

UC Irvine

UC Irvine Previously Published Works

Title

Association of Serum Triglycerides and Renal Outcomes among 1.6 Million US Veterans.

Permalink

<https://escholarship.org/uc/item/03m22763>

Journal

Nephron, 146(5)

ISSN

1660-8151

Authors

Soofoo, Melissa
Hashemi, Leila
Hsiung, Jui-Ting
[et al.](#)

Publication Date

2022

DOI

10.1159/000522388

Peer reviewed

Title:

**Risk of ASCVD and non-ASCVD Hospitalizations for Triglycerides
across CKD Stages
among 2.9 Million US Veterans**

(Running Head: TG and Hospitalizations)

Authors:

Melissa Soohoo¹, Leila Hashemi¹, Jui-Ting Hsiung¹, Hamid Moradi^{1,2},
Matthew J. Budoff³, Csaba P. Kovesdy^{4,5}, Kamyar Kalantar-Zadeh^{1,2}, Elani Streja^{1,2}

Affiliations:

1. Harold Simmons Center for Kidney Disease Research and Epidemiology,
Division of Nephrology and Hypertension,
University of California Irvine Medical Center, Orange, CA;
2. Nephrology Section, Tibor Rubin Veterans Affairs Medical Center, Long Beach, CA;
3. Division of Cardiology, The Lundquist Institute for Biomedical Innovation at Harbor-UCLA
Medical Center, Torrance, CA;
4. Nephrology Section, Memphis Veterans Affairs Medical Center, Memphis, TN;
5. Division of Nephrology, University of Tennessee Health Science Center, Memphis, TN;

Corresponding Author:

Elani Streja MPH, PhD

VA Long Beach Healthcare System

5901 East 7th Street, Long Beach, CA 90822, USA.

Tel: 562-826-5801

Email: elani.streja@va.gov

Word Counts:

Abstract word count: 304

Text word count: 3491

Tables: 1

Figures: 2

Supplemental Material:

Tables: 9

Figures: 2

Abstract

Background: High serum triglycerides (TG) are associated with higher risks of atherosclerotic cardiovascular disease (ASCVD). Studies have shown that in advanced chronic kidney disease (CKD) patients, the association of elevated serum TG levels with mortality is diminished. We sought to investigate the relationship of serum TG with ASCVD and non-ASCVD hospitalizations across CKD stages.

Methods: The cohort comprised 2,963,176 US veterans who received care in 2004-2006 (baseline period) and were followed to 2014. Using Cox models, we evaluated associations of baseline and time-varying TG with time to ASCVD or non-ASCVD hospitalizations, stratified by baseline CKD stage, and adjusted for demographics and baseline or time-updated clinical characteristics. Sensitivity analyses included competing risk regressions and stratification.

Results: The cohort mean age(SD) was 63±14 years old, and included 6% females and 14% African-Americans. The baseline median[IQR] TG was 127[87,189] mg/dL, and a quarter of the patients had prevalent CKD. There was a linear association between baseline TG and ASCVD event risk, however the risk with high TG ≥ 240 mg/dL gradually attenuated with worsening CKD stages (ref: TG 120-<160 mg/dL). Baseline TG was associated with a U-shaped relationship for non-ASCVD events in CKD 3A-3B patients. We additionally observed an incremental decline in non-ASCVD risks among high TG patients and worsening CKD stage. Time-varying associations of TG with ASCVD were similar to that of baseline analyses. Yet, the time-varying TG relationship with non-ASCVD events was now inverse and linear, where elevated TG were associated with lower risks and gradually declined for all stages. Results were robust in sensitivity analyses.

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

Key words:

Atherosclerotic cardiovascular disease; non-atherosclerotic cardiovascular disease; hospitalization; lipids; chronic kidney disease; triglycerides

Introduction

Dyslipidemia, including elevated serum triglycerides (TG), is a recognized 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 are predictors for chronic kidney disease (CKD), including its development and progression into advanced stages.^{4,5} Due to lipid aberrations and accelerated atherosclerosis during CKD progression, CKD 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 TG with CVD mortality incrementally declined across worsening CKD stages and in late-stage CKD patients, it reached a null association.¹⁰ Possible explanations include competing events of other CVD causes such as non-fatal CVD hospitalizations.^{5,10,11} Clinical trials investigating ASCVD events among CKD patients have primarily targeted low-density lipoprotein cholesterol (LDL) in early-stages (3A and 3B), while trials have been null in the advanced CKD patients.¹² Thus, understanding the relationship between other components of dyslipidemia, such as TG, with CVD outcomes is critical for devising risk mitigation strategies, especially in those with advanced CKD.

Prior studies examining serum lipid levels with CVD events among CKD patients have found mixed results.¹³⁻¹⁶ Several studies investigated populations of mainly early-stage CKD patients, despite the literature suggesting a relationship between serum lipids and outcomes in advanced CKD patients. Understanding both the long- and short-term relationship of TG on CVD events may better elucidate their complex relationship as CKD advances. Therefore, using a large national cohort, we hypothesized that the relationships between baseline and time-varying serum TG with ASCVD and non-ASCVD are also impacted by worsening CKD stages.

Methods

Study Population and Longitudinal Construction

The LIPROVET study (Lipid profiles and management in veterans with CKD) is comprised of US Veterans Affairs (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 TG and estimated glomerular filtration rate (eGFR) measurement in the baseline period. We excluded 114,031 patients for missing a TG measurement during baseline, 880,985 patients for missing an eGFR, 98 patients with invalid censoring information and 547 patients for missing data on hospitalization during follow-up. The final cohort comprised 2,963,176 patients (**Supplemental Figure 1**).

Clinical Measurements

The ascertainment of characteristics have been described elsewhere.¹⁰ Data were sourced from combined VA, Centers for Medicare and Medicaid Services (CMS), and the United States Renal Data System (USRDS) databases. The VA databases informed ever smoker and alcoholism statuses, which were defined as any indication of the behavior until censorship.¹⁷ VA/CMS pharmacy records were used to ascertain the prescription of lipid modulating therapies, based on drug class codes and names. Receipt of medication was defined as any dispensation record within each calendar quarter. Comorbidities were derived from VA/CMS databases using International Classification of Diseases, Ninth Revision (ICD-9) Diagnostic and Current Procedural Terminology.^{18, 19}

Laboratory measurements were extracted from the VA database. The Martin-Hopkins equation was used to calculate LDL if it was missing for any quarter.²⁰ eGFR was calculated from serum creatinine using the CKD-EPI formula.²¹ CKD stage according to non-dialysis dependent eGFR cutoffs were categorized as non-CKD, 3A, 3B, 4 and 5. The USRDS identified patients with end-stage renal disease (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

Based on clinically relevant cutoffs, baseline and time-varying TG were categorized as: <80, 80-<120, 120-<160, 160-<200, 200-<240 and ≥ 240 mg/dL.¹⁰

The co-primary outcomes were time to 1) ASCVD hospitalization and 2) non-ASCVD hospitalization. Hospitalizations were obtained from VA/CMS databases. Records with the specific diagnostic code in the first or second position were considered as an event. Event codes are presented in **Supplemental Table 1**. Information on other censoring events were obtained from the aforementioned sources and the National Death Index. Patient follow-up began 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 \pm standard deviation, median [interquartile range] or percentage, as appropriate.

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

Five adjustment models were examined: 1) Unadjusted, 2) Age adjusted, 3) Case-Mix Adjusted, which included baseline characteristics of age, gender, 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, 4) Case-Mix+Lab Adjusted, which additionally included body mass index (BMI) and albumin to the Case-Mix model, and 5) Case-Mix+Lab+Lipid Adjusted, which additionally included low and high-density lipoprotein cholesterol (LDL and HDL) to the Case-Mix+Lab model. For baseline models, data from the baseline quarter were used in analyses. In time-varying models, time-updated variables were used as appropriate, and time-varying CKD stage was also included in Case-Mix and higher models. We predefined the Case-Mix+Lab adjustment as the model of interest.

To consider mortality in each association, we performed competing risk regression, where ASCVD hospitalization was competed against all-cause mortality and non-ASCVD hospitalization, and vice versa when non-ASCVD hospitalization was the outcome.²² We evaluated the TG-hospitalization relationships in subgroup analyses of baseline characteristics to investigate effect modification. In sensitivity analyses, we evaluated the relationship of baseline TG and urinary tract infection (UTI) hospitalization to investigate this negative control outcome in addressing uncontrolled confounding. Moreover, we evaluated 194,801 patients with available data on urine albumin-to-creatinine ratio (UACR) in the year prior to the calendar quarter of

entry. A comparison of characteristics between patients with and without UACR data are presented in **Supplemental Table 2** and evaluated using standardized differences. We repeated baseline analyses with adjustment for averaged logged UACR in the Case-Mix+Lab model.

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

Analyses were performed using SAS Enterprise Guide (7.1) (Cary, NC) and Stata (15) (College Station, TX). Due to the non-intrusive 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 old, and included 6% females and 14% African Americans. The cohort had a median[IQR] averaged TG of 127[87,189] mg/dL, as well as averaged HDL, LDL and total cholesterol 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% on non-dialysis dependent CKD stage 5 or with ESRD. Overall, those with higher TG tended to be younger and white, have a lower prevalence of chronic obstructive pulmonary disease and anemia, and have a higher prevalence of diabetes, depression and anxiety.

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%CI] 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 (**Supplemental Table 3**). Only 11% and 16% of patients experienced more than two ASCVD or non-ASCVD hospitalizations, respectively during follow-up. Among patients with any ASCVD hospitalization, 21% experienced a myocardial infarction as their first event, while the majority (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 TG and ASCVD hospitalization was generally linear compared to the reference group (**Supplemental Table 4**). After adjustment for Case-Mix+Lab covariates, lower TG <120 mg/dL were associated with a lower risk of ASCVD hospitalization across all stages compared to TG 120-<160 mg/dL (**Figure 1A**). Moreover, the magnitude of association for high TG ≥ 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 overall relationships remained similar.

In unadjusted models, we observed a shallow inverse relationship between baseline TG and non-ASCVD hospitalization across CKD stages (**Supplemental Table 5**). Yet, adjustment for Case-Mix+Lab covariates demonstrated a U-shaped relationship for CKD stage 3A-B patients. (**Figure 1B**). Among CKD stage 4 and 5/ESRD patients, we observed an inverse relationship. We also observed a gradual cascade in the risk between high TG and non-ASCVD hospitalization across CKD stages. There was a null association between high TG and non-

ASCVD hospitalization among CKD stage 4 and 5/ESRD patients. Similar relationships were observed with additional lipid adjustment.

Sensitivity Analyses of Baseline Triglycerides and Time to Hospitalizations

Our observed relationships were similar when using a competing risk regression adjusted for Case-Mix+Lab covariates. We observed a relatively linear association with baseline TG and time to ASCVD hospitalization after considering competing events. Elevated TG were associated with a higher risk for ASCVD events for all stages. In competing risk analyses for non-ASCVD hospitalization, we observed a reverse J-shaped association in Case-Mix+Lab adjustment.

In sensitivity analyses using a negative control, we found that association of TG with UTI hospitalization showed a lower to null relationship across all CKD stages. A comparison of patients with and without UACR data showed that those with UACR were more likely to be older, diabetic, have hyperlipidemia, and higher levels of body mass index. After adjustment for log UACR in our main models, we observed an attenuated relationship between TG and ASCVD hospitalization but still reflected that elevated TG were associated with a higher risk of event except for CKD5/ESRD patients (**Supplemental Figure 2**). The TG-non-ASCVD relationship was also attenuated and demonstrated that the risk of non-ASCVD hospitalization diminished across CKD stages.

Subgroup Analyses for Baseline Triglycerides with Time to Hospitalizations

Subgroup analyses were attenuated across strata of age, diabetes, LDL levels, statin use, race and prior CVD (**Supplemental Table 6-7**). In general, we observed that the association of high TG ≥ 240 mg/dL with each outcome depicted a similar cascade across advancing CKD stages. Notably, high TG levels were no longer associated with decreased time to non-ASCVD

hospitalization among CKD stage 5/ESRD patients and <65 years of age. Among patients with LDL <100 mg/dL and CKD stage 5/ESRD, the association of high TG ≥ 240 mg/dL with ASCVD and non-ASCVD event were each strengthened towards close to a 10% lower risk of event. Conversely, patients with high LDL ≥ 100 mg/dL, high TG and CKD stage 4 had a null relationship with ASCVD or non-ASCVD hospitalization, while a slightly higher was observed among persons with CKD stage 5/ESRD and high TG. The relationship of TG and non-ASCVD events among patients without prior CVD was largely flat, while the TG-ASCVD relationship remained linear across prior CVD strata.

Association of Time-Varying Triglycerides with Time to Hospitalizations

In time-varying analyses, we observed similar results to our baseline model (**Supplemental Table 8-9, Figure 2A and B**). After adjustment for time-varying Case-Mix+Lab covariates, low time-varying TG were generally associated with a null or lower risk of ASCVD hospitalization across strata of baseline CKD stage (ref: TG 120-<160 mg/dL). Time-varying TG ≥ 240 mg/dL were associated with a higher risk of ASCVD hospitalization for baseline non-CKD and CKD stage 3A-B. Similar to the baseline analysis, we observed a cascade in effect estimates in the association of high time-varying TG and ASCVD event, including a null association among those with CKD stage 4 and 5/ESRD.

Alternatively, the association of time-varying TG with time to non-ASCVD event was inverse across baseline CKD stages. Time-varying TG <120 mg/dL were associated with a higher risk of non-ASCVD hospitalization across baseline CKD stages, with the exception of CKD stage 5/ESRD patients. We observed a lower to null risk of non-ASCVD hospitalization for time-varying TG ≥ 160 mg/dL. Baseline CKD stage 5/ESRD patients with the highest time-

varying TG ≥ 240 mg/dL had the lowest risk of time to non-ASCVD hospitalization (HR[95%CI]: 0.86[0.81, 0.91]). Results were similar with time-updated lipid adjustment.

Discussion

We evaluated the long- and short-term associations between TG and ASCVD and non-ASCVD hospitalization across CKD stages. Our observations suggest that there was a linear association between baseline and time-varying TG with ASCVD hospitalization across CKD stages. For non-ASCVD outcomes, the relationship with baseline TG was U-shaped but the time-varying TG relationship was inverse. Across all analyses, we observed a similar pattern: the relationship with elevated TG with outcomes incrementally declined in the magnitude of risk across worsening CKD stages, where the advanced CKD (4, 5/ESRD) patients tended to have null or lower associations with CVD hospitalizations.

Cohort studies have examined TG with composite CVD events in CKD patients, yet were unable to examine relationships within individual CKD stages. The Atherosclerosis Risk in Communities Study (ARIC) suggested that each quartile increase in TG was associated with a higher risk of coronary heart disease (CHD) among patients with eGFR 15- <60 mL/min/1.73m², but included minimal adjustment.¹⁶ The Multiethnic Study of Atherosclerosis (MESA) observed the potential interaction between non-CKD and CKD patients (p-interaction: 0.07) for an SD increase of log TG with CHD risk.¹⁵ Finally, the Chronic Renal Insufficiency Cohort (CRIC) study showed linear associations between TG tertiles and ASCVD events among CKD patients.¹³ However, they did not observe interaction by eGFR ($<$ and ≥ 45 mL/min/1.73m²), where associations for TG >160 mg/dL among each strata had a 24-25% higher risk of event (ref: TG <103 mg/dL), but were attenuated. The magnitude of effect estimates from CRIC and MESA studies do suggest a higher risk of ASCVD events with elevated TG among predominantly early-

stage CKD patients. This was similarly observed in our early-stage CKD patients where the larger cohort size allowed for more power to examine individual stages and smaller clinically relevant groups of TG.

A post-hoc analysis of the Study of Heart and Renal Protection (SHARP) trial showed weak to null associations between higher TG and ASCVD events, even when stratified at eGFR 30 mL/min/1.73m².¹⁴ We also observed that CKD stage 5/ ESRD patients had a null risk of ASCVD events, yet the SHARP analyses for early-stage CKD patients not only contrasted our study, but also that of CRIC and MESA. These two studies comprised mostly CKD stage 3A-B patients, and thus were limited in the ability to examine later stages. While the SHARP trial did investigate late-stage CKD and dialysis patients, it also had restrictive enrollment criteria and were limited to those with prior myocardial infarction, which may make study participants less generalizable to the general CKD population. Moreover, these studies were limited in their ability to account for potential confounders without overadjustment. Our data allowed for the adjustment of potential confounders including comorbidities and markers of malnutrition and inflammation that were often absent from prior studies. Notably, we observed a higher risk of ASCVD events with high TG (≥ 160 mg/dL) across CKD stages 3A-4. Akin to SHARP, we also observed an attenuated relationship with TG and ASCVD outcomes with our CKD stage 5/ESRD patients. These results are consistent with findings in hemodialysis patients, where elevated TG levels were associated with lower risks of mortality and possibly due to the malnutrition and inflammation that are prevalent in this population.^{10, 23}

Few studies have examined the relationship of TG and non-ASCVD events. The SHARP trial showed that TG levels were not associated with higher risk of non-ASCVD events among those with early-stage CKD, while 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 TG among non-CKD and CKD 3A patients, while the risk was attenuated or lower in later stages. In our time-varying analyses, we observe a lower risk of non-ASCVD events with elevated TG for all CKD stages. Within the SHARP trial, it was suggested that the relationships may be due 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. While most studies evaluating serum TG have been in the context of ASCVD, future research will need to clarify the association of TG with outcomes not related to ASCVD.

Clinical trials have indicated the important role of remnant cholesterol and triglyceride-rich lipoprotein (TGRL) in the development of ASCVD events.²⁴ The lipoprotein lipase that lies in the vascular endothelial surface can degrade the circulating TG, thereby allowing remnant cholesterol and TGRL to be taken up by the arterial wall without the need of further oxidation.²⁵ ²⁶ While this mechanism may explain the relationships in early-stage CKD patients, animal models have indicated that lipid metabolism is altered in advanced CKD stages.⁸ Prior studies primarily relied on baseline TG measurement, even though lipid metabolism can be dysregulated through CKD, rendering the possibility of an altered impact over time as TG levels change. Thus, a baseline TG measurement in early-stage CKD may not fully capture the TG-hospitalization relationship after patients had progressed to advanced CKD. CKD patients have a higher prevalence of hypertriglyceridemia, in part due to impaired clearance of lipoproteins in conjunction with reduced kidney function.^{27, 28} Particularly in advanced CKD patients, it may be that the greater prevalence of non-traditional risk factors such as malnutrition, cachexia, and

protein-energy-wasting become more prominent and dominate the TGRL relationship.^{29,30} Such conditions are associated with a disordered energy metabolism which explain why elevated TG were not associated with ASCVD and non-ASCVD hospitalizations, as demonstrated in this study. Moreover, clinical trials have noted that treatment with icosapent ethyl and statins were effective in lowering risks of ASCVD events in high-risk patients with established CVD or diabetes, however these trials did not include patients with CKD stage 4-5 or on dialysis.³¹ For non-ASCVD events, a similar explanation of TGRL accumulation in the arterial wall as well as in the heart muscle leading to cardiomyopathy has been suggested in prior studies evaluating elevated TG and heart failure. These studies also suggested that associations may be explained by the pro-inflammatory and toxic role of TG.^{29,30} However, further studies are needed to examine this hypothesis.

Using our repeated measured data, we examined the time-varying relationships of TG and hospitalizations, showing largely similar patterns with TG and ASCVD to our baseline results. Yet, our non-ASCVD relationship had an inverse linear pattern, suggesting that in the short-term, elevated TG levels are not associated with a higher risk of non-ASCVD events in both non-CKD and CKD patients. To date, there is little information on the short-term risk of events with time-varying TG and outcomes in CKD patients. This observation of the lower risk of non-ASCVD events in the short-term for advanced CKD patients 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 TG. Few studies have evaluated serial TG measurements and our ability to examine short-term associations especially as one progresses through CKD are strengths of this study. In addition,

we note several limitations. We cannot rule out residual confounding nor make causal inferences. We were unable adjust for confounders including other markers of nutrition or apolipoproteins. Data on UACR were only available in a select proportion of patients, 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.³³ Our source for outcomes were electronic medical records and there remains the possibility of misclassification. However, we restricted our outcomes to primary or secondary ICD-9 codes in order to obtain adverse events and minimize biases. Finally, our results may not be generalizable to the general population given that our source cohort of VA patients is primarily comprised of older white men.

In conclusion, we showed the short-term and long-term associations of TG with ASCVD and non-ASCVD hospitalizations across CKD stages. Relationships incrementally declined across worse CKD stages for elevated TG, a known CVD risk factor. Given the burden and risk of CVD among CKD patients, it is important to evaluate both immediate and long-term impact of TG 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 TG with a specific focus on late-stage CKD patients.

Disclosures:

KKZ has received honoraria and/or support from Abbott, Abbvie, Alexion, Amgen, American Society of Nephrology, Astra-Zeneca, AVEO Oncology, Chugai, DaVita, Fresenius, Genentech, Haymarket Media, Hofstra Medical School, International Federation of Kidney Foundations, International Society of Hemodialysis, International Society of Renal Nutrition & Metabolism, Japanese Society of Dialysis Therapy, Hospira, Kabi, Keryx, Novartis, National Institutes of Health, National Kidney Foundation, OPKO, Pfizer, Relypsa, Resverlogix, Sandoz, Sanofi, Shire, Vifor, UpToDate, and ZSPharma. CPK has received honoraria from Akebia, Ardelyx, Astra-Zeneca, Bayer, Cara Therapeutics, Reata and Tricida. HM has received research funding from Novartis and Amgen. ES has received support from Astra Zeneca and Edwards Lifesciences.

Acknowledgment

This study was supported by Dr. Streja's Career Development Award IK2- CX 001266-01 from the US Veterans Administration Clinical Sciences Research and Development Program.

The data reported here have been supplied by the US Veterans Administration. Support for VA/CMS data is provided by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Health Services Research and Development, VA Information Resource Center (Project Numbers SDR 02-237 and 98-004). Opinions expressed in this presentation are those of the authors and do not represent the official opinion of the US Department of Veterans Affairs or the US Government.

Data were presented as an oral presentation at the 2019 American Heart Association Scientific Sessions meeting in Philadelphia, PA, a poster presentation at the virtual 2020 American Society for Nephrology Kidney Week meeting.

Funding Source

KKZ has been supported by the NIH/NIDDK mid-career award K24-DK091419. ES is supported by a career development award from the Office of Research and Development of the Department of Veterans Affairs (IK2- CX 001266-01). HM is supported by a career development award from the Office of Research and Development of the Department of Veterans Affairs (1IK- CX 001043-01A2).

References

1. Stauffer ME, Weisenfluh L, Morrison A. Association between triglycerides and cardiovascular events in primary populations: a meta-regression analysis and synthesis of evidence. *Vasc Health Risk Manag.* 2013;9:671-80. doi:10.2147/VHRM.S52713
2. Liu J, Zeng FF, Liu ZM, Zhang CX, Ling WH, Chen YM. Effects of blood triglycerides on cardiovascular and all-cause mortality: a systematic review and meta-analysis of 61 prospective studies. *Lipids Health Dis.* Oct 2013;12:159. doi:10.1186/1476-511X-12-159
3. Klempfner R, Erez A, Sagit BZ, et al. Elevated Triglyceride Level Is Independently Associated With Increased All-Cause Mortality in Patients With Established Coronary Heart Disease: Twenty-Two-Year Follow-Up of the Bezafibrate Infarction Prevention Study and Registry. *Circ Cardiovasc Qual Outcomes.* Mar 2016;9(2):100-8. doi:10.1161/CIRCOUTCOMES.115.002104
4. Holmes MV, Ala-Korpela M, Smith GD. Mendelian randomization in cardiometabolic disease: challenges in evaluating causality. *Nat Rev Cardiol.* Oct 2017;14(10):577-590. doi:10.1038/nrcardio.2017.78
5. Chawla V, Greene T, Beck GJ, et al. Hyperlipidemia and long-term outcomes in nondiabetic chronic kidney disease. *Clin J Am Soc Nephrol.* Sep 2010;5(9):1582-7. doi:10.2215/CJN.01450210
6. System USRD. *2016 USRDS annual data report: Epidemiology of kidney disease in the United States.* 2016.
7. Reiss AB, Voloshyna I, De Leon J, Miyawaki N, Mattana J. Cholesterol Metabolism in CKD. *Am J Kidney Dis.* Dec 2015;66(6):1071-82. doi:10.1053/j.ajkd.2015.06.028
8. Vaziri ND. Dyslipidemia of chronic renal failure: the nature, mechanisms, and potential consequences. *Am J Physiol Renal Physiol.* Feb 2006;290(2):F262-72. doi:10.1152/ajprenal.00099.2005
9. Choudhury D, Tuncel M, Levi M. Disorders of lipid metabolism and chronic kidney disease in the elderly. *Semin Nephrol.* Nov 2009;29(6):610-20. doi:10.1016/j.semnephrol.2009.07.006
10. Soohoo M, Moradi H, Obi Y, Kovesdy CP, Kalantar-Zadeh K, Streja E. Serum triglycerides and mortality risk across stages of chronic kidney disease in 2 million U.S. veterans. *J Clin Lipidol.* Aug 2019;doi:10.1016/j.jacl.2019.08.001
11. Kovesdy CP, Anderson JE, Kalantar-Zadeh K. Inverse association between lipid levels and mortality in men with chronic kidney disease who are not yet on dialysis: effects of case mix and the malnutrition-inflammation-cachexia syndrome. *J Am Soc Nephrol.* Jan 2007;18(1):304-11. doi:10.1681/ASN.2006060674
12. Messow CM, Isles C. Meta-analysis of statins in chronic kidney disease: who benefits? *QJM.* Aug 2017;110(8):493-500. doi:10.1093/qjmed/hcx040
13. Bajaj A, Xie D, Cedillo-Couvert E, et al. Lipids, Apolipoproteins, and Risk of Atherosclerotic Cardiovascular Disease in Persons With CKD. *Am J Kidney Dis.* 06 2019;73(6):827-836. doi:10.1053/j.ajkd.2018.11.010
14. Lamprea-Montealegre JA, Staplin N, Herrington WG, et al. Apolipoprotein B, Triglyceride-Rich Lipoproteins, and Risk of Cardiovascular Events in Persons with CKD. *Clin J Am Soc Nephrol.* Jan 2020;15(1):47-60. doi:10.2215/CJN.07320619
15. Lamprea-Montealegre JA, McClelland RL, Grams M, Ouyang P, Szklo M, de Boer IH. Coronary heart disease risk associated with the dyslipidaemia of chronic

kidney disease. *Heart*. 09 2018;104(17):1455-1460. doi:10.1136/heartjnl-2017-312794

16. Muntner P, He J, Astor BC, Folsom AR, Coresh J. Traditional and nontraditional risk factors predict coronary heart disease in chronic kidney disease: results from the atherosclerosis risk in communities study. *J Am Soc Nephrol*. Feb 2005;16(2):529-38. doi:10.1681/ASN.2004080656

17. McGinnis KA, Brandt CA, Skanderson M, et al. Validating smoking data from the Veteran's Affairs Health Factors dataset, an electronic data source. *Nicotine Tob Res*. Dec 2011;13(12):1233-9. doi:10.1093/ntr/ntr206

18. VIREC. *Calculating a Comorbidity Index for Risk Adjustment Using VA or Medicare Data*. Hines, IL: U.S. Department of Veterans Affairs, Health Services Research and Development Service, VA Information Resource Center; April 2014. (Rev. September 2015).

19. Klabunde CN, Harlan LC, Warren JL. Data sources for measuring comorbidity: a comparison of hospital records and medicare claims for cancer patients. *Med Care*. Oct 2006;44(10):921-8. doi:10.1097/01.mlr.0000223480.52713.b9

20. Martin SS, Blaha MJ, Elshazly MB, et al. Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. *JAMA*. Nov 2013;310(19):2061-8. doi:10.1001/jama.2013.280532

21. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. May 2009;150(9):604-12.

22. Fine J, Gray R. A Proportional Hazards Model for the Subdistribution of a Competing Risk. *Journal of the American Statistical Association*. 1999;94(446):496-509. doi:10.2307/2670170

23. Kilpatrick RD, McAllister CJ, Kovesdy CP, Derose SF, Kopple JD, Kalantar-Zadeh K. Association between serum lipids and survival in hemodialysis patients and impact of race. *J Am Soc Nephrol*. Jan 2007;18(1):293-303. doi:10.1681/ASN.2006070795

24. Nordestgaard BG, Varbo A. Triglycerides and cardiovascular disease. *Lancet*. Aug 2014;384(9943):626-635. doi:10.1016/S0140-6736(14)61177-6

25. Toth PP. Triglyceride-rich lipoproteins as a causal factor for cardiovascular disease. *Vasc Health Risk Manag*. 2016;12:171-83. doi:10.2147/VHRM.S104369

26. Maggi FM, Raselli S, Grigore L, Redaelli L, Fantappiè S, Catapano AL. Lipoprotein remnants and endothelial dysfunction in the postprandial phase. *J Clin Endocrinol Metab*. Jun 2004;89(6):2946-50. doi:10.1210/jc.2003-031977

27. Chan DT, Dogra GK, Irish AB, et al. Chronic kidney disease delays VLDL-apoB-100 particle catabolism: potential role of apolipoprotein C-III. *J Lipid Res*. Dec 2009;50(12):2524-31. doi:10.1194/jlr.P900003-JLR200

28. Sacks FM. The crucial roles of apolipoproteins E and C-III in apoB lipoprotein metabolism in normolipidemia and hypertriglyceridemia. *Curr Opin Lipidol*. Feb 2015;26(1):56-63. doi:10.1097/MOL.0000000000000146

29. Toth PP, Philip S, Hull M, Granowitz C. Elevated Triglycerides (≥ 150 mg/dL) and High Triglycerides (200-499 mg/dL) Are Significant Predictors of New Heart Failure Diagnosis: A Real-World Analysis of High-Risk Statin-Treated Patients. *Vasc Health Risk Manag*. 2019;15:533-538. doi:10.2147/VHRM.S221289

30. Varbo A, Nordestgaard BG. Nonfasting Triglycerides, Low-Density Lipoprotein Cholesterol, and Heart Failure Risk: Two Cohort Studies of 113 554 Individuals. *Arterioscler Thromb Vasc Biol*. 02 2018;38(2):464-472. doi:10.1161/ATVBAHA.117.310269

31. Bhatt DL, Steg PG, Miller M, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. *N Engl J Med*. 01 2019;380(1):11-22. doi:10.1056/NEJMoa1812792
32. Lee Y, Park S, Lee S, et al. Lipid profiles and risk of major adverse cardiovascular events in CKD and diabetes: A nationwide population-based study. *PLoS One*. 2020;15(4):e0231328. doi:10.1371/journal.pone.0231328
33. Lipsitch M, Tchetgen Tchetgen E, Cohen T. Negative controls: a tool for detecting confounding and bias in observational studies. *Epidemiology*. May 2010;21(3):383-8. doi:10.1097/EDE.0b013e3181d61eeb

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 (x 10 ³ /mm ³)	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 (mmHg)	135±18	133±18	134±18	135±18	136±17	136±17	137±17
DBP (mmHg)	76±11	74±11	75±11	76±11	76±11	76±11	77±11
BMI (kg/m ²)	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	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	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
Non-statin	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

Abbreviations: Data presented as mean ± standard deviation, median[interquartile range], or percentage, as appropriate.

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

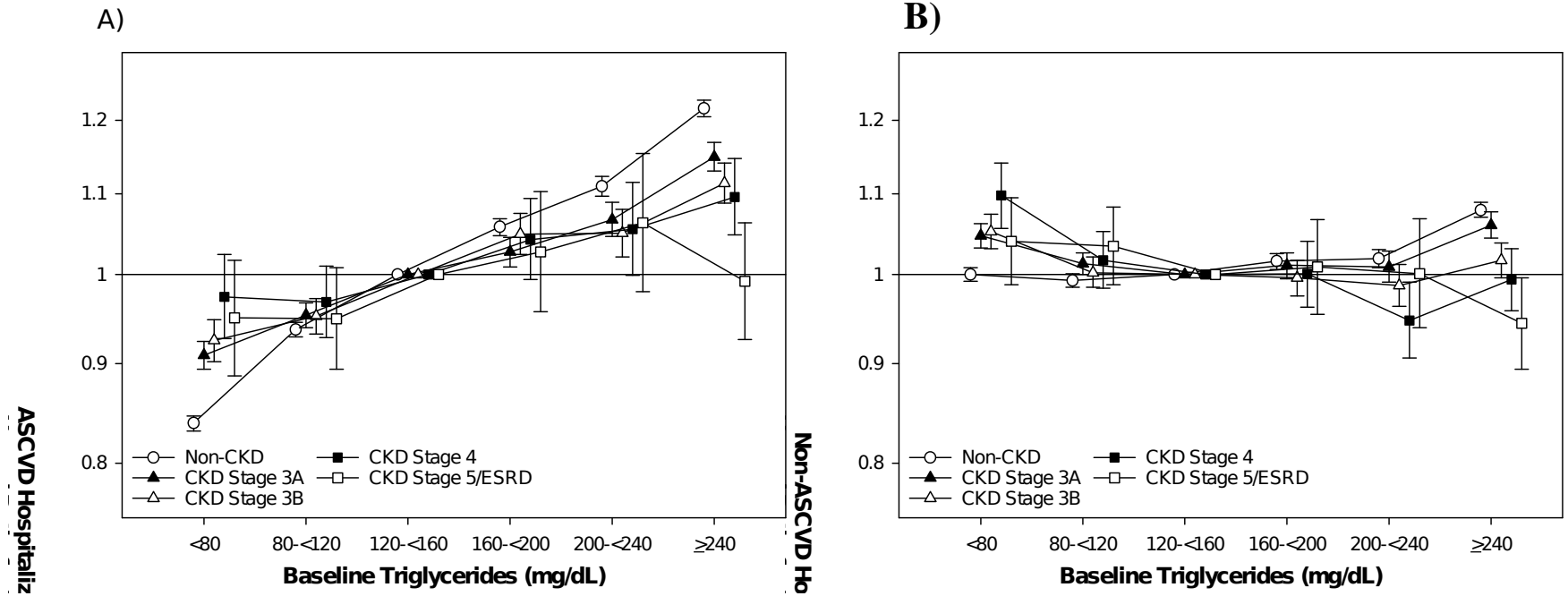
*eGFR provided for only patients classified as CKD stage 5, yet not on ESRD.

Figure Titles

Figure 1. Association of Baseline Triglycerides with Time to A)ASCVD and B) Non-ASCVD Hospitalization Across CKD Stages after adjustment for Case-Mix + Lab covariates

Figure 2. Association of Time-Varying Triglycerides with Time to A)ASCVD and B) Non-ASCVD Hospitalization Across Baseline CKD Stages after adjustment for Case-Mix + Lab covariates

Figure 1. Association of Baseline Triglycerides with Time to A) ASCVD and B) Non-ASCVD Hospitalization Across CKD Stages after adjustment for Case-Mix + Lab covariates

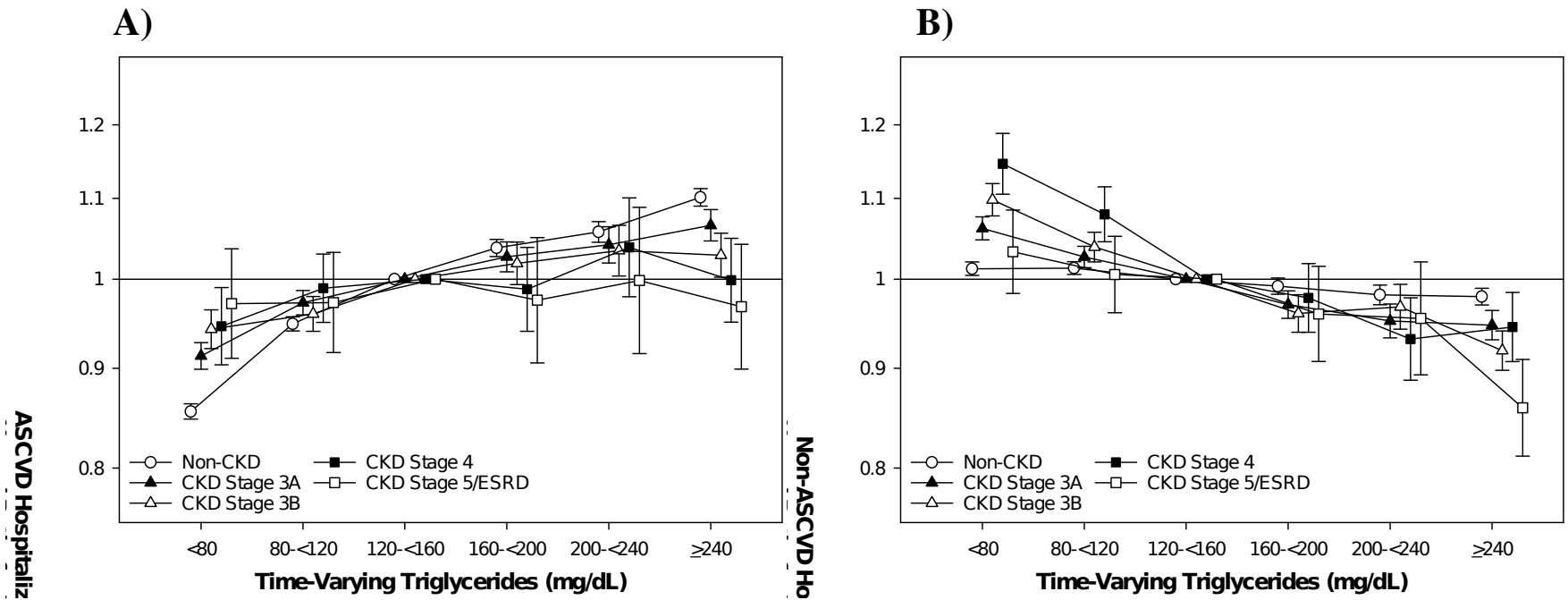


Model Adjustments: age, gender, race, ethnicity, ever smoker, ever alcoholism, Charlson comorbidity index, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disorder, dementia, liver disease, cancer, diabetes, atrial fibrillation,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

Abbreviations:

ASCVD; atherosclerotic cardiovascular disease, CKD; chronic kidney disease, ESRD; end-stage renal disease

Figure 2. Association of Time-Varying Triglycerides with Time to A) ASCVD and B) Non-ASCVD Hospitalization Across Baseline CKD Stages after adjustment for Case-Mix + Lab covariates



Model Adjustments: age, gender, 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, body mass index, albumin and CKD stage.

Abbreviations:

ASCVD; atherosclerotic cardiovascular disease, CKD; chronic kidney disease, ESRD; end-stage renal disease

Supplemental 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
	Non-hemorrhagic 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

Abbreviations:

ASCVD; atherosclerotic cardiovascular disease, CKD; chronic kidney disease, ESRD; end-stage renal disease, PVD; peripheral vascular disease, TIA; transient ischemic attack.

Supplemental Table 2. 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
Gender (% 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

Abbreviations: 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.

Supplemental Table 3. 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	597362	35.9	202445	81.2	105330	131.7	31084	223.7	16138	294.1

	[47.2,47.4]		[35.8,36.0]		[80.9,81.6]		[130.9,132.5]		[221.2,226.2]		[289.6,298.7]
--	-------------	--	-------------	--	-------------	--	---------------	--	---------------	--	---------------

Supplemental Table 4. 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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]

Group (mg/dL)										
<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]
120-<160	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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, gender, 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 cholesterol

Supplemental Table 5. 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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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	
	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]
Serum Triglycerides Group (mg/dL)										
<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]
120-<160	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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	
	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]
Serum Triglycerides Group (mg/dL)										
<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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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, gender, 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 cholesterol

Supplemental Table 6: 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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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]

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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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]
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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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, gender, 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.

Supplemental Table 7: 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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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]
120-<160	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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]
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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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, gender, 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.

Supplemental Table 8. 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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]
<80	<.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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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]	<.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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]
<80	<.0001	0.82[0.81,0.83]	<.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	<.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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
160-<200	<.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	<.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	<.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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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]
120-<160	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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

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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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]
120-<160	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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)	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	HR[95%CI]	<i>P</i>	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	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>	<i>Ref</i>
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**

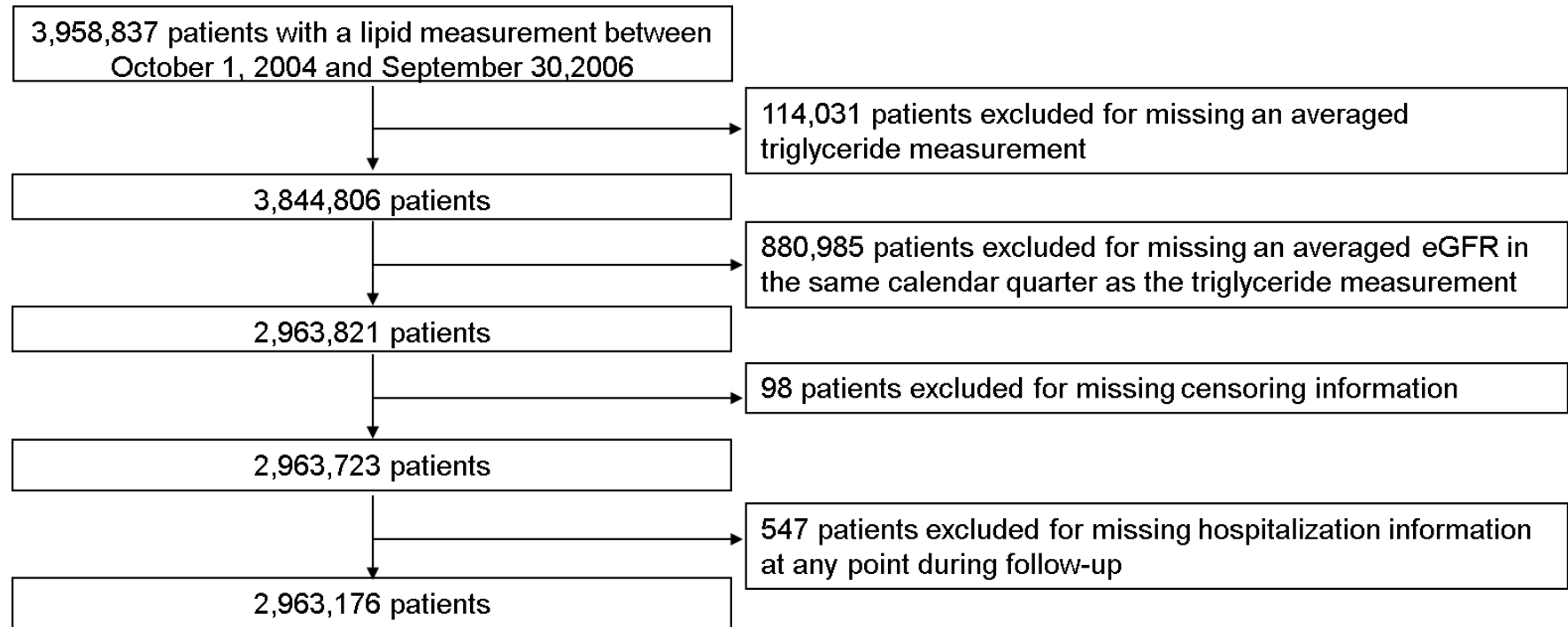
Age Adjusted: age

Case-Mix Adjusted: age, gender, 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 cholesterol

Supplemental Figure 1. Cohort Construction



Supplemental Figure 2. Association of Baseline Triglycerides with Time to A) ASCVD and B) Non-ASCVD Hospitalization Across CKD Stages after adjustment for Case-Mix + Lab + Log UACR among N=194,801 patients with UACR data

