Supplement file

Table of Contents

Appendix 1. Data analysis overview and analytic notes for some of individual studies

Overview:
As previously described,[1] the collaborating cohorts were asked to compile a dataset with approximately 30 variables (key exposures [serum creatinine to estimate GFR and albuminuria], covariates [e.g., age, sex, race/ethnicity, diabetes, hypertension], and outcomes [event variables and corresponding follow-up times]). To be consistent across cohorts, the CKD-PC Data Coordinating Center sent definitions for those variables to participating cohorts. We instructed studies not to impute any variables.

For 20 of the 28 CKD-PC cohorts in this specific study of change in albuminuria, the Data Coordination Center at Johns Hopkins University conducted the analysis; the remainder and the CKD-EPI collaboration coordinating center ran the standard code written in STATA by the Data Coordinating Center and shared the output with the Data Coordinating Center. The standard code was designed to automatically save all estimates and variance-covariance matrices needed for the meta-analysis. Then, the Data Coordinating Center meta-analyzed the estimates across cohorts using STATA. CKD-PC Cohorts needed to have at least 50 outcome events overall to be included in this study, and any cohorts with fewer than 10 outcome events in any particular analysis were excluded. CKD-EPI Trials needed to have at least 30 outcome events overall to be included

As detailed in our previous reports,[2,3] each cohort was instructed to standardize their serum creatinine and report its method when available. The reported creatinine standardization allows grouping studies into studies that reported using a standard IDMS traceable method or conducted some serum creatinine standardization to IDMS traceable methods (CanPREDDICT, CCF, CRIC, Geisinger, GLOMMS 2, Maccabi, MASTERPLAN, NephroTest, PREVEND, Rancho Bernardo, RCAV, SCREAM, SRR-CKD, Takahata; ALTITUDE, HALTPKD_B) and studies where the creatinine standardization was not done (AASK, ADVANCE, BC CKD, Framingham, MDRD, NZDCS, Pima, RENAAL, Sunnybrook, ZODIAC; CSG_Lewis, Hou, IDNT, ORIENT, REIN, REIN2, ROAD). For those cohorts without standardization, the creatinine levels were reduced by 5%, the calibration factor used to adjust non-standardized MDRD Study samples to IDMS.[2,4] We did not adjust creatinine levels in those studies with unknown standardization status (CPRD, Optum/AMGA, Mt Sinai BioMe, and PSP-CKD).

We calculated eGFR using the CKD-EPI equation: $eGFR_{CKD\text{-}EPI} = 141 \times (\text{minimum of standardized serum creatinine [mg/dL]}/\kappa \text{ or } 1)^{\alpha} \times (\text{maximum of standardized serum creatinine [mg/dL]}/\kappa \text{ or } 1)^{-1.209} \times 0.993^{age}$ × (1.018 if female) × (1.159 if black), where κ is 0.7 if female and 0.9 if male and α is -0.329 if female and -0.411 if male.[5] The selection of knots for eGFR and ACR was based on clinical thresholds.[6]

Our primary measure of albuminuria was urine albumin-to-creatinine ratio (ACR), but we also included studies with urine albumin excretion rate (AER), urine protein-to-creatinine ratio (PCR) and urine protein excretion rate (PER). AER or PER in mg/d, were converted to ACR and PCR mg/g by dividing by 1.0 mg/g per mg/d, assuming 24-hour urinary creatinine excretion was 1.0 g/d. Studies with ACR or AER and PCR or PER were analyzed separately. For spot urine collection, first morning void (FMV) urine collection is noted when it was uniformly implemented. Otherwise, the urine is assumed to be collected at a random time.

We examined changes in albuminuria on the log scale to focus on relative changes, normalize the distribution and enable analysis of change across a wide range of baseline albuminuria levels (e.g. 30% decline is possible for all levels while a 300 mg/g decrease is only possible above this level of albuminuria). We expressed albuminuria changes as percent change; a change in albuminuria of +/-

0.515 on the log (base2) scale corresponds to a 30% decrease and 43% increase in albuminuria (these percent changes are symmetric relative changes with 1/0.70=1.43). As the implications for the magnitude of change in albuminuria may vary depending on the time in which the change is observed, we defined three baseline periods (1, 2, and 3 years) to determine the change in albuminuria and repeated the analysis for each baseline period. To include all albuminuria measures during the baseline period and standardize the duration of follow-up we regressed log (base 2) albuminuria on time and multiplied the slope by the duration of the baseline period analyzed (1, 2 and 3 years) to estimate the log change in albuminuria during the baseline. When only two measures one year apart were available, this is identical to $\log_2$(1 year albuminuria/baseline albuminuria).

Adjusted absolute risk was calculated by combining the meta-analyzed adjusted HRs in the primary analysis with the estimated meta-analyzed adjusted baseline subhazards. The adjusted baseline subhazards were estimated from a competing risk models which accounted for death as a competing endpoint in each of the cohorts which contributed ESKD data except two cohorts with <2 years of follow-up (RENAAL and Optum/AMGA). The baseline subhazard was adjusted in each cohort to the following values of the covariates: 60 year old, 50% female, non-black, no change albuminuria, first eGFR of 60 ml/min/1.73m^2, a systolic blood pressure of 140 mm Hg, a total cholesterol of 5.2 mmol/L, 25% diabetes, 25% CVD, and 25% current and 25% former smoking. The baseline subhazards were then meta-analyzed by fitting a Weibull survival distribution to each cohort and averaging these distributions using equal weights. We then fit a Weibull survival distribution to the average survival and used that as the overall baseline survival and corresponding subhazard. Risk was calculated for a baseline ACR of 30, 300 and 600 mg/g and baseline PCR of 50, 500 and 1000 mg/g as well as eGFR levels of 45 and 75 ml/min/1.73 m^2.

Under agreement with the participating cohorts, CKD-PC cannot share individual data with third parties. These data were collected by other institutions.

Notes for individual studies:

CKD-PC studies:

AASK: Clinical trial. Urine PER was obtained from a 24-hour collection.

ADVANCE: This study is an intervention study that includes participants with diabetes only. Urine ACR was obtained from a random spot collection.

BC CKD: Urine ACR or PCR was obtained from a random spot collection.

CanPREDDICT: Urine ACR was obtained from a random spot collection. This cohort does not have data on smoking. Sudden cardiac death was not included in this cohort's definition of cardiovascular mortality.

CCF: Random spot urine was collected for clinical purposes.

CPRD: Random spot urine was collected for clinical purposes.

CRIC: Urine PER was obtained from a 24-hour collection.

Framingham: Urine ACR was obtained from a random spot collection.

Geisinger: Random spot urine was collected for clinical purposes. In <1% of the measurements a 24-hour urine collection was used to calculate the ACR or PCR.

GLOMMS 2: Urine ACR or PCR was obtained from a random spot collection. ACR was often measured routinely in clinical practice for those with known or suspected diabetes. Where proteinuria was suspected or needed to be ruled out in other circumstances, PCR was more often measured. This cohort does not have data on smoking, systolic blood pressure and total cholesterol.

Maccabi: Random spot urine was collected for clinical purposes. ACR was reported when the value was less than 300 mg/g. Otherwise, PCR was reported. PCR was converted to ACR by dividing by 2.655 for men and 1.7566 for women.

MASTERPLAN: Urine AER or PER was obtained from a 24-hour collection.

MDRD: Clinical trial. Urine PER was obtained from a 24-hour collection.

Mt Sinai BioMe: Random spot urine was collected for clinical purposes.

NephroTest: Urine AER or PER was obtained from a 24-hour collection.

NZDCS: Random spot urine was collected for clinical purposes.

Optum/AMGA: Random spot urine was collected for clinical purposes. The analysis in this study was first conducted in each center and then meta-analyzed. This study was not included in the meta-analysis of baseline hazard due to no sufficient follow-up.

Pima: Urine ACR or PCR was obtained from a random spot collection. This cohort does not have data on history of CVD and total cholesterol.

PREVEND: Urine ACR was obtained from a first morning void collection. Urine AER from a 24-hour collection was also available in this study but not used in the analysis.

PSP-CKD: Random spot urine was collected for clinical purposes.

Rancho Bernardo: Urine ACR was obtained from a morning (usually second void of the day) spot collection. Sudden cardiac death was not included in this cohort's definition of cardiovascular mortality.

RCAV: Random spot urine was collected for clinical purposes. This cohort does not have data on smoking.

RENAAL: Clinical trial. Urine ACR was obtained from a first morning void collection. This cohort does not have data on history of CVD and categorizes smoking as current vs. former/never smoking.

SCREAM: Random spot urine was collected for clinical purposes. This cohort does not have data on smoking and blood pressure. This study was not included in the meta-analysis of baseline hazard due to no sufficient follow-up.

SRR-CKD: Random spot urine was collected for clinical purposes. This cohort does not have data on smoking. There may be some overlap with the SCREAM cohort, which would capture participants with advanced CKD in the region of Stockholm.

Sunnybrook: This cohort includes patients seen in the nephrology clinics at Sunnybrook Hospital in Toronto, Ontario, Canada with CKD stage 3-5 or proteinuric CKD stage 1-2. Spot urine was collected for clinical purposes.

Takahata: Urine ACR was obtained from a morning spot collection.

ZODIAC: Urine ACR was obtained from a morning spot collection. This cohort does not have data on former smoker.

CKD-EPI trials that are not included in CKD-PC:

ALTITUDE: Urine ACR was obtained from a first morning void collection.

CSG_Lewis: Urine PER was obtained from a 24-hour collection.

HALTPKD_B: Urine AER was obtained from a 24-hour collection.

Hou: Urine PER was obtained from a 24-hour collection.

IDNT: Urine AER or PER was obtained from a 24-hour collection.

ORIENT: Urine PCR was obtained from a first morning void collection.

REIN: Urine PER was obtained from a 24-hour collection.

REIN2: Urine PER was obtained from a 24-hour collection.

ROAD: Urine PER was obtained from a 24-hour collection.

Percent with missing covariates:

Cohort	DM	Hx of CVD	Smoking	Systolic BP	Total Chol
AASK	0 (0%)	0 (0%)	0 (0%)	0 (0%)	9 (1%)
ADVANCE	0 (0%)	0 (0%)	0 (0%)	1 (0%)	3 (0%)
BC CKD	0 (0%)	0 (0%)	0 (0%)	2870 (37%)	2463 (31%)
CanPREDDICT	0 (0%)	0 (0%)	682 (100%)	8 (1%)	284 (42%)
CCF	0 (0%)	0 (0%)	0 (0%)	54 (3%)	205 (12%)
CPRD	NA	NA	NA	NA	NA
CRIC	0 (0%)	0 (0%)	0 (0%)	1 (0%)	39 (1%)

Framingham	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Geisinger	0 (0%)	0 (0%)	0 (0%)	4074 (15%)	4067 (15%)
GLOMMS 2	0 (0%)	0 (0%)	5953 (100%)	5953 (100%)	5953 (100%)
Maccabi	0 (0%)	0 (0%)	0 (0%)	8558 (7%)	2546 (2%)
MASTERPLAN	0 (0%)	4 (1%)	6 (1%)	0 (0%)	0 (0%)
MDRD	0 (0%)	0 (0%)	1 (0%)	0 (0%)	0 (0%)
Mt Sinai BioMe	0 (0%)	0 (0%)	0 (0%)	514 (18%)	343 (12%)
NephroTest	0 (0%)	0 (0%)	0 (0%)	33 (4%)	10 (1%)
NZDCS	0 (0%)	0 (0%)	36 (0%)	34 (0%)	30 (0%)
Optum/AMGA	0 (0%)	0 (0%)	16579 (20%)	11399 (14%)	9546 (12%)
Pima	0 (0%)	2720 (100%)	911 (33%)	11 (0%)	2720 (100%)
PREVEND	142 (3%)	0 (0%)	0 (0%)	4 (0%)	25 (1%)
PSP-CKD	0 (0%)	0 (0%)	0 (0%)	117 (3%)	629 (17%)
Rancho Bernardo	0 (0%)	0 (0%)	2 (1%)	0 (0%)	0 (0%)
RCAV	0 (0%)	0 (0%)	301816 (100%)	11792 (4%)	21133 (7%)
RENAAL	0 (0%)	1243 (100%)	2 (0%)	1240 (100%)	671 (54%)
SCREAM	0 (0%)	0 (0%)	17811 (100%)	17811 (100%)	2167 (12%)
SRR-CKD	0 (0%)	0 (0%)	420 (100%)	11 (3%)	225 (54%)
Sunnybrook	0 (0%)	0 (0%)	0 (0%)	739 (74%)	646 (64%)
Takahata	20 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ZODIAC	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0%)

Appendix 2. Acronyms or abbreviations for studies included in the current report and their key references linked to the Web references

CKD-PC Cohorts:

AASK:	African American Study of Kidney Disease and Hypertension[7]
ADVANCE:	The Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial[8]
BC CKD:	British Columbia CKD Study[9]
CanPREDDICT:	Canadian Study of Prediction of Death, Dialysis and Interim Cardiovascular Events[10]
CCF:	Cleveland Clinic CKD Registry Study[11]
CPRD:	Clinical Practice Research Datalink
CRIC:	Chronic Renal Insufficiency Cohort
Framingham:	Framingham Heart Study[12]
Geisinger:	Geisinger Health System[13]
GLOMMS 2:	Grampian Laboratory Outcomes, Morbidity and Mortality Studies – 2
Maccabi:	Maccabi Health System[14]
MASTERPLAN:	Multifactorial Approach and Superior Treatment Efficacy in Renal Patients with the Aid of a Nurse Practitioner[15]
MDRD:	Modification of Diet in Renal Disease Study[16]
Mt Sinai BioMe:	Mount Sinai BioMe Biobank Platform[17]
NephroTest:	NephroTest Study[18]
NZDCS:	New Zealand Diabetes Cohort Study[19]
Optum/AMGA:	Optum/AMGA Study
Pima:	Pima Indian Study[20]
PREVEND:	Prevention of Renal and Vascular End-stage Disease Study[21]
PSP-CKD:	Primary-Secondary Care Partnership to Prevent Adverse Outcomes in Chronic Kidney Disease
Rancho Bernardo:	Rancho Bernardo Study[22]
RCAV:	Racial and Cardiovascular Risk Anomalies in CKD Cohort[23]
RENAAL:	Reduction of Endpoints in Non-insulin Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan[24]
SCREAM:	Stockholm CREAtinine Measurements Cohort[25]
SRR-CKD:	Swedish Renal Registry CKD Cohort[26]
Sunnybrook:	Sunnybrook Cohort[27]
Takahata:	Takahata Study[28]
ZODIAC:	Zwolle Outpatient Diabetes project Integrating Available Care[29]

CKD-EPI trials that are not included in CKD-PC:

ALTITIDE:	Aliskiren Trial in Type 2 Diabetes Using Cardiovascular and Renal Disease Endpoints[30]
CSG Lewis:	Collaborative Study Group Lewis study[31]
HALTPKD_B:	HALT Progression of Polycystic Kidney Disease- B[32]
Hou:	Efficacy and safety of benazepril for advanced chronic renal insufficiency[33]
IDNT:	Irbesartan Type II Diabetic Nephropathy Trial[34]
ORIENT:	Olmesartan Reducing Incidence of Endstage Renal Disease in Diabetic Nephropathy Trial[35]
REIN:	Ramipril Efficiency in Nephropathy Study[36]

REIN2: Ramipril Efficiency in Nephropathy Study 2[37]
ROAD: Renoprotection of Optimal Antiproteinuric Doses [38]

Appendix 3. Acknowledgements and funding for collaborating cohorts

CKD-PC Cohorts:

Study	List of sponsors
AASK	AASK was supported by grants to each clinical center and the coordinating center from the National Institute of Diabetes and Digestive and Kidney Diseases. In addition, AASK was supported by the Office of Research in Minority Health (now the National Center on Minority Health and Health Disparities, NCMHD) and the following institutional grants from the National Institutes of Health: M01 RR-00080, M01 RR-00071, M0100032, P20-RR11145, M01 RR00827, M01 RR00052, 2P20 RR11104, RR029887, and DK 2818-02. King Pharmaceuticals provided monetary support and antihypertensive medications to each clinical center. Pfizer Inc, AstraZeneca Pharmaceuticals, Glaxo Smith Kline, Forest Laboratories, Pharmacia and Upjohn also donated antihypertensive medications.
ADVANCE	National Health and Medical Research Council (NHMRC)of Australia program grants 358395 and 571281 and project grant 211086
BC CKD	BC Provincial Renal Agency, an Agency of the Provincial Health Services Authority in collaboration with University of British Columbia.
CanPREDDICT	
CCF	Supported by an unrestricted educational grant from Amgen to the Department of Nephrology and Hypertension.
CPRD	
CRIC	
Framingham	NHLBI Framingham Heart Study (N01-HC-25195).
Geisinger	Geisinger Clinic
GLOMMS-2	
Maccabi	Morris Kahn and Maccabi Health Data Science Institute
MASTERPLAN	The MASTERPLAN study is a clinical trial with trial registration ISRCTN registry: 73187232. Sources of funding: The MASTERPLAN Study was supported by grants from the Dutch Kidney Foundation (Nierstichting Nederland, number PV 01), and the Netherlands Heart Foundation (Nederlandse Hartstichting, number 2003 B261). Unrestricted grants were provided by Amgen, Genzyme, Pfizer and Sanofi-Aventis.
MDRD	NIDDK UO1 DK35073 and K23 DK67303, K23 DK02904
Mt Sinai BioMe	
NephroTest	The NephroTest CKD cohort study is supported by grants from: Inserm GIS-IReSP AO 8113LS TGIR; French Ministry of Health AOM 09114 and AOM 10245; Inserm AO 8022LS; Agence de la Biomédecine R0 8156LL, AURA, and Roche 2009-152-447G. The Nephrotest initiative was also sponsored by unrestricted grants from F.Hoffman-La Roche Ltd. The authors thank the collaborators and the staff of the NephroTest Study: François Vrtovsnik, Eric Daugas, Martin Flamant, Emmanuelle Vidal-Petiot (Bichat

	Hospital); Christian Jacquot, Alexandre Karras, Eric Thervet, Christian d'Auzac, P. Houillier, M. Courbebaisse, D. Eladari et G. Maruani (European Georges Pompidou Hospital); Jean-Jacques Boffa, Pierre Ronco, H. Fessi, Eric Rondeau, Emmanuel Letavernier, Jean Philippe Haymann, P. Urena-Torres (Tenon Hospital)
NZDCS	New Zealand Health Research Council, Auckland Medical Research Foundation and New Zealand Society for the Study of Diabetes
Optum/AMGA	AMGA supported this analysis using the Optum Analytics database comprised of longitudinal ambulatory electronic health record (EHR) data from 25 health care organizations who pool their EHR data as part of a national learning collaborative. Optum extracts data from multiple sources, cleans, normalizes and validates it making it possible to conduct accurate lateral analysis and comparisons.
Pima	This work was supported by the Intramural Research Program of the National Institute of Diabetes and Digestive and Kidney Diseases.
PREVEND	The PREVEND study is supported by several grants from the Dutch Kidney Foundation, and grants from the Dutch Heart Foundation, the Dutch Government (NWO), the US National Institutes of Health (NIH) and the University Medical Center Groningen, The Netherlands (UMCG). Dade Behring, Marburg, Germany supplied equipment and reagents for nephelometric measurement of urinary albumin.
PSP-CKD	The PSP-CKD study was funded by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care (CLAHRC) East Midlands. Ongoing support for the study is funded by NIHR CLAHRC East Midlands and Kidney Research UK (Grant TF2/2015).
Rancho Bernardo	NIA AG07181 and AG028507 NIDDK DK31801
RCAV	This study was supported by grant R01DK096920 from NIH-NIDDK and is the result of work supported with resources and the use of facilities at the Memphis VA Medical Center and the Long Beach VA Medical Center. 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).
RENAAL	The RENAAL trial was supported by Merck and Company.
SCREAM	This study was supported by Stockholm County Council and the Swedish Heart and Lung Foundation.
SRR-CKD	The SRR-CKD is a national health care quality register funded by The Swedish Association of Local Authorities and Regions, which is an organization that represents and advocates for local government in Sweden. All of Sweden's municipalities, county councils and regions are members.
Sunnybrook	
Takahata	A Grant-in-Aid from the 21st Century Center of Excellence (COE) and Global COE program of the Japan Society for the Promotion of Science
ZODIAC	

CKD-EPI trials that are not included in CKD-PC:

Study	**List of sponsors**

ALTITIDE	Supported by Novartis
CSG Lewis	Supported by grants from the Public Health Service (5 R01-DK 39908, 5 R01-DK 39826, MO1-RR00030, MO1-RR00034, MO1-RR00036, MO1-RR00051, MO1-RR00058, MO1-RR00059, and MO1-RR00425) and by the Bristol-Myers Squibb Pharmaceutical Research Institute (Princeton, N.J.).
HALTPKD_B	Supported by grants from the National Institute of Diabetes and Digestive and Kidney Diseases (DK62410 to Dr. Torres, DK62408 to Dr. Chapman, DK62402 to Dr. Schrier, DK082230 to Dr. Moore, DK62411 to Dr. Perrone, and DK62401 to Washington University at St. Louis) and the National Center for Research Resources General Clinical Research Centers (RR000039 to Emory University, RR000585 to the Mayo Clinic, RR000054 to Tufts Medical Center, RR000051 to the University of Colorado, RR023940 to the University of Kansas Medical Center, and RR001032 to Beth Israel Deaconess Medical Center), National Center for Advancing Translational Sciences Clinical and Translational Science Awards (RR025008 and TR000454 to Emory University, RR024150 and TR00135 to the Mayo Clinic, RR025752 and TR001064 to Tufts University, RR025780 and TR001082 to the University of Colorado, RR025758 and TR001102 to Beth Israel Deaconess Medical Center, RR033179 and TR000001 to the University of Kansas Medical Center, and RR024989 and TR000439 to Cleveland Clinic), by funding from the Zell Family Foundation (to the University of Colorado), and by a grant from the PKD Foundation.
Hou	Supported by a National Nature and Sciences Grant for Major Projects (30330300) and a People's Liberation Army Grant for Major Clinical Research (to Dr. Hou) and in part by Novartis
IDNT	Supported by the Bristol-Myers Squibb Institute for Medical Research and Sanofi–Synthelabo.
ORIENT	The ORIENT study was supported by a research grant from Daiichi Sankyo.
REIN	Supported in part by a grant from Aventis Pharma SA, Antony, France.
REIN2	The study was supported in part by a grant from Aventis Pharma SA, Antony, France.
ROAD	Supported by a National Nature and Sciences Grant for Major Projects (30330300), a People's Liberation Army Grant for Major Clinical Research (2000), and National 11th Five-Years Plan Foundation (to F.F.H.)

Table S1. Estimation of variance of measurement error.

Study	Total N	Type of urine sample	Type of measurement	Time window	Error variance (log2)
Brigham and Women's Hospital	49	SUS	ACR	3 visits in 4 weeks	**0.578**
	48	FMV	ACR	2 visits in 2 weeks	0.323
	49	SUS	PCR	3 visits in 4 weeks	**0.448**
	48	FMV	PCR	2 visits in 2 weeks	0.289
SPAAR	241	24h	AER	3 visits in 6 weeks	0.212
	240	FMV	ACR	3 visits in 6 weeks	0.176
	241	SUS	ACR	3 visits in 6 weeks	**0.580**
ALTITUDE	8509	FMV	ACR	3 visits in 3 days	0.213
Mean of FMV or 24h					0.243
Mean of SUS					**0.535**

FMV: first morning void spot urine sample; SUS: random spot urine sample; 24h: 24 hours urine collection

Table S2. Further baseline characteristics for cohorts with a 2-year baseline period and event numbers.

Cohort	N	ESKD events	ACM events	CVM events	Mean (SD) Follow-up, years	Median # ACR/PCR (IQR)	Systolic BP, mmHg	Total Chol, mmol/L	%HTN	% Hx of CVD	% Current Smoker	% Former Smoker
AASK	898	234	160	NA	6 (3)	5 (4-5)	149 (24)	5.5 (1.1)	100%	50%	29%	29%
ADVANCE	9383	61	1556	627	7 (3)	2 (2-2)	144 (21)	5.2 (1.2)	82%	25%	15%	27%
BC CKD	7855	1817	2862	NA	3 (2)	6 (4-9)	135 (22)	4.4 (1.2)	78%	30%	2%	6%
CanPREDDICT	682	109	104	NA	2 (1)	4 (3-4)	132 (19)	4.3 (1.2)	97%	34%	NA	NA
CCF	1739	NA	78	NA	1 (0.7)	3 (2-4)	131 (17)	4.5 (1.2)	96%	31%	7%	42%
CPRD	90172	414	9988	1576	4 (3)	3 (2-3)	137 (17)	4.7 (1.1)	95%	51%	NA	NA
CRIC	2774	594	455	NA	5 (2)	3 (3-3)	127 (21)	4.7 (1.1)	85%	32%	11%	42%
Framingham	893	NA	67	NA	8 (1)	2 (2-2)	129 (18)	5.2 (1.0)	42%	11%	16%	NA
Geisinger	26594	311	4876	NA	6 (4)	3 (2-3)	131 (17)	4.8 (1.1)	66%	28%	5.4%	27%
GLOMMS 2	5953	NA	1074	326	4 (2)	3 (3-4)	NA	NA	5%	9%	NA	NA
Maccabi	117414	746	10466	NA	5 (2)	3 (2-4)	133 (18)	4.9 (1.1)	86%	68%	2.0%	27%
MASTERPLAN	408	81	NA	NA	2 (1)	3 (3-3)	138 (20)	4.9 (1.1)	95%	26%	18%	41%
MDRD	682	509	354	136	14 (6)	12 (11-13)	131 (17)	5.6 (1.1)	83%	10%	9.4%	NA
Mt Sinai BioMe	2895	71	NA	NA	3 (2)	3 (2-4)	132 (20)	4.7 (1.1)	84%	20%	9.3%	16%
NephroTest	783	169	133	NA	5 (3)	3 (2-3)	135 (20)	4.9 (1.1)	93%	18%	14%	35%
NZDCS	8698	299	2241	221	8 (2)	3 (3-5)	138 (19)	5.3 (1.1)	76%	19%	15%	29%
Optum/AMGA	81653	569	6676	NA	1 (1)	3 (2-3)	129 (16)	4.4 (1.1)	75%	8%	17%	32%
Pima	2720	168	530	100	9 (7)	2 (2-2)	119 (17)	NA	19%	NA	27%	17%
PREVEND	4941	NA	230	60	6 (1)	2 (2-2)	126 (18)	5.4 (1.0)	33%	6.2%	26%	44%
PSP-CKD	3598	NA	709	NA	3(1)	3 (2-3)	134 (15)	4.4 (1.2)	85%	37%	6.4%	18%
Rancho Bernardo	369	NA	109	57	9 (4)	2 (2-2)	136 (19)	5.3 (0.9)	58%	15%	3%	47%
RCAV	301816	500	29993	NA	3 (2)	3 (2-3)	132 (16)	4.4 (1.1)	85%	25%	NA	NA
RENAAL	1243	248	182	183	1 (0.6)	10 (9-11)	NA	5.9 (1.4)	37%	NA	18%	NA

SCREAM	17811	290	2364	NA	3 (1)	3 (2-4)	NA	4.9 (1.1)	39%	20%	NA	NA
SRR-CKD	420	172	146	68	3 (2)	4 (3-5)	145 (22)	5.3 (1.3)	98%	25%	NA	NA
Sunnybrook	1003	99	200	NA	3 (2)	4 (3-6)	138 (20)	5.0 (1.4)	56%	5.7%	12%	19%
Takahata	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ZODIAC	419	NA	208	89	9 (4)	3 (3-3)	156 (26)	5.6 (1.1)	78%	31%	19%	NA
Total	693816	7461	75761	3443	4 (2)	3 (2-3)	133 (17)	4.6 (1.1)	82%	29%	6.0%	27%

Table S3. Baseline characteristics for cohorts with a 1-year baseline period.

Cohort	Exposure	N	Age, years	% Female	% Black	Baseline eGFR, ml/min/ 1.73m^2	% DM	Baseline median ACR/PCR (IQR), mg/g	Median ACR/PCR fold change (IQR)
AASK	PCR*	873	55 (10)	37%	100%	46 (15)	0%	71 (27-307)	1.06 (0.58-1.76)
ADVANCE	ACR	6416	70 (6)	45%	0.20%	74 (18)	100%	16 (7-41)	1.02 (0.57-1.95)
BC CKD	ACR/PCR	8351	71 (13)	45%	0%	33 (15)	52%	112 (26-622)	1.06 (0.63-1.87)
CanPREDDICT	ACR/PCR	642	69 (12)	36%	1.2%	28 (10)	51%	158 (33-680)	0.95 (0.49-1.64)
CCF	ACR	1950	71 (10)	53%	15%	49 (12)	86%	18 (7-66)	1.10 (0.64-1.98)
CPRD	ACR	88902	64 (12)	42%	0%	74 (21)	97%	10 (5-26)	1.00 (0.63-1.71)
CRIC	PCR*	3311	58 (11)	45%	42%	45 (15)	47%	139 (55-680)	1.00 (0.61-1.63)
Framingham	NA	NA	NA	NA	NA	NA	NA	NA	NA
Geisinger	ACR/PCR	27508	62 (14)	50%	2.2%	81 (23)	83%	14 (6-41)	1.01 (0.54-1.91)
GLOMMS 2	ACR/PCR	5900	66 (13)	50%	0%	68 (20)	9.5%	9 (8-35)	1.00 (0.87-1.47)
Maccabi	ACR	106520	61 (13)	48%	0%	81 (20)	85%	5 (5-20)	1.00 (0.95-1.14)
MASTERPLAN	PCR*/ACR*	505	61 (12)	31%	0%	36 (14)	24%	256 (82-884)	1.00 (0.70-1.60)
MDRD	PCR*	750	52 (12)	39%	7.3%	35 (13)	9.5%	285 (70-1340)	0.95 (0.56-1.47)
Mt Sinai BioMe	ACR/PCR	2778	58 (13)	63%	33%	75 (26)	73%	14 (5-63)	1.00 (0.50-2.06)
NephroTest	PCR*/ACR*	716	59 (14)	31%	11%	40 (19)	30%	285 (111-931)	0.98 (0.68-1.41)
NZDCS	ACR	13306	62 (13)	50%	0.13%	76 (22)	100%	1 (1-6)	1.00 (0.48-2.00)
Optum/AMGA	ACR	94434	64 (13)	45%	5.9%	78 (24)	79%	15 (7-41)	1.07 (0.65-1.77)
Pima	ACR/PCR	NA	NA	NA	NA	NA	NA	NA	NA
PREVEND	ACR	NA	NA	NA	NA	NA	NA	NA	NA
PSP-CKD	ACR/PCR	3616	75 (9)	54%	0.75%	49 (12)	47%	18 (12-38)	1.00 (0.74-1.70)
Rancho Bernardo	ACR	NA	NA	NA	NA	NA	NA	NA	NA
RCAV	ACR	307130	65 (10)	3%	16%	78 (18)	82%	12 (5-37)	1.02 (0.61-1.80)
RENAAL	ACR*	1364	60 (7)	36%	15%	39 (13)	100%	1157 (519-2346)	0.91 (0.52-1.44)
SCREAM	ACR	18887	54 (13)	41%	0%	83 (27)	46%	17 (7-73)	1.00 (0.58-1.75)

SRR-CKD	ACR	520	65 (15)	32%	0%	22 (8)	36%	129 (24-456)	1.01 (0.53-2.02)
Sunnybrook	PCR/ACR	1186	59 (17)	41%	0%	58 (32)	36%	489 (179-1315)	0.82 (0.45-1.41)
Takahata	ACR	1464	64 (10)	55%	0%	98 (12)	8.9%	9 (6-18)	1.11 (0.82-1.52)
ZODIAC	ACR	520	68 (10)	57%	0%	68 (17)	100%	2 (1-6)	1.04 (0.76-1.75)
Total		697549	64 (12)	30%	6.8%	77 (21)	81%	12 (5-37)	1.02 (0.61-1.80)

ACR: urine albumin-to-creatinine ratio; PCR: urine protein-to-creatinine ratio; DM: diabetes mellitus; IQR: interquartile range.
If both ACR and PCR are included, the first listed in the column is the larger sample size for this baseline period. All characteristics listed are for the larger sample.
*Albuminuria is based on 24-hour urine in these studies as albumin excretion rate (AER) rather than ACR and protein excretion rate (PER) rather than PCR.

Table S4. Further baseline characteristics for cohorts with a 1-year baseline period and event numbers.

Cohort	N	ESKD events	ACM events	CVM events	Mean (SD) Follow-up, years	Median # ACR/PCR (IQR)	Systolic BP, mmHg	Total Chol	%HTN	% Hx of CVD	% Current Smoker	% Former Smoker
AASK	873	234	151	NA	7 (3)	3 (3-3)	149 (24)	5.5 (1.2)	100%	49%	28%	29%
ADVANCE	6416	NA	687	290	4 (2)	2 (2-2)	137 (18)	4.7 (1.1)	81%	27%	15%	22%
BC CKD	8351	2037	3227	NA	4 (2)	4 (3-5)	136 (22)	4.4 (1.2)	77%	29%	1.7%	6.5%
CanPREDDICT	642	114	104	NA	3 (2)	3 (2-3)	133 (20)	4.2 (1.2)	98%	36%	NA	NA
CCF	1950	NA	121	NA	2 (1)	2 (2-3)	131 (17)	4.5 (1.1)	97%	32%	6.9%	42%
CPRD	88902	386	9763	1521	4 (3)	2 (2-2)	137 (16)	4.6 (1.1)	96%	56%	NA	NA
CRIC	3311	757	579	NA	6 (2)	2 (2-2)	127 (21)	4.7 (1.1)	86%	33%	12%	42%
Framingham	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Geisinger	27508	313	4924	NA	6 (4)	2 (2-2)	131 (17)	4.7 (1.1)	70%	30%	11%	32%
GLOMMS 2	5900	NA	1094	332	4 (2)	2 (2-2)	NA	NA	6%	10%	NA	NA
Maccabi	106520	747	9871	NA	5 (2)	2 (2-3)	133 (18)	4.8 (1.1)	87%	70%	2.0%	26%
MASTERPLAN	505	103	70	NA	3 (1)	2 (2-2)	137 (20)	4.8 (1.0)	95%	30%	18%	36%
MDRD	750	568	391	154	15 (6)	5 (4-5)	132 (17)	5.6 (1.1)	84%	11%	10%	NA
Mt Sinai BioMe	2778	69	NA	NA	4 (3)	2 (2-3)	132 (20)	4.7 (1.1)	84%	20%	11%	15%
NephroTest	716	196	144	NA	6 (3)	2 (2-2)	136 (20)	4.8 (1.1)	95%	21%	15%	37%
NZDCS	13306	496	3586	331	8 (2)	2 (2-3)	138 (19)	5.3 (1.1)	85%	20%	15%	28%
Optum/AMGA	94434	817	8795	NA	2 (1)	2 (2-2)	129 (16)	4.4 (1.1)	76%	10%	18%	33%
Pima	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
PREVEND	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
PSP-CKD	3616	NA	698	NA	3 (1)	2 (2-2)	134 (15)	4.4 (1.2)	88%	37%	6.4%	19%
Rancho Bernardo	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
RCAV	307130	537	32109	NA	3 (2)	2 (2-3)	132 (16)	4.3 (1.1)	85%	25.1%	NA	NA
RENAAL	1364	301	251	443	2 (1)	6 (5-7)	125 (15)	5.9 (1.5)	37%	NA	18%	0%

SCREAM	18887	335	2636	NA	3 (1)	2 (2-3)	NA	4.9 (1.1)	41%	NA	NA	NA
SRR-CKD	520	225	203	95	4 (2)	3 (2-4)	145 (23)	5.2 (1.9)	98%	27%	NA	NA
Sunnybrook	1186	130	240	NA	3 (2)	3 (2-4)	136 (20)	5.0 (1.6)	54%	7%	NA	NA
Takahata	1464	NA	101	NA	8 (1)	2 (2-2)	134 (16)	5.2 (0.8)	56%	4.2%	16%	14%
ZODIAC	520	NA	268	109	10 (4)	2 (2-2)	155 (25)	5.6 (1.1)	78%	32%	19%	NA
Total	697549	8365	80013	3275	4 (3)	2 (2-3)	133 (17)	4.5 (1.1)	83%	17%	5.7%	26%

Table S5. Baseline characteristics for cohorts with a 3-year baseline period.

Cohort	Exposure	N	Age, years	% Female	% Black	Baseline eGFR, ml/min/1.73m^2	% DM	Baseline median ACR/PCR (IQR), mg/g	Median ACR/PCR fold change (IQR)
AASK	PCR*	880	55 (10)	39%	100%	47 (14)	0%	67 (27-250)	1.35 (0.74-2.68)
ADVANCE	ACR	9346	66 (6)	43%	0.32%	78 (17)	100%	14 (7-38)	1.03 (0.43-2.46)
BC CKD	ACR/PCR	7015	70 (13)	46%	0%	34 (15)	52%	93 (24-485)	1.34 (0.67-2.90)
CanPREDDICT	ACR	656	68 (12)	36%	1.4%	29 (9)	49%	123 (25-517)	1.19 (0.49-2.89)
CCF	ACR	1264	71 (10)	53%	15%	49 (11)	86%	18 (7-57)	1.32 (0.67-2.88)
CPRD	ACR	89002	63 (12)	43%	0%	73 (21)	95%	10 (5-25)	1.09 (0.59-2.13)
CRIC	PCR*	2950	58 (11)	46%	40%	45 (15)	46%	134 (55-652)	1.25 (0.65-2.32)
Framingham	ACR	1483	58 (10)	55%	0%	88 (18)	8.0%	7 (3-15)	0.90 (0.45-2.16)
Geisinger	ACR/PCR	26876	61 (13)	50%	2.1%	83 (23)	78%	14 (6-39)	1.13 (0.52-2.42)
GLOMMS 2	ACR/PCR	6192	65 (13)	49%	0%	69 (20)	6.0%	9 (8-35)	1.08 (0.91-2.31)
Maccabi	ACR	117208	60 (12)	47%	0%	81 (20)	82%	5 (5-20)	1.00 (0.81-1.44)
MASTERPLAN	PCR*	423	60 (13)	31%	0%	37 (14)	23%	260 (98-798)	1.04 (0.56-2.04)
MDRD	PCR*	449	52 (12)	39%	5.1%	36 (14)	7.8%	220 (70-980)	1.32 (0.74-2.73)
Mt Sinai BioMe	ACR/PCR	2833	58 (13)	63%	34%	77 (26)	71%	12 (5-50)	1.19 (0.53-2.78)
NephroTest	PCR*/ACR*	765	58 (14)	33%	12%	44 (19)	27%	237 (106-735)	1.17 (0.67-2.09)
NZDCS	ACR	6581	61 (13)	51%	0.076%	77 (22)	100%	2 (1-6)	1.00 (0.39-2.91)
Optum/AMGA	ACR	65956	63 (13)	46%	5.6%	78 (23)	78%	14 (7-39)	1.28 (0.70-2.64)
Pima	ACR/PCR	2569	34 (14)	63%	0%	120 (17)	29%	12 (7-24)	1.16 (0.65-2.08)
PREVEND	ACR	5122	52 (12)	49%	0.88%	94 (15)	5.1%	7 (5-12)	1.05 (0.81-1.44)
PSP-CKD	ACR/PCR	2651	75 (10)	53%	0.83%	49 (12)	42%	18 (11-42)	1.14 (0.75-2.83)
Rancho Bernardo	ACR	806	70 (11)	60%	0.12%	70 (16)	14%	12 (7-20)	1.05 (0.67-1.76)
RCAV	ACR	295268	64 (10)	3%	17%	79 (17)	84%	11 (5-33)	1.20 (0.60-2.53)
RENAAL	ACR*	1132	60 (7)	36%	15%	40 (13)	100%	1071 (478-2099)	0.79 (0.33-1.57)
SCREAM	ACR	15908	52 (13)	40%	0%	85 (26)	46%	17 (7-68)	1.10 (0.56-2.18)
SRR-CKD	ACR	285	64 (14)	32%	0%	24 (8)	34%	72 (21-262)	1.38 (0.54-5.99)
Sunnybrook	PCR/ACR	804	58 (17)	41%	0%	60 (31)	38%	476 (170-1256)	0.88 (0.39-1.65)

Takahata	NA	NA	NA	NA	NA	NA	NA	NA	NA
ZODIAC	ACR	413	67 (10)	58%	0%	69 (16)	100%	2 (1-5)	1.00 (0.59-2.06)
Total		664837	62 (12)	29%	6.8%	78 (21)	80%	11 (5-33)	1.20 (0.60-2.53)

ACR: urine albumin-to-creatinine ratio; PCR: urine protein-to-creatinine ratio; DM: diabetes mellitus; IQR: interquartile range.
If both ACR and PCR are included, the first listed in the column is the larger sample size for this baseline period. All characteristics listed are for the larger sample.
*Albuminuria is based on 24-hour urine in these studies as albumin excretion rate (AER) rather than ACR and protein excretion rate (PER) rather than PCR.

Table S6. Further baseline characteristics for cohorts with a 3-year baseline period and event numbers.

Cohort	N	ESKD events	ACM events	CVM events	Mean (SD) Follow-up, years	Median # ACR/PCR (IQR)	Systolic BP, mmHg	Total Chol, mmol/L	%HTN	% Hx of CVD	% Current Smoker	% Former Smoker
AASK	880	214	151	NA	6 (3)	6 (5-7)	149 (24)	5.5 (1.1)	100%	49%	28%	29%
ADVANCE	9346	59	1540	623	7 (3)	2 (2-2)	144 (21)	5.2 (1.2)	82%	25%	15%	27%
BC CKD	7015	1486	2396	NA	2 (2)	8 (6-12)	135 (22)	4.4 (1.2)	79%	31%	1.9%	6.7%
CanPREDDICT	656	84	78	NA	2 (1)	5 (3-6)	132 (19)	4.2 (1.2)	98%	32%	NA	NA
CCF	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
CPRD	89002	370	9629	1507	4 (3)	4 (3-4)	137 (17)	4.7 (1.1)	95%	49%	NA	NA
CRIC	2950	667	450	NA	5 (2)	4 (3-4)	127 (21)	4.7 (1.1)	86%	32%	12%	41%
Framingham	1483	NA	105	59	8 (1)	2 (2-2)	128 (19)	5.3 (1.0)	37%	9.8%	15%	NA
Geisinger	26876	300	4969	NA	5 (4)	3 (3-4)	131 (17)	4.9 (1.1)	63%	26%	12%	28%
GLOMMS 2	6192	NA	1099	326	3 (2)	4 (3-5)	NA	NA	4.1%	6.9%	NA	NA
Maccabi	117208	689	9740	NA	4 (1)	4 (3-5)	133 (18)	4.9 (1.1)	86%	67%	1.9%	27%
MASTERPLAN	423	76	NA	NA	2 (1)	4 (3-4)	138 (20)	4.9 (1.1)	95%	26%	17%	45%
MDRD	449	338	236	93	14 (5)	10 (9-11)	131 (18)	5.6 (1.1)	82%	9.4%	10%	NA
Mt Sinai BioMe	2833	67	NA	NA	3 (2)	3 (3-4)	132 (20)	4.8 (1.1)	83%	19%	8.6%	15%
NephroTest	765	163	126	NA	5 (3)	3 (2-4)	134 (20)	4.9 (1.1)	93%	18%	14%	34%
NZDCS	6581	214	1737	177	7 (2)	3 (3-6)	139 (19)	5.4 (1.1)	85%	19%	15%	30%
Optum/AMGA	65956	287	4369	NA	1 (1)	3 (2-4)	129 (16)	4.4 (1.1)	74%	7%	16%	32%
Pima	2569	167	475	101	8 (7)	2 (2-2)	119 (17)	NA	17%	NA	27%	17%
PREVEND	5122	NA	264	62	6 (2)	2 (2-2)	127 (19)	5.5 (1.1)	33%	5.6%	28%	41%
PSP-CKD	2651	NA	481	NA	2 (1)	3 (2-4)	133 (15)	4.4 (1.2)	79%	34%	5.4%	16%
Rancho Bernardo	806	NA	243	120	10 (4)	2 (2-2)	134 (21)	5.4 (0.9)	53%	14%	5%	48%
RCAV	295268	414	26635	NA	3 (2)	3 (3-4)	132 (16)	4.4 (1.1)	84%	24%	NA	NA
RENAAL	1132	190	116	325	0.6 (0.4)	13 (12-14)	119 (14)	5.8 (1.4)	38%	NA	18%	NA

SCREAM	15908	208	1904	NA	3 (1)	3 (3-5)	NA	4.9 (1.1)	38%	NA	NA	NA
SRR-CKD	285	114	88	NA	3 (2)	5 (3-6)	145 (23)	5.2 (1.4)	99%	21%	NA	NA
Sunnybrook	804	69	146	NA	2 (2)	6 (4-8)	137 (19)	5.1 (1.5)	58%	4.7%	NA	NA
Takahata	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ZODIAC	413	NA	192	77	8 (4)	4 (3-4)	155 (25)	5.6 (1.1)	78%	30%	18%	NA
Total	663573	6176	67169	3470	3 (2)	3 (3-4)	133 (17)	4.6 (1.1)	81%	14%	5.9%	27%

Table S7. Regression dilution coefficients* & summary

	λ-1 year	λ-2 year	λ-3 year
Median study	0.677	0.721	0.789
Low (25th %ile)	0.549	0.650	0.713
High (75th %ile)	0.770	0.808	0.852
AASK	0.770	0.834	0.818
ADVANCE	0.640	0.648	0.820
BC_CKD	0.485	0.649	0.713
CanPREDDICT	0.689	0.696	0.791
CPRD	0.586	0.684	0.720
CRIC	0.699	0.778	0.834
Geisinger	0.576	0.650	0.698
GLOMMS 2	0.195	0.415	0.535
Maccabi	0.302	0.389	0.445
MASTERPLAN	0.842	0.854	0.890
MDRD	0.737	0.808	0.852
Mt Sinai BioMe	0.683	0.721	0.782
NephroTest	0.549	0.703	0.787
NZDCS	0.889	0.907	0.928
RCAV	0.647	0.729	0.789
RENAAL	0.677	0.805	0.870
SCREAM	0.533	0.656	0.703
SRR-CKD	0.796	0.842	0.855
Sunnybrook	0.796	0.776	0.763

* Assumes error variance of 0.535 for random urines and 0.243 for first morning void on log2 scale (includes biological and assay variation). Variance of change is double the variance of each measure.

Table S8. Baseline characteristics of CKD-EPI collaboration trials (not including the trials that overlap with CKD-PC). Sections by baseline windows of 0.5, 1, and 2 years

Cohort	Exposure	N	Age, years	% Female	% Black	Baseline eGFR	% DM	Baseline median ACR/PCR (IQR)	Median ACR/PCR fold change (IQR)	ESKD events	ACM events	Mean (SD) Follow-up
Baseline window: 6 month												
ALTITUDE	ACR	7667	64 (10)	31%	3.3%	58 (21)	100%	285 (59-881)	0.94 (0.56-1.49)	203	530	2.7 (0.9)
CSG_Lewis	PCR	364	34 (8)	48%	7.4%	69 (25)	100%	1838 (966-3703)	0.88 (0.53-1.31)	32	NA	3.0 (1.1)
HALTPKD_B	ACR	414	49 (8)	51%	2.4%	48 (12)	0%	30.1 (17.3-75.4)	0.81 (0.48-1.30)	69	NA	5.0 (1.6)
Hou	PCR	220	45 (15)	50%	0%	16 (4)	0%	1690 (1080-2240)	0.70 (0.47-0.98)	80	NA	1.8 (0.9)
IDNT(CCB)	ACR/PCR	937	59 (7)	36%	12%	47 (18)	100%	1853 (1034-3363)	0.81 (0.48-1.24)	99	94	2.3 (1.0)
IDNT(CNTRL)	ACR/PCR	478	58 (8)	29%	13%	48 (19)	100%	1946 (1050-3404)	0.90 (0.56-1.37)	59	51	2.2 (0.9)
ORIENT	PCR	540	59 (8)	31%	0%	48 (12)	100%	2102 (1010-3786)	0.94 (0.63-1.38)	97	NA	2.1 (1.0)
REIN	PCR	235	48 (13)	25%	0.43%	40 (18)	0%	2348 (1424-3610)	0.85 (0.56-1.22)	53	NA	2.2 (1.2)
REIN 2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ROAD	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Total		10855	61 (12)	33%	4.3%	55 (22)	92%	285 (59-881)	0.94 (0.56-1.49)	692	675	2.6 (1.1)
Baseline window: 12 month												
ALTITUDE	ACR	7656	64 (10)	31%	3.3%	58 (21)	100%	281 (57-860)	1.00 (0.53-1.69)	189	475	2.2 (0.9)
CSG_Lewis	PCR	369	34 (8)	47%	7.3%	69 (25)	100%	1804 (977-3660)	0.84 (0.46-1.44)	31	NA	2.6 (1.0)
HALTPKD_B	ACR	389	49 (8)	51%	2.3%	48 (12)	0%	29.0 (16.9-66.5)	0.86 (0.44-1.33)	61	NA	4.5 (1.5)
Hou	PCR	187	45 (16)	50%	0%	16 (4)	0%	1630 (1030-2240)	0.58 (0.34-0.81)	56	NA	1.5 (0.7)
IDNT(CCB)	ACR/PCR	892	59 (7)	35%	12%	48 (18)	100%	1793 (990-3222)	0.75 (0.39-1.25)	74	73	1.9 (0.9)
IDNT(CNTRL)	ACR/PCR	446	58 (8)	29%	11%	48 (19)	100%	1901 (1017-3380)	0.91 (0.45-1.42)	54	38	1.8 (0.9)
ORIENT	PCR	503	59 (8)	32%	0%	48 (12)	100%	2054 (974-3606)	0.94 (0.55-1.35)	82	NA	1.8 (0.9)
REIN	PCR	218	48 (13)	22%	0.0%	41 (19)	0%	2250 (1395-3500)	0.91 (0.57-1.36)	46	NA	1.9 (1.2)
REIN 2	PCR	284	54 (15)	24%	0.0%	30 (16)	4.9%	2383 (1493-3630)	0.88 (0.63-1.22)	61	NA	1.2 (1.1)
ROAD	PCR	328	51 (14)	38%	0%	29 (13)	0%	1600 (1070-2670)	0.54 (0.37-0.69)	48	NA	2.5 (0.7)
Total		11272	61 (12)	33%	4.0%	54 (22)	88%	281 (57-860)	1.00 (0.53-1.69)	702	586	2.2 (1.0)
Baseline window: 24 month												
ALTITUDE	ACR	6802	64 (10)	31%	3%	59 (21)	100%	276 (56-822)	1.05 (0.48-2.06)	123	274	1.5 (0.6)
CSG_Lewis	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

HALTPKD_B	ACR	357	49 (8)	51%	2.5%	48 (12)	0%	28.6 (16.9-66.5)	0.77 (0.36-1.44)	50	NA	3.6 (1.4)
Hou	PCR	162	45 (16)	49%	0%	16 (4)	0%	1585 (1030-2240)	0.49 (0.33-0.82)	43	NA	0.8 (0.4)
IDNT(CCB)	ACR/PCR	860	59 (8)	34%	13%	48 (17)	100%	1729 (970-3049)	0.70 (0.32-1.31)	58	57	1.0 (0.8)
IDNT(CNTRL)	ACR/PCR	425	58 (8)	28%	12%	49 (19)	100%	1723 (955-3036)	0.84 (0.39-1.62)	36	36	1.0 (0.7)
ORIENT	PCR	438	59 (8)	31%	0%	48 (12)	100%	1898 (918-3204)	0.90 (0.48-1.54)	59	NA	0.9 (0.6)
REIN	PCR	201	47 (13)	24%	0%	42 (18)	0%	2070 (1317-3000)	0.84 (0.52-1.43)	32	NA	1.2 (1.0)
REIN 2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ROAD	PCR	309	51 (13)	37%	0%	30 (13)	0%	1590 (1070-2660)	0.50 (0.34-0.65)	32	NA	1.7 (0.5)
Total		9554	61 (12)	33%	4.1%	55 (22)	90%	276 (56-822)	1.05 (0.48-2.06)	433	367	1.5 (0.8)

Table S9. Hazard Ratio of ESKD with 30% ACR & PCR Reduction – Before and after Adjustment for Measurement Error: CKD-EPI trials

Change Period	Reliability $\lambda_{Median\ (IQR\ high\text{-}low)}$	Unadjusted HR (95% CI)	Regression Dilution adjusted HR estimates (95% CI)		
			median reliability	high reliability	low reliability
ACR					
0.5-year	0.650 (0.733–0.526)	0.73 (0.64-0.85)	0.65 (0.54-0.79)	0.64 (0.53-0.79)	0.55 (0.42-0.73)
1-year	0.749 (0.807–0.673)	0.64 (0.48-0.85)	0.55 (0.38-0.80)	0.57 (0.40-0.82)	0.51 (0.34-0.78)
2-year	0.810 (0.855–0.748)	0.83 (0.69-1.00)	0.79 (0.63-1.00)	0.80 (0.64-1.00)	0.78 (0.61-0.99)
PCR					
0.5-year	0.650 (0.733–0.526)	0.65 (0.56-0.76)	0.52 (0.41-0.66)	0.56 (0.45-0.69)	0.44 (0.33-0.59)
1-year	0.749 (0.807–0.673)	0.64 (0.50-0.81)	0.55 (0.39-0.76)	0.57 (0.42-0.77)	0.51 (0.35-0.73)
2-year	0.810 (0.855–0.748)	0.71 (0.60-0.85)	0.66 (0.53-0.82)	0.67 (0.55-0.83)	0.64 (0.50-0.81)

Based on 19 estimates for ACR and PCR in 15 studies. Reliability estimates are the same for ACR and PCR.

Table S10. Regression dilution coefficients & summary for clinical trials in CKD-EPI

	λ-0.5 year	λ-1 year	λ-2 year
Median study	0.650	0.749	0.810
Low (25th %ile)	0.526	0.673	0.748
High (75th %ile)	0.733	0.807	0.855
AASK(BP)	0.716	0.782	0.848
ADVANCE(ACE)	0.816	0.850	0.862
ALTITUDE	0.751	0.812	0.879
CSG_Lewis	0.705	0.757	0.896
HALTPKD_B	0.764	0.807	0.832
Hou	0.127	0.250	0.461
IDNT(CCB)	0.577	0.735	0.833
IDNT(CNTRL)	0.608	0.675	0.810
MASTERPLAN		0.863	0.855
MDRD_A(BP)	0.699	0.749	0.810
MDRD_B(BP)	0.650	0.749	0.808
ORIENT	0.509	0.673	0.748
REIN	0.323	0.503	0.667
RENAAL	0.542	0.687	0.806
ROAD		0.329	0.466

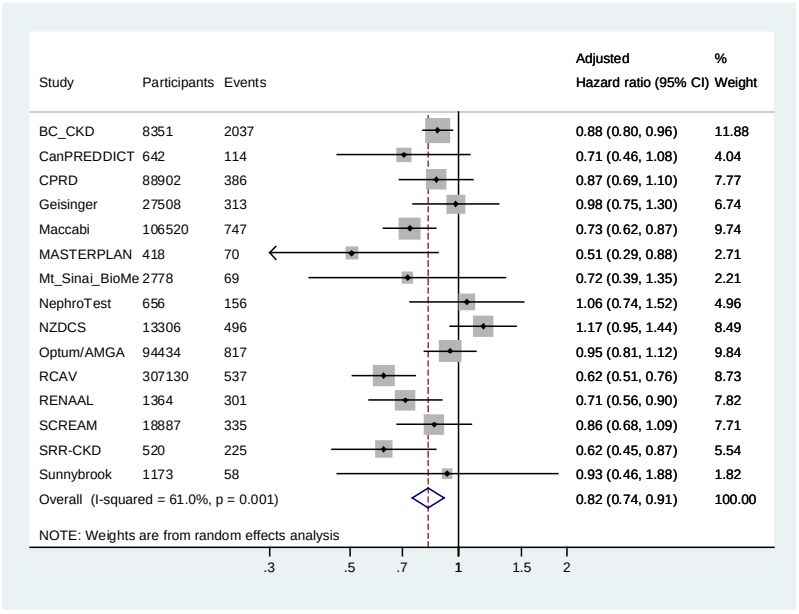
* Assumes error variance of 0.243 on log2 scale (includes biological and assay variation). Variance of change is double the variance of each measure.

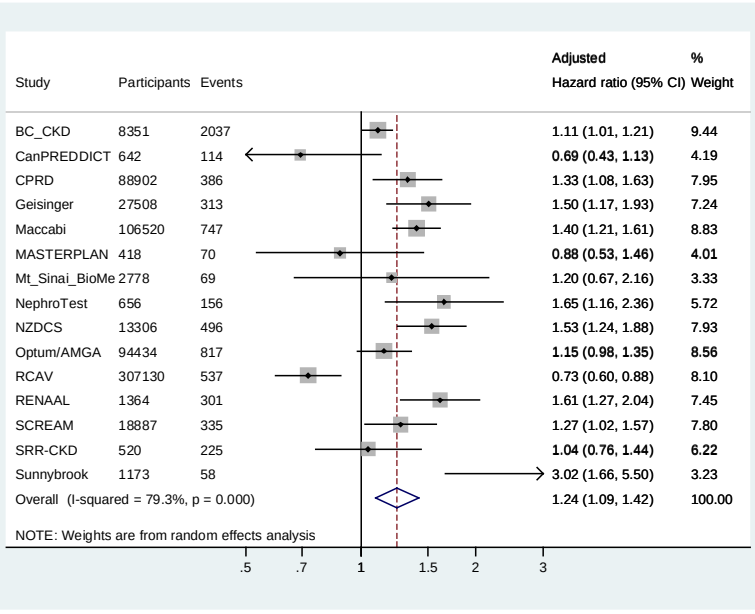
Table S11. Median study correlation of change in albuminuria between baseline periods

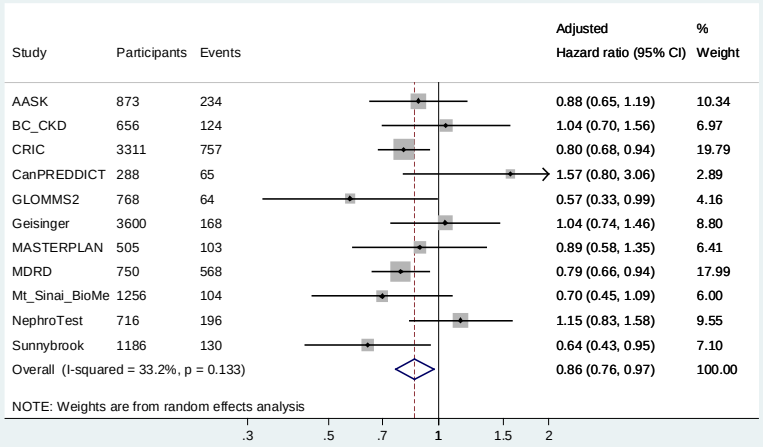
ACR change*	
1-year vs. 2-year	0.591
2-year vs. 3-year	0.702
1-year vs. 3-year	0.423
PCR change	
1-year vs. 2-year	0.601
2-year vs. 3-year	0.740
1-year vs. 3-year	0.442

* Measures are limited to those which share the same initial albuminuria measurement and exclude pairs where the same data were used for the different follow up periods.

Figure S1. Forest plot showing the individual study and meta-analyzed estimate of adjusted hazard ratio of ESKD associated with 1-year ACR change (top row) and PCR change (bottom row) for a 30% reduction (left side) 43% increase (right side)







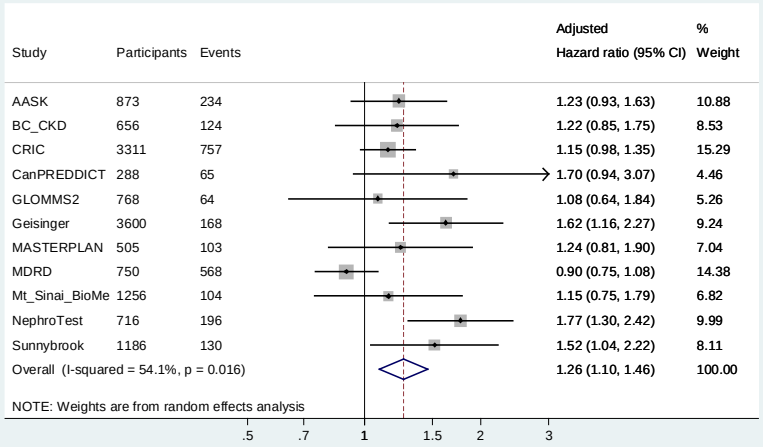
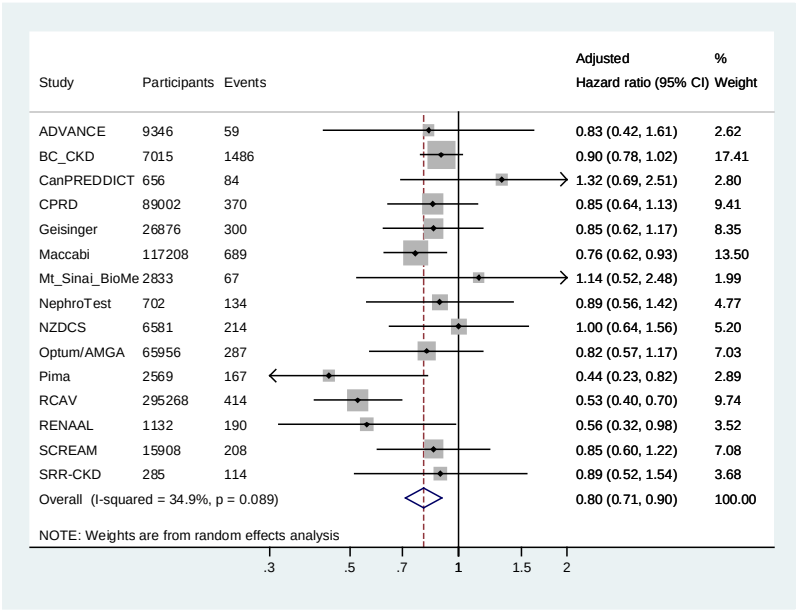
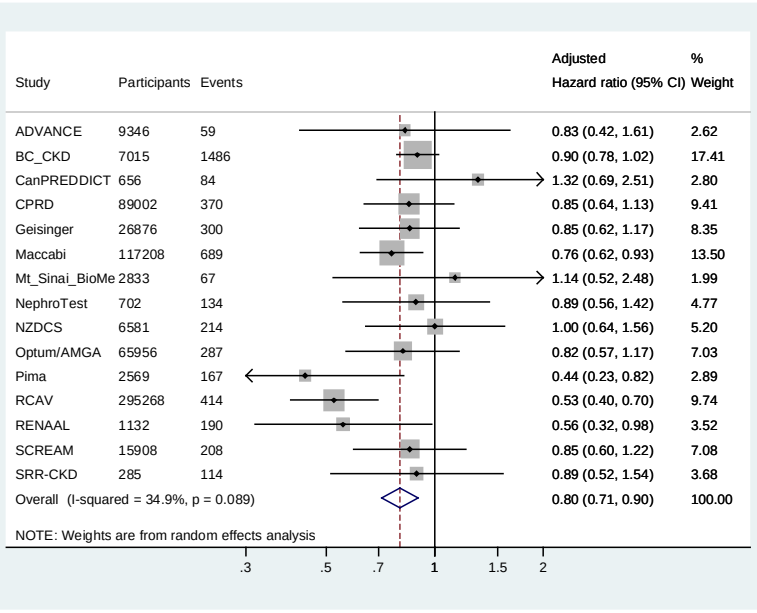
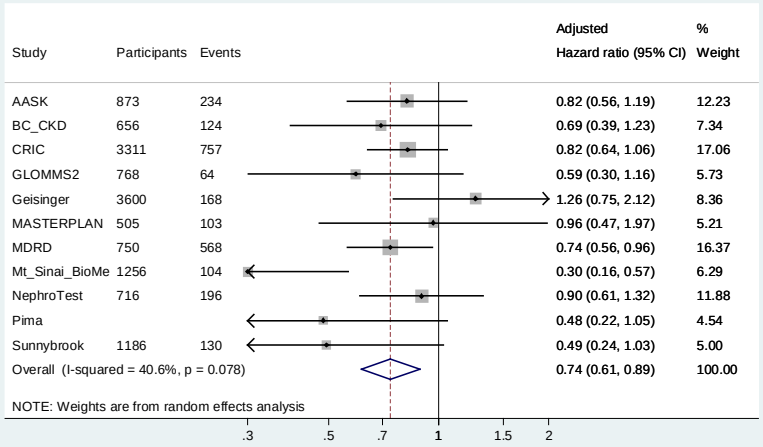


Figure S2. Forest plot showing the individual study and meta-analyzed estimate of adjusted hazard ratio of ESKD associated with 3-year ACR change (top row) and PCR change (bottom row) for a 30% reduction (left side) 43% increase (right side)







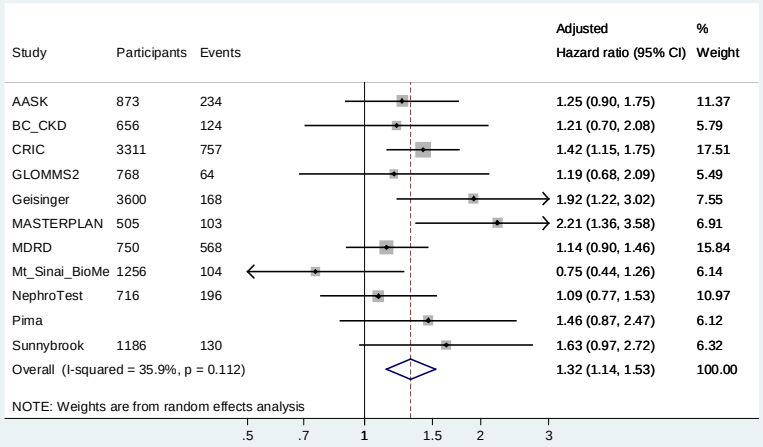
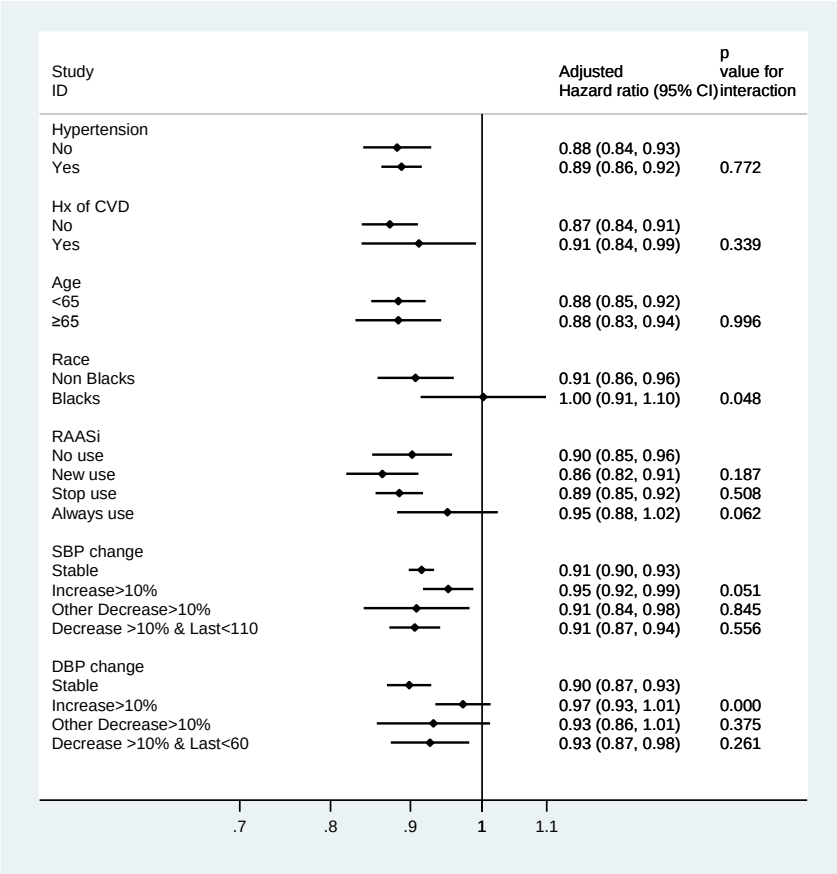
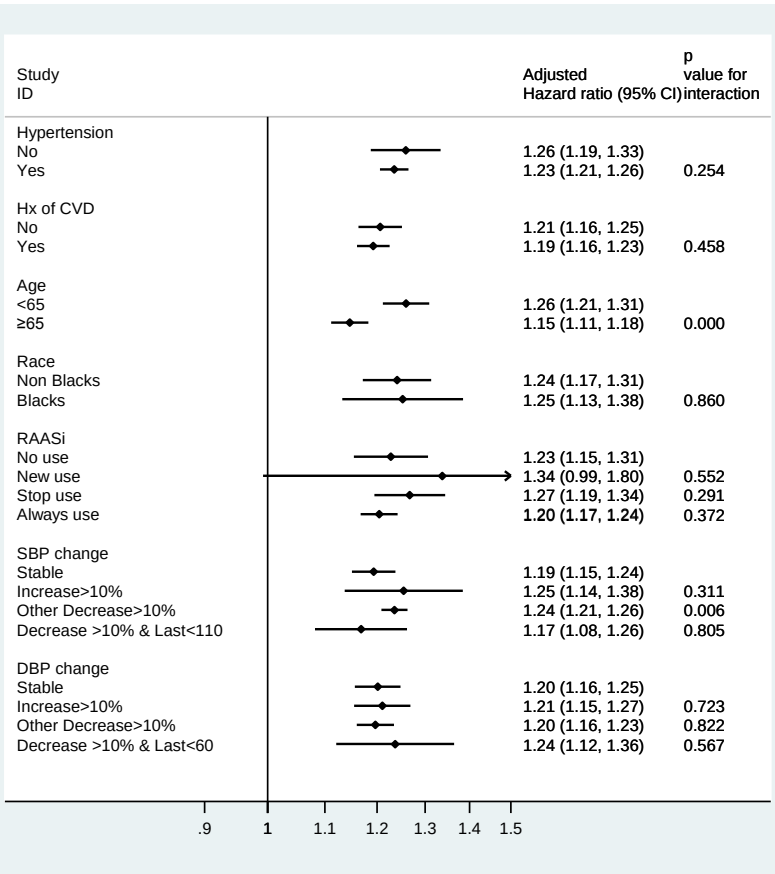


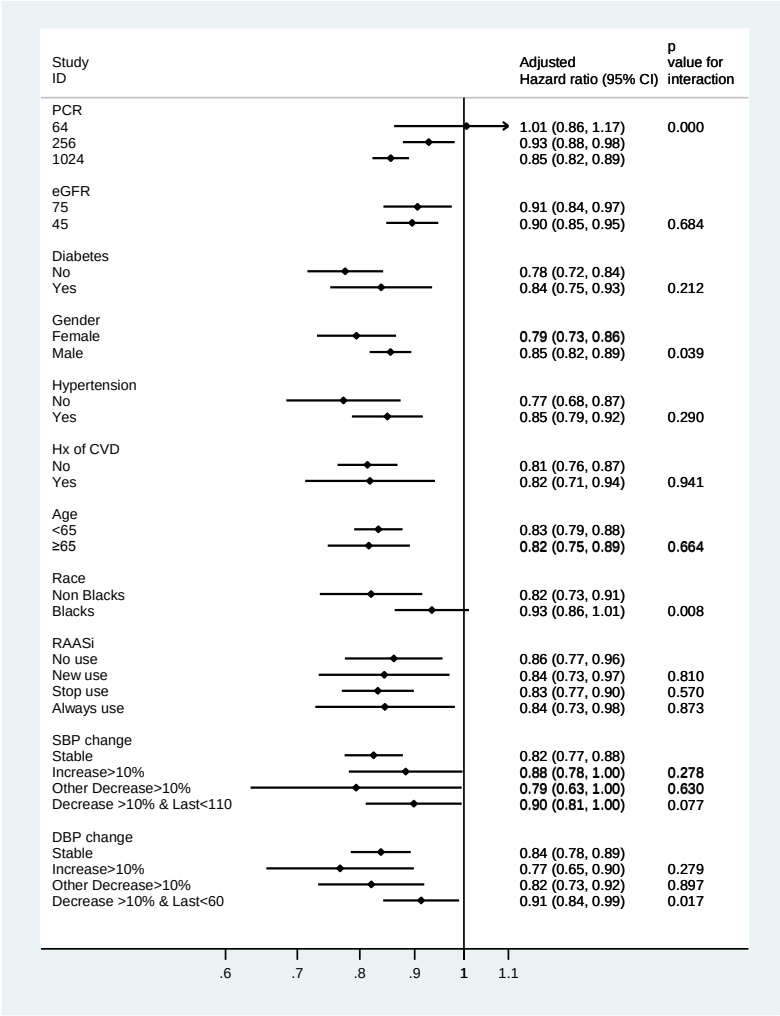
Figure S3. Interaction analysis of the adjusted hazard ratio of ESKD associated with 2-year change in ACR by baseline characteristics for a 30% reduction (left side) 43% increase (right side)

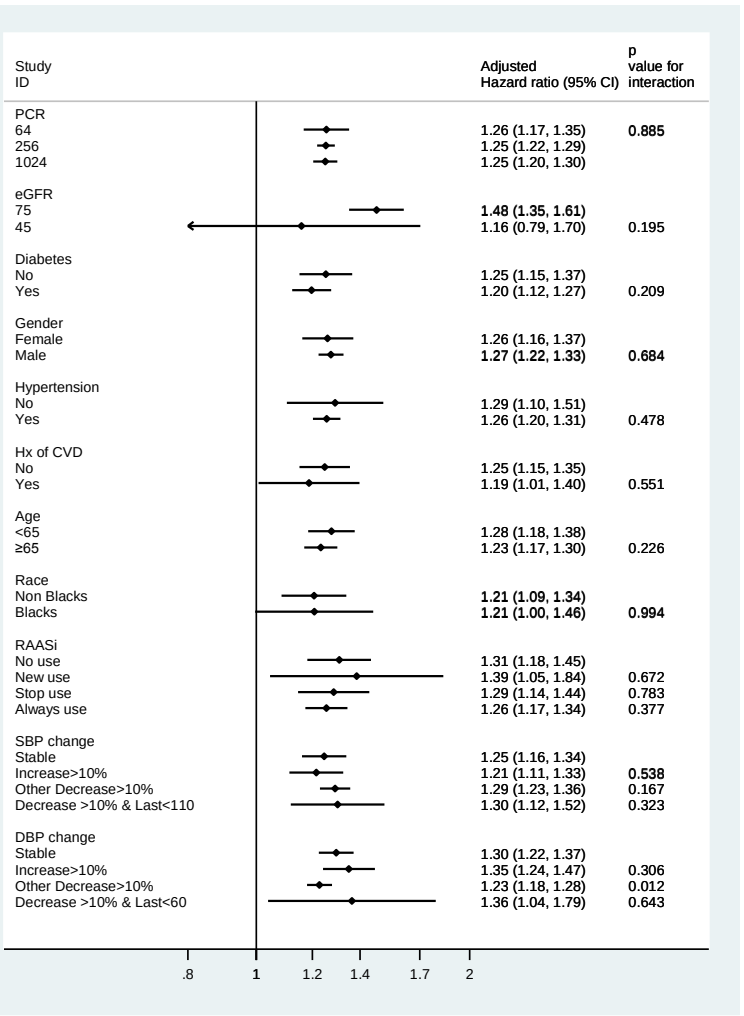




*The same weights were used for the random effects meta-analyses for all main effects and the interaction test. The weights from the random effects meta-analysis for the each reference group were used for each variable to provide more stable estimates.

Figure S4. Interaction analysis of the adjusted hazard ratio of ESKD associated with 2-year change in PCR by baseline characteristics for a 30% reduction (left side) 43% increase (right side)





*The same weights were used for the random effects meta-analyses for all main effects and the interaction test. The weights from the random effects meta-analysis for the each reference group were used for each variable to provide more stable estimates.

Figure S5. Subgroup analysis for ESKD risk and ACR, by ACR group (mg/g)

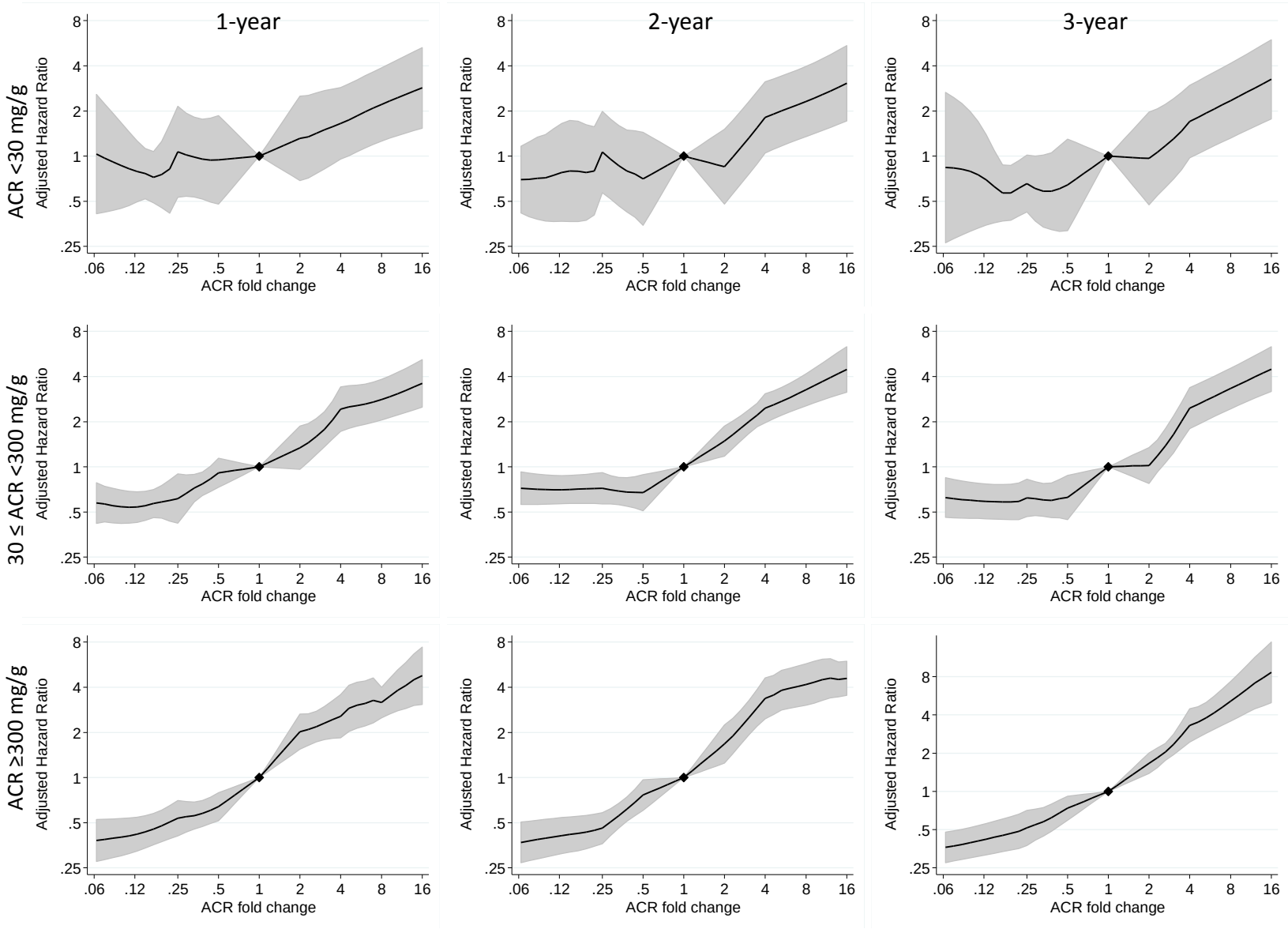


Figure S6. Subgroup analysis for ESKD risk and ACR, by eGFR

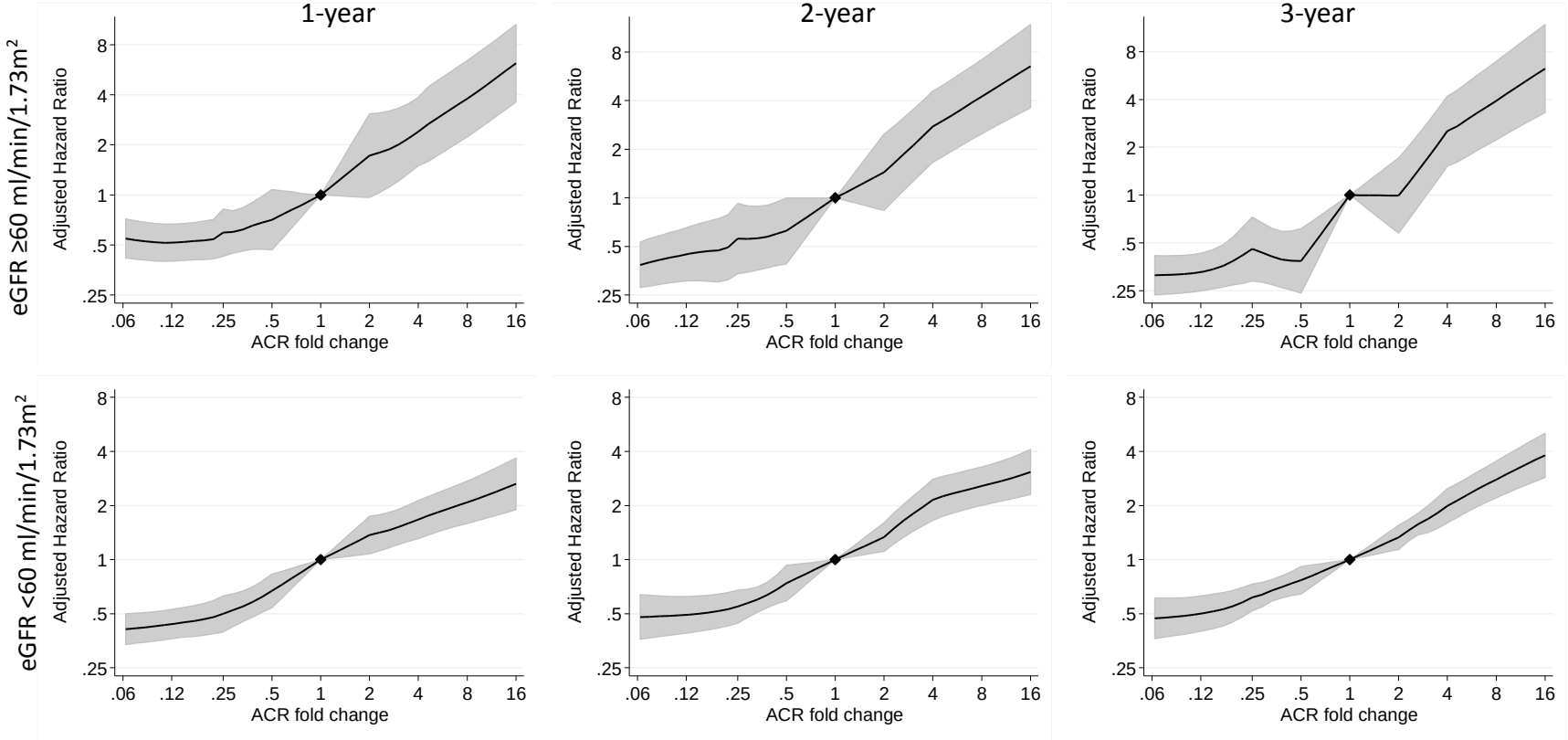


Figure S7. Subgroup analysis for ESKD risk and ACR, by diabetes

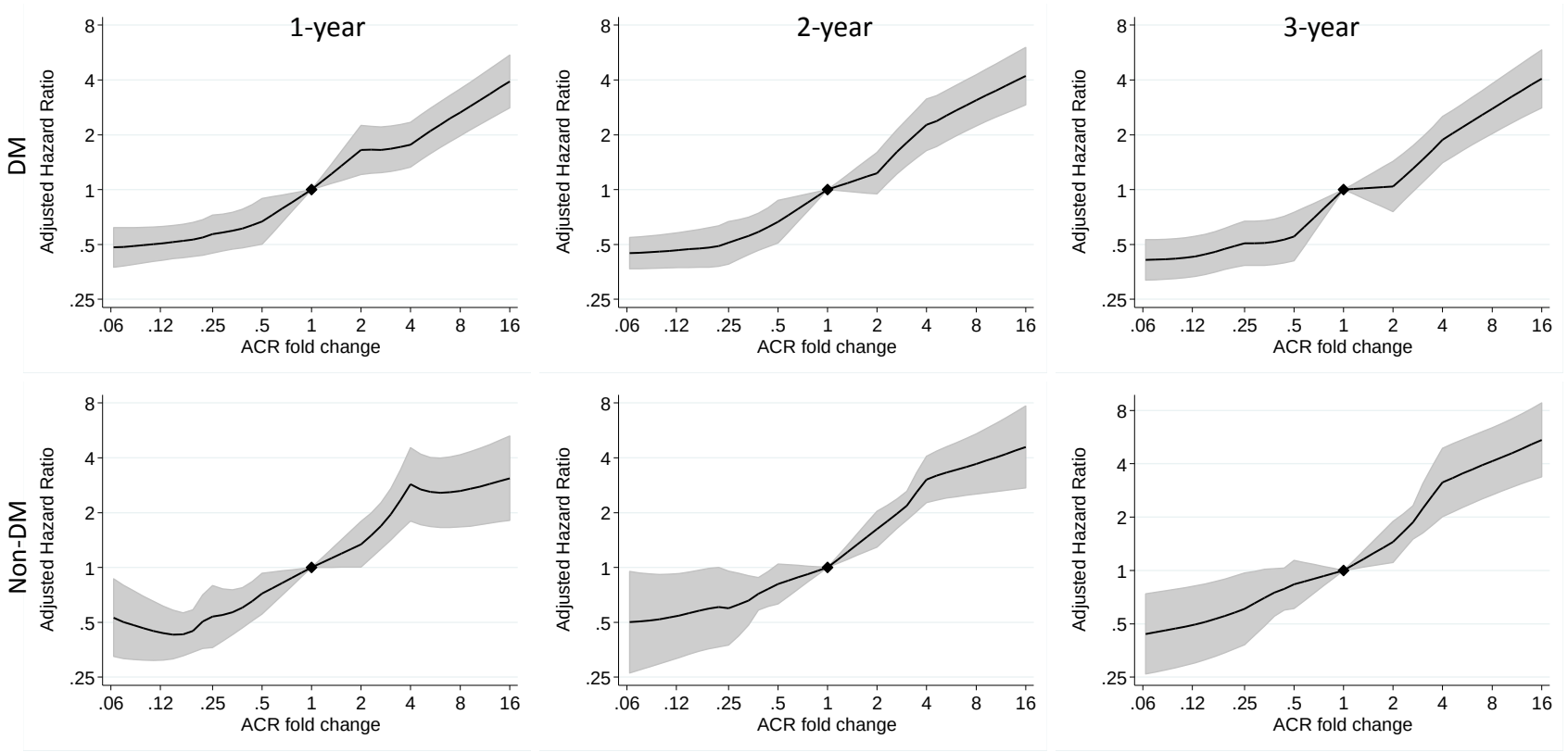
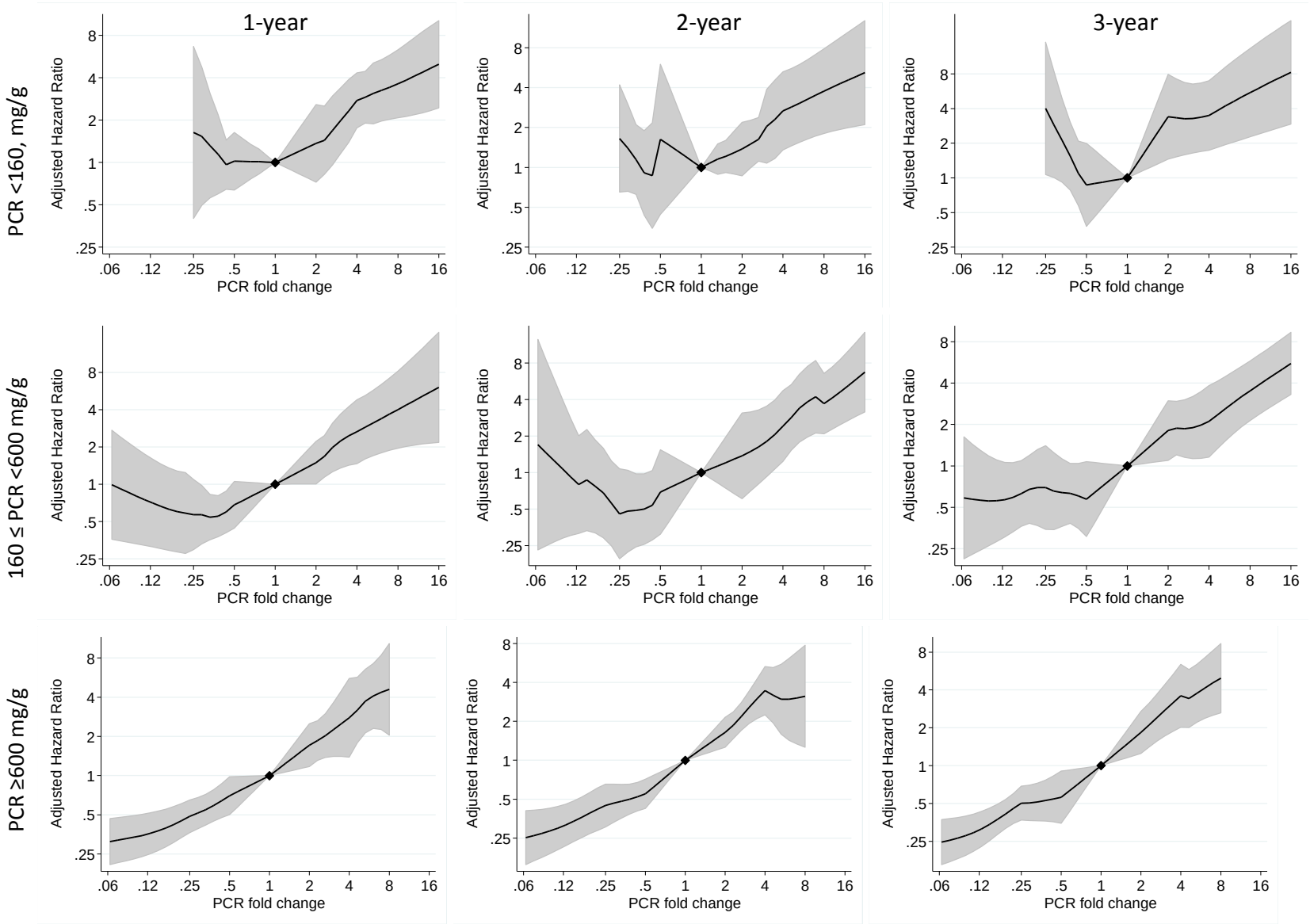


Figure S8. Subgroup analysis for ESKD risk and PCR, by PCR categories*



* PCR cutoffs were from matched percentile to ACR 30 and 300 mg/g in CKD cohorts that had both ACR and PCR data.

Figure S9. Subgroup analysis for ESKD risk and PCR, by eGFR

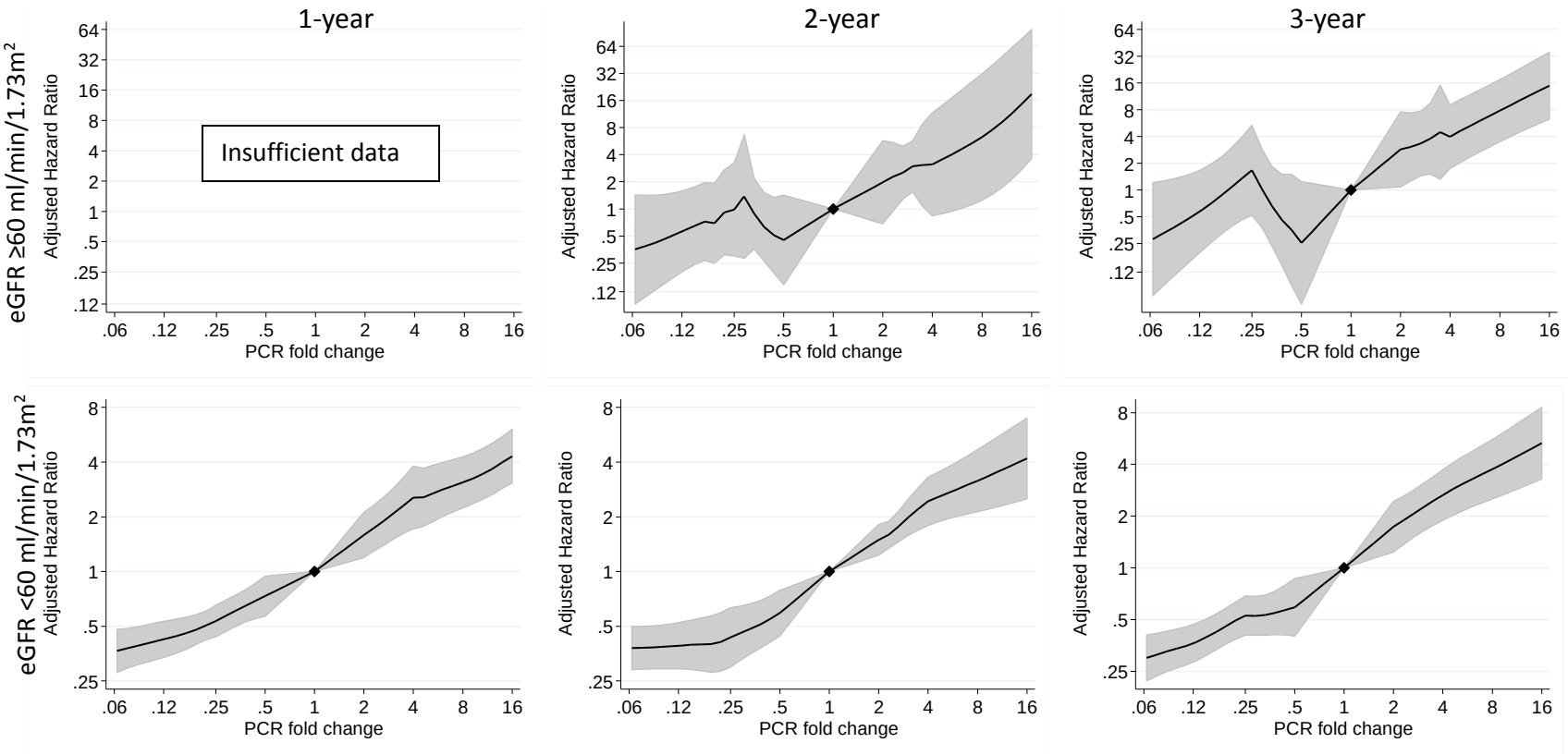


Figure S10. Subgroup analysis for ESKD risk and PCR, by diabetes

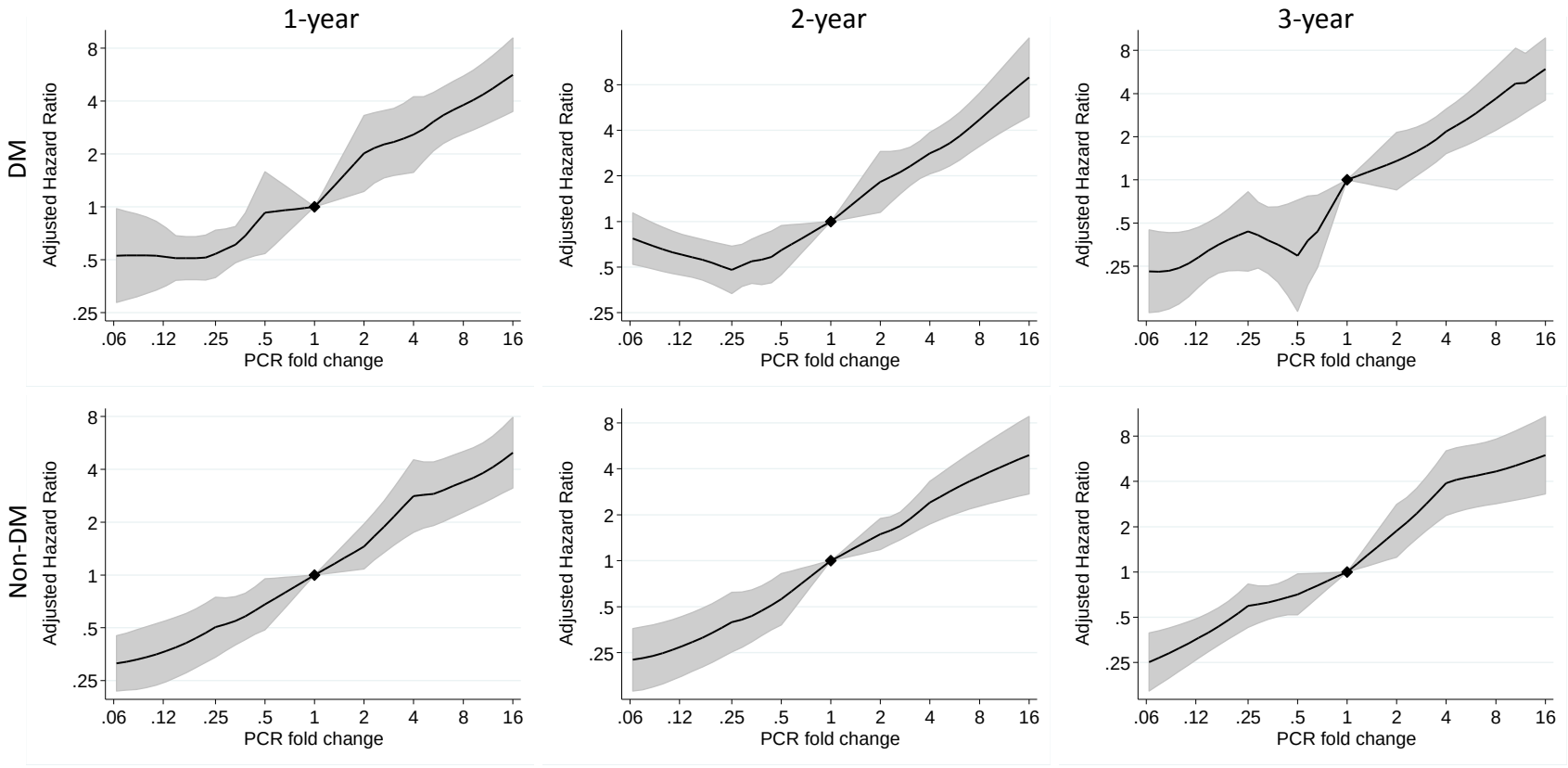


Figure S11. Adjusted hazard ratio of all-cause mortality and change in albuminuria.

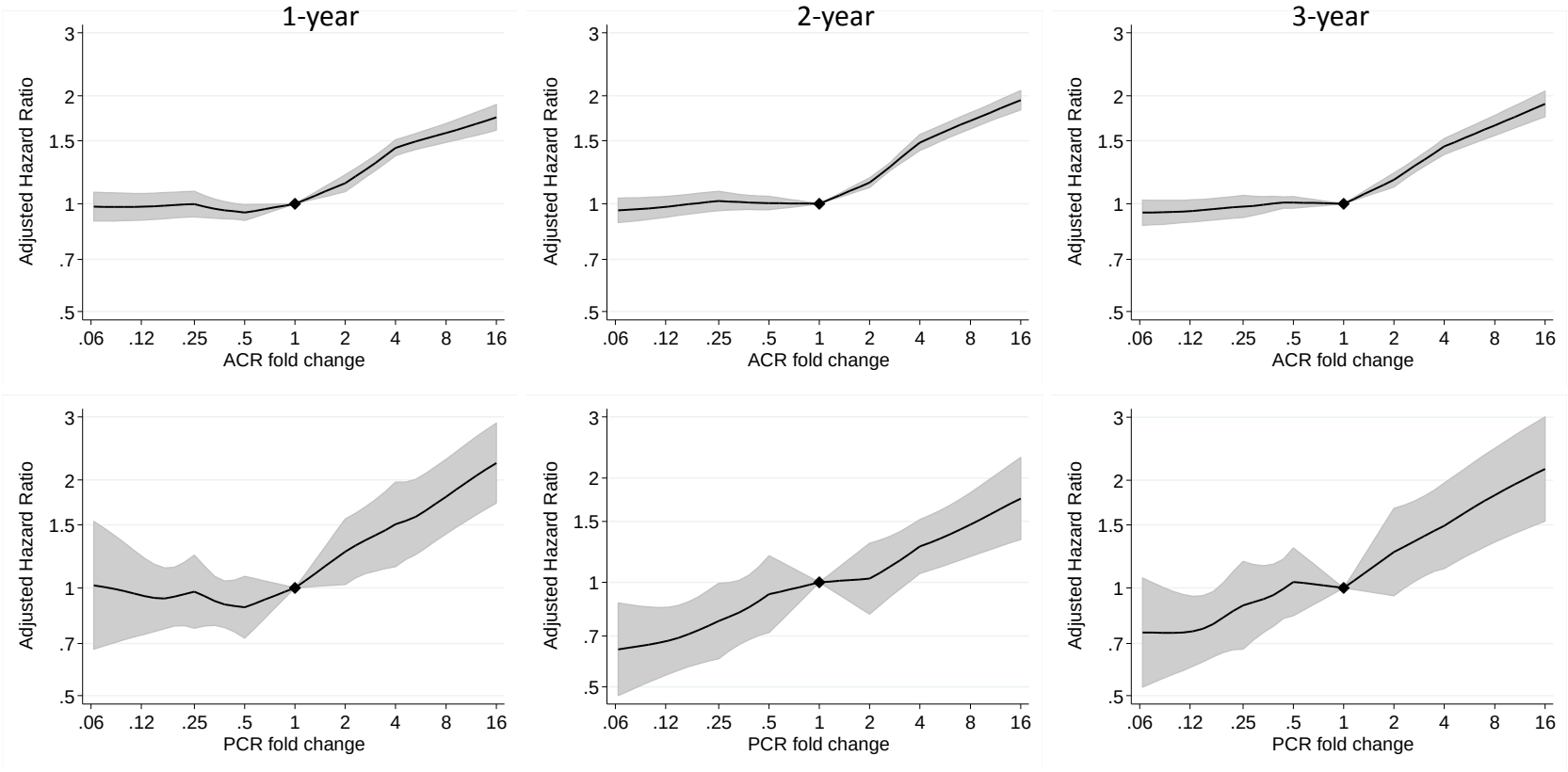
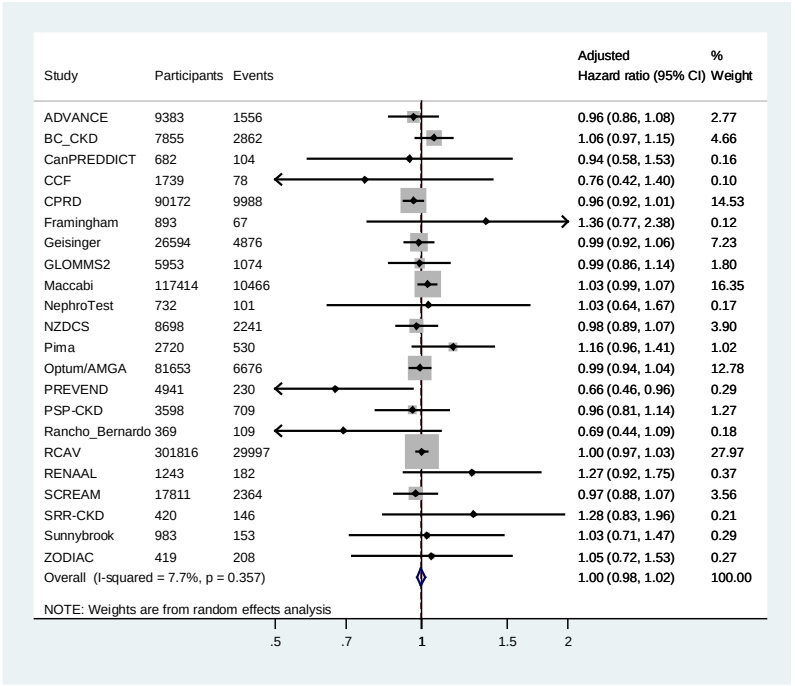
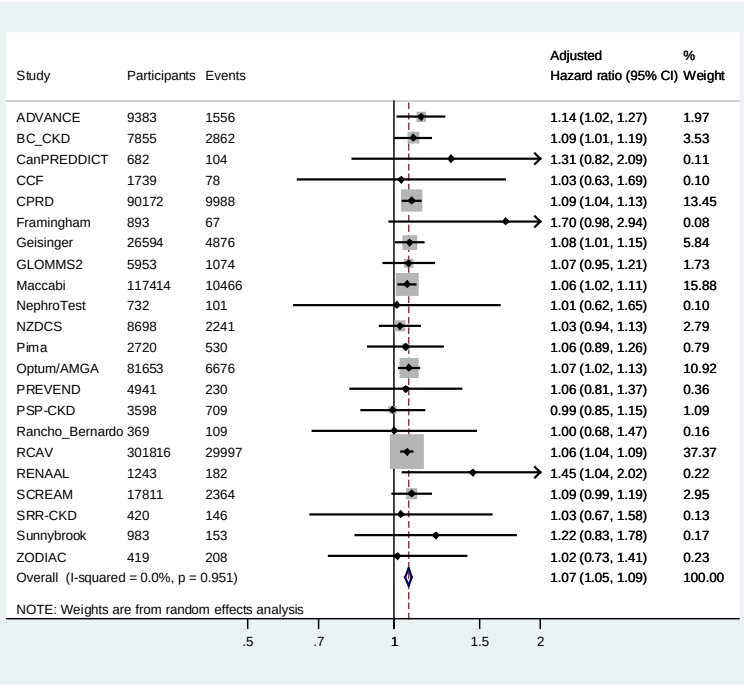
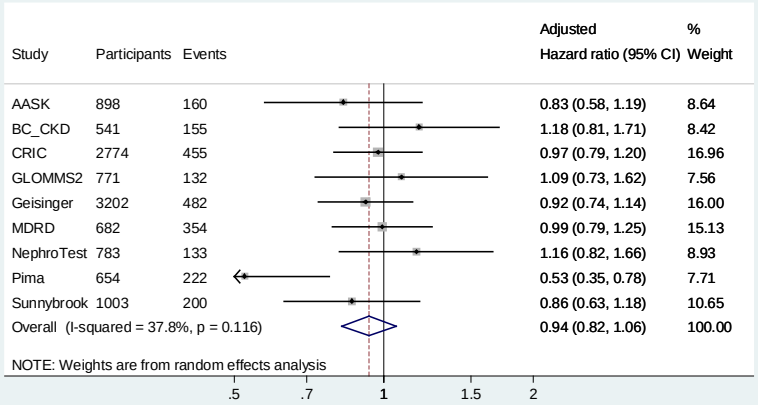


Figure S12. Forest plot showing the individual study and meta-analyzed estimate of adjusted hazard ratio of all-cause mortality associated with 2-year ACR change (top row) and PCR change (bottom row) for a 30% reduction (left side) 43% increase (right side).







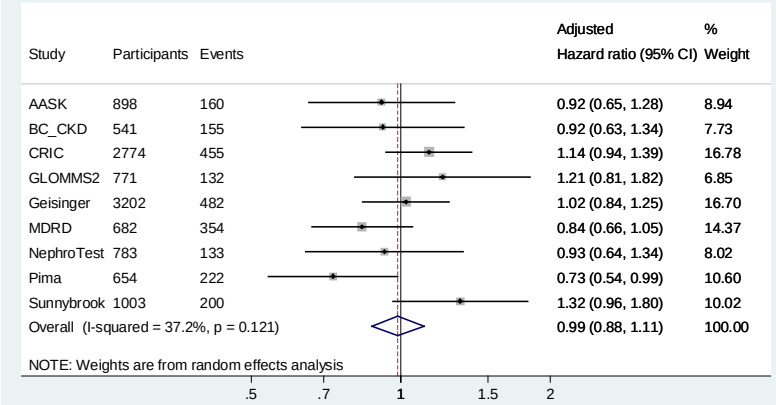


Figure S13. Adjusted hazard ratio of cardiovascular (top row) and non-cardiovascular (bottom row) mortality and change in albuminuria.

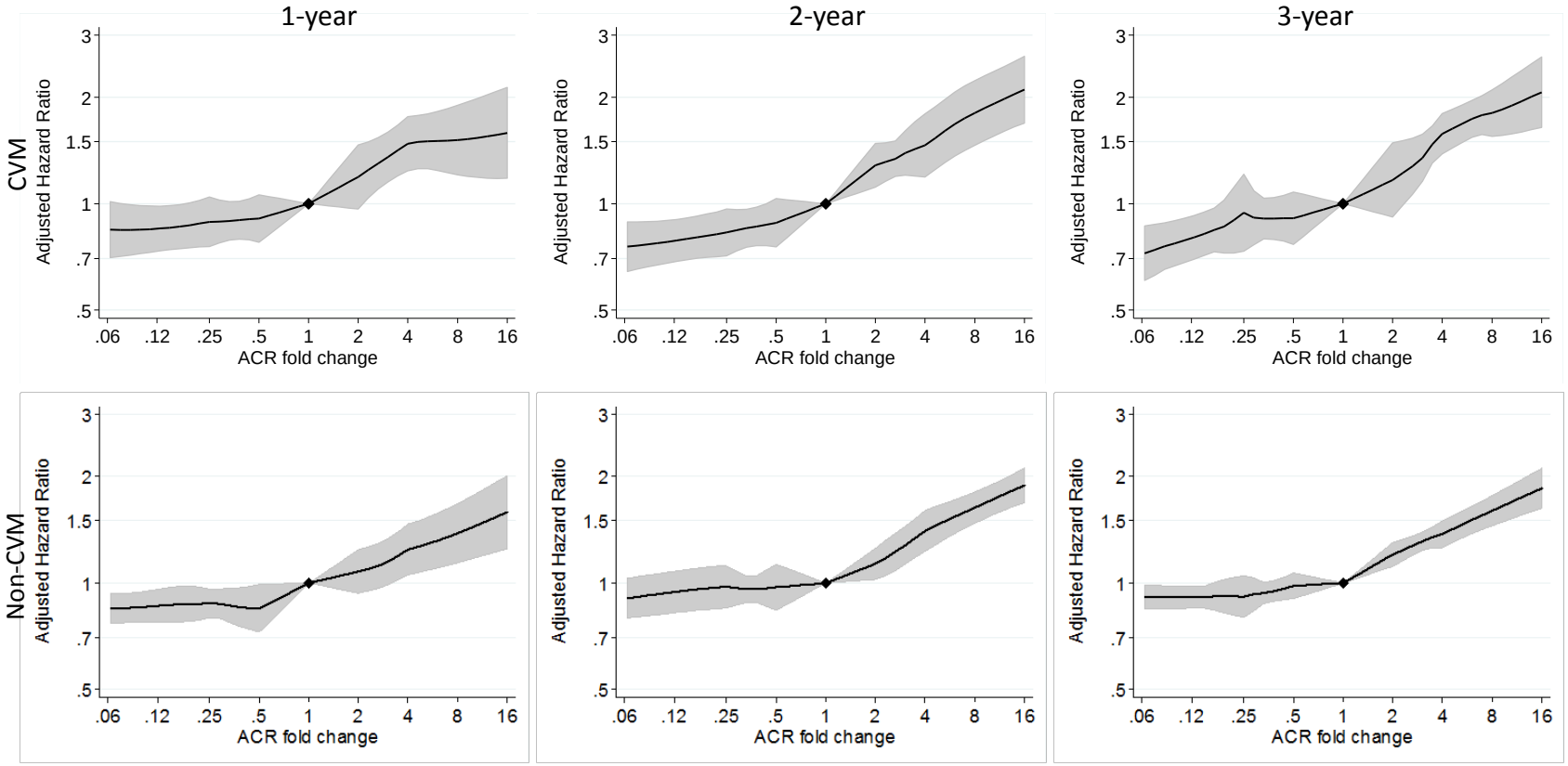


Figure S14. Forest plot showing the individual study and meta-analyzed estimate of adjusted hazard ratio of cardiovascular mortality associated with 2-year ACR change for a 30% reduction (left side) 43% increase (right side).

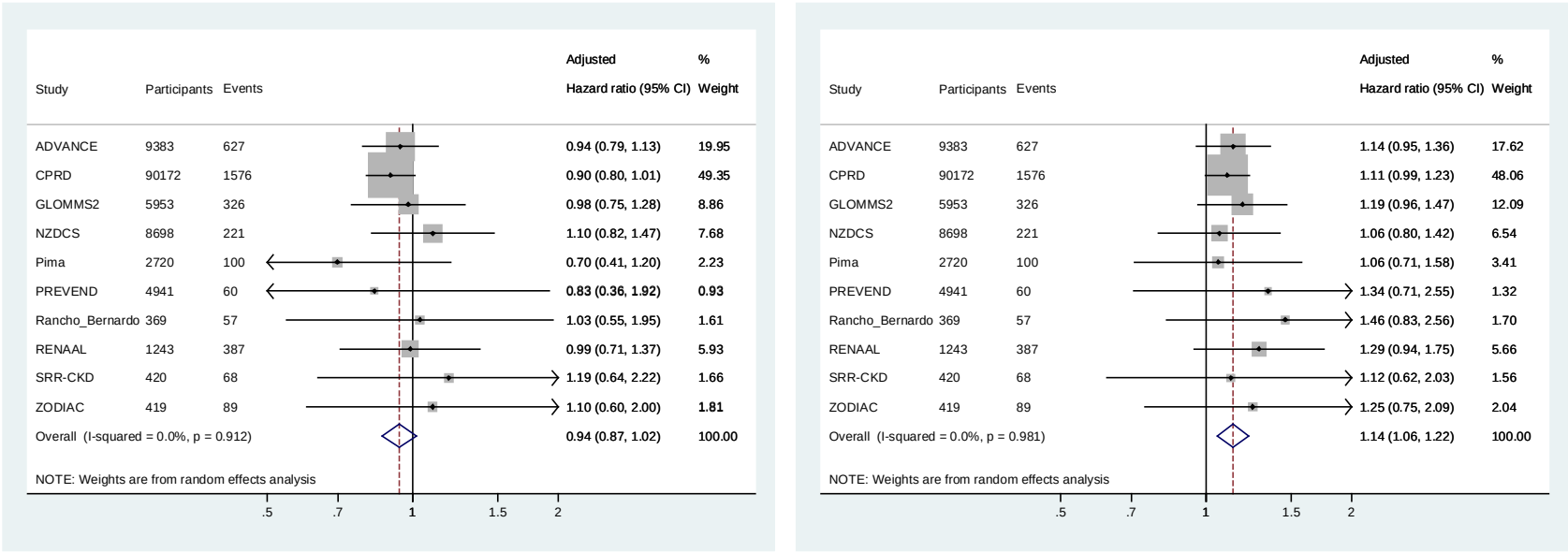


Figure S15. Forest plot showing the individual study and meta-analyzed estimate of adjusted hazard ratio of non-cardiovascular mortality associated with 2-year ACR change for a 30% reduction (left side) 43% increase (right side).

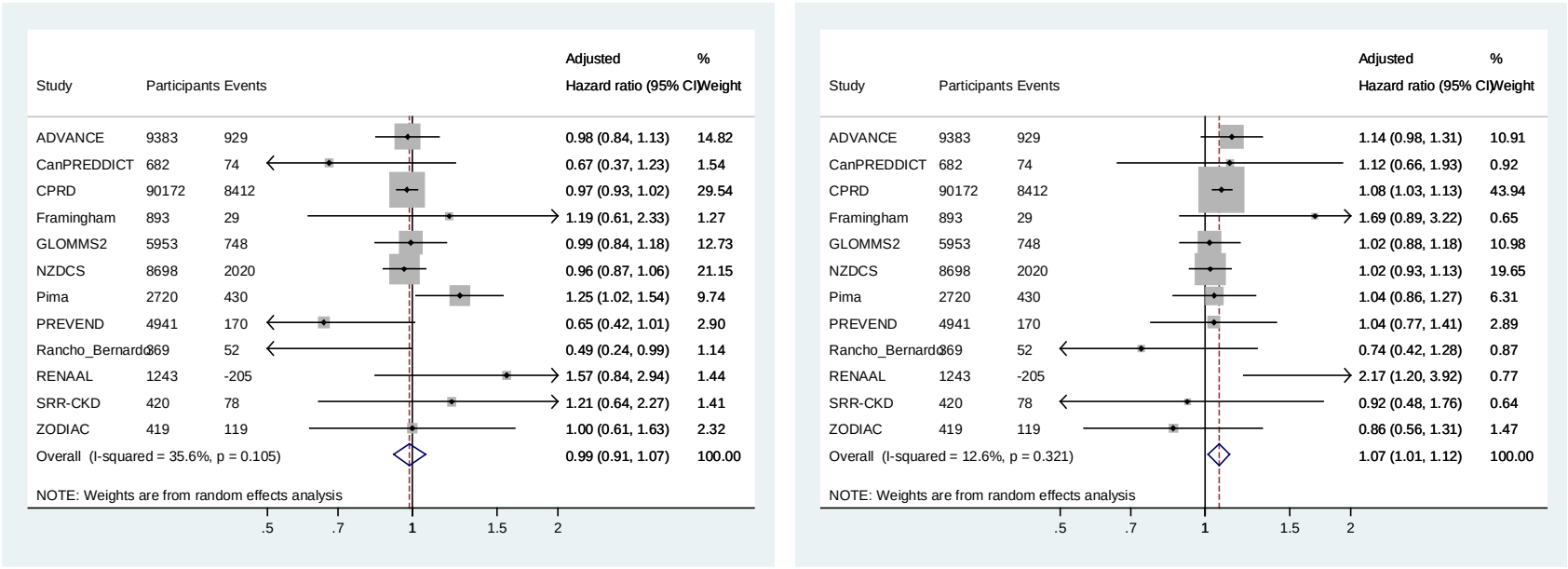


Figure S16. Adjusted hazard ratio of ESKD and population distribution of change in albuminuria in CKD-EPI clinical trials. Black circles denote -30% and +43% change in albuminuria.

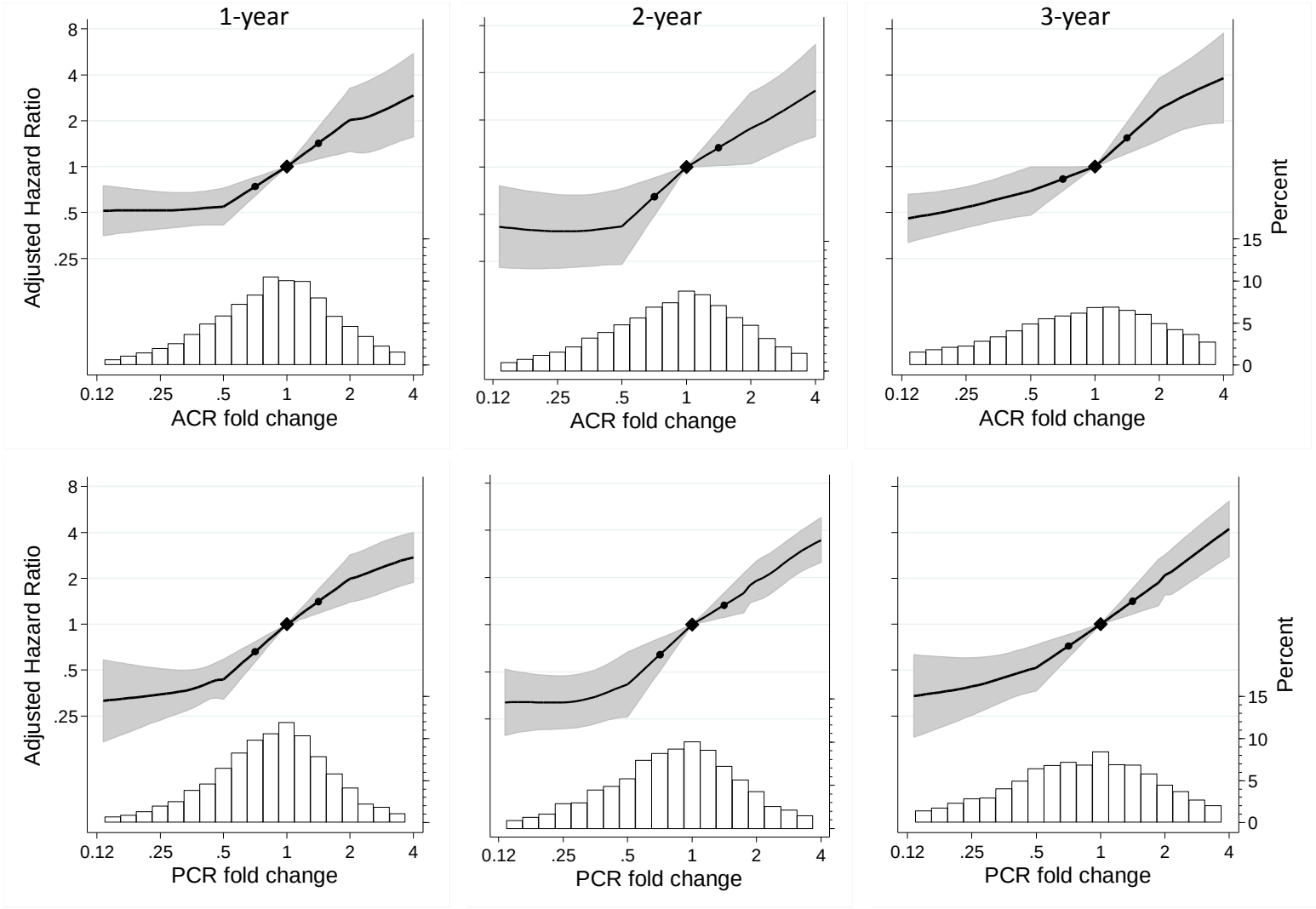
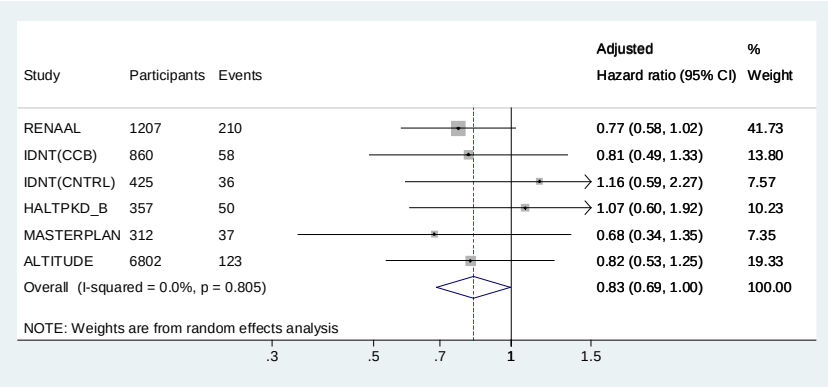
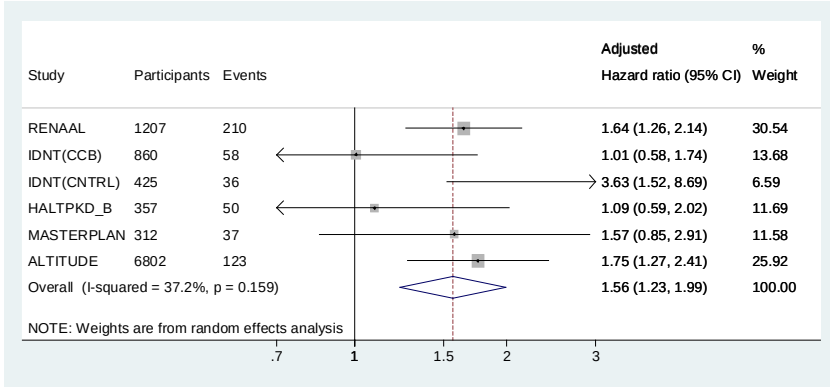
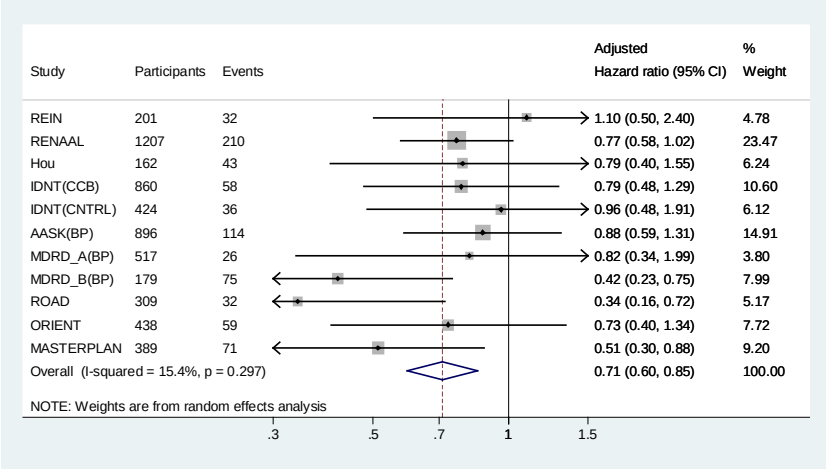


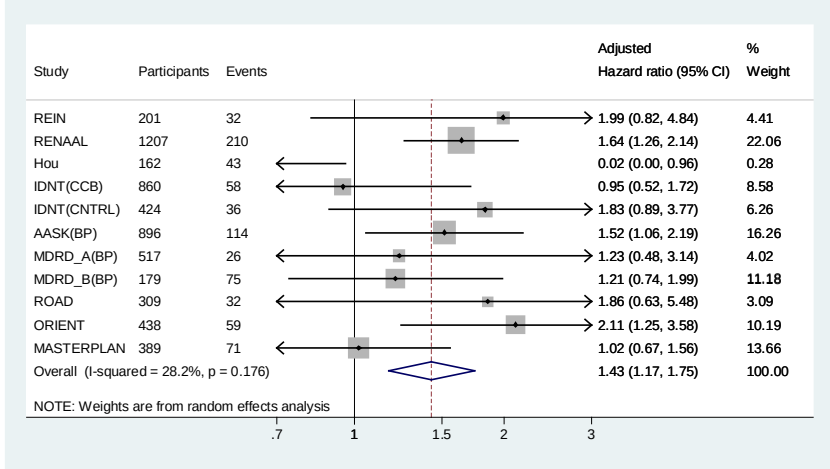
Figure S17. Forest plot showing the individual study and meta-analyzed estimate of adjusted hazard ratio of ESKD associated with 2-year ACR change (top row) and PCR change (bottom row) for a 30% reduction (left side) 43% increase (right side) in the in CKD-EPI clinical trials.





After excluding those included in CKD-PC (MASTERPLAN, RENAAL), overall adjusted hazard ratio is 0.91 (0.70, 1.18) for 30% reduction and 1.53 (0.98, 2.39) for 43% increase.





After excluding those included in CKD-PC (AASK, MASTERPLAN, MDRD, RENAAL), overall adjusted hazard ratio is 0.75 (0.56, 0.99) for 30% reduction and 1.55 (0.97, 2.46) for 43% increase.

Figure S18. Comparison of the association of change in albuminuria with ESKD (top row) to the association with an expanded outcome definition with includes ESKD or eGFR<15 ml/min/1.73m2 (bottom row). This sensitivity analysis was limited to the Geisinger cohort which provided data suitable for this analysis.

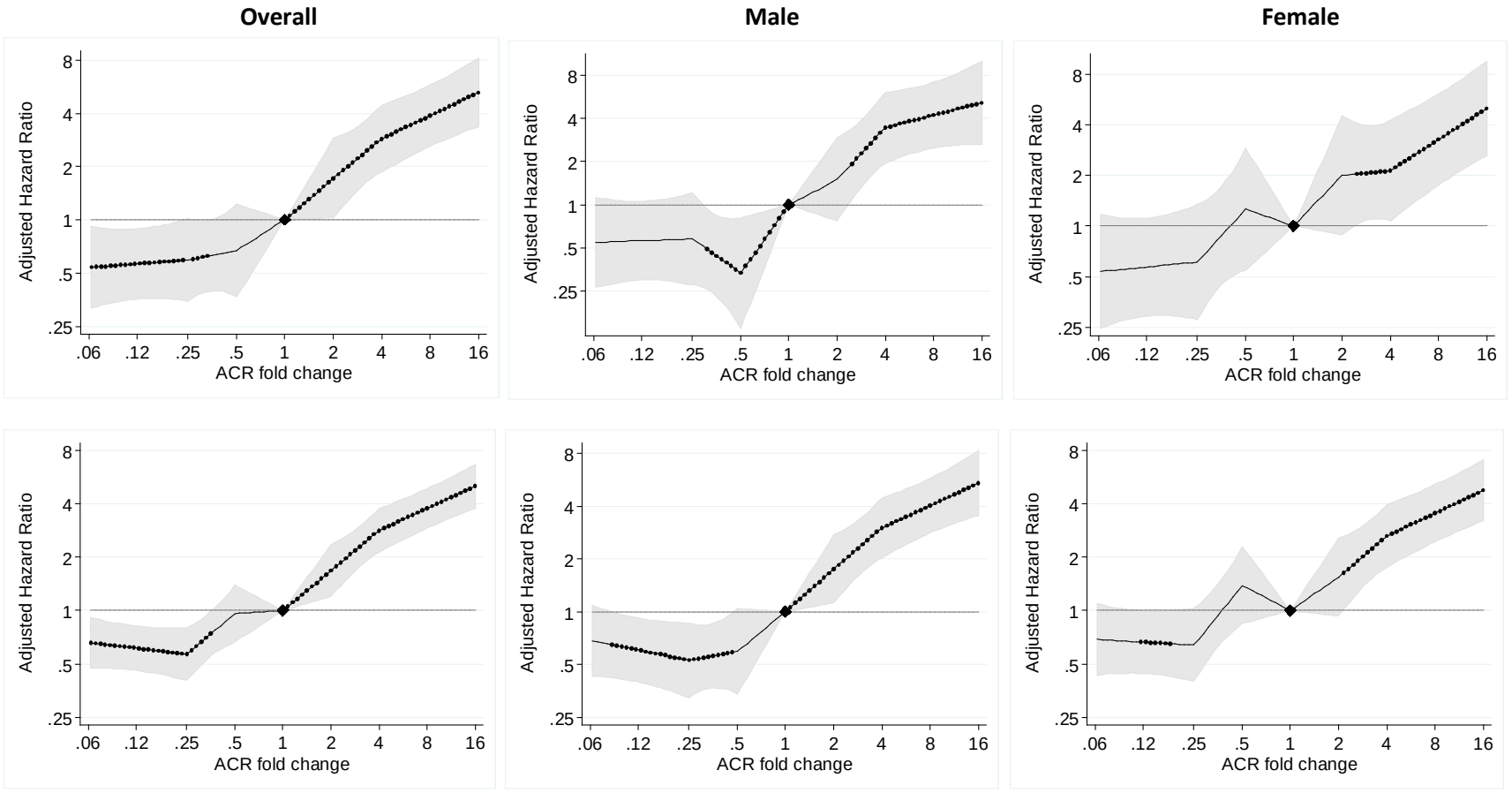
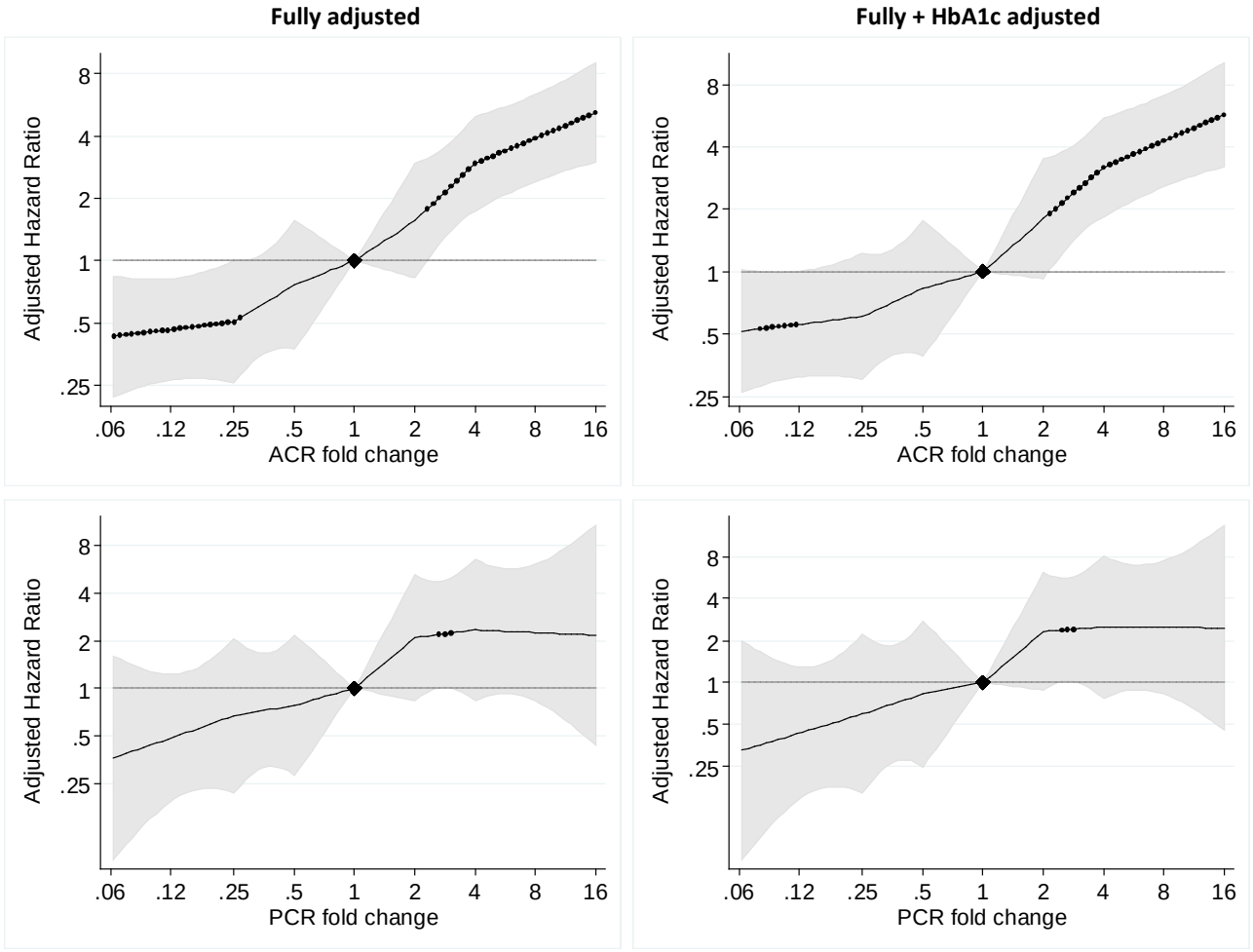


Figure S19. Comparison of the association of change in albuminuria with ESKD in the main fully adjusted model (left column) to a model further adjusted for hemoglobin A1c (HbA1c, right column). This sensitivity analysis was limited to the diabetic patients in the Geisinger cohort which provided data suitable for this analysis.



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