Type 1 and Type 2 diabetes and COVID-19 related mortality in England: a cohort study in people with diabetes

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Abstract

Background

Although diabetes has been associated with COVID-19 mortality, its scale and relationships with modifiable risk factors including hyperglycaemia and obesity in Type 1 and Type 2 diabetes remain unclear.

Methods

National diabetes and mortality data in England identified deaths in people with Type 1 and Type 2 diabetes weekly from 1st January 2017 to 1st May 2020. Cox proportional hazards analysis investigated the relationship between risk factors and COVID-19 related death in a cohort alive on 1st January 2020 and followed to 1st May 2020.

Findings

Weekly deaths in Type 1 and Type 2 diabetes more than doubled from the week ending 3rd April 2020 exceeding expected variation (3SD). Among 265,090 people with Type 1 and 2,889,210 people with Type 2 diabetes there were 418 and 9377 COVID-19 related deaths respectively. The adjusted hazard ratio (HR) of HbA1c >86 mmol/mol compared to HbA1c 48-53 mmol/mol was 2·19 (95% CI 1·46-3·29) for Type 1 and 1·62 (95% CI 1·48-1·79) for Type 2 diabetes. The relationship between BMI and COVID-19 mortality was U-shaped; HRs for BMI >40 kg/m^2 compared to 25-29.9 kg/m^2 were 2·15 (95% 1·37-3·36) and 1·46 (95% CI 1·50-1·79) for Type 1 and Type 2 respectively.

Interpretation

Deaths in people with diabetes in England have more than doubled during the COVID-19 epidemic. Hyperglycaemia and obesity in both Type 1 and Type 2 diabetes were independently associated with increased COVID-19 mortality. Risk factor control could diminish the impact of COVID-19 in diabetes.

Funding

NHS England & Improvement and NHS Digital.

Research in context

Evidence before this study

From March 2020, we performed weekly searches of PubMed and MedRxiv using the terms COVID-19, SARS-CoV-2, coronavirus, SARS virus and diabetes. The scale of the excess mortality risk in people with diabetes attributable to the COVID-19 epidemic in England is unknown. Although previous studies have identified diabetes as a risk factor for mortality from COVID-19, it is unclear whether that increased risk is seen in all sub-types of diabetes. Poorly controlled diabetes has been reported to be a risk factor for adverse outcomes in people with COVID-19, but the relationship with different degrees of hyperglycaemia has not been reported.

Added value of this study

This study shows that the onset of the COVID-19 epidemic in England has been associated with a doubling of the weekly rate of mortality among people with diabetes. The risk of COVID-19 related mortality in people with either Type 1 and Type 2 diabetes is independently associated with the level of hyperglycaemia and degree of obesity.

Implications of all the available evidence

In people with diabetes, efforts to improve glycaemic control and optimise obesity are likely important in order to reduce the adverse outcomes of SARS-CoV-2 infection.

Introduction

By 1st May 2020, 3,394,153 people worldwide, from 213 countries and territories, are known to have had Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 infection, and 239,447 have died[1]. Recent studies from England have reported that 19% of people admitted to hospitals with COVID-19 have diabetes[2] and in a separate analysis we have shown that one third of deaths in hospital with diabetes are in people with diabetes. This excess burden of morbidity and mortality in people with diabetes mirrors that seen in other epidemics, including Middle East respiratory syndrome (MERS), in which the prevalence of diabetes was approximately 50%, and severe acute respiratory syndrome (SARS), for which diabetes was an independent predictor of mortality and morbidity[3-6]. The true number of excess deaths in England among people with diabetes attributable to the COVID-19 epidemic is unknown. Previous reports have focused on mortality within hospitals and the attribution of COVID-19 as a cause can be limited by the extent of diagnostic testing for COVID-19 infection, which until recently has been limited mainly to people admitted to hospital. In order to quantify the true scale of the excess mortality risk, we investigate the weekly number of deaths among the entire population of people with diabetes in England in a period before and during the current epidemic.

Diabetes, cardiovascular disease and hypertension are the commonest chronic long-term co-morbidities in people with severe COVID-19[7-14]. People with Type 1 diabetes have 3·5 (95% CI 3·15-3·89) times the odds, and people with Type 2 diabetes 2·0 (9% CI 1·97-2·09) times the odds, of dying in hospital with COVID-19, compared to the population without known diabetes, independent of age, sex, socioeconomic status and ethnicity. Studies from USA and China have suggested an association between in-hospital hyperglycaemia and poorer outcomes for COVID-19[12, 13], mirroring the known association between hyperglycaemia and increased severity of other infections[15, 16]. It is possible that hyperglycaemia may modulate the hyperimmune response that may underlie severe, life threatening COVID-19 infection[17].

To investigate the relationship between hyperglycaemia and other modifiable risk factors including obesity, and risk of COVID-19 related mortality in both community and hospital environments, we analysed data from a cohort of over three million people with diagnosed Type 1 and Type 2 diabetes in England using a national dataset.

Methods

Data sources

The National Diabetes Audit (NDA) collates data on nearly all people with diagnosed diabetes registered with a healthcare provider in England. Individuals are included if they have a valid code for diabetes mellitus (excluding gestational diabetes) in their electronic health record. Demographic and clinical data are extracted from general practice electronic clinical systems using the General Practice Extraction Service (a national centralised data collection service). This is supplemented by data submitted by specialist diabetes services. Each person with diabetes is identified by a unique NHS number. Data from general practices in England is available from 1st April 2003 to 31st December 2019. For the period 1st January 2018 to 31st March 2019 data was collected from 98% of general practices in England. Data was submitted by 113 specialist diabetes services[18].

Study population, observation period and outcomes

People who had been included in any NDA data collection were used to quantify the weekly number of deaths from all-causes among people with diabetes occurring between 1st January 2017 to 1st May 2020 using data collated by the Office for National Statistics (ONS)[19]. ONS data is collated civil death registrations and therefore includes all deaths, not just those that have occurred in hospital environments.

The diabetes cohort study population used to investigate risk factors for COVID-19 related mortality were people with Type 1 diabetes or Type 2 diabetes who had been included in the 2018/19 NDA data collection, whose most recent General Practice was in England and who were alive on 1st January 2020. People with a recorded date of birth giving an age of 110 or greater were excluded from the analysis. All people included in the study were followed up to 1st May 2020. Using the unique NHS number all individuals were linked to Hospital Episode Statistics (HES), a record of every hospital admission in England (data were available from 1st April 2017 to 31st December 2019) and to deaths including causes of death registered up to 1st May 2020 as collated by the Office for National Statistics (19). COVID-19 related death was defined as a death where an International Classification of Diseases version 10 code of U07.1 (COVID-19, virus identified) or U07.2 (COVID-19, virus not identified) was recorded as either a primary underlying or secondary cause of death. We analysed deaths that occurred after 1st January 2020 and were registered by 1st May 2020.

Definitions of exposures

Type of diabetes was based on the codes recorded in clinical records. There can be inconsistencies in type of diabetes recorded in different settings. In annual care process and treatment target reports the type of diabetes codes received from either primary or secondary care are resolved by attributing diagnosis of diabetes type from

a specialist care provider if one was attended or the most recent code identified from primary care. In complication and mortality reports the type of diagnosis most recently assigned by specialist care in any year is used if available and was the approach adopted for this analysis.

Age was grouped as less than 40 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years and 80 years and older. Social deprivation was defined by the Indices of Multiple Deprivation 2019 based on individual home postcode (20). Ethnicity was classified as White, Mixed, Asian, Black, other ethnic groups or missing. People were allocated to seven regions based on their home postcode to adjust for the geographical variation in SARS-CoV-2 infection rates in England.

We included data on the latest HbA1c and estimated Glomerular Filtration Rate (eGFR) recorded between 1st January 2019 and 31st December 2020. HbA1c data was categorised into < 48 mmol/mol, 48-53 mmol/mol, 54-58 mmol/mol, 59-74 mmol/mol, 75-85 mmol/mol, and ≥86 mmol/mol or missing. The Modification of Diet in Renal Disease (MDRD) formula was used to calculate eGFR and results were grouped into <15, 15 -29, 30-44, 45-59, ≥60 or missing. Body mass index (BMI) and smoking status were identified using the latest recorded measurement between 1st January 2017 and 31st December 2019. Body mass index (BMI) was classified as <20 kg/m^2, 20-24·9 kg/m^2, 25-29·9 kg/m^2, 30-34·9 kg/m^2, 35-39·9 kg/m^2, ≥40 kg/m^2 or missing. Smoking status was identified as current smoker, ex-smoker, non-smoker (not a current smoker but history unknown), never smoked or missing data.

Hypertension was defined on the basis of having a prescription for anti-hypertensive medication between 1st January 2017 and 31st December 2019. A history of myocardial infarction (ICD-10 codes I21-22), stroke (ICD-10 codes I61, I63-63 and I67.9) and heart failure (ICD-10 code I50) were identified from hospital episodes between 1st April 2017 and 31st December 2019 where the condition was included as either the primary or one of up to 14 secondary diagnoses.

Statistical analysis

The weekly mean number of deaths in people with Type 1 and Type 2 diabetes was identified. Two and three standard deviations were calculated to identify control limits outside which special cause variation occurs.

We used Cox proportional hazards survival analysis models with COVID-19 related death as the outcome and a competing risk of death from all other causes to identify the hazard ratios of COVID-19 related death associated with Type 1 and Type 2 diabetes plus demographic characteristics s(age, sex, social deprivation, ethnic group,

region of residence), clinical characteristics (HbA1c, duration of diagnosed diabetes, body mass index, eGFR, smoking status) and co-morbidities (history of myocardial infarction, stroke, heart failure and hypertension).

Statistical calculations were undertaken in SAS Enterprise Guide 7.1 (https://support.sas.com/en/software/enterprise-guide-support.html). All numbers taken directly from the National Diabetes Audit are rounded to the nearest five persons to protect confidentiality.

Information governance

The National Diabetes Audit (NDA) data are collected under the terms of section 254 of the Health and Social Care Act (HSCA) for England 2012. Data are not extracted if the person has registered their dissent from permission to use their record for secondary analysis. NHS England and NHS Digital are the joint data controller for the NDA data and this has been linked with ONS mortality data and hospital episode statistics data under the terms of section 254 of the HSCA.

Data linkage and analysis are undertaken within NHS Digital and further information can be found at https://digital.nhs.uk/data-and-information/looking-after-information.

Results

A total of 17,882 and 372,242 deaths occurred between 1st January 2017 and 24th April 2020 in people with Type 1 and Type 2 diabetes respectively. The weekly number of deaths in people with Type 1 and Type 2 diabetes first exceeded three standard deviations in the week ending 3rd April 2020 for people with both Type 1 diabetes and Type 2 diabetes (see Figure 1) and has remained extremely high since then. The total number of deaths per week among people with diabetes in England has more than doubled since April 3rd 2020 compared to what would be expected in this season.

The cohort analysis included 265,090 people with Type 1 diabetes and 2,889,210 people with Type 2 diabetes. The mean age of those with Type 1 diabetes was 46.7 years, whereas those with Type 2 diabetes were on average 67·6 years old. In people with Type 1 diabetes 5·6% were Asian and 3·5% were from Black ethnic groups. The corresponding figures for those with Type 2 diabetes were 14·0% and 4·8%. Among people with Type 1 diabetes, 11·4% had a last reported HbA1c of 75-85 mmol/mol and 11·8% had a value ≥86 mmol/mol. A quarter (25·1%) of people with Type 2 diabetes had an HbA1c < 48mmol/mol whilst 6·1% had a measurement ≥86 mmol/mol (Table 1).

Between 1st January 2020 and 1st May 2020 71,160 deaths from all causes were registered in people with diabetes. A total of 9795 deaths (418 in people with Type 1 and 9377 in people with Type 2 diabetes) had COVID-19 included on the death certificate and 9341 (95.4%) had COVID-19 as the underlying cause of death.

Older age and male sex were associated with a higher risk of COVID-19 related mortality (see Table 2, Figure 2). In Type 1 diabetes, risk was higher in people of Black ethnicity (HR 1·68, 95% CI 1·23-2·29) compared to the white population, and was similarly elevated in those of Asian ethnicity (HR 1·79, 95% CI 1·21-2·63). The difference in risk for those of mixed ethnicity was not statistically significant. In Type 2 diabetes, the risk was greatest for people of Black ethnicity (HR 1·63 95% CI 1·50-1·77) compared to the white population, and there was only a small increase in risk in those of Asian ethnicity (HR 1·09, 95% CI 1·02-1·17) (See Figure 2).

There was a clear relationship between COVID-19 related death and socio-economic deprivation among people with diabetes of either type. The hazard ratio for COVID-19 related mortality for people with Type 1 diabetes in the most socioeconomically deprived quintile was 1·79 (95% CI 1·24 – 2·57) compared to people living in the least deprived area, The comparable figure for Type 2 diabetes was a HR of 1·45 (95% CI 1·35-1·56).

The degree of hyperglycaemia was strongly associated with risk of death related to COVID-19 after adjusting for other risk factors. For people with Type 2 diabetes, those with an HbA1c of 59-74 mmol/mol had a hazard ratio of 1·23 (95% CI 1·15 – 1·32) compared with people with an HbA1c of 48-53mmol/mol. In people with Type 2 diabetes and an HbA1c of ≥86mmol/mol the HR was 1·62 (95% CI 1·48-1·79). A similar overall pattern of association was seen in people with Type 1 diabetes, but the raised risk was only statistically significant in those with an HbA1c ≥ 86 mmol/mol (HR 2·19 95% CI 1·46-3·29) when compared to those with a HbA1c of 48-53 mmol/mol. The hazard ratio in people with Type 2 diabetes and a low HbA1c (<48mmol/mol) was 1·11 (95% CI 1·04 – 1·18) and a similar, but non-statistically significant risk was seen in the equivalent glycaemic control group in people with Type 1 diabetes (HR 1·22 95% CI 0·78 – 1·91).

In this population of people with diabetes, there was a U-shaped relationship with body mass index. For those with Type 1 diabetes and a BMI of 20 kg/m^2 the hazard ratio compared to people with a BMI of 25 to 29·9 kg/m^2 was 2·11 (95% CI 1·32 – 3·38). The comparable figure for Type 2 diabetes was 2·26 (95% CI 2·04-2·50). People with Type 1 diabetes and a BMI of ≥40 kg/m^2 had a HR of 2·15 (95% CI 1·37-3·36) and that for the same group in people with Type 2 diabetes was 1·46 (95% CI 1·50-1·79).

Impaired renal function was associated with an increased risk of COVID-19 related death. People with Type 1 diabetes and impaired renal function (eGFR of 30-44) had twice (HR 2·16 95% CI 1·59-2·93) the risk of those

with normal renal function (eGFR ≥ 60). The relative risk in those with an eGFR of less than 15 was seven times that of people with normal renal function (HR 6·85 95% CI 4·65 – 10·09). The comparable hazard ratios for people with Type 2 diabetes were 1·75 (95% CI 1·64-1·86) and 4·83 (95% CI 4·28-5·46) respectively.

A history of having a previous hospital stay for stroke and heart failure was associated with increased COVID-19 related mortality risk in both people with Type 1 and Type 2 diabetes (see Table 2). However, neither a history of myocardial infarction or having been prescribed anti-hypertensive drugs were associated with statistically significant increases in risk.

After adjustment for other risk factors, being a current smoker was associated with lower COVID-19 related mortality in the population of people with Type 2 diabetes (HR 0·63 95% CI 0·57 – 0·69).

Discussion

Using data from the entire population of people with Type 1 and Type 2 diabetes in England, we have demonstrated that after the emergence of the COVID-19 epidemic in this country, there has been a rapid and sizeable increase in deaths from all-causes occurring in people with both Type 1 and Type 2 diabetes. The weekly number of deaths exceeded standard control limits (three standard deviations) five weeks after the first recorded death related to COVID-19 in the UK. The scale of the increased number of weekly deaths is sizeable with more than twice the number of people with diabetes dying each week after April 3rd 2020 than would be expected at this time of year. The data suggest that during this period approximately 2500 to 3000 more deaths per week have occurred in the population of people with diabetes.

In the population of people with Type 1 and Type 2 diabetes, we found an independent association between the level of HbA1c and COVID-19 related mortality. Risk was higher in those with an HbA1c > 58mmol/mol and increased as HbA1c levels rose.

A previous study dichotomised people with diabetes without specification of type into those who were 'well-controlled' and 'poorly-controlled' and found a relationship with death from COVID-19. Our observations show that risk of COVID-19 death is related to hyperglycaemia in people with either Type 1 or Type 2 diabetes risk and is proportional to the level of hyperglycaemia.

In people with Type 2 diabetes and poor control (i.e. an HbA1c ≥86 mmol/mol) the increased risk compared to those with an HbA1c between 49-53 mmol/mol was 62%. In people with Type 1 diabetes, those with this level of poor glycaemic control had double the risk of people with good control. There are a number of possible

mechanistic explanations for the association of glycaemia and COVID-19 mortality. People with diabetes are at known increased risk of many serious infections[6] and poor glycaemic control has previously been associated with serious infections and hospitalisation[7]. Hyperglycaemia is known to impair host defences including granulocyte and macrophage function that are more important in bacterial infection.

The association of BMI with risk of COVID-19 related death in the diabetes population was U-shaped. The risk was greatest for those with very high BMI with the nadir of risk being in those with a BMI 25-29·9 kg/m^2. The higher risk seen in people with lower BMI could be linked to the effect of confounding by factors that are associated with weight loss which have either not been considered in our analysis (unmeasured confounding) or for which we have only imperfectly adjusted (residual confounding). The elevated risk of COVID-19 in people with diabetes and severe obesity is marked and adds to evidence that obesity is an important risk factor for death from COVID-19 for which a number of possible mechanisms have been postulated[17].

We also observed independent associations of age, sex, ethnicity, socioeconomic status, smoking status (but in the opposite direction to that usually found in studies of mortality), and some comorbidities (renal impairment, heart failure, stroke) in people with both Type 1 and Type 2 diabetes.

Several of the associations with death related to COVID-19 in these data are with non-modifiable risk factors such as age, sex, ethnicity and socioeconomic status and mirror findings in other recent analyses[17, 18]. The higher mortality risk seen in people with diabetes from black or Asian ethnic groups is a reversal of the pattern usually found for deaths registered pre-pandemic in people with diabetes (21). We also found an increased risk of COVID-19 death associated with established renal disease which was stronger in people with Type 1 diabetes. We observed a high risk in those with heart failure and stroke but no statistically significant association in people with a history of hypertension or recent myocardial infarction.

Categorisation as a current smoker was associated with a lower, not higher, risk of COVID-19 death, compared to being a non-smoker. This unexpected finding has also been described elsewhere[16] and, if confirmed, might point to an interaction with abnormal inflammation as found in ulcerative colitis[22].

While a number of the risk factors identified for COVID-19 mortality cannot readily be modified, obesity and the level of hyperglycaemia in people with diabetes may be influenced by healthcare interventions and patient behaviours. The nature of the epidemic of COVID-19 means that it would be implausible to seek randomised controlled trial evidence to prove that improving glycaemic control and optimising BMI would result in improved outcomes in people with diabetes who are infected with COVID-19. However, these targets are no

different from usual diabetes care. At this time, it would be important to further strengthen health care efforts to support people with diabetes in achieving and sustaining effective self-management and beneficial behavioural changes.

Comparison with other studies

Few previous studies have reported an association of blood glucose control with mortality from COVID-19. One retrospective study from 88 US hospitals of 451 people with COVID-19 and diabetes or hyperglycaemia reported that uncontrolled hyperglycaemia was associated with longer length of stay and higher mortality [12]. However, the definition of diabetes was unclear. Another retrospective study from China of 952 people with Type 2 diabetes (total cohort 7337) reported a higher mortality in people with diabetes (7·8% versus 2·7%; adjusted hazard ratio [HR] 1·49) and higher multiple organ injury than in the individuals without diabetes. They also reported that well controlled blood glucose (glycaemic variability within 3·9 to 10·0 mmol/L) was associated with much lower in-hospital mortality compared to individuals with poorly controlled glycaemia (adjusted HR, 0·14). Similar to our study, the OpenSAFELY Collaborative has taken a population approach by linking English primary care data on approximately 17 million individuals, with mortality data from people who died of COVID-19 in hospitals. The study assessed the independent effects of demographic characteristics and comorbidities. Diabetes was independently associated with a higher risk of death, with an adjusted hazard ratio of 1·50 for those with HbA1c < 58mmol/mol, and of 2·36 for those with HbA1c ≥ 58mmol/mol. However, these data were not available by type of diabetes, and were presented with only a single categorical divide for degree of glycaemic control[2]. Our work meaningfully extends such observations to aid clinical judgements and advice targeted at patients with Type 1 and Type 2 diabetes, and by assessing ONS data on all death registrations, includes deaths in the community as well as deaths in hospital.

Strengths and limitations

A strength of our study is its whole population approach, including nearly all people with Type 1 and Type 2 diabetes in England with risk factor information from prior to the start of the epidemic. This means that it assesses risk throughout the full course of the disease process. However, the lack of accurate population level data on tests for COVID-19 means it is not possible to identify whether the associations between risk factors and COVID-19 related mortality are due to increased susceptibility to infection, more severe illness following infection or a combination of both.

This study also uses all deaths as the end point which helps to overcome concerns about measures of disease severity when just assessing deaths in hospital. The limitations of using admissions to hospital or to ICU as surrogates for disease severity, or indeed using data on deaths to assess the independent impact of diabetes status on infection with COVID-19 have been highlighted[15].

Conclusion

In conclusion, we have demonstrated that there has been a rapid and sizeable increase in deaths occurring in people with diabetes since the beginning of the COVID-19 epidemic in England. Using a cohort approach including the total populations of people with Type 1 and Type 2 diabetes in England, we have shown independent associations with deaths registered with COVID-19 and the potentially modifiable risk factors of HbA1c and BMI, as well as with risk factors which are not clinically modifiable such as age, sex, ethnicity, deprivation and pre-existing co-morbidities.

Funding

NHS England & Improvement and NHS Digital provided resources for these analyses.

Authors contributions

JV, BY, NS, KK, NH, EB, PK conceived the study. NH, PK, JO, MC, EB, AW managed the data and carried out the statistical analysis. All the authors collaborated in interpretation of the results and drafting of the manuscript.

Conflicts of Interest

Jonathan Valabhji is National Clinical Director for Diabetes and Obesity at NHS England & Improvement. Partha Kar is National Specialty Advisor for Diabetes and Obesity at NHS England & Improvement. Bob Young is Clinical Lead for the National Diabetes Audit and a trustee of Diabetes UK. Kamlesh Khunti has acted as a consultant and speaker for Novartis, Novo Nordisk, Sanofi-Aventis, Lilly and Merck Sharp & Dohme. K.K. has also received grants in support of investigator and investigator-initiated trials from Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Merck Sharp & Dohme, Pfizer and Boehringer Ingelheim and has served on advisory boards for Novo Nordisk, Sanofi-Aventis, Lilly and Merck Sharp & Dohme. NH carries out Diabetes UK funded research. Emma Barron is Head of Health Intelligence (Diabetes), Public Health England. Chirag Bakhai is Primary Care advisor to the NHS Diabetes Programme. NS has consulted for Amgen, Astrazeneca, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, Pfizer and Sanofi and received grant support from Boehringer Ingelheim.

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Tables and Figures

Figure 1a: Weekly number of deaths in people with Type 1 diabetes in England January 2017-April 2020

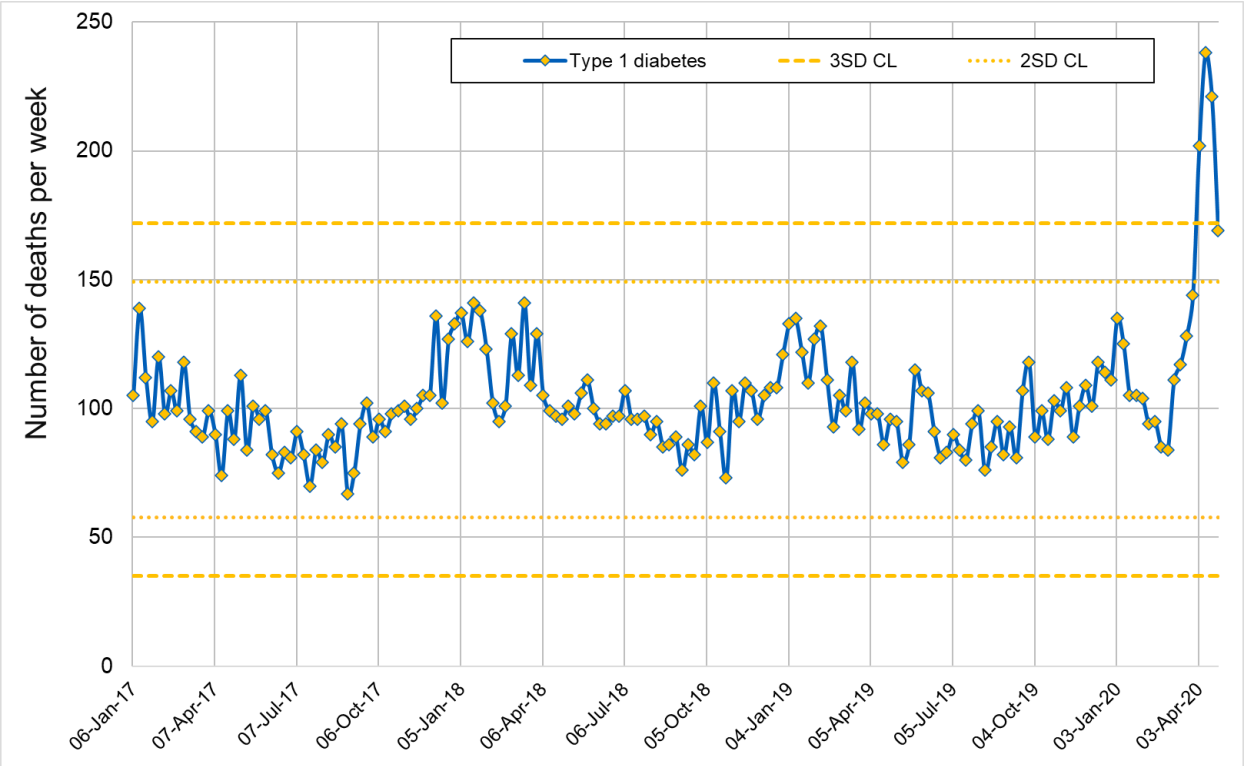


Figure 1b: Weekly number of deaths in people with Type 2 diabetes in England January 2017-April 2020

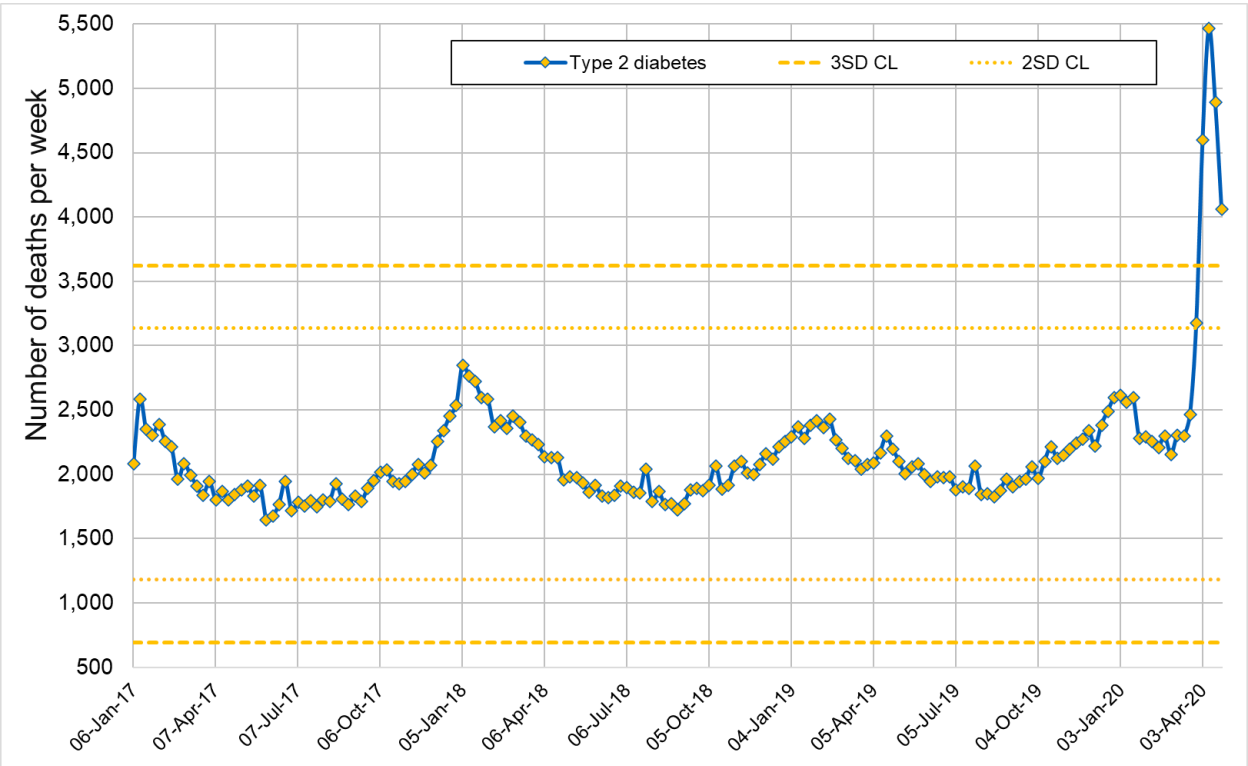


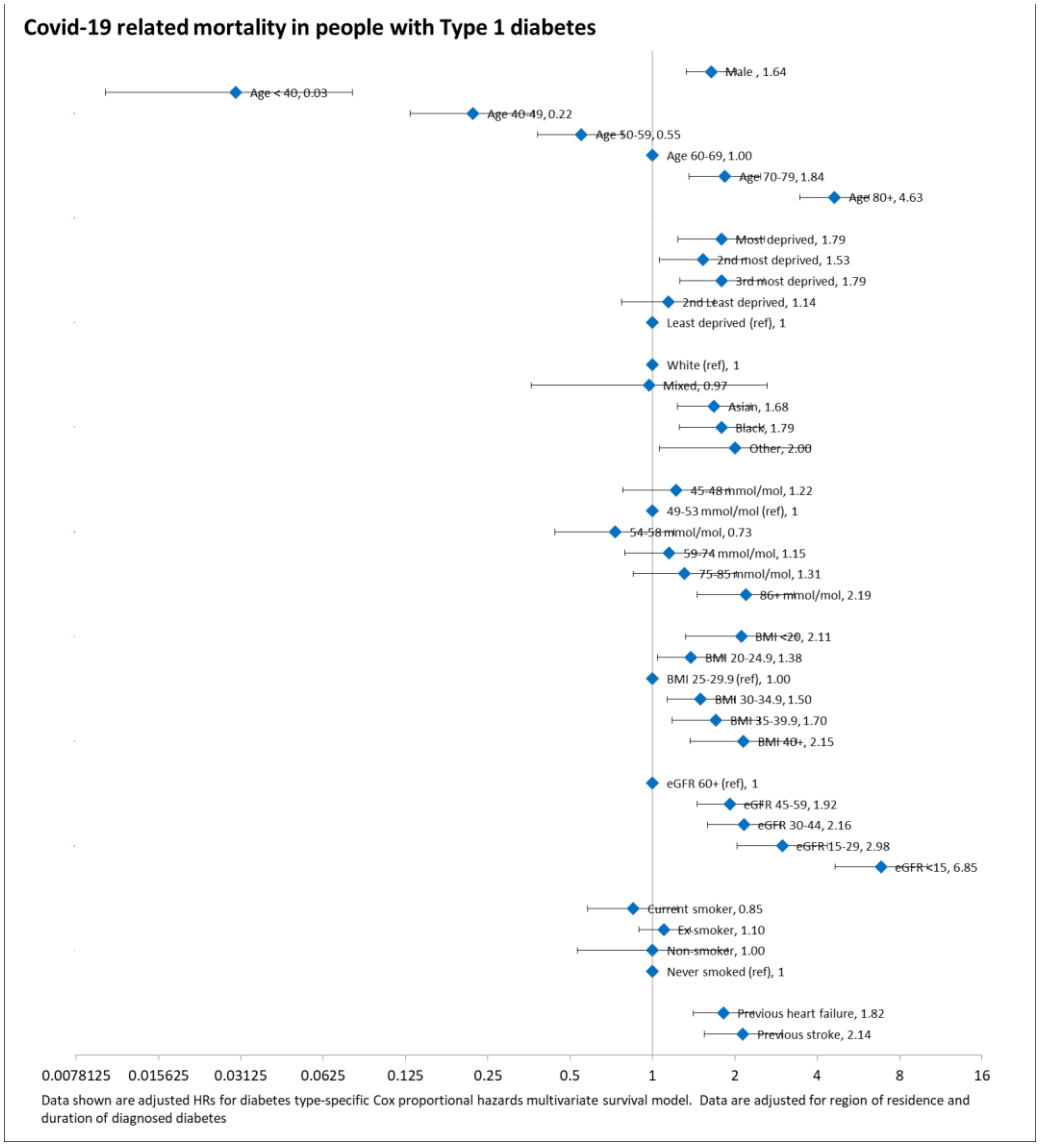
Table 1: Baseline characteristics on 1st January 2020 and number (%) of subsequent deaths with COVID-19 in people with Type 1 (n=265,090) and Type 2 diabetes (n=2,889,210) in England

	Type 1 diabetes				Type 2 diabetes			
	n	%	Deaths	%	n	%	Deaths	%
Sex								
Male	150,070	56·6%	263	62·9%	1,614,815	55·9%	5784	61·7%
Female	115,020	43·4%	155	37·1%	1,274,400	44·1%	3593	38·3%
Age								
<40 years	100,890	38·1%	*	-	67,860	2·3%	23	0·2%
40-49 years	41,785	15·8%	*	-	213,290	7·4%	90	1·0%
50-59 years	49,325	18·6%	52	12·4%	520,995	18·0%	445	4·7%
60-69 years	36,335	13·7%	75	17·9%	726,440	25·1%	1161	12·4%
70-79 years	24,480	9·2%	103	24·6%	772,860	26·7%	2437	26·0%
80+ years	12,275	4·6%	166	39·7%	587,760	20·3%	5221	55·7%
Deprivation								
Most deprived	56,465	21·3%	118	28·2%	704,530	24·4%	2519	26·9%
2nd most deprived	54,415	20·5%	97	23·2%	644,785	22·3%	2300	24·5%
3rd least deprived	53,475	20·2%	100	23·9%	578,140	20·0%	1761	18·8%
2nd least deprived	51,480	19·4%	58	13·9%	516,885	17·9%	1511	16·1%
Least deprived	49,075	18·5%	45	10·8%	443,315	15·3%	1279	13·6%
Missing	180	0·1%	0	0·0%	1,565	0·1%	7	0·1%
Region								
London	33,400	12·6%	102	24·4%	467,770	16·2%	2403	25·6%
South West	27,595	10·4%	21	5·0%	273,465	9·5%	521	5·6%
South East	41,650	15·7%	37	8·9%	403,990	14·0%	1180	12·6%
West Midlands	53,370	20·1%	106	25·4%	588,065	20·4%	1795	19·1%
East of England	32,665	12·3%	54	12·9%	313,825	10·9%	859	9·2%
North West	32,270	12·2%	47	11·2%	375,410	13·0%	1333	14·2%
North East	43,965	16·6%	51	12·2%	465,120	16·1%	1279	13·6%
Missing	180	0·1%	0	0·0%	1,565	0·1%	7	0·1%
Ethnicity								
White	211,000	79·6%	276	66·0%	1,909,470	66·1%	6266	66·8%
Mixed	3,230	1·2%	*	-	30,965	1·1%	120	1·3%
Asian	14,770	5·6%	57	13·6%	404,235	14·0%	1225	13·1%
Black	9,330	3·5%	45	10·8%	138,075	4·8%	818	8·7%
Other	4,045	1·5%	*	-	47,705	1·7%	152	1·6%
Missing	22,720	8·6%	26	6·2%	358,765	12·4%	796	8·5%
HbA1c								
<48 mmol/mol	18,010	6·8%	42	10·0%	726,600	25·1%	2444	26·1%
49-53 mmol/mol	21,610	8·2%	36	8·6%	594,270	20·6%	1618	17·3%
54-58 mmol/mol	25,250	9·5%	27	6·5%	367,365	12·7%	1033	11·0%
59-74 mmol/mol	77,550	29·3%	123	29·4%	553,840	19·2%	1798	19·2%
75-85 mmol/mol	30,235	11·4%	49	11·7%	157,685	5·5%	526	5·6%
86+ mmol/mol	31,380	11·8%	70	16·7%	175,640	6·1%	609	6·5%
Missing HbA1c	61,055	23·0%	71	17·0%	313,815	10·9%	1349	14·4%
Duration								
< 1 year	1,865	0·7%	*	-	52,955	1·8%	90	1·0%
2-3 years	14,955	5·6%	*	-	377,035	13·0%	643	6·9%
4-5 years	16,355	6·2%	*	-	374,790	13·0%	804	8·6%
5-9 years	37,280	14·1%	17	4·1%	791,020	27·4%	1923	20·5%
10-14 years	39,905	15·1%	39	9·3%	626,225	21·7%	2040	21·8%
15-20 years	42,725	16·1%	99	23·7%	422,425	14·6%	2115	22·6%
20+ years	112,005	42·3%	253	60·5%	244,770	8·5%	1762	18·8%

Body mass index								
BMI <20	20,065	7·6%	22	5·3%	43,570	1·5%	428	4·6%
BMI 20-24·9	74,160	28·0%	94	22·5%	402,240	13·9%	1875	20·0%
BMI 25-29·9	82,180	31·0%	103	24·6%	909,400	31·5%	2648	28·2%
BMI 30-34·9	42,175	15·9%	92	22·0%	745,475	25·8%	1897	20·2%
BMI 35-39·9	15,510	5·9%	41	9·8%	368,270	12·7%	873	9·3%
BMI 40+	8,195	3·1%	25	6·0%	242,305	8·4%	623	6·6%
BMI missing	22,815	8·6%	41	9·8%	177,955	6·2%	1033	11·0%
Smoking status								
Current smoker	43,500	16·4%	35	8·4%	370,150	12·8%	487	5·2%
Ex-smoker	61,865	23·3%	158	37·8%	1,013,045	35·1%	4000	42·7%
Non-smoker	6,265	2·4%	10	2·4%	50,920	1·8%	246	2·6%
Never smoked	139,810	52·7%	215	51·4%	1,452,630	50·3%	4629	49·4%
Missing	13,650	5·1%	0	0·0%	2,470	0·1%	15	0·2%
eGFR								
60+	198,790	75·0%	185	44·3%	2,305,915	79·8%	5102	54·4%
45-59	13,550	5·1%	82	19·6%	310,585	10·7%	1819	19·4%
30-44	7,565	2·9%	63	15·1%	147,930	5·1%	1411	15·0%
15-29	3,345	1·3%	36	8·6%	41,305	1·4%	568	6·1%
<15	1,895	0·7%	36	8·6%	10,920	0·4%	293	3·1%
Missing	39,955	15·1%	16	3·8%	72,565	2·5%	184	2·0%
Co-morbidities								
Previous MI	3,145	1·2%	28		49,180	1·7%	380	
Previous stroke	3,230	1·2%	43		58,490	2·0%	723	
Previous heart failure	7,020	2·6%	99		142,350	4·9%	1908	
Hypertension	117,025	44·1%	358		2,213,725	76·6%	8314	

The numbers of people in each category has been rounded to the nearest five to meet information governance rules · * - indicates a small number that has been suppressed to meet information governance rules

Figure 2: Forest plots showing adjusted hazard ratios for COVID-19 related death in people with Type 1 (n=265,090) and Type 2 diabetes (n=2,889,210) in England up until May 1st 2020·



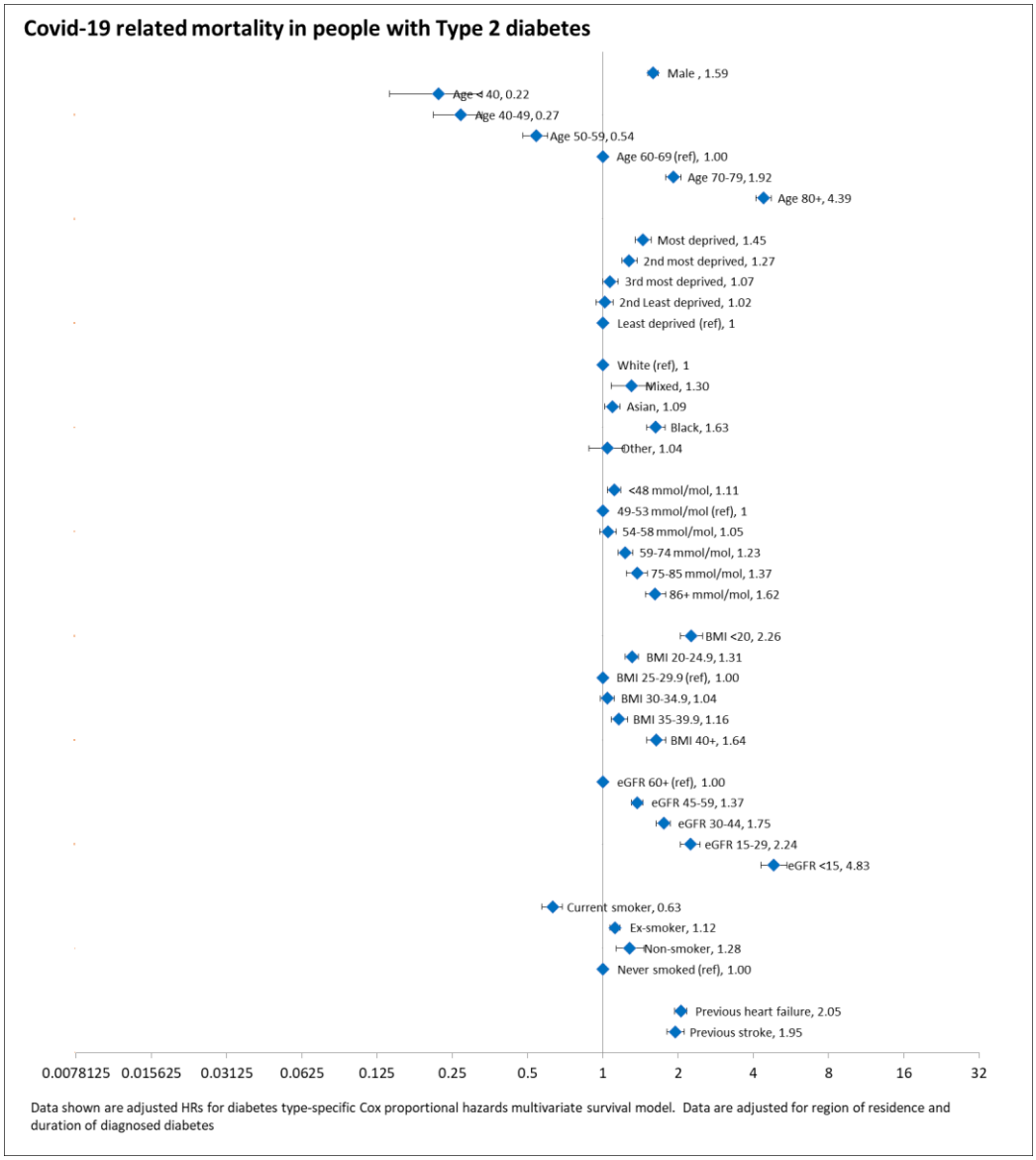


Table 2: Adjusted hazard ratios for COVID-19 related death in people with Type 1 (n=265,090) and Type 2 diabetes (n=2,889,210) in England up until May 1st 2020·

	COVID-19 related deaths	
	Type 1	Type 2
	HR (95% CI)	HR (95% CI)
Sex		
Male	1·64 (1·33 - 2·02)	1·59 (1·52 - 1·66)
Female	-	-
Age		
<40	0·03 (0·01 - 0·08)	0·22 (0·14 - 0·33)
40-49	0·22 (0·13 - 0·37)	0·27 (0·21 - 0·33)
50-59	0·55 (0·38 - 0·78)	0·54 (0·48 - 0·6)
60-69	-	-
70-79	1·84 (1·36 - 2·48)	1·92 (1·79 - 2·06)
80+	4·63 (3·46 - 6·2)	4·39 (4·1 - 4·71)
Deprivation		
Most deprived	1·79 (1·24 - 2·57)	1·45 (1·35 - 1·56)
2nd most deprived	1·53 (1·06 - 2·19)	1·27 (1·19 - 1·37)
3rd most deprived	1·79 (1·26 - 2·56)	1·07 (1 - 1·15)
2nd Least deprived	1·14 (0·77 - 1·69)	1·02 (0·94 - 1·1)
Least deprived	-	-
Region		
London	2·48 (1·67 - 3·69)	1·77 (1·64 - 1·91)
South West	0·77 (0·45 - 1·31)	0·63 (0·57 - 0·7)
South East	-	-
West Midlands	1·44 (0·98 - 2·12)	1·03 (0·95 - 1·11)
East of England	1·85 (1·21 - 2·83)	0·97 (0·88 - 1·06)
North West	1·69 (1·09 - 2·62)	1·17 (1·08 - 1·27)
North East	1·22 (0·79 - 1·87)	0·92 (0·85 - 1)
Ethnic group		
White	-	-
Mixed	0·97 (0·36 - 2·62)	1·3 (1·08 - 1·56)
Asian	1·68 (1·23 - 2·29)	1·09 (1·02 - 1·17)
Black	1·79 (1·25 - 2·55)	1·63 (1·5 - 1·77)
Other	2 (1·06 - 3·78)	1·04 (0·88 - 1·22)
Missing	1·24 (0·82 - 1·86)	0·79 (0·73 - 0·85)
HbA1c		
45-48 mmol/mol	1·22 (0·78 - 1·91)	1·11 (1·04 - 1·18)
49-53 mmol/mol	-	-
54-58 mmol/mol	0·73 (0·44 - 1·2)	1·05 (0·97 - 1·13)
59-74 mmol/mol	1·15 (0·79 - 1·67)	1·23 (1·15 - 1·32)
75-85 mmol/mol	1·31 (0·85 - 2·03)	1·37 (1·24 - 1·51)
86+ mmol/mol	2·19 (1·46 - 3·29)	1·62 (1·48 - 1·79)
Missing	1·6 (1·05 - 2·43)	1·57 (1·46 - 1·7)
Duration of diagnosis		

<1 year	2·81 (0·31 - 25·2)	0·93 (0·74 - 1·15)
1-2 years	1·37 (0·37 - 5·11)	0·87 (0·78 - 0·96)
3-4 years	-	-
5-9 years	1·51 (0·51 - 4·48)	0·96 (0·89 - 1·04)
10-14 years	1·78 (0·63 - 5·01)	0·98 (0·91 - 1·07)
15-19 years	2·51 (0·92 - 6·86)	1·14 (1·05 - 1·24)
20+ years	1·87 (0·69 - 5·06)	1·17 (1·07 - 1·28)
eGFR		
60 or greater	-	-
45-59	1·92 (1·46 - 2·53)	1·37 (1·3 - 1·45)
30-44	2·16 (1·59 - 2·93)	1·75 (1·64 - 1·86)
15-29	2·98 (2·04 - 4·35)	2·24 (2·04 - 2·45)
Less than 15	6·85 (4·65 - 10·09)	4·83 (4·28 - 5·46)
Missing	1·45 (0·83 - 2·55)	0·82 (0·7 - 0·97)
Body mass index		
BMI <20	2·11 (1·32 - 3·38)	2·26 (2·04 - 2·5)
BMI 20-24·9	1·38 (1·04 - 1·83)	1·31 (1·23 - 1·39)
BMI 25-29·9	-	-
BMI 30-34·9	1·5 (1·13 - 1·99)	1·04 (0·98 - 1·11)
BMI 35-39·9	1·7 (1·18 - 2·46)	1·16 (1·08 - 1·26)
BMI 40+	2·15 (1·37 - 3·36)	1·64 (1·5 - 1·79)
Missing	1·8 (1·23 - 2·63)	1·86 (1·73 - 2·01)
Smoking		
Current smoker	0·85 (0·58 - 1·23)	0·63 (0·57 - 0·69)
Ex-smoker	1·1 (0·89 - 1·37)	1·12 (1·07 - 1·17)
Non-smoker	1 (0·53 - 1·89)	1·28 (1·13 - 1·46)
Never smoked	-	-
Missing	-	2·03 (1·22 - 3·37)
Co-morbidities		
Previous stroke	2·14 (1·55 - 2·97)	1·95 (1·81 - 2·11)
Previous heart failure	1·82 (1·41 - 2·34)	2·05 (1·94 - 2·17)

Data shown are adjusted HRs for diabetes type-specific Cox proportional hazards multivariate survival model·