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Mortality and acute complications in children and young adults diagnosed with type 1 diabetes in Yorkshire, UK: a cohort study.

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Duality of interest

There are no conflicts of interest to declare by the authors.

Novelty Statement

- Population-based registers have found decreasing mortality in early onset (under 15 years) type 1 diabetes. Analysis on mortality in late onset (15 – 29 years) is lacking
- The Yorkshire Register of Diabetes in Children and Young People (YRDCYP) is the largest population-based dataset in the UK (5,498 individuals with 100,959 person-years of follow-up). We found that all-cause mortality has

fallen over time, but there was no improvement in mortality for deaths due to acute complications for either onset groups

- We also highlight the importance of clinical verification of death certification data for accurate reporting on cause-specific mortality

Abstract

Aims

Examine all-cause and cause-specific mortality in a population-based cohort of early and late type 1 diabetes onset.

Methods

The Yorkshire Register of Diabetes in Children and Young People (YRDCYP) includes individuals with early (0-14 years) and late (15-29 years) type 1 diabetes onset diagnosed between 1978 and 2013. The YRDCYP was linked to death certification data from the Office for National Statistics (ONS) to calculate standardised mortality ratios (SMRs), cumulative mortality curves using Kaplan-Meier survival estimates and Cox regression modelling. Ethnicity was derived using Onomap. Deprivation was classified using Townsend index. Underlying cause of death was clinically verified.

Results

There were 229 deaths in 5,498 individuals (100,959 person-years of follow-up). Overall SMR was 4.3 (95% CI 3.8 to 4.9). There were no significant differences in SMRs by age of onset, sex or deprivation. SMRs were significantly higher for white ethnicity (8.1 (95% CI 6.9 to 9.4)) compared with South Asian (3.4 (95% CI 1.7 to 6.4)).

Mortality risk was lower in those diagnosed in later years (2002 to 2013 for early onset and 2006 to 2013 for late onset) compared with earlier years (1991 to 1997 for

early onset and 1991 to 1997 for late onset) for early and late onset groups (HR 0.13 (95% CI 0.05 to 0.33); 0.24 (95% CI 0.07 to 0.81)).

Mortality risk improved over time for chronic complications in the early onset group only. There was no improvement in either onset groups for acute complications.

Conclusions

An excess of deaths in the type 1 diabetes population remains. Although all-cause mortality risk has fallen over time, no improvement has been found in mortality due to acute complications.

Introduction

Population-based registers have shown an excess in mortality for individuals with type 1 diabetes compared with the general population (1–10). Reduced mortality in recent years for children diagnosed with type 1 diabetes suggest decreasing excesses in death (1,2,9,11). Few studies have examined this trend in adolescent and young adult onset. In a Finnish cohort, Harjutsalo et al (3) analysed mortality in early (diagnosed under 15 years) and late onset (diagnosed between 15 – 29 years). They found lower mortality over time with early onset, whilst mortality due to acute complications increased with late onset. In the UK, data from the Yorkshire Register of type 1 diabetes in children and young people (YRDCYP) found no difference in standardised mortality ratios (SMRs) between early and late onset (7). However, no comparisons were made between onset groups over time and there was no examination by ethnicity and deprivation, often under-examined demographic factors in UK mortality studies.

Cause-specific mortality from the YRDCYP found a third and a fifth of deaths were due to acute and chronic complications of type 1 diabetes, respectively (7). However, these results were based on death certification data without clinical validation, which may have led to inaccuracies, particularly for diabetes-related deaths. Other studies have noted the frequent omission of type 1 diabetes from death certificates. For example, Laing et al (12) found that only 67% of death certificates for their type 1 diabetes cohort mentioned diabetes. These deaths were reassessed for reclassification under cardiovascular or renal disease. However, no reassessment was made on non-diabetes related deaths.

The YRDCYP now includes data up to 2013, with linked death certification data up to the end of 2015. The aim of this study was to examine associations between demographic factors (onset age, sex, ethnicity and deprivation) with all-cause and cause-specific mortality risk. Mortality risk over time was also analysed, where it was hypothesised that mortality risk would decrease with time.

Research Design and Methods

Study Cohort

The YRDCYP includes data on all under 15 year olds (early onset) diagnosed with diabetes between 1978 and 2013 in the Yorkshire Regional Health Authority (YRHA). The YRHA has an estimated population of 5.3 million (9% of the population of England and Wales) (13). Estimated prevalence of type 1 diabetes in the YRHA is 0.81%, twice the England prevalence (0.4%) (14).

The YRDCYP also includes data on 15 – 29 year olds (late onset) diagnosed between 1991 to 2013 in West Yorkshire (Bradford, Calderdale, Kirklees, Leeds and Wakefield). West Yorkshire includes 57% of the total YRHA population (15).

Individuals diagnosed with type 1 diabetes recorded at the latest diagnosis date were included in the cohort. Individuals diagnosed with type 1 diabetes as a secondary condition were excluded.

In England and Wales, diabetes care is available up to 24 years at specialist Paediatric Diabetes Units, although transfer to adult services can occur from 16

years. The YRDCYP collects data from all specialist diabetes services and from primary care for data validation. Further details on data collection are described in Feltbower et al (2008) (6).

Demographic data

Ethnicity was unavailable due to inconsistent data recording. Onomap software categorised ethnicity by using full name to calculate probability scores according to religion, geographic origin, ethnic background and language. Despite sensitivity issues for classifying non-British identities, Onomap was the preferred ethnicity algorithm for its extensive coverage of ethnicities and number of identity dimensions used to derive a classification (16). Unknown ethnicity was classified for incomplete name or names of ambiguous origin.

The Townsend index categorised individuals into deprivation groups, using a material deprivation definition from the UK decennial census variables (unemployment, overcrowded households, car/van ownership, home ownership) (17). The census year 2001 was chosen as this lies approximately midway within the cohort period. A Townsend index score was assigned to each YRHA 2001 UK census ward area and ordered and divided into five groups from ‘Most deprived fifth’ to ‘Least deprived fifth’. In early onset, deprivation group was assigned according to geocoding YRHA ward area by place of residence at diagnosis. West Yorkshire includes the most deprived and populated wards within the YRHA, so geocoding ward area for late onset using the YRHA would inflate the most deprived groups. Therefore, the late onset group used geocoding from West Yorkshire ward areas only.

Linking the YRDCYP with ONS mortality data

The YRDCYP was linked to ONS death certification data up to 31st December 2015 using National Health Service (NHS) number (this identifies a person's health record in England and Wales), date of birth, gender and name. Consent for data linkage was obtained through the ethics approval granted for this study. Data included date of death, free text from death certificates and the derived ICD-10 codes for underlying cause of death. The ICD-10 code was clinically verified (by HJB) against the free text. Underlying cause of death was defined as "the disease or injury which initiated the train of morbid events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury" (18). Therefore, deaths coded as non-diabetes related (e.g. cardiovascular or renal disease) but was initiated by diabetes were reclassified under diabetes. Underlying cause of death categories included diabetes (E10 – E14), respiratory failure (J00 – J98), ischaemic heart disease (IHD) (I20 – I25), neoplasms (C00 – C97, D00 – D48), mental disorder (F00 – F99), accidents and violence (S00 – T98, V00 – X59, X85 – Y98), suicide (X60 – X84) and other/unknown causes. Deaths due to acute complications were classified as diabetes deaths with coma or ketoacidosis. All other diabetes deaths with other complications were classified under chronic complications.

Statistical analysis

Standardised Mortality Ratios (SMRs)

All analyses was performed using STATA 14. SMRs used 95% confidence intervals assuming a Poisson distribution to compare mortality with the general population. Population and death data for the YRHA were unavailable. Therefore, population

and death totals in England and Wales from 1978 to 2014 by 5-year age bands and sex were used to calculate mortality rates in the general population. Although the England and Wales population and mortality rates include individuals with type 1 diabetes, due to type 1 diabetes prevalence (0.4% (19)), any bias in SMRs is likely to remain low (20). SMRs for diabetes-related deaths were not calculated, as national type 1 diabetes population figures were unavailable.

Survival analysis

Cumulative mortality plots using Kaplan-Meier survival estimates were produced against time since diabetes diagnosis by sex, ethnicity, deprivation and diagnosis year (21). Diagnosis years were categorised into three periods; 1978 to 1989 (period 1), 1990 to 2001 (period 2) and 2002 to 2013 (period 3) for early onset and 1991 to 1997 (period 1), 1998 to 2005 (period 2) and 2006 to 2013 (period 3) for late onset. Analysis time was censored to date of death or to 31st December 2015. Univariable logrank tests assessed differences between survivor functions.

Cox regression models included terms for sex, year of diagnosis, ethnicity and deprivation. An overall model compared the hazard ratios (HRs) between onset groups. Separate models for each onset group assessed all-cause and cause-specific mortality. Schoenfeld residuals and log-log plots of survival were used to assess the proportional hazards assumption.

Cox regression was not completed for non-diabetes related deaths due to small numbers.

Results

Demographics of cohort

The cohort included 5,498 individuals (100, 959 person-years of follow-up); 4,382 (79.7%) with early onset, 1,116 (20.3%) with late onset. Demographic data on the cohort are presented in table 1.

More individuals with early onset were diagnosed with type 1 diabetes in later years, with a third diagnosed from 1999 with 16 years or less follow-up time. This contributed to similar median follow-up times per person to the late onset group, despite data collection beginning 13 years earlier (17.7 years (range 1.5 – 38 years)) in early onset; 16.3 years (range 0.3 – 25 years) in late onset).

All-cause mortality

There were 229 deaths, with median age of death at 29.7 years (range 6.5 – 52.5 years). Median age at death was 28.2 years (range 6.5 – 48.9 years) in early onset and 33.1 years (range 16.2 – 52.5 years) in late onset.

Overall SMR was 4.3 (95% CI 3.8 to 4.9). SMRs between early and late onset were similar (4.1 (95% CI 3.6 to 4.8) vs. 4.7 (95% CI 3.8 to 5.9)) (figure 1a). Although most deaths occurred in males, the SMR (4.4 (95% CI 3.8 to 5.2); n=165) was similar to females (4.0 (95% CI 3.2 to 5.2); n=64) (figure 1b).

Of all deaths, 77.7% had a known ethnicity (169 had white ethnic origin; 9 had South Asian origin). The SMR was significantly higher for white ethnicity compared to South Asian (8.1 (95% CI 6.9 to 9.4) vs. 3.4 (95% CI 1.7 to 6.4)) (figure 1c).

There were no significant differences in SMRs between deprivation categories for the most deprived (4.8 (95% CI 3.8 to 6.1) and for the least deprived (3.3 (95% CI 2.2 to 4.9) (figure 1d). Period 3 had the lowest SMR by diagnosis period (2.1 (95% CI 1.1 to 4.3)), but was not significantly different from period 1 (4.8 (95% CI 4.1 to 5.6)).

Cumulative mortality curves showed lower absolute mortality in later diagnosis periods (figure 2). The curve for period 3 begins to deviate from earlier periods after 13 years and 5 years after diabetes diagnosis for early and late onset respectively. Logrank tests showed significant differences between the survivor functions of the three diagnosis periods in early onset but not in late onset.

Late onset had double the risk of all-cause mortality compared with early onset, when adjusted for sex, year of diagnosis, ethnicity and deprivation (HR 2.1 (95% CI 1.53 to 2.88)). Females, diagnosis period 3 and South Asian ethnicity all had significantly lower mortality risk compared with males, diagnosis period 1 and white ethnicity respectively (table 2). There were no significant differences found between deprivation groups.

The early onset model found that female sex, diagnosis period 3 and South Asian ethnicity were associated with significantly lower mortality rates. In late onset, female sex and diagnosis period 3 had significantly lower mortality compared with males and diagnosis period 1 (table 2).

Diabetes-related mortality

After validation, 53 (23.1%) deaths were reclassified (Supplementary table 1). The majority were reclassified with type 1 diabetes. Of all 229 death certificates, 123 mentioned diabetes; 48 specifically mentioned type 1 diabetes.

There were 119 deaths with an underlying cause of type 1 diabetes. Late onset had a significantly higher risk of death due to type 1 diabetes compared with early onset (HR 1.81 (95%CI 1.13 to 2.89)). In early onset, females and diagnosis period 3 had a significantly lower mortality risk from type 1 diabetes compared with males and diagnosis period 1. In late onset, only deprivation was a significant factor, where the most deprived fifth had a significantly higher mortality risk compared with the least deprived fifth (table 2).

Fifty-six deaths were due to diabetes-related acute complications (median age at death 28.6 years (range 8.9 – 52.5 years)). Forty-three deaths were due to chronic complications (median age at death 35.6 years (range 16.4 – 50.1 years)). Females had a lower mortality risk from acute complications compared with males in early onset (HR 0.46 (95%CI 0.02 to 0.87)). No significant differences were found between diagnosis period. No factors had a significant effect on mortality in late onset.

For deaths due to chronic complications, there was a significantly lower risk in early onset for females and diagnosis period 2. In late onset, there were no significant associations evident with mortality (table 2).

Non-diabetes related mortality

Overall, there were significantly higher SMRs for respiratory failure (3.5 (95% CI 1.7 to 7.4)), mental disorder (4.9 (95% CI 2.6 to 9.1)) and suicide (2.5 (95% CI 1.5 to 4.3)).

Suicide was the only underlying cause of death where there was an excess in deaths for both early (SMR 2.1 (95% CI 1.0 to 4.2)) and late onset (SMR 3.5 (95% CI 1.6 to 7.7)) (figure 1a).

Mental disorder deaths were significantly higher for males (SMR 4.2 (95% CI 2.0 to 8.7) and females 8.4 (SMR 95% CI 2.7 to 26.03) compared with the general population. Males only had a significant excess in deaths for suicide (SMR 2.8 (95% CI 1.6 to 4.8)) and respiratory failure (SMR 4.1 (95% CI 1.7 to 9.8)) (figure 1b).

White ethnicity had an excess in mental health-related mortality (12.9 (95% CI 6.7 to 24.8)) and exhibited an excess of deaths due to accidents (2.8 (95% CI 1.8 to 4.1)). South Asian ethnicity had an excess in deaths due to neoplasms (SMR 6.5 (95% CI 2.1 to 20.1) (figure 1c).

All deprivation groups displayed an excess in deaths due to mental disorder. The two most deprived fifths had an excess in the deaths due to suicide (figure 1d).

Conclusions

The YRDCYP is the largest sub-national population-based cohort to have examined mortality in type 1 diabetes in England. Our study found that mortality risk in the

Yorkshire type 1 diabetes population remains 4 to 5 times greater than the England and Wales general population. Although generalising these results nationally must be considered with caution, the mortality burden is significant.

No significant differences were found in all-cause SMRs between age groups, sex or deprivation. White ethnicity had a significantly higher SMR compared with South Asians, contradicting international studies where minority ethnicities are associated with higher mortality risk (2,22,23). However, this result must be considered in view of Onomap's limitations. Around 32% of the cohort had incomplete full names, so the South Asian total could be underestimated. Additionally, there was no consideration for marital status name changes nor identification of mixed ethnicities.

Classification errors may also have occurred for deprivation. Larger populations live within the most deprived YRHA wards, leading to a higher proportion of the cohort classified in the most deprived fifth. The Index of Multiple Deprivation (IMD) is calculated by Output Areas which are approximately equal in population size, so provides a more equal spread across the five deprivation categories. However, Townsend index was preferred due to its focus on material deprivation. No difference in trends were found in this study when using IMD in comparison to Townsend score.

Despite these limitations, this is the first UK study to our knowledge which has examined mortality by ethnicity and deprivation in the type 1 diabetes population and highlights the importance of accurate recording and/or assignment of ethnicity and deprivation categories to examine future trends.

Absolute all-cause mortality decreased significantly over time. Mortality risk in diagnosis period 3 was significantly lower for both early (HR 0.13 (95%CI 0.05 to 0.33)) and late onset (HR 0.24 (95%CI 0.07 to 0.81)). The follow-up time for period 3 was less for both onset groups compared with period 1, so future analysis with additional follow-up time will determine if this decrease in mortality continues. However, despite improvements in all-cause mortality, no improvements were found in deaths due to acute complications. This is concerning, particularly as this and other studies reveal that these deaths occur at younger ages (7,10,22,24–26). Additionally, Cox regression found that only sex was significantly associated with mortality risk from acute complications, with a notable increased risk in males. The 2015-16 National Diabetes Audit and National Paediatric Diabetes Audit showed only a third of all individuals aged 12 years and over in England and Wales received all recommended annual care processes. Additionally, less than 20% reached recommended HbA1c, blood pressure and cholesterol targets. Improving specifically targeted diabetes care is essential in reducing premature deaths due to diabetes-related complications.

Reduced mortality risk for chronic complications was evident only in early onset, as was found by Harjutsalo et al (3). However, mortality risk due to acute complications was significantly increased in their study in late onset between 1970-1974 and 1985-1989. This study covers a more recent time period, so can provide a contemporary representation of the type 1 diabetes population, including the introduction of intensive insulin treatment. Unfortunately, data on treatment regimen and other clinical variables (e.g. HbA1c value and smoking status) were unavailable. This creates difficulty in ascertaining which variables contribute to mortality risk change.

Differences between the onset groups may be due to self-management education and experience in combination with differences in the transition from paediatric to adult health services. There has been increased recognition of transitional issues, with the introduction of national clinical guidelines for England in 2016 (27). However, the specificity of issues by onset age lack research and are not fully understood.

Sex differences were found in non-diabetes related deaths. Excess deaths due to respiratory failure and suicide were found in males only. The total male deaths due to respiratory failure was small (along with other cause-specific SMRs by other demographic variables), so the SMR should be interpreted with caution.
Nearly 10% of all male deaths were due to suicide. The difficulty in determining whether deaths due to acute complications were self-inflicted with the intention of suicide may mean that suicide rates are underestimated. Other studies have reported higher suicide rates in women (3,26,28), although higher rates in males were found in the DCCT cohort. The DCCT cohort also found nominally more suicides in the intensive treatment group compared with the conventional treatment group (29). There is some evidence for increased mental health issues in type 1 diabetes compared with the general population. However, the rate of increased mental health problems since the introduction of intensive insulin treatment has not been well examined.

We found a larger proportion of diabetes-related deaths compared with our previous study, partly due to the death classification (6). Deaths originally classified as renal

disease and IHD were re-classified as type 1 diabetes. The ICD-10 code E10.2 was used for type 1 diabetes with renal complications. However, there is no ICD-10 code for type 1 diabetes with IHD, so these were coded under E10.6 (type 1 diabetes with specified complications). The accuracy of assigning ICD-10 codes without clinical verification is therefore questionable. This draws attention to possible underestimations in deaths due to type 1 diabetes in previous studies. Only 54% of all death certificates mentioned diabetes and 21% specifically mentioned type 1 diabetes. The absence of type 1 diabetes recorded on death certificates for individuals with a confirmed diagnosis has been highlighted previously (30).

In conclusion, an excess of deaths remains in the type 1 diabetes Yorkshire population compared with the general population of England and Wales. There is some evidence that all-cause mortality rates are falling. However, the lack of improvement in diabetes-related deaths, especially due to acute complications, is concerning. The re-classification of the underlying cause of death due to type 1 diabetes suggests an underestimation of deaths due to type 1 diabetes in previous studies.

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Contribution statement

T.C.E-C. analysed data and wrote the manuscript. H.J.B. provided clinical validation of death certification data and reviewed the manuscript. R.G.F and R.C.P. contributed to the discussion and reviewed/edited the manuscript.

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Table 1a: Demographic characteristics of the Yorkshire Register of Diabetes in Children and Young People cohort by sex

	Males	Females	Total
Total individuals	2,970 (54%)	2,527 (46%)	5,498
Total person-years	53,854.7 (53.3%)	47,097.5 (46.7%)	100,959.0
Mean person-years per individual	18.1	18.6	18.4
Median person-years per individual	17.1	17.5	17.3
Age at diagnosis			
0 to 14 years (early onset)	2,276 (51.9%)	2,105 (48%)	4,382
15 to 29 years (late onset)	694 (62.2%)	422 (37.8%)	1,116
Ethnicity			
White	1,762 (52.7%)	1,581 (47.3%)	3,343
South Asian	188 (52.4%)	171 (47.6%)	359
Other/Unknown ethnicity	1,020 (56.8%)	775 (43.2%)	1,796
Deprivation			
Most deprived fifth	822 (53.7%)	710 (46.3%)	1,532
2nd most deprived fifth	677 (53.3%)	593 (46.7%)	1,270
3rd most deprived fifth	592 (53.3%)	518 (46.6%)	1,111
2nd least deprived fifth	473 (54.1%)	402 (45.9%)	875
Least deprived fifth	406 (57.2%)	304 (42.8%)	710
Diabetes duration			
<10 years	578 (54%)	491 (45.9%)	1,070
10 to 19 years	1,243 (55.2%)	1,007 (44.8%)	2,250
20 to 29 years	1,149 (52.8%)	1,029 (47.2%)	2,178
Underlying cause of death			
All causes	165 (72.1%)	64 (27.9%)	229
Type 1 diabetes related	83 (69.7%)	36 (30.3%)	119
Respiratory failure	*	*	7
Neoplasms	*	*	13
Accidents and violence	19 (70.4%)	8 (29.6%)	27
Mental disorder	*	*	10
Suicide	*	*	14
Other/Unknown	29 (74.4%)	11 (28.2%)	39

*Small (potentially disclosive) numbers under 5

Table 1b: Demographic characteristics of the Yorkshire Register of Diabetes in Children and Young People cohort by onset group

	Early onset	Late onset	Total
Total individuals	4,382 (79.7%)	1,116 (20.3%)	5,498
Total person-years	83,097.2 (82.3%)	17,861.9 (17.7%)	100,959.0
Mean person-years per individual	19	16	18.4
Median person-years per individual	17.7	16.3	17.3
Sex			
Male	2,276 (76.6%)	694 (23.4%)	2,970
Female	2,105 (83.3%)	422 (16.7%)	2,527
Ethnicity			
White	2,707 (81%)	636 (19%)	3,343
South Asian	263 (73.3%)	96 (26.7%)	359
Other/Unknown ethnicity	1,412 (78.6%)	384 (21.4%)	1,796
Deprivation			
Most deprived fifth	1,248 (81.5%)	284 (18.5%)	1,532
2nd most deprived fifth	1,048 (82.5%)	222 (17.5%)	1,270
3rd most deprived fifth	902 (81.2%)	209 (18.8%)	1,111
2nd least deprived fifth	675 (77.1%)	200 (22.9%)	875
Least deprived fifth	509 (71.7%)	201 (28.3%)	710
Diabetes duration			
<10 years	885 (82.7%)	185 (17.3%)	1,070
10 to 19 years	1,650 (73.3%)	1,650 (26.7%)	2,250
20 to 29 years	1,847 (84.8%)	331 (15.2%)	2,178
Underlying cause of death			
All causes	156 (68.1%)	73 (31.9%)	229
Type 1 diabetes related	88 (73.9%)	31 (26.1%)	119
Respiratory failure	*	*	7
Neoplasms	7 (53.8%)	6 (46.2%)	13
Accidents and violence	18 (66.7%)	9 (33.3%)	27
Mental disorder	*	*	10
Suicide	8 (57.1%)	6 (42.9%)	14
Other/Unknown	27 (69.2%)	12 (30.8%)	39

*Small (potentially disclosive) numbers under 5

Table 2: Hazard ratios and 95% confidence intervals associated with mortality following diagnosis of type 1 diabetes by demographic factors

	Late onset vs early onset	Females vs males	South Asian vs white ethnicity	Most deprived fifth vs least deprived fifth	Diagnosis period 2 vs diagnosis period 1	Diagnosis period 3 vs diagnosis period 1	Total deaths
All deaths							
All	**2.1 (1.53 to 2.88)**	**0.41 (0.31 to 0.55)**	**0.35 (0.18 to 0.7)**	1.25 (0.78 to 2)	**0.48 (0.34 to 0.68)**	**0.15 (0.07 to 0.32)**	229
Early onset		**0.41 (0.29 to 0.58)**	**0.35 (0.14 to 0.58)**	0.87 (0.49 to 1.55)	**0.4 (0.26 to 0.6)**	**0.13 (0.05 to 0.33)**	156
Late onset		**0.41 (0.23 to 0.71)**	0.36 (0.12 to 1.02)	1.96 (0.88 to 4.38)	0.7 (0.4 to 1.22)	**0.24 (0.07 to 0.81)**	73
All diabetes-related deaths							
All	**1.81 (1.13 to 2.89)**	**0.45 (0.3 to 0.66)**	**0.18 (0.04 to 0.73)**	1.06 (0.55 to 2.06)	**0.47 (0.29 to 0.78)**	**0.23 (0.09 to 0.62)**	119
Early onset		**0.42 (0.27 to 0.66)**	0.16 (0.02 to 1.15)	0.55 (0.26 to 1.16)	**0.36 (0.2 to 0.65)**	**0.15 (0.04 to 0.54)**	88
Late onset		0.53 (0.24 to 1.2)	0.2 (0.03 to 1.52)	**4.69 (1.02 to 21.61)**	0.84 (0.36 to 1.97)	0.61 (0.13 to 2.87)	31
All diabetes-related deaths - acute complications							
All	1.54 (0.78 to 3.06)	**0.5 (0.28 to 0.88)**	-	0.91 (0.36 to 2.31)	0.84 (0.43 to 1.64)	0.4 (0.12 to 1.31)	56
Early onset		**0.46 (0.02 to 0.87)**	-	0.75 (0.28 to 2.06)	0.59 (0.27 to 1.29)	0.28 (0.07 to 1.08)	43
Late onset		0.66 (0.2 to 2.17)	-	4.31 (0.48 to 38.78)	1.84 (0.51 to 6.61)	1.06 (0.11 to 10.59)	13
All diabetes-related deaths - chronic complications							
All	1.58 (0.69 to 3.58)	**0.57 (0.02 to 0.39)**	0.29 (0.04 to 2.23)	1.02 (0.31 to 3.35)	**0.09 (0.02 to 0.39)**	0.26 (0.03 to 2.37)	43

Early onset		0.49 (0.24 to 1)	-	0.41 (0.11 to 1.5)	**0.06 (0.01 to 0.43)**	-	33
Late onset		1.01 (0.87 to 1.17)	0.57 (0.06 to 5.27)	-	0.27 (0.03 to 2.31)	2.67 (0.21 to 34.06)	10