# Statin Initiation and Risk of Incident Kidney Disease in Patients with Diabetes

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Appendix 1, as supplied by the authors. Appendix to: Zhou S, Su L, Xu R, et al. Statin initiation and risk of incident kidney disease in patients with diabetes. *CMAJ* 2023. doi: 10.1503/cmaj.230093.

## Supplementary Table of Contents

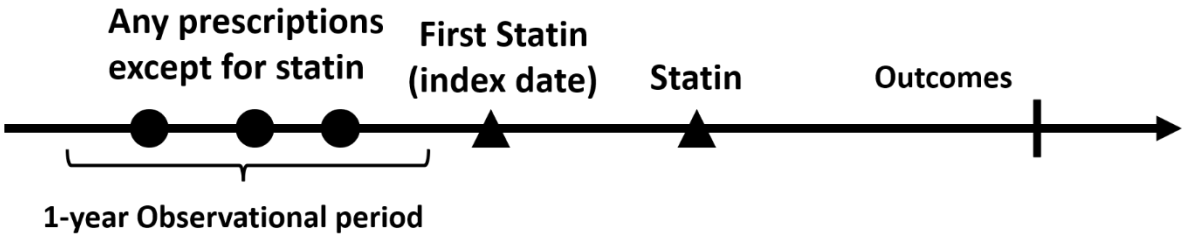
## Supplementary Methods 1. The brief of the China Renal Data System (CRDS)

CRDS (Website: **http://www.crds-network.org.cn/#/database**) is a cooperative network formed by the regional medical centers across China with the aim of facilitating clinical research on kidney disease. Each participating center exported from its proprietary hospital information systems the demographic and the clinical data of the patients who had been hospitalized between 2000 and 2021. The exported data were cleaned up, standardized, anonymized and pooled at the CRDS datacenter located at the National Clinical Research Center of Kidney Disease in Guangzhou. This database contains both the inpatient and outpatient follow-up data for each patient, including demographic information, details of prescriptions, the diagnosis, the results of laboratory testing, information regarding surgery, and vital signs, but does not include data on outpatient visits elsewhere.

Specifically, the age, sex, smoking and alcohol consumption status, date of diagnosis, diagnosis codes on admission and discharge, surgical procedure codes and dates, need for intensive care, occurrence of death in hospital, and blood pressure of the patients were included. The laboratory data included the results and timing of specific laboratory tests. The prescription details included the names, codes, doses, dose units, frequency and route of administration, and initiation and cessation dates for each drug. The data collected at all the participating hospitals were pooled and cleaned at the National Clinical Research Center for Kidney Disease in Guangzhou, China. All the laboratories at the participating hospitals had passed the annual External Quality Assessment of the Chinese National Center for Clinical Laboratories. CRDS database has achieved the ISO9001 quality certification and the approval of China Office of Human Genetic Resources for Data Preservation Application from Ministry of Science and Technology of China (approval number: 2021-BC0037). For data cleaning and standardization, we conducted two-step quality control for the raw data and the standardized data to ensure the high quality of our database. First, a portion of the raw data from each hospital were randomly extracted and reviewed to verify the accuracy and completeness of at least 95%. Second, the quality control was implemented as feedback of the data cleaning cycles, by clinical staff manually reviewing the data and submitting the QC report. The data cleaning process would continuously cycle until the quality control accuracy reach to 95%. As of November 1, 2021, the CRDS databases included data of more than 7 million patients from 19 medical centers.

## Supplementary Methods 2. Definition of the statin initiators

The date of the first statin prescription was assigned as the index date for statin initiators, and subsequent statin use was captured. Persons with any prior statin or without any precipitations except for statin within 1-year before the index-date were excluded. Timelines of statin new-user (initiators) illustrated below.



## Supplementary Methods 3. Propensity score (PS) model

Propensity score methods are used to minimize the confounding bias in estimating treatment effects in observational data. The propensity score (PS) of statin initiation was estimated using a multi-variables logistic regression model including the potential confounding factors: age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, hba1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia. The propensity score ($PS_i$) repented the likelihood to initiate statin therapy for each patient. These scores ranged from 0 to 1, the higher the score, the more likely the patients with statin therapy. According to the propensity score, matching and weighting were performed to adjust the confounding factors.

**Propensity score matching (PSM)**

PSM was used to balance the baseline characteristics by matching. The matching ratio in our study was set to 1:1. The selection of caliper was generally set to 0.2 × SD of the logit of the estimated PS or experientially, 0.02. In our study, we slightly magnified it to 0.05 because the large sample sizes and reasonable comparability between the two group.

**Inverse probability of treatment weighting (IPTW)**

IPTW is defined as $w_i=1/PS_i$ for statin initiators and $w_i=1/(1- PS_i)$ for noninitiators. IPTW allocated to each patient a weight proportional to the reciprocal of the probability of being received statin therapy. The objective of the IPTW was to create a pseudo-population between statin initiators and noninitiators in which there is no association between the confounding factors and the statin initiation. However, the pseudo-population this weighting method will be enlarged. To better reveal the characteristics of original population, two weighting methods were used.

***IPTW for Stabilized weighting***

The stabilized weighting is defined as $w_i$=Pr[statin initiators]/$PS_i$ for statin initiators and $w_i$= Pr[noninitiators]/(1− $PS_i$) for noninitiators, which Pr[statin initiators] and Pr[noninitiators] were the probability statin use in the total population. In our study, Pr[statin initiators]= 7272/19,858 while Pr[noninitiators]= 12,586/19,858. We stabilized the inverse probability weights to obtain a similar number among statin and noninitiators and limited them in a normal range (0.1<weights<10) to avoid the extreme weights.

**Propensity score overlap weighting**

IPTW may perform poorly when patients in exposure (statin initiators) and non-exposure (noninitiators) are initially very different and patients with extreme large or small PS (near to 0 or 1), that is, almost be a statin initiator or noninitiators in some condition. Extreme PS are particularly common in real-world research where inclusion criteria can be defined broadly. In this cohort, patients with statin initiation were more likely to be dyslipidemia at baseline though the guidelines recommended diabetes patients aged 40 years of older initiated statin therapy whether dyslipidemia or not. To clarify to influence of extreme PS, we also used overlap weights (OW) to estimate the association instead of stabilized weights. Overlap weights are defined as $w_i$=1-$PS_i$ for statin initiators and $w_i$=$PS_i$ for noninitiators. These weights eliminate the probability for extreme weights by avoiding

an extreme PS near 0 or 1 as the denominator (like stabilized weight). Therefore, when using overlap weights, many of the concerns about the assessment and the trimming of the weights are eliminated.

## Supplementary Table 1. Classification of Concomitant Drugs based on ATC codes

| Category | Drug name | ATC (3 codes) | ATC (5 codes) |
|---|---|---|---|
| Antihypertensive drugs | Renin-Angiotensin-Aldosterone System | C09 | C09AA\|C09BA\|C09BB\|C09BX\|C09CA\|C09DA\|C09DB\|C09DX |
| | β blockers | C07 | C07AA\|C07AB\|C07AG\|C07BA\|C07BB\|C07BG\|C07CA\|C07CB\|C07CG\|C07DA\|C07DB\|C07EA\|C07EB\|C07FB\|C07FX |
| | Calcium Channel Blocker | C08 | C08CA\|C08CX\|C08DA\|C08DB\|C08EAC08EX\|C08GA |
| | Diuretics | C03 | C03AA\|C03AB\|C03BA\|C03BB\|C03CA\|C03CB\|C03CC\|C03CD\|C03CX\|C03DA\|C03DB\|C03EA\|C03EB\|C03XA |
| | Others | C10 | C02AA\|C02AB\|C02AC\|C02CA\|C02DB\|C02DC\|C02DD\|C02KX\|C02LA |
| Glucose-lowering drugs | Insulin | A10 | A10AB\|A10AC\|A10AD\|A10AE |
| | Metformin | A10 | A10BA02 |
| | Sulfonylureas | A10 | A10BB |
| | DPP4 | A10 | A10BH |
| | SGLT2 | A10 | A10BK |
| | GLP1 | A10 | A10BJ |
| lipid-lowering agents | Statin | C10 | C10AA |
| | Others lipid-lowering agents | C10 | C10AB\|C10AC\|C10AD\|C10AX |
| Anti-inflammatory agents, non-steroids | NSAIDs | S01 | S01BC01\| S01BC02\| S01BC03\| S01BC04\| S01BC05\| S01BC06\| S01BC07\|01BC08\| S01BC09\| S01BC010\| S01BC11\| |

**Supplementary Table 2. Baseline characteristics of study population (Complete)** *

| Characteristics | Total | Before weighting | | | After weighting | | |
|---|---|---|---|---|---|---|---|
| | | Noninitiators | Statin initiators | SMD† | Noninitiators | Statin initiators | SMD† |
| No. | 19 858 | 12 586 | 7272 | - | 2684.39 | 2684.39 | - |
| Age, yr | 62.2 (54.5-69.4) | 60.7 (53.5-67.4) | 65.0 (57.1-72.7) | 0.40 | 62.7 (55.3-69.9) | 62.8 (54.7-70.5) | <0.001 |
| Male (%) | 11012.0 (55.5) | 7140.0 (56.7) | 3872.0 (53.2) | 0.07 | 1423.2 (53.0) | 1423.2 (53.0) | <0.001 |
| BMI, median (IQR), kg/m$^2$ | 23.6 (21.5-26.0) | 23.4 (21.2-25.8) | 24.1 (22.0-26.4) | 0.22 | 23.8 (21.6-26.2) | 23.8 (21.7-26.1) | <0.001 |
| Blood pressure, median (IQR), (mmHg) | | | | | | | |
| SBP | 131 (120-144) | 129 (118-141) | 135 (123-149) | 0.03 | 131 (120-145) | 132 (120-145) | <0.001 |
| DBP | 79 (71-86) | 78 (70-85) | 80 (72-87) | 0.02 | 79 (71-86) | 80 (71-87) | <0.001 |
| Laboratory testing indicators, median (IQR) | | | | | | | |
| Baseline eGFR, 60 ml/min/1.73m$^2$ ‡ | 94.2 (83.7-103.1) | 96.6 (86.8-105.1) | 89.6 (79.2-98.8) | 0.46 | 93.5 (82.8-101.9) | 93.3 (82.9-101.9) | <0.001 |
| Dyslipidemia (%) | | | | | | | |
| LDL-C ≥ 3.4 mmol/L | 4086.0 (20.6) | 1753.0 (13.9) | 2333.0 (32.1) | 0.44 | 668.4 (24.9) | 668.4 (24.9) | <0.001 |
| TC≥ 5.1 mmol/L | 5583.0 (28.1) | 2747.0 (21.8) | 2836.0 (39.0) | 0.38 | 896.7 (33.4) | 896.7 (33.4) | <0.001 |
| TG ≥ 1.7 mmol/L | 4324.0 (21.8) | 2378.0 (18.9) | 1946.0 (26.8) | 0.19 | 661.8 (24.7) | 661.8 (24.7) | <0.001 |
| HDL-C, mmol/L | 1.09 (0.91-1.31) | 1.09 (0.90-1.31) | 1.10 (0.92-1.31) | 0.05 | 1.1 (0.9-1.3) | 1.1 (0.9-1.3) | <0.001 |
| Albumin, g/L | 40.5 (37.6-43.5) | 40.2 (37.1-43.3) | 40.9 (38.2-43.7) | 0.21 | 40.8 (38.0-43.8) | 40.7 (38.0-43.6) | <0.001 |
| HbA1c, % | 7.0 (6.2-8.3) | 6.9 (6.2-8.1) | 7.0 (6.3-8.5) | 0.15 | 7.0 (6.3-8.5) | 7.0 (6.2-8.4) | <0.001 |
| Uric acid, μmol/L | 320 (260-387) | 312 (253-377) | 334 (274-403) | 0.24 | 324 (263-390) | 323 (262-391) | <0.001 |
| Alanine aminotransaminase, U/L | 19 (14-29) | 20 (13-30) | 19 (14-28) | 0.08 | 19 (13-29) | 19 (14-28) | <0.001 |
| Aspartate aminotransaminase, U/L | 20 (16-27) | 21 (16-29) | 20 (16-25) | 0.11 | 20 (16-26) | 20 (16-25) | <0.001 |
| Hemoglobin, g/L | 129 (117-141) | 126 (113-138) | 134 (123-144) | 0.46 | 131 (120-142) | 131 (120-142) | <0.001 |
| White blood cells, ×10$^9$/L | 6.2 (4.9-7.6) | 5.9 (4.5-7.4) | 6.8 (5.6-8.2) | 0.25 | 6.4 (5.1-7.9) | 6.5 (5.3-8.0) | <0.001 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Glucose-lowering agents (%) | | | | | | | |
| Insulin | 9159.0 (46.1) | 6410.0 (50.9) | 2749.0 (37.8) | 0.27 | 1177.5 (43.9) | 1177.5 (43.9) | <0.001 |
| Metformin | 6851.0 (34.5) | 3604.0 (28.6) | 3247.0 (44.7) | 0.34 | 1051.0 (39.2) | 1051.0 (39.2) | <0.001 |
| Sulfonylureas | 4358.0 (21.9) | 2476.0 (19.7) | 1882.0 (25.9) | 0.15 | 644.2 (24.0) | 644.2 (24.0) | <0.001 |
| DPP4 inhibitors | 1345.0 (6.8) | 607.0 (4.8) | 738.0 (10.1) | 0.20 | 231.8 (8.6) | 231.8 (8.6) | <0.001 |
| SGLT2 inhibitors | 82.0 (0.4) | 24.0 (0.2) | 58.0 (0.8) | 0.09 | 13.1 (0.5) | 13.1 (0.5) | <0.001 |
| GLP1 | 84.0 (0.4) | 40.0 (0.3) | 44.0 (0.6) | 0.04 | 17.3 (0.6) | 17.3 (0.6) | <0.001 |
| Anti-hypertension agents (%) | | | | | | | |
| RASi | 4872.0 (24.5) | 1827.0 (14.5) | 3045.0 (41.9) | 0.64 | 734.5 (27.4) | 734.5 (27.4) | <0.001 |
| β-blockers | 3759.0 (18.9) | 1522.0 (12.1) | 2237.0 (30.8) | 0.47 | 514.4 (19.2) | 514.4 (19.2) | <0.001 |
| CCB | 5939.0 (29.9) | 2908.0 (23.1) | 3031.0 (41.7) | 0.41 | 859.9 (32.0) | 859.9 (32.0) | <0.001 |
| Diuretic | 3186.0 (16.0) | 2370.0 (18.8) | 816.0 (11.2) | 0.21 | 340.5 (12.7) | 340.5 (12.7) | <0.001 |
| NSAIDs (%) | 9866.0 (49.7) | 5642.0 (44.8) | 4224.0 (58.1) | 0.27 | 1328.7 (49.5) | 1328.7 (49.5) | <0.001 |
| CCI, median (IQR) [§] | 6 (5-7) | 6 (5-7) | 6 (4-7) | 0.23 | 6 (4-7) | 5 (4-7) | <0.001 |
| Comorbidities (%) | | | | | | | |
| Diabetic complications [¶] | 4297.0 (21.6) | 2297.0 (18.3) | 2000.0 (27.5) | 0.22 | 669.7 (24.9) | 669.7 (24.9) | <0.001 |
| Myocardial infarction | 218.0 (1.1) | 24.0 (0.2) | 194.0 (2.7) | 0.21 | 15.6 (0.6) | 15.6 (0.6) | <0.001 |
| Arrhythmia | 1899.0 (9.6) | 770.0 (6.1) | 1129.0 (15.5) | 0.31 | 271.0 (10.1) | 271.0 (10.1) | <0.001 |
| Hypertension | 9049.0 (45.6) | 4550.0 (36.2) | 4499.0 (61.9) | 0.53 | 1304.6 (48.6) | 1304.6 (48.6) | <0.001 |
| Hyperuricemia | 2154.0 (10.8) | 948.0 (7.5) | 1206.0 (16.6) | 0.28 | 342.4 (12.8) | 342.4 (12.8) | <0.001 |
| Hypothyroidism | 347.0 (1.7) | 159.0 (1.3) | 188.0 (2.6) | 0.10 | 54.5 (2.0) | 54.5 (2.0) | <0.001 |
| PVD | 3469.0 (17.5) | 1659.0 (13.2) | 1810.0 (24.9) | 0.30 | 471.1 (17.5) | 471.1 (17.5) | <0.001 |
| COPD | 1053.0 (5.3) | 618.0 (4.9) | 435.0 (6.0) | 0.05 | 154.9 (5.8) | 154.9 (5.8) | <0.001 |
| Asthma | 400.0 (2.0) | 197.0 (1.6) | 203.0 (2.8) | 0.08 | 61.2 (2.3) | 61.2 (2.3) | <0.001 |
| Cerebral bleeding | 236.0 (1.2) | 103.0 (0.8) | 133.0 (1.8) | 0.09 | 42.9 (1.6) | 42.9 (1.6) | <0.001 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Cerebral infraction | 2492.0 (12.5) | 548.0 (4.4) | 1944.0 (26.7) | 0.65 | 329.3 (12.3) | 329.3 (12.3) | <0.001 |
| Pancreatitis | 198.0 (1.0) | 161.0 (1.3) | 37.0 (0.5) | 0.08 | 21.1 (0.8) | 21.1 (0.8) | <0.001 |

BMI=body mass index, CCB=calcium channel blocker, CCI=Charlson Comorbidity Index, DBP=diastolic blood pressure, COPD=Chronic Obstructive Pulmonary Disease, DPP4=dipeptidyl peptidase-4, eGFR=estimated glomerular filtration rate, HbA1c=glycated hemoglobin, HDL-C=high density lipoprotein cholesterol, IQR=interquartile range, LDL-C=low-density lipoprotein cholesterol, PVD=peripheral vascular disease, RASi=renin-angiotensin system inhibitors, SBP=systolic blood pressure, SGLT2=sodium-glucose co-transporter-2, SMD=standardized mean difference, TC=total cholesterol, TG=triglyceride.

*We defined the time from within 3 months before the index date as the baseline period. The date of the first statin prescription was assigned as the index date for statin initiators. For noninitiators, the index date was assigned as a randomly selected date of any admission

†Covariates with SMD of > 0.1 were regarded as unbalancing the groups. [43]

‡Estimated GFR was calculated using serum creatinine and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[39]

§We calculated the Charlson Comorbidity Index to quantify the overall comorbidity status [40]

¶Diabetic complications including diabetic retinopathy, diabetic peripheral neuropathy, diabetic ketosis, diabetic foot and other diabetic angiopathies.

**Supplementary Table 3. The weighted incidence of kidney outcomes before and after overlap weighting**

| Outcomes | Total | Before weighting | | | After weighting | | |
|---|---|---|---|---|---|---|---|
| | | Noninitiators | Statin initiators | *P* value | Noninitiators | Statin initiators | *P* value |
| No. | 19 858 | 12 586 | 7272 | - | 2684.39 | 2684.39 | - |
| Development of DKD | 1247.0 (6.3) | 743.0 (5.9) | 504.0 (6.9) | 0.004 | 181.7 (6.8) | 164.1 (6.1) | 0.169 |
| New-onset eGFR <60 ml/min/1.73m$^2$ | 571.0 (2.9) | 328.0 (2.6) | 243.0 (3.3) | 0.003 | 88.3 (3.3) | 72.0 (2.7) | 0.070 |
| New-onset proteinuria | 880.0 (4.4) | 539.0 (4.3) | 341.0 (4.7) | 0.180 | 132.0 (4.9) | 118.0 (4.4) | 0.203 |
| >40% decline in eGFR | 316.0 (1.6) | 195.0 (1.5) | 121.0 (1.7) | 0.534 | 50.5 (1.9) | 40.3 (1.5) | 0.144 |

DKD=diabetic kidney disease, eGFR=estimated glomerular filtration rate.

**Supplementary Table 4. The association of different statin subtypes and kidney outcomes**

| Statin subtypes | No. | Development of DKD | | New-onset eGFR <60 ml/min/1.73m$^2$ | | New-onset proteinuria | | >40% decline in eGFR | |
|---|---|---|---|---|---|---|---|---|---|
| | | HR (95%CI) * | *P* value | HR (95%CI) * | *P* value | HR (95%CI) * | *P* value | HR (95%CI) * | *P* value |
| Lipophilic | | | | | | | | | |
| Simvastatin | 766 | 0.88 (0.68-1.15) | 0.347 | 0.68 (0.46-1.02) | 0.063 | 0.94 (0.69-1.27) | 0.675 | 0.62 (0.35-1.09) | 0.099 |
| Pitavastatin | 418 | 0.75 (0.51-1.11) | 0.148 | 0.84 (0.50-1.42) | 0.511 | 0.59 (0.35-0.98) | 0.042 | 0.91 (0.45-1.86) | 0.801 |
| Fluvastatin | 303 | 0.75 (0.50-1.13) | 0.171 | 0.71 (0.39-1.27) | 0.242 | 0.71 (0.43-1.15) | 0.162 | 0.68 (0.33-1.40) | 0.294 |
| Atorvastatin | 4424 | 0.65 (0.54-0.78) | <0.001 | 0.55 (0.42-0.73) | <0.001 | 0.66 (0.53-0.83) | <0.001 | 0.49 (0.33-0.72) | <0.001 |
| Hydrophilic | | | | | | | | | |
| Rosuvastatin | 1135 | 0.75 (0.56-1.00) | 0.053 | 0.62 (0.40-0.96) | 0.032 | 0.65 (0.45-0.93) | 0.019 | 0.63 (0.36-1.09) | 0.100 |
| Pravastatin | 226 | 0.46 (0.23-0.91) | 0.026 | 0.37 (0.13-1.06) | 0.064 | 0.49 (0.23-1.04) | 0.065 | 0.15 (0.02-1.06) | 0.057 |

DKD=diabetic kidney disease, eGFR=estimated glomerular filtration rate, HR=hazard ratio.

* HRs were estimated by cox proportional model after overlap weighting with confounders adjusted including age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, HbA1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia.

**Supplementary Table 5. The association between statin initiation and increase in the number of glucose-lowering medication classes among diabetic patients with and without dyslipidemia**

| Outcomes | Total population | | Without dyslipidemia | | Dyslipidemia | |
|---|---|---|---|---|---|---|
| | OR (95%CI) † | *P* value | OR (95%CI) † | *P* value | OR (95%CI) † | *P* value |
| Increase in number of all glucose-lowering medication | 1.46 (1.27-1.68) | <0.001 | 1.55 (1.28-1.87) | <0.001 | 1.39 (1.13-1.71) | 0.001 |
| Increase in insulin usage | 1.11 (0.92-1.35) | 0.277 | 1.23 (0.95-1.60) | 0.112 | 0.98 (0.73-1.32) | 0.887 |
| Increase in oral glucose-lowering medication * | 1.75 (1.50-2.05) | <0.001 | 1.84 (1.48-2.29) | <0.001 | 1.69 (1.34-2.13) | <0.001 |

OR=odds ratio.

* Oral glucose-lowering medication including metformin, SGLT2 inhibitors, DPP4 inhibitors, GLP1, and Sulfonylureas.

† ORs (odd ratio) were estimated using logistic regression in weighted cohort with confounders adjusted including age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, HbA1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia.

**Supplementary Table 6. Adjusted HR associated with kidney outcomes in patients with long-term (>3 yr) follow-up**

| Outcomes | HR (95%CI) * | *P* value |
|---|---|---|
| Development of DKD | 0.67 (0.57-0.78) | <0.001 |
| New-onset eGFR <60 ml/min/1.73m$^2$ | 0.62 (0.49-0.78) | <0.001 |
| New-onset proteinuria | 0.65 (0.55-0.78) | <0.001 |
| >40% decline in eGFR | 0.58 (0.42-0.80) | 0.001 |

DKD=diabetic kidney disease, eGFR=estimated glomerular filtration rate, HR=hazard ratio.

* HRs were estimated by cox proportional model after propensity score overlap weighting with confounders adjusted including age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, HbA1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia.

**Supplementary Table 7. Adjusted hazard ratio of statin initiation associated with kidney outcomes via propensity-score matching and weighting**

| | Propensity score matching | | IPTW for stabilized weighting | |
|---|---|---|---|---|
| **Outcomes** | **HR (95%CI) *** | ***P* value** | **HR (95%CI) *** | ***P* value** |
| Development of DKD | 0.75 (0.63-0.90) | 0.002 | 0.77 (0.59-0.99) | 0.043 |
| New-onset eGFR <60 ml/min/1.73m$^2$ | 0.67 (0.52-0.87) | 0.003 | 0.68 (0.46-1.00) | 0.052 |
| New-onset proteinuria | 0.75 (0.61-0.93) | 0.007 | 0.74 (0.55-0.98) | 0.036 |
| >40% decline in eGFR | 0.62 (0.44-0.88) | 0.007 | 0.88 (0.52-1.49) | 0.627 |

DKD=diabetic kidney disease, eGFR=estimated glomerular filtration rate, HR=hazard ratio, IPTW=Inverse Probability of Treatment Weighting.

* HRs were estimated by cox proportional model after propensity score matching or weighting with confounders adjusted including age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, HbA1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia.

**Supplementary Table 8. Adjusted hazard ratio of statin initiation associated with kidney outcomes using time-varying Cox model**

| **Outcomes** | **HR (95%CI)** * | ***P* value** |
|---|---|---|
| Development of DKD | 0.76 (0.64-0.89) | 0.001 |
| New-onset eGFR <60 ml/min/1.73m$^2$ | 0.69 (0.54-0.89) | 0.004 |
| New-onset proteinuria | 0.76 (0.62-0.92) | 0.005 |
| >40% decline in eGFR | 0.71 (0.50-0.99) | 0.045 |

DKD=diabetic kidney disease, eGFR=estimated glomerular filtration rate, HR=hazard ratio.

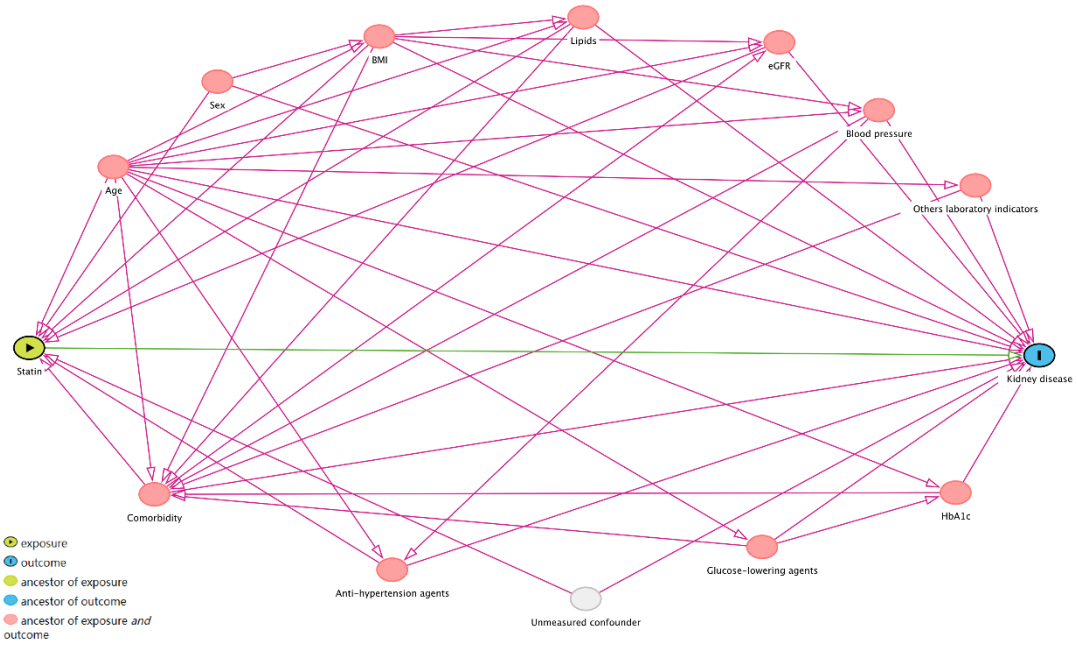
* HRs were estimated by cox proportional model after propensity score overlap weighting with confounders adjusted including age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, HbA1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia.

**Supplementary Table 9. Adjusted HR associated with kidney outcomes after excluding patients who encountered the development of DKD within one-year.**

| Outcomes | HR (95%CI) * | *P* value |
|---|---|---|
| Development of DKD | 0.79 (0.65-0.96) | 0.018 |
| New-onset eGFR <60 ml/min/1.73m$^2$ | 0.68 (0.50-0.91) | 0.009 |
| New-onset proteinuria | 0.81 (0.64-1.02) | 0.077 |
| >40% decline in eGFR | 0.60 (0.41-0.90) | 0.012 |

DKD=diabetic kidney disease, eGFR=estimated glomerular filtration rate, HR=hazard ratio.

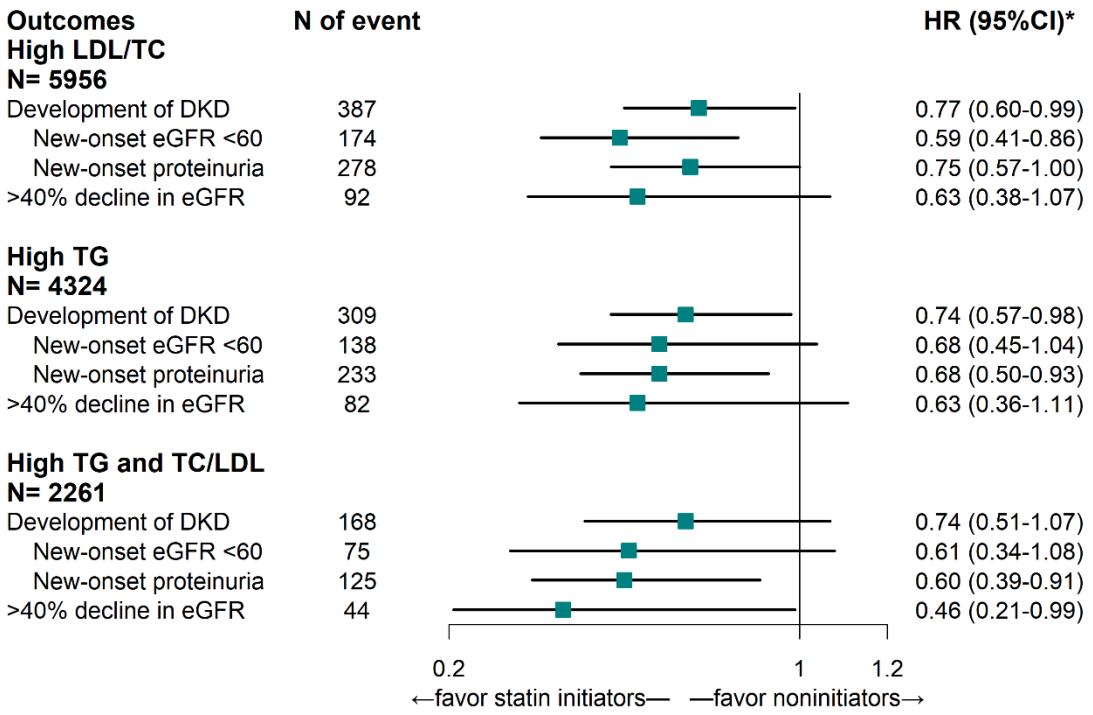
* HRs were estimated by cox proportional model after propensity score overlap weighting with confounders adjusted including age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, HbA1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia.




## Supplementary Figure 1. Directed Acyclic Graph

eGFR=estimated glomerular filtration rate.

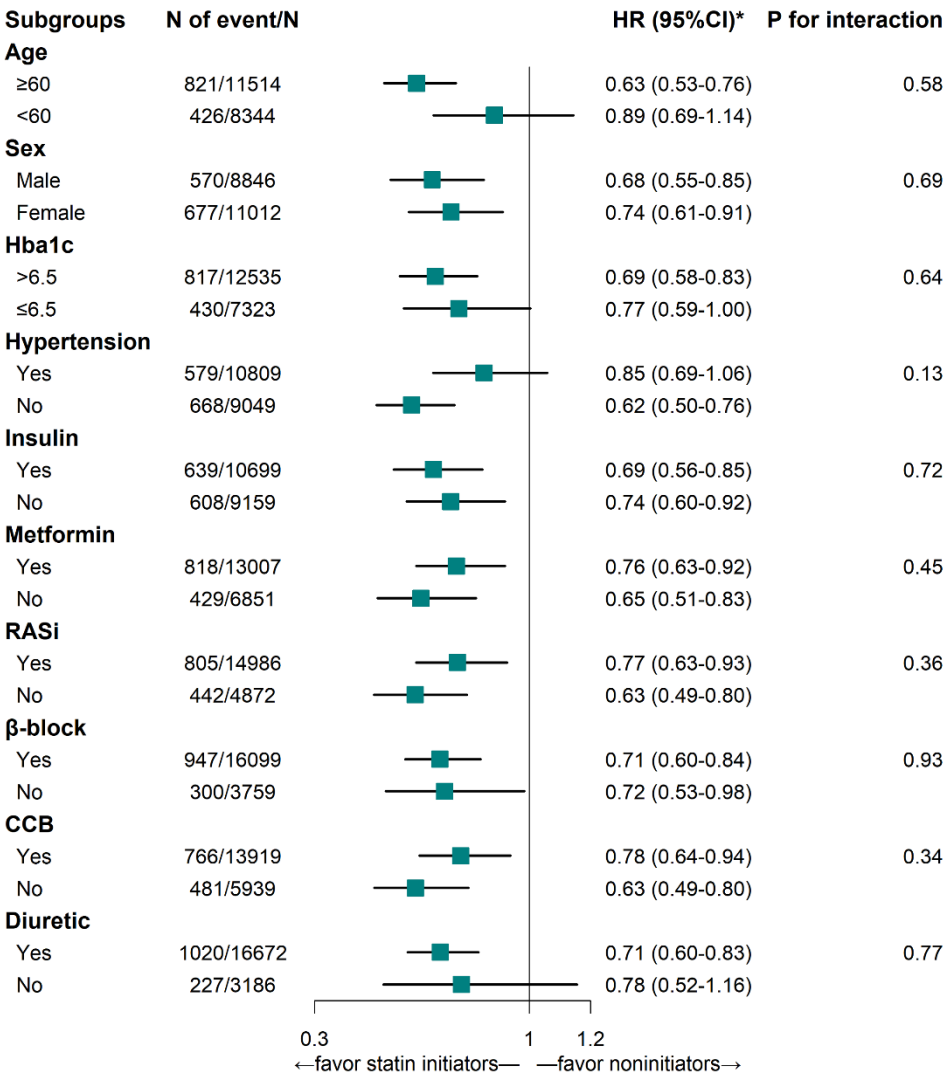
The directed acyclic graph (DAG) is built with variables that are associated with the exposure and/or the outcome based on biological mechanism or evidence from previously published data. Green circle: exposure; Blue circle with black line: outcome; Blue circle: ancestor of outcome. They are variables that may affect the outcome but with no relation with the exposure; Pink circle: ancestor of exposure or outcome.




**Supplementary Figure 2. Adjusted hazard ratio associated with kidney outcomes among different component of dyslipidemia**

DKD=diabetic kidney disease, eGFR=estimated glomerular filtration rate, HR=hazard ratio, LDL-C=low-density lipoprotein-cholesterol, TC=total cholesterol, TG=triglyceride.

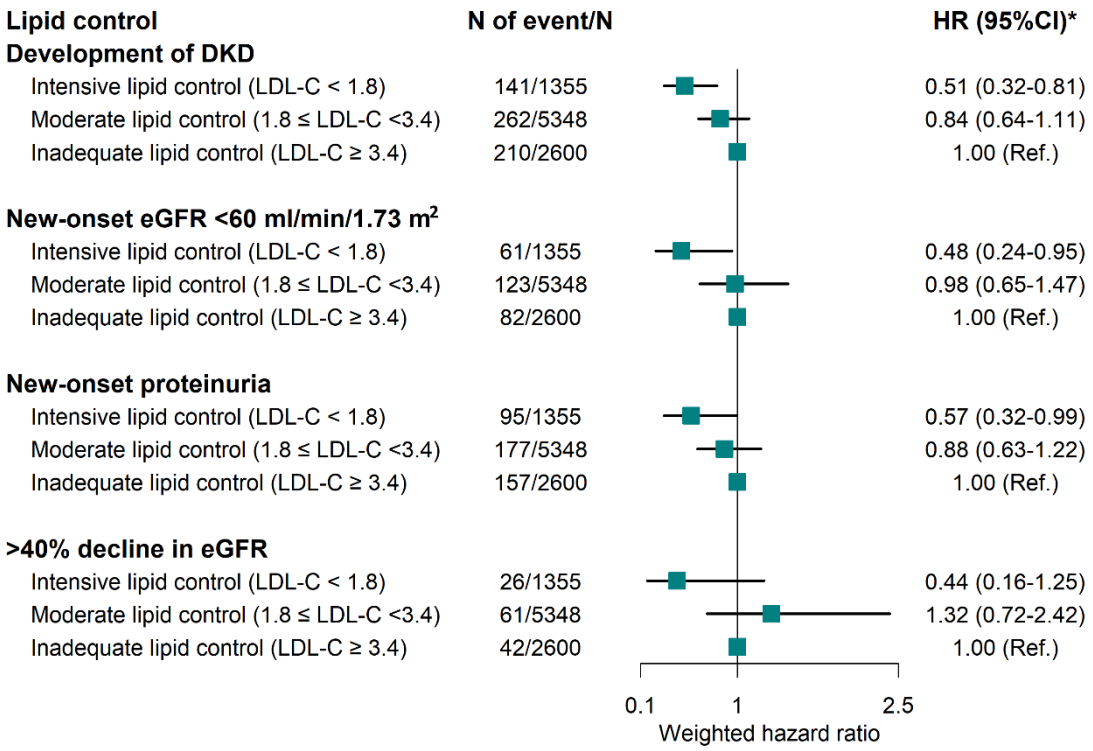
* HRs were estimated by cox proportional model after propensity score overlap weighting with confounders adjusted including age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, HbA1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia.




**Supplementary Figure 3: Adjusted hazard ratio for the development of diabetic kidney disease for statin initiation by baseline characteristics**

CCB=calcium channel blocker, DKD=diabetic kidney disease, LDL-C=low-density lipoprotein cholesterol, RASi=renin-angiotensin system inhibitors, TC=total cholesterol, TG=triglyceride.

* HRs were estimated by cox proportional model after propensity score overlap weighting with confounders adjusted including age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, HbA1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia.




**Supplementary Figure 4. The association of LDL-C control after one year and kidney outcomes.**

DKD=diabetic kidney disease, eGFR=estimated glomerular filtration rate, HR=hazard ratio.

* HRs were estimated by cox proportional model after propensity score overlap weighting with confounders adjusted including age, sex, BMI, SBP, DBP, Baseline eGFR, LDL-C, TC, TG, HDL-C, albumin, HbA1c, Uric acid, ALT, AST, Hemoglobin, WBC, insulin, metformin, SGLT2 inhibitors, GLP1, DPP4 inhibitors, Sulfonylureas, RASi, β-blockers, CCB, Diuretic, NSAIDs, hypertension, Hyperuricemia, PVD, COPD, asthma, cerebral bleeding, cerebral infraction, pancreatitis, and arrhythmia.