ORIGINAL RESEARCH

Risk of Atherosclerotic Cardiovascular Disease and Nonatherosclerotic Cardiovascular Disease Hospitalizations for Triglycerides Across Chronic Kidney Disease Stages Among 2.9 Million US Veterans

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BACKGROUND: High triglycerides are associated with atherosclerotic cardiovascular disease (ASCVD) risks. Among patients with advanced chronic kidney disease (CKD), the association of elevated triglycerides with mortality is diminished and, thus, we investigated the relationship of triglycerides with ASCVD and non-ASCVD hospitalizations across CKD stages.

METHODS AND RESULTS: The cohort comprised 2 963 176 veterans who received care in 2004 to 2006 (baseline) and were followed up to 2014. Using Cox models, we evaluated baseline and time-varying triglycerides with time to ASCVD or non-ASCVD hospitalizations, stratified by baseline CKD stage, and adjusted for demographics and baseline or time-updated clinical characteristics. The cohort mean±SD age was 63±14 years, with a baseline median (interquartile range) triglycerides level of 127 (87–189) mg/dL, and a quarter had prevalent CKD. There was a linear association between baseline triglycerides and ASCVD risk; however, the risk with high triglycerides ≥240 mg/dL attenuated with worsening CKD stages (reference: triglycerides 120 to <160 mg/dL). Baseline triglycerides were associated with a U-shaped relationship for non-ASCVD events in patients with CKD 3A to 3B. Patients with late-stage CKD had lower to null relationships between baseline triglycerides and non-ASCVD events. Time-varying triglycerides associations with ASCVD were similar to baseline analyses. Yet, the time-varying triglycerides relationship with non-ASCVD events was inverse and linear, where elevated triglycerides were associated with lower risks.

CONCLUSIONS: Associations of higher triglycerides with ASCVD and non-ASCVD events declined across advancing CKD stages, where a lower to null risk was observed in patients with advanced CKD. Studies are needed to examine the impact of advanced CKD on triglycerides metabolism and its association with outcomes in this high-risk population.

Key Words: atherosclerosis ■ statistics ■ triglycerides

Dyslipidemia, including elevated serum triglycerides, is a risk factor for atherogenesis and development of cardiovascular disease (CVD) and is thus a primary target for CVD prevention in the general population.[1–3] Studies have suggested that hypertriglyceridemia is a predictor for chronic kidney

CLINICAL PERSPECTIVE

What Is New?

- Elevated triglycerides are associated with higher risk of atherosclerotic and nonatherosclerotic cardiovascular disease events yet not in patients with advanced chronic kidney disease.
- These relationships persisted in evaluating long- and short-term measurements of triglycerides.

What Are the Clinical Implications?

- It is imperative to understand the immediate and long-term impact of triglycerides on these cardiovascular events in patients with chronic kidney disease as to best manage cardiovascular health.

Nonstandard Abbreviations and Acronyms

SHARP	Study of Heart and Renal Protection
UACR	urine albumin/creatinine ratio
VA	Veterans Affairs

disease (CKD), including its development and progression into advanced CKD stages.[4,5] Because of lipid aberrations and accelerated atherosclerosis during CKD progression, these patients have a higher burden and risk of atherosclerotic cardiovascular disease (ASCVD), non-ASCVD, and mortality compared with the general population.[6–9] We previously demonstrated that the association between high serum triglycerides with CVD mortality incrementally declined across worsening CKD stages, where it reached a null association in patients with CKD stage 5 and end-stage renal disease (ESRD).[10] Possible explanations include competing events of other CVD causes, such as nonfatal CVD hospitalizations.[5,10,11] Clinical trials have focused on ASCVD events in patients with CKD, including primarily targeting low-density lipoprotein cholesterol (LDL-C) levels in early CKD stages (3A-3B), while the trials have been null in the patients with advanced CKD.[12] Thus, understanding the relationship between other components of dyslipidemia, such as triglycerides, with CVD outcomes is critical for devising risk mitigation strategies, especially in patients with advanced CKD.

Prior studies examining serum lipids with CVD events in patients with CKD have found mixed results, and have primarily investigated patients with early-stage CKD.[13–16] Understanding both the long- and short-term relationships of triglycerides on CVD events may better elucidate their complex relationships as CKD progresses to advanced stages. Moreover, studies have often focused on the relationship of triglycerides with composite CVD or ASCVD only events given that they are targeted by pharmacologic therapies, but the relationship of triglycerides with vascular yet non-ASCVD events remains less known. Therefore, using a large national cohort, we hypothesized that the relationships between baseline and time-varying serum triglycerides with ASCVD and non-ASCVD are also impacted by worsening CKD stages.

METHODS

Data Availability

Restrictions apply to the availability of data generated or analyzed during this study. The US Department of Veterans Affairs (VA) places legal restrictions on access to veteran's health care data, which includes both identifying data and sensitive patient information. The corresponding author will on request detail the restrictions and any conditions under which access to some data may be provided.

Study Population and Longitudinal Construction

The LIPROVET (Lipid Profiles and Management in Veterans With CKD) study is composed of US VA patients, with a lipid measurement between October 1, 2004, and September 30, 2006 (baseline period).[10] Follow-up was divided into consecutive calendar quarters (91-day intervals), starting from the quarter of the patient's first triglycerides and estimated glomerular filtration rate (eGFR) measurement in the baseline period. We excluded 114 031 patients for missing a triglycerides measurement during baseline, 880 985 patients for missing an eGFR measurement, 98 patients with invalid censoring information, and 547 patients for missing data on hospitalization during follow-up. The final cohort included 2 963 176 patients (Figure S1).

Clinical Measurements

The ascertainment of characteristics has been described elsewhere.[10] Data were sourced from combined VA, Centers for Medicare and Medicaid Services, and the US Renal Data System databases. The VA databases informed ever smoker and alcoholism statuses, which were defined as any indication of the behavior until censorship.[17] VA/Centers for Medicare and Medicaid Services pharmacy records identified lipid-modulating therapy prescriptions based on drug class codes and names. Receipt of medication was defined as any dispensation recorded within each calendar quarter. Comorbidities were derived from VA/Centers for Medicare and Medicaid Services databases using *International Classification of Diseases, Ninth*

Revision (*ICD-9*) Diagnostic and Current Procedural Terminology, and were updated for each quarter.[18,19]

Laboratory measurements were extracted from the VA database. The Martin-Hopkins equation was used to calculate LDL-C if missing for any quarter.[20] eGFR was calculated from serum creatinine using the CKD Epidemiology Collaboration formula.[21] CKD stage according to non–dialysis-dependent eGFR cutoffs was categorized as non-CKD, 3A, 3B, 4, and 5. The US Renal Data System identified patients with ESRD on renal replacement therapy, and they were grouped with CKD stage 5 irrespective of eGFR. All laboratory measurements were averaged per patient per calendar quarter to minimize measurement variability.

Exposure and Outcome Assessment

On the basis of clinically relevant cutoffs and prior studies, baseline and time-varying triglycerides were categorized as follows: <80, 80 to <120, 120 to <160, 160 to <200, 200 to <240, and ≥240 mg/dL.[10,22,23]

The outcomes were time to (1) ASCVD and (2) non-ASCVD hospitalization. VA/Centers for Medicare and Medicaid Services records with the specific diagnostic code in the first or second position were considered as an event (Table 1). Definitions of ASCVD and non-ASCVD hospitalizations were based on clinician judgment and prior studies.[13,14,24] Information on other censoring events was obtained from the aforementioned sources and the National Death Index. Patient follow-up started at the calendar quarter of entry, and ended at death, lost to follow-up, first ASCVD or non-ASCVD hospitalization if the outcome of interest, or December 31, 2014, whichever occurred first.

Statistical Analysis

Baseline characteristics are presented as mean±SD, median (interquartile range), or percentage, as appropriate.

We used Cox models to evaluate the association of baseline or time-varying triglycerides with time to ASCVD or non-ASCVD hospitalization, stratified by baseline CKD stage. In all analyses, the reference group was triglycerides 120 to <160 mg/dL.

Five adjustment models were examined: (1) unadjusted; (2) age adjusted; (3) case-mix adjusted, which included age, sex, race, ethnicity, ever smoker, ever alcoholism, Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disorder, dementia, liver disease, cancer, diabetes, atrial fibrillation, hypertension, depression, ischemic heart disease, prescription of statins, and prescription of nonstatins; (4) case-mix+laboratory adjusted, which additionally included body mass index and albumin to the case-mix model; and (5) case-mix+laboratory+lipid adjusted, which additionally included LDL-C and high-density lipoprotein cholesterol to the case-mix+laboratory model. For baseline models, data from the baseline quarter were used in analyses. In time-varying models, time-updated comorbidities, medications, and laboratory measurements were used, as well as time-varying CKD stage in case-mix adjusted and higher models. We predefined the case-mix+laboratory adjustment as the model of interest.

We performed competing risk regression to account for mortality, where ASCVD hospitalization was competed against all-cause mortality and non-ASCVD hospitalization, and vice versa when non-ASCVD hospitalization was the outcome.[25] We evaluated the triglycerides-hospitalization relationships in subgroup analyses of baseline characteristics to investigate effect modification. In sensitivity analyses, we evaluated the relationship of baseline triglycerides and urinary tract infection hospitalization to investigate this negative control outcome in addressing uncontrolled confounding. Moreover, we evaluated

Table 1. *ICD-9* Codes and Causes of ASCVD and Non-ASCVD Hospitalizations

Hospitalization	Event description	*ICD-9* codes
ASCVD	Myocardial infarction	410, 412
	Unstable angina	411, 413
	Ischemic heart disease–other (coronary artery disease)	414
	Nonhemorrhagic stroke (ischemic TIA)	433–438
	Atherosclerosis (includes PVD and aneurysm)	440–445
Non-ASCVD	Heart failure (includes cardiomyopathy/arrhythmia)	425–429
	Hypertension	401–405
	Hemorrhagic stroke	430–432
	Fatal pulmonary embolism	415
	Phlebitis	451

ASCVD indicates atherosclerotic cardiovascular disease; *ICD-9*, *International Classification of Diseases, Ninth Revision*; PVD, peripheral vascular disease; and TIA, transient ischemic attack.

194 801 patients with available data on urine albumin/creatinine ratio (UACR) in the year before the calendar quarter of entry. A comparison of patients with and without UACR data is presented in Table S1. We repeated baseline analyses with adjustment for log-transformed UACR in the case-mix+laboratory model in this select population.

Data were missing in <2% for demographics, and 6% and 22%, respectively, for smoking status and alcoholism at baseline, and were imputed with a missing category. Baseline medications were missing in 5%, and both baseline and time-varying medications were imputed with a missing category. Albumin and body mass index were missing in 25% and 9%, respectively, at baseline, and were imputed by means. A last measurement carried forward imputation was used for all missing time-varying laboratory data, including triglycerides or eGFR.

Analyses were performed using SAS Enterprise Guide (7.1) (Cary, NC) and Stata (15) (College Station, TX). Because of the nonintrusive nature of the research, patient anonymity, and large sample size, the required written consent was waived; and this study was approved by the institutional review board of the Tibor Rubin VA Medical Center of Long Beach, CA.

RESULTS

In our cohort, the mean age (SD) was 63±14 years, and the cohort included 6% women and 14% Black race. The cohort had a median (interquartile range) averaged triglycerides level of 127 (87–189) mg/dL and averaged high-density lipoprotein cholesterol, LDL-C, and total cholesterol levels of 42 (35–51), 104 (83–129), and 178 (153–206) mg/dL, respectively. A quarter of patients had CKD (stage 3A and higher) at baseline, including 0.8% with CKD stage 5 or ESRD. Those with higher triglycerides tended to be younger and White race, have a lower prevalence of chronic obstructive pulmonary disease and anemia, and have a higher prevalence of diabetes, depression, and anxiety (Table 2).

Association of Baseline Triglycerides With Time to Hospitalizations

We observed 756 917 and 952 359 ASCVD and non-ASCVD hospitalizations, respectively, yielding crude incidence rates (95% CIs) of 36.7 (36.6–36.8) ASCVD and 47.3 (47.2–47.4) non-ASCVD events per 1000 person-years. Both rates increased with advancing CKD stage (Table S2). Only 11% and 16% of patients experienced >2 ASCVD or non-ASCVD hospitalizations, respectively, during follow-up. Among patients with any ASCVD hospitalization, 21% experienced

a myocardial infarction as their first event, whereas most (35%) experienced other ischemic heart disease as their first ASCVD event. Conversely, 60% of the first non-ASCVD hospitalizations were for heart failure.

In unadjusted models, the relationship of baseline triglycerides and ASCVD hospitalization was generally linear compared with triglycerides 120 to <160 mg/dL (Table S3). After adjustment for case-mix+laboratory covariates, lower triglycerides <120 mg/dL were associated with a lower risk of ASCVD hospitalization across all stages (Figure 1A). Moreover, the magnitude of association for high triglycerides ≥240 mg/dL with ASCVD hospitalization gradually decreased across CKD stages, where those with CKD stage 5/ESRD had an attenuated and null relationship. Adjustment for lipid measurements slightly attenuated results, but they were nonetheless similar.

In unadjusted models, we observed a shallow inverse relationship between baseline triglycerides and non-ASCVD hospitalization across CKD stages (Table S4). Yet, adjustment for case-mix+laboratory covariates demonstrated a U-shaped relationship for patients with CKD stage 3A to 3B, and an inverse relationship for patients with CKD stage 4 and 5/ESRD (Figure 1B). We also observed a gradual cascade in the risk between high triglycerides and non-ASCVD hospitalization across CKD stages. There was a lower to null association between high triglycerides and non-ASCVD hospitalization among patients with CKD stage 4 and 5/ESRD. Similar relationships were observed with additional lipid adjustment.

Sensitivity Analyses of Baseline Triglycerides and Time to Hospitalizations

Our observed relationships were comparable when using a competing risk regression adjusted for case-mix+laboratory covariates. We observed a linear association with baseline triglycerides and time to ASCVD hospitalization after considering competing events. Elevated triglycerides were associated with a higher risk for ASCVD events for all CKD stages. In competing risk analyses for non-ASCVD hospitalization, we observed a reverse J-shaped association in case-mix+laboratory adjustment.

In sensitivity analyses using a negative control, we found that association of baseline triglycerides with urinary tract infection hospitalization had a lower to null relationship across all CKD stages. A comparison of patients with and without UACR data demonstrated that those with UACR were more likely to be older, have diabetes, have hypertension, and have higher levels of body mass index (Table S1). After adjustment for log-transformed UACR in our main models, we observed

Table 2. Patient Characteristics Stratified by Baseline Serum Triglycerides Group

Characteristic	Total	Baseline serum triglycerides group, mg/dL					
		<80	80–<120	120–<160	160–<200	200–<240	≥240
No. (%)	2 963 176	594 877 (20)	767 468 (26)	571 781 (19)	368 272 (12)	228 243 (8)	432 535 (15)
eGFR, mL/min per 1.73 m²*	76 (62–91)	80 (64–94)	76 (61–90)	75 (61–89)	75 (60–89)	75 (60–90)	77 (61–92)
CKD stage, %							
Non-CKD	77	81	77	75	75	75	77
CKD 3A	15	13	15	16	16	15	14
CKD 3B	6	5	6	7	7	7	7
CKD 4	2	1	2	2	2	2	2
CKD 5/ESRD	0.8	0.7	0.8	0.8	0.8	0.8	0.8
Age, y	63±14	63±16	64±14	64±14	63±13	62±13	60±13
Sex, % women	6	8	6	5	5	5	4
Married, %	56	54	57	58	58	57	55
Race, %							
White	82	75	80	84	85	86	86
Black	14	22	16	13	11	10	9
Other†	4	3	4	4	4	4	5
Hispanic ethnicity, %	4	4	4	4	4	4	5
CCI	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–2)
Comorbid conditions, %							
MI	7	6	7	7	7	7	6
CHF	10	10	11	10	10	10	10
PVD	10	9	10	10	10	10	9
Cerebrovascular disease	9	9	9	9	9	9	8
Dementia	3	4	3	3	3	2	2
COPD	18	19	19	18	18	17	16
Liver disease	3	4	3	3	3	3	3
Diabetes	27	20	24	28	31	33	38
Cancer	12	12	13	13	12	11	10
Anemia	12	14	13	11	10	10	9
Atrial fibrillation	7	8	8	7	7	6	5
Hypertension	64	57	63	66	67	67	67
ISHD	27	24	27	28	28	27	26
Depression	18	15	17	18	19	20	23
Anxiety	13	11	11	12	13	14	16
PTSD	7	6	6	7	8	8	10
Gallbladder disease	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Ever smoking	64	61	63	64	65	66	68
Ever alcoholism	25	30	26	24	23	22	23
Laboratory measurements							
Albumin, g/dL	4.1±0.4	4.0±0.5	4.0±0.4	4.1±0.4	4.1±0.4	4.1±0.4	4.1±0.4
AST, U/L	23 (19–29)	23 (19–29)	23 (19–28)	23 (19–28)	23 (19–28)	23 (19–29)	24 (20–30)
ALT, U/L	25 (18–35)	23 (17–32)	24 (17–33)	25 (18–35)	26 (19–37)	27 (20–38)	29 (21–41)
Glucose, mg/dL	114.4±41.3	105.1±29.8	109.4±33.5	113.6±37.7	117.2±41.8	120.7±45.4	131.7±59.2
Hemoglobin, g/dL	14.5±1.6	14.1±1.6	14.4±1.6	14.6±1.6	14.7±1.6	14.7±1.6	14.8±1.6
WBC count, ×10³/mm³	7.2±2.7	6.6±2.6	7.1±2.7	7.3±2.7	7.4±2.6	7.5±2.6	7.6±2.7
SBP, mm Hg	135±18	133±18	134±18	135±18	136±17	136±17	137±17
DBP, mm Hg	76±11	74±11	75±11	76±11	76±11	76±11	77±11

(Continued)

Table 2. Continued

Characteristic	Total	Baseline serum triglycerides group, mg/dL					
		<80	80–<120	120–<160	160–<200	200–<240	≥240
BMI, kg/m²	29±6	27±5	28±6	30±6	30±6	31±6	31±6
Lipid panel, mg/dL							
Triglycerides	127 (87–189)	63 (53–72)	99 (89–109)	138 (128–148)	177 (168–188)	217 (208–228)	312 (268–395)
HDL-C	42 (35–51)	51 (42–62)	45 (38–53)	41 (35–49)	39 (33–46)	38 (32–44)	36 (30–42)
Cholesterol	178 (153–206)	164 (142–189)	172 (148–198)	178 (154–205)	184 (159–211)	188 (164–216)	202 (174–233)
LDL-C	104 (83–129)	99 (79–120)	105 (85–129)	108 (86–133)	108 (86–134)	107 (84–133)	100 (75–129)
Lipid-modulating therapy use, %							
Statin	48	39	48	51	52	53	51
Ezetimibe	1	1	1	1	1	1	1
Nonstatin	9	4	6	8	10	13	21
Fibrate	5	2	3	4	6	8	15
Niacin	3	2	2	3	3	4	5
Fish oil	0.3	0.1	0.2	0.3	0.4	0.5	0.8
Bile acid sequestrants	1	1	1	1	1	1	1

Data presented as mean±SD, median (interquartile range), or percentage as appropriate. ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CCI, Charlson comorbidity index; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HDL-C, high-density lipoprotein cholesterol; ISHD, ischemic heart disease; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; PTSD, posttraumatic stress disorder; PVD, peripheral vascular disease; SBP, systolic blood pressure; and WBC, white blood cell.

*eGFR provided for only patients classified as CKD stage 5, yet not on ESRD.

†Other race may include American Indian, Asian, Pacific Islander, multi-race and other race not included in White or Black categories.

an attenuated relationship between triglycerides and ASCVD hospitalization but still reflected that elevated triglycerides were associated with a higher risk of event except for in patients with CKD stage 5/ESRD (Figure S2). The triglycerides and non-ASCVD relationship was also attenuated and demonstrated that the non-ASCVD hospitalization risk diminished across CKD stages in patients with high triglycerides ≥240 mg/dL.

Figure 1. Association of baseline triglycerides with time to atherosclerotic cardiovascular disease (ASCVD) (A) and non-ASCVD (B) hospitalization across chronic kidney disease (CKD) stages after adjustment for case-mix+laboratory covariates.
Model adjustments: age, sex, race, ethnicity, ever smoker, ever alcoholism, Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, dementia, liver disease, cancer, diabetes, atrial fibrillation, hypertension, depression, ischemic heart disease, prescription of statins and prescription of nonstatins, body mass index, and albumin. ESRD indicates end-stage renal disease.

Subgroup Analyses for Baseline Triglycerides With Time to Hospitalizations

Subgroup analyses reflected similar yet attenuated relationships across strata of age, diabetes, LDL-C levels, statin use, race, and prior CVD (Tables S5 and S6). In general, we observed that the association of high triglycerides ≥240 mg/dL with each outcome depicted a similar cascade across advancing CKD stages. Notably, high triglycerides levels were no longer associated with decreased time to non-ASCVD hospitalization among patients with CKD stage 5/ESRD and those aged <65 years. Among patients with LDL-C <100 mg/dL and CKD stage 5/ESRD, the associations of high triglycerides ≥240 mg/dL with ASCVD and non-ASCVD events were each strengthened to an almost 10% lower risk of event. Conversely, patients with high LDL-C ≥100 mg/dL, high triglycerides, and CKD stage 4 had a null relationship with ASCVD or non-ASCVD hospitalization, whereas a slightly higher risk was observed in patients with CKD stage 5/ESRD and high triglycerides. The relationship of triglycerides and non-ASCVD events among patients without prior CVD was largely flat, whereas the triglycerides-ASCVD relationship remained linear across prior CVD strata.

Association of Time-Varying Triglycerides With Time to Hospitalizations

We further explored the relationship of triglycerides with ASCVD and non-ASCVD hospitalizations using time-varying models (Tables S7 and S8 and Figure 2A and 2B). After adjustment for time-varying case-mix+laboratory covariates, low time-varying triglycerides were generally associated with a null or lower risk of ASCVD hospitalization across strata of baseline CKD stage (reference: triglycerides 120–<160 mg/dL). Time-varying triglycerides ≥240 mg/dL were associated with a higher risk of ASCVD hospitalization for baseline non-CKD and CKD stage 3A to 3B. Similar to the baseline analysis, we observed a cascade in effect estimates in the association of high time-varying triglycerides and ASCVD event, including a null association among those with CKD stage 4 and 5/ESRD.

Alternatively, the association of time-varying triglycerides with time to non-ASCVD event was inverse across baseline CKD stages. Time-varying triglycerides <120 mg/dL were associated with a higher risk of non-ASCVD hospitalization across baseline CKD stages, with the exception of patients with CKD stage 5/ESRD in the case-mix+laboratory model. We observed a lower to null risk of non-ASCVD hospitalization for time-varying triglycerides ≥160 mg/dL across all CKD stages. Patients with baseline CKD stage 5/ESRD with the highest time-varying triglycerides ≥240 mg/dL had the lowest risk of non-ASCVD hospitalization (hazard ratio [95% CI], 0.86 [0.81–0.91]). Results were similar with time-updated lipid adjustment.

DISCUSSION

We evaluated long- and short-term associations between triglycerides and ASCVD and non-ASCVD hospitalization across CKD stages. Our observations suggest linear associations between baseline and
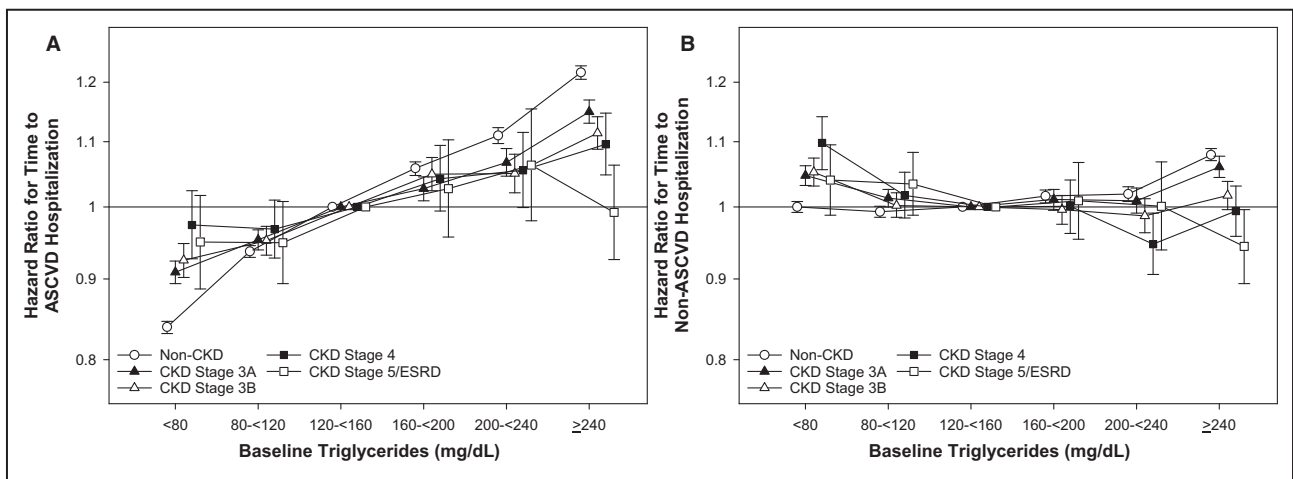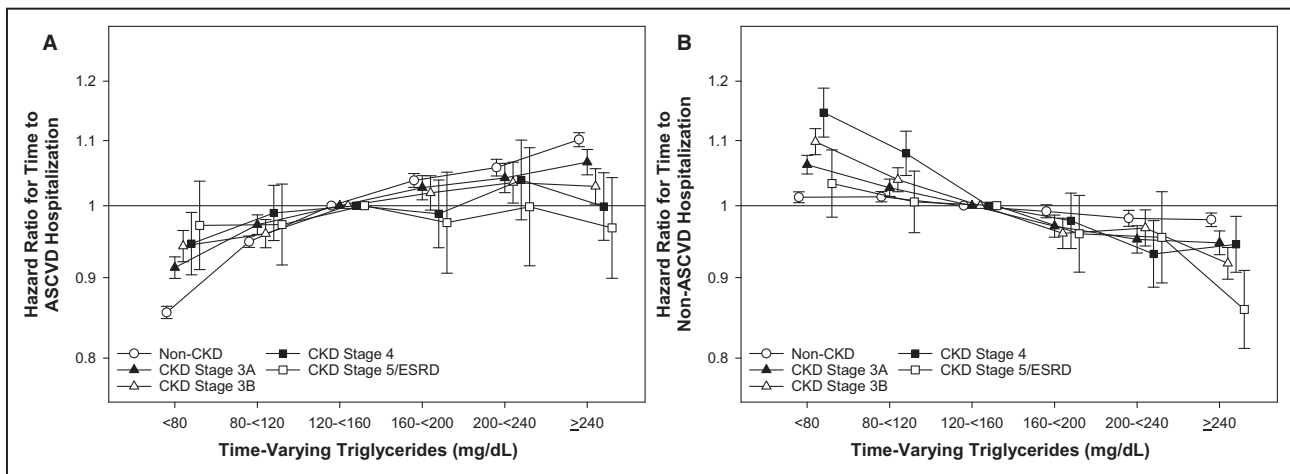

Figure 2. Association of time-varying triglycerides with time to atherosclerotic cardiovascular disease (ASCVD) (A) and non-ASCVD (B) hospitalization across baseline chronic kidney disease (CKD) stages after adjustment for case-mix+laboratory covariates.

Model adjustments: age, sex, race, ethnicity, ever smoker, ever alcoholism, time-updated Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, dementia, liver disease, cancer, diabetes, atrial fibrillation, hypertension, depression, ischemic heart disease, prescription of statins and prescription of nonstatins, body mass index, albumin, and CKD stage. ESRD indicates end-stage renal disease.

time-varying triglycerides with ASCVD hospitalization across CKD stages. For non-ASCVD outcomes, the relationship with baseline triglycerides was U-shaped in CKD stage 3A and 3B patients, but the time-varying triglycerides relationship was inverse and linear for all CKD stages. Across all analyses, we observed a similar pattern: the relationship with elevated triglycerides with hospitalizations incrementally declined in the magnitude of risk across worsening CKD stages, where patients with advanced CKD (stage 4 and 5/ESRD) tended to have null or lower associations with ASCVD and non-ASCVD hospitalizations.

Studies have examined the relationship of triglycerides with CVD events in patients with CKD, yet did not investigate relationships within individual CKD stages. The ARIC (Atherosclerosis Risk in Communities) study suggested that each quartile increase in triglycerides was associated with a higher risk of coronary heart disease among patients with CKD (eGFR 15–<60 mL/min per 1.73 m^2), but included minimal adjustment.[16] The MESA (Multi-Ethnic Study of Atherosclerosis) observed the potential interaction between patients without and with CKD (P-interaction=0.07) for an SD increase of log triglycerides with coronary heart disease risk.[15] Finally, the CRIC (Chronic Renal Insufficiency Cohort) study showed linear associations between triglycerides tertiles and ASCVD events among patients with CKD.[13] However, they did not observe interaction by eGFR (<45 and ≥45 mL/min per 1.73 m^2), where associations for triglycerides >160 mg/dL among each strata had a 24% to 25% higher risk of event (reference: triglycerides <103 mg/dL), and were attenuated. The magnitude of effect estimates from the CRIC study and MESA suggests a higher risk of ASCVD events with elevated triglycerides among patients with predominantly early-stage CKD. This was similarly observed in our patients with CKD 3A and 3B, where we had the power to examine individual stages and smaller clinically relevant groups of triglycerides.

A post hoc analysis of the SHARP (Study of Heart and Renal Protection) showed weak to null associations between higher triglycerides and ASCVD events, even when stratified at eGFR 30 mL/min per 1.73 m^2.[14] We also observed that patients with CKD stage 5/ESRD had a null risk of ASCVD events, yet the SHARP analyses for patients with early-stage CKD not only contrasted our study, but also the CRIC study and MESA. Both the CRIC study and MESA comprised primarily patients with CKD stage 3A to 3B, and thus were limited in the evaluation of later stages. Although SHARP did investigate patients with late-stage CKD and dialysis, it also excluded patients with prior myocardial infarction, which may render these study participants less generalizable to the general population with CKD. Moreover, these studies were limited in their ability to account for confounders without overadjustment. Our data allowed for the adjustment of potential confounders, including comorbidities and markers of malnutrition and inflammation often absent from prior studies. Notably, we observed a higher risk of ASCVD events with high triglycerides (≥160 mg/dL) across non-CKD and CKD stages 3A to 4. Akin to SHARP, we observed an attenuated relationship with triglycerides and ASCVD outcomes in patients with CKD stage 5/ESRD. These results were consistent with findings in patients undergoing hemodialysis, in whom elevated triglycerides levels were associated with lower risks of mortality and possibly attributable to the malnutrition and inflammation that are prevalent in this population.[10,26]

Few studies have examined the relationship of triglycerides and non-ASCVD events. SHARP showed that triglycerides were not associated with higher risk of non-ASCVD events among those with early-stage CKD, whereas there was a lower risk of non-ASCVD events among late-stage CKD. In our baseline study, we observed an elevated risk of non-ASCVD events with high triglycerides among patients without CKD and patients with CKD stage 3A, whereas the risk was attenuated or lower in later stages. In our time-varying analyses, we observed a lower risk of non-ASCVD events with elevated triglycerides for all CKD stages. Within SHARP, it was suggested that the relationships may be attributable to inflammation and reverse causality.[14] Specifically, our time-varying analyses included time-updated covariates to account for temporality. We also adjusted for albumin as a marker of inflammation, but we acknowledge the limitation that stronger markers of inflammation were unavailable in this cohort. Although most studies evaluating triglycerides have been in the context of ASCVD, future research will need to clarify the association of triglycerides with outcomes not related to ASCVD, especially in patients with CKD.

Clinical trials have suggested an important role of remnant cholesterol and triglyceride-rich lipoprotein in the development of ASCVD events.[27] The lipoprotein lipase that lies in the vascular endothelial surface can degrade the circulating triglycerides, thereby allowing remnant cholesterol and triglyceride-rich lipoprotein to be taken up by the arterial wall without the need of further oxidation.[28,29] For non-ASCVD events, a similar explanation of triglyceride-rich lipoprotein accumulation in the arterial wall as well as in the heart muscle, leading to cardiomyopathy, has been suggested in prior studies evaluating triglycerides and heart failure. These studies suggested that associations may be explained by the proinflammatory and toxic role of triglycerides, yet further research is needed.[23,30] Although these mechanisms may explain the relationships in patients with early-stage CKD, animal models

have indicated that lipid metabolism is altered in advanced CKD stages.[8] Prior studies primarily relied on baseline triglycerides measurement, even though lipid metabolism can become dysregulated through CKD progression, rendering the possibility of an altered impact over time as triglycerides levels change. Thus, a baseline triglycerides measurement in early-stage CKD may not fully capture the triglycerides-hospitalization relationship after transition to advanced CKD. Patients with CKD have a higher prevalence of hypertriglyceridemia, in part attributable to impaired clearance of lipoproteins in conjunction with reduced kidney function.[31,32] Particularly in patients with advanced CKD, it may be that the greater prevalence of nontraditional risk factors, such as malnutrition, cachexia, and protein-energy wasting, become more prominent and dominate the triglyceride-rich lipoprotein relationship.[23,30] Such conditions are associated with a disordered energy metabolism that explains why elevated triglycerides were not associated with ASCVD and non-ASCVD hospitalizations in later CKD stages, as demonstrated in this study. Moreover, clinical trials have noted that treatment with icosapent ethyl and statins was effective in lowering risks of ASCVD events in high-risk patients with established CVD or diabetes; however, these trials excluded patients with CKD stage 4 to 5 and those undergoing dialysis.[33] Thus, future studies, including clinical trials, are needed to better understand the effects of elevated triglycerides as well as the impact of pharmacologic treatments, particularly in patients with late-stage CKD, in whom nontraditional risk factors are more prevalent. Such studies will be informative in better tailoring clinical guidelines, including those describing lipid-lowering modulation therapies focused on this high-risk population.

Using our repeated measured data, we examined the time-varying relationships of triglycerides and hospitalizations, showing largely similar patterns with our baseline results. Yet, our non-ASCVD relationship had an inverse and linear pattern, suggesting that in the short-term, elevated triglycerides levels are not associated with a higher risk of non-ASCVD events in both patients without CKD and patients with CKD. To date, there is little information on the short-term risk of events with time-varying triglycerides and outcomes in patients with CKD. This observation of the lower risk of non-ASCVD events in the short-term for patients with advanced CKD further highlights the paradoxical relationships between lipids and outcomes, and merits additional investigation.[11]

Highlighted strengths of this study include the large sample size, use of multiple sources of data, and length of follow-up, which lend the ability to evaluate CKD stages and time-varying triglycerides. Few studies have evaluated serial triglycerides measurements, and our ability to examine short-term associations, especially as one progresses through CKD, is a strength of this study. In addition, we note several limitations. We were unable to adjust for potential confounders, such as diet, apolipoproteins, or other markers of inflammation, including CRP (C-reactive protein). Data on UACR were only available in a select population, yet analysis in this subgroup demonstrated similar but attenuated relationships. Our negative control analyses suggested that our results may be less subject to uncontrolled confounding.[34] We believe our triglycerides measurements were drawn after fasting given standard laboratory practice; however, we are unable to confirm fasting status. Prior studies have demonstrated small differences between fasting and nonfasting triglycerides levels, as well as the utility of nonfasting triglycerides in CVD risk prediction, yet we acknowledge that our results may be subject to misclassification.[35–38] Moreover, we restricted our outcomes to primary or secondary *ICD-9* codes to identify adverse events and minimize potential misclassification that stemmed from health administration medical records. Finally, our results may not be generalizable to the general population given that our source cohort is primarily composed of older White men.

In conclusion, we showed the short- and long-term associations of triglycerides with ASCVD and non-ASCVD hospitalizations across CKD stages. Relationships incrementally declined across worse CKD stages for elevated triglycerides, a known CVD risk factor. Given the burden and risk of CVD among patients with CKD, it is important to evaluate both the immediate and long-term impact of triglycerides on ASCVD and non-ASCVD events as to best manage cardiovascular health in this vulnerable population. Future studies as well as clinical trials are necessary to target and manage triglycerides, with a specific focus on patients with late-stage CKD.

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Supplementary Material

Tables S1–S8
Figures S1–S2

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SUPPLEMENTAL MATERIAL

Table S1. Comparison of Characteristics Between Patients with and without data on UACR.

	Without UACR	With UACR	Std. Diff
N(%)	2,768,375(93%)	194,801(7%)	
eGFR(mL/min/1.73m^2)	77[62,91]	72[56,87]	-0.24
CKD Stage (%)	77	69	-0.19
Non-CKD	14	19	0.12
CKD 3A	6	9	0.12
CKD 3B	2	2	0.05
CKD 4	0.8	0.6	-0.02
CKD 5/ESRD	77	69	-0.19
Serum Triglycerides Group (mg/dL)			
<80	20	15	0.18
80-<120	26	23	
120-<160	19	20	
160-<200	12	14	
200-<240	8	9	
≥240	14	19	
Age (years)	63±14	66±11	0.28
Sex (% Female)	6	3	-0.16
Married(%)	56	58	0.04
Race(%)			
White	82	81	-0.01
African American	14	14	-0.01
Other	4	5	0.05
Hispanic Ethnicity(%)	4	4	0.02
CCI	1[0,2]	2[1,3]	0.56
Comorbid Conditions (%)			
MI	6	9	0.08
CHF	10	15	0.15
PVD	9	14	0.14
Cerebrovascular Disease	9	11	0.08
Dementia	3	2	-0.03
COPD	18	19	0.03
Liver Disease	3	3	0.00
Diabetes	23	88	1.73
Cancer	12	13	0.03
Anemia	11	15	0.10
Atrial Fibrillation	7	8	0.05
Hypertension	62	85	0.55
ISHD	26	38	0.25
Depression	18	19	0.03
Anxiety	12	13	0.02
PTSD	7	9	0.05
Gallbladder Disease	0.4	0.5	0.01
Ever Smoking	64	65	0.02
Ever Alcoholism	26	16	-0.25
Laboratory Measurements			
Albumin (g/dL)	4.1±0.4	4.0±0.4	-0.16
AST(U/L)	23[19,29]	22[18,28]	-0.07
ALT (U/L)	25[18,35]	25[18,35]	-0.04
Glucose (mg/dL)	112.3±39.2	144.6±55.7	0.67

Hemoglobin (g/dL)	14.5±1.6	14.0±1.7	-0.31
WBC (x 10^3/mm^3)	7.2±2.7	7.3±2.8	0.06
SBP (mmHg)	135±18	135±17	0.04
DBP (mmHg)	76±11	73±11	-0.25
BMI (kg/m^2)	29±6	31±6	0.38
Lipid Panel (mg/dL)			
Triglycerides	126[86,187]	143[97,213]	0.16
HDL	42[35,52]	39[33,46]	-0.32
Cholesterol	179[154,207]	164[142,190]	-0.34
LDL	105[84,130]	91[73,112]	-0.40
Lipid Modulating Therapy Use(%)			
Statin	46	69	0.46
Ezetimibe	1	2	0.08
Non-statin	9	17	0.26
Fibrate	5	11	0.22
Niacin	3	5	0.11
Fish Oil	0.3	0.8	0.06
Bile Acid Sequestrants	1	1	0.05

Data presented as mean ± standard deviation, median[interquartile range], or percentage, as appropriate.
Standardized differences of ≥0.2 are considered as a meaningful imbalance, where 0.8, 0.5 and 0.2 represent large, medium and small imbalances, respectively.

ALT; Alanine Aminotransferase, AST; Aspartate Aminotransferase, BMI; Body Mass Index, CCI; Charlson Comorbidity Index, CHF; Congestive Heart Failure, CKD; Chronic Kidney Disease, COPD; Chronic Obstructive Pulmonary Disorder, DBP; Diastolic Blood Pressure, eGFR; estimated glomerular filtration rate, ESRD; end-stage renal disease, HDL; High Density Lipoprotein, ISHD; Ischemic Heart Disease, LDL; Low Density Lipoprotein, MI; Myocardial Infarction, PTSD; Post-traumatic Stress Disorder, PVD; Peripheral Vascular Disease, SBP; Systolic Blood Pressure, WBC; White Blood Cells Count, UACR; urine albumin-to-creatinine ratio
*eGFR provided for only patients classified as CKD stage 5, yet not on ESRD.

Table S2. ASCVD and non-ASCVD Incident Hospitalization Event Rates Stratified by Baseline Serum Triglycerides and Baseline CKD Stage.

ASCVD Hospitalization											
Stage	Total		Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]
<80	126034	30.7 [30.5,30.8]	85532	24.4 [24.2,24.5]	25567	58.8 [58.1,59.5]	10851	84.7 [83.1,86.3]	2563	113.6 [109.3,118.1]	1521	120.4 [114.5,126.6]
80-<120	191356	36.2 [36.1,36.4]	124207	28.8 [28.6,28.9]	41321	60.4 [59.8,61.0]	18671	84.7 [83.5,85.9]	4741	113.0 [109.9,116.3]	2416	116.1 [111.5,120.8]
120-<160	151690	38.2 [38.0,38.3]	96481	30.2 [30.0,30.4]	33106	61.5 [60.8,62.1]	16112	86.6 [85.3,88.0]	4093	113.0 [109.6,116.5]	1898	117.0 [111.9,122.4]
160-<200	100656	39.0 [38.8,39.2]	63987	30.9 [30.7,31.2]	21522	60.9 [60.1,61.7]	11035	89.4 [87.8,91.1]	2837	117.4 [113.2,121.8]	1275	113.0 [107.0,119.4]
200-<240	63726	39.7 [39.4,40.0]	40556	31.5 [31.2,31.8]	13509	62.6 [61.6,63.7]	6948	88.4 [86.4,90.5]	1874	118.1 [112.9,123.6]	839	116.9 [109.2,125.1]
≥240	123455	40.4 [40.2,40.6]	80426	32.3 [32.1,32.5]	24557	65.3 [64.5,66.1]	13169	92.4 [90.9,94.0]	3768	119.0 [115.2,122.8]	1535	104.9 [99.8,110.3]
Total	756917	36.7 [36.6,36.8]	491189	29.1 [29.0,29.2]	159582	61.3 [61.0,61.6]	76786	87.4 [86.7,88.0]	19876	115.3 [113.7,116.9]	9484	114.6 [112.3,116.9]
Non-ASCVD Hospitalization											
Stage	Total		Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]	N Event	Rate per 1000 person-years [95% CI]
<80	181246	45.9 [45.7,46.1]	120552	35.4 [35.2,35.6]	36378	90.0 [89.0,90.9]	16913	150.4 [148.2,152.7]	4576	265.5 [257.9,273.3]	2827	358.0 [345.0,371.4]
80-<120	249345	48.7 [48.5,48.9]	156258	36.9 [36.8,37.1]	54240	83.8 [83.1,84.5]	26760	135.0 [133.4,136.6]	7772	232.7 [227.6,238.0]	4315	323.0 [313.5,332.8]
120-<160	187912	48.4 [48.1,48.6]	115282	36.5 [36.3,36.7]	41232	79.5 [78.7,80.2]	21842	129.1 [127.4,130.8]	6371	216.4 [211.2,221.8]	3185	297.0 [286.9,307.5]
160-<200	121012	47.7 [47.5,48.0]	74035	36.0 [35.8,36.3]	26385	77.4 [76.5,78.3]	14313	126.0 [124.0,128.1]	4211	212.0 [205.7,218.5]	2068	266.7 [255.4,278.4]
200-<240	74092	46.6 [46.3,46.9]	45102	35.0 [34.7,35.4]	15952	75.6 [74.4,76.8]	9000	122.6 [120.1,125.2]	2712	206.5 [198.9,214.4]	1326	264.5 [250.7,279.1]
≥240	138752	45.6 [45.4,45.9]	86133	34.4 [34.2,34.7]	28258	76.4 [75.6,77.3]	16502	124.0 [122.1,125.9]	5442	210.2 [204.6,215.8]	2417	238.9 [229.5,248.6]
Total	952359	47.3 [47.2,47.4]	597362	35.9 [35.8,36.0]	202445	81.2 [80.9,81.6]	105330	131.7 [130.9,132.5]	31084	223.7 [221.2,226.2]	16138	294.1 [289.6,298.7]

Table S3. Hazard Ratios for the Association of Baseline Serum Triglycerides with Time to ASCVD Hospitalization Stratified by Baseline CKD Stage across levels of adjustment.

Unadjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.81[0.80,0.81]	<.0001	0.95[0.94,0.97]	0.01	0.97[0.95,0.99]	0.78	0.99[0.95,1.04]	0.98	1.00[0.94,1.07]
80-<120	<.0001	0.95[0.95,0.96]	0.01	0.98[0.97,1.00]	0.02	0.98[0.95,1.00]	0.79	0.99[0.95,1.04]	0.61	0.98[0.93,1.05]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.03[1.02,1.04]	0.44	0.99[0.98,1.01]	0.01	1.03[1.01,1.06]	0.11	1.04[0.99,1.09]	0.44	0.97[0.91,1.04]
200-<240	<.0001	1.04[1.03,1.06]	0.05	1.02[1.00,1.04]	0.13	1.02[0.99,1.05]	0.08	1.05[0.99,1.11]	0.93	1.00[0.93,1.09]
≥240	<.0001	1.07[1.06,1.08]	<.0001	1.06[1.05,1.08]	<.0001	1.07[1.05,1.09]	0.01	1.06[1.01,1.11]	0.01	0.92[0.86,0.98]

Age Adjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.79[0.78,0.79]	<.0001	0.90[0.89,0.91]	<.0001	0.94[0.92,0.97]	0.43	0.98[0.93,1.03]	0.48	0.98[0.91,1.04]
80-<120	<.0001	0.91[0.91,0.92]	<.0001	0.95[0.94,0.96]	0.0001	0.96[0.94,0.98]	0.50	0.99[0.95,1.03]	0.23	0.96[0.91,1.02]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.08[1.07,1.09]	0.004	1.03[1.01,1.04]	0.0002	1.05[1.02,1.07]	0.04	1.05[1.00,1.10]	0.77	0.99[0.92,1.06]
200-<240	<.0001	1.15[1.14,1.16]	<.0001	1.09[1.07,1.11]	0.002	1.05[1.02,1.08]	0.01	1.07[1.02,1.13]	0.37	1.04[0.96,1.13]
≥240	<.0001	1.33[1.32,1.34]	<.0001	1.20[1.19,1.23]	<.0001	1.13[1.11,1.16]	<.0001	1.12[1.07,1.17]	0.84	1.01[0.94,1.08]

Case-Mix Adjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.88[0.87,0.89]	<.0001	0.95[0.94,0.97]	0.01	0.97[0.94,0.99]	0.64	1.01[0.96,1.06]	0.76	0.99[0.92,1.06]
80-<120	<.0001	0.96[0.95,0.96]	0.0001	0.97[0.96,0.99]	0.004	0.97[0.95,0.99]	0.64	0.99[0.95,1.03]	0.18	0.96[0.90,1.02]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.04[1.03,1.05]	0.10	1.02[1.00,1.03]	0.01	1.04[1.01,1.06]	0.18	1.03[0.99,1.08]	0.96	1.00[0.93,1.07]
200-<240	<.0001	1.09[1.08,1.10]	<.0001	1.05[1.03,1.07]	0.06	1.03[1.00,1.06]	0.26	1.03[0.98,1.09]	0.49	1.03[0.95,1.12]
≥240	<.0001	1.19[1.18,1.20]	<.0001	1.12[1.10,1.14]	<.0001	1.08[1.06,1.11]	0.01	1.06[1.02,1.11]	0.10	0.94[0.88,1.01]

Case-Mix+Lab Adjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.84[0.83,0.85]	<.0001	0.91[0.89,0.92]	<.0001	0.93[0.90,0.95]	0.31	0.97[0.93,1.02]	0.14	0.95[0.89,1.02]
80-<120	<.0001	0.94[0.93,0.95]	<.0001	0.95[0.94,0.97]	<.0001	0.95[0.93,0.97]	0.13	0.97[0.93,1.01]	0.09	0.95[0.89,1.01]

Stage	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
	P	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.06[1.05,1.07]	0.002	1.03[1.01,1.05]	<.0001	1.05[1.02,1.08]	0.09	1.04[0.99,1.09]	0.46	1.03[0.96,1.10]
200-<240	<.0001	1.11[1.10,1.12]	<.0001	1.07[1.05,1.09]	0.001	1.05[1.02,1.08]	0.05	1.06[1.00,1.12]	0.14	1.06[0.98,1.15]
≥240	<.0001	1.22[1.21,1.23]	<.0001	1.15[1.13,1.17]	<.0001	1.11[1.09,1.14]	<.0001	1.10[1.05,1.15]	0.83	0.99[0.93,1.06]
Case-Mix+Lab+Lipid Adjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.90[0.89,0.91]	<.0001	0.96[0.94,0.97]	0.01	0.97[0.94,0.99]	0.40	1.02[0.97,1.08]	0.59	0.98[0.91,1.05]
80-<120	<.0001	0.96[0.95,0.97]	<.0001	0.97[0.96,0.98]	0.002	0.97[0.95,0.99]	0.47	0.99[0.94,1.03]	0.22	0.96[0.91,1.02]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.05[1.04,1.06]	0.04	1.02[1.00,1.04]	0.001	1.04[1.02,1.07]	0.25	1.03[0.98,1.08]	0.59	1.02[0.95,1.10]
200-<240	<.0001	1.10[1.08,1.11]	<.0001	1.06[1.04,1.08]	0.01	1.04[1.01,1.07]	0.20	1.04[0.98,1.10]	0.24	1.05[0.97,1.14]
≥240	<.0001	1.21[1.20,1.22]	<.0001	1.14[1.12,1.16]	<.0001	1.10[1.08,1.13]	0.001	1.08[1.03,1.13]	0.48	0.98[0.91,1.05]

Model Adjustments:
Unadjusted
Age Adjusted: age
Case-Mix Adjusted: age, sex, race, ethnicity, ever smoker, ever alcoholism, Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disorder, dementia, liver disease, cancer, diabetes, atrial fibrillation, hypertension, depression, ischemic heart disease, prescription of statins and prescription of non-statins
Case-Mix+Lab Adjusted: Case-Mix covariates and body mass index and albumin
Case-Mix+Lab+Lipid Adjusted: Case-Mix+Lab covariates and HDL and LDL cholesterols

Table S4. Hazard Ratios for the Association of Baseline Serum Triglycerides with Time to Non-ASCVD Hospitalization Stratified by Baseline CKD Stage across levels of adjustment.

Unadjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.97[0.96,0.98]	<.0001	1.13[1.11,1.14]	<.0001	1.15[1.13,1.18]	<.0001	1.20[1.16,1.25]	<.0001	1.15[1.09,1.21]
80-<120	0.005	1.01[1.00,1.02]	<.0001	1.05[1.04,1.07]	<.0001	1.04[1.02,1.06]	0.0002	1.07[1.03,1.10]	0.01	1.07[1.02,1.12]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.01	0.99[0.98,1.00]	0.002	0.98[0.96,0.99]	0.05	0.98[0.96,1.00]	0.38	0.98[0.95,1.02]	0.01	0.93[0.88,0.98]
200-<240	<.0001	0.96[0.95,0.97]	<.0001	0.95[0.94,0.97]	0.0002	0.95[0.93,0.98]	0.07	0.96[0.92,1.00]	0.01	0.92[0.86,0.98]
≥240	<.0001	0.95[0.94,0.95]	<.0001	0.96[0.95,0.98]	0.0006	0.97[0.95,0.99]	0.20	0.98[0.94,1.01]	<.0001	0.84[0.80,0.89]
Age Adjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.95[0.95,0.96]	<.0001	1.05[1.04,1.06]	<.0001	1.12[1.09,1.14]	<.0001	1.19[1.15,1.24]	<.0001	1.13[1.08,1.19]
80-<120	<.0001	0.97[0.96,0.98]	0.20	1.01[1.00,1.02]	0.02	1.02[1.00,1.04]	0.001	1.06[1.03,1.10]	0.02	1.06[1.01,1.10]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.04[1.03,1.05]	0.05	1.02[1.00,1.03]	0.71	1.00[0.98,1.02]	0.57	0.99[0.95,1.03]	0.01	0.93[0.88,0.98]
200-<240	<.0001	1.06[1.05,1.07]	0.001	1.03[1.01,1.05]	0.17	0.98[0.96,1.01]	0.19	0.97[0.93,1.02]	0.04	0.94[0.88,1.00]
≥240	<.0001	1.17[1.16,1.18]	<.0001	1.12[1.11,1.14]	0.0002	1.04[1.02,1.06]	0.80	1.01[0.97,1.04]	<.0001	0.88[0.84,0.93]
Case-Mix Adjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	0.79	1.00[0.99,1.01]	<.0001	1.07[1.05,1.08]	<.0001	1.08[1.06,1.11]	<.0001	1.15[1.11,1.19]	0.001	1.09[1.04,1.15]
80-<120	0.09	0.99[0.99,1.00]	0.002	1.02[1.01,1.03]	0.10	1.02[1.00,1.03]	0.01	1.04[1.01,1.08]	0.10	1.04[0.99,1.09]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.001	1.02[1.01,1.03]	0.49	1.01[0.99,1.02]	0.15	0.99[0.96,1.01]	0.66	0.99[0.95,1.03]	0.22	0.97[0.91,1.02]
200-<240	0.004	1.02[1.01,1.03]	1.00	1.00[0.98,1.02]	0.02	0.97[0.95,0.99]	0.001	0.93[0.88,0.97]	0.16	0.96[0.90,1.02]
≥240	<.0001	1.08[1.07,1.08]	<.0001	1.05[1.03,1.06]	0.49	0.99[0.97,1.01]	0.04	0.96[0.93,1.00]	<.0001	0.88[0.84,0.93]
Case-Mix+Lab Adjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	0.97	1.00[0.99,1.01]	<.0001	1.05[1.03,1.06]	<.0001	1.05[1.03,1.07]	<.0001	1.10[1.06,1.14]	0.14	1.04[0.99,1.10]
80-<120	0.07	0.99[0.99,1.00]	0.05	1.01[1.00,1.03]	0.79	1.00[0.99,1.02]	0.32	1.02[0.98,1.05]	0.15	1.03[0.99,1.08]

Serum Triglycerides Group (mg/dL)	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.001	1.02[1.01,1.03]	0.18	1.01[1.00,1.03]	0.69	1.00[0.98,1.02]	0.97	1.00[0.96,1.04]	0.75	1.01[0.95,1.07]
200-<240	0.001	1.02[1.01,1.03]	0.34	1.01[0.99,1.03]	0.30	0.99[0.96,1.01]	0.02	0.95[0.91,0.99]	0.97	1.00[0.94,1.07]
≥240	<.0001	1.08[1.07,1.09]	<.0001	1.06[1.04,1.08]	0.1184	1.02[1.00,1.04]	0.74	0.99[0.96,1.03]	0.04	0.94[0.89,1.00]
Case-Mix+Lab+Lipid Adjusted										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	0.001	0.99[0.98,0.99]	<.0001	1.04[1.03,1.06]	<.0001	1.05[1.03,1.07]	<.0001	1.10[1.05,1.14]	0.15	1.04[0.99,1.10]
80-<120	0.002	0.99[0.98,1.00]	0.08	1.01[1.00,1.03]	0.91	1.00[0.98,1.02]	0.33	1.02[0.98,1.05]	0.15	1.04[0.99,1.08]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.0001	1.02[1.01,1.03]	0.16	1.01[1.00,1.03]	0.74	1.00[0.98,1.02]	0.96	1.00[0.96,1.04]	0.75	1.01[0.95,1.07]
200-<240	<.0001	1.02[1.01,1.03]	0.31	1.01[0.99,1.03]	0.34	0.99[0.96,1.01]	0.02	0.95[0.91,0.99]	0.99	1.00[0.94,1.07]
≥240	<.0001	1.08[1.07,1.09]	<.0001	1.06[1.04,1.08]	0.12	1.02[1.00,1.04]	0.69	0.99[0.96,1.03]	0.01	0.93[0.88,0.98]

Model Adjustments:
Unadjusted
Age Adjusted: age
Case-Mix Adjusted: age, sex, race, ethnicity, ever smoker, ever alcoholism, Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disorder, dementia, liver disease, cancer, diabetes, atrial fibrillation, hypertension, depression, ischemic heart disease, prescription of statins and prescription of non-statins
Case-Mix+Lab Adjusted: Case-Mix covariates and body mass index and albumin
Case-Mix+Lab+Lipid Adjusted: Case-Mix+Lab covariates and HDL and LDL cholesterols

Table S5. Association of Baseline Serum Triglycerides with Time to ASCVD Hospitalization across Strata under Case-Mix + Lab adjustment.

Age<65 years (N =1,594,293)										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.80[0.79,0.81]	<.0001	0.84[0.80,0.89]	0.29	0.95[0.87,1.05]	0.98	1.00[0.86,1.17]	0.41	0.96[0.86,1.07]
80-<120	<.0001	0.93[0.92,0.94]	0.01	0.94[0.91,0.99]	0.89	0.99[0.92,1.08]	0.63	1.03[0.91,1.17]	0.47	0.97[0.88,1.06]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.07[1.05,1.09]	0.18	1.03[0.99,1.08]	0.003	1.13[1.04,1.22]	0.16	1.10[0.96,1.26]	0.30	1.06[0.95,1.18]
200-<240	<.0001	1.12[1.10,1.14]	0.01	1.07[1.01,1.12]	0.01	1.12[1.03,1.22]	0.08	1.14[0.98,1.31]	0.03	1.14[1.01,1.29]
≥240	<.0001	1.23[1.22,1.25]	<.0001	1.18[1.13,1.22]	<.0001	1.19[1.11,1.28]	0.01	1.16[1.04,1.30]	0.83	1.01[0.92,1.12]
Age ≥65 years (N =1,368,883)										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.88[0.87,0.89]	<.0001	0.92[0.90,0.94]	<.0001	0.93[0.90,0.95]	0.25	0.97[0.92,1.02]	0.14	0.94[0.86,1.02]
80-<120	<.0001	0.95[0.94,0.96]	<.0001	0.96[0.94,0.97]	<.0001	0.95[0.93,0.97]	0.08	0.96[0.92,1.01]	0.12	0.94[0.87,1.02]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.04[1.02,1.05]	0.01	1.02[1.01,1.04]	0.003	1.04[1.01,1.07]	0.20	1.03[0.98,1.09]	0.93	1.00[0.91,1.10]
200-<240	<.0001	1.08[1.06,1.10]	<.0001	1.07[1.04,1.09]	0.01	1.04[1.01,1.07]	0.17	1.04[0.98,1.11]	0.81	1.01[0.91,1.13]
≥240	<.0001	1.16[1.14,1.17]	<.0001	1.13[1.11,1.16]	<.0001	1.10[1.08,1.13]	0.001	1.09[1.04,1.15]	0.57	0.97[0.88,1.07]
Non-Diabetics (N =2,150,024)										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.84[0.83,0.85]	<.0001	0.90[0.89,0.92]	<.0001	0.92[0.89,0.95]	0.24	0.96[0.89,1.03]	0.003	0.84[0.75,0.94]
80-<120	<.0001	0.94[0.93,0.95]	<.0001	0.96[0.94,0.97]	0.0002	0.95[0.92,0.98]	0.55	1.02[0.96,1.08]	0.49	0.97[0.87,1.07]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.06[1.04,1.07]	0.15	1.02[0.99,1.04]	0.001	1.06[1.03,1.10]	0.03	1.08[1.01,1.17]	0.24	1.08[0.95,1.22]
200-<240	<.0001	1.11[1.09,1.13]	<.0001	1.07[1.04,1.10]	0.0004	1.08[1.03,1.12]	0.20	1.06[0.97,1.15]	0.07	1.14[0.99,1.31]
≥240	<.0001	1.20[1.19,1.22]	<.0001	1.14[1.11,1.16]	<.0001	1.09[1.06,1.13]	0.01	1.10[1.03,1.19]	0.54	0.96[0.85,1.09]
Diabetics (N =813,152)										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.83[0.82,0.85]	<.0001	0.91[0.89,0.94]	<.0001	0.92[0.89,0.96]	0.81	0.99[0.92,1.06]	0.88	1.01[0.93,1.10]
80-<120	<.0001	0.93[0.92,0.95]	<.0001	0.95[0.92,0.97]	0.004	0.95[0.92,0.99]	0.01	0.92[0.87,0.98]	0.08	0.94[0.87,1.01]

Serum Triglycerides Group (mg/dL)	Non-CKD P	Non-CKD HR[95%CI]	CKD Stage 3A P	CKD Stage 3A HR[95%CI]	CKD Stage 3B P	CKD Stage 3B HR[95%CI]	CKD Stage 4 P	CKD Stage 4 HR[95%CI]	CKD Stage 5/ESRD P	CKD Stage 5/ESRD HR[95%CI]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.06[1.04,1.08]	0.00	1.04[1.01,1.07]	0.03	1.04[1.00,1.08]	0.63	1.02[0.95,1.08]	0.89	1.01[0.92,1.10]
200-<240	<.0001	1.11[1.09,1.13]	<.0001	1.07[1.04,1.10]	0.16	1.03[0.99,1.07]	0.15	1.05[0.98,1.13]	0.59	1.03[0.93,1.14]
≥240	<.0001	1.21[1.20,1.23]	<.0001	1.15[1.12,1.18]	<.0001	1.12[1.09,1.16]	0.01	1.09[1.03,1.15]	0.89	0.99[0.92,1.08]

LDL <100 mg/dL (N =1,300,948)

Stage	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.87[0.86,0.89]	<.0001	0.94[0.92,0.96]	<.0001	0.93[0.90,0.96]	0.54	1.02[0.96,1.08]	0.53	0.97[0.90,1.06]
80-<120	<.0001	0.95[0.94,0.96]	0.0001	0.96[0.94,0.98]	<.0001	0.95[0.92,0.97]	0.48	1.02[0.97,1.08]	0.54	0.98[0.91,1.05]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.04[1.03,1.06]	0.15	1.02[0.99,1.04]	0.05	1.03[1.00,1.07]	0.02	1.08[1.01,1.15]	0.72	1.02[0.93,1.11]
200-<240	<.0001	1.08[1.06,1.10]	0.02	1.03[1.01,1.06]	0.02	1.04[1.01,1.08]	0.04	1.08[1.00,1.16]	0.23	1.07[0.96,1.19]
≥240	<.0001	1.18[1.16,1.20]	<.0001	1.13[1.10,1.16]	<.0001	1.12[1.09,1.16]	<.0001	1.16[1.10,1.23]	0.11	0.93[0.85,1.02]

LDL ≥100 mg/dL (N = 1,608,920)

Stage	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.82[0.81,0.83]	<.0001	0.88[0.86,0.90]	0.002	0.94[0.90,0.98]	0.13	0.93[0.85,1.02]	0.02	0.84[0.73,0.97]
80-<120	<.0001	0.93[0.92,0.95]	<.0001	0.95[0.93,0.97]	0.06	0.97[0.94,1.00]	0.005	0.90[0.84,0.97]	0.02	0.88[0.78,0.98]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.07[1.05,1.08]	0.004	1.04[1.01,1.07]	0.001	1.07[1.03,1.11]	0.52	0.98[0.90,1.05]	0.59	1.03[0.92,1.17]
200-<240	<.0001	1.14[1.12,1.16]	<.0001	1.11[1.08,1.15]	0.01	1.06[1.02,1.11]	0.72	1.02[0.93,1.11]	0.58	1.04[0.91,1.19]
≥240	<.0001	1.26[1.25,1.28]	<.0001	1.19[1.15,1.22]	<.0001	1.10[1.06,1.15]	0.89	1.00[0.92,1.07]	0.11	1.10[0.98,1.23]

No Statin Prescription (N = 1,466,566)

Stage	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.83[0.81,0.84]	<.0001	0.89[0.86,0.91]	<.0001	0.92[0.88,0.96]	0.33	0.96[0.88,1.05]	0.05	0.90[0.81,1.00]
80-<120	<.0001	0.94[0.92,0.95]	<.0001	0.95[0.92,0.97]	0.04	0.96[0.92,1.00]	0.62	0.98[0.91,1.06]	0.02	0.88[0.80,0.98]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.07[1.05,1.08]	0.02	1.04[1.01,1.07]	0.12	1.04[0.99,1.09]	0.15	1.07[0.98,1.17]	0.73	0.98[0.87,1.10]
200-<240	<.0001	1.12[1.10,1.14]	<.0001	1.08[1.04,1.12]	0.32	1.03[0.97,1.08]	0.74	1.02[0.92,1.13]	0.45	1.06[0.92,1.21]
≥240	<.0001	1.23[1.21,1.25]	<.0001	1.15[1.11,1.18]	<.0001	1.12[1.07,1.17]	<.0001	1.18[1.09,1.28]	0.09	0.90[0.80,1.02]

Statin Prescription (N = 1,353,351)

Stage	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.86[0.85,0.87]	<.0001	0.92[0.91,0.94]	<.0001	0.93[0.91,0.96]	0.61	0.98[0.93,1.05]	0.63	0.98[0.89,1.07]

	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
80-<120	<.0001	0.95[0.94,0.96]	<.0001	0.96[0.94,0.98]	<.0001	0.95[0.92,0.97]	0.12	0.96[0.91,1.01]	0.69	0.99[0.91,1.06]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.05[1.03,1.06]	0.05	1.02[1.00,1.04]	0.0003	1.06[1.03,1.09]	0.29	1.03[0.97,1.09]	0.28	1.05[0.96,1.15]
200-<240	<.0001	1.09[1.08,1.11]	<.0001	1.06[1.03,1.09]	0.001	1.06[1.02,1.09]	0.06	1.06[1.00,1.14]	0.22	1.07[0.96,1.18]
≥240	<.0001	1.18[1.17,1.19]	<.0001	1.14[1.12,1.17]	<.0001	1.11[1.08,1.14]	0.06	1.05[1.00,1.11]	0.43	1.04[0.95,1.13]
No Prior CVD (N = 2,070,569)										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.81[0.80,0.83]	<.0001	0.86[0.84,0.89]	<.0001	0.90[0.85,0.94]	0.00	0.82[0.74,0.92]	0.15	0.91[0.79,1.04]
80-<120	<.0001	0.93[0.92,0.94]	<.0001	0.93[0.91,0.96]	0.01	0.95[0.91,0.99]	0.00	0.88[0.81,0.96]	0.01	0.86[0.76,0.97]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.07[1.05,1.09]	0.04	1.03[1.00,1.06]	0.01	1.06[1.02,1.12]	0.07	1.10[0.99,1.21]	0.26	0.92[0.80,1.06]
200-<240	<.0001	1.14[1.12,1.16]	<.0001	1.08[1.04,1.11]	0.01	1.08[1.02,1.14]	0.43	1.05[0.94,1.17]	0.69	1.03[0.89,1.20]
≥240	<.0001	1.26[1.25,1.28]	<.0001	1.20[1.17,1.23]	<.0001	1.11[1.06,1.16]	0.04	1.10[1.01,1.21]	0.22	1.08[0.95,1.23]
Prior CVD (N =892,607)										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.88[0.87,0.89]	<.0001	0.94[0.92,0.95]	<.0001	0.94[0.91,0.96]	0.56	1.02[0.96,1.08]	0.37	0.96[0.89,1.04]
80-<120	<.0001	0.95[0.94,0.96]	0.0002	0.97[0.95,0.99]	0.0003	0.96[0.93,0.98]	0.89	1.00[0.95,1.05]	0.70	0.99[0.92,1.06]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<.0001	1.04[1.03,1.06]	0.05	1.02[1.00,1.04]	0.005	1.04[1.01,1.07]	0.35	1.03[0.97,1.09]	0.08	1.08[0.99,1.17]
200-<240	<.0001	1.07[1.06,1.09]	<.0001	1.06[1.03,1.09]	0.03	1.04[1.00,1.07]	0.07	1.06[1.00,1.13]	0.11	1.08[0.98,1.19]
≥240	<.0001	1.15[1.13,1.16]	<.0001	1.12[1.10,1.14]	<.0001	1.11[1.08,1.14]	0.001	1.10[1.04,1.16]	0.43	0.97[0.89,1.05]

Model Adjustments: age, sex, race, ethnicity, ever smoker, ever alcoholism, Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disorder, dementia, liver disease, cancer, diabetes, atrial fibrillation, hypertension, depression, ischemic heart disease, prescription of statins and prescription of non-statins, body mass index and albumin.

Table S6. Association of Baseline Serum Triglycerides with Time to Non-ASCVD Hospitalization across Strata under Case-Mix + Lab adjustment.

	Age<65 years (N =1,594,293)									
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.95[0.94,0.96]	0.44	1.02[0.97,1.07]	0.88	0.99[0.92,1.07]	0.002	1.19[1.07,1.33]	0.005	1.12[1.04,1.21]
80-<120	0.001	0.98[0.97,0.99]	0.21	1.02[0.99,1.06]	0.31	0.97[0.91,1.03]	0.18	1.07[0.97,1.18]	0.02	1.09[1.02,1.17]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.001	1.02[1.01,1.04]	0.20	1.03[0.99,1.07]	0.40	1.03[0.96,1.10]	0.49	1.04[0.94,1.15]	0.04	1.09[1.00,1.18]
200-<240	0.003	1.02[1.01,1.04]	0.51	1.02[0.97,1.06]	0.19	0.95[0.88,1.03]	0.36	1.05[0.94,1.18]	0.34	1.05[0.95,1.15]
≥240	<.0001	1.09[1.07,1.10]	<.0001	1.09[1.05,1.13]	0.77	0.99[0.94,1.05]	0.19	1.06[0.97,1.16]	0.93	1.00[0.93,1.08]
	Age ≥65 years (N =1,368,883)									
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	1.04[1.03,1.05]	<.0001	1.05[1.04,1.07]	<.0001	1.06[1.04,1.08]	0.0002	1.08[1.04,1.13]	0.40	0.97[0.91,1.04]
80-<120	0.25	1.01[1.00,1.02]	0.10	1.01[1.00,1.03]	0.53	1.01[0.99,1.03]	0.60	1.01[0.97,1.05]	0.63	0.99[0.93,1.05]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.65	1.00[0.99,1.02]	0.35	1.01[0.99,1.03]	0.43	0.99[0.97,1.01]	0.91	1.00[0.96,1.04]	0.09	0.94[0.87,1.01]
200-<240	0.63	1.00[0.99,1.02]	0.42	1.01[0.99,1.03]	0.37	0.99[0.96,1.01]	0.003	0.93[0.88,0.98]	0.50	0.97[0.89,1.06]
≥240	<.0001	1.04[1.03,1.05]	<.0001	1.04[1.03,1.06]	0.17	1.02[0.99,1.04]	0.29	0.98[0.94,1.02]	0.01	0.90[0.83,0.97]
	Non-Diabetics (N =2,150,024)									
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	0.03	1.01[1.00,1.02]	<.0001	1.05[1.03,1.07]	<.0001	1.06[1.04,1.09]	0.004	1.08[1.03,1.14]	0.80	1.01[0.93,1.10]
80-<120	0.16	0.99[0.98,1.00]	0.07	1.02[1.00,1.03]	0.14	1.02[0.99,1.04]	0.28	1.03[0.98,1.08]	0.19	1.05[0.98,1.13]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.09	1.01[1.00,1.02]	0.32	1.01[0.99,1.03]	0.99	1.00[0.97,1.03]	0.56	0.98[0.93,1.04]	0.89	1.01[0.92,1.10]
200-<240	0.09	1.01[1.00,1.03]	0.95	1.00[0.98,1.03]	0.55	0.99[0.96,1.03]	0.47	0.98[0.91,1.05]	0.50	1.04[0.93,1.16]
≥240	<.0001	1.06[1.05,1.07]	0.0001	1.04[1.02,1.07]	0.26	1.02[0.99,1.05]	0.44	0.98[0.92,1.04]	0.57	0.97[0.89,1.07]
	Diabetics (N =813,152)									
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.97[0.95,0.98]	0.01	1.04[1.01,1.06]	0.06	1.03[1.00,1.06]	0.0002	1.11[1.05,1.18]	0.11	1.06[0.99,1.13]
80-<120	0.17	0.99[0.98,1.00]	0.54	1.01[0.99,1.03]	0.16	0.98[0.95,1.01]	0.76	1.01[0.96,1.06]	0.52	1.02[0.96,1.08]

Serum Triglycerides Group (mg/dL)	Non-CKD P	Non-CKD HR[95%CI]	CKD Stage 3A P	CKD Stage 3A HR[95%CI]	CKD Stage 3B P	CKD Stage 3B HR[95%CI]	CKD Stage 4 P	CKD Stage 4 HR[95%CI]	CKD Stage 5/ESRD P	CKD Stage 5/ESRD HR[95%CI]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.002	1.03[1.01,1.04]	0.31	1.01[0.99,1.04]	0.52	0.99[0.96,1.02]	0.62	1.01[0.96,1.07]	0.77	1.01[0.94,1.08]
200-<240	0.004	1.03[1.01,1.05]	0.17	1.02[0.99,1.05]	0.35	0.98[0.95,1.02]	0.02	0.93[0.88,0.99]	0.66	0.98[0.91,1.07]
≥240	<.0001	1.09[1.08,1.11]	<.0001	1.07[1.04,1.09]	0.59	1.01[0.98,1.04]	0.89	1.00[0.96,1.05]	0.02	0.93[0.87,0.99]

LDL <100 mg/dL (N =1,300,948)

Stage	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	0.001	1.02[1.01,1.03]	<.0001	1.06[1.04,1.08]	<.0001	1.08[1.05,1.11]	<.0001	1.13[1.08,1.18]	0.21	1.04[0.98,1.11]
80-<120	0.53	1.00[0.99,1.02]	0.21	1.01[0.99,1.03]	0.95	1.00[0.98,1.02]	0.005	1.06[1.02,1.11]	0.36	1.03[0.97,1.09]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.42	1.01[0.99,1.02]	0.84	1.00[0.98,1.02]	0.10	0.98[0.95,1.01]	0.50	1.02[0.97,1.07]	0.97	1.00[0.93,1.08]
200-<240	0.998	1.00[0.98,1.02]	0.12	0.98[0.96,1.01]	0.63	0.99[0.96,1.03]	0.03	0.94[0.88,0.99]	0.34	0.96[0.88,1.04]
≥240	<.0001	1.05[1.04,1.07]	0.0003	1.04[1.02,1.06]	0.84	1.00[0.98,1.03]	0.88	1.00[0.95,1.05]	0.002	0.90[0.84,0.96]

LDL ≥100 mg/dL (N = 1,608,920)

Stage	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<.0001	0.97[0.96,0.98]	0.34	1.01[0.99,1.04]	0.23	0.98[0.94,1.01]	0.13	1.06[0.98,1.14]	0.15	0.92[0.83,1.03]
80-<120	0.003	0.98[0.97,1.00]	0.18	1.01[0.99,1.03]	0.65	1.01[0.98,1.04]	0.03	0.94[0.89,1.00]	0.92	1.00[0.92,1.08]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.001	1.02[1.01,1.04]	0.03	1.03[1.00,1.05]	0.29	1.02[0.99,1.05]	0.60	0.98[0.93,1.05]	0.77	1.01[0.92,1.12]
200-<240	<.0001	1.03[1.02,1.05]	0.002	1.05[1.02,1.08]	0.25	0.98[0.94,1.02]	0.42	0.97[0.91,1.04]	0.14	1.08[0.98,1.20]
≥240	<.0001	1.09[1.08,1.11]	<.0001	1.08[1.05,1.11]	0.02	1.04[1.01,1.07]	0.79	0.99[0.93,1.05]	0.38	1.04[0.95,1.14]

No Statin Prescription (N = 1,466,566)

Stage	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	0.14	1.01[1.00,1.02]	0.0001	1.05[1.02,1.07]	0.001	1.06[1.02,1.09]	<.0001	1.17[1.10,1.25]	0.54	0.98[0.91,1.05]
80-<120	0.59	1.00[0.99,1.01]	0.22	1.01[0.99,1.04]	0.30	1.02[0.99,1.05]	0.09	1.05[0.99,1.11]	0.67	1.02[0.95,1.09]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.88	1.00[0.99,1.02]	0.66	0.99[0.97,1.02]	0.54	0.99[0.95,1.03]	0.11	1.06[0.99,1.13]	0.01	0.89[0.82,0.98]
200-<240	0.29	1.01[0.99,1.03]	0.92	1.00[0.97,1.03]	0.78	0.99[0.95,1.04]	0.42	0.97[0.89,1.05]	0.57	1.03[0.93,1.14]
≥240	<.0001	1.05[1.03,1.06]	0.06	1.03[1.00,1.05]	0.63	1.01[0.97,1.05]	0.09	1.06[0.99,1.13]	0.02	0.91[0.83,0.99]

Statin Prescription (N = 1,353,351)

Stage	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	0.77	1.00[0.99,1.01]	<.0001	1.05[1.03,1.07]	0.0004	1.05[1.02,1.08]	0.04	1.05[1.00,1.11]	0.02	1.09[1.02,1.17]

Serum Triglycerides Group (mg/dL)	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]
80-<120	0.14	0.99[0.98,1.00]	0.08	1.01[1.00,1.03]	0.52	0.99[0.97,1.02]	0.95	1.00[0.96,1.04]	0.14	1.05[0.98,1.11]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.0004	1.02[1.01,1.04]	0.04	1.02[1.00,1.04]	0.82	1.00[0.97,1.02]	0.24	0.97[0.93,1.02]	0.01	1.10[1.02,1.18]
200-<240	0.01	1.02[1.01,1.03]	0.34	1.01[0.99,1.04]	0.19	0.98[0.95,1.01]	0.03	0.94[0.89,0.99]	0.84	0.99[0.91,1.08]
≥240	<.0001	1.09[1.08,1.10]	<.0001	1.08[1.06,1.10]	0.19	1.02[0.99,1.04]	0.10	0.96[0.92,1.01]	0.42	0.97[0.91,1.04]
No Prior CVD (N = 2,070,569)										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]
<80	0.03	0.99[0.98,1.00]	0.04	1.02[1.00,1.05]	0.10	1.03[0.99,1.07]	0.09	1.06[0.99,1.14]	0.55	0.97[0.89,1.06]
80-<120	0.02	0.99[0.98,1.00]	0.48	1.01[0.99,1.03]	0.69	0.99[0.96,1.03]	0.40	0.97[0.92,1.04]	0.82	1.01[0.93,1.09]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.02	1.01[1.00,1.03]	0.74	1.00[0.98,1.03]	0.69	1.01[0.97,1.05]	0.93	1.00[0.93,1.08]	0.57	0.97[0.89,1.07]
200-<240	0.0002	1.03[1.01,1.04]	0.36	1.01[0.99,1.04]	0.68	0.99[0.95,1.04]	0.90	1.01[0.93,1.09]	0.42	0.96[0.86,1.07]
≥240	<.0001	1.08[1.07,1.09]	<.0001	1.05[1.03,1.08]	0.03	1.04[1.00,1.08]	0.38	1.03[0.96,1.10]	0.92	1.01[0.92,1.10]
Prior CVD (N =892,607)										
Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]	P	HR[95%CI]
<80	<.0001	1.03[1.02,1.04]	<.0001	1.07[1.05,1.09]	<.0001	1.06[1.04,1.09]	<.0001	1.11[1.06,1.16]	0.02	1.08[1.01,1.15]
80-<120	0.57	1.00[0.99,1.02]	0.03	1.02[1.00,1.04]	0.56	1.01[0.99,1.03]	0.10	1.03[0.99,1.08]	0.08	1.05[0.99,1.11]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.12	1.01[1.00,1.03]	0.17	1.01[0.99,1.04]	0.39	0.99[0.96,1.02]	0.97	1.00[0.95,1.05]	0.41	1.03[0.96,1.10]
200-<240	1.00	1.00[0.98,1.02]	0.66	1.01[0.98,1.03]	0.30	0.98[0.96,1.01]	0.01	0.93[0.88,0.98]	0.53	1.03[0.95,1.11]
≥240	<.0001	1.06[1.05,1.08]	<.0001	1.06[1.04,1.08]	0.71	1.01[0.98,1.03]	0.35	0.98[0.94,1.02]	0.01	0.91[0.85,0.98]

Model Adjustments: age, sex, race, ethnicity, ever smoker, ever alcoholism, Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disorder, dementia, liver disease, cancer, diabetes, atrial fibrillation, hypertension, depression, ischemic heart disease, prescription of statins and prescription of non-statins, body mass index and albumin.

Table S7. Hazard Ratios for the Association of Time-Varying Serum Triglycerides with Time to ASCVD Hospitalization Stratified by Baseline CKD Stage across levels of adjustment.

Unadjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<0.0001	0.87[0.86,0.88]	0.573	1.00[0.99,1.02]	0.01	1.03[1.01,1.05]	0.18	1.03[0.99,1.08]	0.02	1.08[1.01,1.15]
80-<120	0.001	0.99[0.98,0.99]	0.01	1.02[1.01,1.03]	0.96	1.00[0.98,1.02]	0.43	1.02[0.98,1.06]	0.18	1.04[0.98,1.10]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.90	1.00[0.99,1.01]	0.59	1.00[0.98,1.01]	0.373	0.99[0.96,1.01]	0.16	0.96[0.92,1.01]	0.01	0.90[0.84,0.97]
200-<240	0.06	0.99[0.98,1.00]	0.10	0.98[0.96,1.00]	0.76	1.00[0.97,1.03]	0.48	0.98[0.92,1.04]	0.21	0.95[0.87,1.03]
≥240	0.03	0.99[0.98,1.00]	0.841	1.00[0.98,1.02]	0.104	0.98[0.95,1.00]	0.01	0.93[0.89,0.98]	<0.0001	0.87[0.81,0.93]
Age Adjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<0.0001	0.82[0.81,0.83]	<0.0001	0.95[0.93,0.96]	0.99	1.00[0.98,1.02]	0.91	1.00[0.95,1.04]	0.14	1.05[0.98,1.12]
80-<120	<0.0001	0.94[0.93,0.94]	0.08	0.99[0.97,1.00]	0.11	0.98[0.96,1.00]	0.99	1.00[0.96,1.04]	0.53	1.02[0.96,1.08]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<0.0001	1.06[1.04,1.07]	0.01	1.03[1.01,1.04]	0.79	1.00[0.98,1.03]	0.45	0.98[0.93,1.03]	0.04	0.92[0.86,1.00]
200-<240	<0.0001	1.10[1.08,1.11]	0.001	1.04[1.01,1.06]	0.16	1.02[0.99,1.05]	0.69	1.01[0.95,1.07]	0.78	0.99[0.91,1.08]
≥240	<0.0001	1.22[1.21,1.23]	0	1.11[1.09,1.13]	0.02	1.03[1.00,1.06]	0.82	0.99[0.95,1.04]	0.23	0.96[0.89,1.03]
Case-Mix Adjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<0.0001	0.96[0.95,0.97]	0.89	1.00[0.99,1.02]	0.03	1.03[1.00,1.05]	0.16	1.03[0.99,1.08]	0.04	1.07[1.00,1.14]
80-<120	0.08	0.99[0.98,1.00]	0.13	1.01[1.00,1.03]	0.69	1.00[0.98,1.02]	0.18	1.03[0.99,1.07]	0.94	1.00[0.94,1.06]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.09	1.01[1.00,1.02]	0.84	1.00[0.98,1.02]	0.82	1.00[0.97,1.02]	0.15	0.96[0.92,1.01]	0.11	0.94[0.87,1.01]
200-<240	0.08	1.01[1.00,1.02]	0.92	1.00[0.98,1.02]	0.73	0.99[0.97,1.02]	0.93	1.00[0.94,1.06]	0.18	0.94[0.86,1.03]
≥240	<0.0001	1.04[1.03,1.05]	0.19	1.01[0.99,1.03]	0.04	0.97[0.95,1.00]	0.01	0.93[0.89,0.98]	<0.0001	0.88[0.81,0.94]
Case-Mix+Lab Adjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<0.0001	0.86[0.85,0.86]	<0.0001	0.91[0.90,0.93]	<0.0001	0.94[0.92,0.96]	0.02	0.95[0.90,0.99]	0.38	0.97[0.91,1.04]
80-<120	<0.0001	0.95[0.94,0.96]	<0.0001	0.97[0.96,0.99]	<0.0001	0.96[0.94,0.98]	0.60	0.99[0.95,1.03]	0.36	0.97[0.92,1.03]

	Non-CKD		CKD Stage 3A		CKD Stage 3B		CKD Stage 4		CKD Stage 5/ESRD	
	P	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<0.0001	1.04[1.03,1.05]	0.003	1.03[1.01,1.04]	0.14	1.02[0.99,1.04]	0.64	0.99[0.94,1.04]	0.51	0.98[0.91,1.05]
200-<240	<0.0001	1.06[1.04,1.07]	<0.0001	1.04[1.02,1.06]	0.03	1.03[1.00,1.07]	0.21	1.04[0.98,1.10]	0.97	1.00[0.92,1.09]
≥240	<0.0001	1.10[1.09,1.11]	<0.0001	1.07[1.05,1.09]	0.03	1.03[1.00,1.06]	0.96	1.00[0.95,1.05]	0.39	0.97[0.90,1.04]
Case-Mix+Lab+Lipid Adjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<0.0001	0.94[0.93,0.95]	0.019	0.98[0.96,1.00]	0.75	1.00[0.98,1.03]	0.81	0.99[0.95,1.04]	0.95	1.00[0.94,1.07]
80-<120	<0.0001	0.98[0.97,0.99]	0.79	1.00[0.98,1.01]	0.09	0.98[0.96,1.00]	0.70	1.01[0.97,1.05]	0.66	0.99[0.93,1.05]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<0.0001	1.02[1.01,1.03]	0.16	1.01[1.00,1.03]	0.672	1.01[0.98,1.03]	0.35	0.98[0.93,1.03]	0.39	0.97[0.90,1.04]
200-<240	<0.0001	1.03[1.02,1.05]	0.04	1.02[1.00,1.05]	0.34	1.01[0.98,1.05]	0.51	1.02[0.96,1.08]	0.77	0.99[0.91,1.08]
≥240	<0.0001	1.07[1.06,1.08]	<0.0001	1.04[1.03,1.06]	0.653	1.01[0.98,1.03]	0.37	0.98[0.93,1.03]	0.17	0.95[0.88,1.02]

Model Adjustments:
Unadjusted
Age Adjusted: age
Case-Mix Adjusted: age, sex, race, ethnicity, ever smoker and ever alcoholism as well as time-updated Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disorder, dementia, liver disease, cancer, diabetes, atrial fibrillation, hypertension, depression, ischemic heart disease, prescription of statins and prescription of non-statins, and time-updated CKD stage
Case-Mix+Lab Adjusted: Case-Mix covariates and time-updated body mass index and albumin
Case-Mix+Lab+Lipid Adjusted: Case-Mix+Lab covariates and time-updated HDL and LDL cholesterols

Table S8. Hazard Ratios for the Association of Time-Varying Serum Triglycerides with Time to Non-ASCVD Hospitalization Stratified by Baseline CKD Stage across levels of adjustment.

Unadjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<0.0001	1.08[1.07,1.09]	<0.0001	1.23[1.22,1.25]	<0.0001	1.27[1.25,1.30]	<0.0001	1.34[1.30,1.39]	<0.0001	1.20[1.14,1.26]
80-<120	<0.0001	1.06[1.05,1.07]	<0.0001	1.10[1.08,1.11]	<0.0001	1.10[1.08,1.12]	<0.0001	1.14[1.10,1.18]	0.004	1.07[1.02,1.12]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<0.0001	0.95[0.94,0.96]	<0.0001	0.93[0.92,0.95]	<0.0001	0.93[0.91,0.95]	0.01	0.94[0.91,0.98]	<0.0001	0.88[0.83,0.93]
200-<240	<0.0001	0.91[0.90,0.92]	<0.0001	0.89[0.88,0.91]	<0.0001	0.92[0.90,0.95]	<0.0001	0.90[0.86,0.94]	<0.0001	0.87[0.81,0.92]
≥240	<0.0001	0.86[0.85,0.87]	<0.0001	0.88[0.86,0.89]	<0.0001	0.86[0.84,0.88]	<0.0001	0.87[0.84,0.91]	<0.0001	0.74[0.70,0.79]
Age Adjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<0.0001	1.03[1.03,1.04]	<0.0001	1.16[1.14,1.17]	<0.0001	1.23[1.21,1.26]	<0.0001	1.32[1.27,1.36]	<0.0001	1.18[1.13,1.24]
80-<120	<0.0001	1.01[1.01,1.02]	<0.0001	1.06[1.04,1.07]	<0.0001	1.08[1.06,1.10]	<0.0001	1.13[1.10,1.17]	0.01	1.06[1.01,1.11]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.86	1.00[0.99,1.01]	<0.0001	0.97[0.95,0.98]	<0.0001	0.95[0.92,0.97]	0.04	0.96[0.92,1.00]	<0.0001	0.89[0.84,0.94]
200-<240	0.96	1.00[0.99,1.01]	<0.0001	0.95[0.93,0.97]	<0.0001	0.95[0.93,0.98]	0.001	0.92[0.88,0.97]	<0.0001	0.88[0.83,0.94]
≥240	<0.0001	1.06[1.05,1.07]	0.30	0.99[0.97,1.01]	<0.0001	0.91[0.89,0.93]	<0.0001	0.92[0.88,0.95]	<0.0001	0.78[0.74,0.83]
Case-Mix Adjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<0.0001	1.10[1.09,1.11]	<0.0001	1.15[1.14,1.17]	<0.0001	1.19[1.17,1.22]	<0.0001	1.26[1.22,1.31]	<0.0001	1.13[1.08,1.19]
80-<120	<0.0001	1.05[1.04,1.06]	<0.0001	1.06[1.05,1.07]	<0.0001	1.08[1.06,1.09]	<0.0001	1.12[1.09,1.16]	0.13	1.04[0.99,1.08]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	<0.0001	0.97[0.96,0.98]	<0.0001	0.95[0.93,0.96]	<0.0001	0.94[0.92,0.96]	0.03	0.96[0.92,1.00]	0.002	0.91[0.86,0.97]
200-<240	<0.0001	0.95[0.94,0.96]	<0.0001	0.92[0.90,0.93]	<0.0001	0.93[0.91,0.96]	<0.0001	0.89[0.85,0.93]	0.001	0.89[0.83,0.95]
≥240	<0.0001	0.93[0.92,0.94]	<0.0001	0.90[0.89,0.92]	<0.0001	0.87[0.85,0.89]	<0.0001	0.88[0.84,0.91]	<0.0001	0.78[0.74,0.82]
Case-Mix+Lab Adjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	0.002	1.01[1.00,1.02]	<0.0001	1.06[1.05,1.08]	<0.0001	1.10[1.08,1.12]	<0.0001	1.15[1.11,1.19]	0.20	1.03[0.98,1.08]
80-<120	0.001	1.01[1.01,1.02]	<0.0001	1.03[1.01,1.04]	<0.0001	1.04[1.02,1.06]	<0.0001	1.08[1.05,1.12]	0.81	1.01[0.96,1.05]

Baseline Stage / Serum Triglycerides Group (mg/dL)	Non-CKD P	Non-CKD HR[95%CI]	CKD Stage 3A P	CKD Stage 3A HR[95%CI]	CKD Stage 3B P	CKD Stage 3B HR[95%CI]	CKD Stage 4 P	CKD Stage 4 HR[95%CI]	CKD Stage 5/ESRD P	CKD Stage 5/ESRD HR[95%CI]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.09	0.99[0.98,1.00]	<0.0001	0.97[0.95,0.99]	<0.0001	0.96[0.94,0.98]	0.28	0.98[0.94,1.02]	0.15	0.96[0.91,1.02]
200-<240	0.002	0.98[0.97,0.99]	<0.0001	0.95[0.93,0.97]	0.02	0.97[0.94,0.99]	0.004	0.93[0.89,0.98]	0.17	0.95[0.89,1.02]
≥240	<0.0001	0.98[0.97,0.99]	<0.0001	0.95[0.93,0.96]	<0.0001	0.92[0.90,0.94]	0.01	0.94[0.91,0.98]	<0.0001	0.86[0.81,0.91]
Case-Mix+Lab+Lipid Adjusted										
Baseline Stage	**Non-CKD**		**CKD Stage 3A**		**CKD Stage 3B**		**CKD Stage 4**		**CKD Stage 5/ESRD**	
Serum Triglycerides Group (mg/dL)	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]	*P*	HR[95%CI]
<80	<0.0001	1.02[1.01,1.03]	<0.0001	1.08[1.06,1.09]	<0.0001	1.11[1.09,1.13]	<0.0001	1.16[1.11,1.20]	0.38	1.02[0.97,1.08]
80-<120	<0.0001	1.02[1.01,1.02]	<0.0001	1.03[1.02,1.05]	<0.0001	1.04[1.02,1.06]	<0.0001	1.08[1.05,1.12]	0.96	1.00[0.96,1.05]
120-<160	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
160-<200	0.05	0.99[0.98,1.00]	<0.0001	0.97[0.95,0.98]	<0.0001	0.96[0.94,0.98]	0.22	0.98[0.94,1.02]	0.16	0.96[0.91,1.02]
200-<240	0.001	0.98[0.97,0.99]	<0.0001	0.95[0.93,0.97]	0.01	0.96[0.94,0.99]	0.003	0.93[0.88,0.97]	0.20	0.96[0.90,1.02]
≥240	<0.0001	0.98[0.97,0.99]	<0.0001	0.94[0.92,0.96]	<0.0001	0.91[0.89,0.94]	0.001	0.94[0.90,0.97]	<0.0001	0.85[0.80,0.90]

Model Adjustments:
Unadjusted
Age Adjusted: age
Case-Mix Adjusted: age, sex, race, ethnicity, ever smoker and ever alcoholism as well as time-updated Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disorder, dementia, liver disease, cancer, diabetes, atrial fibrillation, hypertension, depression, ischemic heart disease, prescription of statins and prescription of non-statins, and time-updated CKD stage
Case-Mix+Lab Adjusted: Case-Mix covariates and time-updated body mass index and albumin
Case-Mix+Lab+Lipid Adjusted: Case-Mix+Lab covariates and time-updated HDL and LDL cholesterols

Figure S1. Cohort Construction.

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┌─────────────────────────────────────────────────┐
│ 3,958,837 patients with a lipid measurement between │
│   October 1, 2004 and September 30,2006          │
└─────────────────────────────────────────────────┘
                    │
                    │          ┌──────────────────────────────────────────────┐
                    ├─────────▶│ 114,031 patients excluded for missing an averaged │
                    │          │ triglyceride measurement                     │
                    ▼          └──────────────────────────────────────────────┘
┌─────────────────────────────────────────────────┐
│            3,844,806 patients                    │
└─────────────────────────────────────────────────┘
                    │
                    │          ┌──────────────────────────────────────────────┐
                    ├─────────▶│ 880,985 patients excluded for missing an averaged eGFR in │
                    │          │ the same calendar quarter as the triglyceride measurement │
                    ▼          └──────────────────────────────────────────────┘
┌─────────────────────────────────────────────────┐
│            2,963,821 patients                    │
└─────────────────────────────────────────────────┘
                    │
                    │          ┌──────────────────────────────────────────────┐
                    ├─────────▶│ 98 patients excluded for missing censoring information │
                    │          └──────────────────────────────────────────────┘
                    ▼
┌─────────────────────────────────────────────────┐
│            2,963,723 patients                    │
└─────────────────────────────────────────────────┘
                    │
                    │          ┌──────────────────────────────────────────────┐
                    ├─────────▶│ 547 patients excluded for missing hospitalization information │
                    │          │ at any point during follow-up                │
                    ▼          └──────────────────────────────────────────────┘
┌─────────────────────────────────────────────────┐
│            2,963,176 patients                    │
└─────────────────────────────────────────────────┘
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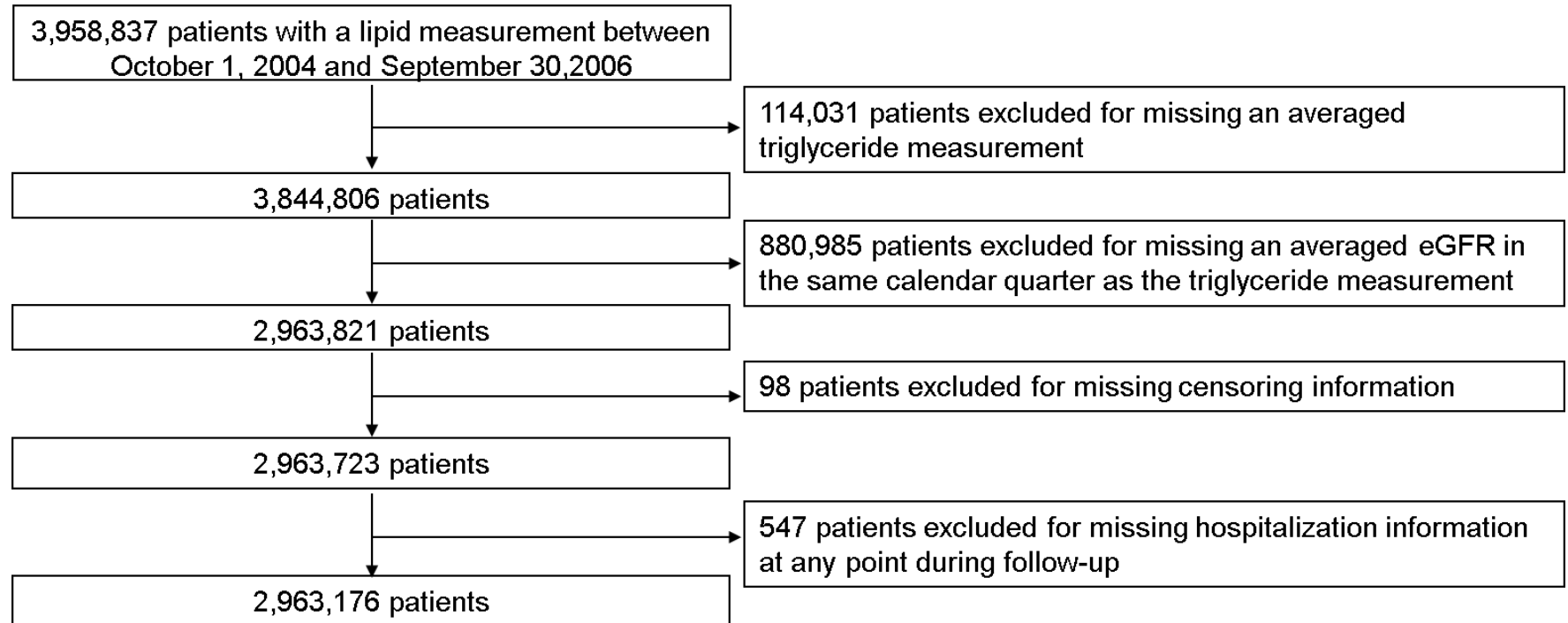
Figure S2. Association of Baseline Triglycerides with Time to A) ASCVD and B) Non-ASCVD Hospitalization Across CKD Stages after adjustment for Case-Mix + Lab + Log Transformed UACR among N=194,801 patients with UACR data.