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Supplementary Table 1. ICD-10 codes and Read codes for diabetic retinopathy

ICD-10 code	Description	Read code	Description
H36.0	Diabetic retinopathy	F420.00	Diabetic retinopathy
		F420000	Background diabetic retinopathy
		2BBP.00	O/E - right eye background diabetic retinopathy
		2BBQ.00	O/E - left eye background diabetic retinopathy
		F420400	Diabetic maculopathy
		F420100	Proliferative diabetic retinopathy
		2BBW.00	O/E - right eye diabetic maculopathy
		2BBX.00	O/E - left eye diabetic maculopathy
		7276	Pan retinal photocoagulation for diabetes
		F420200	Preproliferative diabetic retinopathy
		2BBL.00	O/E - diabetic maculopathy present both eyes
		2BBR.00	O/E - right eye preproliferative diabetic retinopathy
		2BBS.00	O/E - left eye preproliferative diabetic retinopathy
		2BBT.00	O/E - right eye proliferative diabetic retinopathy
		F420z00	Diabetic retinopathy NOS
		F420.00	Diabetic retinopathy
		2BBV.00	O/E - left eye proliferative diabetic retinopathy
		C10F600	Type 2 diabetes mellitus with retinopathy
		2BBF.00	Retinal abnormality - diabetes related
		F420300	Advanced diabetic maculopathy
		C108700	Insulin dependent diabetes mellitus with retinopathy
		C10FQ00	Type 2 diabetes mellitus with exudative maculopathy
		F420500	Advanced diabetic retinal disease
		C109600	Non-insulin-dependent diabetes mellitus with retinopathy
		2BBk.00	O/E - right eye stable treated proliferative diabetic retinopathy
		2BBl.00	O/E - left eye stable treated proliferative diabetic retinopathy
		2BBo.00	O/E - sight threatening diabetic retinopathy
		F420700	High risk proliferative diabetic retinopathy
		C10F611	Type II diabetes mellitus with retinopathy
		F420800	High risk non proliferative diabetic retinopathy
		C109611	Type II diabetes mellitus with retinopathy
		C109612	Type 2 diabetes mellitus with retinopathy
		C10E712	Insulin dependent diabetes mellitus with retinopathy
		2BBr.00	Impaired vision due to diabetic retinopathy

Abbreviations: ICD-10, International Statistical Classification of Diseases and Health-Related Problems, Tenth Revision; O/E, on examination

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Supplementary Table 2. Crude and adjusted hazard ratios for the association between the use of individual GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	2386	48,692	49.0 (47.1 to 51.0)	1.00 [Reference]	1.00 [Reference]
Exenatide only	75	1915	39.2 (30.8 to 49.1)	0.84 (0.67 to 1.06)	0.89 (0.70 to 1.12)
Liraglutide only	92	2219	41.5 (33.4 to 50.8)	0.98 (0.79 to 1.21)	1.10 (0.89 to 1.35)
≤6 months of use					
≥2 oral antidiabetic drugs	1203	23,473	51.3 (48.4 to 54.2)	1.00 [Reference]	1.00 [Reference]
Exenatide	36	1093	32.9 (23.1 to 45.6)	0.71 (0.51 to 0.98)	0.74 (0.53 to 1.03)
Liraglutide	49	1180	41.5 (30.7 to 54.9)	1.00 (0.75 to 1.33)	1.12 (0.84 to 1.49)
6.1-12 months of use					
≥2 oral antidiabetic drugs	394	8586	45.9 (41.5 to 50.7)	1.00 [Reference]	1.00 [Reference]
Exenatide	21	344	61.0 (37.8 to 93.3)	1.37 (0.88 to 2.12)	1.45 (0.94 to 2.26)
Liraglutide	24	454	52.9 (33.9 to 78.7)	1.25 (0.83 to 1.88)	1.39 (0.92 to 2.11)
>12 months of use					
≥2 oral antidiabetic drugs	789	16,633	47.4 (44.2 to 50.9)	1.00 [Reference]	1.00 [Reference]
Exenatide	18	478	37.7 (22.3 to 59.5)	0.83 (0.52 to 1.32)	0.89 (0.55 to 1.41)
Liraglutide	19	585	32.5 (19.6 to 50.7)	0.77 (0.49 to 1.21)	0.86 (0.54 to 1.35)
					P for heterogeneity for exenatide = 0.10
					P for heterogeneity for liraglutide = 0.32

Abbreviations: HR, hazard ratio; GLP-1, glucagon-like peptide-1; CI, confidence interval; BMI, Body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year.

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

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Supplementary Table 3. Adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (interaction with duration of treated diabetes)

Exposure [a]	Duration of treated diabetes <5 years Adjusted HR (95% CI) [b]	Duration of treated diabetes ≥5 years Adjusted HR (95% CI) [b]	P for interaction
≥2 oral antidiabetic drugs	1.00 (reference)	1.00 (reference)	
GLP-1 receptor agonists	0.99 (0.82 to 1.20)	1.08 (0.81 to 1.43)	*0.08*
≤6 months of use			
≥2 oral antidiabetic drugs	1.00 (reference)	1.00 (reference)	
GLP-1 receptor agonists	0.91 (0.70 to 1.18)	1.19 (0.80 to 1.76)	*0.01*
6.1-12 months of use			
≥2 oral antidiabetic drugs	1.00 (reference)	1.00 (reference)	
GLP-1 receptor agonists	1.53 (1.07 to 2.18)	1.18 (0.66 to 2.12)	*0.01*
>12 months of use			
≥2 oral antidiabetic drugs	1.00 (reference)	1.00 (reference)	
GLP-1 receptor agonists	0.80 (0.53 to 1.20)	0.91 (0.53 to 1.57)	*0.01*

Abbreviations: HR, hazard ratio; GLP-1, glucagon-like peptide-1; CI, confidence interval; BMI, Body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

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Supplementary Table 4. Adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (interaction with hemoglobin A1c levels)

Exposure [a]	≤7.0%	7.1%-8.0%	>8.0%	P for interaction
	Adjusted HR (95% CI) [b]	Adjusted HR (95% CI) [b]	Adjusted HR (95% CI) [b]	
≥2 oral antidiabetic drugs	1.00 [Reference]	1.00 [Reference]	1.00 [Reference]	
GLP-1 receptor agonists	0.78 (0.19-3.24)	0.69 (0.22-2.19)	1.29 (0.80-2.10)	*0.53*

Abbreviations: HR, hazard ratio; GLP-1, glucagon-like peptide-1; CI, confidence interval; BMI, Body mass index

* Arterial hypertension defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90mmHg or use of any antihypertensive medication

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

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Supplementary Table 5. Adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (interaction with arterial hypertension*)

Exposure [a]	Without arterial hypertension Adjusted HR (95% CI) [b]	With arterial hypertension Adjusted HR (95% CI) [b]	P for interaction
≥2 oral antidiabetic drugs	1.00 [Reference]	1.00 [Reference]	
GLP-1 receptor agonists	0.76 (0.56-1.03)	1.12 (0.94-1.35)	*0.0013*
≤6 months of use			
≥2 oral antidiabetic drugs	1.00 [Reference]	1.00 [Reference]	
GLP-1 receptor agonists	0.76 (0.50-1.14)	1.04 (0.80-1.34)	*0.0152*
6.1-12 months of use			
≥2 oral antidiabetic drugs	1.00 [Reference]	1.00 [Reference]	
GLP-1 receptor agonists	1.09 (0.61-1.96)	1.61 (1.13-2.30)	*0.0152*
>12 months of use			
≥2 oral antidiabetic drugs	1.00 [Reference]	1.00 [Reference]	
GLP-1 receptor agonists	0.54 (0.27-1.10)	0.97 (0.67-1.41)	*0.0152*

Abbreviations: HR, hazard ratio; GLP-1, glucagon-like peptide-1; CI, confidence interval; BMI, Body mass index

* Arterial hypertension defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90mmHg or use of any antihypertensive medication

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits

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Supplementary Table 6. Adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (interaction with use of ACE inhibitors or ARBs)

Exposure [a]	Without ACE inhibitors or ARBs Adjusted HR (95% CI) [b]	With ACE inhibitors or ARBs Adjusted HR (95% CI) [b]	P for interaction
≥2 oral antidiabetic drugs	1.00 [Reference]	1.00 [Reference]	
GLP-1 receptor agonists	0.89 (0.69-1.14)	1.08 (0.89-1.32)	*0.0137*
≤6 months of use			
≥2 oral antidiabetic drugs	1.00 [Reference]	1.00 [Reference]	
GLP-1 receptor agonists	0.89 (0.64-1.25)	0.99 (0.75-1.32)	*0.0486*
6.1-12 months of use			
≥2 oral antidiabetic drugs	1.00 [Reference]	1.00 [Reference]	
GLP-1 receptor agonists	1.34 (0.83-2.18)	1.50 (1.02-2.21)	*0.0486*
>12 months of use			
≥2 oral antidiabetic drugs	1.00 [Reference]	1.00 [Reference]	
GLP-1 receptor agonists	0.59 (0.32-1.07)	1.00 (0.68-1.48)	*0.0486*

Abbreviations: HR, hazard ratio; GLP-1, glucagon-like peptide-1; ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; CI, confidence interval; BMI, Body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits

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Supplementary Table 7. Crude and adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (90-day grace period)

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	2593	52,632	49.3 (47.4 to 51.2)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	180	4443	40.5 (34.8 to 46.9)	0.92 (0.79 to 1.07)	1.01 (0.86 to 1.17)
≤6 months of use					
≥2 oral antidiabetic drugs	810	14,988	54.0 (50.4 to 57.9)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	53	1410	37.6 (28.2 to 49.2)	0.87 (0.66 to 1.15)	0.94 (0.71 to 1.25)
6.1-12 months of use					
≥2 oral antidiabetic drugs	419	9181	45.6 (41.4 to 50.2)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	48	924	51.9 (38.3 to 68.9)	1.21 (0.90 to 1.64)	1.33 (0.99 to 1.80)
>12 months of use					
≥2 oral antidiabetic drugs	1364	28,463	47.9 (45.4 to 50.5)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	79	2108	37.5 (29.7 to 46.7)	0.85 (0.68 to 1.07)	0.93 (0.74 to 1.17)
					P for heterogeneity = 0.26

Abbreviations: GLP-1, glucagon-like peptide-1; CI, confidence interval; HR, hazard ratio; BMI, body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year.

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

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Supplementary Table 8. Crude and adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (additionally adjusting for use of antidiabetic drugs in the year prior to cohort entry)

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	2386	48,692	49.0 (47.1 to 51.0)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	173	4281	40.4 (34.6 to 46.9)	0.92 (0.78 to 1.07)	0.98 (0.84 to 1.15)
≤6 months of use					
≥2 oral antidiabetic drugs	1203	23,473	51.3 (48.4 to 54.2)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	88	2305	38.2 (30.6 to 47.0)	0.87 (0.70 to 1.08)	0.93 (0.75 to 1.16)
6.1-12 months of use					
≥2 oral antidiabetic drugs	394	8586	45.9 (41.5 to 50.7)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	47	831	56.6 (41.6 to 75.2)	1.31 (0.97 to 1.78)	1.42 (1.05 to 1.93)
>12 months of use					
≥2 oral antidiabetic drugs	789	16,633	47.4 (44.2 to 50.9)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	38	1144	33.2 (23.5 to 45.6)	0.76 (0.55 to 1.05)	0.82 (0.59 to 1.14)
					P for heterogeneity = 0.07

Abbreviations: GLP-1, glucagon-like peptide-1; CI, confidence interval; HR, hazard ratio; BMI, body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year.

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

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Supplementary Table 9. Crude and adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (excluding thiazolidinedione users from the 2 main exposure categories)

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	1856	37,539	49.4 (47.2 to 51.7)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	147	3823	38.5 (32.5 to 45.2)	0.87 (0.73 to 1.03)	0.93 (0.79 to 1.11)
≤6 months of use					
≥2 oral antidiabetic drugs	1015	19,542	51.9 (48.8 to 55.2)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	82	2087	39.3 (31.2 to 48.8)	0.87 (0.70 to 1.10)	0.94 (0.75 to 1.18)
6.1-12 months of use					
≥2 oral antidiabetic drugs	299	6680	44.8 (39.8 to 50.1)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	37	733	50.5 (35.5 to 69.6)	1.20 (0.85 to 1.68)	1.30 (0.92 to 1.82)
>12 months of use					
≥2 oral antidiabetic drugs	542	11,318	47.9 (43.9 to 52.1)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	28	1004	27.9 (18.5 to 40.3)	0.63 (0.43 to 0.93)	0.68 (0.46 to 1.00)
					P for heterogeneity = 0.09

Abbreviations: GLP-1, glucagon-like peptide-1; CI, confidence interval; HR, hazard ratio; BMI, body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year.

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

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Supplementary Table 10. Crude and adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (multiple imputation for missing values)

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	2386	48,692	49.0 (47.1 to 51.0)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	173	4281	40.4 (34.6 to 46.9)	0.92 (0.78 to 1.07)	1.00 (0.85 to 1.17)
≤6 months of use					
≥2 oral antidiabetic drugs	1203	23,473	51.3 (48.4 to 54.2)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	88	2305	38.2 (30.6 to 47.0)	0.87 (0.70 to 1.08)	0.94 (0.76 to 1.17)
6.1-12 months of use					
≥2 oral antidiabetic drugs	394	8586	45.9 (41.5 to 50.7)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	47	831	56.6 (41.6 to 75.2)	1.31 (0.97 to 1.78)	1.44 (1.06 to 1.95)
>12 months of use					
≥2 oral antidiabetic drugs	789	16,633	47.4 (44.2 to 50.9)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	38	1144	33.2 (23.5 to 45.6)	0.76 (0.55 to 1.05)	0.83 (0.60 to 1.15)
					P for heterogeneity = 0.07

Abbreviations: GLP-1, glucagon-like peptide-1; CI, confidence interval; HR, hazard ratio; BMI, body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year.

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

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Supplementary Table 11. Crude and adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (competing risk analysis)

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	2386	48,692	49.0 (47.1 to 51.0)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	173	4281	40.4 (34.6 to 46.9)	0.92 (0.78 to 1.07)	1.00 (0.85 to 1.17)
≤6 months of use					
≥2 oral antidiabetic drugs	1203	23,473	51.3 (48.4 to 54.2)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	88	2305	38.2 (30.6 to 47.0)	0.88 (0.70 to 1.09)	0.95 (0.76 to 1.18)
6.1-12 months of use					
≥2 oral antidiabetic drugs	394	8586	45.9 (41.5 to 50.7)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	47	831	56.6 (41.6 to 75.2)	1.32 (0.97 to 1.79)	1.44 (1.06 to 1.96)
>12 months of use					
≥2 oral antidiabetic drugs	789	16,633	47.4 (44.2 to 50.9)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	38	1144	33.2 (23.5 to 45.6)	0.76 (0.55 to 1.06)	0.83 (0.60 to 1.16)
					P for heterogeneity = 0.08

Abbreviations: GLP-1, glucagon-like peptide-1; CI, confidence interval; HR, hazard ratio; BMI, body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

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Supplementary Table 12. Crude and adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy (stratification on high-dimensional disease risk score deciles)

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	2386	48,692	49.0 (47.1 to 51.0)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	173	4281	40.4 (34.6 to 46.9)	0.92 (0.78 to 1.07)	1.05 (0.90 to 1.23)
≤6 months of use					
≥2 oral antidiabetic drugs	1203	23,473	51.3 (48.4 to 54.2)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	88	2305	38.2 (30.6 to 47.0)	0.87 (0.70 to 1.08)	0.96 (0.77 to 1.19)
6.1-12 months of use					
≥2 oral antidiabetic drugs	394	8586	45.9 (41.5 to 50.7)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	47	831	56.6 (41.6 to 75.2)	1.31 (0.97 to 1.78)	1.52 (1.12 to 2.06)
>12 months of use					
≥2 oral antidiabetic drugs	789	16,633	47.4 (44.2 to 50.9)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	38	1144	33.2 (23.5 to 45.6)	0.76 (0.55 to 1.05)	0.95 (0.68 to 1.31)
					P for heterogeneity = 0.09

Abbreviations: GLP-1, glucagon-like peptide-1; CI, confidence interval; HR, hazard ratio

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year.

[c] Stratified by high-dimensional disease risk score deciles.

SUPPLEMENTARY DATA

Supplementary Table 13. Crude and adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy in patients without screening for diabetic retinopathy in the year prior to cohort entry

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	1523	30,249	50.3 (47.9 to 52.9)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	95	2485	38.2 (30.9 to 46.7)	0.84 (0.52 to 1.34)	0.93 (0.75 to 1.15)
≤6 months of use					
≥2 oral antidiabetic drugs	807	14,869	54.3 (50.6 to 58.2)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	50	1349	37.1 (27.5 to 48.9)	0.85 (0.64 to 1.13)	0.93 (0.70 to 1.24)
6.1-12 months of use					
≥2 oral antidiabetic drugs	236	5258	44.9 (39.3 to 41.0)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	24	477	50.3 (32.2 to 74.9)	1.21 (0.80 to 1.84)	1.34 (0.88 to 2.05)
>12 months of use					
≥2 oral antidiabetic drugs	453	9412	48.1 (43.8 to 52.8)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	16	607	26.4 (15.1 to 42.8)	0.61 (0.37 to 1.00)	0.67 (0.41 to 1.10)
					P for heterogeneity = 0.20

Abbreviations: GLP-1, glucagon-like peptide-1; CI, confidence interval; HR, hazard ratio; BMI, body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year.

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

SUPPLEMENTARY DATA

Supplementary Table 14. Crude and adjusted hazard ratios for the association between the use of GLP-1 receptor agonists compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy in patients with screening for diabetic retinopathy in the year prior to cohort entry

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	863	18,443	46.8 (43.7 to 50.0)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	78	1796	43.4 (34.3 to 54.2)	0.97 (0.77 to 1.22)	1.08 (0.86 to 1.36)
≤6 months of use					
≥2 oral antidiabetic drugs	396	8604	46.0 (41.6 to 50.8)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	38	956	39.7 (28.1 to 54.6)	0.90 (0.65 to 1.26)	0.95 (0.68 to 1.33)
6.1-12 months of use					
≥2 oral antidiabetic drugs	158	3328	47.5 (40.4 to 55.5)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	23	355	64.8 (41.1 to 97.2)	1.44 (0.93 to 2.23)	1.55 (1.00 to 2.41)
>12 months of use					
≥2 oral antidiabetic drugs	336	7220	46.5 (41.7 to 51.8)	1.00 [Reference]	1.00 [Reference]
GLP-1 receptor agonists	22	537	41.0 (25.7 to 62.0)	0.93 (0.60 to 1.43)	1.04 (0.67 to 1.60)
					P for heterogeneity = 0.27

Abbreviations: GLP-1, glucagon-like peptide-1; CI, confidence interval; HR, hazard ratio; BMI, body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year.

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits.

SUPPLEMENTARY DATA

Supplementary Table 15. Bounds on corrected estimates and 95% confidence intervals for unmeasured confounding (sensitivity analysis without assumptions)*

	1.2	1.3	1.5	1.8	2	2.5	3	4	5	6	8	10
1.2	1.41 (1.06-1.89)	1.39 (1.05-1.87)	1.37 (1.03-1.83)	1.34 (1.01-1.80)	1.33 (1.00-1.78)	1.31 (0.98-1.75)	1.29 (0.97-1.72)	1.27 (0.95-1.7)	1.26 (0.94-1.68)	1.25 (0.94-1.67)	1.24 (0.93-1.66)	1.23 (0.93-1.65)
1.3	1.39 (1.05-1.87)	1.37 (1.03-1.84)	1.34 (1.01-1.79)	1.30 (0.98-1.74)	1.28 (0.96-1.72)	1.25 (0.94-1.67)	1.23 (0.92-1.64)	1.20 (0.90-1.60)	1.18 (0.89-1.58)	1.17 (0.88-1.57)	1.16 (0.87-1.55)	1.15 (0.86-1.54)
1.5	1.37 (1.03-1.83)	1.34 (1.01-1.79)	1.29 (0.97-1.72)	1.24 (0.93-1.65)	1.21 (0.91-1.62)	1.16 (0.87-1.55)	1.13 (0.85-1.51)	1.09 (0.82-1.46)	1.06 (0.80-1.42)	1.05 (0.79-1.40)	1.03 (0.77-1.37)	1.02 (0.76-1.36)
1.8	1.34 (1.01-1.80)	1.30 (0.98-1.74)	1.24 (0.93-1.65)	1.16 (0.87-1.56)	1.13 (0.85-1.51)	1.06 (0.80-1.42)	1.02 (0.77-1.37)	0.97 (0.73-1.29)	0.93 (0.70-1.25)	0.91 (0.69-1.22)	0.89 (0.67-1.19)	0.87 (0.65-1.16)
2	1.33 (1.00-1.78)	1.28 (0.96-1.72)	1.21 (0.91-1.62)	1.13 (0.85-1.51)	1.09 (0.82-1.46)	1.02 (0.76-1.36)	0.97 (0.73-1.29)	0.91 (0.68-1.21)	0.87 (0.65-1.16)	0.85 (0.64-1.13)	0.82 (0.61-1.09)	0.80 (0.60-1.07)
2.5	1.31 (0.98-1.75)	1.25 (0.94-1.67)	1.16 (0.87-1.55)	1.06 (0.80-1.42)	1.02 (0.76-1.36)	0.93 (0.7-1.24)	0.87 (0.65-1.16)	0.80 (0.60-1.07)	0.75 (0.57-1.01)	0.73 (0.55-0.97)	0.69 (0.52-0.92)	0.67 (0.50-0.89)
3	1.29 (0.97-1.72)	1.23 (0.92-1.64)	1.13 (0.85-1.51)	1.02 (0.77-1.37)	0.97 (0.73-1.29)	0.87 (0.65-1.16)	0.81 (0.61-1.08)	0.73 (0.55-0.97)	0.68 (0.51-0.91)	0.64 (0.48-0.86)	0.60 (0.45-0.81)	0.58 (0.44-0.78)
4	1.27 (0.95-1.70)	1.20 (0.90-1.60)	1.09 (0.82-1.46)	0.97 (0.73-1.29)	0.91 (0.68-1.21)	0.80 (0.60-1.07)	0.73 (0.55-0.97)	0.63 (0.48-0.85)	0.58 (0.44-0.78)	0.54 (0.41-0.73)	0.50 (0.37-0.67)	0.47 (0.35-0.63)
5	1.26 (0.94-1.68)	1.18 (0.89-1.58)	1.06 (0.80-1.42)	0.93 (0.70-1.25)	0.87 (0.65-1.16)	0.75 (0.57-1.01)	0.68 (0.51-0.91)	0.58 (0.44-0.78)	0.52 (0.39-0.70)	0.48 (0.36-0.65)	0.44 (0.33-0.58)	0.41 (0.31-0.54)
6	1.25 (0.94-1.67)	1.17 (0.88-1.57)	1.05 (0.79-1.40)	0.91 (0.69-1.22)	0.85 (0.64-1.13)	0.73 (0.55-0.97)	0.64 (0.48-0.86)	0.54 (0.41-0.73)	0.48 (0.36-0.65)	0.44 (0.33-0.59)	0.39 (0.30-0.53)	0.36 (0.27-0.49)
8	1.24 (0.93-1.66)	1.16 (0.87-1.55)	1.03 (0.77-1.37)	0.89 (0.67-1.19)	0.82 (0.61-1.09)	0.69 (0.52-0.92)	0.60 (0.45-0.81)	0.50 (0.37-0.67)	0.44 (0.33-0.58)	0.39 (0.30-0.53)	0.34 (0.26-0.45)	0.31 (0.23-0.41)
10	1.23 (0.93-1.65)	1.15 (0.86-1.54)	1.02 (0.76-1.36)	0.87 (0.65-1.16)	0.80 (0.60-1.07)	0.67 (0.50-0.89)	0.58 (0.44-0.78)	0.47 (0.35-0.63)	0.41 (0.31-0.54)	0.36 (0.27-0.49)	0.31 (0.23-0.41)	0.28 (0.21-0.37)

* Rows correspond to increasing strength of the risk ratio of unmeasured confounding on the outcome and columns correspond to increasing strength of risk ratio of unmeasured confounding on the exposure.

SUPPLEMENTARY DATA

Supplementary Table 16. Baseline demographics and clinical characteristics of the cohort and stratified by used of DPP-4 inhibitors and insulin at cohort entry

		Use at Cohort Entry	
Characteristic	**Entire Cohort**	**DPP-4 inhibitors**	**Insulins**
Total	77,115	2605	1544
Age, years (mean, SD)	61.6 (13.6)	65.3 (11.6)	64.7 (13.0)
Male, n (%)	44,155 (57.3)	1484 (57.0)	866 (56.1)
Index of Multiple Deprivation, n (%)			
Quintile 1	14,799 (19.2)	§	307 (19.9)
Quintile 2	15,947 (20.7)	585 (22.5)	286 (18.5)
Quintile 3	15,993 (20.7)	521 (20.0)	321 (20.8)
Quintile 4	15,732 (20.4)	501 (19.2)	331 (21.4)
Quintile 5	14,595 (18.9)	521 (20.0)	299 (19.4)
Unknown	49 (0.1)	§	0 (0.0)
Alcohol-related disorders, n (%)	10,671 (13.8)	506 (19.4)	286 (18.5)
Smoking status, n (%)			
Current	12,434 (16.1)	360 (13.8)	§
Past	28,540 (37.0)	1054 (40.5)	667 (43.2)
Never	35,864 (46.5)	1191 (45.7)	643 (41.7)
Unknown	277 (0.4)	0 (0.0)	§
Body mass index, n (%)			
<25 kg/m^2	8484 (11.0)	251 (9.6)	252 (16.3)
25-30 kg/m^2	22,938 (29.8)	754 (28.9)	467 (30.3)
≥30 kg/m^2	43,730 (56.7)	1590 (61.0)	816 (52.9)
Unknown	1963 (2.5)	10 (0.4)	9 (0.6)
Hemoglobin A1c, n (%)			
≤7.0% or ≤53 mmol/mol,	13,453 (17.4)	420 (16.1)	140 (9.1)
7.1%-8.0% or 54-64 mmol/mol	16,658 (21.6)	861 (33.1)	193 (12.5)
>8.0% or >64 mmol/mol	24,031 (31.2)	1211 (46.5)	1205 (78.0)
Unknown	22,973 (29.8)	113 (4.3)	6 (0.4)
Blood pressure, n (%)			
Systolic <140 mm Hg and diastolic <90 mm Hg	39,307 (51.0)	1548 (59.4)	919 (59.5)
Systolic ≥140 mm Hg or diastolic ≥90 mm Hg	32,196 (41.7)	979 (37.6)	573 (37.1)
Unknown	5612 (7.3)	78 (3.0)	52 (3.4)
Dyslipidemia, n (%)	17,931 (23.3)	833 (32.0)	468 (30.3)
Duration of treated diabetes in years (mean, SD)	1.0 (2.4)	6.7 (3.5)	6.0 (2.9)
Neuropathy, n (%)	7364 (9.5)	679 (26.1)	385 (24.9)
Nephropathy, n (%)	25,476 (33.0)	1250 (48.0)	770 (49.0)
Peripheral arteriopathy, n (%)	3056 (4.0)	164 (6.3)	143 (9.3)
Myocardial infarction, n (%)	5774 (7.5)	239 (9.2)	242 (15.7)
Ischemic stroke, n (%)	3778 (4.9)	150 (5.8)	124 (8.0)
Cataract surgery, n (%)	5800 (7.5)	281 (10.8)	159 (10.3)
Albuminuria or proteinuria, n (%)	6339 (8.2)	520 (20.0)	396 (25.7)
Uveitis, n (%)	302 (0.4)	17 (0.7)	10 (0.7)
Sickle-cell disease, n (%)	123 (0.2)	6 (0.2)	§
Statins, n (%)	47,765 (61.9)	2161 (83.0)	1245 (80.6)
Fibrates, n (%)	1231 (1.6)	82 (3.2)	46 (3.0)
Antihypertensive drugs, n (%)			
Calcium channel blockers	20,705 (26.8)	840 (32.3)	513 (33.2)
Angiotensin-converting enzyme inhibitors	29,310 (38.0)	1371 (52.6)	829 (54.0)
Angiotensin receptor blockers	10,161 (13.2)	547 (21.0)	282 (18.3)
Beta-blockers	17,524 (22.7)	722 (27.7)	501 (32.5)

SUPPLEMENTARY DATA

		Use at Cohort Entry	
Characteristic	**Entire Cohort**	**DPP-4 inhibitors**	**Insulins**
Diuretics	22,781 (29.5)	936 (35.9)	647 (41.9)
Mineralocorticoid receptor antagonists	1671 (2.2)	73 (2.8)	101 (6.5)
Other antihypertensive drugs	742 (1.0)	38 (1.5)	27 (1.8)
Ophthalmic agents	1758 (2.3)	75 (2.9)	50 (3.2)
Antimalarial drugs	258 (0.3)	8 (0.3)	5 (0.3)
Fluconazole	1897 (2.5)	60 (2.3)	53 (3.4)
Tamoxifen	306 (0.4)	9 (0.4)	10 (0.7)
Number of non-antidiabetic drugs (mean, SD)	8.0 (6.1)	10.2 (6.2)	12.2 (6.6)
0	3775 (4.9)	24 (0.9)	6 (0.4)
1	4327 (5.6)	36 (1.4)	5 (0.3)
2	5106 (6.6)	54 (2.1)	19 (1.2)
3	5605 (7.3)	102 (3.9)	41 (2.7)
≥4	58,302 (75.6)	2389 (91.7)	1473 (95.4)
Number of physician visits, mean (SD)	7.6 (9.1)	9.3 (10.4)	11.7 (12.2)

Abbreviations: SD, standard deviation; DPP-4, dipeptidy1 peptidase-4

[a] Patients exposed to other antidiabetic drugs at cohort entry (n=72,976) are not displayed in the table.

§ Numbers <5 are not displayed, as per the confidentiality policies of the Clinical Practice Research Datalink

SUPPLEMENTARY DATA

Supplementary Table 17. Crude and adjusted hazard ratios for the association between the use of DPP-4 inhibitors compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	2386	48,692	49.0 (47.1 to 51.0)	1.00 [Reference]	1.00 [Reference]
DPP-4 inhibitors	853	20,037	42.6 (39.8 to 45.5)	0.94 (0.87 to 1.02)	1.03 (0.95 to 1.11)
≤6 months of use					
≥2 oral antidiabetic drugs	1203	23,473	51.3 (48.4 to 54.2)	1.00 [Reference]	1.00 [Reference]
DPP-4 inhibitors	351	7719	45.5 (40.8 to 50.5)	0.96 (0.85 to 1.08)	1.04 (0.92 to 1.17)
6.1-12 months of use					
≥2 oral antidiabetic drugs	394	8586	45.9 (41.5 to 50.7)	1.00 [Reference]	1.00 [Reference]
DPP-4 inhibitors	181	4071	44.5 (38.2 to 51.4)	1.01 (0.85 to 1.21)	1.10 (0.92 to 1.31)
>12 months of use					
≥2 oral antidiabetic drugs	789	16,633	47.4 (44.2 to 50.9)	1.00 [Reference]	1.00 [Reference]
DPP-4 inhibitors	321	8247	38.9 (34.8 to 43.4)	0.87 (0.76 to 0.99)	0.95 (0.84 to 1.09)
					P for heterogeneity = 0.56

Abbreviations: DPP-4, dipeptidyl peptidase-4; CI, confidence interval; HR, hazard ratio; BMI, body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table.

[b] Per 1000 persons per year.

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits

SUPPLEMENTARY DATA

Supplementary Table 18. Crude and adjusted hazard ratios for the association between the use of insulin compared with the use of ≥2 oral antidiabetic drugs and the risk of diabetic retinopathy

Exposure [a]	Events	Person-years	Incidence rate [b] (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI) [c]
≥2 oral antidiabetic drugs	2386	48,692	49.0 (47.1 to 51.0)	1.00 [Reference]	1.00 [Reference]
Insulin	659	12,282	53.7 (49.6 to 57.9)	1.17 (1.08 to 1.28)	1.17 (1.07 to 1.28)
≤6 months of use					
≥2 oral antidiabetic drugs	1203	23,473	51.3 (48.4 to 54.2)	1.00 [Reference]	1.00 [Reference]
Insulin	374	7184	52.1 (46.9 to 57.6)	1.14 (1.01 to 1.28)	1.14 (1.01 to 1.28)
6.1-12 months of use					
≥2 oral antidiabetic drugs	394	8586	45.9 (41.5 to 50.7)	1.00 [Reference]	1.00 [Reference]
Insulin	107	1947	55.0 (45.0 to 66.4)	1.25 (1.01 to 1.55)	1.25 (1.01 to 1.55)
>12 months of use					
≥2 oral antidiabetic drugs	789	16,633	47.4 (44.2 to 50.9)	1.00 [Reference]	1.00 [Reference]
Insulin	178	3151	56.5 (48.5 to 65.4)	1.27 (1.08 to 1.49)	1.26 (1.07 to 1.48)
					P for heterogeneity = 0.001

Abbreviations: CI, confidence interval; HR, hazard ratio; BMI, body mass index

[a] Use of other antidiabetic agents is considered in the model, but not presented in the table

[b] Per 1000 persons per year

[c] Adjusted for year of cohort entry, age, sex, quintiles of the Index of Multiple Deprivation, alcohol-related disorders, smoking status, BMI category, hemoglobin A1c, systolic and diastolic blood pressure, dyslipidemia, duration of treated diabetes, neuropathy, nephropathy, peripheral arteriopathy, myocardial infarction, ischemic stroke, history of cataract surgery, albuminuria or proteinuria, uveitis, sickle disease, use of statins, fibrates, antihypertensive drugs, ophthalmic agents, antimalarial drugs, fluconazole, tamoxifen, the number of non-antidiabetic drugs, and the number of physician visits

SUPPLEMENTARY DATA

Supplementary Table 19. Baseline demographics and clinical characteristics of new users of GLP-1 receptor agonists and new users of insulin

Characteristic	GLP-1 receptor agonists	Insulin
Total	2606	5556
Age, years (mean, SD)	55.9 (10.4)	61.0 (14.4)
Male, n (%)	1419 (54.5)	3078 (55.4)
Index of Multiple Deprivation, n (%)		
Quintile 1	428 (16.4)	1022 (18.4)
Quintile 2	497 (19.1)	1074 (19.3)
Quintile 3	549 (21.1)	1133 (20.4)
Quintile 4	564 (21.6)	1192 (21.5)
Quintile 5	568 (21.8)	1135 (20.4)
unknown	0 (0.0)	0 (0.0)
Alcohol-related disorders, n (%)	480 (18.4)	1084 (19.5)
Smoking status, n (%)		
Current	388 (14.9)	1013 (18.2)
Past	1121 (43.0)	2183 (39.3)
Never	1097 (42.1)	2360 (42.5)
Unknown	0 (0.0)	0 (0.0)
Body mass index, n (%)		
<25 kg/m^2	15 (0.6)	1111 (20.0)
25-30 kg/m^2	152 (5.8)	1752 (31.5)
≥30.0 kg/m^2	2434 (93.4)	2616 (47.1)
Unknown	5 (0.2)	77 (1.4)
Hemoglobin A1c, n (%)		
≤7.0%	324 (12.4)	611 (11.0)
7.1%-8.0%	536 (20.6)	748 (13.5)
>8.0%	1619 (62.1)	3653 (65.8)
Unknown	127 (4.9)	544 (9.8)
Blood pressure, n (%)		
Systolic <140 mm Hg and diastolic <90 mm Hg	1553 (59.6)	3544 (63.8)
Systolic ≥140 mm Hg or diastolic ≥90 mm Hg	989 (38.0)	1770 (31.9)
Unknown	64 (2.5)	242 (4.4)
Dyslipidemia, n (%)	682 (26.2)	1448 (26.1)
Duration of treated diabetes in years (median)	4.6	3.9
Neuropathy, n (%)	533 (20.5)	1047 (18.8)
Nephropathy, n (%)	684 (26.3)	2408 (43.3)
Peripheral arteriopathy, n (%)	85 (3.3)	370 (6.7)
Myocardial infarction, n (%)	151 (5.8)	650 (11.7)
Ischemic stroke, n (%)	88 (3.4)	354 (6.4)
Cataract surgery, n (%)	94 (3.6)	467 (8.4)
Albuminuria or proteinuria, n (%)	461 (17.7)	991 (17.8)
Uveitis, n (%)	12 (0.5)	25 (0.5)
Sickle-cell disease, n (%)	§	9 (0.2)
Statins, n (%)	2100 (80.6)	3925 (70.6)
Fibrates, n (%)	91 (3.5)	176 (3.2)
Antihypertensive drugs, n (%)		
Calcium channel blockers	753 (28.9)	1492 (26.9)

SUPPLEMENTARY DATA

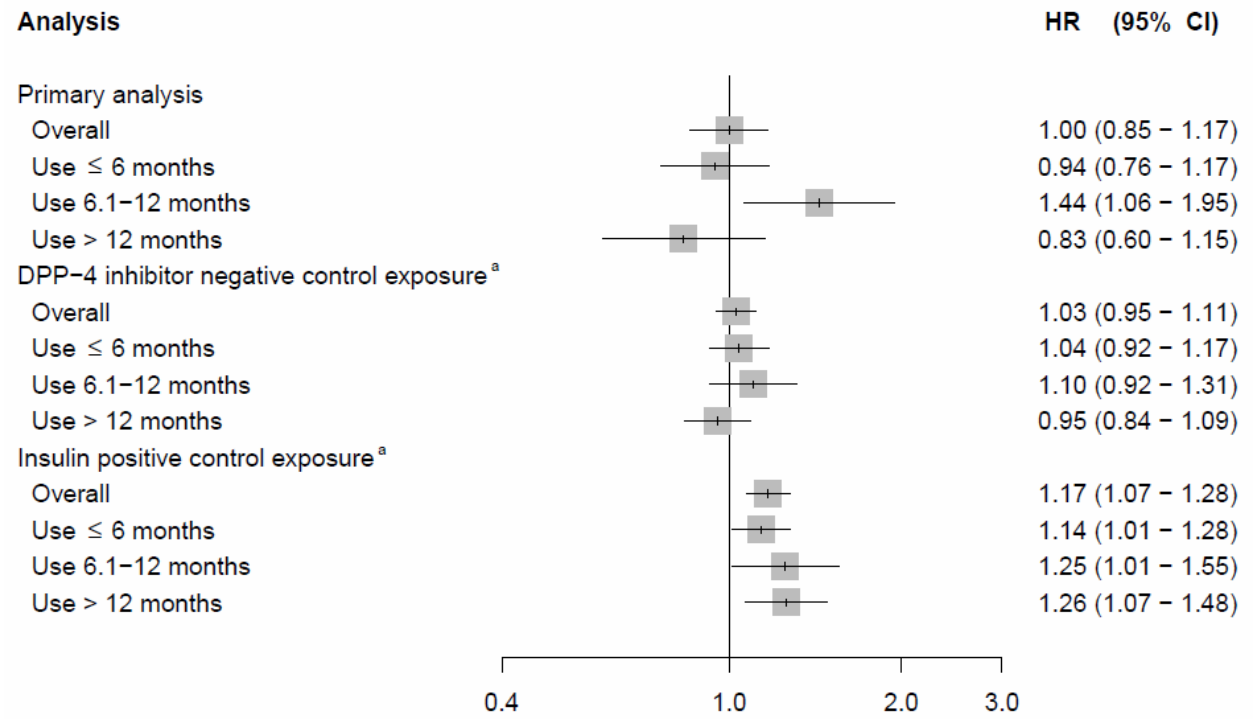
Characteristic	GLP-1 receptor agonists	Insulin
Angiotensin-converting enzyme inhibitors	1298 (49.8)	2445 (44.0)
Angiotensin receptor blockers	516 (19.8)	872 (15.7)
Beta-blockers	549 (21.1)	1540 (27.7)
Diuretics	820 (31.5)	1856 (33.4)
Mineralocorticoid receptor antagonists	54 (2.1)	307 (5.5)
Other antihypertensive drugs	51 (2.0)	83 (1.5)
Ophthalmic agents	30 (1.2)	131 (2.4)
Antimalarial drugs	15 (0.6)	31 (0.6)
Fluconazole	136 (5.2)	291 (5.2)
Tamoxifen	§	19 (0.3)
Number of non-antidiabetic drugs (mean, SD)	10.9 (6.2)	12.0 (7.3)
0	§	31 (0.6)
1	§	50 (0.9)
2	46 (1.8)	126 (2.3)
3	94 (3.6)	195 (3.5)
≥4	2438 (93.6)	5154 (92.8)
Number of physician visits, mean (SD)	10.0 (10.4)	11.4 (12.3)

Abbreviations: SD, standard deviation; GLP-1, glucagon-like peptide-1

§ Numbers <5 are not displayed, as per the confidentiality policies of the Clinical Practice Research Datalink

SUPPLEMENTARY DATA

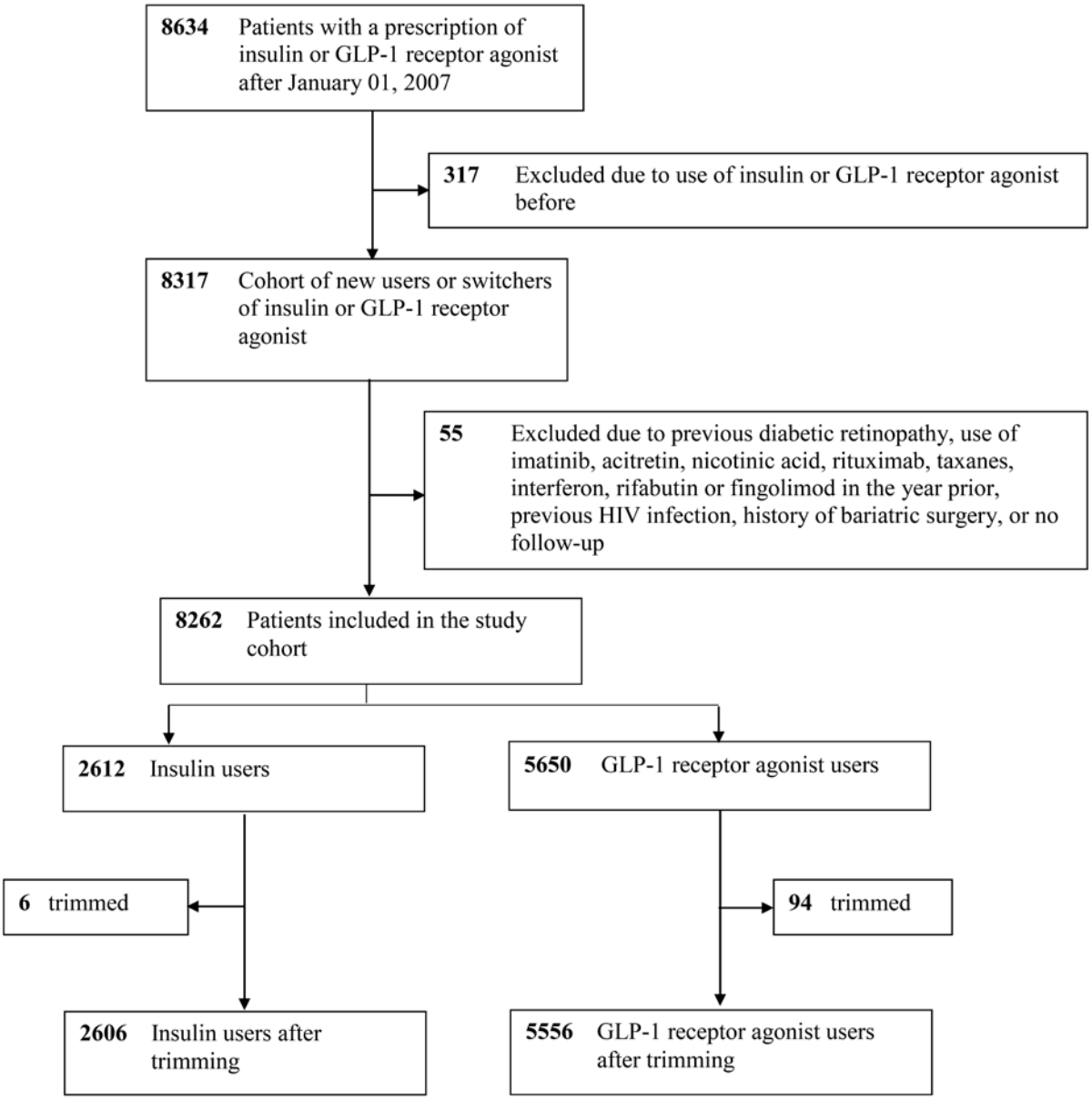
Supplementary Figure 1. Forest plot summarizing the primary analysis and the analyses using negative (DPP-4 inhibitors) and positive control (insulin) exposures.



Abbreviations: DPP-4, dipeptidyl peptidase-4; HR, hazard ratio; CI, confidence interval
[a] Use of ≥2 oral antidiabetic drugs as comparator

SUPPLEMENTARY DATA

Supplementary Figure 2. Flowchart describing the construction of the study cohort for the ancillary analysis including new users of GLP-1 receptor agonists and new users of insulin



SUPPLEMENTARY DATA

Supplementary Figure 3. Incidence rate of diabetic retinopathy in the base cohort according to duration of treated diabetes