

Insulin treated diabetes mellitus: causes of death determined from record linkage of population based registers in Leicestershire, UK

N T Raymond, J D Langley, E Goyder, J L Botha, A C Burden, J R Hearnshaw

Abstract

Study objective - Analyses of causes of mortality in people with diabetes using data from death certificates mentioning diabetes provide unreliable estimates of mortality. Under-recording of diabetes as a cause on death certificates has been widely reported, ranging from 15-60%. Using a population based register of people with diabetes and linking data from this with causes of death data from another source is a viable alternative. Data from the Office of Population Censuses and Surveys (OPCS) are the most acceptable mortality data available for such an exercise, as direct comparison with other published mortality rates is then possible.

Design - A locally maintained population-based mortality register and all insulin-treated diabetes mellitus cases notified to the Leicestershire diabetes register (n = 4680) were linked using record linkage software developed in-house (Lynx). This software has been extensively used in a maintenance and update cycle designed to maximise accuracy and minimise duplication and false registration on the diabetes register. Deaths identified were initially coded locally to the International Classification of Diseases, 9th revision (ICD9), and later a linkage was performed to use official OPCS coding. Mortality data identified by the linkage was indirectly standardised using population data for Leicestershire for 1991. Standardised mortality ratios (SMR) were estimated, with 95% confidence intervals. Insulin dependent diabetes (IDDM) was defined as diabetes diagnosed before age 30 years with insulin therapy begun within one year of diagnosis. All other types were considered non-insulin dependent diabetes (NIDDM). Analyses were performed for the whole sample and then for the NIDDM subgroup. Results from these analyses were similar and therefore only whole group analyses are presented.

Main results - A total of 370 deaths were identified for the period 1990-92 inclusive - 56% were in men and 44% in women, median age (range) 71 years (12-94). Approximately 90% of deaths were subjects with NIDDM. Diabetes was mentioned on 215 (58%) death certificates. The all causes SMRs were significantly raised for men and women for all ages less than 75 years. Ischaemic heart disease (ICD9 rubrics

410-414) accounted for 146 (40%) deaths - 41% of male and 38% of female deaths. Male and female SMRs were significantly raised for the age groups 45-64, 65-74, and 75-84 years. Cerebrovascular disease (ICD9 rubrics 430-438) accounted for 38 (10%) deaths and the SMR for women was significantly raised. For women the external causes of death (ICD9 rubrics E800-E999) were also significantly raised overall and in age groups 15-44 and 45-64 years. This was not true for men, although numbers of deaths in this category were small for both men (4) and women (9).

Conclusions - Record linkage has been used successfully to link two local, population based registers. This has enabled an analysis of mortality in people with diabetes to be performed which overcomes the problems associated with using as a sample, death certificates where diabetes is mentioned. The mortality rates and SMRs estimated should more accurately reflect the true rates than would be possible using other methods. The persisting excess mortality identified for people with diabetes is of a similar magnitude and attributable to similar causes as has been reported elsewhere in population based studies.

(J Epidemiol Community Health 1995;49:570-574)

Comparative analysis of the mortality of people with diabetes is complicated by the problem of selecting and identifying the population at risk. Using death certificates that mention diabetes is unreliable as between 15% and 60% of these fail to mention diabetes as a cause.¹⁻⁵ A hospital diabetes clinic based population may result in biased results as those attending may have more severe disease,^{4,6} particularly those with microvascular complications attending for diabetes care. A population based study, in a centre such as Leicestershire where most people with insulin treated diabetes are cared for by a centralised diabetes service,^{7,8} provides an opportunity to study a representative population of insulin-takers.

Previous studies have reported an overall excess mortality for people with diabetes.^{1,4,9-12} Ischaemic heart disease has been implicated as a particular contributor to excess mortality as has cerebrovascular disease.^{1,3,4,6,12} There have been conflicting reports of cancer mortality.^{1,3,4,10,12} Different study methods and

Department of
Epidemiology and
Public Health,
University of
Leicester,
Faculty of Medicine,
22-28 Princess Road
West,
Leicester LE1 6TP
N T Raymond
J D Langley
E Goyder
J L Botha

Department of Public
Health Medicine,
Leicestershire Health
E Goyder
J L Botha

Department of
Diabetes, Leicester
General Hospital and
Leicester Royal
Infirmary
A C Burden
J R Hearnshaw

Correspondence to:
Mr N T Raymond.

Accepted for publication
March 1995

different samples make comparison of results between studies difficult. This study aimed to investigate the possibility of using record linkage and a population based register of people with diabetes to detect deaths, and to examine causes of deaths and patterns of excess mortality in the deaths detected.

Methods

A population based register of people with insulin treated diabetes was established in Leicestershire during 1983–84, when the conversion to U100 insulin was implemented. This register was reinstated and computerised in 1986 using hospital and consultants' records, and data from diabetes specialist nurses, the family health services authority (FHSA), and district dietitians. In 1991 an ascertainment exercise using capture-recapture methods and patients themselves as an "independent" information source estimated the completeness of the register at 86%. A record of people removed from the register because of death or migration is maintained. Register data for 1992 were used as denominators for estimating the mortality rates of people with insulin treated diabetes.

In Leicestershire there is also a locally maintained population based register of residents' deaths – the Leicestershire mortality list (LML).¹³ This register contains all data recorded on death certificates, including uncoded causes of death. Record linkage software¹⁴ (Lynx) developed within the Department of Epidemiology and Public Health and the Leicestershire Health Authority has been used extensively in a maintenance and up date cycle designed to maximise accuracy and minimise duplication and false registration on the diabetes register. The diabetes register, including deletions, was linked to the mortality register to produce a list of deaths. The linkage software used is a probabilistic record linker, which uses a phonetic name matching algorithm to link records despite misspellings or alternative spell-

ings. We analysed deaths that occurred from 1 January 1990 to 31 December 1992, a three year period for which we were certain to have all deaths.

All causes of death mentioned on death certificates were available on computer as text strings. These were searched to check for mention of diabetes, hypoglycaemia, and renal failure to allow analysis of possible under-reporting of diabetes and examine associations between causes listed on death certificates and final underlying cause recorded. Causes of death were coded locally to ICD9 and later further record linkage was performed to incorporate OPCS coding.¹⁵ An analysis of the similarity of local and OPCS coding of the underlying cause of death was undertaken, and showed an overall agreement for 82% of death certificates. The main disagreement between local and OPCS coding was that local coders were less likely to assign diabetes as underlying cause of death (57 OPCS *v* 22 local). Analyses presented are all based on final OPCS coding.

Population and mortality data for Leicestershire for 1991 were used to standardise the data indirectly. Standardised mortality ratios (SMR) and 95% confidence intervals (95% CI) were estimated separately for men and women and within standard age bands. All cause mortality and deaths from diabetes mellitus (DM, ICD9 rubrics 250), ischaemic heart disease (IHD, ICD9 rubrics 410–414), cerebrovascular disease (CVA, ICD9 rubrics 430–438), neoplasms (ICD9 rubrics 140–239), and external causes (E-codes, ICD9 rubrics E800–E999) were examined independently.

To investigate the potential influence of the distribution of insulin dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM) in the sample of deaths, IDDM was defined as diabetes diagnosed before age 30 and with insulin therapy started within one year of diagnosis. A comparative analysis of causes and age of death was performed by type and duration of diabetes.

Analyses were performed using the SAS¹⁵ statistical package, calculating Fisher's exact tests, and χ^2 tests of independence where appropriate. SMRs with 95% CIs were estimated using the *Confidence Interval Analysis*¹⁶ (CIA) microcomputer program.

Results

In 1992 the Leicestershire diabetes register included 4680 people with insulin-treated diabetes. The age-sex distribution is shown in figure 1. A total of 370 deaths during the years 1990–92 were identified by linking the diabetes register and the local mortality list – 163 (44%) were in females and 207 (56%) in males. One female death at age 12 years from cystic fibrosis, was excluded from the main analyses as this was the only recorded death at age less than 15 years. The median age at death was 71 years (range 12–94).

Diabetes mellitus (DM) was mentioned on 215 (58%) death certificates – 60% in 1990, 55% in 1991, and 58% in 1992. For 57 (15%) deaths diabetes was the underlying cause of

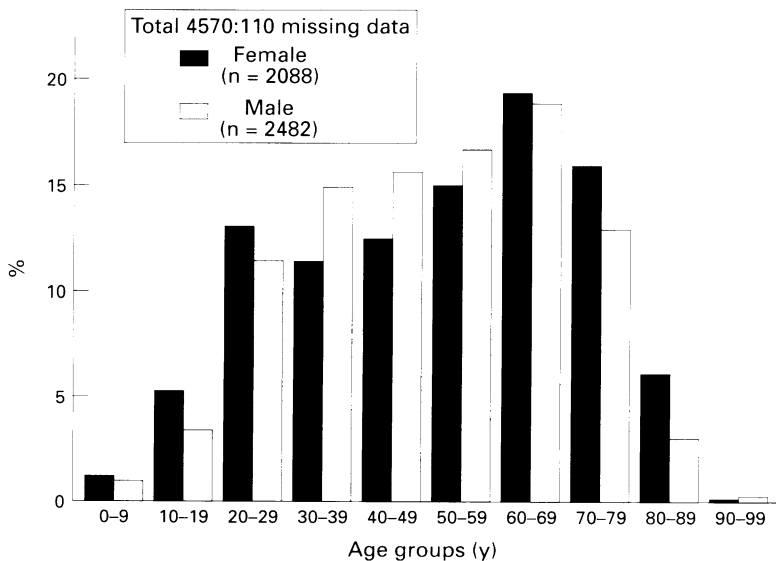


Figure 1 Leicestershire diabetes register (insulin treated diabetes), 1992, age-sex distribution.

Table 1 Mention of diabetes mellitus (DM) on death certificates in relation to underlying cause of death and sex.

Underlying cause of death	Men		Women	
	No of certificates	Mention of DM (%)	No of certificates	Mention of DM (%)
Cerebrovascular disease	16	10 (63)	22	17 (77)
Diabetes	32	32 (100)	25	25 (100)
External causes	4	1 (25)	9	4 (44)
Ischaemic heart disease	85	41 (48)	61	40 (66)
Neoplasms	29	9 (31)	22	5 (23)
All other causes of death	41	18 (44)	23	13 (57)
All causes of death	207	111 (54)	162	104 (64)

death. Most mentions of diabetes were in *part ii* of the death certificate (167 (78%) *v* 48 (22%) in *part i*). Where diabetes was mentioned in *part i*, the underlying cause of death was significantly more likely to be ascribed to diabetes than when it was mentioned in *part ii* (34 (71%) *v* 23 (14%); Fisher's exact test, two-tail $p < 0.001$).

Women were significantly more likely to have DM mentioned than men (65% *v* 54% respectively; Fisher's exact test, two-tail $p = 0.0428$) and the rate of mention of DM also varied in relation to the cause of death (table 1). DM was more likely to be mentioned on death certificates of those aged 85 and older than any other age group (85+ 80%, 75-84 57%, 65-74 59%, 45-64 57%, 15-44 38%), although the differences were not statistically significant.

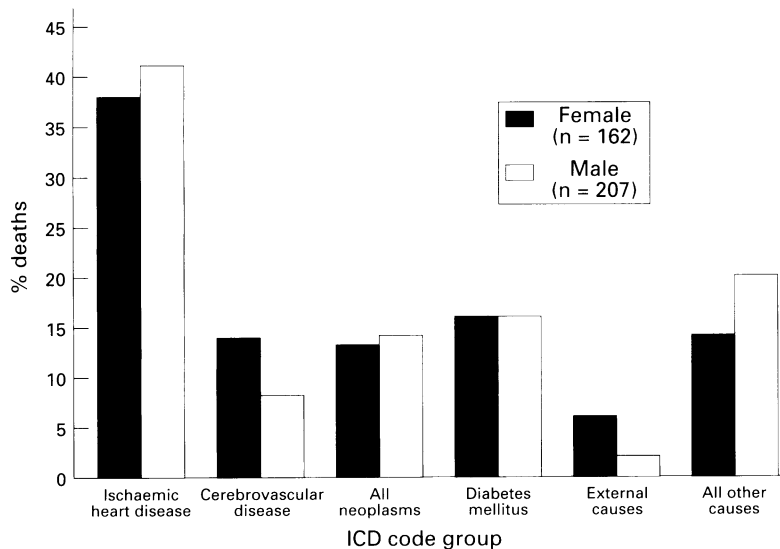


Figure 2 Distribution of underlying causes of deaths 1990-92 inclusive (n=369).

Table 2 Age and sex specific standardised mortality rates (SMRs) for all causes of death

Age group	Observed deaths	Expected deaths	SMR	(95% CI)
Women:				
15-44	6	1.26	4.76*	(1.75, 10.40)
45-64	44	9.53	4.62*	(3.35, 6.20)
65-74	43	24.89	1.73*	(1.25, 2.33)
75-84	54	36.27	1.49*	(1.12, 1.94)
85+	15	19.65	0.76	(0.43, 1.26)
All ages	162	91.60	1.77*	(1.51, 2.06)
Men:				
15-44	10	3.05	3.28*	(1.57, 6.03)
45-64	51	21.19	2.41*	(1.79, 3.16)
65-74	76	46.85	1.62*	(1.28, 2.03)
75-84	60	47.16	1.27	(0.97, 1.64)
85+	10	20.77	0.48*	(0.23, 0.89)
All ages	207	139.03	1.49*	(1.29, 1.71)

* Significant at the 5% level.

Renal failure (chronic, acute, or end stage) was mentioned in 29 (8%) death certificates. Certificates that mentioned renal failure were more likely to mention diabetes (66% *v* 58%), but this was not significant. Significantly more certificates that mentioned renal failure (11, 38%), were allocated to DM as the underlying cause of death than those not mentioning renal failure (46, 14%; Fisher's exact test, two-tail $p = 0.00183$). Hypoglycaemia was mentioned on two death certificates (one man, one woman). In each case hypoglycaemia was listed as cause *ia*, resulting from an insulin overdose. Underlying causes of both deaths were external causes, with one case assigned a coroner's verdict of suicide and the other misadventure. The distribution of causes of death in relation to sex is shown in figure 2. There were 10 (3%) deaths due to cancer of the pancreas (ICD9 rubrics 157) - five in men and five in women. In two cases, examination of the medical notes suggested that DM had developed as a result of pancreatic cancer. Ischaemic heart disease accounted for 146 (40%) deaths, cerebrovascular disease for 38 (10%), neoplasms for 51 (14%), and external causes for 13 (4%). Of the 57 (15%) deaths due to DM, 25 (15%) were in women and 32 (15%) in men.

The SMRs for all causes of death are shown by age and sex in table 2. Men and women have significantly raised SMRs compared with the Leicestershire population overall and for all ages under 75 years. Women also have a significantly raised SMR for the age group 75-84 years and men have a significantly reduced SMR for age group 85+ years.

Ischaemic heart disease was the most common cause of death. It accounted for 38% of female and 41% of male mortality. The overall SMRs (95% CI) were 2.68 (2.05, 3.44) for women and 1.92 (1.53, 2.37) for men (table 3). For women, the main excess was observed in the age group 45-64 years, with an SMR 9.69 (5.84, 15.10) and 19 deaths. For both men and women, the SMR was significantly raised in all age groups from 45 to under 85 years.

Cerebrovascular disease accounted for 38 (10%) deaths - 22 (14%) in women and 16 (8%) in men. The SMRs for men (2.90 (1.33, 5.50)) and women (3.17, (1.37, 6.25)) aged 65-74 were significantly raised, and the overall SMR for women was also raised (1.76 (1.10, 2.66)). A total of 13 deaths were allocated E-codes as causes - nine in women and four in men. SMRs for women were significantly raised overall (5.01 (2.29, 9.51)) and in the age bands

Table 3 Age and sex specific standardised mortality rates (SMRs) for deaths from ischaemic heart disease

Age group	Observed deaths	Expected deaths	SMR	(95% CI)
Women:				
15-44	0	0.04	—	—
45-64	19	1.96	9.69*	(5.84, 15.10)
65-74	18	6.94	2.59*	(1.54, 4.10)
75-84	20	9.94	2.01*	(1.23, 3.11)
85+	4	3.87	1.03	(0.28, 2.65)
All ages	61	22.75	2.68*	(2.05, 3.44)
Men:				
15-44	1	0.35	2.86	(0.07, 15.90)
45-64	22	8.55	2.57*	(1.61, 3.90)
65-74	31	16.24	1.91*	(1.30, 2.71)
75-84	28	14.74	1.90*	(1.26, 2.75)
85+	3	4.42	0.68	(0.14, 1.98)
All ages	85	44.29	1.92*	(1.53, 2.37)

* Significant at the 5% level.

15-44 (11.6 (2.39, 33.80)), and 45-64 (11.48 (3.13, 29.40)).

Fifty one deaths were attributed to neoplasms - 22 (14%) in women and 29 (14%) in men. The overall SMRs for men 0.82 (0.55, 1.18) and for women 0.98 (0.61, 1.48) were both slightly low, but not significantly so.

Eighteen (5%) deaths were defined as IDDM, 322 (88%) NIDDM, and for 27 (7%) there was insufficient data to determine the type of diabetes. Considering all IDDM and NIDDM only, IDDM was associated with death at younger ages but after longer durations of diabetes.

Information on the duration of diabetes was available for 334 (91%) of the deaths. Using these deaths only, the median duration of diabetes at death was 14 years, with a range from 0-56 years. There was some variation in the distribution of causes of death in relation to the duration of diabetes, with more underlying causes ascribed to diabetes in longer duration groups, 13 (11%) at 0-9 years, 18 (16%) at 10-19 years, and 22 (20%) at 20 years duration or more. Conversely, ischaemic heart disease mortality accounted for 56 (49%) deaths at 0-9 years, 44 (39%) at 10-19, and 38 (35%) at 20 or more years of duration.

Discussion

The under-reporting of diabetes on death certificates observed in this study confirms the problems of using death certificates that record diabetes as the underlying cause of death to investigate diabetes related mortality. In this study, diabetes was significantly more likely to be entered on the death certificates of women than men. While this finding has been reported previously, the difference (48% *v* 24% respectively, $p=0.08$) was not significant.¹⁷ An explanation for the discrepancy has been suggested - men are more likely to have their deaths attributed to heart disease because of the known risk for men, while other reasons may be sought for women.

In a population based study reported by Wong *et al*,⁴ ischaemic heart disease, cerebrovascular disease, and neoplasms accounted for 70% of deaths in the population with diabetes, and the all cause SMR was significantly raised, with excess ischaemic heart disease in women accounting for most of this. In the

current study, ischaemic heart disease, cerebrovascular disease, and neoplasms accounted for 63% of deaths compared with 64% due to the same causes for the Leicestershire population in 1991. The cause specific distribution differed appreciably, with excess ischaemic heart disease and cerebrovascular disease and reduced neoplastic mortality for those with diabetes. The differing age structure of the population with insulin treated diabetes compared with the background population may explain these differences. Calculation of SMRs shows that there are excess deaths in the population with insulin treated diabetes after allowing for varying age and sex distributions. Most of this excess can be explained by ischaemic heart disease for men and a combination of ischaemic heart disease and cerebrovascular disease for women.

In this study, an estimated excess mortality of 50% was found for men and one of 80% for women. Differing methods and sample compositions necessitate caution in interpretation of comparisons with other studies reporting higher or lower excesses.^{4,6,9-11,18} Raised SMRs were found for ischaemic heart disease for men and women in all age groups from 45 to 84 years, for cerebrovascular disease for women overall but not for men. There was a significant excess in cerebrovascular disease mortality for men and women aged 65-74 years. The raised all cause SMRs observed can be explained by these ischaemic heart disease and cerebrovascular disease excesses. While the SMRs for all neoplasms were less than 1.0 for men and for women in all age groups except ages 45-64 years, none of these decreases was significant, nor were they sufficient to counter balance the ischaemic heart disease excesses, as has been reported previously for men.⁴

There was an excess of deaths entered as E-codes for women - nine deaths occurred at ages less than 75 years. This has not been reported in previous epidemiological studies and could be an area for future audit and research.

This study focused on insulin-treated DM, a group comprising both IDDM and NIDDM. The age, duration of disease, and causes of mortality distributions differed between the IDDM and NIDDM groups. The IDDM group comprised only 5% of the total mortality, 18 deaths over 3 years. While it is important to bear in mind the differences, the very small numbers of IDDM make separate analyses redundant without considerably more years' worth of data. Using just NIDDM in the analyses made very little difference to the SMR estimates. Despite reported improvements in prognosis for people with diabetes¹⁸⁻²⁰ those with insulin-treated DM still experience high mortality compared with the general population. Most of the excess deaths are attributable to vascular diseases. Future analyses when mortality data for more years are available should enable time trends to be described, for different ethnic groups and for different durations of diabetes.

The use of record linkage and local population based registers has been shown to be effective in estimating mortality in the popu-

lation with diabetes. While this study has focused on insulin treated DM, the methods described are applicable to the whole population with diabetes where appropriate computerised records are available. Similarly, record linkage techniques could be used in other areas where suitable data exist. Focusing on end points other than mortality, purchasers may find uses for record linkage and local registers in identifying high risk groups and monitoring health care delivery and achievement of targets.

We thank Leicestershire Health for funding the diabetes register and Janet Jones and Beverley Ward for their invaluable contribution to its upkeep.

- 1 Green A, Hougaard P. Epidemiological studies of diabetes mellitus in Denmark: 5. Mortality and causes of death among insulin-treated diabetic patients. *Diabetologia* 1984; 26:190-4.
- 2 Whittall DE, Glatthaar C, Knuiman MW, Welborn TA. Deaths from diabetes are under-reported in national mortality statistics. *Med J Aust* 1990;152:598-600.
- 3 Fuller JH, Elford J, Goldblatt P, Adelstein AM. Diabetes mortality: new light on an underestimated public health problem. *Diabetologia* 1983;24:336-41.
- 4 Wong JSK, Pearson DWM, Murchison LE, Williams MJ, Narayan V. Mortality in diabetes mellitus: experience of a geographically defined population. *Diabetic Med* 1991; 8:135-9.
- 5 Ochi JW, Melton III LJ, Palumbo PJ, Chu C. A population-based study of diabetes mortality. *Diabetes Care* 1985;8: 224-9.
- 6 Moss SE, Klein R, Klein BEK. Cause-specific mortality in a population-based study of diabetes. *Am J Public Health* 1991;81:1158-62.
- 7 Walker JB. *Chronicle of a diabetic service*. London: The British Diabetic Association, 1989.
- 8 McNally PG, Burden AC, Swift PGF, Walls J, Hearnshaw JR. The prevalence and risk factors associated with the onset of diabetic nephropathy in juvenile-onset (insulin-dependent) diabetics diagnosed under the age of 17 years in Leicestershire 1930-1985. *Q J Med* 1990;280:831-44.
- 9 Nystrom L, Ostman J, Wall S, Wibell L, DISS Group. Mortality of all incident cases of diabetes mellitus in Sweden diagnosed 1983-1987 at age 15-34 years. *Diabetic Med* 1992;9:422-7.
- 10 Dorman JS, LaPorte RE, Kuller LH *et al*. The Pittsburgh insulin-dependent diabetes mellitus (IDDM) morbidity and mortality study: mortality results. *Diabetes* 1984;33: 271-6.
- 11 Kleinman JC, Donahue RP, Harris MI, Finucane FF, Madans JH, Brock DB. Mortality among diabetics in a national sample. *Am J Epidemiol* 1988;128:389-401.
- 12 Sprafka JM, Pankow J, McGovern PG, French LR. Mortality among type 2 diabetic individuals and associated risk factors: the three city study. *Diabetic Med* 1993;10: 627-33.
- 13 Langley JD, Jackson D, Botha JL. The Leicestershire mortality list: A population-based mortality information system. *J Epidemiol Community Health* 1994;48:A509.
- 14 Langley JD, Botha JL. Use of record linkage techniques to maintain the Leicestershire diabetes register. *Computer Methods and Programs in Biomedicine* 1994;41:287-95.
- 15 SAS Institute Inc. *SAS language reference*. Version 6. 1st ed. Cary, NC: SAS Institute Inc, 1990.
- 16 Gardner MJ, Gardner SB, Winter P. *Confidence interval analysis (CIA)*. Version 1.2. London; BMJ Publishing Group, 1991.
- 17 MacLeod JM. Death certificates and diabetes. *Diabetic Med* 1993;10(suppl):S33.
- 18 Sartor G, Nystrom L, Dahlquist G. The Swedish childhood diabetes study: a seven-fold decrease in short-term mortality. *Diabetic Med* 1990;8:18-21.
- 19 Borch-Johnsen K, Kreiner S, Deckert T. Mortality of type 1 (insulin-dependent) diabetes mellitus in Denmark: a study of relative mortality in 2930 Danish type 1 diabetic patients diagnosed from 1933 to 1972. *Diabetologia* 1986; 29:767-72.
- 20 Green A, Borch-Johnsen K, Anderson PK *et al*. Relative mortality of Type 1 (insulin-dependent) diabetes in Denmark: 1933-1981. *Diabetologia* 1985;28:339-42.