

Supplementary Online Content

Kang EY-C, Chen T-H, Garg SJ, et al. Association of statin therapy with prevention of vision-threatening diabetic retinopathy. *JAMA Ophthalmol*. Published online January 10, 2019. doi:10.1001/jamaophthalmol.2018.6399

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. ICD-9-CM Codes of Diagnoses Used for Defining the Population, Comorbidities, and Outcomes

Diagnosis	ICD-9-CM Code
Select study cohort	
Diabetes mellitus	250.xx and any oral hypoglycemic drugs or insulin
Type 1 diabetes	250.01, 250.03, 250.11, 250.13, 250.21, 250.23, 250.31, 250.33, 250.41, 250.43, 250.51, 250.53, 250.61, 250.63, 250.71, 250.73, 250.81, 250.83, 250.91, 250.93
Other background retinopathy	362.1x
Other proliferative retinopathy	362.2x
Retinal vascular occlusion	362.3x
Separation of retinal layer	361.xx, 362.4x
Degeneration of retina	362.5x, 362.6x, 362.7x
Chorioretinal inflammation	363.0x, 363.1x, 363.2x
Other retinal disorder	362.8x, 379.23
Liver cirrhosis	571.2, 571.5, 571.6 (with catastrophic illness card)
Primary outcomes	
Diabetic retinopathy	362.0x
Non-proliferative DR	362.01, 362.03, 362.04, 362.05, 362.06
Proliferative DR	362.02
Vitreous hemorrhage	379.23, 362.81
Tractional retinal detachment	361.0x, 361.8x, 361.9
Diabetic macular edema	362.07, 362.53
Safety outcomes	
Acute ischemic stroke	433.xx-437.xx
Heart failure	428.xx
Acute myocardial infarction	410.xx
Diabetic neuropathy	250.6x, 357.2
Diabetic foot	250.7x, 785.4 (gangrene)
Dialysis	585.xx

Comorbidities	
Hypertension	401.xx, 402.xx, 403.xx, 404.xx, 405.xx and any anti-hypertension drugs
Ischemic heart disease	410.xx-414.xx
Chronic kidney disease	580.xx-589.xx, 403.xx-404.xx, 016.0x, 095.4x, 236.9x, 250.4x, 274.1x, 442.1x, 447.3x, 440.1x, 572.4x, 642.1x, 646.2x, 753.1x, 283.11, 403.01, 404.02, 446.21
Diabetic neuropathy	250.6x, 357.2
Diabetic foot ulcers	250.7x, 785.4 (gangrene)
Peripheral arterial disease	440.0x, 440.2x, 440.3x, 440.8x, 440.9x, 443.xx, 444.0x, 444.22, 444.8x, 447.8x, 447.9x
Dialysis	585.xx (with catastrophic illness card)
Ischemic stroke	433.xx-437.xx
Heart failure	428.xx

Abbreviation: DR, diabetic retinopathy; *ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification.*

eTable 2. Anatomical Therapeutic Chemical (ATC) Codes of the Medications Used in This Study

Medications	ATC codes
Study drugs	
Statin	C10AA01, C10AA02, C10AA03, C10AA04, C10AA05, C10AA07, C10AA08, C10BA01, C10BA02
Rosuvastatin	C10AA07
Atorvastatin	C10AA05
Simvastatin	C10AA01, C10BA02
Fluvastatin	C10AA04
Pravastatin	C10AA03
Lovastatin	C10AA02, C10BA01,
Pitavastatin	C10AA08
Diabetes medication	
Insulin	A10AB01, A10AB03, A10AB04, A10AB05, A10AB06, A10AB30, A10AC01, A10AC03, A10AC30, A10AD01, A10AD03, A10AD05, A10AE01, A10AE04, A10AE05
Sulfonylurea	A10BB01, A10BB02, A10BB03, A10BB04, A10BB05, A10BB07, A10BB08, A10BB09, A10BB12, A10BB31
Metformin	A10BA02, A10BA03, A10BD, A10BD02, A10BD03, A10BD05, A10BD07, A10BD08, A10BD10, A10BD11, A10BD13, A10BX02
DPP4i	A10BH01, A10BH02, A10BH03, A10BH04, A10BH05
Thiazolidinediones	A10BG02, A10BG03
Alpha-glucosidase inhibitors	A10BF01, A10BF02
Meglitinides	A10BX08
Hypertension medication	
Calcium channel blocker (Dihydropyridine)	C08CA01, C08CA02, C08CA03, C08CA04, C08CA05, C08CA06, C08CA07, C08CA08, C08CA09, C08CA12, C08CA13, C08CA15

Beta blocker	C07AA01, C07AA02, C07AA03, C07AA05, C07AA06, C07AA07, C07AA12, C07AA15, C07AA19, C07AB02, C07AB03, C07AB04, C07AB05, C07AB07, C07AB09, C07AB12, C07AG01, C07AG02, C07BA68, C07BB02, C07BB03, C07CA03, C07DA06
ACEi	C09AA01, C09AA03, C09AA02, C09AA09, C09AA05, C09AA04, C09BA04, C09AA06, C09AA08, C09AA07, C09BB05, C09BA01, C09AA16, C09BB, C09BA02
ARB	C09DA07, C09CA06, C09CA01, C09DA08, C09CA03, C09DA01, C09CA04, C09DA03, C09DB01, C09CA07, C09CA08, C09DA04, C09CA02, C09DA06, C09DX01, C09DX03, C09DB04, C09DB02, C09CA09
Thiazide	C03AA03, C03AA06, C03AA91, C03AA07
Alpha blocker	C02CA91, C02CA01, C02CA04

eTable 3. Demographic Information of the Study Population before Propensity Score Matching

Variables	Statin (<i>n</i> = 199 760) No. (%)	Non-Statin (<i>n</i> = 19 599) No. (%)	ASMD
Sex			
Male	97 376 (48.7)	8747 (44.6)	0.083
Female	102 384 (51.3)	10 852 (55.4)	0.083
Outpatient visit in previous year ^a	22.9 ± 13.0	15.2 ± 14.2	0.564
Diabetes duration, y ^a	3.3 ± 3.7	2.7 ± 3.2	0.175
Age (y) ^a	60.6 ± 10.6	61.0 ± 11.0	0.037
Age ≥65 y	66 619 (33.3)	7259 (37.0)	0.077
Comorbidity			
Hypertension	114 805 (57.5)	8217 (41.9)	0.315
Ischemic heart disease	31 688 (15.9)	2451 (12.5)	0.096
Chronic kidney disease	15 369 (7.7)	1162 (5.9)	0.070
Diabetic neuropathy	11 556 (5.8)	914 (4.7)	0.050
Diabetic foot	3337 (1.7)	328 (1.7)	0.000
Peripheral arterial disease	3102 (1.6)	279 (1.4)	0.011
Dialysis	446 (0.2)	53 (0.3)	0.010
History of event			
Ischemic stroke	16 491 (8.3)	1734 (8.8)	0.021
Heart failure	5367 (2.7)	624 (3.2)	0.029
Amputation	767 (0.4)	77 (0.4)	0.001
Diabetes medication			
Insulin	19 405 (9.7)	2328 (11.9)	0.070
Sulfonylurea	149 310 (74.7)	15 681 (80.0)	0.126
Metformin	165 367 (82.8)	14 519 (74.1)	0.213
DPP4i	18 160 (9.1)	536 (2.7)	0.272
Thiazolidinediones	37 384 (18.7)	2065 (10.5)	0.233
Alpha-glucosidase inhibitors	32 217 (16.1)	2100 (10.7)	0.159
Meglitinides	19 242 (9.6)	1696 (8.7)	0.034
Hypertension medication			
Calcium channel blocker	93 406 (46.8)	9021 (46.0)	0.015
Beta blocker	81 765 (40.9)	8304 (42.4)	0.029
ACEi	61 985 (31.0)	7374 (37.6)	0.139
ARB	83 334 (41.7)	5098 (26.0)	0.337

Thiazide	20 766 (10.4)	2529 (12.9)	0.078
Alpha blocker	12 882 (6.4)	1489 (7.6)	0.045
CCI score ^a	1.8 ± 1.3	1.6 ± 1.5	0.130

Abbreviation: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ASMD, absolute standardized mean difference; CCI, Charlson comorbidity index; DM, diabetes mellitus; DPP4i, dipeptidyl peptidase-4 inhibitors.

^aPresented as mean ± standard deviation.

eTable 4. The Effect of Statin on Diabetic Retinopathy in Patients with Type 2 Diabetes Mellitus by Intensity

	No.	Event (%)	HR (95% CI) ^a	<i>P</i> value ^b
Intensity ^c				
Low	41 160	5523 (13.4)	1 (Reference)	
Moderate	140 002	8404 (6.0)	0.66 (0.64-0.68)	<.001
High	11 329	383 (3.4)	0.49 (0.44-0.54)	<.001
<i>P</i> trend ^d				<.001

Abbreviations: CI, confidence interval; HR, hazard ratio; NA, not applicable.

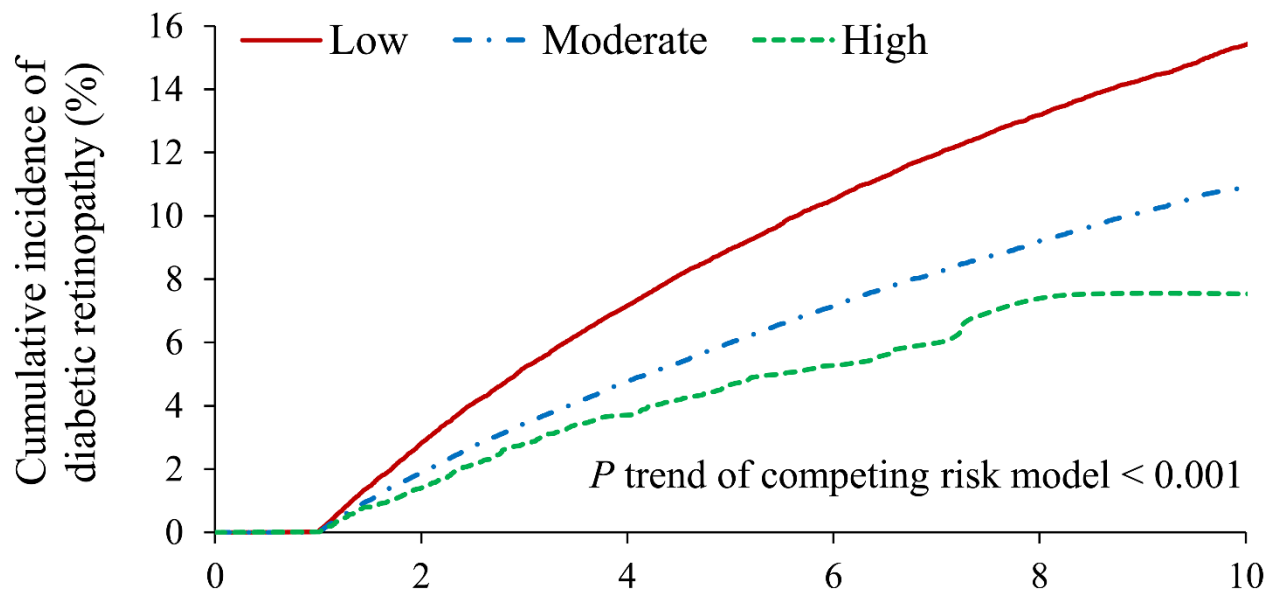
^a Estimated from a sub-distribution hazard model.

^b The *P* values were derived from two separate models in the same column of the table, there were three *P* values at total in which 2 were from the first model and 1 was from the second model (the latter one was *P* trend).

^c 26 868 patients were excluded because of a switch among low-intensity, moderate-intensity, and high-intensity statin.

^d The intensity of statin was treated as a continuous variable in which the coding of low-, moderate-, and high-intensity was 1, 2, and 3 respectively.

eFigure 1. Cumulative Incidence of All Diabetic Retinopathy With Low-, Moderate-, and High-Intensity Statin Therapy



No. at risk:

	0	2	4	6	8	10
Low	41160	38254	31180	24864	18996	11147
Moderate	140002	115684	76710	45915	22663	8985
High	11329	8946	4546	1531	133	6

eFigure 2. Distribution of the Index date in the Statin and Nonstatin Groups After Propensity Score Matching

