

Supplementary Information

Effects of antidiabetic drugs on mortality risks in individuals with type 2 diabetes: A prospective cohort study of UK Biobank participants

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Supplementary Methods

Datasets

Clinical and prescription NHS data (primary care general practice (GP) datasets, data providers TPP (<https://www.tpp-uk.com/>) and EMIS (<https://www.emishealth.com/>) were retrieved on Oct. 1st, 2021. Codes for diabetes diagnosis and anti-diabetic medication prescriptions were obtained from using SNOMED (EMIS dataset), CTV3 and TPP local codes (TPP dataset). Only participants with clinical data and prescription data were included in the study, under the assumption that the data for the other participants was not available, rather than that these individuals never sought NHS services.

The fields from UK Biobank data download (retrieved on Oct 1st, 2021) used for this analysis were: '53-0.0' Date of Recruitment, '21022-0.0' Age at Recruitment, '34-0.0' Year of birth, '52-0.0' Month of Birth, '40007-0.0' Age at Death, '40000-0.0' Date of Death, '40001-0.0' Cause of Death, '31-0.0' Sex, '22009-0.1' to '22009-0.10' Genetic principal components (PC) 1-10, '22040-0.0' Summed MET minutes per week for all activity, '21001-0.0' BMI, '189-0.0' Townsend deprivation index, '20161-0.0' PackYears, '20116-0.0' Smoking status, '1160-0.0' Sleep duration, '2453-0.0' Cancer diagnosed by doctor, '2463-0.0' Fractured/broken bones in last 5 years, '2473-0.0' Other serious medical condition/disability diagnosed by doctor, '6150-0.0' Vascular/heart problems diagnosed by doctor.

The British National Formulary (BNF) and ATC codes were used to annotate T2D treatments. In particular, we BNF codes 6.1.1 – ‘Insulin’ and 6.1.2 ‘Antidiabetic drugs’ within the broad category “Drugs used in Diabetes” were used to select for prescriptions of antidiabetic medications. ATC10 4th level super-codes A10A - ‘INSULINS AND ANALOGUES’ and A10B - BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS in the broad category “Drugs used in Diabetes”) were used to subdivide the non-insulin antidiabetic drugs (A10B) into functional classes, which are the ones used for the classification in this manuscript, if they reached a critical number of prescribed patients. In particular:

- o A10BA Biguanides;
- o A10BB Sulfonylureas;
- o A10BF Alpha glucosidase inhibitors or acarbose – present in the dataset, but in low numbers and therefore excluded from the study;
- o A10BG Thiazolidinediones;
- o A10BH Dipeptidyl peptidase 4 (DPP-4) inhibitors;
- o A10BJ Glucagon-like peptide-1 (GLP-1) analogues;
- o A10BK Sodium-glucose co-transporter 2 (SGLT2) inhibitors;
- o A10BX Other blood glucose lowering drugs, excl. insulins – in this category there are meglitinides present in the dataset, but in low numbers and therefore excluded from the study.

The categories: A10BC Sulfonamides (heterocyclic) were not found among NHS prescriptions, and A10BD Combinations of oral blood glucose lowering drugs were subdivided into individual components.

Criteria for Inclusion and Exclusion of Participants

Individuals that had not taken anti-diabetic medications for at least three consecutive months, and that were not taking these medications within six months of the last recorded event (either death or last censoring), were not considered users of that medication. Individuals with missing values for the covariates analysed were eliminated from the analysis.

Observation Time, Length of Exposure, and End Points

The data on deaths was available for all individuals as linked to the national death registry, updated every six or three months (<https://biobank.ndph.ox.ac.uk/showcase/ukb/docs/DeathLinkage.pdf>), and the last recorded date of death (anteceding the date of data retrieval of more than six months) was chosen as the day of censoring to ensure completeness of the death registry data.

For the T2D with drug vs T2D without drug matching strategy (see below), the age at first drug was included in the covariates to match, to avoid immortal time bias¹. By matching each patient by age at recruitment and age at first drug use, we ensured that the length of exposure to the target drug treatment was the same as the control drug.

Survival Analyses: General Remarks

The day of birth is not available for privacy and data protection regulations, therefore the precise age of the participant at the age of recruitment was estimated, taking into account the age between date of birth (DOB) and date of recruitment, assuming that the DOB is on the 15th of the month². This was not the case for 4520 participants, whose birthday was between the beginning

of the month and the recruitment date before the 15th of the month. For these participants the estimated age was rounded up to the declared age of recruitment. In the dataset used for these analyses (retrieved on Oct 1st, 2021) is the date of the last reported death, therefore that was considered the time of censoring and used to calculate the inferred age of the live participants from the estimated age at recruitment². The inferred age at death was calculated from the estimated age at recruitment and the date of death. The censoring status = 1 indicates that an event occurred (i.e., death), status = 0 indicates that the observation was right censored (i.e., participant was alive at the time of censoring; March 20th, 2021).

Survival Analyses of Observational Cohort

In Kaplan-Meier survival estimates, the entire cohort was subdivided into non-T2D-diagnosed and T2D-diagnosed, or into non-T2D-diagnosed, T2D-diagnosed taking the drug of interest or T2D-diagnosed not taking the drug of interest (**Fig. 1b**). The survival probability of each group is expressed as proportion of individuals that are alive at that age versus total number of individuals that have died at that age³. P values shown were calculated with log-rank test.

Multivariate analysis of survival was analysed with Cox proportional-hazard regression model (**Fig. 1c**). Proportional hazard assumption was checked and it was met for all covariates. The difference between the age of recruitment and the age of last censoring was the survival time of the model.⁴ Age at recruitment, sex, genetic principal components 1-20 (as proxy for population ethnic diversity), lifestyle factors (BMI, smoking, alcohol intake, physical exercise, Townsend deprivation index, sleep duration), comorbidities (Fractured/Broken Bones, Cancer, Cardiovascular disease, Blood Clots, DVT, Bronchitis, Emphysema, Other serious medical condition), and Use of Anti-Diabetic Drugs, were covariates of the model.

Nearest Neighbour Covariate Matching (NNCM) Strategy

(i) Introduction

We opted to individually match the users of each drug to control individuals with similar characteristics to evaluate the effect of the target drug with minimal confounding on outcomes. Individual matching, differently from frequency-based matching which selects controls based on similar distribution of variables, ensures that treated individuals and their respective controls are selected based on the exact matching of selected features, and resembles as closely as possible a randomised clinical trial⁵. Among the available algorithms developed for individual matching^{6,7}, we opted to use a previously established nearest neighbours algorithm-based strategy⁶⁻⁸ based on data-driven covariate-specific distance metrics (**Fig. S5a-b**). This method has greater power in dealing with non-homogenous cohorts, such as the ones we have (**Fig. S6**), and provided the most accurate matching for covariates heavily responsible for outcomes.

With a data-driven approach based on a Cox proportional hazard model, we selected for each cohort covariates that mostly affect longevity, called priority-matched covariates (**Fig. S5a-d**), and thanks to *ad hoc* distance metrics, they were the ones contributing mostly for the matching (**Fig. S5e-f**). This ensured that priority-matched covariates were matched most accurately to minimise the differences among individuals mostly contributing to age at death. In the first analysis, we compared T2D individuals who were either taking the drug of interest (and potentially other drugs) with matched controls who were T2D-diagnosed and using another anti-diabetic drug (or multiple other drugs), while in the second analysis, we compared T2D individuals who were taking the drug with control individuals that were not T2D-diagnosed (non-T2Ds).

(ii) Matching Algorithm

For each individual diagnosed with T2D treated with the drug of interest (T2D with drug) the unsupervised nearest neighbours algorithm (adapted from the Python library scikit-learn 1.0.2 NearestNeighbors) would assign one individual from T2D subjects not taking that drug (T2D without drug) or from the non-T2D-diagnosed subjects cohort (non T2D without drug) with the smallest cumulative covariate distance (computed *ad hoc* as explained below). Males and females were matched separately, to ensure precise matching of the sex. If more than one patient matched to the same control individual, the matching was reassigned to ensure univocal 1:1 matching. The cumulative covariate distance was calculated by assigning a custom distance metric according to their data type and priority level (**Fig. S5**).

(iii) Data-driven Selection of Priority-matched Covariates

A Cox proportional hazard multivariate model was used to determine within each cohort comparison the covariates contributing mostly to the observed mortality (having $\log(\text{HR}) > 0.05$ or $\log(\text{HR}) < -0.05$), hereafter referred to as priority-matched covariates (**Fig. S5a-b and 5c-d**).

The priority-matched covariates were assigned an exponentially growing distance weight if differing between individuals more than one standard deviation or more than one mismatched comorbidity. The other covariates, including use of additional anti-diabetic drugs and age at first use of the anti-diabetic drug of interest to estimate exposure, were assigned a Euclidean distance, if continuous, or a Hamming distance, if binary.

(iv) Ad hoc Distance Metrics for Priority-matched Covariates and Other Distance Metrics

To match treated and control individuals, we calculated how different each pair of treated and control individuals was, and for each treated individual we took the most similar control individual, without using the same control individual twice. To calculate how different each treated-control pair was, we created an algorithm that assessed how distant the covariates of each individuals were. Novel sets of metrics, named here *ad hoc* distance metrics, were created to establish the cumulative distance between covariates of treated and control individuals. These *ad hoc* distances were devised to increase exponentially if two covariates were differing more than one standard deviation (if quantitative such as age) or of more than one yes/no answer in morbidity status (the binary covariates). In this way, the likelihood of matching very distant individuals was very low. More in detail, distance between priority-matched rescaled (mean = 0, standard deviation = 1) quantitative covariates (Age at recruitment) was determined as a distance that would exponentially increase for differences in the covariates greater than 0.1 standard deviations

with the formula $e^{\frac{(x_{T2D+drug} - x_{control})^2}{0.1^2}} - 1$ (where $x_{T2D+drug}$ and $x_{control}$ are respectively the covariate values for each treated-control pair) (**Fig. S5e**). Distance between priority-matched binary covariates (cancer, cardiovascular, etc.) was coded as a distance that would exponentially increase for cumulative Hamming distances greater than 1, and calculated with the formula $e^{\sum_{i=0}^n |x_{i(T2D+drug)} - x_{i(control)}|} - 1$ (where $x_{i(T2D+drug)}$ and $x_{i(control)}$ are the treated-control pair values of the i th binary priority-matched covariate) (**Fig. S5f**). This strategy ensures that each matched individual is allowed to differ by at most one mismatched priority-matched diagnoses, otherwise the distance becomes exponentially big. Distances between other quantitative covariates used for matching were calculated as Euclidean distances, while for binary covariates as Hamming distances (**Fig. S5**).

Individuals with T2D which are not prescribed the drug of interest (the control group to individuals with T2D using the drug of interest) take any other antidiabetic drug which is not the drug of

interest. Therefore, for the T2D with drug vs T2D without drug matching strategy, the age at first drug was included in the covariates to match, to avoid immortal time bias.¹ By matching each patient by age at recruitment and age at first drug use (either drug of interest or any other antidiabetic drug in the control group), we ensured that the length of exposure to the target drug treatment was the same as the control drug.

(v) Cohorts Homogeneity after NNCM

The matching strategy used ensured that the average standardised mean difference of all covariates within the treated and matched cohort was below 5%. All treated individuals were matched to untreated controls, excluding individuals who did not have data for the features used for matching.

Survival Analyses of NNCM Cohorts

For each drug, survival analysis was performed between T2D with drug vs T2D without drug NNCM Cohorts (**Fig. 2a-b**) or between T2D with drug vs non-T2D without drug NNCM Cohorts (**Fig. 3a-b**), or between T2D with DPP4I/SGLT2I with metformin vs T2D with metformin only vs non-T2D without drug NNCM Cohorts (**Fig. 4a-b**), survival analyses were performed as in the observational cohort, with the difference that the analysis of NNCM cohorts T2D with drug and T2D without drug (**Fig. 3a-b**), the use of other diabetic drugs, as well as the age at first use (to take into account exposure time) were added as exogenous variables, while in T2D with DPP4I/SGLT2I with metformin vs T2D with metformin only vs non-T2D without drug NNCM Cohorts (**Fig. 4a-b**) age at first use was added as exogenous variable.

Statistical Analyses

All the analyses, figures and tables were created with Python3.7 using the following libraries: pandas v.1.1.4, matplotlib v.3.3.4, seaborn v. 0.11.1, scipy v. 1.4.1, sklearn v.0.0, statsmodels v. 0.11.0, numpy v.1.19.5, and lifelines v.0.25.11 (<https://doi.org/10.21105/joss.01317>)

Survival curves were generated with the Python 3.7 and Lifelines (lifelines v.0.25.11) package KaplanMeierFitter function, and P-values calculated with log-rank test (lifelines v.0.25.11). Multivariate analysis of survival was analysed with Cox proportional-hazard regression model using lifelines v.0.25.11 CoxPHFitter. Proportional hazard assumption was checked with lifelines v.0.25.11 function *check_assumption* and it was met for all covariates. Aberrations from the proportion of expected versus observed deaths of a certain cause within the case-control cohorts were calculated with a chi-squared test (scipy v. 1.4.1).

Supplemental References

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Supplementary Table 1

Absolute number and percentage of deaths aggregated as ICD10 codes level 3 in the entire cohort, divided between T2Ds vs not T2Ds. P values obtained by chi-squared contingency test.

Causes of death	Number of Deaths in not T2Ds	Percentage of Deaths in not T2Ds	Number of Deaths in T2Ds	Percentage of Deaths in T2Ds	p-value
[A02] Other salmonella infections	0	0	1	0.00229305	0.20138
[A04] Other bacterial intestinal infections	8	0.00218115	1	0.00229305	1
[A08] Viral and other specified intestinal infections	1	0.00027264	0	0	1
[A09] Other gastroenteritis and colitis of infectious and unspecified origin	8	0.00218115	1	0.00229305	1
[A16] Respiratory tuberculosis, not confirmed bacteriologically or histologically	2	0.00054529	0	0	1
[A19] Miliary tuberculosis	2	0.00054529	0	0	1
[A28] Other zoonotic bacterial diseases, not elsewhere classified	1	0.00027264	1	0.00229305	0.50951 2
[A31] Infection due to other mycobacteria	1	0.00027264	0	0	1
[A32] Listeriosis	1	0.00027264	1	0.00229305	0.50951 2
[A39] Meningococcal infection	1	0.00027264	0	0	1
[A40] Streptococcal sepsis	6	0.00163586	0	0	0.85537 1
[A41] Other sepsis	24	0.00654345	9	0.02063747	0.00479 3
[A49] Bacterial infection of unspecified site	7	0.00190851	1	0.00229305	1
[A81] Atypical virus infections of central nervous system	17	0.00463494	0	0	0.30383 5
[A85] Other viral encephalitis, not elsewhere classified	1	0.00027264	0	0	1
[B00] Herpesviral [herpes simplex] infections	1	0.00027264	0	0	1
[B02] Zoster [herpes zoster]	1	0.00027264	0	0	1
[B18] Chronic viral hepatitis	4	0.00109057	0	0	1
[B20] Human immunodeficiency virus [HIV] disease resulting in infectious and parasitic diseases	3	0.00081793	0	0	1
[B24] Unspecified human immunodeficiency virus [HIV] disease	1	0.00027264	1	0.00229305	0.50951 2
[B25] Cytomegaloviral disease	1	0.00027264	0	0	1
[B27] Infectious mononucleosis	1	0.00027264	0	0	1

[B34] Viral infection of unspecified site	2	0.00054529	0	0	1
[B59] Pneumocystosis (J17.3*)	1	0.00027264	1	0.00229305	0.50951 2
[B91] Sequelae of poliomyelitis	1	0.00027264	0	0	1
[B99] Other infectious disease	1	0.00027264	0	0	1
[C01] Malignant neoplasm of base of tongue	2	0.00054529	0	0	1
[C02] Malignant neoplasm of other and unspecified parts of tongue	16	0.0043623	2	0.0045861	1
[C03] Malignant neoplasm of gum	1	0.00027264	0	0	1
[C04] Malignant neoplasm of floor of mouth	1	0.00027264	0	0	1
[C05] Malignant neoplasm of palate	3	0.00081793	0	0	1
[C06] Malignant neoplasm of other and unspecified parts of mouth	9	0.00245379	2	0.0045861	0.74599 2
[C07] Malignant neoplasm of parotid gland	3	0.00081793	0	0	1
[C08] Malignant neoplasm of other and unspecified major salivary glands	1	0.00027264	0	0	1
[C09] Malignant neoplasm of tonsil	17	0.00463494	1	0.00229305	0.75222 6
[C10] Malignant neoplasm of oropharynx	9	0.00245379	2	0.0045861	0.74599 2
[C11] Malignant neoplasm of nasopharynx	4	0.00109057	1	0.00229305	1
[C12] Malignant neoplasm of piriform sinus	5	0.00136322	1	0.00229305	1
[C13] Malignant neoplasm of hypopharynx	6	0.00163586	0	0	0.85537 1
[C14] Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx	7	0.00190851	2	0.0045861	0.55653 4
[C15] Malignant neoplasm of oesophagus	281	0.07661289	38	0.08713598	0.51274 9
[C16] Malignant neoplasm of stomach	149	0.04062392	28	0.06420546	0.03398 7
[C17] Malignant neoplasm of small intestine	16	0.0043623	1	0.00229305	0.80938
[C18] Malignant neoplasm of colon	332	0.09051772	49	0.11235955	0.18262 7
[C19] Malignant neoplasm of rectosigmoid junction	128	0.0348984	19	0.04356799	0.44090 4
[C20] Malignant neoplasm of rectum	125	0.03408047	17	0.03898188	0.70089 2
[C21] Malignant neoplasm of anus and anal canal	22	0.00599816	1	0.00229305	0.52295 3
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	170	0.04634944	62	0.14216923	4.10E-15
[C23] Malignant neoplasm of gallbladder	36	0.00981517	5	0.01146526	0.94217 3
[C24] Malignant neoplasm of other and unspecified parts of biliary tract	24	0.00654345	4	0.00917221	0.74768 2
[C25] Malignant neoplasm of pancreas	376	0.10251405	124	0.28433845	1.65E-24

[C26] Malignant neoplasm of other and ill-defined digestive organs	99	0.02699173	18	0.04127494	0.12844 4
[C30] Malignant neoplasm of nasal cavity and middle ear	1	0.00027264	0	0	1
[C31] Malignant neoplasm of accessory sinuses	2	0.00054529	0	0	1
[C32] Malignant neoplasm of larynx	20	0.00545287	0	0	0.23827 3
[C33] Malignant neoplasm of trachea	3	0.00081793	0	0	1
[C34] Malignant neoplasm of bronchus and lung	969	0.26419179	151	0.34625086	0.00223 7
[C37] Malignant neoplasm of thymus	2	0.00054529	1	0.00229305	0.73425
[C38] Malignant neoplasm of heart, mediastinum and pleura	2	0.00054529	1	0.00229305	0.73425
[C40] Malignant neoplasm of bone and articular cartilage of limbs	1	0.00027264	0	0	1
[C41] Malignant neoplasm of bone and articular cartilage of other and unspecified sites	9	0.00245379	0	0	0.62155 6
[C43] Malignant melanoma of skin	127	0.03462576	16	0.03668883	0.93422 3
[C44] Other malignant neoplasms of skin	20	0.00545287	3	0.00687916	0.96982 6
[C45] Mesothelioma	108	0.02944552	15	0.03439578	0.67574 2
[C47] Malignant neoplasm of peripheral nerves and autonomic nervous system	1	0.00027264	0	0	1
[C48] Malignant neoplasm of retroperitoneum and peritoneum	43	0.01172368	2	0.0045861	0.26964 8
[C49] Malignant neoplasm of other connective and soft tissue	45	0.01226897	9	0.02063747	0.22262 8
[C50] Malignant neoplasm of breast	473	0.12896049	43	0.09860124	0.10525 7
[C51] Malignant neoplasm of vulva	5	0.00136322	3	0.00687916	0.05838
[C52] Malignant neoplasm of vagina	5	0.00136322	0	0	0.96374 2
[C53] Malignant neoplasm of cervix uteri	10	0.00272644	2	0.0045861	0.83320 2
[C54] Malignant neoplasm of corpus uteri	68	0.01853977	14	0.03210273	0.08629 5
[C55] Malignant neoplasm of uterus, part unspecified	21	0.00572552	2	0.0045861	1
[C56] Malignant neoplasm of ovary	219	0.05970898	22	0.05044715	0.51554 8
[C57] Malignant neoplasm of other and unspecified female genital organs	14	0.00381701	3	0.00687916	0.58520 8
[C60] Malignant neoplasm of penis	4	0.00109057	1	0.00229305	1
[C61] Malignant neoplasm of prostate	379	0.10333198	77	0.17656501	2.01E-05
[C62] Malignant neoplasm of testis	2	0.00054529	0	0	1

[C64] Malignant neoplasm of kidney, except renal pelvis	164	0.04471357	26	0.05961935	0.21121 6
[C65] Malignant neoplasm of renal pelvis	2	0.00054529	0	0	1
[C66] Malignant neoplasm of ureter	11	0.00299908	1	0.00229305	1
[C67] Malignant neoplasm of bladder	128	0.0348984	22	0.05044715	0.14063 6
[C68] Malignant neoplasm of other and unspecified urinary organs	10	0.00272644	3	0.00687916	0.31408 7
[C69] Malignant neoplasm of eye and adnexa	7	0.00190851	0	0	0.76487 9
[C70] Malignant neoplasm of meninges	1	0.00027264	0	0	1
[C71] Malignant neoplasm of brain	296	0.08070255	26	0.05961935	0.16269
[C73] Malignant neoplasm of thyroid gland	19	0.00518023	1	0.00229305	0.65003 3
[C74] Malignant neoplasm of adrenal gland	3	0.00081793	1	0.00229305	0.90322 6
[C75] Malignant neoplasm of other endocrine glands and related structures	3	0.00081793	0	0	1
[C76] Malignant neoplasm of other and ill-defined sites	9	0.00245379	0	0	0.62155 6
[C78] Secondary malignant neoplasm of respiratory and digestive organs	5	0.00136322	1	0.00229305	1
[C80] Malignant neoplasm without specification of site	277	0.07552232	47	0.10777345	0.02949 8
[C81] Hodgkin lymphoma	9	0.00245379	6	0.01375831	0.00106 6
[C82] Follicular lymphoma	14	0.00381701	1	0.00229305	0.93724 2
[C83] Non-follicular lymphoma	65	0.01772184	9	0.02063747	0.81027 3
[C84] Mature T/NK-cell lymphomas	25	0.00681609	2	0.0045861	0.81767 4
[C85] Other and unspecified types of non-Hodgkin lymphoma	114	0.03108139	18	0.04127494	0.32656 9
[C86] Other specified types of T/NK-cell lymphoma	1	0.00027264	0	0	1
[C88] Malignant immunoproliferative diseases	3	0.00081793	0	0	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	148	0.04035127	21	0.04815409	0.52579 7
[C91] Lymphoid leukaemia	27	0.00736138	11	0.02522357	0.00067
[C92] Myeloid leukaemia	124	0.03380782	16	0.03668883	0.86433 8
[C93] Monocytic leukaemia	5	0.00136322	1	0.00229305	1
[C95] Leukaemia of unspecified cell type	8	0.00218115	2	0.0045861	0.65359
[C96] Other and unspecified malignant neoplasms of lymphoid, haematopoietic and related tissue	1	0.00027264	0	0	1

[C97] Malignant neoplasms of independent (primary) multiple sites	8	0.00218115	0	0	0.68792 2
[D15] Benign neoplasm of other and unspecified intrathoracic organs	1	0.00027264	0	0	1
[D18] Haemangioma and lymphangioma, any site	1	0.00027264	0	0	1
[D32] Benign neoplasm of meninges	10	0.00272644	1	0.00229305	1
[D35] Benign neoplasm of other and unspecified endocrine glands	1	0.00027264	0	0	1
[D37] Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs	7	0.00190851	1	0.00229305	1
[D38] Neoplasm of uncertain or unknown behaviour of middle ear and respiratory and intrathoracic organs	2	0.00054529	0	0	1
[D39] Neoplasm of uncertain or unknown behaviour of female genital organs	1	0.00027264	0	0	1
[D41] Neoplasm of uncertain or unknown behaviour of urinary organs	1	0.00027264	2	0.0045861	0.02690 3
[D43] Neoplasm of uncertain or unknown behaviour of brain and central nervous system	14	0.00381701	3	0.00687916	0.58520 8
[D44] Neoplasm of uncertain or unknown behaviour of endocrine glands	2	0.00054529	1	0.00229305	0.73425
[D46] Myelodysplastic syndromes	19	0.00518023	5	0.01146526	0.19656 4
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	23	0.00627081	3	0.00687916	1
[D48] Neoplasm of uncertain or unknown behaviour of other and unspecified sites	4	0.00109057	1	0.00229305	1
[D57] Sickle-cell disorders	1	0.00027264	0	0	1
[D58] Other hereditary haemolytic anaemias	2	0.00054529	0	0	1
[D59] Acquired haemolytic anaemia	1	0.00027264	1	0.00229305	0.50951 2
[D61] Other aplastic anaemias	5	0.00136322	1	0.00229305	1
[D64] Other anaemias	0	0	2	0.0045861	0.00313 6
[D65] Disseminated intravascular coagulation [defibrination syndrome]	1	0.00027264	0	0	1
[D69] Purpura and other haemorrhagic conditions	0	0	1	0.00229305	0.20138
[D70] Agranulocytosis	5	0.00136322	0	0	0.96374 2
[D75] Other diseases of blood and blood-forming organs	1	0.00027264	1	0.00229305	0.50951 2
[D76] Other specified diseases with participation of lymphoreticular and reticulohistiocytic tissue	5	0.00136322	0	0	0.96374 2

[D80] Immunodeficiency with predominantly antibody defects	0	0	1	0.00229305	0.20138
[D84] Other immunodeficiencies	0	0	1	0.00229305	0.20138
[D86] Sarcoidosis	2	0.00054529	2	0.0045861	0.08115 2
[D89] Other disorders involving the immune mechanism, not elsewhere classified	1	0.00027264	1	0.00229305	0.50951 2
[E10] Type 1 diabetes mellitus	4	0.00109057	2	0.0045861	0.25326 2
[E11] Type 2 diabetes mellitus	7	0.00190851	39	0.08942903	3.42E-58
[E14] Unspecified diabetes mellitus	19	0.00518023	28	0.06420546	1.69E-26
[E16] Other disorders of pancreatic internal secretion	0	0	2	0.0045861	0.00313 6
[E27] Other disorders of adrenal gland	1	0.00027264	0	0	1
[E34] Other endocrine disorders	1	0.00027264	0	0	1
[E66] Obesity	13	0.00354437	1	0.00229305	1
[E78] Disorders of lipoprotein metabolism and other lipidaemias	0	0	1	0.00229305	0.20138
[E83] Disorders of mineral metabolism	0	0	3	0.00687916	4.38E-05
[E84] Cystic fibrosis	1	0.00027264	0	0	1
[E85] Amyloidosis	27	0.00736138	1	0.00229305	0.36557 2
[E87] Other disorders of fluid, electrolyte and acid-base balance	4	0.00109057	3	0.00687916	0.03125 2
[E88] Other metabolic disorders	4	0.00109057	0	0	1
[F01] Vascular dementia	57	0.01554069	29	0.06649851	1.24E-11
[F03] Unspecified dementia	181	0.04934852	37	0.08484293	0.00337 6
[F05] Delirium, not induced by alcohol and other psychoactive substances	0	0	1	0.00229305	0.20138
[F10] Mental and behavioural disorders due to use of alcohol	14	0.00381701	0	0	0.39167 1
[F31] Bipolar affective disorder	1	0.00027264	0	0	1
[F50] Eating disorders	1	0.00027264	0	0	1
[F81] Specific developmental disorders of scholastic skills	1	0.00027264	0	0	1
[G00] Bacterial meningitis, not elsewhere classified	1	0.00027264	0	0	1
[G04] Encephalitis, myelitis and encephalomyelitis	4	0.00109057	2	0.0045861	0.25326 2
[G06] Intracranial and intraspinal abscess and granuloma	1	0.00027264	1	0.00229305	0.50951 2
[G10] Huntington's disease	2	0.00054529	0	0	1
[G11] Hereditary ataxia	4	0.00109057	0	0	1

[G12] Spinal muscular atrophy and related syndromes	141	0.03844277	11	0.02522357	0.22069 3
[G20] Parkinson's disease	164	0.04471357	18	0.04127494	0.83980 4
[G23] Other degenerative diseases of basal ganglia	51	0.01390483	4	0.00917221	0.55629 9
[G30] Alzheimer's disease	203	0.05534668	39	0.08942903	0.00764 5
[G31] Other degenerative diseases of nervous system, not elsewhere classified	82	0.02235679	3	0.00687916	0.05148 4
[G35] Multiple sclerosis	34	0.00926989	3	0.00687916	0.81781 2
[G40] Epilepsy	8	0.00218115	0	0	0.68792 2
[G41] Status epilepticus	2	0.00054529	1	0.00229305	0.73425
[G45] Transient cerebral ischaemic attacks and related syndromes	1	0.00027264	0	0	1
[G47] Sleep disorders	0	0	2	0.0045861	0.00313 6
[G51] Facial nerve disorders	1	0.00027264	0	0	1
[G60] Hereditary and idiopathic neuropathy	1	0.00027264	0	0	1
[G61] Inflammatory polyneuropathy	2	0.00054529	0	0	1
[G62] Other polyneuropathies	0	0	1	0.00229305	0.20138
[G70] Myasthenia gravis and other myoneural disorders	0	0	1	0.00229305	0.20138
[G71] Primary disorders of muscles	4	0.00109057	3	0.00687916	0.03125 2
[G72] Other myopathies	2	0.00054529	0	0	1
[G80] Cerebral palsy	1	0.00027264	0	0	1
[G82] Paraplegia and tetraplegia	2	0.00054529	0	0	1
[G83] Other paralytic syndromes	1	0.00027264	0	0	1
[G90] Disorders of autonomic nervous system	16	0.0043623	2	0.0045861	1
[G91] Hydrocephalus	1	0.00027264	0	0	1
[G93] Other disorders of brain	3	0.00081793	1	0.00229305	0.90322 6
[G95] Other diseases of spinal cord	5	0.00136322	0	0	0.96374 2
[G96] Other disorders of central nervous system	2	0.00054529	0	0	1
[H70] Mastoiditis and related conditions	1	0.00027264	0	0	1
[I05] Rheumatic mitral valve diseases	11	0.00299908	1	0.00229305	1
[I07] Rheumatic tricuspid valve diseases	2	0.00054529	0	0	1
[I08] Multiple valve diseases	3	0.00081793	0	0	1
[I10] Essential (primary) hypertension	9	0.00245379	0	0	0.62155 6
[I11] Hypertensive heart disease	48	0.0130869	20	0.04586104	1.36E-06

[I12] Hypertensive renal disease	4	0.00109057	0	0	1
[I13] Hypertensive heart and renal disease	3	0.00081793	4	0.00917221	0.00072 4
[I20] Angina pectoris	1	0.00027264	0	0	1
[I21] Acute myocardial infarction	394	0.10742164	151	0.34625086	6.02E-38
[I24] Other acute ischaemic heart diseases	7	0.00190851	1	0.00229305	1
[I25] Chronic ischaemic heart disease	623	0.16985705	263	0.60307269	2.19E-75
[I26] Pulmonary embolism	56	0.01526805	14	0.03210273	0.01872
[I27] Other pulmonary heart diseases	5	0.00136322	6	0.01375831	2.26E-05
[I31] Other diseases of pericardium	6	0.00163586	1	0.00229305	1
[I33] Acute and subacute endocarditis	7	0.00190851	3	0.00687916	0.14023 4
[I34] Nonrheumatic mitral valve disorders	9	0.00245379	2	0.0045861	0.74599 2
[I35] Nonrheumatic aortic valve disorders	49	0.01335954	16	0.03668883	0.00054 3
[I38] Endocarditis, valve unspecified	18	0.00490759	3	0.00687916	0.84924 5
[I40] Acute myocarditis	2	0.00054529	0	0	1
[I42] Cardiomyopathy	43	0.01172368	14	0.03210273	0.00137 8
[I44] Atrioventricular and left bundle-branch block	1	0.00027264	0	0	1
[I45] Other conduction disorders	1	0.00027264	0	0	1
[I46] Cardiac arrest	2	0.00054529	0	0	1
[I47] Paroxysmal tachycardia	1	0.00027264	0	0	1
[I48] Atrial fibrillation and flutter	42	0.01145104	12	0.02751662	0.01094 7
[I49] Other cardiac arrhythmias	4	0.00109057	0	0	1
[I50] Heart failure	34	0.00926989	26	0.05961935	1.13E-15
[I51] Complications and ill-defined descriptions of heart disease	22	0.00599816	5	0.01146526	0.30845 8
[I60] Subarachnoid haemorrhage	86	0.02344736	2	0.0045861	0.01778
[I61] Intracerebral haemorrhage	123	0.03353518	24	0.05503325	0.03493 8
[I62] Other nontraumatic intracranial haemorrhage	45	0.01226897	10	0.02293052	0.10970 8
[I63] Cerebral infarction	46	0.01254161	10	0.02293052	0.12378 5
[I64] Stroke, not specified as haemorrhage or infarction	128	0.0348984	51	0.11694565	2.24E-14
[I67] Other cerebrovascular diseases	33	0.00899724	15	0.03439578	1.07E-05
[I69] Sequelae of cerebrovascular disease	4	0.00109057	2	0.0045861	0.25326 2
[I70] Atherosclerosis	2	0.00054529	1	0.00229305	0.73425
[I71] Aortic aneurysm and dissection	112	0.0305361	13	0.02980968	1

[I72] Other aneurysm and dissection	8	0.00218115	1	0.00229305	1
[I73] Other peripheral vascular diseases	13	0.00354437	4	0.00917221	0.18259 4
[I77] Other disorders of arteries and arterioles	2	0.00054529	0	0	1
[I78] Diseases of capillaries	1	0.00027264	0	0	1
[I80] Phlebitis and thrombophlebitis	62	0.01690391	9	0.02063747	0.71297
[I81] Portal vein thrombosis	2	0.00054529	1	0.00229305	0.73425
[I82] Other venous embolism and thrombosis	3	0.00081793	0	0	1
[I83] Varicose veins of lower extremities	1	0.00027264	1	0.00229305	0.50951 2
[I87] Other disorders of veins	1	0.00027264	0	0	1
[J10] Influenza due to other identified influenza virus	7	0.00190851	1	0.00229305	1
[J11] Influenza, virus not identified	6	0.00163586	4	0.00917221	0.01238 2
[J12] Viral pneumonia, not elsewhere classified	2	0.00054529	1	0.00229305	0.73425
[J13] Pneumonia due to Streptococcus pneumoniae	1	0.00027264	1	0.00229305	0.50951 2
[J15] Bacterial pneumonia, not elsewhere classified	1	0.00027264	1	0.00229305	0.50951 2
[J18] Pneumonia, organism unspecified	145	0.03953334	44	0.10089429	3.24E-08
[J20] Acute bronchitis	1	0.00027264	0	0	1
[J21] Acute bronchiolitis	1	0.00027264	0	0	1
[J22] Unspecified acute lower respiratory infection	15	0.00408966	2	0.0045861	1
[J40] Bronchitis, not specified as acute or chronic	2	0.00054529	0	0	1
[J42] Unspecified chronic bronchitis	2	0.00054529	0	0	1
[J43] Emphysema	16	0.0043623	4	0.00917221	0.31853 2
[J44] Other chronic obstructive pulmonary disease	274	0.07470439	71	0.1628067	3.34E-09
[J45] Asthma	10	0.00272644	8	0.01834442	1.93E-05
[J47] Bronchiectasis	34	0.00926989	5	0.01146526	0.85337 7
[J60] Coalworker's pneumoconiosis	1	0.00027264	1	0.00229305	0.50951 2
[J61] Pneumoconiosis due to asbestos and other mineral fibres	2	0.00054529	0	0	1
[J67] Hypersensitivity pneumonitis due to organic dust	5	0.00136322	3	0.00687916	0.05838
[J69] Pneumonitis due to solids and liquids	10	0.00272644	3	0.00687916	0.31408 7
[J80] Adult respiratory distress syndrome	0	0	1	0.00229305	0.20138
[J81] Pulmonary oedema	1	0.00027264	0	0	1

[J82] Pulmonary eosinophilia, not elsewhere classified	1	0.00027264	0	0	1
[J84] Other interstitial pulmonary diseases	174	0.04744001	51	0.11694565	8.73E-09
[J85] Abscess of lung and mediastinum	4	0.00109057	1	0.00229305	1
[J86] Pyothorax	1	0.00027264	2	0.0045861	0.02690 3
[J90] Pleural effusion, not elsewhere classified	2	0.00054529	1	0.00229305	0.73425
[J94] Other pleural conditions	2	0.00054529	0	0	1
[J98] Other respiratory disorders	10	0.00272644	3	0.00687916	0.31408 7
[K20] Oesophagitis	0	0	1	0.00229305	0.20138
[K21] Gastro-oesophageal reflux disease	1	0.00027264	0	0	1
[K22] Other diseases of oesophagus	5	0.00136322	1	0.00229305	1
[K25] Gastric ulcer	5	0.00136322	3	0.00687916	0.05838
[K26] Duodenal ulcer	18	0.00490759	4	0.00917221	0.42138 2
[K27] Peptic ulcer, site unspecified	1	0.00027264	2	0.0045861	0.02690 3
[K29] Gastritis and duodenitis	4	0.00109057	1	0.00229305	1
[K31] Other diseases of stomach and duodenum	2	0.00054529	0	0	1
[K35] Acute appendicitis	0	0	1	0.00229305	0.20138
[K37] Unspecified appendicitis	1	0.00027264	0	0	1
[K41] Femoral hernia	1	0.00027264	0	0	1
[K43] Ventral hernia	0	0	1	0.00229305	0.20138
[K44] Diaphragmatic hernia	4	0.00109057	0	0	1
[K46] Unspecified abdominal hernia	1	0.00027264	0	0	1
[K50] Crohn's disease [regional enteritis]	7	0.00190851	1	0.00229305	1
[K51] Ulcerative colitis	3	0.00081793	1	0.00229305	0.90322 6
[K52] Other noninfective gastroenteritis and colitis	1	0.00027264	1	0.00229305	0.50951 2
[K55] Vascular disorders of intestine	42	0.01145104	10	0.02293052	0.07370 3
[K56] Paralytic ileus and intestinal obstruction without hernia	25	0.00681609	8	0.01834442	0.02408 7
[K57] Diverticular disease of intestine	28	0.00763402	7	0.01605136	0.12719 5
[K61] Abscess of anal and rectal regions	1	0.00027264	0	0	1
[K62] Other diseases of anus and rectum	1	0.00027264	0	0	1
[K63] Other diseases of intestine	10	0.00272644	2	0.0045861	0.83320 2
[K65] Peritonitis	7	0.00190851	2	0.0045861	0.55653 4
[K66] Other disorders of peritoneum	1	0.00027264	0	0	1

[K70] Alcoholic liver disease	107	0.02917288	23	0.0527402	0.01342 6
[K71] Toxic liver disease	1	0.00027264	0	0	1
[K72] Hepatic failure, not elsewhere classified	7	0.00190851	3	0.00687916	0.14023 4
[K74] Fibrosis and cirrhosis of liver	35	0.00954253	11	0.02522357	0.00725 2
[K75] Other inflammatory liver diseases	8	0.00218115	6	0.01375831	0.00050 2
[K76] Other diseases of liver	16	0.0043623	11	0.02522357	1.88E-06
[K80] Cholelithiasis	16	0.0043623	1	0.00229305	0.80938
[K81] Cholecystitis	7	0.00190851	4	0.00917221	0.02256 6
[K82] Other diseases of gallbladder	1	0.00027264	0	0	1
[K83] Other diseases of biliary tract	12	0.00327172	8	0.01834442	9.62E-05
[K85] Acute pancreatitis	24	0.00654345	5	0.01146526	0.39274 4
[K86] Other diseases of pancreas	1	0.00027264	2	0.0045861	0.02690 3
[K92] Other diseases of digestive system	15	0.00408966	5	0.01146526	0.08487 5
[L03] Cellulitis	6	0.00163586	4	0.00917221	0.01238 2
[L08] Other local infections of skin and subcutaneous tissue	1	0.00027264	0	0	1
[L12] Pemphigoid	1	0.00027264	0	0	1
[L51] Erythema multiforme	1	0.00027264	1	0.00229305	0.50951 2
[L97] Ulcer of lower limb, not elsewhere classified	3	0.00081793	1	0.00229305	0.90322 6
[L98] Other disorders of skin and subcutaneous tissue, not elsewhere classified	1	0.00027264	0	0	1
[M00] Pyogenic arthritis	1	0.00027264	0	0	1
[M06] Other rheumatoid arthritis	16	0.0043623	1	0.00229305	0.80938
[M25] Other joint disorders, not elsewhere classified	6	0.00163586	1	0.00229305	1
[M30] Polyarteritis nodosa and related conditions	0	0	1	0.00229305	0.20138
[M31] Other necrotizing vasculopathies	3	0.00081793	1	0.00229305	0.90322 6
[M32] Systemic lupus erythematosus	2	0.00054529	0	0	1
[M34] Systemic sclerosis	8	0.00218115	0	0	0.68792 2
[M35] Other systemic involvement of connective tissue	9	0.00245379	1	0.00229305	1
[M41] Scoliosis	3	0.00081793	0	0	1
[M46] Other inflammatory spondylopathies	2	0.00054529	2	0.0045861	0.08115 2

[M60] Myositis	2	0.00054529	0	0	1
[M62] Other disorders of muscle	1	0.00027264	0	0	1
[M72] Fibroblastic disorders	1	0.00027264	0	0	1
[M80] Osteoporosis with pathological fracture	3	0.00081793	1	0.00229305	0.903226
[M81] Osteoporosis without pathological fracture	1	0.00027264	0	0	1
[M84] Disorders of continuity of bone	1	0.00027264	0	0	1
[M86] Osteomyelitis	5	0.00136322	3	0.00687916	0.05838
[N02] Recurrent and persistent haematuria	3	0.00081793	0	0	1
[N03] Chronic nephritic syndrome	0	0	1	0.00229305	0.20138
[N04] Nephrotic syndrome	1	0.00027264	0	0	1
[N10] Acute tubulo-interstitial nephritis	1	0.00027264	1	0.00229305	0.509512
[N12] Tubulo-interstitial nephritis, not specified as acute or chronic	2	0.00054529	2	0.0045861	0.081152
[N15] Other renal tubulo-interstitial diseases	1	0.00027264	0	0	1
[N17] Acute renal failure	5	0.00136322	0	0	0.963742
[N18] Chronic kidney disease	18	0.00490759	6	0.01375831	0.050727
[N19] Unspecified kidney failure	1	0.00027264	0	0	1
[N20] Calculus of kidney and ureter	0	0	2	0.0045861	0.003136
[N26] Unspecified contracted kidney	1	0.00027264	0	0	1
[N28] Other disorders of kidney and ureter, not elsewhere classified	2	0.00054529	0	0	1
[N30] Cystitis	0	0	1	0.00229305	0.20138
[N39] Other disorders of urinary system	29	0.00790667	20	0.04586104	3.45E-11
[N40] Hyperplasia of prostate	0	0	1	0.00229305	0.20138
[N41] Inflammatory diseases of prostate	1	0.00027264	0	0	1
[N49] Inflammatory disorders of male genital organs, not elsewhere classified	1	0.00027264	0	0	1
[N50] Other disorders of male genital organs	1	0.00027264	0	0	1
[R09] Other symptoms and signs involving the circulatory and respiratory systems	1	0.00027264	0	0	1
[R54] Senility	2	0.00054529	1	0.00229305	0.73425
[R68] Other general symptoms and signs	3	0.00081793	0	0	1
[R96] Other sudden death, cause unknown	0	0	1	0.00229305	0.20138
[R99] Other ill-defined and unspecified causes of mortality	21	0.00572552	1	0.00229305	0.562159
[U071] COVID	470	0.12814256	225	0.51593671	7.02E-77
[U07] Emergency use of U07	2	0.00054529	0	0	1
[U50] Drug resistant tuberculosis	14	0.00381701	1	0.00229305	0.937242

Supplementary Table 2

Absolute number and percentage of deaths agglomerated as ICD10 codes level 3 in each cohort of T2D using each selected drug and matched T2D individuals. P values obtained by chi-squared contingency test.

Metformin

Causes of death	Number of Deaths in T2D matched controls	Percentage of Deaths in T2D matched controls	Number of Deaths in Metformin users	Percentage of Deaths in Metformin users	p-value
[A41] Other sepsis	0	0	1	0.038491147	1
[C15] Malignant neoplasm of oesophagus	4	0.153964588	2	0.076982294	0.682918
[C16] Malignant neoplasm of stomach	2	0.076982294	0	0	0.479416
[C18] Malignant neoplasm of colon	4	0.153964588	2	0.076982294	0.682918
[C19] Malignant neoplasm of rectosigmoid junction	1	0.038491147	0	0	1
[C20] Malignant neoplasm of rectum	1	0.038491147	3	0.115473441	0.616939
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	10	0.38491147	2	0.076982294	0.043067
[C23] Malignant neoplasm of gallbladder	2	0.076982294	0	0	0.479416
[C24] Malignant neoplasm of other and unspecified parts of biliary tract	3	0.115473441	0	0	0.248076
[C25] Malignant neoplasm of pancreas	14	0.538876059	4	0.153964588	0.033586
[C26] Malignant neoplasm of other and ill-defined digestive organs	1	0.038491147	1	0.038491147	1
[C34] Malignant neoplasm of bronchus and lung	4	0.153964588	7	0.269438029	0.546068
[C37] Malignant neoplasm of thymus	1	0.038491147	0	0	1
[C44] Other malignant neoplasms of skin	1	0.038491147	0	0	1
[C49] Malignant neoplasm of other connective and soft tissue	1	0.038491147	0	0	1
[C50] Malignant neoplasm of breast	5	0.192455735	2	0.076982294	0.449386
[C53] Malignant neoplasm of cervix uteri	0	0	1	0.038491147	1
[C54] Malignant neoplasm of corpus uteri	2	0.076982294	0	0	0.479416
[C55] Malignant neoplasm of uterus, part unspecified	1	0.038491147	0	0	1
[C56] Malignant neoplasm of ovary	4	0.153964588	2	0.076982294	0.682918
[C61] Malignant neoplasm of prostate	7	0.269438029	4	0.153964588	0.546068
[C64] Malignant neoplasm of kidney, except renal pelvis	2	0.076982294	2	0.076982294	1

[C67] Malignant neoplasm of bladder	3	0.115473441	0	0	0.248076
[C68] Malignant neoplasm of other and unspecified urinary organs	1	0.038491147	0	0	1
[C71] Malignant neoplasm of brain	3	0.115473441	2	0.076982294	1
[C74] Malignant neoplasm of adrenal gland	0	0	1	0.038491147	1
[C80] Malignant neoplasm without specification of site	4	0.153964588	3	0.115473441	1
[C83] Non-follicular lymphoma	1	0.038491147	1	0.038491147	1
[C84] Mature T/NK-cell lymphomas	1	0.038491147	0	0	1
[C85] Other and unspecified types of non-Hodgkin lymphoma	2	0.076982294	1	0.038491147	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	5	0.192455735	0	0	0.0735
[C91] Lymphoid leukaemia	2	0.076982294	0	0	0.479416
[C92] Myeloid leukaemia	1	0.038491147	1	0.038491147	1
[D32] Benign neoplasm of meninges	0	0	1	0.038491147	1
[D37] Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs	1	0.038491147	0	0	1
[D41] Neoplasm of uncertain or unknown behaviour of urinary organs	1	0.038491147	0	0	1
[D46] Myelodysplastic syndromes	1	0.038491147	0	0	1
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	1	0.038491147	0	0	1
[D64] Other anaemias	1	0.038491147	0	0	1
[D69] Purpura and other haemorrhagic conditions	1	0.038491147	0	0	1
[D84] Other immunodeficiencies	1	0.038491147	0	0	1
[E11] Type 2 diabetes mellitus	7	0.269438029	2	0.076982294	0.182043
[E14] Unspecified diabetes mellitus	3	0.115473441	2	0.076982294	1
[E16] Other disorders of pancreatic internal secretion	2	0.076982294	0	0	0.479416
[F01] Vascular dementia	4	0.153964588	2	0.076982294	0.682918
[F03] Unspecified dementia	4	0.153964588	1	0.038491147	0.370863
[G04] Encephalitis, myelitis and encephalomyelitis	1	0.038491147	0	0	1.00E+00
[G12] Spinal muscular atrophy and related syndromes	1	0.038491147	1	0.038491147	1
[G23] Other degenerative diseases of basal ganglia	1	0.038491147	0	0	1
[G30] Alzheimer's disease	3	0.115473441	1	0.038491147	6.17E-01
[I05] Rheumatic mitral valve diseases	0	0	1	0.038491147	1

[I11] Hypertensive heart disease	3	0.115473441	0	0	0.248076
[I13] Hypertensive heart and renal disease	1	0.038491147	0	0	1
[I21] Acute myocardial infarction	16	0.615858353	9	0.346420323	0.229016
[I25] Chronic ischaemic heart disease	28	1.077752117	11	0.423402617	0.010119
[I26] Pulmonary embolism	1	0.038491147	0	0	1
[I27] Other pulmonary heart diseases	1	0.038491147	1	0.038491147	1
[I34] Nonrheumatic mitral valve disorders	1	0.038491147	0	0	1
[I35] Nonrheumatic aortic valve disorders	0	0	1	0.038491147	1
[I42] Cardiomyopathy	1	0.038491147	0	0	1
[I48] Atrial fibrillation and flutter	0	0	1	0.038491147	1
[I50] Heart failure	4	0.153964588	0	0	0.133465
[I51] Complications and ill-defined descriptions of heart disease	1	0.038491147	0	0	1
[I60] Subarachnoid haemorrhage	0	0	1	0.038491147	1
[I61] Intracerebral haemorrhage	2	0.076982294	0	0	0.479416
[I62] Other nontraumatic intracranial haemorrhage	1	0.038491147	0	0	1
[I63] Cerebral infarction	1	0.038491147	2	0.076982294	1
[I64] Stroke, not specified as haemorrhage or infarction	7	0.269438029	1	0.038491147	0.076872
[I67] Other cerebrovascular diseases	3	0.115473441	0	0	0.248076
[I73] Other peripheral vascular diseases	1	0.038491147	0	0	1
[I80] Phlebitis and thrombophlebitis	1	0.038491147	0	0	1
[J11] Influenza, virus not identified	1	0.038491147	0	0	1
[J18] Pneumonia, organism unspecified	7	0.269438029	2	0.076982294	0.182043
[J44] Other chronic obstructive pulmonary disease	4	0.153964588	4	0.153964588	1
[J45] Asthma	3	0.115473441	1	0.038491147	0.616939
[J60] Coalworker's pneumoconiosis	1	0.038491147	0	0	1.00E+00
[J84] Other interstitial pulmonary diseases	1	0.038491147	1	0.038491147	1
[J86] Pyothorax	1	0.038491147	0	0	1
[K20] Oesophagitis	1	0.038491147	0	0	1
[K27] Peptic ulcer, site unspecified	0	0	1	0.038491147	1
[K29] Gastritis and duodenitis	1	0.038491147	0	0	1
[K57] Diverticular disease of intestine	1	0.038491147	1	0.038491147	1
[K70] Alcoholic liver disease	7	0.269438029	1	0.038491147	0.076872
[K72] Hepatic failure, not elsewhere classified	1	0.038491147	0	0	1
[K74] Fibrosis and cirrhosis of liver	2	0.076982294	0	0	0.479416
[K75] Other inflammatory liver diseases	2	0.076982294	0	0	0.479416

[K76] Other diseases of liver	1	0.038491147	0	0	1
[K81] Cholecystitis	0	0	1	0.038491147	1
[K86] Other diseases of pancreas	1	0.038491147	0	0	1
[K92] Other diseases of digestive system	1	0.038491147	0	0	1
[L03] Cellulitis	0	0	1	0.038491147	1
[M25] Other joint disorders, not elsewhere classified	1	0.038491147	0	0	1
[M46] Other inflammatory spondylopathies	0	0	1	0.038491147	1
[M86] Osteomyelitis	0	0	1	0.038491147	1
[N18] Chronic kidney disease	3	0.115473441	0	0	0.248076
[N30] Cystitis	1	0.038491147	0	0	1
[N39] Other disorders of urinary system	1	0.038491147	0	0	1
[N40] Hyperplasia of prostate	0	0	1	0.038491147	1
[R99] Other ill-defined and unspecified causes of mortality	1	0.038491147	0	0	1
[U071] COVID	19	0.731331794	11	0.423402617	0.199939

Sulfonylureas

Causes of death	Number of Deaths in T2D matched controls	Percentage of Deaths in T2D matched controls	Number of Deaths in Sulfonylureas users	Percentage of Deaths in Sulfonylureas users	p-value
[A41] Other sepsis	0	0	1	0.027203482	1
[C06] Malignant neoplasm of other and unspecified parts of mouth	1	0.027203482	0	0	1
[C15] Malignant neoplasm of oesophagus	5	0.13601741	5	0.13601741	1
[C16] Malignant neoplasm of stomach	3	0.081610446	5	0.13601741	0.723529
[C17] Malignant neoplasm of small intestine	1	0.027203482	0	0	1
[C18] Malignant neoplasm of colon	6	0.163220892	2	0.054406964	0.288582
[C19] Malignant neoplasm of rectosigmoid junction	1	0.027203482	1	0.027203482	1
[C20] Malignant neoplasm of rectum	1	0.027203482	2	0.054406964	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	4	0.108813928	5	0.13601741	1
[C23] Malignant neoplasm of gallbladder	0	0	1	0.027203482	1
[C24] Malignant neoplasm of other and unspecified parts of biliary tract	1	0.027203482	0	0	1
[C25] Malignant neoplasm of pancreas	7	0.190424374	17	0.462459195	0.06575

[C26] Malignant neoplasm of other and ill-defined digestive organs	0	0	2	0.054406964	0.47944
[C34] Malignant neoplasm of bronchus and lung	8	0.217627856	15	0.408052231	0.210188
[C37] Malignant neoplasm of thymus	0	0	1	0.027203482	1
[C43] Malignant melanoma of skin	1	0.027203482	1	0.027203482	1
[C44] Other malignant neoplasms of skin	0	0	1	0.027203482	1
[C45] Mesothelioma	1	0.027203482	0	0	1
[C49] Malignant neoplasm of other connective and soft tissue	1	0.027203482	2	0.054406964	1
[C50] Malignant neoplasm of breast	4	0.108813928	5	0.13601741	1
[C53] Malignant neoplasm of cervix uteri	0	0	1	0.027203482	1
[C54] Malignant neoplasm of corpus uteri	0	0	3	0.081610446	0.248117
[C56] Malignant neoplasm of ovary	1	0.027203482	4	0.108813928	0.370931
[C57] Malignant neoplasm of other and unspecified female genital organs	1	0.027203482	0	0	1
[C60] Malignant neoplasm of penis	1	0.027203482	0	0	1
[C61] Malignant neoplasm of prostate	8	0.217627856	9	0.244831338	1
[C64] Malignant neoplasm of kidney, except renal pelvis	1	0.027203482	5	0.13601741	0.220483
[C67] Malignant neoplasm of bladder	3	0.081610446	3	0.081610446	1
[C71] Malignant neoplasm of brain	1	0.027203482	1	0.027203482	1
[C80] Malignant neoplasm without specification of site	4	0.108813928	6	0.163220892	0.751666
[C83] Non-follicular lymphoma	1	0.027203482	3	0.081610446	6.17E-01
[C84] Mature T/NK-cell lymphomas	0	0	1	0.027203482	1.00E+00
[C85] Other and unspecified types of non-Hodgkin lymphoma	1	0.027203482	4	0.108813928	0.370931
[C90] Multiple myeloma and malignant plasma cell neoplasms	1	0.027203482	3	0.081610446	0.616979
[C91] Lymphoid leukaemia	1	0.027203482	0	0	1
[C92] Myeloid leukaemia	1	0.027203482	2	0.054406964	1
[D32] Benign neoplasm of meninges	0	0	1	0.027203482	1
[D37] Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs	1	0.027203482	0	0	1.00E+00
[D41] Neoplasm of uncertain or unknown behaviour of urinary organs	1	0.027203482	0	0	1
[D46] Myelodysplastic syndromes	0	0	3	0.081610446	0.248117
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	0	0	1	0.027203482	1
[D48] Neoplasm of uncertain or unknown behaviour of other and unspecified sites	0	0	1	0.027203482	1

[D69] Purpura and other haemorrhagic conditions	0	0	1	0.027203482	1.00E+00
[E11] Type 2 diabetes mellitus	2	0.054406964	8	0.217627856	0.1136
[E14] Unspecified diabetes mellitus	2	0.054406964	0	0	0.47944
[E16] Other disorders of pancreatic internal secretion	1	0.027203482	0	0	1
[E78] Disorders of lipoprotein metabolism and other lipidaemias	1	0.027203482	0	0	1
[E85] Amyloidosis	1	0.027203482	0	0	1
[E87] Other disorders of fluid, electrolyte and acid-base balance	0	0	1	0.027203482	1
[F01] Vascular dementia	2	0.054406964	3	0.081610446	1
[F03] Unspecified dementia	5	0.13601741	3	0.081610446	0.723529
[G04] Encephalitis, myelitis and encephalomyelitis	0	0	1	0.027203482	1
[G12] Spinal muscular atrophy and related syndromes	3	0.081610446	0	0	0.248117
[G23] Other degenerative diseases of basal ganglia	1	0.027203482	1	0.027203482	1
[G30] Alzheimer's disease	1	0.027203482	3	0.081610446	0.616979
[G90] Disorders of autonomic nervous system	0	0	1	0.027203482	1
[G93] Other disorders of brain	1	0.027203482	0	0	1
[I05] Rheumatic mitral valve diseases	0	0	1	0.027203482	1
[I11] Hypertensive heart disease	3	0.081610446	3	0.081610446	1
[I13] Hypertensive heart and renal disease	0	0	2	0.054406964	0.47944
[I21] Acute myocardial infarction	11	0.299238303	11	0.299238303	1
[I25] Chronic ischaemic heart disease	17	0.462459195	27	0.734494015	0.173552
[I26] Pulmonary embolism	0	0	2	0.054406964	0.47944
[I27] Other pulmonary heart diseases	0	0	2	0.054406964	0.47944
[I34] Nonrheumatic mitral valve disorders	0	0	1	0.027203482	1
[I35] Nonrheumatic aortic valve disorders	1	0.027203482	0	0	1
[I42] Cardiomyopathy	1	0.027203482	1	0.027203482	1
[I48] Atrial fibrillation and flutter	1	0.027203482	1	0.027203482	1
[I50] Heart failure	1	0.027203482	2	0.054406964	1
[I51] Complications and ill-defined descriptions of heart disease	0	0	1	0.027203482	1
[I61] Intracerebral haemorrhage	2	0.054406964	2	0.054406964	1
[I63] Cerebral infarction	2	0.054406964	2	0.054406964	1
[I64] Stroke, not specified as haemorrhage or infarction	3	0.081610446	4	0.108813928	1
[I67] Other cerebrovascular diseases	0	0	1	0.027203482	1

[I71] Aortic aneurysm and dissection	2	0.054406964	0	0	0.47944
[I80] Phlebitis and thrombophlebitis	0	0	2	0.054406964	0.47944
[J11] Influenza, virus not identified	1	0.027203482	1	0.027203482	1
[J12] Viral pneumonia, not elsewhere classified	1	0.027203482	0	0	1
[J18] Pneumonia, organism unspecified	1	0.027203482	7	0.190424374	0.076939
[J44] Other chronic obstructive pulmonary disease	8	0.217627856	3	0.081610446	0.227452
[J45] Asthma	0	0	1	0.027203482	1
[J84] Other interstitial pulmonary diseases	7	0.190424374	5	0.13601741	0.772649
[J85] Abscess of lung and mediastinum	0	0	1	0.027203482	1
[J86] Pyothorax	0	0	1	0.027203482	1
[J98] Other respiratory disorders	2	0.054406964	0	0	0.47944
[K52] Other noninfective gastroenteritis and colitis	0	0	1	0.027203482	1
[K55] Vascular disorders of intestine	1	0.027203482	1	0.027203482	1
[K56] Paralytic ileus and intestinal obstruction without hernia	1	0.027203482	0	0	1
[K57] Diverticular disease of intestine	0	0	1	0.027203482	1
[K70] Alcoholic liver disease	0	0	3	0.081610446	0.248117
[K72] Hepatic failure, not elsewhere classified	0	0	1	0.027203482	1
[K76] Other diseases of liver	1	0.027203482	2	0.054406964	1
[K81] Cholecystitis	0	0	1	0.027203482	1
[K83] Other diseases of biliary tract	0	0	1	0.027203482	1
[K85] Acute pancreatitis	0	0	1	0.027203482	1
[K92] Other diseases of digestive system	3	0.081610446	0	0	0.248117
[L03] Cellulitis	0	0	1	0.027203482	1
[M46] Other inflammatory spondylopathies	0	0	1	0.027203482	1
[N18] Chronic kidney disease	1	0.027203482	0	0	1
[N39] Other disorders of urinary system	1	0.027203482	1	0.027203482	1
[R99] Other ill-defined and unspecified causes of mortality	0	0	1	0.027203482	1
[U071] COVID	22	0.598476605	23	0.625680087	1

DPP4I

Causes of death	Number of Deaths in T2D matched controls	Percentage of Deaths in T2D matched controls	Number of Deaths in DPP4I users	Percentage of Deaths in DPP4I users	p-value
[A41] Other sepsis	1	0.035893754	0	0	1

[C06] Malignant neoplasm of other and unspecified parts of mouth	1	0.035893754	0	0	1.00E+00
[C15] Malignant neoplasm of oesophagus	1	0.035893754	1	0.035893754	1
[C16] Malignant neoplasm of stomach	3	0.107681263	1	0.035893754	0.616949
[C18] Malignant neoplasm of colon	1	0.035893754	3	0.107681263	6.17E-01
[C20] Malignant neoplasm of rectum	0	0	2	0.071787509	0.479421
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	3	0.107681263	2	0.071787509	1
[C24] Malignant neoplasm of other and unspecified parts of biliary tract	1	0.035893754	0	0	1
[C25] Malignant neoplasm of pancreas	10	0.358937545	7	0.251256281	0.6271
[C26] Malignant neoplasm of other and ill-defined digestive organs	2	0.071787509	1	0.035893754	1
[C34] Malignant neoplasm of bronchus and lung	5	0.179468772	9	0.32304379	0.422094
[C37] Malignant neoplasm of thymus	1	0.035893754	0	0	1
[C43] Malignant melanoma of skin	2	0.071787509	0	0	0.479421
[C49] Malignant neoplasm of other connective and soft tissue	0	0	1	0.035893754	1
[C50] Malignant neoplasm of breast	0	0	1	0.035893754	1
[C54] Malignant neoplasm of corpus uteri	0	0	1	0.035893754	1
[C56] Malignant neoplasm of ovary	2	0.071787509	1	0.035893754	1
[C61] Malignant neoplasm of prostate	4	0.143575018	3	0.107681263	1
[C64] Malignant neoplasm of kidney, except renal pelvis	0	0	4	0.143575018	0.133475
[C67] Malignant neoplasm of bladder	1	0.035893754	1	0.035893754	1
[C71] Malignant neoplasm of brain	1	0.035893754	0	0	1
[C73] Malignant neoplasm of thyroid gland	0	0	1	0.035893754	1
[C80] Malignant neoplasm without specification of site	3	0.107681263	0	0	0.248086
[C85] Other and unspecified types of non-Hodgkin lymphoma	1	0.035893754	0	0	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	5	0.179468772	0	0	0.073509
[C92] Myeloid leukaemia	0	0	1	0.035893754	1
[D32] Benign neoplasm of meninges	0	0	1	0.035893754	1
[D46] Myelodysplastic syndromes	0	0	1	0.035893754	1
[D84] Other immunodeficiencies	0	0	1	0.035893754	1
[E11] Type 2 diabetes mellitus	2	0.071787509	2	0.071787509	1
[E14] Unspecified diabetes mellitus	1	0.035893754	0	0	1.00E+00
[E16] Other disorders of pancreatic internal secretion	1	0.035893754	0	0	1

[F01] Vascular dementia	4	0.143575018	2	0.071787509	0.68293
[F03] Unspecified dementia	4	0.143575018	2	0.071787509	0.68293
[G30] Alzheimer's disease	1	0.035893754	2	0.071787509	1
[G93] Other disorders of brain	1	0.035893754	0	0	1
[I05] Rheumatic mitral valve diseases	0	0	1	0.035893754	1
[I11] Hypertensive heart disease	3	0.107681263	3	0.107681263	1
[I21] Acute myocardial infarction	3	0.107681263	13	0.466618808	0.024244
[I25] Chronic ischaemic heart disease	14	0.502512563	10	0.358937545	0.539417
[I26] Pulmonary embolism	1	0.035893754	0	0	1
[I35] Nonrheumatic aortic valve disorders	0	0	1	0.035893754	1
[I42] Cardiomyopathy	0	0	1	0.035893754	1
[I48] Atrial fibrillation and flutter	0	0	3	0.107681263	0.248086
[I50] Heart failure	1	0.035893754	1	0.035893754	1
[I51] Complications and ill-defined descriptions of heart disease	0	0	1	0.035893754	1
[I60] Subarachnoid haemorrhage	1	0.035893754	0	0	1
[I62] Other nontraumatic intracranial haemorrhage	1	0.035893754	0	0	1
[I63] Cerebral infarction	0	0	1	0.035893754	1
[I64] Stroke, not specified as haemorrhage or infarction	1	0.035893754	3	0.107681263	0.616949
[I67] Other cerebrovascular diseases	1	0.035893754	1	0.035893754	1
[I73] Other peripheral vascular diseases	0	0	1	0.035893754	1
[J12] Viral pneumonia, not elsewhere classified	0	0	1	0.035893754	1
[J13] Pneumonia due to Streptococcus pneumoniae	0	0	1	0.035893754	1
[J18] Pneumonia, organism unspecified	2	0.071787509	4	0.143575018	0.68293
[J43] Emphysema	0	0	1	0.035893754	1
[J44] Other chronic obstructive pulmonary disease	4	0.143575018	0	0	0.133475
[J47] Bronchiectasis	1	0.035893754	0	0	1
[J84] Other interstitial pulmonary diseases	3	0.107681263	1	0.035893754	0.616949
[J85] Abscess of lung and mediastinum	1	0.035893754	0	0	1
[J86] Pyothorax	1	0.035893754	0	0	1
[J98] Other respiratory disorders	0	0	1	0.035893754	1
[K55] Vascular disorders of intestine	0	0	1	0.03589375	1
[K56] Paralytic ileus and intestinal obstruction without hernia	1	0.03589375	0	0	1
[K57] Diverticular disease of intestine	1	0.03589375	1	0.03589375	1
[K70] Alcoholic liver disease	2	0.071787509	2	0.071787509	1
[K72] Hepatic failure, not elsewhere classified	0	0	1	0.035893754	1

[K75] Other inflammatory liver diseases	1	0.035893754	0	0	1
[K76] Other diseases of liver	0	0	1	0.035893754	1
[K81] Cholecystitis	0	0	1	0.035893754	1
[K83] Other diseases of biliary tract	1	0.035893754	0	0	1
[K85] Acute pancreatitis	1	0.035893754	0	0	1
[K92] Other diseases of digestive system	1	0.035893754	1	0.035893754	1
[L03] Cellulitis	1	0.035893754	0	0	1
[L51] Erythema multiforme	0	0	1	0.035893754	1
[N18] Chronic kidney disease	0	0	1	0.035893754	1
[N39] Other disorders of urinary system	0	0	2	0.071787509	0.479421
[U071] COVID	13	0.466618808	12	0.430725054	1

Long/Interm.-Acting Insulins

Causes of death	Number of Deaths in T2D matched controls	Percentage of Deaths in T2D matched controls	Number of Deaths in Long/Interm.-Acting Insulins users	Percentage of Deaths in Long/Interm.-Acting Insulins users	p-value
[A41] Other sepsis	1	0.039856517	1	0.039856517	1
[C06] Malignant neoplasm of other and unspecified parts of mouth	0	0	1	0.039856517	1
[C14] Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx	0	0	1	0.039856517	1
[C15] Malignant neoplasm of oesophagus	0	0	3	0.11956955	0.248072
[C16] Malignant neoplasm of stomach	3	0.11956955	1	0.039856517	0.616935
[C18] Malignant neoplasm of colon	2	0.079713033	3	0.11956955	1
[C19] Malignant neoplasm of rectosigmoid junction	0	0	1	0.039856517	1
[C20] Malignant neoplasm of rectum	0	0	1	0.039856517	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	2	0.079713033	7	0.278995616	0.18203
[C23] Malignant neoplasm of gallbladder	0	0	1	0.039856517	1
[C24] Malignant neoplasm of other and unspecified parts of biliary tract	0	0	2	0.079713033	0.479413
[C25] Malignant neoplasm of pancreas	6	0.239139099	11	0.438421682	0.331155
[C26] Malignant neoplasm of other and ill-defined digestive organs	2	0.079713033	0	0	0.479413

[C34] Malignant neoplasm of bronchus and lung	8	0.318852132	6	0.239139099	0.78898
[C44] Other malignant neoplasms of skin	0	0	1	0.039856517	1
[C49] Malignant neoplasm of other connective and soft tissue	2	0.079713033	0	0	0.479413
[C50] Malignant neoplasm of breast	1	0.039856517	3	0.11956955	0.616935
[C53] Malignant neoplasm of cervix uteri	0	0	1	0.039856517	1
[C55] Malignant neoplasm of uterus, part unspecified	0	0	1	0.039856517	1
[C56] Malignant neoplasm of ovary	0	0	1	0.039856517	1
[C60] Malignant neoplasm of penis	1	0.039856517	0	0	1
[C61] Malignant neoplasm of prostate	6	0.239139099	7	0.278995616	1
[C64] Malignant neoplasm of kidney, except renal pelvis	3	0.11956955	3	0.11956955	1
[C67] Malignant neoplasm of bladder	1	0.039856517	2	0.079713033	1
[C68] Malignant neoplasm of other and unspecified urinary organs	0	0	1	0.039856517	1
[C71] Malignant neoplasm of brain	1	0.039856517	0	0	1
[C80] Malignant neoplasm without specification of site	0	0	4	0.159426066	0.13346
[C81] Hodgkin lymphoma	0	0	1	0.039856517	1
[C83] Non-follicular lymphoma	0	0	1	0.039856517	1
[C84] Mature T/NK-cell lymphomas	1	0.039856517	0	0	1
[C85] Other and unspecified types of non-Hodgkin lymphoma	2	0.079713033	0	0	4.79E-01
[C90] Multiple myeloma and malignant plasma cell neoplasms	2	0.079713033	3	0.11956955	1
[C91] Lymphoid leukaemia	0	0	2	0.079713033	0.479413
[D37] Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs	0	0	1	0.039856517	1.00E+00
[D41] Neoplasm of uncertain or unknown behaviour of urinary organs	0	0	1	0.039856517	1
[D46] Myelodysplastic syndromes	0	0	1	0.039856517	1
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	2	0.079713033	0	0	0.479413
[D48] Neoplasm of uncertain or unknown behaviour of other and unspecified sites	1	0.039856517	0	0	1
[E11] Type 2 diabetes mellitus	3	0.11956955	6	0.239139099	0.504603
[E14] Unspecified diabetes mellitus	0	0	3	0.11956955	0.248072
[E16] Other disorders of pancreatic internal secretion	0	0	2	0.079713033	0.479413

[E78] Disorders of lipoprotein metabolism and other lipidaemias	0	0	1	0.039856517	1
[E83] Disorders of mineral metabolism	0	0	1	0.039856517	1
[F01] Vascular dementia	2	0.079713033	4	0.159426066	0.682912
[F03] Unspecified dementia	3	0.11956955	2	0.079713033	1
[G04] Encephalitis, myelitis and encephalomyelitis	0	0	1	0.039856517	1
[G12] Spinal muscular atrophy and related syndromes	1	0.039856517	1	0.039856517	1
[G30] Alzheimer's disease	0	0	3	0.11956955	0.248072
[G47] Sleep disorders	0	0	1	0.039856517	1
[G71] Primary disorders of muscles	1	0.039856517	0	0	1
[G90] Disorders of autonomic nervous system	0	0	2	0.079713033	0.479413
[I11] Hypertensive heart disease	2	0.079713033	1	0.039856517	1
[I13] Hypertensive heart and renal disease	0	0	1	0.039856517	1
[I21] Acute myocardial infarction	5	0.199282583	17	0.677560781	0.018755
[I25] Chronic ischaemic heart disease	11	0.438421682	19	0.757273814	0.199893
[I26] Pulmonary embolism	1	0.039856517	1	0.039856517	1
[I27] Other pulmonary heart diseases	1	0.039856517	1	0.039856517	1
[I42] Cardiomyopathy	0	0	1	0.039856517	1
[I48] Atrial fibrillation and flutter	1	0.039856517	0	0	1
[I50] Heart failure	0	0	5	0.199282583	7.35E-02
[I51] Complications and ill-defined descriptions of heart disease	2	0.079713033	1	0.039856517	1
[I61] Intracerebral haemorrhage	1	0.039856517	0	0	1
[I62] Other nontraumatic intracranial haemorrhage	1	0.039856517	1	0.039856517	1
[I63] Cerebral infarction	3	0.11956955	1	0.039856517	0.616935
[I64] Stroke, not specified as haemorrhage or infarction	0	0	6	0.239139099	0.041106
[I67] Other cerebrovascular diseases	0	0	3	0.11956955	0.248072
[I73] Other peripheral vascular diseases	1	0.039856517	0	0	1
[J11] Influenza, virus not identified	0	0	1	0.039856517	1
[J18] Pneumonia, organism unspecified	1	0.039856517	5	0.199282583	0.220395
[J44] Other chronic obstructive pulmonary disease	0	0	5	0.199282583	0.073495
[J45] Asthma	0	0	2	0.079713033	0.479413
[J47] Bronchiectasis	0	0	1	0.039856517	1
[J60] Coalworker's pneumoconiosis	0	0	1	0.039856517	1
[J84] Other interstitial pulmonary diseases	7	0.278995616	4	0.159426066	0.546053
[J98] Other respiratory disorders	1	0.039856517	1	0.039856517	1

[K20] Oesophagitis	0	0	1	0.039856517	1
[K27] Peptic ulcer, site unspecified	0	0	1	0.039856517	1
[K29] Gastritis and duodenitis	0	0	1	0.039856517	1
[K55] Vascular disorders of intestine	1	0.039856517	1	0.039856517	1
[K57] Diverticular disease of intestine	2	0.079713033	0	0	0.479413
[K70] Alcoholic liver disease	1	0.039856517	3	0.11956955	0.616935
[K72] Hepatic failure, not elsewhere classified	1	0.039856517	0	0	1
[K74] Fibrosis and cirrhosis of liver	1	0.039856517	2	0.079713033	1
[K75] Other inflammatory liver diseases	0	0	2	0.079713033	0.479413
[K76] Other diseases of liver	2	0.079713033	0	0	0.479413
[K81] Cholecystitis	0	0	1	0.039856517	1
[K86] Other diseases of pancreas	0	0	1	0.039856517	1
[K92] Other diseases of digestive system	0	0	1	0.039856517	1
[L03] Cellulitis	0	0	1	0.039856517	1
[M25] Other joint disorders, not elsewhere classified	0	0	1	0.039856517	1
[M46] Other inflammatory spondylopathies	1	0.039856517	0	0	1
[N10] Acute tubulo-interstitial nephritis	0	0	1	0.039856517	1
[N18] Chronic kidney disease	0	0	2	0.079713033	0.479413
[N30] Cystitis	0	0	1	0.039856517	1
[N39] Other disorders of urinary system	0	0	1	0.039856517	1
[U071] COVID	10	0.398565165	20	0.797130331	0.099332

SGLT2i

Causes of death	Number of Deaths in T2D matched controls	Percentage of Deaths in T2D matched controls	Number of Deaths in SGLT2i users	Percentage of Deaths in SGLT2i users	p-value
[C09] Malignant neoplasm of tonsil	1	0.054914882	0	0	1
[C17] Malignant neoplasm of small intestine	1	0.054914882	0	0	1
[C18] Malignant neoplasm of colon	1	0.054914882	0	0	1
[C20] Malignant neoplasm of rectum	1	0.054914882	1	0.054914882	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	2	0.109829764	1	0.054914882	1
[C23] Malignant neoplasm of gallbladder	0	0	1	0.054914882	1
[C25] Malignant neoplasm of pancreas	6	0.329489292	3	0.164744646	0.504458
[C26] Malignant neoplasm of other and ill-defined digestive organs	0	0	1	0.054914882	1
[C34] Malignant neoplasm of bronchus and lung	3	0.164744646	1	0.054914882	0.616882

[C45] Mesothelioma	1	0.054914882	0	0	1
[C50] Malignant neoplasm of breast	3	0.164744646	0	0	0.248018
[C54] Malignant neoplasm of corpus uteri	1	0.054914882	0	0	1
[C55] Malignant neoplasm of uterus, part unspecified	0	0	1	0.054914882	1
[C61] Malignant neoplasm of prostate	6	0.329489292	1	0.054914882	0.1302
[C67] Malignant neoplasm of bladder	1	0.054914882	0	0	1
[C71] Malignant neoplasm of brain	1	0.054914882	0	0	1
[C80] Malignant neoplasm without specification of site	2	0.109829764	1	0.054914882	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	2	0.109829764	0	0	0.479379
[D32] Benign neoplasm of meninges	0	0	1	0.054914882	1
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	0	0	1	0.054914882	1
[E11] Type 2 diabetes mellitus	1	0.054914882	0	0	1
[E14] Unspecified diabetes mellitus	0	0	1	0.054914882	1
[F01] Vascular dementia	2	0.109829764	0	0	0.479379
[F03] Unspecified dementia	1	0.054914882	0	0	1
[I11] Hypertensive heart disease	1	0.054914882	1	0.054914882	1
[I21] Acute myocardial infarction	1	0.054914882	0	0	1
[I25] Chronic ischaemic heart disease	8	0.439319055	6	0.329489292	0.788871
[I26] Pulmonary embolism	1	0.054914882	0	0	1
[I42] Cardiomyopathy	1	0.054914882	0	0	1
[J18] Pneumonia, organism unspecified	1	0.054914882	1	0.054914882	1
[J44] Other chronic obstructive pulmonary disease	3	0.164744646	0	0	0.248018
[J84] Other interstitial pulmonary diseases	2	0.109829764	0	0	4.79E-01
[K55] Vascular disorders of intestine	0	0	1	0.054914882	1
[K57] Diverticular disease of intestine	1	0.054914882	0	0	1
[M86] Osteomyelitis	0	0	1	0.054914882	1.00E+00
[U071] COVID	5	0.27457441	8	0.439319055	0.578421

GLP1RA

Causes of death	Number of Deaths in T2D matched controls	Percentage of Deaths in T2D matched controls	Number of Deaths in GLP1RA users	Percentage of Deaths in GLP1RA users	p-value
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[C16] Malignant neoplasm of stomach	1	0.098135427	1	0.098135427	1
[C18] Malignant neoplasm of colon	1	0.098135427	0	0	1
[C20] Malignant neoplasm of rectum	0	0	1	0.098135427	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	1	0.098135427	2	0.196270854	1
[C25] Malignant neoplasm of pancreas	3	0.294406281	0	0	0.247865
[C34] Malignant neoplasm of bronchus and lung	1	0.098135427	2	0.196270854	1
[C43] Malignant melanoma of skin	1	0.098135427	0	0	1
[C45] Mesothelioma	1	0.098135427	0	0	1
[C49] Malignant neoplasm of other connective and soft tissue	0	0	1	0.098135427	1
[C50] Malignant neoplasm of breast	1	0.098135427	0	0	1
[C56] Malignant neoplasm of ovary	1	0.098135427	0	0	1
[C61] Malignant neoplasm of prostate	0	0	1	0.098135427	1
[C64] Malignant neoplasm of kidney, except renal pelvis	2	0.196270854	1	0.098135427	1
[C67] Malignant neoplasm of bladder	0	0	1	0.098135427	1
[C80] Malignant neoplasm without specification of site	0	0	1	0.098135427	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	2	0.196270854	0	0	0.479284
[E83] Disorders of mineral metabolism	0	0	1	0.098135427	1
[F03] Unspecified dementia	2	0.196270854	0	0	0.479284
[G20] Parkinson's disease	1	0.098135427	0	0	1
[I21] Acute myocardial infarction	2	0.196270854	0	0	0.479284
[I25] Chronic ischaemic heart disease	2	0.196270854	5	0.490677134	0.448912
[I26] Pulmonary embolism	1	0.098135427	0	0	1.00E+00
[I42] Cardiomyopathy	0	0	1	0.098135427	1
[I64] Stroke, not specified as haemorrhage or infarction	0	0	1	0.098135427	1
[J44] Other chronic obstructive pulmonary disease	2	0.196270854	0	0	0.479284
[J84] Other interstitial pulmonary diseases	1	0.098135427	3	0.294406281	0.616729
[J85] Abscess of lung and mediastinum	0	0	1	0.098135427	1
[J86] Pyothorax	1	0.098135427	0	0	1
[K70] Alcoholic liver disease	1	0.098135427	0	0	1
[K81] Cholecystitis	0	0	1	0.098135427	1
[M25] Other joint disorders, not elsewhere classified	0	0	1	0.098135427	1
[M86] Osteomyelitis	0	0	1	0.098135427	1
[U071] COVID	1	0.098135427	5	0.490677134	0.219991

Short-Acting Insulins

Causes of death	Number of Deaths in T2D matched controls	Percentage of Deaths in T2D matched controls	Number of Deaths in Short-Acting Insulins users	Percentage of Deaths in Short-Acting Insulins users	p-value
[A41] Other sepsis	1	0.101317123	1	0.101317123	1
[C14] Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx	0	0	1	0.101317123	1
[C15] Malignant neoplasm of oesophagus	1	0.101317123	1	0.101317123	1
[C17] Malignant neoplasm of small intestine	1	0.101317123	0	0	1
[C20] Malignant neoplasm of rectum	0	0	2	0.202634245	0.479277
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	0	0	3	0.303951368	0.247853
[C25] Malignant neoplasm of pancreas	5	0.506585613	2	0.202634245	0.448886
[C26] Malignant neoplasm of other and ill-defined digestive organs	0	0	1	0.101317123	1
[C34] Malignant neoplasm of bronchus and lung	2	0.202634245	0	0	0.479277
[C49] Malignant neoplasm of other connective and soft tissue	2	0.202634245	1	0.101317123	1
[C50] Malignant neoplasm of breast	1	0.101317123	0	0	1
[C55] Malignant neoplasm of uterus, part unspecified	0	0	1	0.101317123	1
[C56] Malignant neoplasm of ovary	0	0	1	0.101317123	1
[C61] Malignant neoplasm of prostate	3	0.303951368	1	0.101317123	0.616718
[C64] Malignant neoplasm of kidney, except renal pelvis	2	0.202634245	0	0	0.479277
[C67] Malignant neoplasm of bladder	0	0	2	0.202634245	0.479277
[C68] Malignant neoplasm of other and unspecified urinary organs	1	0.101317123	0	0	1
[C80] Malignant neoplasm without specification of site	0	0	2	0.202634245	0.479277
[C84] Mature T/NK-cell lymphomas	1	0.101317123	0	0	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	0	0	1	0.101317123	1
[C91] Lymphoid leukaemia	1	0.101317123	0	0	1
[D37] Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs	0	0	1	0.101317123	1

[D41] Neoplasm of uncertain or unknown behaviour of urinary organs	0	0	1	0.101317123	1
[D64] Other anaemias	1	0.101317123	0	0	1
[E11] Type 2 diabetes mellitus	0	0	3	0.303951368	0.247853
[E83] Disorders of mineral metabolism	0	0	1	0.101317123	1
[F01] Vascular dementia	0	0	2	0.202634245	0.479277
[G04] Encephalitis, myelitis and encephalomyelitis	0	0	1	0.101317123	1
[G12] Spinal muscular atrophy and related syndromes	1	0.101317123	1	0.101317123	1
[G30] Alzheimer's disease	1	0.101317123	1	0.101317123	1
[I21] Acute myocardial infarction	1	0.101317123	6	0.607902736	0.129888
[I25] Chronic ischaemic heart disease	1	0.101317123	11	1.114488349	0.00916
[I26] Pulmonary embolism	0	0	1	0.101317123	1
[I50] Heart failure	0	0	2	0.202634245	0.479277
[I51] Complications and ill-defined descriptions of heart disease	1	0.101317123	0	0	1
[I61] Intracerebral haemorrhage	0	0	1	0.101317123	1
[I62] Other nontraumatic intracranial haemorrhage	0	0	2	0.202634245	0.479277
[I63] Cerebral infarction	1	0.101317123	0	0	1
[I64] Stroke, not specified as haemorrhage or infarction	2	0.202634245	2	0.202634245	1
[I67] Other cerebrovascular diseases	1	0.101317123	0	0	1
[J11] Influenza, virus not identified	0	0	1	0.101317123	1
[J18] Pneumonia, organism unspecified	1	0.101317123	2	0.202634245	1
[J43] Emphysema	0	0	1	0.101317123	1
[J44] Other chronic obstructive pulmonary disease	1	0.101317123	1	0.101317123	1
[J45] Asthma	0	0	2	0.202634245	0.479277
[J84] Other interstitial pulmonary diseases	0	0	2	0.202634245	0.479277
[K20] Oesophagitis	0	0	1	0.101317123	1
[K70] Alcoholic liver disease	1	0.101317123	1	0.101317123	1
[K74] Fibrosis and cirrhosis of liver	1	0.101317123	2	0.202634245	1
[K75] Other inflammatory liver diseases	0	0	1	0.101317123	1
[K76] Other diseases of liver	1	0.101317123	0	0	1
[K86] Other diseases of pancreas	0	0	1	0.101317123	1
[M25] Other joint disorders, not elsewhere classified	0	0	1	0.101317123	1
[M86] Osteomyelitis	1	0.101317123	0	0	1

[R99] Other ill-defined and unspecified causes of mortality	1	0.101317123	0	0	1
[U071] COVID	3	0.303951368	6	0.607902736	0.504011

Thiazolidinediones

Causes of death	Number of Deaths in T2D matched controls	Percentage of Deaths in T2D matched controls	Number of Deaths in Thiazolidinediones users	Percentage of Deaths in Thiazolidinediones users	p-value
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	0	0	1	0.210970464	1
[C25] Malignant neoplasm of pancreas	1	0.210970464	4	0.843881857	0.369828
[C26] Malignant neoplasm of other and ill-defined digestive organs	0	0	1	0.210970464	1
[C34] Malignant neoplasm of bronchus and lung	1	0.210970464	2	0.421940928	1
[C43] Malignant melanoma of skin	1	0.210970464	0	0	1
[C50] Malignant neoplasm of breast	0	0	1	0.210970464	1
[C54] Malignant neoplasm of corpus uteri	0	0	1	0.210970464	1
[C61] Malignant neoplasm of prostate	1	0.210970464	3	0.632911392	0.61633
[C64] Malignant neoplasm of kidney, except renal pelvis	1	0.210970464	0	0	1
[C67] Malignant neoplasm of bladder	0	0	1	0.210970464	1
[C80] Malignant neoplasm without specification of site	1	0.210970464	1	0.210970464	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	1	0.210970464	0	0	1
[C92] Myeloid leukaemia	1	0.210970464	0	0	1
[E11] Type 2 diabetes mellitus	0	0	1	0.210970464	1
[F03] Unspecified dementia	1	0.210970464	0	0	1
[I21] Acute myocardial infarction	0	0	2	0.421940928	0.479036
[I25] Chronic ischaemic heart disease	3	0.632911392	2	0.421940928	1
[I26] Pulmonary embolism	1	0.210970464	1	0.210970464	1
[I51] Complications and ill-defined descriptions of heart disease	0	0	1	0.210970464	1
[I80] Phlebitis and thrombophlebitis	1	0.210970464	1	0.210970464	1
[J18] Pneumonia, organism unspecified	2	0.421940928	0	0	0.479036
[J44] Other chronic obstructive pulmonary disease	0	0	1	0.210970464	1
[K70] Alcoholic liver disease	0	0	1	0.210970464	1

[K75] Other inflammatory liver diseases	0	0	1	0.210970464	1
[K92] Other diseases of digestive system	0	0	1	0.210970464	1
[U071] COVID	1	0.210970464	3	0.632911392	0.61633

Supplementary Table 3

Absolute number and percentage of deaths agglomerated as ICD10 codes level 3 in each cohort of T2D using each selected drug and matched not T2D individuals. P values obtained by chi-squared contingency test.

Metformin

Causes of death	Number of Deaths in not T2D matched controls	Percentage of Deaths in not T2D matched controls	Number of Deaths in Metformin users	Percentage of Deaths in Metformin users	p-value
[A04] Other bacterial intestinal infections	1	0.006416014	0	0	1
[A16] Respiratory tuberculosis, not confirmed bacteriologically or histologically	1	0.006416014	0	0	1
[A41] Other sepsis	2	0.012832029	3	0.019248043	1
[B27] Infectious mononucleosis	1	0.006416014	0	0	1
[C02] Malignant neoplasm of other and unspecified parts of tongue	2	0.012832029	0	0	0.479486
[C06] Malignant neoplasm of other and unspecified parts of mouth	1	0.006416014	0	0	1
[C09] Malignant neoplasm of tonsil	2	0.012832029	1	0.006416014	1
[C13] Malignant neoplasm of hypopharynx	1	0.006416014	0	0	1
[C14] Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx	0	0	1	0.006416014	1
[C15] Malignant neoplasm of oesophagus	17	0.109072244	10	0.064160144	0.248008
[C16] Malignant neoplasm of stomach	11	0.070576158	12	0.076992172	1
[C17] Malignant neoplasm of small intestine	2	0.012832029	1	0.006416014	1
[C18] Malignant neoplasm of colon	21	0.134736302	17	0.109072244	0.626286
[C19] Malignant neoplasm of rectosigmoid junction	2	0.012832029	6	0.038496086	0.288782
[C20] Malignant neoplasm of rectum	8	0.051328115	6	0.038496086	0.789222
[C21] Malignant neoplasm of anus and anal canal	1	0.006416014	0	0	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	9	0.057744129	15	0.096240216	0.307248

[C23] Malignant neoplasm of gallbladder	3	0.019248043	0	0	0.24819
[C24] Malignant neoplasm of other and unspecified parts of biliary tract	2	0.012832029	0	0	0.479486
[C25] Malignant neoplasm of pancreas	22	0.141152316	40	0.256640575	0.030684
[C26] Malignant neoplasm of other and ill-defined digestive organs	4	0.025664057	5	0.032080072	1
[C34] Malignant neoplasm of bronchus and lung	58	0.372128834	58	0.372128834	1
[C41] Malignant neoplasm of bone and articular cartilage of other and unspecified sites	1	0.006416014	0	0	1
[C43] Malignant melanoma of skin	2	0.012832029	6	0.038496086	0.288782
[C44] Other malignant neoplasms of skin	2	0.012832029	1	0.006416014	1
[C45] Mesothelioma	6	0.038496086	2	0.012832029	0.288782
[C48] Malignant neoplasm of retroperitoneum and peritoneum	3	0.019248043	0	0	0.24819
[C49] Malignant neoplasm of other connective and soft tissue	5	0.032080072	3	0.019248043	0.72364
[C50] Malignant neoplasm of breast	13	0.083408187	12	0.076992172	1
[C51] Malignant neoplasm of vulva	0	0	1	0.006416014	1
[C53] Malignant neoplasm of cervix uteri	1	0.006416014	1	0.006416014	1
[C54] Malignant neoplasm of corpus uteri	4	0.025664057	3	0.019248043	1
[C56] Malignant neoplasm of ovary	7	0.044912101	5	0.032080072	0.772787
[C57] Malignant neoplasm of other and unspecified female genital organs	0	0	1	0.006416014	1
[C60] Malignant neoplasm of penis	0	0	1	0.006416014	1
[C61] Malignant neoplasm of prostate	31	0.198896446	25	0.160400359	0.503652
[C64] Malignant neoplasm of kidney, except renal pelvis	11	0.070576158	9	0.057744129	0.823007
[C67] Malignant neoplasm of bladder	11	0.070576158	7	0.044912101	0.479373
[C68] Malignant neoplasm of other and unspecified urinary organs	3	0.019248043	0	0	0.24819
[C69] Malignant neoplasm of eye and adnexa	1	0.006416014	0	0	1
[C71] Malignant neoplasm of brain	16	0.10265623	7	0.044912101	0.095171
[C73] Malignant neoplasm of thyroid gland	1	0.006416014	1	0.006416014	1
[C74] Malignant neoplasm of adrenal gland	0	0	1	0.006416014	1
[C76] Malignant neoplasm of other and ill-defined sites	1	0.006416014	0	0	1
[C78] Secondary malignant neoplasm of respiratory and digestive organs	1	0.006416014	0	0	1
[C80] Malignant neoplasm without specification of site	11	0.070576158	12	0.076992172	1
[C81] Hodgkin lymphoma	0	0	1	0.006416014	1.00E+00
[C82] Follicular lymphoma	1	0.006416014	0	0	1

[C83] Non-follicular lymphoma	3	0.019248043	5	0.032080072	0.72364
[C84] Mature T/NK-cell lymphomas	1	0.006416014	0	0	1.00E+00
[C85] Other and unspecified types of non-Hodgkin lymphoma	2	0.012832029	3	0.019248043	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	7	0.044912101	6	0.038496086	1
[C91] Lymphoid leukaemia	1	0.006416014	1	0.006416014	1
[C92] Myeloid leukaemia	5	0.032080072	5	0.032080072	1
[C93] Monocytic leukaemia	1	0.006416014	1	0.006416014	1
[C95] Leukaemia of unspecified cell type	1	0.006416014	0	0	1
[C97] Malignant neoplasms of independent (primary) multiple sites	1	0.006416014	0	0	1
[D32] Benign neoplasm of meninges	0	0	1	0.006416014	1
[D37] Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs	1	0.006416014	0	0	1
[D43] Neoplasm of uncertain or unknown behaviour of brain and central nervous system	1	0.006416014	0	0	1
[D44] Neoplasm of uncertain or unknown behaviour of endocrine glands	1	0.006416014	0	0	1
[D46] Myelodysplastic syndromes	2	0.012832029	3	0.019248043	1
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	1	0.006416014	1	0.006416014	1
[D48] Neoplasm of uncertain or unknown behaviour of other and unspecified sites	0	0	1	0.006416014	1
[D59] Acquired haemolytic anaemia	0	0	1	0.006416014	1
[D61] Other aplastic anaemias	1	0.006416014	0	0	1
[D75] Other diseases of blood and blood-forming organs	0	0	1	0.006416014	1
[E11] Type 2 diabetes mellitus	0	0	9	0.057744129	0.007652
[E14] Unspecified diabetes mellitus	2	0.012832029	5	0.032080072	0.449641
[E78] Disorders of lipoprotein metabolism and other lipidaemias	0	0	1	0.006416014	1
[E83] Disorders of mineral metabolism	0	0	1	0.006416014	1
[E85] Amyloidosis	1	0.006416014	1	0.006416014	1
[E87] Other disorders of fluid, electrolyte and acid-base balance	0	0	2	0.012832029	0.479486
[F01] Vascular dementia	4	0.025664057	11	0.070576158	0.121246
[F03] Unspecified dementia	11	0.070576158	14	0.089824201	0.689038
[G04] Encephalitis, myelitis and encephalomyelitis	0	0	1	0.006416014	1.00E+00

[G12] Spinal muscular atrophy and related syndromes	6	0.038496086	4	0.025664057	0.751791
[G20] Parkinson's disease	12	0.076992172	5	0.032080072	0.1455
[G23] Other degenerative diseases of basal ganglia	2	0.012832029	1	0.006416014	1
[G30] Alzheimer's disease	9	0.057744129	8	0.051328115	1
[G35] Multiple sclerosis	1	0.006416014	0	0	1
[G40] Epilepsy	2	0.012832029	0	0	0.479486
[G45] Transient cerebral ischaemic attacks and related syndromes	1	0.006416014	0	0	1
[G47] Sleep disorders	0	0	1	0.006416014	1
[G71] Primary disorders of muscles	0	0	1	0.006416014	1
[G90] Disorders of autonomic nervous system	0	0	2	0.012832029	0.479486
[G93] Other disorders of brain	0	0	1	0.006416014	1
[G95] Other diseases of spinal cord	1	0.006416014	0	0	1
[I05] Rheumatic mitral valve diseases	0	0	1	0.006416014	1
[I10] Essential (primary) hypertension	1	0.006416014	0	0	1
[I11] Hypertensive heart disease	2	0.012832029	9	0.057744129	0.070391
[I13] Hypertensive heart and renal disease	0	0	1	0.006416014	1
[I21] Acute myocardial infarction	22	0.141152316	41	0.263056589	0.023203
[I24] Other acute ischaemic heart diseases	1	0.006416014	0	0	1
[I25] Chronic ischaemic heart disease	47	0.301552675	73	0.468369049	0.02222
[I26] Pulmonary embolism	2	0.012832029	5	0.032080072	0.449641
[I27] Other pulmonary heart diseases	1	0.006416014	2	0.012832029	1
[I31] Other diseases of pericardium	1	0.006416014	0	0	1
[I35] Nonrheumatic aortic valve disorders	2	0.012832029	4	0.025664057	0.683063
[I38] Endocarditis, valve unspecified	1	0.006416014	0	0	1
[I42] Cardiomyopathy	2	0.012832029	3	0.019248043	1
[I48] Atrial fibrillation and flutter	3	0.019248043	4	0.025664057	1
[I50] Heart failure	2	0.012832029	3	0.019248043	1
[I51] Complications and ill-defined descriptions of heart disease	2	0.012832029	2	0.012832029	1
[I60] Subarachnoid haemorrhage	4	0.025664057	1	0.006416014	0.371055
[I61] Intracerebral haemorrhage	2	0.012832029	3	0.019248043	1
[I62] Other nontraumatic intracranial haemorrhage	2	0.012832029	3	0.019248043	1
[I63] Cerebral infarction	2	0.012832029	7	0.044912101	0.182359
[I64] Stroke, not specified as haemorrhage or infarction	9	0.057744129	11	0.070576158	0.823007
[I67] Other cerebrovascular diseases	1	0.006416014	1	0.006416014	1

[I71] Aortic aneurysm and dissection	4	0.025664057	5	0.032080072	1
[I80] Phlebitis and thrombophlebitis	4	0.025664057	4	0.025664057	1
[J11] Influenza, virus not identified	0	0	1	0.006416014	1
[J12] Viral pneumonia, not elsewhere classified	0	0	1	0.006416014	1
[J13] Pneumonia due to Streptococcus pneumoniae	0	0	1	0.006416014	1
[J18] Pneumonia, organism unspecified	7	0.044912101	12	0.076992172	0.358649
[J22] Unspecified acute lower respiratory infection	2	0.012832029	0	0	0.479486
[J42] Unspecified chronic bronchitis	1	0.006416014	0	0	1
[J43] Emphysema	2	0.012832029	2	0.012832029	1
[J44] Other chronic obstructive pulmonary disease	25	0.160400359	20	0.128320287	0.550697
[J45] Asthma	0	0	2	0.012832029	0.479486
[J47] Bronchiectasis	1	0.006416014	2	0.012832029	1
[J69] Pneumonitis due to solids and liquids	1	0.006416014	0	0	1
[J84] Other interstitial pulmonary diseases	10	0.064160144	18	0.115488259	0.185679
[J85] Abscess of lung and mediastinum	0	0	1	0.006416014	1
[J98] Other respiratory disorders	0	0	2	0.012832029	0.479486
[K22] Other diseases of oesophagus	1	0.006416014	0	0	1
[K26] Duodenal ulcer	1	0.006416014	1	0.006416014	1
[K27] Peptic ulcer, site unspecified	0	0	1	0.006416014	1
[K50] Crohn's disease [regional enteritis]	0	0	1	0.006416014	1
[K52] Other noninfective gastroenteritis and colitis	0	0	1	0.006416014	1
[K55] Vascular disorders of intestine	3	0.019248043	4	0.025664057	1
[K56] Paralytic ileus and intestinal obstruction without hernia	0	0	1	0.006416014	1
[K57] Diverticular disease of intestine	2	0.012832029	3	0.019248043	1.00E+00
[K65] Peritonitis	0	0	1	0.006416014	1.00E+00
[K70] Alcoholic liver disease	3	0.019248043	3	0.019248043	1
[K72] Hepatic failure, not elsewhere classified	1	0.006416014	1	0.006416014	1
[K74] Fibrosis and cirrhosis of liver	1	0.006416014	2	0.012832029	1
[K75] Other inflammatory liver diseases	3	0.019248043	1	0.006416014	0.617052
[K76] Other diseases of liver	2	0.012832029	3	0.019248043	1
[K81] Cholecystitis	1	0.006416014	3	0.019248043	6.17E-01
[K83] Other diseases of biliary tract	0	0	3	0.019248043	0.24819
[K85] Acute pancreatitis	2	0.012832029	1	0.006416014	1
[K92] Other diseases of digestive system	0	0	2	0.012832029	0.479486
[L03] Cellulitis	0	0	4	0.025664057	0.133589

[L12] Pemphigoid	1	0.006416014	0	0	1.00E+00
[L51] Erythema multiforme	0	0	1	0.006416014	1
[M06] Other rheumatoid arthritis	2	0.012832029	0	0	0.479486
[M25] Other joint disorders, not elsewhere classified	1	0.006416014	0	0	1
[M46] Other inflammatory spondylopathies	0	0	2	0.012832029	0.479486
[M86] Osteomyelitis	1	0.006416014	1	0.006416014	1
[N03] Chronic nephritic syndrome	0	0	1	0.006416014	1
[N10] Acute tubulo-interstitial nephritis	0	0	1	0.006416014	1
[N12] Tubulo-interstitial nephritis, not specified as acute or chronic	0	0	1	0.006416014	1
[N17] Acute renal failure	1	0.006416014	0	0	1
[N39] Other disorders of urinary system	2	0.012832029	4	0.025664057	0.683063
[N40] Hyperplasia of prostate	0	0	1	0.006416014	1
[R96] Other sudden death, cause unknown	0	0	1	0.006416014	1
[U071] COVID	28	0.179648402	73	0.468369049	1.16E-05
[U50] Drug resistant tuberculosis	2	0.012832029	0	0	0.479486

Sulfonylureas

Causes of death	Number of Deaths in not T2D matched controls	Percentage of Deaths in not T2D matched controls	Number of Deaths in Sulfonylureas users	Percentage of Deaths in Sulfonylureas users	p-value
[A04] Other bacterial intestinal infections	1	0.02236136	0	0	1
[A41] Other sepsis	0	0	1	0.02236136	1
[C02] Malignant neoplasm of other and unspecified parts of tongue	1	0.02236136	0	0	1
[C09] Malignant neoplasm of tonsil	1	0.02236136	0	0	1
[C15] Malignant neoplasm of oesophagus	8	0.178890877	5	0.111806798	0.578824
[C16] Malignant neoplasm of stomach	1	0.02236136	5	0.111806798	0.220516
[C18] Malignant neoplasm of colon	7	0.156529517	4	0.089445438	0.546247
[C19] Malignant neoplasm of rectosigmoid junction	1	0.02236136	2	0.044722719	1
[C20] Malignant neoplasm of rectum	2	0.044722719	3	0.067084079	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	3	0.067084079	10	0.223613596	0.095851
[C23] Malignant neoplasm of gallbladder	0	0	1	0.02236136	1
[C25] Malignant neoplasm of pancreas	3	0.067084079	22	0.491949911	0.000312

[C26] Malignant neoplasm of other and ill-defined digestive organs	1	0.02236136	2	0.044722719	1
[C34] Malignant neoplasm of bronchus and lung	16	0.357781753	17	0.380143113	1
[C37] Malignant neoplasm of thymus	0	0	1	0.02236136	1
[C43] Malignant melanoma of skin	0	0	1	0.02236136	1
[C44] Other malignant neoplasms of skin	1	0.02236136	1	0.02236136	1
[C45] Mesothelioma	2	0.044722719	0	0	0.479451
[C49] Malignant neoplasm of other connective and soft tissue	1	0.02236136	2	0.044722719	1
[C50] Malignant neoplasm of breast	3	0.067084079	6	0.134168157	0.504771
[C53] Malignant neoplasm of cervix uteri	0	0	1	0.02236136	1
[C54] Malignant neoplasm of corpus uteri	0	0	4	0.089445438	0.133528
[C56] Malignant neoplasm of ovary	4	0.089445438	4	0.089445438	1
[C61] Malignant neoplasm of prostate	12	0.268336315	12	0.268336315	1
[C64] Malignant neoplasm of kidney, except renal pelvis	2	0.044722719	5	0.111806798	0.449514
[C67] Malignant neoplasm of bladder	4	0.089445438	3	0.067084079	1
[C71] Malignant neoplasm of brain	7	0.156529517	3	0.067084079	0.342512
[C78] Secondary malignant neoplasm of respiratory and digestive organs	1	0.02236136	0	0	1
[C80] Malignant neoplasm without specification of site	5	0.111806798	7	0.156529517	0.772682
[C83] Non-follicular lymphoma	2	0.044722719	3	0.067084079	1
[C84] Mature T/NK-cell lymphomas	0	0	1	0.02236136	1
[C85] Other and unspecified types of non-Hodgkin lymphoma	2	0.044722719	4	0.089445438	0.682991
[C90] Multiple myeloma and malignant plasma cell neoplasms	3	0.067084079	4	0.089445438	1
[C91] Lymphoid leukaemia	0	0	1	0.02236136	1
[C92] Myeloid leukaemia	1	0.02236136	2	0.044722719	1
[C97] Malignant neoplasms of independent (primary) multiple sites	1	0.02236136	0	0	1
[D32] Benign neoplasm of meninges	0	0	1	0.02236136	1
[D43] Neoplasm of uncertain or unknown behaviour of brain and central nervous system	1	0.02236136	0	0	1
[D44] Neoplasm of uncertain or unknown behaviour of endocrine glands	1	0.02236136	0	0	1
[D46] Myelodysplastic syndromes	1	0.02236136	3	0.067084079	0.616996
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	0	0	1	0.02236136	1

[D48] Neoplasm of uncertain or unknown behaviour of other and unspecified sites	0	0	1	0.02236136	1
[D69] Purpura and other haemorrhagic conditions	0	0	1	0.02236136	1
[D75] Other diseases of blood and blood-forming organs	0	0	1	0.02236136	1
[E11] Type 2 diabetes mellitus	0	0	8	0.178890877	0.013287
[E87] Other disorders of fluid, electrolyte and acid-base balance	0	0	1	0.02236136	1
[F01] Vascular dementia	3	0.067084079	3	0.067084079	1.00E+00
[F03] Unspecified dementia	4	0.089445438	4	0.089445438	1
[G04] Encephalitis, myelitis and encephalomyelitis	0	0	1	0.02236136	1
[G12] Spinal muscular atrophy and related syndromes	1	0.02236136	0	0	1.00E+00
[G20] Parkinson's disease	4	0.089445438	0	0	0.133528
[G23] Other degenerative diseases of basal ganglia	1	0.02236136	1	0.02236136	1
[G30] Alzheimer's disease	3	0.067084079	3	0.067084079	1
[G31] Other degenerative diseases of nervous system, not elsewhere classified	1	0.02236136	0	0	1
[G71] Primary disorders of muscles	1	0.02236136	0	0	1
[G90] Disorders of autonomic nervous system	0	0	1	0.02236136	1
[I05] Rheumatic mitral valve diseases	0	0	1	0.02236136	1
[I11] Hypertensive heart disease	0	0	4	0.089445438	0.133528
[I13] Hypertensive heart and renal disease	0	0	2	0.044722719	0.479451
[I21] Acute myocardial infarction	6	0.134168157	18	0.402504472	0.024552
[I25] Chronic ischaemic heart disease	16	0.357781753	35	0.782647585	0.011481
[I26] Pulmonary embolism	1	0.02236136	5	0.111806798	0.220516
[I27] Other pulmonary heart diseases	1	0.02236136	3	0.067084079	0.616996
[I31] Other diseases of pericardium	1	0.02236136	0	0	1
[I34] Nonrheumatic mitral valve disorders	0	0	1	0.02236136	1
[I35] Nonrheumatic aortic valve disorders	0	0	1	0.02236136	1
[I42] Cardiomyopathy	1	0.02236136	1	0.02236136	1
[I48] Atrial fibrillation and flutter	0	0	1	0.02236136	1
[I50] Heart failure	1	0.02236136	3	0.067084079	0.616996
[I51] Complications and ill-defined descriptions of heart disease	1	0.02236136	1	0.02236136	1
[I60] Subarachnoid haemorrhage	2	0.044722719	0	0	0.479451
[I61] Intracerebral haemorrhage	0	0	2	0.044722719	0.479451
[I62] Other nontraumatic intracranial haemorrhage	1	0.02236136	0	0	1

[I63] Cerebral infarction	2	0.044722719	2	0.044722719	1
[I64] Stroke, not specified as haemorrhage or infarction	3	0.067084079	6	0.134168157	0.504771
[I67] Other cerebrovascular diseases	0	0	1	0.02236136	1.00E+00
[I71] Aortic aneurysm and dissection	1	0.02236136	0	0	1
[I80] Phlebitis and thrombophlebitis	0	0	2	0.044722719	0.479451
[J11] Influenza, virus not identified	0	0	1	0.02236136	1
[J18] Pneumonia, organism unspecified	1	0.02236136	7	0.156529517	0.076968
[J43] Emphysema	4	0.089445438	0	0	0.133528
[J44] Other chronic obstructive pulmonary disease	8	0.178890877	4	0.089445438	0.386157
[J45] Asthma	0	0	1	0.02236136	1
[J69] Pneumonitis due to solids and liquids	1	0.02236136	0	0	1
[J84] Other interstitial pulmonary diseases	3	0.067084079	5	0.111806798	0.723555
[J85] Abscess of lung and mediastinum	0	0	1	0.02236136	1
[J86] Pyothorax	0	0	1	0.02236136	1
[K50] Crohn's disease [regional enteritis]	0	0	1	0.02236136	1
[K52] Other noninfective gastroenteritis and colitis	0	0	1	0.02236136	1
[K55] Vascular disorders of intestine	2	0.044722719	1	0.02236136	1
[K57] Diverticular disease of intestine	0	0	1	0.02236136	1
[K70] Alcoholic liver disease	0	0	4	0.089445438	0.133528
[K72] Hepatic failure, not elsewhere classified	0	0	2	0.044722719	0.479451
[K74] Fibrosis and cirrhosis of liver	0	0	1	0.02236136	1
[K75] Other inflammatory liver diseases	3	0.067084079	0	0	0.248134
[K76] Other diseases of liver	0	0	2	0.044722719	0.479451
[K81] Cholecystitis	0	0	2	0.044722719	0.479451
[K83] Other diseases of biliary tract	0	0	1	0.02236136	1
[K85] Acute pancreatitis	0	0	1	0.02236136	1
[L03] Cellulitis	0	0	1	0.02236136	1
[M46] Other inflammatory spondylopathies	0	0	1	0.02236136	1
[M86] Osteomyelitis	1	0.02236136	0	0	1
[N17] Acute renal failure	1	0.02236136	0	0	1
[N39] Other disorders of urinary system	0	0	1	0.02236136	1
[R99] Other ill-defined and unspecified causes of mortality	1	0.02236136	1	0.02236136	1
[U071] COVID	4	0.089445438	28	0.626118068	4.64E-05
[U50] Drug resistant tuberculosis	1	0.02236136	0	0	1

DPP4I

Causes of death	Number of Deaths in not T2D matched controls	Percentage of Deaths in not T2D matched controls	Number of Deaths in DPP4I users	Percentage of Deaths in DPP4I users	p-value
[A04] Other bacterial intestinal infections	1	0.027277687	0	0	1
[C09] Malignant neoplasm of tonsil	2	0.054555374	0	0	0.47944
[C13] Malignant neoplasm of hypopharynx	1	0.027277687	0	0	1
[C15] Malignant neoplasm of oesophagus	9	0.245499182	2	0.054555374	0.07023
[C16] Malignant neoplasm of stomach	2	0.054555374	1	0.027277687	1
[C17] Malignant neoplasm of small intestine	2	0.054555374	0	0	0.47944
[C18] Malignant neoplasm of colon	2	0.054555374	3	0.081833061	1
[C19] Malignant neoplasm of rectosigmoid junction	1	0.027277687	1	0.027277687	1
[C20] Malignant neoplasm of rectum	1	0.027277687	2	0.054555374	1
[C21] Malignant neoplasm of anus and anal canal	1	0.027277687	0	0	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	3	0.081833061	3	0.081833061	1
[C23] Malignant neoplasm of gallbladder	1	0.027277687	0	0	1
[C24] Malignant neoplasm of other and unspecified parts of biliary tract	1	0.027277687	0	0	1
[C25] Malignant neoplasm of pancreas	5	0.136388434	9	0.245499182	0.422235
[C26] Malignant neoplasm of other and ill-defined digestive organs	1	0.027277687	1	0.027277687	1
[C34] Malignant neoplasm of bronchus and lung	17	0.463720676	11	0.300054555	0.343781
[C44] Other malignant neoplasms of skin	0	0	1	0.027277687	1
[C45] Mesothelioma	1	0.027277687	0	0	1
[C49] Malignant neoplasm of other connective and soft tissue	3	0.081833061	1	0.027277687	0.616979
[C50] Malignant neoplasm of breast	6	0.163666121	2	0.054555374	0.288581
[C54] Malignant neoplasm of corpus uteri	0	0	1	0.027277687	1
[C56] Malignant neoplasm of ovary	1	0.027277687	1	0.027277687	1
[C60] Malignant neoplasm of penis	0	0	1	0.027277687	1
[C61] Malignant neoplasm of prostate	6	0.163666121	3	0.081833061	0.504723
[C64] Malignant neoplasm of kidney, except renal pelvis	2	0.054555374	5	0.136388434	0.449475
[C67] Malignant neoplasm of bladder	7	0.190943808	1	0.027277687	0.076939
[C71] Malignant neoplasm of brain	4	0.109110747	0	0	0.133508
[C73] Malignant neoplasm of thyroid gland	0	0	1	0.027277687	1
[C76] Malignant neoplasm of other and ill-defined sites	1	0.027277687	0	0	1

[C78] Secondary malignant neoplasm of respiratory and digestive organs	1	0.027277687	0	0	1
[C80] Malignant neoplasm without specification of site	4	0.109110747	1	0.027277687	0.37093
[C83] Non-follicular lymphoma	2	0.054555374	0	0	0.47944
[C90] Multiple myeloma and malignant plasma cell neoplasms	2	0.054555374	1	0.027277687	1
[C92] Myeloid leukaemia	1	0.027277687	2	0.054555374	1
[C95] Leukaemia of unspecified cell type	1	0.027277687	0	0	1
[C97] Malignant neoplasms of independent (primary) multiple sites	1	0.027277687	0	0	1
[D32] Benign neoplasm of meninges	0	0	1	0.027277687	1
[D43] Neoplasm of uncertain or unknown behaviour of brain and central nervous system	2	0.054555374	0	0	0.47944
[D46] Myelodysplastic syndromes	1	0.027277687	1	0.027277687	1
[D84] Other immunodeficiencies	0	0	1	0.027277687	1
[E11] Type 2 diabetes mellitus	0	0	3	0.081833061	0.248116
[E14] Unspecified diabetes mellitus	0	0	1	0.027277687	1
[F01] Vascular dementia	1	0.027277687	3	0.081833061	0.616979
[F03] Unspecified dementia	3	0.081833061	2	0.054555374	1
[G04] Encephalitis, myelitis and encephalomyelitis	0	0	1	0.027277687	1
[G12] Spinal muscular atrophy and related syndromes	0	0	1	0.027277687	1
[G20] Parkinson's disease	4	0.109110747	0	0	1.34E-01
[G23] Other degenerative diseases of basal ganglia	1	0.027277687	0	0	1
[G30] Alzheimer's disease	2	0.054555374	3	0.081833061	1
[G35] Multiple sclerosis	1	0.027277687	0	0	1.00E+00
[G45] Transient cerebral ischaemic attacks and related syndromes	1	0.027277687	0	0	1
[G71] Primary disorders of muscles	1	0.027277687	0	0	1
[I05] Rheumatic mitral valve diseases	0	0	1	0.027277687	1
[I11] Hypertensive heart disease	1	0.027277687	3	0.081833061	0.616979
[I21] Acute myocardial infarction	8	0.218221495	14	0.381887616	0.285698
[I25] Chronic ischaemic heart disease	14	0.381887616	13	0.354609929	1
[I26] Pulmonary embolism	2	0.054555374	0	0	0.47944
[I27] Other pulmonary heart diseases	1	0.027277687	0	0	1
[I31] Other diseases of pericardium	1	0.027277687	0	0	1
[I35] Nonrheumatic aortic valve disorders	0	0	1	0.027277687	1
[I42] Cardiomyopathy	2	0.054555374	1	0.027277687	1

[I48] Atrial fibrillation and flutter	1	0.027277687	3	0.081833061	0.616979
[I50] Heart failure	2	0.054555374	2	0.054555374	1
[I51] Complications and ill-defined descriptions of heart disease	1	0.027277687	1	0.027277687	1
[I60] Subarachnoid haemorrhage	2	0.054555374	0	0	0.47944
[I61] Intracerebral haemorrhage	1	0.027277687	0	0	1
[I62] Other nontraumatic intracranial haemorrhage	0	0	1	0.027277687	1
[I63] Cerebral infarction	1	0.027277687	1	0.027277687	1
[I64] Stroke, not specified as haemorrhage or infarction	2	0.054555374	5	0.136388434	0.449475
[I67] Other cerebrovascular diseases	1	0.027277687	1	0.027277687	1
[I71] Aortic aneurysm and dissection	1	0.027277687	0	0	1
[I73] Other peripheral vascular diseases	1	0.027277687	1	0.027277687	1
[I80] Phlebitis and thrombophlebitis	1	0.027277687	0	0	1
[J12] Viral pneumonia, not elsewhere classified	0	0	1	0.027277687	1
[J13] Pneumonia due to Streptococcus pneumoniae	0	0	1	0.027277687	1
[J18] Pneumonia, organism unspecified	2	0.054555374	4	0.109110747	6.83E-01
[J22] Unspecified acute lower respiratory infection	1	0.027277687	0	0	1
[J43] Emphysema	1	0.027277687	1	0.027277687	1
[J44] Other chronic obstructive pulmonary disease	6	0.163666121	0	0	0.041144
[J69] Pneumonitis due to solids and liquids	1	0.027277687	0	0	1
[J84] Other interstitial pulmonary diseases	3	0.081833061	3	0.081833061	1
[J98] Other respiratory disorders	0	0	1	0.027277687	1
[K55] Vascular disorders of intestine	1	0.027277687	1	0.027277687	1
[K57] Diverticular disease of intestine	1	0.027277687	1	0.027277687	1
[K70] Alcoholic liver disease	1	0.027277687	2	0.054555374	1
[K72] Hepatic failure, not elsewhere classified	0	0	1	0.027277687	1
[K75] Other inflammatory liver diseases	4	0.109110747	0	0	0.133508
[K76] Other diseases of liver	0	0	1	0.027277687	1
[K81] Cholecystitis	2	0.054555374	1	0.027277687	1
[K92] Other diseases of digestive system	0	0	1	0.027277687	1
[L51] Erythema multiforme	0	0	1	0.027277687	1
[M34] Systemic sclerosis	1	0.027277687	0	0	1
[N18] Chronic kidney disease	0	0	1	0.027277687	1
[N39] Other disorders of urinary system	1	0.027277687	2	0.054555374	1
[N40] Hyperplasia of prostate	0	0	1	0.027277687	1

[R99] Other ill-defined and unspecified causes of mortality	1	0.027277687	0	0	1
[U071] COVID	9	0.245499182	19	0.51827605	0.088363

Long/Interm.-Acting Insulins

Causes of death	Number of Deaths in not T2D matched controls	Percentage of Deaths in not T2D matched controls	Number of Deaths in Long/Interm.-Acting Insulins users	Percentage of Deaths in Long/Interm.-Acting Insulins users	p-value
[A41] Other sepsis	0	0	1	0.035087719	1
[C06] Malignant neoplasm of other and unspecified parts of mouth	0	0	1	0.035087719	1
[C09] Malignant neoplasm of tonsil	1	0.035087719	0	0	1
[C14] Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx	0	0	1	0.035087719	1
[C15] Malignant neoplasm of oesophagus	3	0.105263158	3	0.105263158	1
[C16] Malignant neoplasm of stomach	1	0.035087719	1	0.035087719	1
[C18] Malignant neoplasm of colon	5	0.175438596	4	0.140350877	1
[C19] Malignant neoplasm of rectosigmoid junction	1	0.035087719	1	0.035087719	1
[C20] Malignant neoplasm of rectum	1	0.035087719	1	0.035087719	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	1	0.035087719	9	0.315789474	0.026723
[C23] Malignant neoplasm of gallbladder	1	0.035087719	1	0.035087719	1
[C24] Malignant neoplasm of other and unspecified parts of biliary tract	0	0	3	0.105263158	0.248089
[C25] Malignant neoplasm of pancreas	1	0.035087719	15	0.526315789	0.001136
[C26] Malignant neoplasm of other and ill-defined digestive organs	3	0.105263158	1	0.035087719	0.616951
[C34] Malignant neoplasm of bronchus and lung	13	0.456140351	6	0.210526316	0.167958
[C43] Malignant melanoma of skin	2	0.070175439	0	0	0.479423
[C44] Other malignant neoplasms of skin	1	0.035087719	1	0.035087719	1
[C50] Malignant neoplasm of breast	1	0.035087719	4	0.140350877	0.370883
[C53] Malignant neoplasm of cervix uteri	1	0.035087719	1	0.035087719	1
[C55] Malignant neoplasm of uterus, part unspecified	0	0	1	0.035087719	1
[C56] Malignant neoplasm of ovary	5	0.175438596	1	0.035087719	0.220428
[C61] Malignant neoplasm of prostate	5	0.175438596	7	0.245614035	0.772597

[C64] Malignant neoplasm of kidney, except renal pelvis	2	0.070175439	3	0.105263158	1
[C67] Malignant neoplasm of bladder	3	0.105263158	2	0.070175439	1
[C68] Malignant neoplasm of other and unspecified urinary organs	2	0.070175439	1	0.035087719	1
[C71] Malignant neoplasm of brain	2	0.070175439	0	0	0.479423
[C80] Malignant neoplasm without specification of site	6	0.210526316	4	0.140350877	0.751619
[C81] Hodgkin lymphoma	0	0	1	0.035087719	1
[C82] Follicular lymphoma	1	0.035087719	0	0	1
[C83] Non-follicular lymphoma	1	0.035087719	1	0.035087719	1
[C85] Other and unspecified types of non-Hodgkin lymphoma	1	0.035087719	0	0	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	2	0.070175439	4	0.140350877	0.682934
[C91] Lymphoid leukaemia	1	0.035087719	2	0.070175439	1
[C92] Myeloid leukaemia	1	0.035087719	0	0	1
[C93] Monocytic leukaemia	1	0.035087719	0	0	1
[D37] Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs	0	0	1	0.035087719	1
[D41] Neoplasm of uncertain or unknown behaviour of urinary organs	0	0	1	0.035087719	1
[D46] Myelodysplastic syndromes	0	0	1	0.035087719	1
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	1	0.035087719	0	0	1
[D64] Other anaemias	0	0	1	0.035087719	1
[E11] Type 2 diabetes mellitus	0	0	6	0.210526316	0.04112
[E14] Unspecified diabetes mellitus	1	0.035087719	5	0.175438596	0.220428
[E16] Other disorders of pancreatic internal secretion	0	0	2	0.070175439	0.479423
[E78] Disorders of lipoprotein metabolism and other lipidaemias	0	0	1	0.035087719	1
[E83] Disorders of mineral metabolism	0	0	1	0.035087719	1
[F01] Vascular dementia	1	0.035087719	5	0.175438596	0.220428
[F03] Unspecified dementia	2	0.070175439	2	0.070175439	1.00E+00
[G04] Encephalitis, myelitis and encephalomyelitis	0	0	1	0.035087719	1
[G12] Spinal muscular atrophy and related syndromes	1	0.035087719	1	0.035087719	1
[G20] Parkinson's disease	3	0.105263158	0	0	2.48E-01
[G30] Alzheimer's disease	3	0.105263158	3	0.105263158	1

[G35] Multiple sclerosis	1	0.035087719	0	0	1
[G47] Sleep disorders	0	0	1	0.035087719	1
[G90] Disorders of autonomic nervous system	0	0	2	0.070175439	0.479423
[G95] Other diseases of spinal cord	1	0.035087719	0	0	1
[I11] Hypertensive heart disease	0	0	3	0.105263158	0.248089
[I13] Hypertensive heart and renal disease	0	0	1	0.035087719	1
[I21] Acute myocardial infarction	4	0.140350877	19	0.666666667	0.003443
[I25] Chronic ischaemic heart disease	12	0.421052632	22	0.771929825	0.121595
[I26] Pulmonary embolism	0	0	1	0.035087719	1
[I27] Other pulmonary heart diseases	0	0	1	0.035087719	1
[I38] Endocarditis, valve unspecified	1	0.035087719	0	0	1
[I42] Cardiomyopathy	1	0.035087719	1	0.035087719	1
[I48] Atrial fibrillation and flutter	1	0.035087719	0	0	1
[I50] Heart failure	0	0	5	0.175438596	0.073512
[I51] Complications and ill-defined descriptions of heart disease	0	0	1	0.035087719	1
[I60] Subarachnoid haemorrhage	2	0.070175439	0	0	0.479423
[I61] Intracerebral haemorrhage	1	0.035087719	0	0	1
[I62] Other nontraumatic intracranial haemorrhage	0	0	1	0.035087719	1
[I63] Cerebral infarction	0	0	1	0.035087719	1
[I64] Stroke, not specified as haemorrhage or infarction	1	0.035087719	7	0.245614035	0.076892
[I67] Other cerebrovascular diseases	2	0.070175439	4	0.140350877	0.682934
[I71] Aortic aneurysm and dissection	1	0.035087719	0	0	1
[I80] Phlebitis and thrombophlebitis	1	0.035087719	0	0	1
[J11] Influenza, virus not identified	0	0	1	0.035087719	1
[J18] Pneumonia, organism unspecified	4	0.140350877	6	0.210526316	7.52E-01
[J22] Unspecified acute lower respiratory infection	1	0.035087719	0	0	1
[J44] Other chronic obstructive pulmonary disease	7	0.245614035	7	0.245614035	1
[J45] Asthma	0	0	2	0.070175439	0.479423
[J47] Bronchiectasis	0	0	1	0.035087719	1
[J60] Coalworker's pneumoconiosis	0	0	1	0.035087719	1
[J84] Other interstitial pulmonary diseases	3	0.105263158	5	0.175438596	0.723487
[J98] Other respiratory disorders	0	0	1	0.035087719	1
[K20] Oesophagitis	0	0	1	0.035087719	1
[K27] Peptic ulcer, site unspecified	0	0	1	0.035087719	1
[K29] Gastritis and duodenitis	0	0	1	0.035087719	1

[K55] Vascular disorders of intestine	1	0.035087719	1	0.035087719	1
[K70] Alcoholic liver disease	1	0.035087719	3	0.105263158	0.616951
[K74] Fibrosis and cirrhosis of liver	0	0	3	0.105263158	0.248089
[K75] Other inflammatory liver diseases	2	0.070175439	2	0.070175439	1
[K81] Cholecystitis	0	0	1	0.035087719	1
[K86] Other diseases of pancreas	0	0	1	0.035087719	1
[K92] Other diseases of digestive system	0	0	1	0.035087719	1
[L03] Cellulitis	0	0	1	0.035087719	1
[M25] Other joint disorders, not elsewhere classified	0	0	1	0.035087719	1
[M34] Systemic sclerosis	1	0.035087719	0	0	1
[M86] Osteomyelitis	0	0	1	0.035087719	1
[N10] Acute tubulo-interstitial nephritis	0	0	1	0.035087719	1
[N18] Chronic kidney disease	0	0	2	0.070175439	0.479423
[N30] Cystitis	0	0	1	0.035087719	1
[N39] Other disorders of urinary system	0	0	1	0.035087719	1
[U071] COVID	3	0.105263158	22	0.771929825	0.000309

SLGT2I

Causes of death	Number of Deaths in not T2D matched controls	Percentage of Deaths in not T2D matched controls	Number of Deaths in SLGT2 I users	Percentage of Deaths in SLGT2I users	p-value
[A16] Respiratory tuberculosis, not confirmed bacteriologically or histologically	1	0.043497173	0	0	1
[C15] Malignant neoplasm of oesophagus	5	0.217485863	0	0	0.073482
[C16] Malignant neoplasm of stomach	2	0.086994345	0	0	0.479405
[C18] Malignant neoplasm of colon	3	0.130491518	0	0	0.248059
[C19] Malignant neoplasm of rectosigmoid junction	1	0.043497173	0	0	1
[C20] Malignant neoplasm of rectum	1	0.043497173	1	0.043497173	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	1	0.043497173	1	0.043497173	1
[C23] Malignant neoplasm of gallbladder	1	0.043497173	1	0.043497173	1
[C24] Malignant neoplasm of other and unspecified parts of biliary tract	1	0.043497173	0	0	1
[C25] Malignant neoplasm of pancreas	0	0	3	0.130491518	0.248059
[C26] Malignant neoplasm of other and ill-defined digestive organs	0	0	1	0.043497173	1
[C34] Malignant neoplasm of bronchus and lung	3	0.130491518	1	0.043497173	0.616922

[C45] Mesothelioma	2	0.086994345	0	0	0.479405
[C55] Malignant neoplasm of uterus, part unspecified	0	0	1	0.043497173	1
[C56] Malignant neoplasm of ovary	2	0.086994345	0	0	0.479405
[C61] Malignant neoplasm of prostate	3	0.130491518	1	0.043497173	0.616922
[C64] Malignant neoplasm of kidney, except renal pelvis	1	0.043497173	0	0	1
[C67] Malignant neoplasm of bladder	2	0.086994345	0	0	0.479405
[C71] Malignant neoplasm of brain	3	0.130491518	0	0	0.248059
[C76] Malignant neoplasm of other and ill-defined sites	1	0.043497173	0	0	1
[C80] Malignant neoplasm without specification of site	1	0.043497173	2	0.086994345	1
[C85] Other and unspecified types of non-Hodgkin lymphoma	1	0.043497173	0	0	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	2	0.086994345	0	0	0.479405
[D32] Benign neoplasm of meninges	0	0	1	0.043497173	1
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	0	0	1	0.043497173	1
[E14] Unspecified diabetes mellitus	1	0.043497173	1	0.043497173	1
[F03] Unspecified dementia	1	0.043497173	0	0	1
[G20] Parkinson's disease	3	0.130491518	0	0	0.248059
[I11] Hypertensive heart disease	0	0	2	0.086994345	0.479405
[I21] Acute myocardial infarction	2	0.086994345	0	0	0.479405
[I25] Chronic ischaemic heart disease	7	0.304480209	7	0.304480209	1
[I31] Other diseases of pericardium	1	0.043497173	0	0	1
[I60] Subarachnoid haemorrhage	2	0.086994345	0	0	0.479405
[I63] Cerebral infarction	1	0.043497173	0	0	1
[I71] Aortic aneurysm and dissection	1	0.043497173	0	0	1
[J18] Pneumonia, organism unspecified	1	0.043497173	2	0.086994345	1
[J43] Emphysema	2	0.086994345	0	0	0.479405
[J44] Other chronic obstructive pulmonary disease	2	0.086994345	0	0	0.479405
[K55] Vascular disorders of intestine	0	0	1	0.043497173	1
[M86] Osteomyelitis	0	0	1	0.043497173	1
[U071] COVID	3	0.130491518	9	0.391474554	0.148384

GLP1RA

Causes of death	Number of Deaths in not T2D matched controls	Percentage of Deaths in not T2D matched controls	Number of Deaths in GLP1R A users	Percentage of Deaths in GLP1RA users	p-value
[A16] Respiratory tuberculosis, not confirmed bacteriologically or histologically	1	0.088967972	0	0	1
[C10] Malignant neoplasm of oropharynx	1	0.088967972	0	0	1
[C15] Malignant neoplasm of oesophagus	2	0.177935943	0	0	0.479305
[C16] Malignant neoplasm of stomach	1	0.088967972	1	0.088967972	1
[C18] Malignant neoplasm of colon	1	0.088967972	0	0	1
[C20] Malignant neoplasm of rectum	1	0.088967972	1	0.088967972	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	1	0.088967972	2	0.177935943	1
[C25] Malignant neoplasm of pancreas	3	0.266903915	0	0	0.247897
[C34] Malignant neoplasm of bronchus and lung	3	0.266903915	2	0.177935943	1
[C49] Malignant neoplasm of other connective and soft tissue	0	0	1	0.088967972	1
[C50] Malignant neoplasm of breast	1	0.088967972	0	0	1
[C53] Malignant neoplasm of cervix uteri	1	0.088967972	0	0	1
[C55] Malignant neoplasm of uterus, part unspecified	0	0	1	0.088967972	1
[C56] Malignant neoplasm of ovary	1	0.088967972	0	0	1
[C61] Malignant neoplasm of prostate	1	0.088967972	1	0.088967972	1
[C64] Malignant neoplasm of kidney, except renal pelvis	0	0	1	0.088967972	1
[C67] Malignant neoplasm of bladder	0	0	1	0.088967972	1
[C71] Malignant neoplasm of brain	4	0.355871886	0	0	0.133269
[C80] Malignant neoplasm without specification of site	1	0.088967972	1	0.088967972	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	1	0.088967972	0	0	1
[E14] Unspecified diabetes mellitus	0	0	1	0.088967972	1
[E83] Disorders of mineral metabolism	0	0	1	0.088967972	1
[G20] Parkinson's disease	1	0.088967972	0	0	1
[G40] Epilepsy	1	0.088967972	0	0	1
[I21] Acute myocardial infarction	1	0.088967972	1	0.088967972	1
[I25] Chronic ischaemic heart disease	4	0.355871886	5	0.444839858	1
[I42] Cardiomyopathy	0	0	1	0.088967972	1
[I60] Subarachnoid haemorrhage	1	0.088967972	0	0	1
[I64] Stroke, not specified as haemorrhage or infarction	0	0	1	0.088967972	1

[I71] Aortic aneurysm and dissection	1	0.088967972	0	0	1
[I80] Phlebitis and thrombophlebitis	1	0.088967972	0	0	1
[J12] Viral pneumonia, not elsewhere classified	0	0	1	0.088967972	1
[J44] Other chronic obstructive pulmonary disease	1	0.088967972	0	0	1
[J84] Other interstitial pulmonary diseases	1	0.088967972	3	0.266903915	0.616761
[J85] Abscess of lung and mediastinum	0	0	1	0.088967972	1
[K81] Cholecystitis	0	0	1	0.088967972	1
[M25] Other joint disorders, not elsewhere classified	0	0	1	0.088967972	1
[M86] Osteomyelitis	0	0	1	0.088967972	1
[U071] COVID	1	0.088967972	6	0.533807829	0.129971

Short-Acting Insulins

Causes of death	Number of Deaths in not T2D matched controls	Percentage of Deaths in not T2D matched controls	Number of Deaths in Short-Acting Insulins users	Percentage of Deaths in Short-Acting Insulins users	p-value
[A41] Other sepsis	0	0	1	0.094339623	1
[C14] Malignant neoplasm of other and ill-defined sites in the lip, oral cavity and pharynx	0	0	1	0.094339623	1
[C15] Malignant neoplasm of oesophagus	0	0	1	0.094339623	1
[C20] Malignant neoplasm of rectum	0	0	2	0.188679245	0.479293
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	0	0	3	0.283018868	0.247878
[C25] Malignant neoplasm of pancreas	1	0.094339623	4	0.377358491	0.370529
[C26] Malignant neoplasm of other and ill-defined digestive organs	0	0	1	0.094339623	1
[C34] Malignant neoplasm of bronchus and lung	4	0.377358491	1	0.094339623	0.370529
[C43] Malignant melanoma of skin	1	0.094339623	0	0	1
[C49] Malignant neoplasm of other connective and soft tissue	0	0	1	0.094339623	1
[C53] Malignant neoplasm of cervix uteri	1	0.094339623	0	0	1
[C55] Malignant neoplasm of uterus, part unspecified	0	0	1	0.094339623	1
[C56] Malignant neoplasm of ovary	2	0.188679245	1	0.094339623	1
[C61] Malignant neoplasm of prostate	1	0.094339623	1	0.094339623	1
[C64] Malignant neoplasm of kidney, except renal pelvis	1	0.094339623	0	0	1

[C67] Malignant neoplasm of bladder	1	0.094339623	2	0.188679245	1
[C68] Malignant neoplasm of other and unspecified urinary organs	1	0.094339623	0	0	1
[C80] Malignant neoplasm without specification of site	3	0.283018868	2	0.188679245	1
[C82] Follicular lymphoma	1	0.094339623	0	0	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	0	0	1	0.094339623	1
[D37] Neoplasm of uncertain or unknown behaviour of oral cavity and digestive organs	0	0	1	0.094339623	1
[D41] Neoplasm of uncertain or unknown behaviour of urinary organs	0	0	1	0.094339623	1
[D47] Other neoplasms of uncertain or unknown behaviour of lymphoid, haematopoietic and related tissue	1	0.094339623	0	0	1
[E11] Type 2 diabetes mellitus	0	0	3	0.283018868	0.247878
[E14] Unspecified diabetes mellitus	0	0	1	0.094339623	1
[E83] Disorders of mineral metabolism	0	0	1	0.094339623	1
[F01] Vascular dementia	0	0	2	0.188679245	0.479293
[G04] Encephalitis, myelitis and encephalomyelitis	0	0	1	0.094339623	1
[G12] Spinal muscular atrophy and related syndromes	1	0.094339623	1	0.094339623	1
[G20] Parkinson's disease	2	0.188679245	0	0	0.479293
[G30] Alzheimer's disease	0	0	1	0.094339623	1
[I21] Acute myocardial infarction	1	0.094339623	6	0.566037736	0.129935
[I25] Chronic ischaemic heart disease	1	0.094339623	11	1.037735849	0.009175
[I26] Pulmonary embolism	0	0	1	0.094339623	1
[I38] Endocarditis, valve unspecified	1	0.094339623	0	0	1
[I48] Atrial fibrillation and flutter	1	0.094339623	0	0	1
[I50] Heart failure	0	0	2	0.188679245	0.479293
[I61] Intracerebral haemorrhage	0	0	1	0.094339623	1
[I62] Other nontraumatic intracranial haemorrhage	0	0	2	0.188679245	0.479293
[I64] Stroke, not specified as haemorrhage or infarction	0	0	2	0.188679245	0.479293
[I67] Other cerebrovascular diseases	1	0.094339623	0	0	1
[J11] Influenza, virus not identified	0	0	1	0.094339623	1
[J18] Pneumonia, organism unspecified	1	0.094339623	2	0.188679245	1
[J43] Emphysema	0	0	1	0.094339623	1
[J44] Other chronic obstructive pulmonary disease	0	0	1	0.094339623	1

[J45] Asthma	0	0	2	0.188679245	0.479293
[J84] Other interstitial pulmonary diseases	1	0.094339623	2	0.188679245	1
[K20] Oesophagitis	0	0	1	0.094339623	1
[K70] Alcoholic liver disease	0	0	1	0.094339623	1
[K74] Fibrosis and cirrhosis of liver	0	0	2	0.188679245	0.479293
[K75] Other inflammatory liver diseases	0	0	1	0.094339623	1
[K86] Other diseases of pancreas	0	0	1	0.094339623	1
[M25] Other joint disorders, not elsewhere classified	0	0	1	0.094339623	1
[U071] COVID	2	0.188679245	6	0.566037736	0.287933

Thiazolidinediones

Causes of death	Number of Deaths in not T2D matched controls	Percentage of Deaths in not T2D matched controls	Number of Deaths in Thiazolidinediones users	Percentage of Deaths in Thiazolidinediones users	p-value
[C15] Malignant neoplasm of oesophagus	1	0.208768267	1	0.208768267	1
[C22] Malignant neoplasm of liver and intrahepatic bile ducts	1	0.208768267	1	0.208768267	1
[C25] Malignant neoplasm of pancreas	0	0	4	0.835073069	0.132803
[C26] Malignant neoplasm of other and ill-defined digestive organs	0	0	1	0.208768267	1
[C34] Malignant neoplasm of bronchus and lung	0	0	3	0.626304802	0.247471
[C45] Mesothelioma	1	0.208768267	0	0	1
[C50] Malignant neoplasm of breast	0	0	1	0.208768267	1
[C54] Malignant neoplasm of corpus uteri	0	0	1	0.208768267	1
[C56] Malignant neoplasm of ovary	1	0.208768267	0	0	1
[C61] Malignant neoplasm of prostate	0	0	3	0.626304802	0.247471
[C67] Malignant neoplasm of bladder	0	0	1	0.208768267	1
[C73] Malignant neoplasm of thyroid gland	1	0.208768267	0	0	1
[C80] Malignant neoplasm without specification of site	0	0	1	0.208768267	1
[C90] Multiple myeloma and malignant plasma cell neoplasms	1	0.208768267	0	0	1
[C92] Myeloid leukaemia	1	0.208768267	0	0	1
[E11] Type 2 diabetes mellitus	0	0	1	0.208768267	1
[G12] Spinal muscular atrophy and related syndromes	1	0.208768267	0	0	1
[G30] Alzheimer's disease	1	0.208768267	0	0	1

[I21] Acute myocardial infarction	1	0.208768267	2	0.417536534	1
[I25] Chronic ischaemic heart disease	1	0.208768267	2	0.417536534	1
[I26] Pulmonary embolism	0	0	1	0.208768267	1
[I50] Heart failure	0	0	1	0.208768267	1
[I51] Complications and ill-defined descriptions of heart disease	0	0	1	0.208768267	1
[I80] Phlebitis and thrombophlebitis	0	0	1	0.208768267	1
[J44] Other chronic obstructive pulmonary disease	0	0	1	0.208768267	1
[K70] Alcoholic liver disease	0	0	1	0.208768267	1
[K75] Other inflammatory liver diseases	0	0	1	0.208768267	1
[K92] Other diseases of digestive system	0	0	1	0.208768267	1
[U071] COVID	0	0	3	0.626304802	0.247471