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ARTICLE

Area-based socioeconomic status, type 2 diabetes and cardiovascular mortality in Scotland

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Abstract
Aims/hypothesis The aim of this study was to explore the relationships between type 2 diabetes mellitus, area-based socioeconomic status (SES) and cardiovascular disease mortality in Scotland.

Methods We used an area-based measure of SES, Scottish national diabetes register data linked to mortality records, and general population cause-specific mortality data to investigate the relationships between SES, type 2 diabetes and mortality from ischaemic heart disease (IHD)

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and cerebrovascular disease (CbVD), for 2001–2007. We used negative binomial regression to obtain age-adjusted RRs of mortality (by sex), comparing people with type 2 diabetes with the non-diabetic population.

Results Among 216,652 people aged 40 years or older with type 2 diabetes (980,687 person-years), there were 10,554 IHD deaths and 4,378 CbVD deaths. Age-standardised mortality increased with increasing deprivation, and was higher among men. IHD mortality RRs were highest among the least deprived quintile and lowest in the most deprived quintile (men: least deprived, RR 1.94 [95% CI 1.61, 2.33]; most deprived, RR 1.46 [95% CI 1.23, 1.74]) and were higher in women than men (women: least deprived, RR 2.84 [95% CI 2.12, 3.80]; most deprived, RR 2.04 [95% CI 1.55, 2.69]). A similar, weaker, pattern was observed for cerebrovascular mortality.

Conclusions/interpretation Absolute risk of cardiovascular mortality is higher in people with diabetes than in the non-diabetic population and increases with increasing deprivation. The relative impact of diabetes on cardiovascular mortality differs by SES, and further efforts to reduce cardiovascular risk both in deprived groups and people with diabetes are required. Prevention of diabetes may reduce socioeconomic health inequalities.

Keywords Cerebrovascular disorders · Diabetes mellitus · Epidemiology · Myocardial ischaemia · Scotland · Socioeconomic factors · Type 2

Abbreviations

CbVD	Cerebrovascular disease
IHD	Ischaemic heart disease
NHS NSS	National Health Service National Services Scotland
RERI	Relative excess risk due to interaction
SCI-DC	Scottish Care Information – Diabetes Collaboration
SES	Socioeconomic status
SIMD	Scottish Index of Multiple Deprivation

Introduction

The role of socioeconomic status (SES) in morbidity and mortality from common chronic diseases has been widely investigated [1]. It is well documented that the prevalence of type 2 diabetes mellitus and risk factors associated with its development are higher among lower socioeconomic groups [2–5]. Long-term outcomes, such as all-cause mortality, among people with diabetes have also been shown to be associated with SES [6–10].

Few studies have examined the relationship between SES and cardiovascular disease mortality. Among those that have, results are mixed, with most studies reporting that cardiovascular mortality increases with decreasing SES [6, 7, 9, 11], and others reporting no association [12, 13]. Even fewer studies have determined whether the SES gradient for cardiovascular mortality differs by diabetes status [6, 9, 13]. Many studies have included small numbers of people with type 2 diabetes, limiting the power to detect relationships between SES and cardiovascular mortality.

A better understanding of the impact of SES on cardiovascular disease incidence and mortality among people with type 2 diabetes is needed to help develop and direct improved interventions for reducing complications and risk of death. Measures of SES may, for example, improve the predictive power of current cardiovascular risk models for people with diabetes [14, 15].

In Scotland, population-based data on almost all people with diagnosed diabetes are collected electronically from primary and secondary care where they are used for individual patient management. The database includes information on more than 200,000 people with diabetes, and is a valuable resource for research. Previous analyses of these data found an inverse relationship between SES and the RR of all-cause mortality [10]. This SES gradient for all-cause mortality differed between those with and without type 2 diabetes, with a lower RR among the most deprived SES group [10]. In this study, we sought to investigate whether a similar relationship is observed between SES and cardiovascular mortality among people with and without diabetes in Scotland between 2001 and 2007.

Methods

Scottish national electronic diabetes dataset In Scotland, which has a population of 5.2 million, population-based data for people diagnosed with type 1 or type 2 diabetes mellitus are collected in the Scottish Care Information – Diabetes Collaboration (SCI-DC) dataset. National collation of demographic and diabetes clinical care data started in 2000. SCI-DC is populated through daily downloads from primary care databases, with data collated from all except five of the approximately 1000 general practices in Scotland, and from most hospital diabetes clinics.

Population of people with type 2 diabetes In this study, we identified individuals included in the SCI-DC dataset between 2001 and 2007 who were diagnosed with type 2 diabetes and were aged 40 years or over during this period, as both type 2 diabetes and cardiovascular disease mortality are rare in younger people. Presence of type 2 diabetes was defined by excluding people with type 1 diabetes (defined by applying an algorithm including diagnosis before 30 years of age, a prescribing history showing continuous

insulin prescription from diagnosis of diabetes and no record of prescription of non-metformin oral diabetes drugs, and clinically defined type of diabetes). We included individuals for whom data on year of birth, sex, SES and dead/alive status were available.

Our colleagues at the Information Services Division of the National Health Service National Services Scotland (NHS NSS) used the Scottish unique health record identifier, the Community Health Index, and probabilistic linkage methods to link the Scottish national diabetes register data to mortality records [16]. A research database containing no identifiable information was used for analysis. Approval for the generation and analysis of the linked dataset was obtained from the SCI-DC steering committee, the Scottish multicentre research ethics committee, the Privacy Advisory Committee of NHS NSS, and Caldicott guardians of all 14 Health Boards in Scotland.

For the main analysis, we identified deaths among people with diabetes from ischaemic heart disease (IHD) (International Classification of Disease [ICD10] codes I20–25) and cerebrovascular disease (CbVD) (ICD10 I60–69, G45), where these codes were given as the underlying (primary) cause of death. Individuals were considered to be at risk between January 2001 (if aged at least 40 years during this year) until 31 December 2007 or date of death, whichever was earliest. People who reached 40 years of age during this period were considered at risk from that point onwards, and people who were diagnosed with type 2 diabetes during the study period were considered at risk from the date of diagnosis.

Population without diabetes We obtained data on the total population and numbers of ischaemic heart disease (ICD I20–I25) and CbVD (ICD I60–69, G45) deaths in the Scottish population by calendar year, age, sex and Scottish Index of Multiple Deprivation (SIMD) quintile from the Information Services Division of NHS NSS. We subtracted the number of deaths and person-years at risk among people with diabetes (types 1 and 2) from the total deaths and person-years at risk in the Scottish population to obtain a non-diabetic comparison population.

Socioeconomic status We used the SIMD, an area-based measure of SES assigned on the basis of place of residence at datazone level (an area with a median population of 769 people) [17]. The 2006 version of the SIMD combines 31 indicators across seven domains of income, employment, health, education, housing, geographic access and crime. The overall index is a weighted sum of these seven domain scores for each datazone and is assigned using postal codes. Quintiles of the index are defined at a national level, with quintile 1 used to identify the least deprived and quintile 5 used to identify the most deprived 20% of datazones.

Statistical analyses We calculated IHD and CbVD mortality for the populations with type 2 diabetes and the non-diabetic population, age-standardised to the European Standard Population, from 40 years of age upwards, by sex and SES.

Since the data did not fit the Poisson distribution, we used negative binomial regression, which takes account of overdispersion [18], to obtain RRs with 95% CIs for the association between diabetes status and IHD mortality and CbVD mortality. We investigated whether there was effect modification of diabetes by SES by both testing for multiplicative interaction and investigating the presence of supra-additive interaction between diabetes and the most deprived compared with the most affluent quintile using the methodology and resources described by Andersson et al [19]. A relative excess risk of interaction (RERI) of greater than 0 and a synergy index greater than 1 derived from the latter method suggests that the combined effects of two exposures are greater than expected from adding the individual effects. Testing for multiplicative interactions is more conventional and is used to test the fit of statistical models, but the investigation of additive interaction is more relevant to understanding population health [20].

Sensitivity analyses Identifying IHD or CbVD deaths in our main analysis from the underlying cause of death may underestimate numbers of cardiovascular deaths among people with diabetes. Death certificate coding rules lead to the assignment of diabetes as the underlying cause of death in death records when both cardiovascular disease and diabetes are listed in part I of the death certificate. We therefore repeated our analyses using a broader definition of cardiovascular death, including deaths in which diabetes was recorded as underlying cause, with IHD or CbVD mentioned elsewhere on the death record.

To investigate the effect of the incompleteness of the diabetes register between 2001 and 2004, before its widespread use in primary care which results in artificially low mortality in those years, we performed a further sensitivity analysis in which we restricted our analyses to only people included in the register between 2005 and 2007, when register coverage was almost universal.

Analyses were performed using Stata version 11 (College Station, TX, USA).

Results

Absolute mortality by diabetes status, sex and SES After excluding people for whom SES data were unavailable (n= 1,282), 216,652 people with type 2 diabetes of 40 years of age and above were included. Of these, 116,145 (54%) were men and 100,507 (46%) were women. During 525,077 person-years of follow-up in men, 22,033 died—6,000

(27%) from IHD and 1,942 (9%) from CbVD. During 455,610 person-years of follow-up in women, 20,571 died—4,554 (22%) from IHD and 2,436 (12%) from CbVD (Table 1).

Age-standardised IHD and CbVD mortality increased with increasing deprivation, irrespective of diabetes status (Figs. 1 and 2). In people with diabetes, IHD mortality was 80% higher in the most deprived than the least deprived quintile in both men and women (Fig. 1). Among men with diabetes, CbVD mortality was about 50% higher in the most deprived versus least deprived quintile, with a smaller difference among women (Fig. 2). IHD and CbVD mortality in people without diabetes also increased with increasing deprivation, although this relationship was less steep for CbVD than for IHD. As the slightly divergent lines of Fig. 1 demonstrate, the difference in absolute risks of mortality from cardiovascular disease between people with diabetes and those without increases modestly across each deprivation category, although the combination of deprivation and diabetes appears to be particularly detrimental for women. The age-adjusted absolute risk difference in IHD mortality in women with diabetes and without was 1.77/1000 person-years for the least deprived quintile and 2.82/1000 person-years for the most deprived quintile.

Relative mortality risk, comparing people with and without diabetes Cardiovascular mortality risk was significantly greater among people with diabetes than in the non-diabetic population, both before and after adjustment for SES, with inclusion of SES improving the fit of the models for men and women. In analyses adjusted for age alone, IHD mortality risk among men with diabetes was 73% greater than for those without diabetes (RR 1.73; 95% CI 1.51, 1.98), and was attenuated slightly upon further adjustment for SES (RR 1.71; 95% CI 1.57, 1.86). The RR for type 2 diabetes and IHD mortality was higher in women (age-adjusted RR 2.40 [95% CI 2.01, 2.87]; age- and SES-adjusted RR 2.34 [95% CI 2.05, 2.67]). As expected, the age- and SES-adjusted RRs were higher when the broader definition of IHD mortality including any mention on a death certificate was applied in a sensitivity analysis (men, RR 2.06 [95% CI 1.89, 2.24]; women, 2.60 [95% CI 2.93, 3.03]).

The presence of type 2 diabetes also conferred an increased risk of CbVD, although the RRs were lower than for IHD, with little difference between men and women (men: age-adjusted RR 1.25 [95% CI 1.10, 1.42], age- and SES-adjusted RR 1.24 [95% CI 1.13, 1.26]; women: age-adjusted RR 1.33 [95% CI 1.18, 1.51], age- and SES-adjusted RR 1.31 [95% CI 1.18, 1.45]). Again, the RRs were higher when the broader definition of CbVD mortality was applied (men, RR 1.49 [95% CI 1.36, 1.63]; women, RR 1.59 [95% CI 1.43, 1.77]). RRs of IHD and CbVD associated with diabetes stratified by SES are shown in Table 2. There were no statistically significant multiplicative interactions between deprivation and type 2 diabetes but there were lower relative risks associated with type 2 diabetes in more deprived quintiles than among more affluent quintiles (see Table 2).

In addition there was evidence of non-statistically significant supra-additive interaction between diabetes and SES for IHD mortality (RERI 0.63 and synergy index 2.98 for men; RERI 1.09 and synergy index 3.70 for women; see electronic supplementary material [ESM] Table 1 for more information). The excess risks due to diabetes and being in the most compared with the least deprived quintile and their interaction after adjustment for age are shown by sex in Fig. 3. For CbVD, estimates of the synergy index and RERI had wide confidence intervals and are therefore difficult to interpret (data available from authors).

When we restricted our analyses to patients included in the diabetes register between 2005 and 2007, we found similar results, albeit with less precision, given the smaller sample size (data available from authors).

Table 1 Deaths from IHD and CbVD among people aged≥40 years, between 2001 and 2007, by sex and SES

SES quintile	People with type 2 diabetes						People without diabetes					
	Men (*n*=116,145)			Women (*n*=100,507)			Men (*n*=2,433,748)			Women (*n*=2,630,482)		
	Person-years	IHD deaths	CbVD deaths	Person-years	IHD deaths	CbVD deaths	Person-years	IHD deaths	CbVD deaths	Person-years	IHD deaths	CbVD deaths
1 (least deprived)	84,067	746	278	59,773	505	349	1,839,545	4,761	2,021	2,101,479	4,467	4,035
2	101,110	1,033	414	78,656	727	464	1,882,780	6,246	2,476	2,151,994	5,811	4,834
3	110,008	1,278	371	93,603	930	527	1,832,739	7,670	2,850	2,135,428	6,736	5,067
4	116,010	1,446	442	108,986	1,108	545	1,698,901	8,658	2,823	2,077,940	7,824	5,029
5 (most deprived)	113,882	1,497	437	114,593	1,284	551	1,561,147	9,466	3,021	1,931,388	7,611	4,667
All	525,077	6,000	1,942	455,610	4,554	2,436	8,815,112	36,801	13,191	10,398,229	32,449	23,632

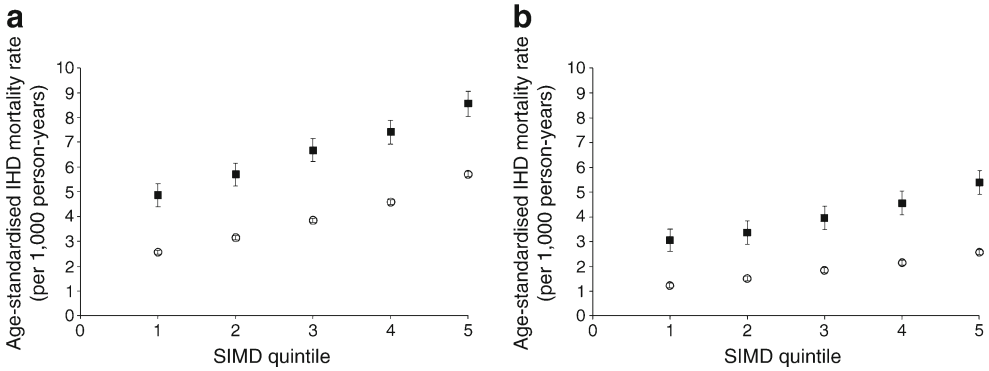

Fig. 1 Age-standardised IHD mortality rates by SES for men (**a**) and women (**b**) with (black squares) and without (white circles) type 2 diabetes. Error bars are 95% CIs

Discussion

Using a national diabetes register with near-complete population coverage, we found that absolute rates of cardiovascular mortality increased with increasing deprivation and were higher among people with type 2 diabetes than those without diabetes. There was evidence of both multiplicative and additive interaction between diabetes and SES.

The relationship between cardiovascular mortality and SES may be mediated partly by an increased prevalence of cardiovascular risk factors among lower socioeconomic groups [21]. However, a previous study of diabetes register data from two areas of Scotland found little difference by SES in control of blood pressure, cholesterol levels or diabetes, suggesting that there is equitable treatment of these risk factors [5]. In contrast, other risk factors that require behaviour change including smoking and obesity were more common in lower than higher socioeconomic groups [5]. Although the Scottish Health Survey contains data on risk factor prevalence on a survey sample, similar data for the whole non-diabetic population included in our analyses were not available. Consequently we were unable to investigate to what extent differences in risk factor patterns contribute to the observed differences in cardiovascular mortality between people with and without diabetes at a population level.

Current predictive models for coronary heart disease in people with diabetes include factors such as age, sex, smoking status, glycaemic control, cholesterol and blood pressure [14, 15], but do not include SES. Inclusion of social deprivation improves cardiovascular risk prediction in the ASSIGN score, a cardiovascular risk score, when compared with the Framingham Score in a Scottish population, and allows targeting of preventive treatment for the most socially deprived groups [22]. Similarly, QRISK2, which also includes a deprivation measure (the Townsend Score) performs better than Framingham in identifying high-risk populations for cardiovascular disease [23]. Further work is required to investigate whether the inclusion of SES improves the predictive capabilities of cardiovascular disease prediction models for people with diabetes.

Comparisons with previous studies The observed increase in cardiovascular disease mortality associated with diabetes is in keeping with results of previous studies, which report an increased risk of ~2–3-fold [24–32]. The overall RRs we obtained for diabetes are slightly lower than in studies from other parts of the UK [30, 31], and from some other countries [24, 25, 27, 29]. We found that presentation of an overall RR for diabetes and cardiovascular disease mortality masks differences by SES in the Scottish population. Differences in distribution of SES may contribute to differences in the effect of diabetes on mortality between populations. Some of the variability in the findings of previous studies is due to differences in cardiovascular death coding, particularly whether underlying cause of death only or

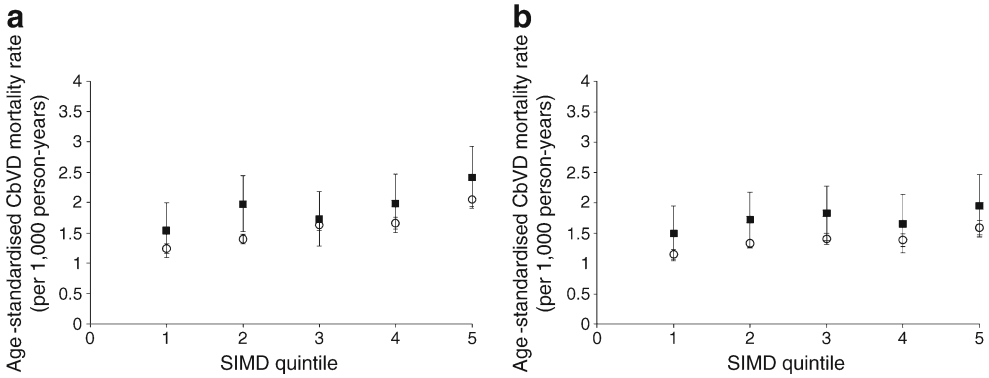

Fig. 2 Age-standardised CbVD mortality rates by SES for men (**a**) and women (**b**) with (black squares) and without (white circles) type 2 diabetes. Error bars are 95% CIs

Table 2 Age-adjusted mortality RRs for IHD and CbVD mortality, by sex and SES, comparing people with and without type 2 diabetes, estimated from negative binomial regression models

Values are RR (95% CI)

[a]Interaction between SES and diabetes status on mortality (likelihood ratio test)

SES quintile	IHD		CbVD	
	Men	Women	Men	Women
1 (least deprived)	1.94 (1.61, 2.33)	2.84 (2.12, 3.80)	1.38 (1.12, 1.70)	1.64 (1.32, 2.05)
2	1.86 (1.55, 2.23)	2.50 (1.89, 3.32)	1.45 (1.19, 1.76)	1.40 (1.13, 1.74)
3	1.75 (1.46, 2.09)	2.20 (1.67, 2.91)	1.13 (0.93, 1.37)	1.36 (1.10, 1.68)
4	1.61 (1.35, 1.92)	2.20 (1.67, 2.91)	1.22 (1.00, 1.47)	1.16 (0.94, 1.43)
5 (most deprived)	1.46 (1.23, 1.74)	2.04 (1.55, 2.69)	1.07 (0.89, 1.30)	1.07 (0.87, 1.32)
p value for interaction[a]	0.192	0.527	0.154	0.055

secondary causes of death are counted. The former method, which we used in our main analysis, is likely to result in conservative RR estimates, as demonstrated by the higher RRs reported from our sensitivity analyses using mention of cardiovascular disease anywhere on the death certificate when the underlying cause of death was reported as diabetes. This broader definition may overestimate cardiovascular death rates among people with diabetes because it will include cardiovascular disease reported in part II of the death certificate (i.e. as a condition that has contributed to death but is not part of the main causal sequence leading to death) when comparable information is not available for the non-diabetic population. Lower RRs in our study may also partly reflect the decreasing relative mortality associated with diabetes over time that has been observed in studies of time trends [29, 33].

Our finding that the RR of cardiovascular mortality associated with diabetes is higher in women than men also concurs with the findings of previous studies [25, 34]. Recent evidence suggests that this sex difference may be due to women with diabetes having greater relative differences compared with women without diabetes in cardiovascular risk factors, including abdominal adiposity, insulin resistance and inflammation, than similar comparisons for men [35].

Results from previous studies that examined the effect of SES on cardiovascular mortality in people with diabetes have been mixed. In the UK, a study using the South Tees District Diabetes Register found increasing cardiovascular mortality with increasing area-based deprivation [9]. Other studies have examined the effect of individual SES measures on cardiovascular mortality, including the Whitehall Study, which found increasing cardiovascular mortality with decreasing occupational social class [6]. An analysis of US health survey data showed increasing cardiovascular mortality with decreasing education level in people with type 2 diabetes [7]. In contrast, an Italian diabetes register found no association between individual educational level and cardiovascular mortality [13]. Comparisons of Finnish data over time found widening socioeconomic disparities in cardiovascular mortality by social class in people with type 2 diabetes [11, 12]. The findings of the different studies suggest that both individual and area-based SES influence the effect of diabetes on cardiovascular mortality. These studies also reported that the RR for diabetes and IHD mortality was higher than that for CbVD mortality, similar to our findings.

We are not aware of any other studies that have compared area-based SES gradients in cardiovascular mortality between people with and without diabetes. However, two

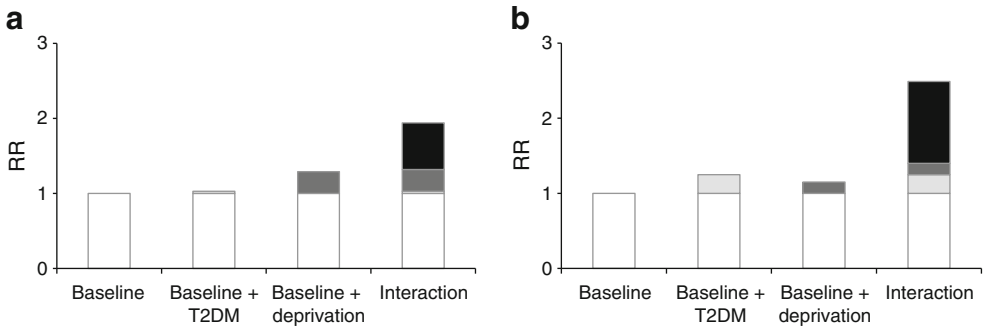

Fig. 3 Contribution to age-adjusted RR of IHD from type 2 diabetes, SES and effect modification of diabetes by SES, comparing quintile 5 with quintile 1 for men (**a**) and women (**b**). White block, baseline RR; light grey block, RR due to type 2 diabetes; dark grey block, RR due to deprivation; black block, RR due to interaction between deprivation and type 2 diabetes. T2DM, type 2 diabetes mellitus

studies have compared individual-based SES gradients in cardiovascular mortality. One study found that the social class gradients in cardiovascular or IHD mortality did not differ by diabetic status [6]. However, this study included only men and very few cases of diabetes, and may have therefore been underpowered to detect differences in SES mortality gradients. A second study found that the relative difference in cardiovascular mortality risk was greater in the highest than the lowest educated group, similar to the pattern we report [13]. The South Tees study reported that relative differences in all-cause mortality were highest in the most deprived groups and decreased with increasing affluence, but did not report RR for cardiovascular disease mortality stratified by SES [9]. The differences between our study and the latter study may reflect secular trends and better management of cardiovascular risk factors, particularly in people with diabetes, since the latter study was performed in 1994–1999 [33, 36].

Study strengths Our study includes data on over 99% of people diagnosed with type 2 diabetes in Scotland in recent years, and is therefore at minimal risk of selection bias. With data on over 200,000 people with type 2 diabetes and almost 15,000 cardiovascular deaths, this is the largest study to date to have examined the relationship between cardiovascular disease mortality and SES, with sufficient power to stratify by sex and SES, and to examine IHD and CbVD mortality separately. We were also able to make comparisons using routinely collected national data on cardiovascular mortality, removing all deaths and follow-up time for people with diabetes from this comparison group to generate a non-diabetic comparison group.

Study limitations Our study has some limitations. Although the diabetes register includes data on cardiovascular risk factors such as blood pressure and body mass index, these data were not available for the general population comparison group and we were therefore unable to investigate the effect of such variables. Type of diabetes was determined from a combination of clinical record, age at onset and prescription records, and there may be some misclassification. We were also unable to examine whether individual-based measures of SES, such as education and occupational social class, followed the same pattern of association with diabetes status and cardiovascular disease mortality as the area-based measure of SES. There are some limitations to using routinely collected data in that errors (e.g. in the coding of cause of death) will have occurred. Death coding errors are unlikely to have varied systematically by SES, but it is possible that accuracy of recording of cause of death varies by diabetes status. A final potential limitation is that the diabetes register does not include all people who had diabetes who died before 2004/5. Therefore people included in the early period of the register may be unrepresentative in that they reflect a healthier subgroup. However, when we restricted our analyses to only people included in the register between 2005 and 2007, we obtained very similar results, suggesting that this limitation does not introduce serious bias.

Conclusions and implications There is a marked socioeconomic gradient in cardiovascular disease mortality for both people with diabetes and the non-diabetic population, and the absolute increase in risk associated with diabetes increased modestly with increasing deprivation. These findings demonstrate the potential impact of type 2 diabetes prevention on cardiovascular mortality and highlight the need for sustained efforts to prevent and reduce cardiovascular risk in populations living in more deprived areas, irrespective of diabetes status. The role of SES as an independent predictor of cardiovascular disease in models of vascular outcomes for people with diabetes should be explored further. Prevention of diabetes may contribute to reducing socioeconomic health inequalities.

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Duality of interest The authors declare that there is no duality of interest associated with this manuscript.

Contribution statement CAJ, CMF, JJW, NRVJ and SHW designed the study; CAJ, JJW and NRVJ performed analyses; CAJ wrote the first draft of the paper, and CMF, JJW, NRVJ, HMC, GPL, RSL, JAM, ADM, JRP, NS and SHW contributed to acquisition and/or interpretation of data and critical revision of the manuscript. All authors approved the final version of the manuscript.

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