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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplementary information

Further details on the National Diabetes Audit

The National Diabetes Audit (NDA) collates data on nearly all people with diagnosed diabetes registered with a healthcare provider in England. Individuals are included if they have a valid code for diabetes mellitus (excluding gestational diabetes) in their electronic health record. Diagnosis of diabetes is based on usual clinical practice in England, which follows guidance from the National Institute for Health and Clinical Excellence that recommends a diagnosis based on a HbA1c persistently above 48mmol/mol; a 2-hour post 75g glucose load ≥11.1 mmol/l; a fasting glucose ≥7.0 mmol/l; or a random plasma glucose ≥11.1 mmol/l. Demographic and clinical data are extracted from general practice electronic clinical systems using the General Practice Extraction Service (a national centralised data collection service). This is supplemented by data submitted by specialist diabetes services. Each person with diabetes is identified by a unique National Health Service (NHS) number.

Data from general practices in England is available from 1st April 2003 to 31st December 2019. For the period 1st January 2018 to 31st March 2019, data was collected from 98% of general practices in England and 113 specialist diabetes services.

Data on demographic characteristics and clinical markers of cardiovascular risk and co-morbidity are extracted from clinical systems. This clinical record data is linked to the Hospital Episode Statistics for data on hospital admissions and discharge diagnoses and to the Office of National Statistics data for dates and causes of death. The type of diabetes was based on the coded diagnostic information recorded in clinical records. Where there were inconsistencies in the type of diabetes recorded over time or in different settings, the code most recently assigned by a specialist service was used, if available; or the most recently recorded code noted in primary care, if not.

The legal basis for the NDA data collection and linkage is a direction from NHS England to NHS Digital according to section 254 of the Health and Social Care Act for England 2012 [NHS Digital.

Directions and Data Provision Notices. Available at: https://digital.nhs.uk/about-nhs-digital/corporate-information-and-documents/directions-and-data-provision-notices. Accessed on July 13, 2020]. Data are not extracted if the person has withdrawn their permission to use their record for secondary analysis, which is estimated to apply to 2.6% of records.

NHS England and NHS Digital are the joint data controllers. Data linkage and analysis are undertaken within NHS Digital. In March 2020, the Secretary of State for Health and Social Care used powers under the UK Health Service (Control of Patient Information) Regulations 2002 to require organisations to process confidential patient information for the purposes of protecting public health, providing healthcare services to the public, and monitoring and managing the COVID-19 outbreak and incidents of exposure. Ethnics approval was not required for this analysis.

Data from the NDA can be requested through the NHS Digital DARS process. For further information please contact diabetes@nhs.net.

Table S1: Univariable hazard ratios

Variable	HR	95% LCI	95% UCI
Sex			
Female	1	-	-
Male	1.193	1.152	1.234
Age (years)			
<40	0.17	0.12	0.241
40 - 44	0.176	0.127	0.245
45 - 49	0.285	0.233	0.349
50 - 54	0.398	0.344	0.46
55 - 59	0.517	0.46	0.581
60 - 64	0.788	0.714	0.869
65 - 69	1	-	-
70 - 74	1.466	1.351	1.591
75 - 79	2.542	2.354	2.746
80+	5.836	5.452	6.248
Deprivation			
Most deprived	1.183	1.119	1.251
2nd most deprived	1.165	1.1	1.233
3rd most deprived	1.041	0.981	1.105
2nd least deprived	1.019	0.959	1.084
Least deprived	1	-	-
Unknown	1.727	0.956	3.117
Region			
London	1.371	1.292	1.455
South West	0.603	0.553	0.658
South East	1	-	-
Midlands	1.065	1.003	1.131
East	0.952	0.886	1.022
North West	1.221	1.145	1.301
North East & Yorkshire	1.049	0.985	1.118
Unknown	1.675	0.926	3.031
Ethnicity			
White	1	-	-
Mixed	1.01	0.861	1.184
Asian	0.782	0.741	0.825
Black	1.419	1.328	1.516
Other	0.831	0.721	0.958
Unknown	0.687	0.647	0.729
HbA1c (mmol/mol)			
<48	1.306	1.24	1.376
48 - <54 [6.5% - <7.1%]	1	-	-
54 - <59 [7.1% - <7.5%]	1.011	0.947	1.08
59 - <75 [7.5% - <9.0%]	1.157	1.094	1.224
75 - <86 [9.0% - <10.0%]	1.196	1.101	1.299
86+	1.216	1.123	1.315
Unknown	1.684	1.586	1.79
Diabetes duration (years)			
< 1	0.859	0.669	1.103
1 - 2	0.833	0.763	0.909
3 - 4	1	-	-
5 - 9	1.186	1.106	1.272
10 - 14	1.631	1.522	1.747
15 - 19	2.495	2.329	2.673
20+	3.59	3.345	3.854
eGFR (ml/min*1.73m^2)			
90+	1	-	-
60 - <90	1.654	1.576	1.736
45 - <60	3.706	3.509	3.914
30 - <45	6.186	5.836	6.556
15 - <30	9.132	8.442	9.879
<15	16.309	14.638	18.171
Unknown	1.79	1.582	2.025

Body mass index (kg/ m^2)			
<20	3.983	3.67	4.324
20 - <25	1.726	1.644	1.812
25 - <30	1	-	-
30 - <35	0.847	0.806	0.891
35 - <40	0.789	0.739	0.841
40+	0.823	0.763	0.887
Unknown	2.078	1.956	2.206
Hypertension			
≤ 140 mmHg	1	-	-
> 140 mmHg	1.148	1.099	1.2
Unknown	0.813	0.76	0.87
Cholesterol (mmol/l)			
<5 [193 mg/dl]	1	-	-
5+	0.819	0.779	0.861
Unknown	1.706	1.637	1.778
Smoking			
Current smoker	0.459	0.426	0.495
Ex - smoker	1.286	1.241	1.332
Non - smoker, history unknown	1.488	1.333	1.66
Never smoked	1	-	-
Unknown	2.275	1.524	3.396
History of cardiovascular disease			
No	1	-	-
Yes	3.509	3.393	3.63
Statins			
No	1	-	-
Yes	0.819	0.79	0.85
Antihypertensive medication			
No	1	-	-
Yes	2.362	2.24	2.491
Number of glucose-lowering drug classes			
0	1	-	-
1	0.863	0.828	0.9
2	0.836	0.797	0.876
3+	0.646	0.609	0.686
DPP-4is			
No prescription	1	-	-
Prescription	1.26	1.208	1.314
GLP1-RAs			
No prescription	1	-	-
Prescription	0.52	0.462	0.585
Insulin			
No prescription	1	-	-
Prescription	1.901	1.824	1.982
Meglitinides			
No prescription	1	-	-
Prescription	0.953	0.615	1.477
Metformin			
No prescription	1	-	-
Prescription	0.508	0.491	0.525
SGLT-2is			
No prescription	1	-	-
Prescription	0.339	0.309	0.372
Sulphonylureas			
No prescription	1	-	-
Prescription	0.987	0.946	1.03
Thiazolidinediones			
No prescription	1	-	-
Prescription	0.79	0.692	0.9
α-Glucosidase Inhibitors			
No prescription	1	-	-
Prescription	1.913	1.153	3.174

Table S2: Multivariable hazard ratios

Variable	Metformin	Thiazolidinediones	SGLT-2is	GLP1-RAs	Sulphonylureas	DPP-4is	Meglitinides	Insulin	α-Glucosidase Inhibitors
Prescribed vs no prescribed drug class	0.77 (0.73-0.81)	0.94 (0.82-1.07)	0.82 (0.74-0.91)	0.94 (0.83-1.07)	0.94 (0.89-0.99)	1.07 (1.01-1.13)	0.75 (0.49-1.17)	1.42 (1.35-1.49)	1.26 (0.76-2.09)
Sex									
Male	1.5 (1.44-1.55)	1.49 (1.44-1.55)	1.49 (1.44-1.55)	1.49 (1.44-1.55)	1.49 (1.44-1.55)	1.49 (1.44-1.55)	1.49 (1.44-1.55)	1.5 (1.44-1.55)	1.49 (1.44-1.55)
Female	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Age									
<40 years	0.16 (0.11-0.22)	0.16 (0.11-0.22)	0.16 (0.11-0.22)	0.16 (0.11-0.22)	0.16 (0.11-0.22)	0.16 (0.11-0.22)	0.16 (0.11-0.22)	0.16 (0.11-0.22)	0.16 (0.11-0.22)
40-44 years	0.18 (0.13-0.24)	0.18 (0.13-0.24)	0.18 (0.13-0.25)	0.18 (0.13-0.24)	0.18 (0.13-0.24)	0.18 (0.13-0.24)	0.18 (0.13-0.24)	0.18 (0.13-0.24)	0.18 (0.13-0.24)
45-49 years	0.29 (0.24-0.36)	0.29 (0.24-0.36)	0.29 (0.24-0.36)	0.29 (0.24-0.36)	0.29 (0.24-0.35)	0.29 (0.24-0.36)	0.29 (0.24-0.36)	0.29 (0.24-0.36)	0.29 (0.24-0.36)
50-54 years	0.41 (0.35-0.47)	0.41 (0.35-0.47)	0.41 (0.35-0.47)	0.41 (0.35-0.47)	0.41 (0.35-0.47)	0.41 (0.35-0.47)	0.41 (0.35-0.47)	0.41 (0.35-0.47)	0.41 (0.35-0.47)
55-59 years	0.53 (0.47-0.6)	0.53 (0.47-0.6)	0.53 (0.47-0.6)	0.53 (0.47-0.6)	0.53 (0.47-0.6)	0.53 (0.47-0.6)	0.53 (0.47-0.6)	0.53 (0.47-0.6)	0.53 (0.47-0.6)
60-64 years	0.79 (0.72-0.88)	0.79 (0.72-0.88)	0.8 (0.72-0.88)	0.79 (0.72-0.88)	0.79 (0.72-0.88)	0.79 (0.72-0.88)	0.79 (0.72-0.88)	0.79 (0.72-0.88)	0.79 (0.72-0.88)
65-69 years	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
70-74 years	1.43 (1.32-1.55)	1.43 (1.32-1.56)	1.43 (1.31-1.55)	1.43 (1.32-1.55)	1.43 (1.32-1.56)	1.43 (1.32-1.55)	1.43 (1.32-1.56)	1.44 (1.32-1.56)	1.43 (1.32-1.56)
75-79 years	2.25 (2.08-2.43)	2.25 (2.08-2.44)	2.23 (2.07-2.42)	2.25 (2.08-2.43)	2.26 (2.09-2.44)	2.25 (2.08-2.43)	2.25 (2.08-2.44)	2.26 (2.09-2.45)	2.25 (2.08-2.44)
≥80 years	4.16 (3.87-4.47)	4.18 (3.89-4.49)	4.14 (3.85-4.45)	4.17 (3.88-4.49)	4.19 (3.9-4.51)	4.16 (3.87-4.47)	4.18 (3.89-4.49)	4.24 (3.94-4.56)	4.18 (3.88-4.49)
Deprivation									
Most deprived	1.46 (1.38-1.55)	1.46 (1.38-1.55)	1.46 (1.37-1.55)	1.46 (1.38-1.55)	1.46 (1.37-1.55)	1.46 (1.37-1.55)	1.46 (1.37-1.55)	1.46 (1.37-1.54)	1.46 (1.38-1.55)
2nd most deprived	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.3 (1.23-1.38)
3rd most deprived	1.11 (1.05-1.18)	1.11 (1.05-1.18)	1.11 (1.05-1.18)	1.11 (1.05-1.18)	1.11 (1.05-1.18)	1.11 (1.05-1.18)	1.11 (1.05-1.18)	1.11 (1.05-1.18)	1.11 (1.05-1.18)
2nd Least deprived	1.05 (0.99-1.12)	1.05 (0.99-1.12)	1.05 (0.99-1.12)	1.05 (0.99-1.12)	1.05 (0.99-1.12)	1.05 (0.99-1.12)	1.05 (0.99-1.12)	1.05 (0.99-1.12)	1.05 (0.99-1.12)
Least deprived	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Unknown	2.15 (1.19-3.9)	2.14 (1.18-3.87)	2.13 (1.18-3.86)	2.13 (1.18-3.87)	2.14 (1.18-3.87)	2.14 (1.18-3.87)	2.13 (1.18-3.86)	2.17 (1.2-3.92)	2.13 (1.18-3.87)
Region									
London	1.46 (1.37-1.56)	1.45 (1.36-1.54)	1.45 (1.35-1.54)	1.45 (1.36-1.54)	1.45 (1.36-1.55)	1.45 (1.36-1.54)	1.45 (1.36-1.55)	1.47 (1.37-1.56)	1.45 (1.36-1.54)
South West	0.55 (0.51-0.61)	0.55 (0.51-0.6)	0.55 (0.51-0.6)	0.55 (0.51-0.6)	0.55 (0.51-0.6)	0.55 (0.51-0.6)	0.55 (0.51-0.6)	0.56 (0.51-0.61)	0.55 (0.51-0.6)
South East	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Midlands	1.04 (0.98-1.1)	1.04 (0.97-1.1)	1.03 (0.97-1.1)	1.04 (0.97-1.1)	1.04 (0.98-1.1)	1.04 (0.97-1.1)	1.04 (0.97-1.1)	1.04 (0.98-1.1)	1.04 (0.97-1.1)
East of England	0.96 (0.89-1.03)	0.96 (0.89-1.03)	0.96 (0.89-1.03)	0.96 (0.89-1.03)	0.96 (0.89-1.03)	0.96 (0.89-1.03)	0.96 (0.89-1.03)	0.96 (0.9-1.03)	0.96 (0.89-1.03)
North West	1.17 (1.09-1.25)	1.17 (1.09-1.25)	1.17 (1.09-1.25)	1.17 (1.09-1.25)	1.17 (1.09-1.25)	1.17 (1.09-1.25)	1.17 (1.09-1.25)	1.18 (1.1-1.26)	1.17 (1.09-1.25)
North East	1.01 (0.95-1.08)	1.01 (0.94-1.08)	1.01 (0.94-1.07)	1.01 (0.94-1.08)	1.01 (0.95-1.08)	1.01 (0.95-1.08)	1.01 (0.94-1.08)	1.01 (0.95-1.08)	1.01 (0.94-1.08)
Unknown	-	-	-	-	-	-	-	-	-
Ethnic group									
Asian	1.04 (0.98-1.11)	1.04 (0.98-1.1)	1.03 (0.97-1.1)	1.04 (0.98-1.1)	1.04 (0.98-1.1)	1.04 (0.98-1.1)	1.04 (0.98-1.1)	1.05 (0.99-1.11)	1.04 (0.98-1.1)
Black	1.55 (1.44-1.67)	1.55 (1.44-1.67)	1.54 (1.43-1.66)	1.55 (1.44-1.67)	1.55 (1.44-1.67)	1.55 (1.44-1.67)	1.55 (1.44-1.67)	1.55 (1.44-1.67)	1.55 (1.44-1.67)
Mixed	1.28 (1.09-1.5)	1.27 (1.08-1.49)	1.26 (1.08-1.49)	1.27 (1.08-1.49)	1.27 (1.08-1.49)	1.27 (1.08-1.49)	1.27 (1.08-1.49)	1.27 (1.08-1.5)	1.27 (1.08-1.49)
Other	0.97 (0.84-1.12)	1.04 (0.98-1.1)	1.03 (0.97-1.1)	1.04 (0.98-1.1)	1.04 (0.98-1.1)	1.04 (0.98-1.1)	1.04 (0.98-1.1)	1.05 (0.99-1.11)	1.04 (0.98-1.1)
White	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Unknown	0.8 (0.76-0.85)	0.8 (0.75-0.85)	0.8 (0.75-0.85)	0.8 (0.75-0.85)	0.8 (0.75-0.85)	0.8 (0.75-0.85)	0.8 (0.84-0.85)	0.81 (0.76-0.86)	0.8 (0.75-0.85)
HbA1c (mmol/mol)									
<48	1.15 (1.09-1.21)	1.14 (1.08-1.2)	1.14 (1.08-1.2)	1.14 (1.08-1.2)	1.14 (1.08-1.2)	1.14 (1.08-1.2)	1.14 (1.08-1.2)	1.14 (1.08-1.2)	1.14 (1.08-1.2)
49-53	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
54-58	1.04 (0.97-1.11)	1.05 (0.98-1.12)	1.05 (0.98-1.12)	1.05 (0.98-1.12)	1.05 (0.98-1.12)	1.05 (0.98-1.12)	1.05 (0.98-1.12)	1.04 (0.97-1.11)	1.05 (0.98-1.12)
59-74	1.2 (1.13-1.27)	1.23 (1.16-1.31)	1.24 (1.17-1.31)	1.23 (1.16-1.31)	1.23 (1.16-1.31)	1.23 (1.16-1.31)	1.23 (1.16-1.31)	1.18 (1.11-1.25)	1.24 (1.16-1.31)
75-85	1.33 (1.22-1.45)	1.39 (1.28-1.52)	1.4 (1.29-1.52)	1.4 (1.28-1.52)	1.39 (1.28-1.52)	1.4 (1.28-1.52)	1.39 (1.28-1.52)	1.29 (1.18-1.4)	1.4 (1.28-1.52)
≥86	1.58 (1.45-1.71)	1.66 (1.53-1.8)	1.66 (1.53-1.8)	1.66 (1.53-1.8)	1.66 (1.53-1.8)	1.66 (1.53-1.81)	1.66 (1.53-1.8)	1.52 (1.4-1.65)	1.66 (1.53-1.8)
Unknown	1.23 (1.14-1.33)	1.24 (1.15-1.34)	1.24 (1.15-1.34)	1.24 (1.15-1.34)	1.24 (1.15-1.34)	1.24 (1.15-1.34)	1.24 (1.15-1.34)	1.23 (1.14-1.32)	1.24 (1.15-1.34)
Diabetes duration (years)									
<1	1.01 (0.79-1.3)	1.01 (0.79-1.3)	1.01 (0.79-1.3)	1.01 (0.79-1.3)	1.01 (0.79-1.3)	1.01 (0.79-1.3)	1.01 (0.79-1.3)	1.01 (0.78-1.29)	1.01 (0.79-1.3)
1-2	0.91 (0.83-0.99)	0.91 (0.84-1)	0.91 (0.83-0.99)	0.91 (0.83-0.99)	0.91 (0.84-1)	0.91 (0.83-0.99)	0.91 (0.84-1)	0.91 (0.83-0.99)	0.91 (0.84-1)
3-4	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
5-9	1.01 (0.94-1.08)	1.01 (0.94-1.08)	1.01 (0.94-1.09)	1.01 (0.94-1.08)	1.01 (0.94-1.08)	1.01 (0.94-1.09)	1.01 (0.94-1.08)	1.01 (0.95-1.09)	1.01 (0.94-1.08)

10-14	1.08 (1-1.16)	1.08 (1.01-1.16)	1.08 (1.01-1.16)	1.08 (1.01-1.16)	1.08 (1.01-1.16)	1.09 (1.01-1.17)	1.08 (1.01-1.16)	1.08 (1-1.15)	1.08 (1.01-1.16)
15-19	1.23 (1.14-1.32)	1.25 (1.16-1.34)	1.25 (1.16-1.34)	1.25 (1.16-1.34)	1.25 (1.16-1.34)	1.25 (1.16-1.34)	1.25 (1.16-1.34)	1.2 (1.12-1.29)	1.25 (1.16-1.34)
≥20	1.25 (1.16-1.35)	1.3 (1.2-1.4)	1.29 (1.2-1.39)	1.3 (1.2-1.4)	1.29 (1.2-1.39)	1.3 (1.21-1.41)	1.3 (1.2-1.4)	1.18 (1.09-1.27)	1.29 (1.2-1.4)
eGFR (ml/min*1.73m^2)									
≥90	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
60-89	0.97 (0.92-1.02)	0.97 (0.93-1.02)	0.97 (0.92-1.02)	0.97 (0.93-1.02)	0.97 (0.93-1.02)	0.97 (0.92-1.02)	0.97 (0.93-1.02)	0.97 (0.92-1.02)	0.97 (0.93-1.02)
45-59	1.28 (1.2-1.35)	1.3 (1.23-1.38)	1.29 (1.22-1.37)	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.3 (1.23-1.38)	1.28 (1.21-1.36)	1.3 (1.23-1.38)
30-44	1.59 (1.49-1.7)	1.71 (1.61-1.82)	1.7 (1.59-1.81)	1.71 (1.61-1.82)	1.72 (1.61-1.83)	1.69 (1.59-1.81)	1.71 (1.61-1.82)	1.65 (1.54-1.75)	1.71 (1.6-1.82)
15-29	2.05 (1.88-2.23)	2.32 (2.14-2.52)	2.31 (2.12-2.51)	2.32 (2.14-2.52)	2.33 (2.14-2.53)	2.28 (2.1-2.49)	2.32 (2.14-2.52)	2.17 (1.99-2.36)	2.32 (2.14-2.52)
<15	4.4 (3.92-4.93)	5 (4.47-5.59)	4.97 (4.45-5.56)	5 (4.47-5.59)	5.01 (4.48-5.6)	4.92 (4.39-5.5)	5 (4.47-5.59)	4.6 (4.11-5.15)	5 (4.47-5.59)
Unknown	0.81 (0.71-0.93)	0.83 (0.73-0.95)	0.83 (0.72-0.95)	0.83 (0.73-0.95)	0.83 (0.73-0.95)	0.83 (0.72-0.95)	0.83 (0.73-0.95)	0.82 (0.71-0.94)	0.83 (0.73-0.95)
Body mass index (kg/m^2)									
BMI <20	2.47 (2.28-2.69)	2.47 (2.28-2.69)	2.48 (2.28-2.69)	2.48 (2.28-2.69)	2.48 (2.28-2.69)	2.47 (2.27-2.69)	2.48 (2.28-2.69)	2.5 (2.3-2.72)	2.47 (2.28-2.69)
BMI 20-24.9	1.39 (1.33-1.46)	1.39 (1.32-1.46)	1.39 (1.32-1.46)	1.39 (1.32-1.46)	1.39 (1.32-1.46)	1.39 (1.32-1.46)	1.39 (1.32-1.46)	1.4 (1.33-1.47)	1.39 (1.32-1.46)
BMI 25-29.9	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
BMI 30-34.9	1.03 (0.98-1.08)	1.03 (0.98-1.09)	1.03 (0.98-1.09)	1.03 (0.98-1.09)	1.03 (0.98-1.08)	1.03 (0.98-1.09)	1.03 (0.98-1.08)	1.02 (0.97-1.07)	1.03 (0.98-1.08)
BMI 35-39.9	1.16 (1.09-1.24)	1.17 (1.1-1.25)	1.17 (1.1-1.25)	1.17 (1.1-1.25)	1.17 (1.09-1.25)	1.17 (1.1-1.25)	1.17 (1.1-1.25)	1.15 (1.08-1.23)	1.17 (1.1-1.25)
BMI ≥40	1.61 (1.49-1.74)	1.63 (1.51-1.76)	1.63 (1.51-1.76)	1.63 (1.51-1.77)	1.62 (1.5-1.75)	1.63 (1.51-1.77)	1.63 (1.51-1.76)	1.59 (1.47-1.71)	1.63 (1.51-1.76)
Unknown	1.86 (1.75-1.98)	1.87 (1.75-1.99)	1.87 (1.75-1.99)	1.87 (1.75-1.99)	1.87 (1.75-1.99)	1.87 (1.75-1.99)	1.87 (1.75-1.99)	1.86 (1.75-1.98)	1.87 (1.75-1.99)
Systolic blood pressure									
≤140 mmHg	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
>140 mmHg	0.93 (0.89-0.97)	0.93 (0.89-0.97)	0.93 (0.89-0.97)	0.93 (0.89-0.97)	0.93 (0.89-0.97)	0.93 (0.89-0.97)	0.93 (0.89-0.97)	0.93 (0.89-0.97)	0.93 (0.89-0.97)
Unknown	0.73 (0.68-0.79)	0.73 (0.68-0.79)	0.73 (0.68-0.79)	0.73 (0.68-0.79)	0.73 (0.68-0.79)	0.73 (0.68-0.79)	0.73 (0.68-0.79)	0.73 (0.68-0.79)	0.73 (0.68-0.79)
On anti-hypertensive drugs									
Yes	1 (0.95-1.06)	1 (0.94-1.06)	1 (0.94-1.06)	1 (0.94-1.06)	1 (0.94-1.06)	1 (0.94-1.06)	1 (0.94-1.06)	1 (0.94-1.06)	1 (0.94-1.06)
No	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Total cholesterol (mmol/l)									
≤5	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
>5	1.01 (0.96-1.07)	1.02 (0.97-1.07)	1.02 (0.97-1.08)	1.02 (0.97-1.07)	1.02 (0.96-1.07)	1.02 (0.96-1.07)	1.02 (0.97-1.07)	1.02 (0.97-1.07)	1.02 (0.97-1.07)
Unknown	1.69 (1.6-1.78)	1.7 (1.61-1.79)	1.7 (1.61-1.79)	1.7 (1.61-1.79)	1.7 (1.61-1.79)	1.7 (1.61-1.79)	1.7 (1.61-1.79)	1.69 (1.6-1.78)	1.7 (1.61-1.79)
On statins									
Yes	0.67 (0.65-0.7)	0.67 (0.64-0.7)	0.67 (0.64-0.7)	0.67 (0.64-0.7)	0.67 (0.64-0.69)	0.67 (0.64-0.7)	0.67 (0.64-0.7)	0.67 (0.64-0.7)	0.67 (0.64-0.7)
No	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Smoking									
Current smoker	0.72 (0.66-0.77)	0.72 (0.66-0.77)	0.72 (0.66-0.77)	0.72 (0.66-0.77)	0.72 (0.66-0.77)	0.72 (0.66-0.77)	0.72 (0.66-0.77)	0.71 (0.66-0.77)	0.72 (0.66-0.77)
Ex-smoker	1.12 (1.08-1.16)	1.12 (1.08-1.16)	1.12 (1.08-1.16)	1.12 (1.08-1.16)	1.12 (1.08-1.16)	1.12 (1.08-1.16)	1.12 (1.08-1.16)	1.11 (1.07-1.16)	1.12 (1.08-1.16)
Non-smoker	1.22 (1.09-1.36)	1.22 (1.09-1.36)	1.22 (1.09-1.36)	1.22 (1.09-1.36)	1.22 (1.09-1.36)	1.22 (1.09-1.36)	1.22 (1.09-1.36)	1.22 (1.09-1.36)	1.22 (1.09-1.36)
Never smoked	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Unknown	2.37 (1.58-3.54)	2.36 (1.58-3.53)	2.35 (1.57-1.46)	2.36 (1.58-3.53)	2.36 (1.58-3.53)	2.36 (1.58-3.53)	2.36 (0.64-3.53)	2.34 (1.57-3.5)	2.36 (1.58-3.53)
History of cardiovascular disease									
Yes	1.89 (1.83-1.96)	1.91 (1.84-1.98)	1.91 (1.84-1.98)	1.91 (1.84-1.98)	1.91 (1.84-1.98)	1.91 (1.84-1.98)	1.91 (1.84-1.98)	1.88 (1.81-1.95)	1.91 (1.84-1.98)
No	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Number of glucose-lowering drug classes prescribed									
0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1	1.18 (1.12-1.25)	1 (0.95-1.04)	0.99 (0.95-1.04)	0.99 (0.95-1.04)	1 (0.96-1.05)	0.99 (0.94-1.03)	1 (0.95-1.04)	0.95 (0.91-1)	0.99 (0.95-1.04)
2	1.21 (1.13-1.29)	0.98 (0.93-1.03)	0.98 (0.93-1.04)	0.98 (0.92-1.03)	1 (0.94-1.07)	0.95 (0.89-1.01)	0.98 (0.92-1.03)	0.91 (0.86-0.97)	0.98 (0.92-1.03)
3+	1.23 (1.12-1.34)	0.95 (0.89-1.02)	0.99 (0.92-1.06)	0.95 (0.89-1.03)	1 (0.92-1.08)	0.9 (0.83-0.98)	0.95 (0.89-1.02)	0.88 (0.82-0.94)	0.95 (0.88-1.02)
R^2 statistic	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007	0.007

The RECORD statement for pharmacoepidemiology (RECORD-PE) checklist of items, extended from the STROBE and RECORD statements, which should be reported in non-interventional pharmacoepidemiological studies using routinely collected health data

Item No	STROBE items	RECORD items	RECORD-PE items	Page No
Title and abstract				
1	(a) Indicate the study's design with a commonly used term in the title or the abstract. (b) Provide in the abstract an informative and balanced summary of what was done and what was found.	1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. 1.2: If applicable, the geographical region and timeframe within which the study took place should be reported in the title or abstract. 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	—	1,3
Introduction				
Background rationale				
2	Explain the scientific background and rationale for the investigation being reported.	—	—	5
Objectives				
3	State specific objectives, including any prespecified hypotheses.	—	—	5,6
Methods				
Study design				
4	Present key elements of study design early in the paper.	—	4.a: Include details of the specific study design (and its features) and report the use of multiple designs if used. 4.b: The use of a diagram(s) is recommended to illustrate key aspects of the study design(s), including exposure, washout, lag and observation periods, and covariate definitions as relevant.	7
Setting				
5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.	—	—	7
Participants				
6	(a) Cohort study—give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. Case-control study—give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. Cross sectional study—give the eligibility criteria, and the sources and methods of selection of participants. (b) Cohort study—for matched studies, give matching criteria and number of exposed and unexposed. Case-control study—for matched studies, give matching criteria and the number of controls per case.	6.1: The methods of study population selection (such as codes or algorithms used to identify participants) should be listed in detail. If this is not possible, an explanation should be provided. 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	6.1.a: Describe the study entry criteria and the order in which these criteria were applied to identify the study population. Specify whether only users with a specific indication were included and whether patients were allowed to enter the study population once or if multiple entries were permitted. See explanatory document for guidance related to matched designs.	7
Variables				
7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	7.1.a: Describe how the drug exposure definition was developed. 7.1.b: Specify the data sources from which drug exposure information for individuals was obtained. 7.1.c: Describe the time window(s) during which an individual is considered exposed to the drug(s). The rationale for selecting a particular time window should be provided. The extent of potential left truncation or left censoring should be specified. 7.1.d: Justify how events are attributed to current, prior, ever, or cumulative drug exposure. 7.1.e: When examining drug dose and risk attribution, describe how current, historical or time on therapy are considered. 7.1.f: Use of any comparator groups should be outlined and justified. 7.1.g: Outline the approach used to handle individuals with more than one relevant drug exposure during the study period.	7,8
Data sources/measurement				
8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.	—	8.a: Describe the healthcare system and mechanisms for generating the drug exposure records. Specify the care setting in which the drug(s) of interest was prescribed.	7,8

(*Continued*)

Item No	STROBE items	RECORD items	RECORD-PE items	Page No
Bias				
9	Describe any efforts to address potential sources of bias.	—	—	8,9
Study size				
10	Explain how the study size was arrived at.	—	—	Fig. 1
Quantitative variables				
11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why.	—	—	8
Statistical methods				
12	(a) Describe all statistical methods, including those used to control for confounding. (b) Describe any methods used to examine subgroups and interactions. (c) Explain how missing data were addressed. (d) Cohort study—if applicable, explain how loss to follow-up was addressed. Case-control study—if applicable, explain how matching of cases and controls was addressed. Cross sectional study—if applicable, describe analytical methods taking account of sampling strategy. (e) Describe any sensitivity analyses.	—	12.1.a: Describe the methods used to evaluate whether the assumptions have been met. 12.1.b: Describe and justify the use of multiple designs, design features, or analytical approaches.	8,9
Data access and cleaning methods				
12	—	12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. 12.2: Authors should provide information on the data cleaning methods used in the study.	—	Sup. Mat.
Linkage				
12	—	12.3: State whether the study included person level, institutional level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	—	Sup. Mat.
Results				
Participants				
13	(a) Report the numbers of individuals at each stage of the study (eg, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed). (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram.	13.1: Describe in detail the selection of the individuals included in the study (that is, study population selection) including filtering based on data quality, data availability, and linkage. The selection of included individuals can be described in the text or by means of the study flow diagram.	—	10, Fig. 1
Descriptive data				
14	(a) Give characteristics of study participants (eg, demographic, clinical, social) and information on exposures and potential confounders. (b) Indicate the number of participants with missing data for each variable of interest. (c) Cohort study—summarise follow-up time (eg, average and total amount).	—	—	10, Tab. :
Outcome data				
15	Cohort study—report numbers of outcome events or summary measures over time. Case-control study—report numbers in each exposure category, or summary measures of exposure. Cross sectional study—report numbers of outcome events or summary measures.	—	—	10, Fig. 2
Main results				
16	(a) Give unadjusted estimates and, if applicable, confounder adjusted estimates and their precision (eg, 95% confidence intervals). Make clear which confounders were adjusted for and why they were included. (b) Report category boundaries when continuous variables are categorised. (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.	—	—	10, Fig. 2

Item No	STROBE items	RECORD items	RECORD-PE items	Page No
Other analyses				
17	Report other analyses done—eg, analyses of subgroups and interactions, and sensitivity analyses.	—	—	10, Fig. 3
Discussion				
Key results				
18	Summarise key results with reference to study objectives.	—	—	12
Limitations				
19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	19.1.a: Describe the degree to which the chosen database(s) adequately captures the drug exposure(s) of interest.	12
Interpretation				
20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	—	20.a: Discuss the potential for confounding by indication, contraindication or disease severity or selection bias (healthy adherer/sick stopper) as alternative explanations for the study findings when relevant.	12-14
Generalisability				
21	Discuss the generalisability (external validity) of the study results.	—	—	13,14
Other information				
Funding				
22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.	—	—	4
Accessibility of protocol, raw data, and programming code				
22	—	22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	—	Sup. Mat.

RECORD=reporting of studies conducted using observational routinely collected data; RECORD-PE=RECORD for pharmacoepidemiological research; STROBE=strengthening the reporting of observational studies in epidemiology. This checklist has been duplicated from table 1 in *BMJ* 2018;363:k3532, as a standalone document for readers to print out or fill in electronically.