% per life year for men and by 7.7% for women. These associations were essentially similar in all studies. Systematic screening, performed with an oral glucose tolerance test, revealed a prevalence which was 1.5-2 times higher.Depending on the method used, the number of subjects with known diabetes in the Netherlands in 1993 varied between 235,000 and 285,000. After systematic screening, this prevalence will be 1.5-2 times higher. These estimates may serve various goals. The prevalence rates based on self-reports or reports by general practitioners are important for estimating health care use. Prevalence rates based on screening are relevant for preventive strategies and latent health care needs.

Key words: diabetes mellitus, pooled analysis, prevalence

Diabetes mellitus is a major cause of morbidity and mortality in the world. Non-insulin-dependent diabetes mellitus (NIDDM) is by far the most common form and thus causes the most co-morbidity.[1,2] As prevalence increases sharply with age, it is an important determinant of health care needs in an ageing society. To assess future needs for health care, policy makers need more information on the number of patients and changes in prevalence over time. This requires reliable estimates of age- and sex-specific prevalence rates. However, prevalence studies are hard to interpret. Reported prevalence rates may vary due to various population characteristics or differences in methodology. Populations may vary by composition (age and sex) or by other characteristics such as obesity and other determinants of diabetes. Methodological diversity is caused by selection of the study population, case definition and case ascertainment. The study population may, for instance, be a random sample of the general population (survey) or have been selected on the basis of health care use (population in a general practice). Case definitions have changed over time. In 1965, diagnostic criteria were first formulated by the World Health Organization (WHO) and revised and standardized in 1980 and 1985.[3,4] Moreover, cases can be ascertained from self-reports, general practitioners reports or by screening with an oral glucose tolerance test (OGTT). Obviously, systematic screening for an often asymptomatic disease will yield much higher prevalence rates.

To obtain a best possible estimate of the prevalence of diabetes in the adult population in The Netherlands, we compared all the studies performed since 1970 and tried to account for differences in methodological characteristics by using logistic regression models. The estimated prevalence rates will be judged according to their relevance to health policy.

METHODS

Data sources

The data were collected from all studies conducted since 1970 on the prevalence of diabetes mellitus in the adult population in The Netherlands. Few were published in peer reviewed papers and most were identified through the snowball method (checking references in all the publications found) and expert advice. We turned up 22 studies reporting the prevalence of diabetes mellitus in The Netherlands. For inclusion in our analyses, the studies were required to report, for men and women

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separately, age-specific prevalences for age groups which differed by a maximum of 20 years. This excluded five studies.[5–9] One study was excluded from analysis because of its highly selective study population (patients in nursing homes and homes for the elderly).[10]. Another study was excluded from analysis because all the diabetic patients who visited the general practitioner were registered during a three month period. This period was too short to estimate the prevalence of diabetes reliably.[11] Fifteen studies qualified for analysis. *Table 1* gives an overview of the characteristics of these studies. They were performed either in general practices or as surveys. Cases of known diabetic patients were ascertained by means of reports from general practitioners or self-reports in a questionnaire. Two studies measured the prevalence of diabetes at several points in time.[12,13] Four studies identified, next to all known cases of diabetes, unknown cases of diabetes by systematic screening of the remaining population with an OGTT. These four studies differed from each other in type of OGTT (fasting or non-fasting) and study population (survey or population from a general practice).[14,24–26]

Analyses of prevalence

The data were analysed using a logistic regression model with the presence or absence of diabetes mellitus as a dependent variable. The same method was used for estimating the prevalence of hypertension on the basis of a number of studies.[27] The statistical package EGRET was used in all the analyses. We restricted the analyses to ages 30 years and above. All the analyses were performed for men and women separately. Age was always specified as an independent variable; the median age of each age group was used. When open-ended, age groups were excluded from the analyses, as the median age in such open-ended age groups may differ strongly between studies. The numbers in each age and sex group were used as weights. Two studies[12,17] reported only aggregated sample sizes. However the distribution by age and sex of these studies was equal to the Dutch population during that period, which made it possible to calculate the number in each age and sex group.

In the first analysis, the study was chosen as an independent (dummy) variables in order to identify the differences between the studies, adjusted for different age structures. The Sentinel Station study performed in 1980–1983 was taken as a reference, because this study has the largest sample size. Because four studies also measured asymptomatic diabetes by screening with an OGTT, we performed the analysis twice. First, the reported prevalence rates of known diabetes were entered as a dependent variable in the model, while for the second analysis for these four studies[14,24–26] we used the sum of known and newly diagnosed diabetes.

Next, we tried to find an explanation for the difference in the prevalence rates of known diabetes between studies by estimating the influence of methodological variation on the prevalence of diabetes. Report by general practitioner and self-report in a survey were chosen as independent variables, adjusted for age and calendar year. Because the four studies using an OGTT used a different test and methodology, a pooled estimate of the effect of systematic screening on the prevalence rate could not be calculated. The regression equations, used for the two analyses are given in the appendix.

The coefficients from the logistic regression models were used to estimate the prevalence of diabetes in The Netherlands.

Table 1 Characteristics of the 15 studies on the prevalence of diabetes mellitus in The Netherlands used in the analysis

Name of the study	Period	Sample size	Age (years)	Case ascertainment
General practice (GP)				
Sentinel Station[12]	1980–1983 1990–1991	162,626	0– ≥65 0– ≥80	Report by GP
CMR-Nijmegen[13]	1971–1993	12,000	0– ≥75	Report by GP
Twello Study[14]	1985	516	65– ≥80	Report by GP and fasting OGTT
Autonomy Project[15]	1986	5,163	65–74	Report by GP
Transition Project[16]	1987	40,796	0– ≥75	Report by GP
Heerde study[17]	1987	11,800	0– ≥80	Report by GP
Survey				
EPOZ[18]	1975–1978	10,616	0–95	Self-report
LSO[19]	1983+1986	7,968	18–75	Self-report
CFRM[20]	1987–1991	36,000	20–59	Self-report
Health Survey[21]	1989–1993	41,450	0–85	Self-report
GLOBE[22]	1991	18,973	14–78	Self-report
LASA[23]	1992–1993	3,108	55–85	Self-report
Hoorn Study[24]	1989–1991	2,484	50–75	Self-report and fasting OGTT
Zutphen Study[25]	1990	492	70–90	Self-report and fasting OGTT
Rotterdam Study[26]	1991–1993	7,983	55– ≥85	Self-report and non-fasting OGTT

CMR: Continuous Morbidity Registration
EPOZ: Epidemiologic Preventive Research Zoetermeer
LSO: Living-Situation Study
CFRM: Cardiovascular Risk Factors Monitorings Project
GLOBE: Health and Living Conditions of the population of Eindhoven and surroundings
LASA: Longitudinal Ageing Study Amsterdam
OGTT: oral glucose tolerance test

RESULTS

The surveys reported higher prevalences as compared with the Sentinel Station, with the exception of the Epidemiologic Preventive Research Zoetermeer (EPOZ) study (*table 2*). Within the studies performed in a general practice, the Continuous Morbidity Registration (CMR)-Nijmegen and the Twello study reported significant higher prevalences than the reference study. The two studies which measured the prevalence at several points in time[12,13] showed contradictory results. The Sentinel Stations reported a lower prevalence in 1989–1990 as compared with 1980–1983. CMR-Nijmegen study showed a slight increase in prevalence over time, for both men and women.

The four studies which identified unknown cases of diabetes in addition to all known cases of diabetes by systematically screening the remaining population with an OGTT, reported higher prevalence estimates compared with the studies identifying only the known cases of diabetes. The number of known diabetic patients could be separated from the newly diagnosed patients in these studies, enabling us to compare the prevalence estimates of known versus known and newly diagnosed within the four studies. Three of the four studies reported prevalences 1.5–2 times as high as their own prevalence rate of known diabetes. The fourth study[14] reported prevalences six times as high as its own prevalence rate of known diabetes and can be considered as an outlier.

Some of the differences between the studies may be explained by methodological variation. Measuring known diabetes in a survey using self-reported cases resulted in higher prevalence rates than those based on reports made by general practitioners (*table 3*). These differences were somewhat larger for men than for women but did not differ significantly: an odds ratio of 1.47 (95% CI: 1.35–1.60) for men versus 1.14 (95% CI: 1.06–1.23) for women. The prevalence of known diabetes mellitus increased for men by 7.1% (95% CI: 6.8–7.4) for each year of age and by 7.7% (95% CI: 7.4–8.0) for women. When estimating the increase in prevalence by age for each of the studies separately, we found that the pooled estimate of the increase by age fell within the confidence

Table 2 Variation in the prevalence of diabetes mellitus in The Netherlands expressed as odds ratios (95% confidence intervals) adjusted for age

		Known diabetes		Known and newly diagnosed diabetes	
Variable	Period	Men	Women	Men	Women
General practice					
Sentinal Station	1980–1983	1.00	1.00	1.00	1.00
	1989–1990	0.82 (0.72–0.94)	0.74 (0.66–0.84)	a	a
CMR-Nijmegen	1971–1975	1.19 (0.88–1.59)	1.08 (0.84–.40)	a	a
	1976–1980	1.43 (1.08–1.87)	1.22 (0.95–1.56)	a	a
	1981–1985	1.56 (1.20–2.01)	1.27 (1.00–1.62)	a	a
	1986–1990	1.48 (1.15–1.90)	1.33 (1.06–1.67)	a	a
	1991–1993	1.48 (1.16–1.89)	1.44 (1.14–1.77)	a	a
Twello Study		1.76 (1.02–3.04)	1.70 (1.11–2.61)	7.08 (4.90–10.24)	5.59 (4.08–7.66)
Autonomy Study		0.93 (0.71–1.23)	1.04 (0.83–1.29)	a	a
Transition Study		1.04 (0.87–1.24)	0.97 (0.83–1.13)		
Heerde Study		1.12 (0.85–1.48)	1.08 (0.86–1.36)		
Survey					
EPOZ		0.83 (0.59–1.16)	0.74 (0.56–0.97)	a	a
LSO		1.23 (0.92–1.65)	1.15 (0.89–1.49)	a	a
CFRM		1.32 (1.11–1.58)	0.92 (0.78–1.10)	a	a
Health Survey		1.30 (1.11–1.52)	1.11 (0.96–1.28)	a	a
GLOBE		1.71 (1.45–2.03)	1.17 (0.99–1.37)	a	a
LASA		1.39 (1.09–1.76)	1.05 (0.84–1.31)	a	a
Hoorn Study		1.05 (0.74–1.50)	0.98 (0.73–1.32)	2.93 (2.30–3.74)	2.32 (1.87–2.88)
Zutphen Study		1.59 (1.12–2.25)	–	3.10 (2.36–4.09)	–
Rotterdam Study		2.08 (1.75–2.47)	0.94 (0.79–1.10)	2.84 (2.40–3.36)	1.77 (1.53–2.05)

a: No newly diagnosed diabetes available

Table 3 Influence of methodological variation on the reported prevalence estimates expressed as odds ratios (95% confidence intervals) adjusted for age and calender year

Variable	Men		Women	
Age (continuous)	1.071	(1.068–1.074)	1.077	(1.074–1.080)
Calender year (continuous)	1.00	(0.99–1.01)	0.99	(0.98–1.00)
Self-report in a survey versus report by GP	1.47	(1.35–1.60)	1.14	(1.06–1.23)

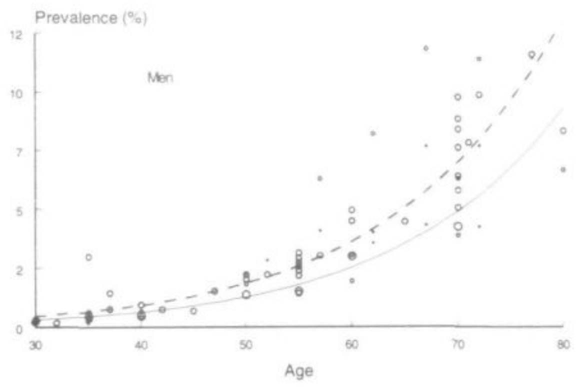

Figure 1 Prevalence of diabetes for men according to a survey with self-reported data (– – –) or a report by a general practitioner (——). The study prevalences are plotted with the size of the ball as an indicator for the sample size.

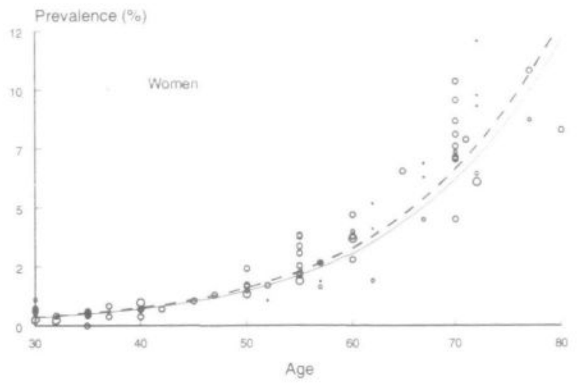

Figure 2 Prevalence of diabetes for women according to a survey with self-reported data (– – –) or a report by a general practitioner (——). The study prevalences are plotted with the size of the ball as an indicator for the sample size.

intervals of each individual study (data not shown). No effect of calender year could be observed.

The coefficients estimated from the logistic model were used to estimate the prevalence of known diabetes in The Netherlands in 1993 (*figures 1 and 2*). The best possible estimate of the age-specific prevalence varied with the methodology used. In The Netherlands, the total number of diabetic patients above the age of 30 years in 1993 was 235,000 (2.7%) based on cases reported by general practitioners and 285,000 (3.2%) based on self-reported cases in a survey. The prevalence is higher for women of all ages. Systematic screening with an OGTT will yield prevalence rates 1.5–2 times as high. Assuming this increase in the prevalence rate is similar in all age groups, the total number of subjects with diabetes after a systematic screening of the total population will amount to 460,000 (5.2%) based on the reports of general practitioners or 560,000 (6.4%) based on self-reports in a survey. These estimates should be interpreted as an upper limit, as they are based on systematic screening with a single glucose tolerance test. The use of repeated measurements will result in a lower prevalence of diabetes.[28]

DISCUSSION

We evaluated all the studies published in The Netherlands in order to obtain a tentative estimate of the prevalence of diabetes. The age-standardized prevalence of known diabetes varied considerably among the studies, with a higher prevalence in surveys using self-reported data. The prevalence increase by age is clear-cut. When systematic screening with an OGTT was performed, the prevalence rates were 1.5–2 times higher.

Pooling the data from heterogeneous studies to arrive at a single estimate might be considered a scientifically unsound undertaking. However, it seemed the only way to overcome the shortcomings of each individual study and to minimize the loss of information. If only selected data sources are considered, the selection might be guided by the (often unconscious) wishes of the reviewer and yield biased results. Furthermore, pooling offers an insight into the effect of methodological variations on the estimates of the prevalence of diabetes. Obviously, the results need to be interpreted with caution, but it is also important to realize that the studies are not heterogeneous in all aspects. For instance, the prevalence increase by age, estimated from the pooled analysis, was more or less similar in all studies.

The analyses started from age 30 years. The incidence and prevalence of NIDDM are by far the greatest[29,30] at older ages. Almost 85% of all diabetic patients, registered in 19 general practices, has the insulin-dependent form of diabetes.[31] The percentage of insulin-dependent diabetes (IDDM) patients diagnosed before age 30 years, but who were older than 30 years when the studies were carried out, is expected to be low and decreases with age. In the Heerde study in which a discrimination could be made between NIDDM and IDDM based on age of diagnosis and treatment with insulin, the percentage of IDDM patients decreased from 30% at age 30 years to less than 10% at age 80 years.[17] Therefore, the results of our analyses mainly concern NIDDM patients.

A changing case definition over time is a major problem in the interpretation of the different studies and in the interpretation of time series. As the definition becomes more and more specific, it may be assumed that the number of wrongly classified cases will drop and that, moreover, the prevalence of diabetes was relatively overestimated in the past. Part of the differences in prevalence rates observed between the studies might be explained by these changes in case definition. In several studies it was checked whether the diagnostic criteria had changed and how this might have influenced the prevalences reported.[17,32] The effect of changed criteria on the reported prevalence differed among these studies. The CMR-Nijmegen study reported that 13% of the diabetic patients did not have diabetes according to the WHO criteria of 1985. Moreover, the CMR-Nijmegen study also reported that for 14% of the subjects, the diagnostic criteria could not be traced anymore.[32] The Heerde study found that in 12.8% of the previously diagnosed diabetic patients the diagnosis could not be reconfirmed with an OGTT when the WHO criteria of 1985 were applied. In general, patients diagnosed by a single glucose tolerance test and/or treated with a diet were shown to be non-diabetic according to the WHO criteria of 1985.[17] For the surveys which used self-reported data, it is impossible to judge if and how case definition influenced the reported prevalence. In studies using a screening with an OGTT, newly diagnosed diabetes was defined according to the WHO criteria of 1985.[4]

Another explanation for the observed differences in the prevalence rates between the studies could be the differences in the prevailing interest of general practitioners in NIDDM. Since the presence of NIDDM is not always clinically manifest, some of the subjects with diabetes are undiagnosed as such.[33,34] Some general practitioners will be more aware of this phenomon and may be more attentive to diagnosing diabetes.

Surveys using self-reported data resulted in higher prevalence estimates as compared with those based on reports made by general practitioners. A possible explanation is that those responding to a survey may state that they are diabetic but are no longer registered in general practice as diabetic patients (because of, for example, changed diagnostic criteria or repeated measurements). On the other hand, in registering the cases in a general practice diabetic patients can be missed due to administration problems (hospital visits fail to be reported to the general practitioner) or the approach to registration (only patients who visit the general practitioner in a certain period are counted).[35] In particular, those patients who are treated with a diet only may cause a discrepancy between self-reported data and those reported by general practitioners. As neither the general practitioners nor the surveys took into account persons who are institutionalized in nursing homes or rest homes (only the Longitudinal Ageing Study Amsterdam (LASA) included the institutionalized population) underestimation of the prevalence is likely. A study in nursing homes and rest-homes,[10] which was excluded from our analysis for reasons of comparability, reported a higher prevalence of diabetes than the estimated prevalences of our analysis: 13% (95% CI: 10–16) for men aged 75–79 years and 21% (95% CI: 19–23) for women of this age, compared with our estimated prevalences of 5.7 and 8.4% for men and women respectively. In The Netherlands, 4.3% of all men and 7.9% of all women aged 75–79 years are institutionalized.[10]

Comparing the prevalence estimates with other countries, The Netherlands appears to be low in the hierarchy. In other European countries, surveys reveal an age-adjusted prevalence of known diabetes between 30 and 64 years of age which varies from 1.8% in Russia to 10.7% in Italy.[1] In American surveys, the age-standardized prevalences of known diabetes in the White population varies between 3 and 8%.[1,33] This is comparable to our estimate of known diabetes of 1.7% between the ages of 30 and 64 years.

The effect of systematic screening on the prevalence rates can best be estimated by comparing studies measuring known and unknown diabetes. Three studies which systematically screened for unknown diabetes reported 1.5–2 times higher prevalence estimates.[24–26] The Twello study reported prevalence rates 6 times as high and is considered to be an outlier. Although it is unclear why this study reported such extreme prevalence rates, a few comments are in order. The study population of this study was relatively small (n=560) and was based on a general practice in a rural village. The almost doubled prevalence found when systematic screening with an OGTT was carried out corresponds with studies which found that approximately 50% or more of the subjects with NIDDM are undiagnosed.[33,34] The three screening studies used a single glucose tolerance test, which is known to be prone to intra individual variation.[36,37] This may explain part of the different prevalence estimates among the four studies using an OGTT. The Hoorn Study assessed the prevalence of diabetes in a sample using two OGTTs, repeated during a period of 2–6 weeks. The prevalence of newly diagnosed diabetes after two OGTTs was lower compared with a single test (3.4 versus 4.3%), probably due to regression towards the mean.[28] Repeated measurements are advisable to avoid possible misclassification and to obtain a more valid estimate of the prevalence of diabetes.

In our analysis, we included studies conducted in the period 1970–1993. However, trends in time were difficult to interpret. As noted before, case definitions became more specific, inducing an artificial decrease by minimizing false positives. The two studies which measured prevalence at several points in time were contradictory. The Sentinel Station showed a decrease in prevalence, but only measured the diabetes the prevalence at two points in time. The decreased prevalence is probably due to a clearance of the diabetic register in general practice.[38] The only study with a continuous registration of diabetes since 1970, the CMR-Nijmegen study, showed a slight increase in prevalence. However, these estimates were based on small numbers. In other populations too, little is known about secular time trends. Two studies reported an increase in prevalence in the US over the past decades.[39,40] This issue also merits further study in The Netherlands.

In this study, the prevalence of known diabetes increased for men by 7.1% for each year of age and by 7.7% for women. Age appears to be a reliable predictor for the future numbers of patients in an ageing society. The number of patients aged 30 years and up will increase by 36% (95% CI: 19–41%) between 1993 and 2010 based on age-specific prevalence rates.

For health policy makers, it is important to realize that, depending on the way prevalence rates are measured, the prevalence of known diabetes in The Netherlands varies between 235,000 and 285,000 known diabetic patients or is 2.7–3.2% of the total population. Systematic screening with an OGTT yields prevalences which are twice as high. Depending on the intended application, different estimates can be of use. Prevalence rates based on self-reported data may be used when estimating total health care use, while the prevalence based on cases reported by general practitioners may be of use for that specific aspect of the health care system. Prevalence rates of diabetes based on screening are relevant for preventive strategies and latent health care needs.

This study is part of a research project supported by grants from the National Institute for Health Sciences (NIHES).
The authors are grateful to P.J. van der Maas, D. Kromhout, P.J. van de Mheen, J. Barendregt, R.P. Stolk and R. Gijsen for helpful comments and E.H. van de Lisdonk and the staff of the department of General Practice in Nijmegen, R.P. Stolk and D.J.H. Deeg for generously providing prevalence data.

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Received 3 January 1997, accepted 24 April 1997

Appendix

In the first analysis, the differences in prevalence estimates between the studies were identified adjusted for different age structures, by using the following regression equation:

$$logit\,(y)sex = logit\,(\alpha + \beta 1 \times age + \beta 2 \times study)$$

where age is a continuous variable and the study is a dummy variable.
In the second analysis, the influence of methodological variation on the prevalence of diabetes was estimated by using the following regression equation:

$$logit\,(y)sex = logit\,(\alpha + \beta 1 \times age + \beta 2 \times calender\ year + \beta 3 \times \mathrm{Mr})$$

where age and calander year are continuous variables and Mr is the methodology used: 0 is a report by a general practitioner and 1 is a self-report in a survey.