Associations between Type 1 and Type 2 diabetes with COVID-19 related mortality in England: a whole population-based study

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Abstract

Background

Although diabetes has been associated with COVID-19 mortality, the absolute and relative risks for Type 1 and Type 2 diabetes are unknown.

Methods

A population cohort study assessing risks of in-hospital death with COVID-19 between 1st March and 11th May 2020, including individuals registered with a General Practice in England and alive on February 16th 2020. Multivariable logistic regression examined diabetes status, by type, and association with in-hospital death, adjusting for demographic factors and comorbidities.

Findings

Of the 61,414,470 individuals registered, 263,830 (0·4%) had a recorded diagnosis of Type 1 and 2,864,670 (4·7%) of Type 2 diabetes. There were 23,698 in-hospital COVID-19 related deaths. One third occurred in people with diabetes: 7,434 (31·4%) with Type 2 and 364 (1·5%) with Type 1 diabetes. Crude mortality rates per 100,000 persons over the 72 days for those without diabetes, and those with Type 1 and Type 2 diabetes were 27 (27-28), 138 (124-153), and 260 (254-265) respectively. Adjusted for age, sex, deprivation, ethnicity and geographical region, people with Type 1 and Type 2 diabetes had 3·51 (3·16-3·90) and 2·03 (1·97-2·09) times the odds respectively of in-hospital death with COVID-19 compared to those without diabetes, effects that were attenuated to 2·86 and 1·80 respectively when also adjusted for previous hospital admissions with coronary heart disease, cerebrovascular disease or heart failure.

Interpretation

This nationwide analysis in England demonstrates that Type 1 and Type 2 diabetes were independently associated with a significant increased odds of in-hospital death with COVID-19.

Funding

NHS England & Improvement and Public Health England.

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. Studies from China, Italy, the USA and the UK have suggested that people with diabetes have higher risks of more severe outcomes with COVID-19, including death. One population-based UK study reported a higher risk of COVID-19 related death in those with diabetes after adjustment for demographic factors and other comorbidities. However, none of these studies have reported differences in risk by type of diabetes, which is important given the need for specific advice to people with different types of diabetes and their families.

Added value of this study

To our knowledge, this is the largest COVID-19 related study, covering almost the entire population of England, and the first study to investigate the relative and absolute risks of death in hospital with COVID-19 by type of diabetes, adjusting for key confounders. It demonstrates that one third of all in-hospital deaths with COVID-19 occur in people with diabetes. Adjusted for age, sex, deprivation, ethnicity and geographical region, people with Type 1 and Type 2 diabetes had 3·51 and 2·03 times the odds respectively of dying in hospital with COVID-19 compared to those without diabetes. These relative odds were attenuated to 2.86 and 1.80 respectively when further adjusted for previous hospital admissions with certain cardiovascular comorbidities.

Implications of all the available evidence

People with diabetes are at higher risk of COVID-19 related death than people without diabetes. However, mortality risk was very low for people under 40 years of age with either types of diabetes. Future studies should determine the key pathophysiological mechanisms underlying the determinants of more severe outcomes with COVID-19 and inform potential clinical and public health responses to the pandemic.

Introduction

By 11th May 2020, 4,252,290 people worldwide, from 213 countries and territories, were known to have had Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 infection, and 287,131 had died.[1] A recent systematic review and studies using univariate analyses from China,[2,3] Italy and the USA,[4,5] and multivariable analyses from China,[6,7] the USA and the UK,[8,9] have all suggested that people with diabetes have higher risks of more severe outcomes with COVID-19, including death. The latter study, using data from General Practices in England covering approximately 40% of the English population, included adjustments for age, ethnicity and socioeconomic deprivation.[9] However, none of these studies differentiated between Type 1 diabetes and Type 2 diabetes, a distinction which is important in both understanding the pathophysiological mechanisms underlying the increased risk of people with diabetes and in informing potential clinical and public health responses to that risk.

Data, including type of diabetes, are routinely collected for people diagnosed with diabetes through the National Diabetes Audit (NDA) and, in 2018/19, 98% of General Practices in England participated in the NDA.[10] We present two sets of analyses as linked publications. In this paper, we assessed the independent effects of diabetes status, by type, on in-hospital death in England with COVID-19 during the period from 1st March 2020 to 11th May 2020. This required a whole population approach, and only parameters recorded reliably for the whole population, including age, sex, ethnicity, socioeconomic deprivation, diabetes status, and previous hospital admissions with certain cardiovascular comorbidities, were assessed.

In the other paper, we assessed total numbers of deaths, in both hospital and community environments, and risk factors associated with COVID-19 related deaths, in people with Type 1 diabetes and people with Type 2 diabetes. As demographic and clinical characteristics, and some microvascular and cardiovascular complications, were recorded reliably in the datasets used for this analysis, the independent effects of each factor in each cohort on COVID-19 related mortality, including the role of prior glycaemic control and associations with body mass index (BMI) were assessed.[11]

Methods

Study design

A population cohort study assessing the risk of in-hospital death relating to COVID-19, covering all individuals registered with a General Practice in England and alive on February 16th 2020, assessing risk in people with Type 1 diabetes and people with Type 2 diabetes.

Data sources

In response to the increasing demand for analysis relating to the COVID-19 outbreak, NHS England created a bespoke hub of relevant datasets in the National Commissioning Data Repository (see Supplementary materials, S1).

This study used de-identified data from the February 2020 Master Patient Index (MPI), a reference data set of every individual registered with a General Practice in England. Patient demographics, birth-month and year, sex and Lower Super Output Area (LSOA) based on postcode of residence are included in the dataset.

The latest full extract of the NDA, covering the period 1st January 2018 to 31st March 2019, was used to identify individuals with diagnosed diabetes.[10] Individuals were identified for inclusion in the NDA if they had a valid code for diabetes (excluding gestational diabetes) in their electronic health record. Type of diabetes was based on the codes recorded in clinical records: Type 1 diabetes, Type 2 diabetes or other diabetes (such as Maturity Onset Diabetes of the Young (MODY)).

The Bridges to Health National Population Segmentation dataset was used to identify individuals' long-term conditions and ethnicity. [12] The model utilises hospital data sources, including over 10 years of Secondary Uses Service, a collection of data from all hospitals in England including Admitted Patient Care Data, Outpatient data and Emergency Care data. The Segmentation dataset includes comorbidity and ethnicity data for individuals, derived using activity occurring up to 31st March 2019 for comorbidity and 28th February 2020 for ethnicity.

Deaths in hospital with COVID-19 were taken from the COVID Patient Notification System (CPNS), a bespoke daily data collection set up on 1st March 2020 as part of the response to support COVID-19. Inclusion in this dataset initially required a positive test for SARS-CoV-2 infection. However, this was subsequently extended on the 28th April 2020 to include those without a positive test but with COVID-19 registered as a cause of death based on clinical judgement. This study used data reported and occurring up to the 11th May 2020.

Antigen testing for COVID-19 during the observation period was largely performed on patients in hospital and it was not possible to determine the true number of people in the total population who were infected. Therefore, we calculated mortality rates for the population as a whole, rather than for the population who were infected as the latter was unknown.

Outcomes

The outcome was death in hospital with COVID-19 between 1st March and 11th May 2020 ascertained through the CPNS. COVID-19 related in-hospital death was used rather than total deaths with COVID-19 due to limitations in available data linkages; unlike CPNS data, data from the Office for National Statistics (ONS) regarding total deaths could not be linked to the MPI dataset.

Covariates

In addition to diabetes status, age, sex, ethnicity, and deprivation were identified as potential confounding factors. Diabetes status was categorised as Type 1, Type 2, other diabetes or no diabetes recorded. Age was calculated as at 1st February 2020 from birth-month and –year and grouped into 10-year age bands. Sex was recorded as male, female or missing. Ethnicity was classified as white, Asian, black, mixed, other or unknown. Social deprivation was measured using Quintiles of the Index of Multiple Deprivation 2019 associated with the LSOA derived from the individual's postcode.[13] Given the geographical variation in population exposure to SARS-CoV-2 across England, region was also identified as a potential outcome moderator. Individuals were allocated to one of the seven regions in England used for healthcare administration purposes according to the home postcode.

We included data on significant cardiovascular comorbidities (coronary heart disease (CHD), cerebrovascular disease (CBVD) and heart failure (HF)) ascertained through coding in the Bridges to Health Segmentation Model.[12] Cardiovascular comorbidities were identified by searching through hospital records for CHD, CBVD and HF codes. Full details of the criteria used can be found in the Supplementary material, S1.

Other factors of interest including BMI, chronic kidney disease, hypertension and smoking status were either not recorded reliably or not recorded at all at population-level in the hospital-derived datasets available, and hence could not be included; these factors were examined in detail in our paired publication looking at risk factors for COVID-19 related mortality in people with diabetes.[11]

Statistical analysis

The associations between diabetes status, sex, age group, ethnicity, deprivation, region and comorbidities and in-hospital death with COVID-19 were determined. Crude mortality rates over the 72-day observation period per 100,000 people were calculated using the MPI population as the denominator. Mortality rates for a given subgroup were calculated with respect to the MPI population for the given subgroup.

A multivariable logistic regression analysis was used to examine whether diabetes status was associated with in-hospital death in England with COVID-19 adjusting for age, sex, ethnicity, deprivation quintile and region. A further logistic regression model included CHD, CBVD and HF to assess the impact of these comorbidities on the association between diabetes and in-hospital death with COVID-19. Separate models were run by sex, age-group (aged less than 70 years and aged 70 and older), by ethnicity and deprivation quintile. The C-statistic was calculated to assess model fit. A sensitivity analysis was performed excluding people of unknown ethnicity. The proportions of different ethnicities in the population with known ethnicity were compared to the 2011 census and the characteristics of people with unknown ethnicity were investigated.[14]

Statistical significance was defined as p-value <0.05 and confidence intervals (CI) were set at 95%. All data were analysed using Stata version 16. All numbers taken directly from the NDA were rounded to the nearest five persons to protect re-identification. Data cells with between 1-4 counts in the CPNS were suppressed due to data protection regulations.

Information Governance

In order to fulfil its statutory duties, NHS England requires access to and linkage of a variety of national pseudonymised datasets, in line with the requirements of General Data Protection Regulation. Furthermore, in March 2020, the Secretary of State for Health and Social Care used powers under the UK Health Service (Control of Patient Information) Regulations 2002 to require organisations to process confidential patient information for the purposes of protecting public health, providing healthcare services to the public and monitoring and managing the COVID-19 outbreak and incidents of exposure.

Results

There were 61,414,470 individuals registered with a GP practice in England and alive on the 16th February 2020. Of those, 263,830 (0·4%) had a recorded diagnosis of Type 1 diabetes, 2,864,670 (4.7%) had a recorded diagnosis of Type 2 diabetes and 41,750 had other types of diabetes (0·1%). The characteristics of the baseline population in England are provided in Table 1; 49·9% were male, the mean (SD) age was 40·9 (23·2) years and 13·4% were of black, Asian, mixed and other (BAME) ethnicity (6·1% Asian, 3·0% black, 1·5% mixed and 2·7% other). Previous CHD was recorded in 3·5% of the population, CBVD in 1·5% and HF in 1·0%. Data were missing for; sex (<0.01%), ethnicity (21.2%), deprivation quintile (0.1%) and region (0.1%). There were no missing data for age.

Table 1 provides the characteristics of the population by diabetes type. Compared to people without diabetes, individuals with Type 1 diabetes and Type 2 diabetes were older (mean age: 46·6 (19·5) years, 67·4 (13·4) years and 39·5 (22·8) years for Type 1, Type 2 and those without diabetes respectively) with a higher proportion of men and higher proportions of people with previous CHD, CBVD and HF. A higher proportion of individuals with Type 2 diabetes were of BAME ethnicities and from the most deprived quintile, compared to those with Type 1 diabetes and those without diabetes. The proportion of missing ethnicity data was lower for people with Type 1 diabetes (4.0%) and Type 2 diabetes (9.0%) than for those without diabetes (21.9%).

There were 23,698 hospital deaths with COVID-19 in England reported up to 11th May 2020. Overall, one third of these deaths occurred in people with diabetes, with Type 2 diabetes accounting for 7,434 (31·4%) deaths, Type 1 diabetes 364 (1·5%) deaths and other types of diabetes 69 (0·3%) deaths. The characteristics of people recorded as having died in hospital with COVID-19 are provided in Table 2. Overall, 61·5% were male, the mean age was 78·6 (12·1) years and 16·0% were from BAME ethnicities (7·5% Asian, 5·7% black, 0·7% mixed and 2·1% other). The highest proportion of deaths were in people from the most deprived quintile of the population (23·8%), with 15·9% being in the least deprived quintile. Previous CHD, CBVD and HF were recorded for 30·9%, 19·8% and 17·8% respectively.

Table 2 shows the characteristics of in-hospital COVID-19 deaths by diabetes type. Compared to those without diabetes, individuals with Type 1 diabetes and Type 2 diabetes were younger (mean: 72·2 (13·0) years, 77·9 (11·0) years and 79·2 (12·5) years for Type 1, Type 2 and no diabetes respectively) with a higher proportion of deaths in people from BAME ethnicities and higher proportions of people with a history of CHD, CBVD and HF. There was a marked inverse relationship with deprivation with substantially more deaths from the most deprived quintile than in the least deprived quintile, in particular for individuals with Type 1 diabetes and Type 2 diabetes, and to a lesser extent, for those without diabetes.

The crude rate of in-hospital mortality with COVID-19 up to 11th May 2020 was 39 (38-39) per 100,000 persons over the 72-day period for the general population (Figure 1). The rate per 100,000 persons in this period was 138 (124-153) for the population with Type 1 diabetes, 260 (254-266) for those with Type 2 diabetes,165 (129-209) for people with other types of diabetes and 27 (27-28) for those without diagnosed diabetes (Table 2).

Mortality rates increased markedly by age group (Figure 1). Within each age group, rates were significantly higher for people with Type 1 and Type 2 diabetes than for those without diabetes.

Regression analysis showed that there was a strong association between death in-hospital with COVID-19 and age. The odds ratio (OR) was 0·012 (95% CI: 0·010 to 0·014) for individuals <40 years and 9·20 (8·83 to 9·58) for individuals aged 80+ years compared to the 60-69-year old reference group. Odds were higher for men (1·94 (1·89 to 1·99)) and were higher in those living in more deprived areas with an OR of 1·88 (1·80 to 1·96) compared to the least deprived quintile of the population. There were higher odds for BAME ethnicities with ORs of 1·35 (1·28 to 1·42) for Asian groups and 1·71 (1·61 to 1·82) for black groups compared to the white population. There were significant differences by region (Figure 2).

Adjusted for age, sex, deprivation, ethnicity and region, people with Type 1 diabetes had 3·51 (3·16-3·90) times the odds of dying in hospital with COVID-19, compared to the population without known diabetes, while people with Type 2 diabetes had 2·03 (1·97-2·09) times the odds of dying in hospital with COVID-19. The C-statistic was 0.934 (0.933 to 0.935).

In the model which included history of comorbidities; CHD, CBVD and HF were each significantly associated with in-hospital death with COVID-19 with ORs of 1·32 (1·28 to 1·36), 2·23 (2·16 to 2·31) and 2·23 (2·15 to 2·31) respectively. Adjustment for these comorbidities slightly attenuated the association with age seen in the model without comorbidity data. A modest attenuation was also seen for the association with type of diabetes. Adjusted for age, sex, deprivation, ethnicity, region and cardiovascular comorbidities, the OR for dying in-hospital with COVID-19 was 2·86 (2·58 to 3·18) for people with Type 1 diabetes and 1·80 (1·75 to 1·86) for people with Type 2 diabetes compared to the population without known diabetes (supplementary material, S2).

Separate modelling showed that the relative impact of having diabetes was greater in younger people, women and those of black ethnicity (supplementary material, S3). In a model restricted to those under-70-years, ORs were 6·39 (5·40 to 7·56) for Type 1 diabetes and 3·74 (3·50 to 3·99) for Type 2 diabetes compared to 2·81 (2·46 to 3·22) and 1·79 (1·74-1·85) respectively in a model restricted to those over 70 years. In a model restricted to women only, the OR for Type 2 diabetes was 2.19 (2.09-2.29) compared to 1.94 (1.87-2.01) in a model restricted to men. In a regression model restricted to people of black ethnicity, the OR was 2.76 (2.46-3.09) in people with Type 2 diabetes, which was significantly higher than in people with Type 2 diabetes for Asian and white ethnicities. Other factors also showed differences between models (supplementary material, S3).

Overall, the proportions of people of different ethnicity amongst those whose ethnicity was known, were broadly similar to those of the 2011 Census. There was a greater proportion of missing data for ethnicity in younger age groups and in men but in a sensitivity analysis excluding individuals with missing ethnicity data the results were unchanged (Supplementary material, S4).

Discussion

To our knowledge, this is the largest COVID-19 related study of its kind, covering almost the entire population of England, and is the first study to investigate the relative and absolute risk of death in hospital with COVID-19 by type of diabetes, adjusting for key confounding factors. It demonstrates an increased risk in people with, and by type of, diabetes, with one third of all deaths in-hospital with COVID-19 occurring in people with diabetes.

After adjusting for age, sex, ethnicity, socioeconomic deprivation and region, individuals with Type 1 diabetes had three and a half times the odds of in-hospital death with COVID-19, while those with Type 2 diabetes had twice the odds, compared to those without a diagnosis of diabetes. Further adjustment for certain cardiovascular comorbidities attenuated these risks slightly but they remained significantly elevated.

Given the endpoint in this study was death with COVID-19 in hospital settings, there is potential for underestimation of the association of Type 2 diabetes with COVID-19 related mortality. The prevalence of Type 2 diabetes increases with age, and so Type 2 diabetes is likely to be over-represented in people with advanced age, frailty and multimorbidity, who in turn are likely to be over-represented in deaths out of hospital with COVID-19. Data analyses by the ONS reveal that over 70% of the deaths relating to COVID-19 in people who resided in care homes, from 2nd March 2020 to 1st May 2020, occurred in care home settings rather than in-hospital and were therefore not included in the data sets analysed in this study.[15]

The risk of all-cause mortality in people with diabetes is higher than in people without diabetes under normal circumstances, but the observed increased odds for in-hospital death with COVID-19 is higher than that reported for all-cause mortality for Type 1 diabetes (148%) and Type 2 diabetes (50%) in the most recently published NDA Complications and Mortality Report.[16] People with other diagnoses of diabetes had similar risk to people with Type 2 diabetes in both models in our analyses. However, as this category of people is relatively small and represents a highly heterogeneous group, further inferences are limited.

Adjusting for comorbidities allows an interpretation of the independent effect of diabetes on in-hospital death with COVID-19 beyond the well-established link between diabetes and cardiovascular comorbidities which are themselves determinants of COVID-19 mortality risk. We recognise that being unable to adjust for BMI, hypertension, kidney disease and smoking, amongst other potential confounders, is likely to have left large residual confounding in the associations described.

In this and previous analyses, HF and CBVD have been shown to be associated with serious outcomes related to COVID-19.[8,9] We demonstrate an association between previous CHD and in-hospital mortality with COVID-19, an association seen in some, but not all, previous studies.[8,9] Although we have adjusted for these factors, this may represent an over-adjustment as diabetes itself predisposes to the development of cardiovascular disease.

As reported in a recently published multivariable analysis using data from England, [9] our analyses showed increased odds of in-hospital death with COVID-19 for older people, men, people of black, Asian or mixed ethnicities and those who live in areas of high socioeconomic deprivation. While a number of studies have reported an association between diabetes and severe outcomes of COVID-19, [2-9] the findings here are novel in suggesting that the influence of diabetes on risk of death with COVID-19 is independent of age, ethnicity, deprivation and cardiovascular comorbidities, and is seen in people with all types of diabetes.

There were differences in the ORs for in-hospital mortality with COVID-19 for Type 1 diabetes and Type 2 diabetes by age, sex and ethnicity, with increased odds for Type 2 diabetes for women, increased odds for both Type 1 and Type 2 diabetes for younger age groups and increased odds for Type 2 diabetes for black ethnicity. For younger age groups, while the relative risk of in-hospital death for Type 1 diabetes and Type 2 diabetes was significantly higher than in older age groups, the absolute risk in the lower age groups was small. At least in part, this may be due to the endpoint used in this study of in-hospital death with COVID-19, with older age groups with frailty and multimorbidity potentially disproportionately represented in deaths with COVID-19 out of hospital.

Implications of this study

There are many possible reasons for the increased odds of in-hospital death from COVID-19 in people with Type 1 diabetes compared to those with Type 2 diabetes. It may be hypothesised that the difference in odds of in-hospital death with COVID-19 could relate to the different aetiologies and pathophysiologies of the types of diabetes, varying patterns of diabetes complications or iatrogenic harms (such as hypoglycaemia), differing patterns, treatments, intensity and duration of glycaemia, or the influence of comorbidities which were either not adjusted for in these analyses or for which we only imperfectly adjusted.

An excess risk of other infectious disease morbidity and mortality has previously been observed in Type 1 compared to Type 2 diabetes. The risk of developing pneumonia was reported to be 2.98 times higher for Type 1 diabetes and 1.58 times greater for Type 2 diabetes compared to the general population.[17] As we could not express mortality risk among those who were truly infected (since this was unknown), it is possible that increased susceptibility to infection with SARS-CoV-2 could explain some of the excess mortality risk associated with diabetes that was observed in this study.

On a relative scale, our analyses show that Type 1 diabetes was associated with 3.51 higher odds of in-hospital death with COVID-19 and Type 2 diabetes was associated with 2.03 higher odds, compared to the population without known diabetes. However, on an absolute scale, the unadjusted rates of in-hospital death with COVID-19 over this 72-day period for Type 1 diabetes (138 per 100,000 persons) were approximately half that for Type 2 diabetes (260 per 100,000 person), largely reflecting the different age structure of the two populations. Even with the additional odds identified, people under the age of 40 years with either type of diabetes were at very low absolute risk of in-hospital death with COVID-19 during the observation period of this study in England.

Strengths and Limitations

A strength of the study is its size, covering almost the whole population of England and nearly all people with Type 1 diabetes and Type 2 diabetes. However, there were a number of limitations. Only the comorbidities CHD, CBVD and HF were included in analyses; we did not adjust for other comorbidities due to limitations in the datasets used and available. In particular, hypertension and chronic kidney disease were not included due to incomplete recording in the hospital-derived Segmentation Model. A previous systematic review suggested an association between poor COVID-19 related outcomes and hypertension,[18] although this has not been detected in some multivariable analyses which showed significant associations with chronic kidney disease.[8,9] Similarly, BMI and smoking status could not be reliably ascertained at population level from the datasets used.

Only data regarding diabetes status and comorbidities up to the end of March 2019 were used. Therefore, a small proportion of the population for whom diabetes or cardiovascular comorbidities were first recorded after April 2019 will have been misclassified.

The endpoint used in this study was in-hospital death with COVID-19. Out-of-hospital deaths with COVID-19 may have occurred disproportionally in people of advanced age, frailty and multimorbidity, and would not have been included in these analyses, potentially resulting in underestimation of the risks associated with Type 2 diabetes in particular.

Conclusion

The findings of the study have important implications for people with diabetes, healthcare professionals and policy makers. We would encourage the use of these findings, along with those from other studies investigating risk factors for COVID-19 related outcomes, to provide reassurance for people who are at low absolute risk, despite having diabetes. For those who are at higher absolute risk, the results can inform public guidance including recommendations for shielding. Further elucidation of the modifiable risk factors for poorer COVID-19 outcomes in people with diabetes will be critical in guiding management and providing targeted support.

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Author contributions

Jonathan Valabhji, Emma Barron, Chirag Bakhai, Andy Weaver, Naomi Holman, Kamlesh Khunti, Naveed Sattar, Nick Wareham, and Bob Young conceived the study. Emma Barron, Dominique Bradley, Hassan Ismail, Naomi Holman and Peter Knighton managed the data and carried out the statistical analysis. All the authors collaborated in interpretation of the results and drafting of the manuscript.

Declarations of Interest

Jonathan Valabhji is the 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. Chirag Bakhai is the Primary Care Advisor to the NHS Diabetes Programme. 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. Kamlesh Khunti 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. Kamlesh Khunti is supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands (ARC EM) and the NIHR Leicester Biomedical Research Centre (BRC). Naveed Sattar 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

Table 1: Number of individuals registered with a GP practice in England and alive at 16th February 2020 by diabetes type

		N					Percentage				
		Overall	Type 1	Type 2	Other Diabetes	No Diabetes	Overall	Type 1	Type 2	Other Diabetes	No Diabetes
	Total	61,414,470	263,830	2,864,670	41,750	58,244,220	100·0%	100·0%	100·0%	100·0%	100·0%
Age	0 to 39 years	30,506,055	100,760	67,735	6,815	30,330,745	49·7%	38·2%	2·4%	16·3%	52·1%
	40 to 49 years	8,073,780	41,680	212,945	5,630	7,813,525	13·1%	15·8%	7·4%	13·5%	13·4%
	50 to 59 years	8,266,300	49,160	519,825	8,520	7,688,795	13·5%	18·6%	18·1%	20·4%	13·2%
	60 to 69 years	6,359,460	36,125	723,790	8,510	5,591,035	10·4%	13·7%	25·3%	20·4%	9·6%
	70 to 79 years	5,057,230	24,180	766,815	7,215	4,259,020	8·2%	9·2%	26·8%	17·3%	7·3%
	80+	3,151,645	11,925	573,560	5,060	2,561,095	5·1%	4·5%	20·0%	12·1%	4·4%
Sex	Male	30,635,515	149,330	1,601,045	22,610	28,862,530	49·9%	56·6%	55·9%	54·2%	49·6%
	Female	30,778,160	114,495	1,263,615	19,140	29,380,910	50·1%	43·4%	44·1%	45·8%	50·4%
	Unknown	790	5	10	-	775	0·0%	0·0%	0·0%	0·0%	0·0%
Ethnicity	Asian	3,769,395	14,030	344,780	4,355	3,406,230	6·1%	5·3%	12·0%	10·4%	5·8%
	Black	1,867,605	8,570	122,985	2,095	1,733,955	3·0%	3·2%	4·3%	5·0%	3·0%
	Mixed	937,125	3,025	22,265	465	911,365	1·5%	1·1%	0·8%	1·1%	1·6%
	Other	1,671,615	4,880	74,385	1,265	1,591,085	2·7%	1·8%	2·6%	3·0%	2·7%
	White	40,132,970	222,795	2,042,950	28,370	37,838,855	65·3%	84·4%	71·3%	68·0%	65·0%
	Unknown	13,035,760	10,530	257,300	5,200	12,762,725	21·2%	4·0%	9·0%	12·5%	21·9%
Deprivation quintile	IMD 1 (most deprived)	12,757,060	55,930	696,675	10,360	11,994,095	20·8%	21·2%	24·3%	24·8%	20·6%
	IMD 2	12,817,805	53,965	638,920	9,430	12,115,490	20·9%	20·5%	22·3%	22·6%	20·8%
	IMD 3	12,306,130	53,325	573,660	8,430	11,670,715	20·0%	20·2%	20·0%	20·2%	20·0%

		N					Percentage				
		Overall	Type 1	Type 2	Other Diabetes	No Diabetes	Overall	Type 1	Type 2	Other Diabetes	No Diabetes
	IMD 4	11,876,020	51,425	513,315	7,245	11,304,040	19·3%	19·5%	17·9%	17·3%	19·4%
	IMD 5 (least deprived)	11,606,690	48,985	440,200	6,250	11,111,255	18·9%	18·6%	15·4%	15·0%	19·1%
	Unknown	50,765	200	1,905	30	48,625	0·1%	0·1%	0·1%	0·1%	0·1%
Region	East	7,071,470	32,500	311,680	5,275	6,722,010	11·5%	12·3%	10·9%	12·6%	11·5%
	London	10,499,665	33,080	461,510	7,130	9,997,945	17·1%	12·5%	16·1%	17·1%	17·2%
	Midlands	11,396,320	53,135	583,655	8,495	10,751,035	18·6%	20·1%	20·4%	20·3%	18·5%
	NE & Yorks	9,164,525	43,765	461,285	6,160	8,653,315	14·9%	16·6%	16·1%	14·8%	14·9%
	North West	7,670,550	32,100	371,930	4,335	7,262,185	12·5%	12·2%	13·0%	10·4%	12·5%
	South East	9,591,390	41,500	401,230	5,600	9,143,060	15·6%	15·7%	14·0%	13·4%	15·7%
	South West	5,969,785	27,550	271,470	4,725	5,666,040	9·7%	10·4%	9·5%	11·3%	9·7%
	Unknown	50,765	200	1,905	30	48,625	0·1%	0·1%	0·1%	0·1%	0·1%
Coronary Heart Disease	No admission	59,259,570	238,460	2,314,195	36,680	56,670,235	96·5%	90·4%	80·8%	87·9%	97·3%
	Admission	2,154,900	25,375	550,475	5,065	1,573,985	3·5%	9·6%	19·2%	12·1%	2·7%
Cerebrovascular Disease	No admission	60,498,915	254,155	2,674,260	39,735	57,530,765	98·5%	96·3%	93·4%	95·2%	98·8%
	Admission	915,555	9,680	190,410	2,010	713,455	1·5%	3·7%	6·6%	4·8%	1·2%
Heart failure	No admission	60,783,235	255,350	2,686,460	39,880	57,801,545	99·0%	96·8%	93·8%	95·5%	99·2%
	Admission	631,235	8,485	178,210	1,865	442,675	1·0%	3·2%	6·2%	4·5%	0·8%

Table 2: Deaths in-hospital with COVID-19 in England between 1st March 2020 and 11th May 2020 by diabetes type

		Number of COVID-19 deaths					Percentage					Rate per 100,000 persons over 72 days				
		Overall	Type 1	Type 2	Other diabetes	No Diabetes	Overall	Type 1	Type 2	Other diabetes	No Diabetes	Overall	Type 1	Type 2	Other diabetes	No Diabetes
	Total	23,698	364	7,434	69	15,831	100·0%	100·0%	100·0%	100·0%	100·0%	39 (38-39)	138 (124-153)	260 (254-265)	165 (129-209)	27 (27-28)
Age	0 to 39 years	160	*	18	*	*	0·7%	*	0·2%	*	*	1 (0-1)	*	27 (16-42)	*	*
	40 to 49 years	384	*	89	*	275	1·6%	*	1·2%	*	1·7%	5 (4-5)	*	42 (34-51)	*	4 (3-4)
	50 to 59 years	1,313	49	399	*	*	5·5%	13·5%	5·4%	*	*	16 (15-17)	100 (74-132)	77 (69-85)	*	*
	60 to 69 years	2,865	73	1,042	7	1,743	12·1%	20·1%	14·0%	10·1%	11·0%	45 (43-47)	202 (158-254)	144 (135-153)	82 (33-170)	31 (30-33)
	70 to 79 years	5,904	97	2,096	22	3,689	24·9%	26·6%	28·2%	31·9%	23·3%	117 (114-120)	401 (325-489)	273 (262-285)	305 (191-462)	87 (84-89)
	80+	13,072	125	3,790	32	9,125	55·2%	34·3%	51·0%	46·4%	57·6%	415 (408-422)	1048 (872-1249)	661 (640-682)	632 (432-892)	356 (349-364)
Sex	Male	14,579	232	4,801	46	9,500	61·5%	63·7%	64·6%	66·7%	60·0%	48 (47-48)	155 (136-177)	300 (291-308)	203 (149-271)	33 (32-34)
	Female	9,119	132	2,633	23	6,331	38·5%	36·3%	35·4%	33·3%	40·0%	30 (29-30)	115 (96-137)	208 (200-216)	120 (76-180)	22 (21-22)
	Unknown	0	0	0	0	0	0·0%	0·0%	0·0%	0·0%	0·0%	0 (0-466)	0 (0-61481)	0 (0-46111)	n/a	0 (0-475)
Ethnicity	Asian	1,769	44	955	*	*	7·5%	12·1%	12·8%	*	*	47 (45-49)	314 (228-421)	277 (260-295)	*	*
	Black	1,354	37	695	5	617	5·7%	10·2%	9·3%	7·2%	3·9%	72 (69-76)	432 (304-595)	565 (524-609)	239 (77-557)	36 (33-39)
	Mixed	171	*	75	*	91	0·7%	*	1·0%	*	0·6%	18 (16-21)	*	337 (265-422)	*	10 (8-12)
	Other	509	11	202	0	296	2·1%	3·0%	2·7%	0·0%	1·9%	30 (28-33)	225 (113-403)	272 (235-312)	0 (0-292)	19 (17-21)
	White	18,968	266	5,328	53	13,321	80·0%	73·1%	71·7%	76·8%	84·1%	47 (47-48)	119 (105-135)	261 (254-268)	187 (140-244)	35 (35-36)
	Unknown	927	*	179	*	*	3·9%	*	2·4%	*	*	7 (7-8)	*	70 (60-81)	*	*

		Number of COVID-19 deaths					Percentage					Rate per 100,000 persons over 72 days				
		Overall	Type 1	Type 2	Other diabetes	No Diabetes	Overall	Type 1	Type 2	Other diabetes	No Diabetes	Overall	Type 1	Type 2	Other diabetes	No Diabetes
Deprivation quintile	IMD 1 (most deprived)	5,632	107	2,065	14	3,446	23·8%	29·4%	27·8%	20·3%	21·8%	44 (43-45)	191 (157-231)	296 (284-309)	135 (74-227)	29 (28-30)
	IMD 2	5,342	80	1,854	17	3,391	22·5%	22·0%	24·9%	24·6%	21·4%	42 (41-43)	148 (118-185)	290 (277-304)	180 (105-289)	28 (27-29)
	IMD 3	4,624	88	1,404	12	3,120	19·5%	24·2%	18·9%	17·4%	19·7%	38 (36-39)	165 (132-203)	245 (232-258)	142 (74-249)	27 (26-28)
	IMD 4	4,308	51	1,153	12	3,092	18·2%	14·0%	15·5%	17·4%	19·5%	36 (35-37)	99 (74-130)	225 (212-238)	166 (86-289)	27 (26-28)
	IMD 5 (least deprived)	3,762	38	948	14	2,762	15·9%	10·4%	12·8%	20·3%	17·4%	32 (31-33)	78 (55-106)	215 (202-230)	224 (122-376)	25 (24-26)
	Unknown	30	0	10	0	20	0·1%	0·0%	0·1%	0·0%	0·1%	59 (40-84)	0 (0-1826)	525 (252-965)	0 (0-11528)	41 (25-64)
Region	East of England	2,777	50	750	16	1,961	11·7%	13·7%	10·1%	23·2%	12·4%	39 (38-41)	154 (114-203)	241 (224-258)	303 (173-493)	29 (28-30)
	London	5,336	81	1,920	14	3,321	22·5%	22·3%	25·8%	20·3%	21·0%	51 (49-52)	245 (194-304)	416 (398-435)	196 (107-329)	33 (32-34)
	Midlands	4,671	96	1,500	9	3,066	19·7%	26·4%	20·2%	13·0%	19·4%	41 (40-42)	181 (146-221)	257 (244-270)	106 (48-201)	29 (28-30)
	North East and Yorkshire	3,319	41	990	10	2,278	14·0%	11·3%	13·3%	14·5%	14·4%	36 (35-37)	94 (67-127)	215 (201-228)	162 (78-299)	26 (25-27)
	North West	3,586	43	1,058	6	2,479	15·1%	11·8%	14·2%	8·7%	15·7%	47 (45-48)	134 (97-180)	284 (268-302)	138 (51-301)	34 (33-36)
	South East	2,903	33	874	8	1,988	12·2%	9·1%	11·8%	11·6%	12·6%	30 (29-31)	80 (55-112)	218 (204-233)	143 (62-282)	22 (21-23)
	South West	1,076	20	332	6	718	4·5%	5·5%	4·5%	8·7%	4·5%	18 (17-19)	73 (44-112)	122 (109-136)	127 (47-276)	13 (12-14)
	Unknown	30	0	10	0	20	0·1%	0·0%	0·1%	0·0%	0·1%	59 (40-84)	0 (0-1826)	525 (252-965)	0 (0-11528)	41 (25-64)
Coronary Heart Disease	No admission	16,375	190	4,545	46	11,594	69·1%	52·2%	61·1%	66·7%	73·2%	28 (27-28)	80 (69-92)	196 (191-202)	125 (92-167)	20 (20-21)
	Admission	7,323	174	2,889	23	4,237	30·9%	47·8%	38·9%	33·3%	26·8%	340 (332-348)	686 (588-796)	525 (506-544)	454 (288-681)	269 (261-277)
Cerebrovascular Disease	No admission	18,995	256	5,798	53	12,888	80·2%	70·3%	78·0%	76·8%	81·4%	31 (31-32)	101 (89-114)	217 (211-222)	133 (100-174)	22 (22-23)
	Admission	4,703	108	1,636	16	2,943	19·8%	29·7%	22·0%	23·2%	18·6%	514	1116	859 (818-902)	796	413 (398-428)

		Number of COVID-19 deaths					Percentage					Rate per 100,000 persons over 72 days				
		Overall	Type 1	Type 2	Other diabetes	No Diabetes	Overall	Type 1	Type 2	Other diabetes	No Diabetes	Overall	Type 1	Type 2	Other diabetes	No Diabetes
												(499-529)	(915-1347)		(455-1292)	
Heart failure	No admission	19,484	257	5,734	55	13,438	82·2%	70·6%	77·1%	79·7%	84·9%	32 (32-33)	101 (89-114)	213 (208-219)	138 (104-180)	23 (23-24)
	Admission	4,214	107	1,700	14	2,393	17·8%	29·4%	22·9%	20·3%	15·1%	668 (648-688)	1261 (1034-1524)	954 (909-1000)	750 (410-1259)	541 (519-563)

*Suppressed due to small numbers

Figure 1: Unadjusted in-hospital COVID-19 mortality rate per 100,000 persons between 1st March 2020 to 11th May 2020 by type of diabetes

*Age groups for 0-39 and 40-49 for Type 1 diabetes and 0-39 and 50-59 for no diabetes have been suppressed due to small numbers of events to comply with data protection regulations.

Figure 2: Adjusted odds ratios for in-hospital deaths with COVID-19 in England (number of deaths=23,698) between 1st March 2020 and 11th May 2020 by different risk factors

*Data shown are the results of a multivariable logistic regression which included the explanatory variables shown, plus region, in a population of 61,414,470 people.