Diabetologia (2013) 56:2601–2608
DOI 10.1007/s00125-013-3063-1

ARTICLE

Mortality trends in patients with and without diabetes in Ontario, Canada and the UK from 1996 to 2009: a population-based study

M. Lind · L. A. Garcia-Rodriguez · G. L. Booth · L. Cea-Soriano · B. R. Shah · G. Ekeroth · L. L. Lipscombe

Received: 26 November 2012 / Accepted: 29 April 2013 / Published online: 11 October 2013

Abstract
Aims/hypothesis The aim of this study was to determine the contemporary rate ratio of mortality and changes over time in individuals with vs without diabetes.
Methods Annual age- and sex-adjusted mortality rates were compared for adults (>20 years) with and without diabetes in Ontario, Canada, and the UK from January 1996 to December 2009 using The Health Improvement Network (THIN) and Ontario databases. The total number of individuals evaluated increased from 8,757,772 in 1996 to 12,696,305 in 2009.
Results The excess risk of mortality for individuals with diabetes in both cohorts was significantly lower during later vs earlier years of the follow-up period (1996–2009). In Ontario the diabetes mortality rate ratio decreased from 1.90 (95% CI 1.86, 1.94) in 1996 to 1.51 (1.48, 1.54) in 2009, and in THIN from 2.14 (1.97, 2.32) to 1.65 (1.57, 1.72), respectively. In Ontario and THIN, the mortality rate ratios among diabetic patients in 2009 were 1.67 (1.61, 1.72) and 1.81 (1.68, 1.94) for those aged 65–74 years and 1.11 (1.10, 1.13) and 1.19 (1.14, 1.24) for those aged over 74 years, respectively. Corresponding rate ratios in Ontario and THIN were 2.45 (2.36, 2.54) and 2.64 (2.39, 2.89) for individuals aged 45–64 years, and 4.89 (4.35, 5.45) and 5.18 (3.73, 6.69) for those aged 20–44 years.
Conclusions/interpretation The excess risk of mortality in individuals with vs without diabetes has decreased over time in both Canada and the UK. This may be in part due to earlier detection and higher prevalence of early diabetes, as well as to improvements in diabetes care.

Keywords Adult · Diabetes · Incidence · Mortality · Prevalence

Abbreviations
ODD Ontario Diabetes Database
THIN The Health Improvement Network

Introduction

The global burden of diabetes has risen dramatically over the last two decades and diabetes is expected to affect more than 500 million adults worldwide by 2030 [1]. Diabetes is a

Electronic supplementary material The online version of this article (doi:10.1007/s00125-013-3063-1) contains peer-reviewed but unedited supplementary material, which is available to authorised users.

M. Lind
Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

M. Lind (✉)
Department of Medicine, Uddevalla Hospital, 451 80 Uddevalla, Sweden
e-mail: lind.marcus@telia.com

L. A. Garcia-Rodriguez · L. Cea-Soriano
Spanish Centre for Pharmacoepidemiologic Research (CEIFE), Madrid, Spain

G. L. Booth
Li Ka Shing Knowledge Institute of St Michael's Hospital, Toronto, ON, Canada

B. R. Shah
Sunnybrook Health Sciences Centre, Toronto, ON, Canada

G. Ekeroth
Statistiska Konsultgruppen, Gothenburg, Sweden

L. L. Lipscombe
Women's College Research Institute, Women's College Hospital, University of Toronto, Toronto, ON, Canada

leading cause of blindness, the most common cause of end-stage renal disease in the developed world [2], and a major cause of cardiovascular complications such as heart attack and stroke [3–5]. As a result, mortality rates are significantly higher in individuals with diabetes than in those without diabetes [6–13], with the majority of deaths being due to cardiovascular disease [3–6].

A comprehensive review of prospective studies of diabetes-related mortality estimated that diabetes is associated with an approximate 80% increase in mortality [6]. It is important to note that several studies included in the review were carried out before the year 2000. Several other studies that examined this question before the year 2000 had suggested that while diabetes mortality rates were declining, excess mortality had not changed and remained approximately double that seen in the general population [9, 11–13]. However, three studies of individuals with diabetes carried out during the initial years of the 21st century in the UK, USA and Denmark, respectively, found a lower excess risk of mortality during later vs earlier time periods [14–16].

The aim of the current study was to estimate the contemporary mortality rate ratio in individuals with vs without diabetes and whether it has changed over time. We analysed data from two large population-based cohorts from Ontario, Canada, and the UK, from 1 January 1996 until 31 December 2009.

Methods

We used population-based healthcare databases from the province of Ontario, Canada, and The Health Improvement Network (THIN) database from the UK over the years 1996–2009 to calculate mortality rates in persons with and without diabetes. Both data sources have been previously described in detail [10, 17]. In Ontario, we obtained data from administrative healthcare databases, which included anonymous records for virtually all residents covered by the government-funded provincial health plan, comprising approximately ten million adults, as well as vital statistical information from linked death-certificate data. The annual count of individuals with diabetes was recorded from the Ontario Diabetes Database (ODD), a validated registry of Ontario residents with diagnosed diabetes based on hospitalisation and physicians' claims data. Based on a validated algorithm that has been shown to have 86% sensitivity and 97% specificity, persons were defined as having diabetes in a given year and being aged at least 20 years if they had one hospitalisation or two physician's claims bearing a diagnosis of diabetes within a 2-year period [18]. In addition, we identified all individuals without a diagnosis of diabetes. In both populations mortality rates were based on the annual number of deaths obtained from death-certificate data enriched with in-hospital deaths from hospital discharge abstracts.

UK data were obtained from the THIN database, a computerised medical research database that contains systematically recorded data on more than three million patients seen at primary-care practices in the UK. This database is representative of this population with respect to age, sex and geographical distribution [19]. Participating primary-care practitioners record data as part of their routine care of patients, including demographic characteristics, consultation rates, referrals, hospital admissions, laboratory results, diagnoses and prescriptions, and send these to the network for research purposes. The Read classification is used to code specific diagnoses [17], and a drug dictionary based on data from the MULTILEX classification is used to code prescriptions [20]. We identified annually all individuals with a diagnosis of diabetes mellitus recorded by the primary-care practitioner with an automatic search using Read Codes as described elsewhere in more detail [21], and all other remaining patients without a diabetes diagnosis were also identified. In both cohorts we identified the number of patients with a recorded death in a given year. Ethics approval was obtained from the institutional review board at Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada, for the ODD and the Multicentre Research Ethics Committee (06/MRE01/29) for the THIN database.

We investigated the excess risk of mortality in adult individuals (aged 20 years or older) with diabetes compared with those free of diabetes each year in both cohorts over the study period (1 January 1996 to 31 December 2009). Annual age- and sex-adjusted mortality rates and rate ratios were estimated on a group level comparing all diabetic patients with all individuals without diabetes each year during the follow-up period. Estimated mortality rates and rate ratios for each year were also calculated by sex and age groups (ages: 20–44, 45–64, 65–74 and 75+ years) in both countries and populations. To make comparisons between countries and over time possible, all estimations of excess risk of mortality, on a group level, by age and sex, and in both countries were standardised to the age and sex distributions of the 2006 Canadian Census population.

Statistics Crude mortality rates were calculated annually during follow-up in both the Ontario and THIN databases for individuals with and without diabetes. Annual age- and sex-adjusted mortality rates for each population were adjusted for differences in population distributions over time, with direct standardisation using the age and sex distribution of the 2006 Canadian Census population in both databases. Mortality rate ratios within each age group in both cohorts were adjusted to the age and sex distributions for the corresponding age group of the 2006 Canadian Census population. In the Ontario cohort, the number of deaths per 1,000 persons

was calculated, whereas number of deaths per 1,000 person-years was estimated for THIN. Annual mortality rate ratios and CIs associated with diabetes were calculated for each database by dividing the corresponding death rates in the diabetic populations by the death rates in the non-diabetic populations. The SE for the directly adjusted standardised rates was obtained by assuming a Poisson distribution for the individual observed rates for each age–sex subgroup and using weights for each subgroup according to Canada Census 2006. For each age–sex subgroup, individual terms were calculated for the product of the number of deaths and the square of the weight multiplied by 1,000 and divided by the person-years (Canada) or patient-years (UK), and the SE of the directly adjusted rate obtained as the square root of the sum of these terms. All calculations were performed with SAS 9.2 (SAS Institute, Cary, NC, USA).

Results

The number of individuals with and without diabetes together with the prevalence of diabetes each year during 1996–2009 are shown for the Ontario and THIN cohorts in Table 1. In Ontario, the number of individuals with diabetes increased from 439,123 to 1,140,248, and the number of individuals without diabetes increased from 7,668,753 to 8,847,360 during the corresponding time period. The prevalence of diabetes increased consistently with time, from 5.4% in 1996 to 11.4% in 2009. In THIN, there were 17,969 persons with diabetes and 548,906 without diabetes in 1996. In 2009 there were 160,348 patients with diabetes and 2,548,349 persons without diabetes, and the prevalence of diabetes increased from 3.2% to 5.9% from 1996 to 2009 (Table 1). The mean age of individuals with and without diabetes, and the proportion of men and women each year during follow-up are shown in Table 1 and Table 2 of the electronic supplementary material (ESM). In both cohorts the mean age and proportion of men remained similar over all years of follow-up in both individuals with and without diabetes. When standardising the prevalence of diabetes in both cohorts to the age and sex distribution of the 2006 Canadian Census population, similar patterns towards an increase in the prevalence, with higher proportion in the Ontario cohort than in the THIN cohort, were found over the whole study period (ESM Table 3)

In Ontario in 1996 the mean age of diabetic patients was 60.8 years and this increased to 61.5 years in 2009; in both years the proportion of men was 52%. The mean age of the non-diabetic population was 45.1 and 46.2 years in 1996 and 2009, respectively, and in both years 48% were men. In THIN, the mean age of diabetic patients was 62.7 years (54% men) in 1996 and 63.0 years (55% men) in 2009. In the non-diabetic population, the mean ages in 1996 and 2009 were 50.1 years (47% men) and 48.1 years (48% men), respectively.

Standardised annual mortality rates by diabetes status for all diabetic patients as a group, for the Ontario and THIN populations, are presented in Fig. 1. The age- and sex-adjusted annual mortality rate in the Ontario cohort decreased by 37.2% over the study period, from 19.4 to 12.2 per 1,000 persons. There was a corresponding 55.0% reduction in adjusted rates in the THIN population, from 31.4 to 14.1 per 1,000 patients. In contrast, adjusted annual mortality rates in persons without diabetes declined by 20.8% (from 10.2 to

Table 1 Number of adults (20 years or older) with and without diabetes and the prevalence of diabetes each year during the follow-up period 1996–2009 in the Ontario and THIN cohorts

Calendar year	Ontario			THIN		
	Diabetes	Without diabetes	Prevalence	Diabetes	Without diabetes	Prevalence
1996	439,123	7,668,753	0.054	17,969	548,906	0.032
1997	476,833	7,751,774	0.058	22,254	655,263	0.033
1998	514,360	7,823,744	0.062	27,453	782,280	0.034
1999	555,599	7,900,855	0.066	34,441	936,509	0.035
2000	597,995	8,007,432	0.069	44,901	1,144,820	0.038
2001	646,586	8,137,155	0.074	59,216	1,412,980	0.040
2002	699,623	8,260,212	0.078	71,884	1,576,296	0.044
2003	749,896	8,361,180	0.082	82,545	1,680,718	0.047
2004	807,774	8,451,336	0.087	97,048	1,850,521	0.050
2005	872,033	8,527,302	0.093	111,475	2,012,337	0.052
2006	945,833	8,591,842	0.099	123,357	2,139,019	0.055
2007	1,014,098	8,664,394	0.105	135,898	2,275,532	0.056
2008	1,075,839	8,747,448	0.110	148,792	2,418,697	0.058
2009	1,140,248	8,847,360	0.114	160,348	2,548,349	0.059

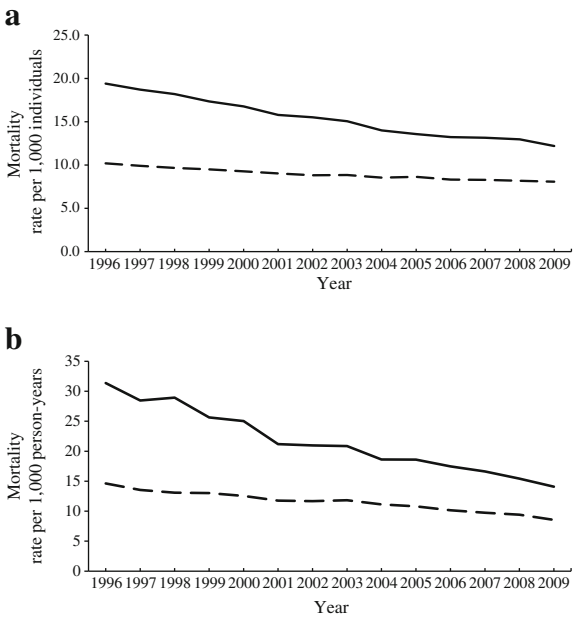

Fig. 1 Adjusted absolute rates of mortality for diabetic (solid line) and non-diabetic (dashed line) adults (20 years or older) in (**a**) Ontario (Canada) and (**b**) the THIN database (UK). Standard population: Canada Census 1996

8.08 per 1,000 individuals) and 41.6% (from 14.6 to 8.55 per 1,000 individuals) in Ontario and THIN, respectively.

The annual mortality rate ratios and 95% CIs each year from 1996 to 2009 for patients with vs without diabetes are shown in Table 2. Excess mortality for patients with diabetes decreased by 44% in Ontario, from a rate ratio of 1.90 (1.86, 1.94) to 1.51 (CI 1.48, 1.54), and by 43% in THIN, from 2.14 (1.97, 2.32) to 1.65 (1.57, 1.72). Similar trends were observed for men and women (Fig. 2). The mortality rate ratio for women decreased in Ontario by 47.1%, from 1.94 (1.88, 1.99) to 1.48 (1.45, 1.52); for men, the mortality rate ratio decreased by 39.0% from 1.87 (1.82, 1.93) to 1.54 (1.50, 1.58) during the corresponding time period. In THIN, the corresponding decline for women was 49.6%, from 2.25 (2.00, 2.50) to 1.63 (1.52, 1.74) and for men it was 35.6%, from 2.04 (1.79, 2.29) to 1.67 (1.56, 1.77). The mortality rate ratios by age group for each year in the Ontario and the THIN groups are shown in Table 2. The mortality rate ratios became lower over time for all age groups except for the youngest group and in both cohorts. In individuals aged 65–74 and 75 years or older the excess risk of mortality was lower in both cohorts and over the whole study period than in individuals younger than 65 years (Table 2). In Ontario and THIN, the mortality rate ratios among diabetic patients in 2009 were 1.67 (1.61, 1.72) and 1.81 (1.68, 1.94) for those aged 65–74 years and 1.11 (1.10, 1.13) and 1.19 (1.14, 1.24) for those aged over 74 years, respectively. Corresponding rate ratios in Ontario and THIN were 2.45 (2.36, 2.54) and 2.64 (2.39, 2.89) for individuals aged 45–64 years, and 4.89 (4.35, 5.45) and 5.18 (3.73, 6.69) for those aged 20–44 years. The underlying adjusted mortality rates for the estimations of adjusted mortality rate ratios by age group are shown in ESM Table 4 and Table 5.

Most deaths in diabetes patients occurred in patients above 64 years of age (84.6% in Ontario and 86.1% in THIN in 1996 and 85.1% in Ontario and 87.5% in THIN in 2009). Similar proportions of deaths in diabetic patients above 64 years of age were found from 1997 to 2008 (data not shown).

Discussion

In these cohorts from Ontario, Canada, and THIN in the UK, the excess risk of mortality for patients with diabetes was significantly lower during later vs earlier years of the study period (1996–2009). The contemporary excess risk of mortality estimated during 2009 was 51% in Ontario and 65% in THIN for diabetic patients on a group level, compared with 90% and 114%, respectively, in 1996.

The excess risk of mortality for diabetic patients was lower over time for all age groups except for the youngest group—approximately 20–45% lower in those 45–64 years old, 35–40% lower in those 65–74 years old, and 65–75% in those older than 74 years over the study period. In 2009 the excess risk of mortality for individuals with diabetes who were aged 20–44 years was five times higher in both cohorts. The excess risk of mortality was approximately 2.5 times higher in those aged 45–64 years, 70–80% higher for individuals aged 65–74 years, and 10–20% greater in those aged over 74 years. The excess risk of mortality for diabetic patients declined to a similar extent for men and women over the study period, and no significant differences were observed in 2009. Although not a primary objective of the study it is worth noting that the prevalence of diabetes in Ontario (adults 20 years or older) increased from 5.4% to 11.4% over the study period, and in the THIN cohort there was an increase in prevalence from 3.2% to 5.9% over the corresponding time period. Moreover, we observed that 85–88% of deaths in diabetic patients, consistently over the study period, occurred in individuals above the age of 64 years.

To our knowledge, estimates of excess mortality risk in diabetic patients during more recent years and from population-based samples are limited. In a recent comprehensive review of 40,116 individuals with diabetes from a series of prospective cohort studies the excess risk of mortality for individuals with diabetes, as a group, was estimated to be 1.8-fold greater than that of individuals without diabetes [6]. It should be noted that several of these studies were performed before the year 2000. Our findings indicate that for diabetic patients as a group, the excess risk of mortality is lower today, by approximately 50–65%, and differs largely by age group, being considerably lower in individuals above 64 years of age.

Table 2 Adjusted mortality rate ratios[a] for adults (20 years or older) with vs without diabetes overall and by age group for each year from 1996 until 2009 in the Ontario and the THIN cohorts

Calendar year	Ontario					THIN				
	Total	20–44 years	45–64 years	65–74 years	75+ years	Total	20–44 years	45–64 years	65–74 years	75+ years
1996	1.90 (1.86, 1.94)	4.77 (4.16, 5.39)	2.85 (2.72, 2.99)	2.05 (1.98, 2.12)	1.44 (1.41, 1.48)	2.14 (1.97, 2.32)	3.79 (1.30, 6.38)	4.14 (3.41, 4.90)	2.35 (2.07, 2.64)	1.52 (1.39, 1.65)
1997	1.89 (1.85, 1.93)	4.54 (3.95, 5.15)	2.93 (2.80, 3.06)	2.08 (2.01, 2.14)	1.43 (1.40, 1.46)	2.10 (1.93, 2.27)	5.25 (2.48, 8.15)	3.67 (3.02, 4.33)	2.34 (2.07, 2.62)	1.50 (1.39, 1.62)
1998	1.88 (1.85, 1.92)	4.95 (4.34, 5.57)	3.12 (2.98, 3.25)	1.97 (1.91, 2.04)	1.40 (1.37, 1.43)	2.21 (2.05, 2.38)	6.40 (3.63, 9.31)	3.71 (3.14, 4.30)	2.33 (2.08, 2.59)	1.55 (1.44, 1.67)
1999	1.83 (1.79, 1.86)	4.73 (4.15, 5.33)	2.89 (2.76, 3.02)	1.91 (1.84, 1.97)	1.39 (1.36, 1.42)	1.97 (1.83, 2.10)	5.21 (2.78, 7.74)	3.50 (2.98, 4.03)	2.08 (1.87, 2.30)	1.43 (1.34, 1.53)
2000	1.81 (1.77, 1.84)	4.90 (4.32, 5.49)	2.92 (2.79, 3.04)	1.91 (1.85, 1.98)	1.35 (1.32, 1.37)	2.00 (1.87, 2.12)	5.38 (3.20, 7.65)	3.42 (2.99, 3.88)	2.12 (1.92, 2.32)	1.41 (1.33, 1.50)
2001	1.75 (1.72, 1.78)	4.59 (4.05, 5.15)	2.84 (2.72, 2.97)	1.87 (1.81, 1.93)	1.30 (1.27, 1.32)	1.80 (1.70, 1.91)	3.91 (2.30, 5.58)	2.99 (2.62, 3.37)	1.83 (1.67, 2.00)	1.37 (1.30, 1.45)
2002	1.76 (1.73, 1.79)	4.76 (4.22, 5.30)	2.81 (2.69, 2.92)	1.85 (1.79, 1.91)	1.31 (1.28, 1.33)	1.80 (1.71, 1.89)	3.73 (2.25, 5.25)	2.79 (2.46, 3.13)	2.03 (1.87, 2.20)	1.40 (1.33, 1.47)
2003	1.70 (1.67, 1.73)	4.20 (3.70, 4.70)	2.68 (2.58, 2.79)	1.79 (1.73, 1.85)	1.30 (1.27, 1.32)	1.76 (1.67, 1.85)	5.22 (3.53, 6.97)	2.78 (2.47, 3.09)	1.95 (1.80, 2.10)	1.30 (1.24, 1.36)
2004	1.64 (1.61, 1.67)	4.04 (3.57, 4.53)	2.54 (2.44, 2.65)	1.71 (1.65, 1.76)	1.26 (1.24, 1.29)	1.67 (1.59, 1.75)	4.10 (2.74, 5.51)	2.54 (2.27, 2.82)	1.71 (1.58, 1.85)	1.30 (1.25, 1.36)
2005	1.57 (1.55, 1.60)	3.83 (3.38, 4.29)	2.47 (2.37, 2.57)	1.69 (1.63, 1.74)	1.21 (1.19, 1.23)	1.72 (1.64, 1.80)	4.22 (2.88, 5.61)	2.66 (2.40, 2.93)	1.94 (1.80, 2.08)	1.31 (1.26, 1.36)
2006	1.59 (1.56, 1.62)	4.30 (3.82, 4.79)	2.53 (2.43, 2.63)	1.69 (1.63, 1.75)	1.19 (1.17, 1.21)	1.72 (1.64, 1.80)	4.56 (3.25, 5.92)	2.74 (2.48, 3.01)	1.84 (1.71, 1.98)	1.27 (1.22, 1.32)
2007	1.59 (1.56, 1.62)	4.08 (3.63, 4.55)	2.53 (2.44, 2.62)	1.77 (1.71, 1.83)	1.19 (1.17, 1.21)	1.70 (1.63, 1.78)	5.70 (4.16, 7.30)	2.59 (2.34, 2.84)	1.89 (1.76, 2.03)	1.23 (1.19, 1.28)
2008	1.59 (1.56, 1.61)	4.88 (4.37, 5.41)	2.51 (2.42, 2.60)	1.75 (1.69, 1.81)	1.16 (1.14, 1.18)	1.64 (1.57, 1.71)	4.07 (2.77, 5.41)	2.77 (2.51, 3.04)	1.85 (1.73, 1.98)	1.21 (1.17, 1.26)
2009	1.51 (1.48, 1.54)	4.89 (4.35, 5.45)	2.45 (2.36, 2.54)	1.67 (1.61, 1.72)	1.11 (1.10, 1.13)	1.65 (1.57, 1.72)	5.18 (3.73, 6.69)	2.64 (2.39, 2.89)	1.81 (1.68, 1.94)	1.19 (1.14, 1.24)

95% CIs are shown in parentheses

[a] All mortality rate ratios, overall and within each age group, are adjusted to the age and sex distributions in the 2006 Canada Census population

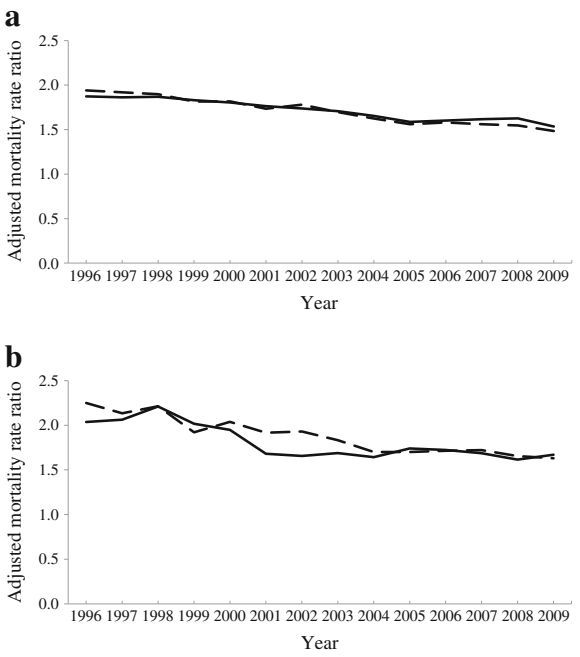

Fig. 2 Mortality rate ratios for men (solid line) and women (dashed line) for each year during 1996–2009 in (**a**) Ontario (Canada) and (**b**) the THIN database (UK). Standard population: Canada Census 2006

However, this result must be interpreted with caution, since it is possible that there are more diabetic patients with a shorter duration of disease in more recent years, since contemporary guidelines focus on screening high-risk groups for diabetes [2]. On the other hand, a recent study showed that patients with the shortest diabetes duration had the highest excess risk of mortality whereas this excess risk declined with longer diabetes duration [15], presumably explained by the greater prevalence of cardiovascular disease when diabetes is diagnosed [22]. Moreover, an earlier study from the UK, including cases of incident type 2 diabetes in individuals older than 30 years of age, found a reduction in excess mortality with time when adjusted for diabetes duration [15]. In addition, in a previous study in the USA that examined 4,399 individuals with self-reported diabetes in 2003–2004, it was found that mortality rates among diabetic patients had declined over time since 1997 [14]. Similar trends were also found in a Danish study over a corresponding time period [16].

In addition to limited previous studies including contemporary estimates of the excess risk of mortality for diabetic patients, the excess risk of mortality over time for diabetic patients grouped by age has to our knowledge not been studied [6–15]. This is possibly because large study sizes are needed to obtain close CIs, especially among younger age groups where fewer deaths occur. It is, however, worth noting that a recent study showed lower mortality rates over time in various age groups, but these were not compared with individuals without diabetes [14]. Our results, showing consistent and large differences in the excess risk of mortality in relation to age, warrant caution when comparing results of the excess risk of mortality for diabetic patients on a group level between different studies. The fact that the excess risk of mortality is strongly related to age could mean that the age of the reference population (i.e. individuals without diabetes to which mortality rates are standardised) will strongly influence the results. To our knowledge this has rarely been highlighted in previous studies of the excess risk of mortality in diabetic populations [6–16]. In our study the excess risk of mortality decreased consistently with age. Although caution should be exercised in identifying a trend-shift in the prognosis of patients with diabetes, more aggressive treatment during recent decades may be applicable to the present results. In 1998, the United Kingdom Prospective Diabetes Study (UKPDS) showed the beneficial effects of blood pressure reduction and improved glycaemic control on diabetic complications [23, 24], and several studies have similarly shown that statin therapy can significantly prevent cardiovascular disease and mortality in virtually all individuals with diabetes [2, 25]. Practice guidelines for diabetes management over the last decade have reflected this evidence and have emphasised the need for aggressive control of blood pressure, lipid levels and hyperglycaemia in patients with diabetes [2, 26]. As a consequence, patients with diabetes now receive more intensive care and are taking substantially more medications [27]. While our findings are likely to be representative of developed nations, different risks might apply to developing nations. Recently it has been estimated that there are up to 100 million diabetic individuals in both China and India, with the majority undiagnosed, and the prevalence is also increasing in many other developing nations [1, 28, 29]. Patients in developing nations are more often diagnosed long after the actual onset of type 2 diabetes [28, 29], and resources for intensive diabetes care are more limited, potentially leading to very different contemporary excess risks of mortality and trends over time in these nations.

Although not a primary aim of the current study, it should be noted that the prevalence of diabetes was considerably higher in the Ontario cohort than in THIN during the study period. The reasons for this discrepancy are unclear, but may be related to differences in factors known to influence the incidence of diabetes, such as screening programmes, ethnicity, eating habits or physical activity patterns, between the two cohorts. Further research would be needed to explore these possibilities.

The present study has several limitations. Some of the factors influencing mortality, such as cardiovascular disease and smoking, were not explored. Hence, the estimated excess risks of mortality might differ considerably for certain patient groups within each age group. Moreover, as is generally the case in previous studies, excess risks of mortality by type of diabetes were not compared [6–16], which would be important and might also, to a certain extent, explain the patterns of excess mortality risk by age. However, it can be noticed that a

higher excess risk of mortality for younger individuals with diabetes has previously been found for both type 1 and type 2 diabetes in two separate studies carried out in individuals from the same background population [8, 30]. The reason why the type of diabetes was not explored was the complexity involved in retrieving this information in the Ontario cohort and also the difficulty in tracking all participants. The Ontario cohort was relatively constant in size over time, including eight to ten million individuals, whereas the THIN cohort increased considerably over time, since this prospective database was initiated around the beginning of the follow-up period. However, although it included fewer individuals, the THIN database was already quite large, with 600,000–800,000 individuals, during the initial years and already having a population-based design. Moreover, different measures were used in the two cohorts—number of deaths per 1,000 individuals in Ontario and number of deaths per 1,000 patient-years in THIN—due to the structure of the data in Ontario, whereas the number of deaths per 1,000 individuals has been used in other studies. However, we believe it is unlikely that this had any major impact on the results. Further, it should be noticed that THIN mortality rates were standardised to the Canadian Census population to enable comparisons of excess risk of mortality in the two cohorts to be made. Finally, it would have strengthened the results if similar patterns could have been shown for cause-specific mortality, improved risk factor control and extension over time of therapies according to guidelines. However, this was not possible in the current project, involving these two large databases over long time periods, and needs to be addressed in future studies.

In conclusion, the excess risk of mortality in patients with vs without diabetes has decreased over time in both Canada and the UK and was five times greater in individuals 20–44 years of age in 2009, approximately 2.5 times greater in those aged 45–64 years, 70–80% greater in those aged 65–74 years and 10–20% greater in individuals aged over 74 years. During the corresponding time period the prevalence of diabetes increased in both countries. It is therefore important to interpret the current findings with caution, since it cannot be excluded that the lower excess risk of mortality for diabetic patients today is due to shorter diabetes duration, rather than successful preventive strategies, bearing in mind the different nature of both sources of information applied in the current study. Further studies are needed to confirm these findings during contemporary time periods compared with historical estimates, and to include the type of diabetes and individuals in developing nations.

Acknowledgements J. Murphy, an independent consultant, based in Kansas City, KS, USA, assisted in language editing of a first draft of the manuscript. S. Dahlqvist from the NU-Hospital Organization assisted in manuscript preparation. The authors thank P. Li (Institute for Clinical Evaluative Sciences) for assistance with statistical analyses and V. Urosevic (Women's College Research Institute) for assistance with manuscript preparation and data presentation. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication. This study was supported through provision of data by the Institute for Clinical Evaluative Sciences (ICES) and through funding support to ICES from an annual grant by the Ontario Ministry of Health and Long-Term Care (MOHLTC). The opinions, results and conclusions reported in this paper are those of the authors. No endorsement by ICES or the Government of Ontario is intended or should be inferred.

Funding This study was supported by the National Diabetes Surveillance System funding from Ontario's Ministry of Health and Long-Term Care and an unrestricted grant from AstraZeneca and Novo Nordisk Scandinavia. The NU-Hospital Organization supports ML for research. LLL was supported by the Canadian Diabetes Association/Canadian Institute of Health Research (CDA/CIHR) Clinician Scientist Award, and currently receives support from a CIHR New Investigator Award. BRS receives support from the CDA, CIHR and the Banting and Best Diabetes Centre at the University of Toronto. GLB is supported by a new investigator award from the Ontario Women's Health Council and CIHR and by a Helene and Reuben Dennis Scholar Award from the Banting and Best Diabetes Centre at the University of Toronto.

The funding agencies had no role in the original protocol design, data collection, data analysis, data interpretation, writing of the report or the decision to submit the report for publication.

Duality of interest ML has received honoraria or served as a consultant for Bayer, Eli Lilly, Novartis, Novo Nordisk Scandinavia, Medtronic Pfizer and Sanofi and has been a member of an advisory board for Novo Nordisk Scandinavia. ML's institution (NU-Hospital Organization) has received grants from Abbot Scandinavia, AstraZeneca and Novo Nordisk Scandinavia. CEIFE has received research grants from AstraZeneca and Bayer. Other authors declare that there is no duality of interest associated with their contribution to this manuscript.

Contribution statement ML, LAGR, GLB, BRS and LLL designed the study protocol. ML, LAGR, LCS and GE performed the statistical analyses. ML and LLL wrote a draft of the manuscript. All authors participated in reviewing and finalising the report. ML had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final version of the manuscript.

References

1. Whiting DR, Guariguata L, Weil C, Shaw J (2011) IDF Diabetes Atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 94:311–321
2. American Diabetes Association (2011) Standards of medical care in diabetes—2011. Diabetes Care 34(Suppl. 1):S11–S61
3. Booth GL, Kapral MK, Fung K, Tu JV (2006) Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. Lancet 368:29–36
4. Booth GL, Kapral MK, Fung K, Tu JV (2006) Recent trends in cardiovascular complications among men and women with and without diabetes. Diabetes Care 29:32–37
5. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA (2008) 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 359:1577–1589
6. Seshasai SR, Kaptoge S, Thompson A et al (2011) Diabetes mellitus, fasting glucose, and risk of cause-specific death. N Engl J Med 364: 829–841

7. Eberly LE, Cohen JD, Prineas R, Yang L, Intervention Trial Research Group (2003) Impact of incident diabetes and in incident nonfatal cardiovascular disease on 18-year mortality: the multiple risk factor intervention trial experience. Diabetes Care 26:848–854
8. Mulnier HE, Seaman HE, Raleigh VS, Soedamah-Muthu SS, Colhoun HM, Lawrenson RA (2006) Mortality in people with type 2 diabetes in the UK. Diabet Med 23:516–521
9. Gregg EW, Gu Q, Cheng YJ, Narayan KM, Cowie CC (2007) Mortality trends in men and women with diabetes, 1971 to 2000. Ann Intern Med 147:149–155
10. Lipscombe LL, Hux JE (2007) Trends in diabetes prevalence, incidence, and mortality in Ontario, Canada 1995–2005: a population-based study. Lancet 369:750–756
11. Dale AC, Vatten LJ, Nilsen TI, Midthjell K, Wiseth R (2008) Secular decline in mortality from coronary heart disease in adults with diabetes mellitus: cohort study. BMJ 337:a236
12. Eliasson M, Talbäck M, Rosén M (2008) Improved survival in both men and women with diabetes between 1980 and 2004—a cohort study in Sweden. Cardiovasc Diabetol 7:32
13. Fox CS, Coady S, Sorlie PD et al (2004) Trends in cardiovascular complications of diabetes. JAMA 292:2495–2499
14. Gregg EW, Cheng YJ, Saydah S et al (2012) Trends in death rates among U.S. adults with and without diabetes between 1997 and 2006: findings from the National Health Interview Survey. Diabetes Care 35:1252–1257
15. Gulliford MC, Charlton J (2009) Is relative mortality of type 2 diabetes mellitus decreasing? Am J Epidemiol 169:455–461
16. Carstensen B, Kristensen JK, Ottosen P, Borch-Johnsen K, Steering Group of the National Diabetes Register (2008) The Danish National Diabetes Register: trends in incidence, prevalence and mortality. Diabetologia 51:2187–2196
17. Rodriguez LA, Cea-Soriano L, Martin-Merino E, Johansson S (2011) Discontinuation of low dose aspirin and risk of myocardial infarction: case-control study in UK primary care. BMJ 343:d4094
18. Hux JE, Ivis F, Flintoft V, Bica A (2002) Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. Diabetes Care 25:512–516
19. Bourke A, Dattani H, Robinson M (2004) Feasibility study and methodology to create a quality-evaluated database of primary care data. Inform Prim Care 12:171–177
20. First Databank (2010) MULTILEX for primary care, 2010. Available from: www.firstdatabank.co.uk/8/multilex-drug-data-file. Accessed May 2013
21. González EL, Johansson S, Wallander MA, Rodríguez LA (2009) Trends in the prevalence and incidence of diabetes in the UK: 1996–2005. J Epidemiol Community Health 63:332–336
22. Gulliford MC, Latinovic R, Charlton J (2008) Diabetes diagnosis, resource utilization, and health outcomes. Am J Manage Care 14:32–38
23. UK Prospective Diabetes Study Group (1998) Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 317:703–713
24. UK Prospective Diabetes Study (UKPDS) Group (1998) Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 352:837–853
25. Colhoun HM, Betteridge DJ, Durrington PN, CARDS investigators et al (2004) Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet 364:685–696
26. Harper W, Woo V, Dawson K et al (2008) Pharmacologic management of type 2 diabetes: Canadian Diabetes Association 2008 Clinical Practice Guidelines. Can J Diabetes 32(Suppl. 1):S53–S61
27. Grant RW, Pirraglia PA, Meigs JB, Singer DE (2004) Trends in complexity of diabetes care in the United States from 1991 to 2000. Arch Intern Med 164:1134–1139
28. Misra P, Upadhyay RP, Misra A, Anand K (2011) A review of the epidemiology of diabetes in rural India. Diabetes Res Clin Pract 92:303–311
29. Yang W, Lu J, Weng J, China National Diabetes and Metabolic Disorders Study Group et al (2010) Prevalence of diabetes among men and women in China. N Engl J Med 362:1090–1101
30. Soedamah-Muthu SS, Fuller JH, Mulnier HE, Raleigh VS, Lawrenson RA, Colhoun HM (2006) All-cause mortality rates in patients with type 1 diabetes mellitus compared with a non-diabetic population from the UK general practice research database, 1992–1999. Diabetologia 49:660–666