Supplementary Material

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eAppendix 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 20 variables (key exposures [serum creatinine to estimate GFR], 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.

Cohorts participated in this analysis if they had the required data and agreed to be included in the paper. This decision was made prior to any analysis or knowledge of the results. For 9 of the 14 cohorts in this specific study, the Data Coordination Center at Johns Hopkins University conducted the analysis; the remainder 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. 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.

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 (CCF, Geisinger, Maccabi, MASTERPLAN, RCAV, SCREAM) and studies where the creatinine standardization was not done (AASK, ADVANCE, BC CKD, KP Hawaii, MDRD, NZDCS, RENAAL, Sunnybrook). 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 calculated eGFR using the CKD-EPI equation: $eGFR_{CKD\text{-}EPI} = 141 \times (\text{minimum of standardized serum creatinine [mg/dL]}/\kappa \text{ or } 1)^{\alpha} \times (\text{maximum of standardized serum creatinine [mg/dL]}/\kappa \text{ or } 1)^{-1.209} \times 0.993^{age} \times (1.018 \text{ if female}) \times (1.159 \text{ if black})$, 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]

Notes for individual studies:

ADVANCE: This study is an intervention study which includes participants with diabetes only.

RCAV: This cohort does not have data on smoking.

RENAAL: This cohort categorizes smoking as current vs. former/never smoking.

SCREAM: This cohort does not have data on smoking and blood pressure.

Percent with missing covariates:

	DM	Hx of CVD	Smoking	Systolic BP	Total Cholesterol
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%)	1937 (20%)	5446 (56%)
CCF	0 (0%)	0 (0%)	0 (0%)	1870 (9%)	9084 (42%)
Geisinger	0 (0%)	0 (0%)	0 (0%)	11840 (9%)	45517 (34%)
KP Hawaii	0 (0%)	447 (2%)	765 (3%)	1682 (6%)	7518 (27%)
Maccabi	0 (0%)	0 (0%)	0 (0%)	212668 (28%)	68434 (9%)
MASTERPLAN	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
MDRD	0 (0%)	0 (0%)	1 (0%)	0 (0%)	0 (0%)
NZDCS	0 (0%)	0 (0%)	69 (2%)	90 (3%)	82 (2%)
RCAV	0 (0%)	0 (0%)	2151271 (100%)	904797 (42%)	1740365 (81%)
RENAAL	0 (0%)	1317 (100%)	2 (0%)	1317 (100%)	1308 (100%)
SCREAM	0 (0%)	0 (0%)	333820 (100%)	333820 (100%)	139321 (42%)
Sunnybrook	0 (0%)	0 (0%)	0 (0%)	1056 (82%)	1049 (81%)

ESKD ascertainment by study:

Study	Ascertainment type
AASK	Active
ADVANCE	Active
BC CKD	Active
CCF	Linkage to registry
Geisinger	Linkage to registry
KP Hawaii	Active
Maccabi	Active
MASTERPLAN	Active
MDRD	Active, Linkage to registry
NZDCS	Linkage to registry, ICD codes
RCAV	Linkage to registry
RENAAL	Active (with adjudication)
SCREAM	Linkage to registry
Sunnybrook	Linkage to registry

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

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]
CCF:	Cleveland Clinic CKD Registry Study[10]
Geisinger:	Geisinger Health System[11]
KP Hawaii:	Kaiser Permanente Hawaii cohort[12]
Maccabi:	Maccabi Health System[13]
MASTERPLAN:	Multifactorial Approach and Superior Treatment Efficacy in Renal Patients with the Aid of a Nurse Practitioner[14]
MDRD:	Modification of Diet in Renal Disease Study[15]
NZDCS:	New Zealand Diabetes Cohort Study[16]
RCAV:	Racial and Cardiovascular Risk Anomalies in CKD Cohort[17]
RENAAL:	Reduction of Endpoints in Non-insulin Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan[18]
SCREAM:	Stockholm CREAtinine Measurements Cohort[19]
Sunnybrook:	Sunnybrook Cohort[20]

eAppendix 3. Acknowledgements and funding for collaborating 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.
CCF	Supported by an unrestricted educational grant from Amgen to the Department of Nephrology and Hypertension.
Geisinger	Geisinger Clinic
KP Hawaii	
Maccabi	
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
NZDCS	Health Research Council of New Zealand, Auckland Medical Research Foundation and New Zealand Society for the Study of Diabetes
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.
Sunnybrook	

eTable 1. Baseline characteristics of individuals in cohorts participating in the 1-year observation period for change in estimated glomerular filtration rate over time, stratified by baseline estimated glomerular filtration rate

eGFR<60	N	Age, years	Female, %	Black, %	eGFR, ml/min /1.73m^2	SBP, mmHg	Diabetes, %	History of CVD, %	Current smoker, %	Former smoker, %	TC, mmol/L
AASK	825	55 (11)	40	100	41 (11)	150 (23)	0	52	43	28	5.5 (1.2)
BC CKD	9783	70 (13)	46	0.40	32 (11)	136 (23)	45	23	2.5	6.1	NA
CCF	21678	72 (12)	54	12	47 (11)	131 (19)	25	26	0.35	3.0	4.7 (1.1)
Geisinger	18947	74 (12)	61	0.84	46 (11)	134 (20)	31	44	8.4	28	4.9 (1.1)
KP Hawaii	7043	71 (11)	53	0	47 (10)	137 (22)	47	34	7.9	NA	4.7 (1.1)
Maccabi	29208	75 (11)	50	0	48 (10)	134 (19)	32	48	1.04	19	4.8 (1.1)
MASTERPLAN	540	61 (12)	32	0	36 (11)	137 (21)	24	30	21	54	4.9 (1.1)
MDRD	721	52 (12)	38	7.4	35 (12)	132 (17)	5.1	13	10	NA	5.6 (1.2)
NZDCS	3581	71 (10)	57	0	47 (10)	141 (21)	100	2.2	8.4	31	5.3 (1.2)
RENAAL	1317	60 (7)	38	14	37 (11)	NA	100	NA	17.3	NA	NA
SCREAM	32660	69 (11)	59	0	47 (11)	NA	17	39	NA	NA	5.1 (1.2)
Sunnybrook	1289	71 (14)	43	0	35 (12)	NA	53	17	7.5	18	NA
Subtotal	**127,592**	**71 (12)**	**55**	**3**	**47 (11)**	**134 (20)**	**30**	**38**	**4.3**	**18**	**4.9 (1.2)**
eGFR 60+											
ADVANCE	8722	66 (6)	40	0.34	83 (13)	144 (21)	100	24	16	27	5.2 (1.2)
Geisinger	114429	56 (15)	56	1.8	91 (17)	129 (18)	18	17	17	25	5.1 (1.1)
KP Hawaii	20518	58 (13)	50	0	86 (16)	135 (20)	58	15	14	NA	4.9 (1.2)
Maccabi	617351	48 (16)	59	0	100 (17)	124 (17)	10.2	9.7	2.1	23	5.0 (1.0)
NZDCS	12167	59 (13)	48	0.18	85 (16)	137 (19)	100	0.76	16	27	5.3 (1.1)
RCAV	2151271	61 (13)	5.5	16	83 (15)	134 (18)	29	21	NA	NA	NA
SCREAM	301160	51 (15)	53	0	95 (17)	NA	8.6	12	NA	NA	5.3 (1.1)
Subtotal	**3225618**	**58 (15)**	**23**	**11**	**88 (17)**	**132 (18)**	**24**	**18**	**5.0**	**23**	**4.9 (1.1)**
Total	**3353210**	**58 (15)**	**24**	**10**	**86 (19)**	**132 (19)**	**24**	**19**	**5.0**	**23**	**4.9 (1.1)**

eTable 2. Baseline characteristics of individuals in cohorts participating in the 3-year observation period for change in estimated glomerular filtration rate over time, stratified by baseline estimated glomerular filtration rate

eGFR<60	**N**	**Age, years**	**Female, %**	**Black, %**	**eGFR, ml/min /1.73m^2**	**SBP, mmHg**	**Diabetes, %**	**History of CVD, %**	**Current smoker, %**	**Former smoker, %**	**TC, mmol/L**
AASK	664	55 (11)	40	100	43 (11)	149 (24)	0	52	42	28	5.5 (1.1)
BC CKD	8168	70 (13)	47	0	33 (11)	136 (23)	44	25	2.5	6.0	4.7 (1.3)
CCF	14631	72 (11)	55	12	47 (10)	132 (19)	25	25	0.18	1.8	4.7 (1.1)
Geisinger	17695	73 (11)	62	0.71	48 (10)	134 (20)	27	41	8.2	26	5.0 (1.1)
KP Hawaii	3484	70 (10)	52	0	47 (10)	136 (21)	64	37	7.2	NA	4.6 (1.1)
Maccabi	28039	74 (11)	51	0	49 (10)	134 (19)	31	46	1.06	19	4.8 (1.1)
MASTERPLAN	481	61 (12)	32	0	36 (11)	136 (20)	23	30	20	53	4.9 (1.1)
MDRD	301	52 (12)	38	4.7	35 (12)	131 (18)	4.0	12	10	NA	5.6 (1.1)
NZDCS	909	71 (9)	56	0	48 (10)	142 (20)	100	0.88	7.7	36	5.4 (1.1)
RENAAL	728	61 (7)	37	13	38 (11)	NA	100	NA	15.3	NA	7.2 (1.6)
SCREAM	33122	69 (10)	62	0	48 (10)	NA	15	34	NA	NA	5.2 (1.2)
Sunnybrook	732	69 (13)	41	0	36 (12)	141 (22)	53	12	7.0	18	4.8 (1.2)
Subtotal	**108,954**	**71 (11)**	**57**	**3**	**48 (10)**	**134 (20)**	**26**	**37**	**3.9**	**18**	**5.0 (1.2)**
eGFR 60+											
ADVANCE	7970	66 (6)	40	0.40	83 (13)	144 (21)	100	23	16	26	5.2 (1.2)
Geisinger	144273	54 (15)	57	1.6	92 (17)	128 (18)	15	14	17	23	5.1 (1.0)
KP Hawaii	9866	59 (13)	49	0	86 (16)	134 (20)	77	17	13	NA	4.8 (1.2)
Maccabi	758347	46 (15)	59	0	101 (17)	123 (17)	8.7	8.5	2.2	24	5.0 (1.0)
NZDCS	3479	59 (13)	49	0.057	86 (17)	138 (19)	100	0.20	16	31	5.4 (1.1)
RCAV	2430178	60 (13)	6.2	17.35	84 (15)	134 (18)	26	18.64	NA	NA	4.9 (1.1)
SCREAM	480145	48 (15)	54	0	97 (17)	NA	6.0	8.3	NA	NA	5.4 (1.1)
Subtotal	**3,834,258**	**56 (15)**	**25**	**11**	**89 (18)**	**132 (18)**	**20**	**15**	**4.9**	**24**	**5.0 (1.1)**
Total	**3,943,212**	**56 (15)**	**26**	**11**	**88 (19)**	**132 (19)**	**20**	**16**	**4.8**	**23**	**5.0 (1.1)**

eTable 3. Median number of creatinine measurements within individuals in cohorts participating in the 2-year observation period for change in estimated glomerular filtration rate over time, with subsequent follow-up and number of events

eGFR<60	N	Median # (IQR) of measurements	Follow-up, years (SD)	# of ESKD events	# of ACM events
AASK	744	7 (6-7)	5.8 (3.0)	243	112
BC CKD	8950	10 (8-15)	3.9 (2.6)	2113	3739
CCF	18873	5 (4-9)	1.2 (0.8)	366	2010
Geisinger	19200	5 (4-8)	5.0 (3.6)	761	9785
KP Hawaii	5468	7 (5-11)	1.2 (0.7)	134	353
Maccabi	29211	6 (4-8)	3.9 (1.7)	968	9683
MASTERPLAN	513	8 (7-9)	3.5 (1.3)	111	79
MDRD	591	8 (7-8)	6.6 (5.1)	431	270
NZDCS	1913	3 (3-4)	5.4 (2.2)	152	728
RENAAL	1139	13 (12-14)	1.2 (0.6)	183	170
SCREAM	35049	5 (3-8)	3.1 (1.6)	500	16900
Sunnybrook	1013	7 (5-10)	2.4 (1.8)	121	306
Subtotal	**122,664**	**7 (5-9)**	**3.3 (2.4)**	**6,083**	**44,135**
eGFR 60+					
ADVANCE	8457	4 (4-4)	2.9 (0.5)	21	407
Geisinger	138682	4 (3-5)	6.2 (3.4)	463	21826
KP Hawaii	15140	5 (4-7)	1.2 (0.7)	19	316
Maccabi	720012	3 (2-4)	3.8 (1.6)	342	23491
NZDCS	7093	3 (3-5)	6.2 (1.5)	100	1081
RCAV	2408814	5 (3-7)	4.4 (0.6)	5471	425718
SCREAM	460353	3 (2-5)	3.5 (1.2)	136	47222
Subtotal	**3,758,551**	**5 (3-7)**	**4.2 (1.3)**	**6,552**	**520,061**
Total	**3,881,215**	**5 (3-7)**	**4.2 (1.3)**	**12,635**	**564,196**

eTable 4. Median number of creatinine measurements within individuals in cohorts participating in the 1-year observation period for change in estimated glomerular filtration rate over time, with subsequent follow-up and number of events

eGFR<60	N	Median # (IQR) of measurements	Follow-up, years (SD)	# of ESKD events	# of ACM events
AASK	825	5 (4-5)	6.4 (3.3)	285	126
BC CKD	9783	6 (5-8)	4.4 (2.9)	2499	4296
CCF	21678	4 (3-6)	1.8 (1.0)	556	3074
Geisinger	18947	4 (3-6)	5.3 (3.8)	863	9937
KP Hawaii	7043	4 (3-6)	1.8 (1.0)	181	595
Maccabi	29208	4 (3-5)	4.5 (2.0)	1090	10383
MASTERPLAN	540	5 (4-5)	4.3 (1.5)	118	94
MDRD	721	5 (5-5)	7.0 (5.3)	532	328
NZDCS	3581	2 (2-2)	5.7 (2.4)	356	1433
RENAAL	1317	9 (8-10)	2.0 (0.8)	297	250
SCREAM	32660	4 (3-5)	3.4 (1.7)	594	15889
Sunnybrook	1289	4 (3-6)	2.7 (2.0)	176	394
Subtotal	**127,592**	**4 (3-5)**	**3.7 (2.6)**	**7,547**	**46,799**
eGFR 60+					
ADVANCE	8722	3 (3-3)	3.9 (0.6)	20	553
Geisinger	114429	3 (2-4)	6.7 (3.8)	419	20285
KP Hawaii	20518	3 (2-4)	1.7 (1.0)	23	501
Maccabi	617351	2 (2-3)	4.3 (1.9)	326	24032
NZDCS	12167	2 (2-3)	6.6 (1.7)	162	1749
RCAV	2151271	3 (2-4)	5.4 (0.6)	5486	433308
SCREAM	301160	3 (2-4)	3.7 (1.4)	106	38139
Subtotal	**3,225,618**	**3 (2-4)**	**5.0 (1.5)**	**6,542**	**518,567**
Total	**3,353,210**	**3 (2-4)**	**5.0 (1.5)**	**14,089**	**565,366**

eTable 5. Median number of creatinine measurements within individuals in cohorts participating in the 3-year observation period for change in estimated glomerular filtration rate over time, with subsequent follow-up and number of events

eGFR<60 ml/min/1.73m^2	N	Median # (IQR) of measurements	Follow-up, years (SD)	# of ESKD events	# of ACM events
AASK	664	9 (8-9)	5.3 (2.7)	198	91
BC CKD	8168	15 (11-20)	3.3 (2.4)	1795	3207
CCF	14631	5 (5-12)	0.7 (0.5)	215	1175
Geisinger	17695	7 (5-11)	4.7 (3.3)	639	8866
KP Hawaii	3484	11 (8-6)	0.7 (0.4)	69	150
Maccabi	28039	8 (5-11)	3.2 (1.4)	806	8434
MASTERPLAN	481	11 (9-12)	2.7 (1.1)	91	64
MDRD	301	11 (10-11)	6.1 (5.1)	229	142
NZDCS	909	4 (3-6)	5.1 (1.9)	69	340
RENAAL	728	17 (16-19)	0.6 (0.4)	81	93
SCREAM	33122	7 (5-10)	2.5 (1.3)	384	14838
Sunnybrook	732	9 (6-13)	2.2 (1.7)	83	206
Total	**108,954**	**9 (7-11)**	**2.8 (2.2)**	**4,659**	**37,606**
eGFR 60+ ml/min/1.73m^2					
ADVANCE	7970	5 (5-5)	2.0 (0.4)	14	275
Geisinger	144273	4 (3-7)	5.7 (3.1)	449	21196
KP Hawaii	9866	7 (5-10)	0.7 (0.4)	14	137
Maccabi	758347	4 (3-6)	3.0 (1.3)	335	21173
NZDCS	3479	4 (3-7)	5.7 (1.4)	53	539
RCAV	2430178	6 (4-9)	3.3 (0.6)	4763	381615
SCREAM	480145	4 (3-6)	2.8 (1.0)	99	43471
Subtotal	**3,834,258**	**6 (4-9)**	**3.3 (1.2)**	**5,727**	**468,406**
Total	**3,943,212**	**6 (4-9)**	**3.3 (1.2)**	**10,386**	**506,012**

eTable 6. Mean and standard deviation of change in estimated glomerular filtration rate over time in cohorts, separately by 1- 2- and 3-year observation period, stratified by baseline estimated glomerular filtration rate, estimated using linear mixed models and linear regression

	1-year eGFR Slope, ml/min/1.73m^2/year				2-year, ml/min/1.73m^2/year				3-year, ml/min/1.73m^2/year			
	Mean slope		SD slope		Mean slope		SD slope		Mean slope		SD slope	
eGFR<60 ml/min/1.73m^2	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**
AASK	-0.31	-0.27	5.69	8.34	-1.06	-1.09	4.19	5.09	-1.11	-1.11	3.20	3.65
BC CKD	-1.14	-1.17	6.44	8.06	-1.12	-1.14	4.13	4.68	-1.12	-1.14	3.21	3.50
CCF	0.82	0.94	7.07	11.09	-0.30	-0.23	4.27	5.82	-0.55	-0.48	3.23	4.11
Geisinger	1.91	1.95	9.03	12.80	0.02	0.07	5.01	6.61	-0.41	-0.36	3.59	4.54
KP Hawaii	1.69	2.04	6.97	11.51	0.27	0.39	4.60	5.92	-0.37	-0.32	3.34	3.92
Maccabi	1.09	1.17	6.24	10.12	-0.33	-0.26	4.05	5.37	-0.38	-0.34	3.19	3.85
MASTERPLAN	-1.92	-1.97	3.68	5.87	-1.42	-1.39	2.89	3.59	-1.27	-1.27	2.44	2.76
MDRD	-4.01	-4.13	5.07	6.73	-3.19	-3.20	3.47	4.00	-2.58	-2.58	2.76	3.01
NZDCS	1.22	1.32	8.83	14.73	-0.33	-0.12	4.42	7.29	-1.03	-0.91	3.36	4.56
RENAAL	-6.04	-6.05	6.86	8.26	-4.92	-4.92	4.56	4.99	-4.12	-4.12	3.18	3.38
SCREAM	1.41	1.47	7.61	11.31	0.02	0.09	4.61	6.14	-0.42	-0.36	3.47	4.33
Sunnybrook	-0.52	-0.33	9.29	12.25	-1.43	-1.43	5.25	6.06	-1.63	-1.62	3.60	3.96
eGFR 60+ ml/min/1.73m^2	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**
ADVANCE	-3.67	-3.67	6.44	13.29	-2.24	-2.24	3.70	6.80	-1.83	-1.84	3.42	4.89
Geisinger	-2.83	-2.67	5.99	12.18	-2.28	-2.17	3.73	6.38	-1.87	-1.78	2.82	4.33
KP Hawaii	-1.42	-1.24	4.09	12.78	-1.49	-1.35	3.95	6.37	-1.29	-1.21	3.29	4.42
Maccabi	-1.24	-1.20	2.81	9.15	-1.06	-1.04	2.16	4.64	-0.75	-0.72	1.71	3.10
NZDCS	-4.54	-4.72	7.14	16.95	-3.71	-3.72	3.98	8.54	-3.35	-3.30	3.35	5.66
RCAV	-2.54	-2.42	6.07	12.71	-2.14	-2.07	4.03	6.62	-1.43	-1.36	3.19	4.57
SCREAM	-1.69	-1.62	5.15	10.87	-1.39	-1.32	3.12	5.67	-1.36	-1.30	2.45	3.95

Mixed effects indicates the best linear unbiased prediction from linear mixed models; the least squares is the beta coefficient from linear regression of eGFR on time. All eGFR values within a given observation period (1-, 2-, 3- years +/- 30%) were used to estimate slope coefficient.

eTable 7. Hazard ratios for end-stage kidney disease associated with a 0.75 ml/min per 1.73 m^2 per year change in estimated glomerular filtration rate over time, separately by 1- 2- and 3-year observation period, stratified by baseline estimated glomerular filtration rate, estimated using linear mixed models and linear regression

	1-year		2-year		3-year	
eGFR<60	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**
AASK	0.72 (0.69, 0.76)	0.87 (0.84, 0.90)	0.69 (0.66, 0.72)	0.77 (0.74, 0.80)	0.65 (0.62, 0.69)	0.72 (0.68, 0.75)
BC CKD	0.84 (0.83, 0.85)	0.89 (0.88, 0.90)	0.77 (0.76, 0.78)	0.81 (0.80, 0.82)	0.72 (0.70, 0.73)	0.75 (0.74, 0.76)
CCF	0.74 (0.72, 0.76)	0.87 (0.86, 0.89)	0.67 (0.65, 0.70)	0.78 (0.76, 0.80)	0.63 (0.61, 0.66)	0.72 (0.69, 0.75)
Geisinger	0.82 (0.80, 0.83)	0.91 (0.90, 0.92)	0.76 (0.74, 0.78)	0.86 (0.84, 0.87)	0.71 (0.69, 0.73)	0.79 (0.77, 0.81)
KP Hawaii	0.70 (0.66, 0.74)	0.84 (0.80, 0.87)	0.62 (0.58, 0.67)	0.72 (0.68, 0.76)	0.54 (0.48, 0.60)	0.65 (0.59, 0.71)
Maccabi	0.76 (0.75, 0.78)	0.87 (0.86, 0.88)	0.71 (0.70, 0.73)	0.79 (0.78, 0.81)	0.61 (0.59, 0.62)	0.69 (0.67, 0.70)
MASTERPLAN	0.76 (0.70, 0.84)	0.88 (0.84, 0.93)	0.61 (0.56, 0.67)	0.72 (0.67, 0.78)	0.57 (0.50, 0.64)	0.64 (0.58, 0.70)
MDRD	0.90 (0.87, 0.93)	0.94 (0.92, 0.96)	0.82 (0.79, 0.85)	0.86 (0.84, 0.89)	0.71 (0.67, 0.76)	0.75 (0.71, 0.79)
NZDCS	0.89 (0.88, 0.91)	0.96 (0.95, 0.96)	0.72 (0.68, 0.76)	0.82 (0.79, 0.86)	0.64 (0.58, 0.70)	0.73 (0.68, 0.78)
RENAAL	0.80 (0.77, 0.83)	0.85 (0.82, 0.88)	0.71 (0.68, 0.75)	0.75 (0.71, 0.78)	0.64 (0.58, 0.70)	0.68 (0.62, 0.73)
SCREAM	0.78 (0.76, 0.80)	0.85 (0.84, 0.87)	0.71 (0.69, 0.73)	0.82 (0.80, 0.83)	0.62 (0.60, 0.64)	0.70 (0.68, 0.73)
Sunnybrook	0.81 (0.77, 0.85)	0.86 (0.83, 0.89)	0.70 (0.65, 0.75)	0.78 (0.74, 0.82)	0.52 (0.46, 0.59)	0.62 (0.56, 0.68)
Meta-analysis	**0.79 (0.76, 0.83)**	**0.88 (0.86, 0.91)**	**0.71 (0.68, 0.74)**	**0.79 (0.77, 0.81)**	**0.63 (0.60, 0.67)**	**0.71 (0.68, 0.73)**
eGFR 60+	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**
ADVANCE	0.83 (0.76, 0.90)	0.95 (0.92, 0.97)	0.63 (0.56, 0.71)	0.85 (0.82, 0.89)	0.64 (0.56, 0.74)	0.80 (0.74, 0.86)
Geisinger	0.80 (0.78, 0.82)	0.95 (0.93, 0.97)	0.73 (0.71, 0.75)	0.90 (0.88, 0.92)	0.69 (0.67, 0.71)	0.83 (0.81, 0.85)
KP Hawaii	0.60 (0.55, 0.66)	0.92 (0.91, 0.94)	0.75 (0.70, 0.80)	0.83 (0.79, 0.87)	0.64 (0.57, 0.72)	0.76 (0.71, 0.82)
Maccabi	0.64 (0.63, 0.66)	0.93 (0.90, 0.95)	0.70 (0.69, 0.71)	0.82 (0.79, 0.84)	0.67 (0.66, 0.68)	0.72 (0.70, 0.75)
NZDCS	0.82 (0.78, 0.86)	0.92 (0.89, 0.95)	0.68 (0.63, 0.74)	0.83 (0.79, 0.87)	0.72 (0.66, 0.79)	0.76 (0.71, 0.82)
RCAV	0.79 (0.78, 0.80)	0.93 (0.93, 0.94)	0.71 (0.71, 0.72)	0.85 (0.84, 0.85)	0.67 (0.66, 0.67)	0.76 (0.76, 0.77)
SCREAM	0.75 (0.71, 0.78)	0.89 (0.85, 0.93)	0.63 (0.61, 0.66)	0.83 (0.79, 0.86)	0.58 (0.55, 0.61)	0.74 (0.70, 0.78)
Meta-analysis	**0.74 (0.69, 0.80)**	**0.93 (0.92, 0.94)**	**0.70 (0.68, 0.72)**	**0.84 (0.82, 0.87)**	**0.66 (0.64, 0.68)**	**0.77 (0.74, 0.80)**

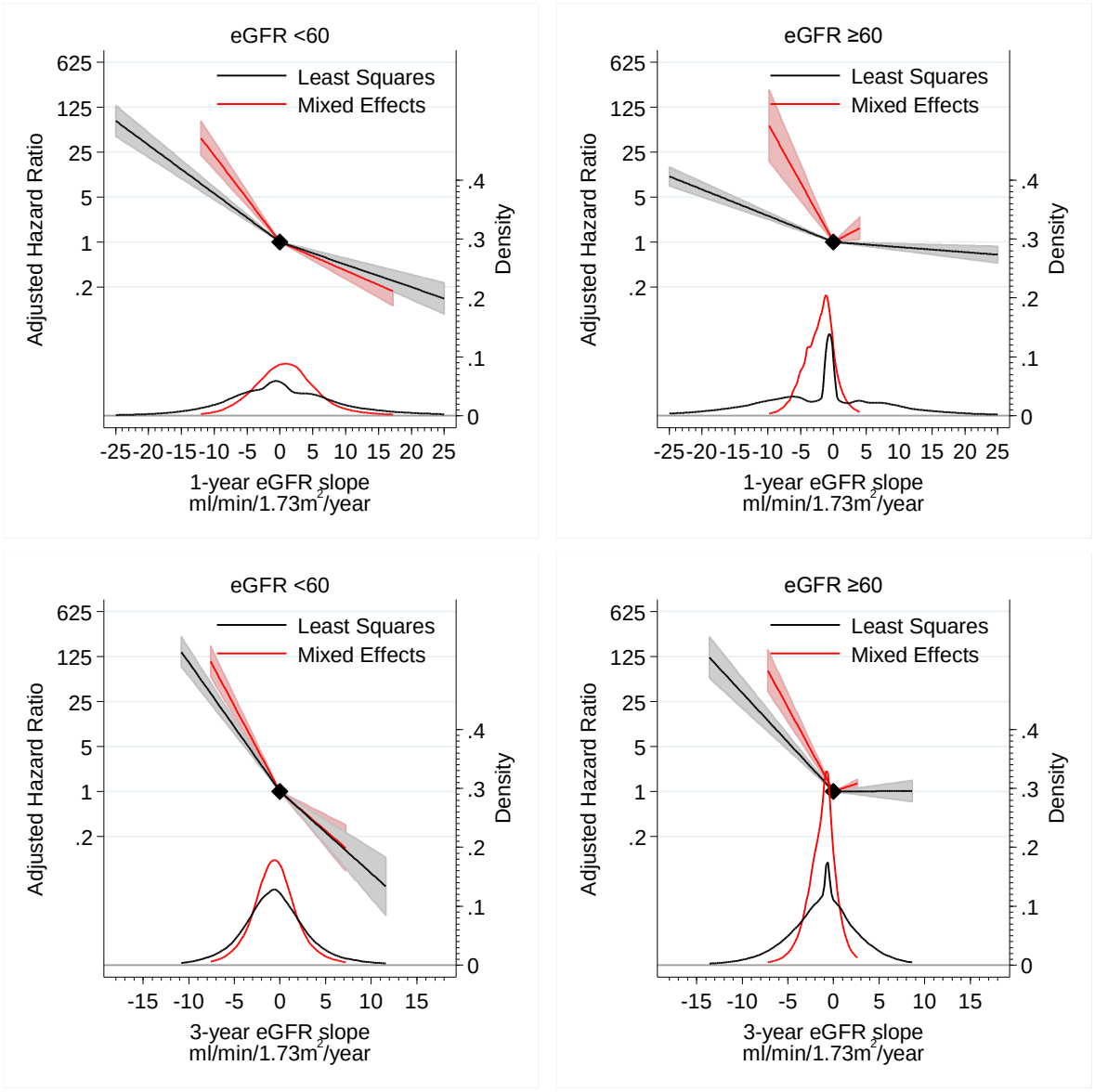
Mixed effects indicates the best linear unbiased prediction from linear mixed models; the least squares is the beta coefficient from linear regression of eGFR on time. All eGFR values within a given observation period (1-, 2-, 3- years +/- 30%) were used to estimate slope coefficient.

eTable 8. Hazard ratios for all-cause mortality associated with a 0.75 ml/min per 1.73 m^2 per year improvement in estimated glomerular filtration rate decline over time, separately by 1- 2- and 3-year observation period, stratified by baseline estimated glomerular filtration rate, estimated using linear mixed models and linear regression

	1-year		2-year		3-year	
eGFR<60	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**
AASK	0.90 (0.84, 0.98)	0.95 (0.90, 0.99)	0.87 (0.81, 0.94)	0.92 (0.87, 0.97)	0.84 (0.76, 0.92)	0.91 (0.84, 0.99)
BC CKD	0.93 (0.92, 0.94)	0.96 (0.95, 0.96)	0.89 (0.88, 0.90)	0.91 (0.90, 0.92)	0.87 (0.86, 0.89)	0.89 (0.88, 0.90)
CCF	0.89 (0.88, 0.90)	0.95 (0.95, 0.96)	0.85 (0.83, 0.86)	0.91 (0.90, 0.93)	0.82 (0.80, 0.84)	0.88 (0.86, 0.89)
Geisinger	0.94 (0.93, 0.95)	0.98 (0.97, 0.98)	0.91 (0.90, 0.92)	0.96 (0.95, 0.96)	0.90 (0.89, 0.90)	0.93 (0.93, 0.94)
KP Hawaii	0.86 (0.84, 0.89)	0.94 (0.92, 0.95)	0.81 (0.79, 0.84)	0.88 (0.85, 0.90)	0.80 (0.76, 0.85)	0.85 (0.81, 0.89)
Maccabi	0.92 (0.91, 0.93)	0.96 (0.96, 0.97)	0.89 (0.89, 0.90)	0.93 (0.93, 0.94)	0.87 (0.87, 0.88)	0.90 (0.90, 0.91)
MASTERPLAN	0.87 (0.79, 0.95)	0.93 (0.88, 0.98)	0.78 (0.70, 0.86)	0.85 (0.79, 0.93)	0.83 (0.72, 0.94)	0.84 (0.76, 0.94)
MDRD	0.96 (0.93, 1.00)	0.98 (0.96, 1.01)	0.97 (0.93, 1.02)	0.98 (0.94, 1.02)	0.98 (0.91, 1.06)	0.98 (0.92, 1.05)
NZDCS	0.94 (0.93, 0.96)	0.96 (0.95, 0.98)	0.92 (0.89, 0.95)	0.95 (0.93, 0.97)	0.88 (0.84, 0.93)	0.92 (0.89, 0.95)
RENAAL	0.96 (0.93, 0.99)	0.97 (0.94, 1.00)	0.92 (0.88, 0.96)	0.93 (0.89, 0.97)	0.89 (0.84, 0.95)	0.90 (0.84, 0.95)
SCREAM	0.93 (0.93, 0.94)	0.97 (0.97, 0.98)	0.90 (0.90, 0.91)	0.95 (0.94, 0.95)	0.89 (0.88, 0.89)	0.92 (0.92, 0.93)
Sunnybrook	0.91 (0.89, 0.94)	0.95 (0.92, 0.97)	0.88 (0.84, 0.92)	0.92 (0.89, 0.95)	0.84 (0.79, 0.89)	0.87 (0.83, 0.92)
Meta-analysis	**0.92 (0.91, 0.94)**	**0.96 (0.95, 0.97)**	**0.89 (0.87, 0.90)**	**0.93 (0.92, 0.94)**	**0.87 (0.86, 0.89)**	**0.90 (0.89, 0.92)**
eGFR 60+	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**	**Mixed Effects**	**Least Squares**
ADVANCE	0.95 (0.93, 0.98)	0.98 (0.96, 1.00)	0.89 (0.86, 0.93)	0.96 (0.94, 0.99)	0.87 (0.83, 0.90)	0.93 (0.90, 0.96)
Geisinger	0.98 (0.97, 0.98)	0.99 (0.99, 0.99)	0.95 (0.95, 0.96)	0.98 (0.98, 0.99)	0.94 (0.93, 0.94)	0.96 (0.96, 0.97)
KP Hawaii	0.88 (0.84, 0.92)	0.99 (0.97, 1.01)	0.86 (0.83, 0.89)	0.94 (0.91, 0.96)	0.82 (0.78, 0.86)	0.89 (0.85, 0.93)
Maccabi	0.95 (0.94, 0.96)	0.99 (0.99, 0.99)	0.90 (0.90, 0.91)	0.96 (0.96, 0.97)	0.86 (0.86, 0.87)	0.93 (0.93, 0.93)
NZDCS	0.97 (0.95, 0.98)	0.98 (0.97, 0.99)	0.95 (0.93, 0.98)	0.98 (0.97, 1.00)	0.93 (0.90, 0.97)	0.95 (0.93, 0.98)
RCAV	0.98 (0.98, 0.98)	1.00 (0.99, 1.00)	0.96 (0.96, 0.97)	0.98 (0.98, 0.98)	0.93 (0.93, 0.94)	0.96 (0.96, 0.96)
SCREAM	0.96 (0.95, 0.96)	0.99 (0.99, 0.99)	0.93 (0.93, 0.93)	0.97 (0.97, 0.97)	0.92 (0.91, 0.92)	0.95 (0.95, 0.96)
Meta-analysis	**0.96 (0.95, 0.97)**	**0.99 (0.99, 0.99)**	**0.93 (0.91, 0.95)**	**0.97 (0.96, 0.98)**	**0.90 (0.88, 0.92)**	**0.95 (0.94, 0.96)**

Mixed effects indicates the best linear unbiased prediction from linear mixed models; the least squares is the beta coefficient from linear regression of eGFR on time. All eGFR values within a given observation period (1-, 2-, 3- years +/- 30%) were used to estimate slope coefficient.

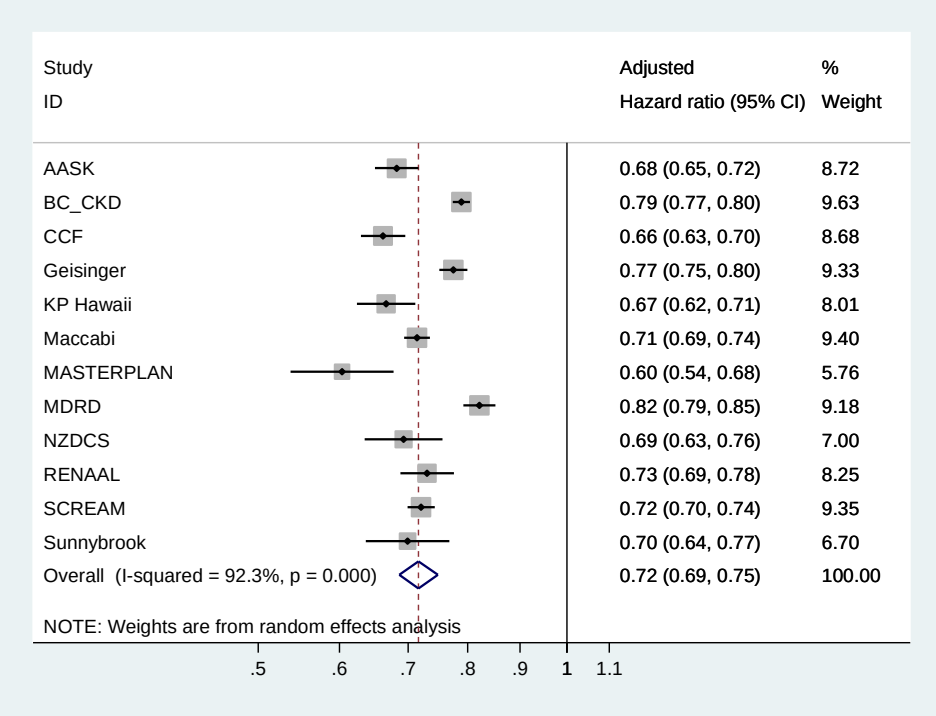
eFigure 1. Adjusted hazard ratios and density of 1-year (top row) and 3-year (bottom row) eGFR slopes



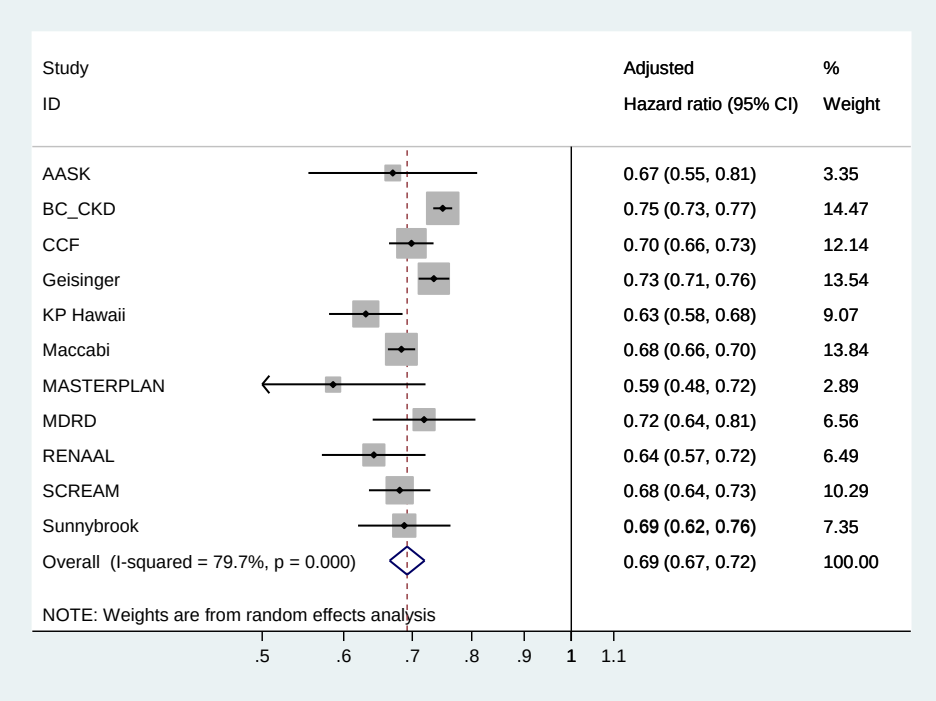
Mixed effects indicates the best linear unbiased prediction from linear mixed models; the least squares is the beta coefficient from linear regression of eGFR on time.

eFigure 2. Forest plot of adjusted hazard ratios for end-stage kidney disease associated with a 0.75 ml/min per 1.73 m^2 per year change in estimated glomerular filtration rate over 2-years estimated using linear mixed models, stratified by baseline estimated glomerular filtration rate and age

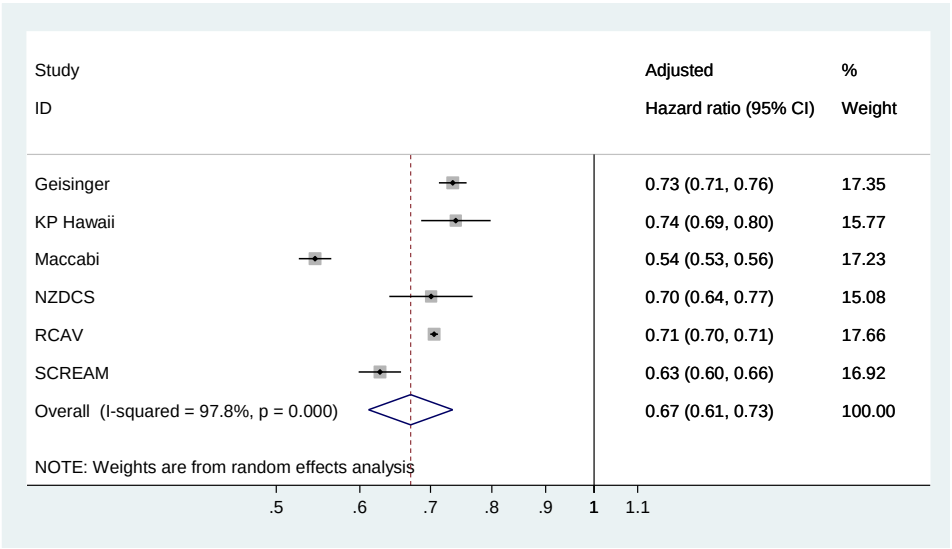
eGFR<60 ml/min/1.73 m^2; Age <65 years



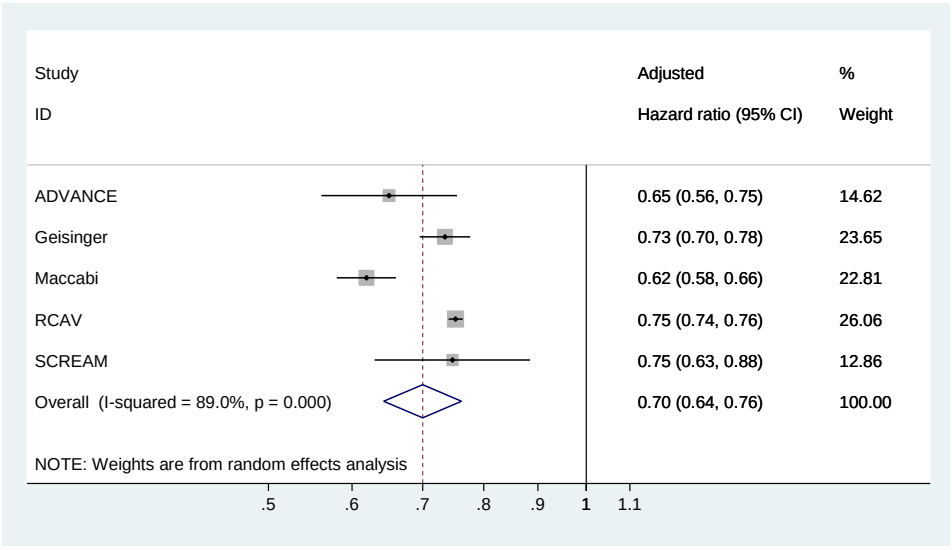
eGFR<60 ml/min/1.73 m^2; Age ≥65 years



eGFR 60+ ml/min/1.73 m^2; Age <65 years

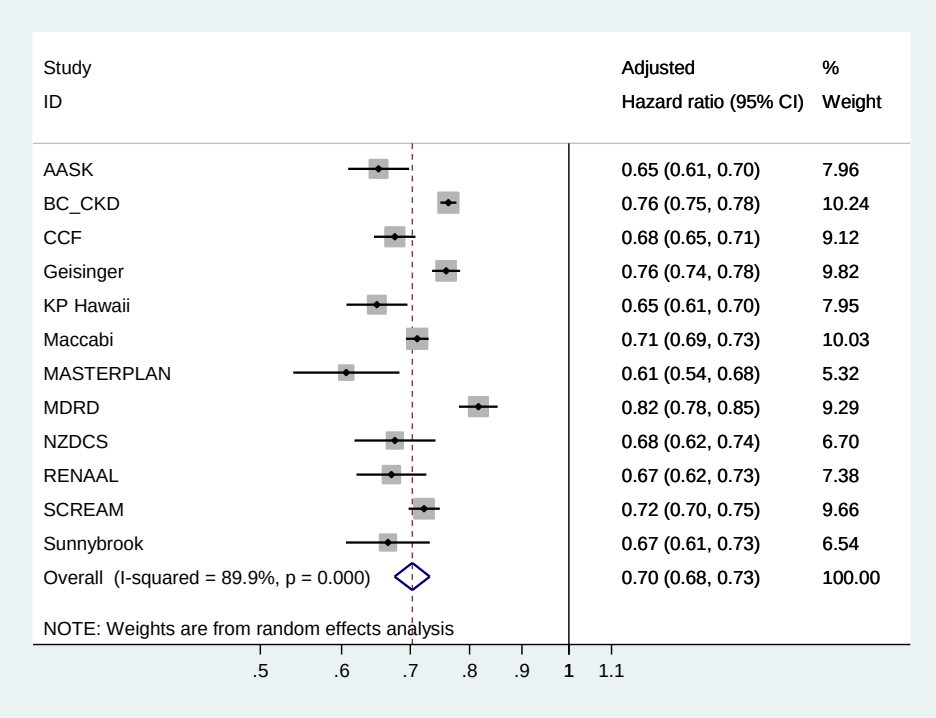


eGFR 60+ ml/min/1.73 m^2; Age ≥65 years

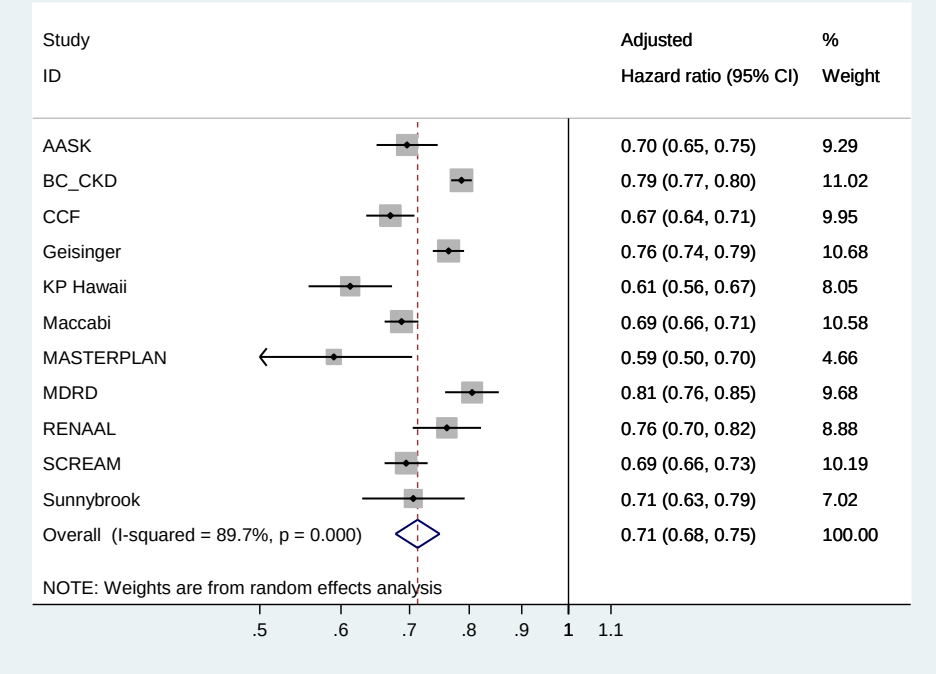


eFigure 3. Forest plot of adjusted hazard ratios for end-stage kidney disease associated with a 0.75 ml/min per 1.73 m^2 per year change in estimated glomerular filtration rate over 2-years estimated using linear mixed models, stratified by baseline estimated glomerular filtration rate and sex

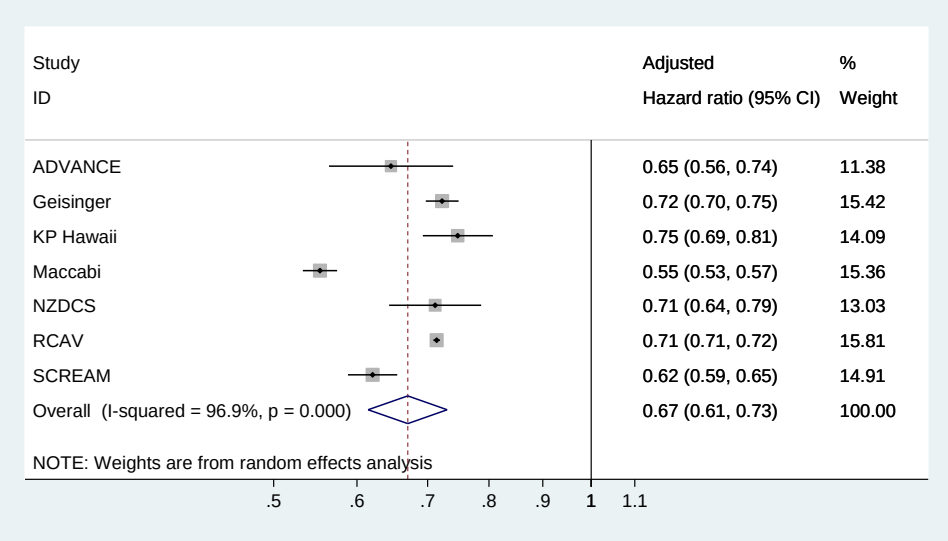
eGFR<60 ml/min/1.73 m^2; Male



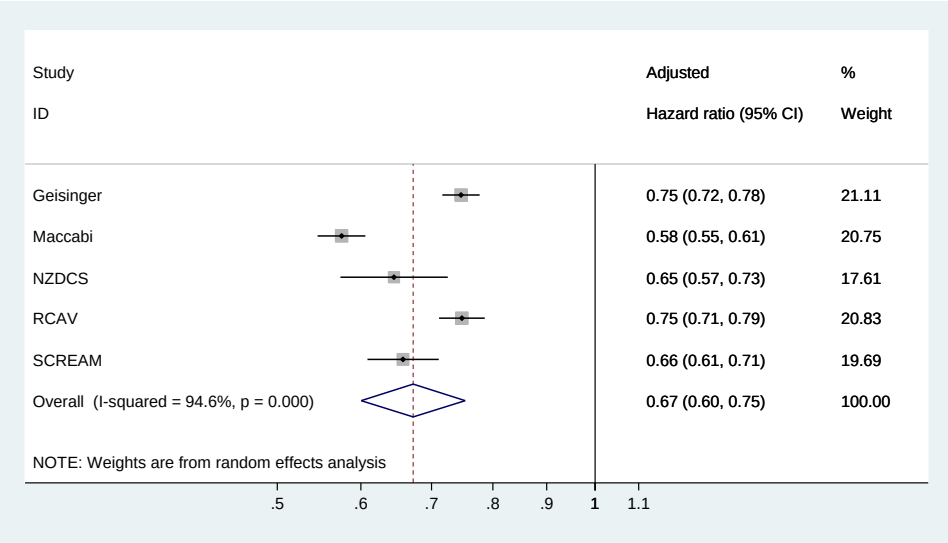
eGFR<60 ml/min/1.73 m^2; Female



eGFR 60+ ml/min/1.73 m^2; Male

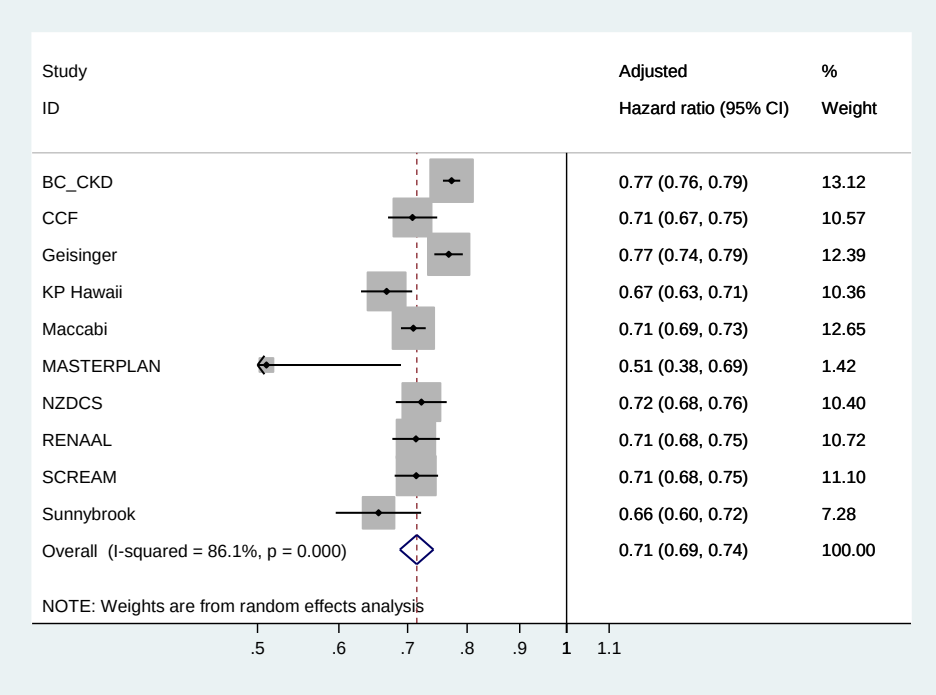


eGFR 60+ ml/min/1.73 m^2; Female

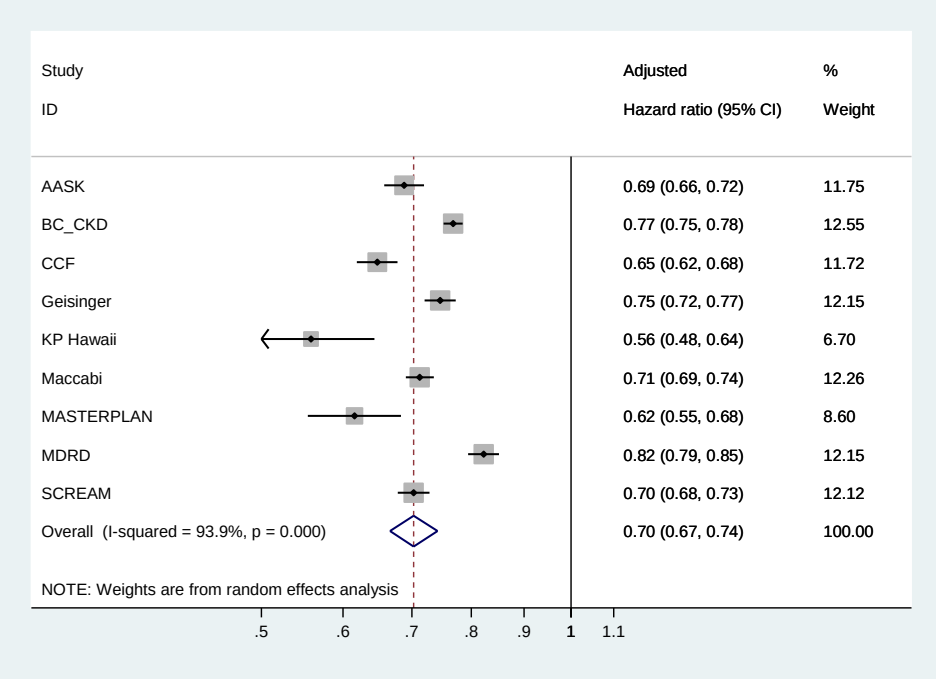


eFigure 4. Forest plot of adjusted hazard ratios for end-stage kidney disease associated with a 0.75 ml/min per 1.73 m^2 per year change in estimated glomerular filtration rate over 2-years estimated using linear mixed models, stratified by baseline estimated glomerular filtration rate and diabetes status

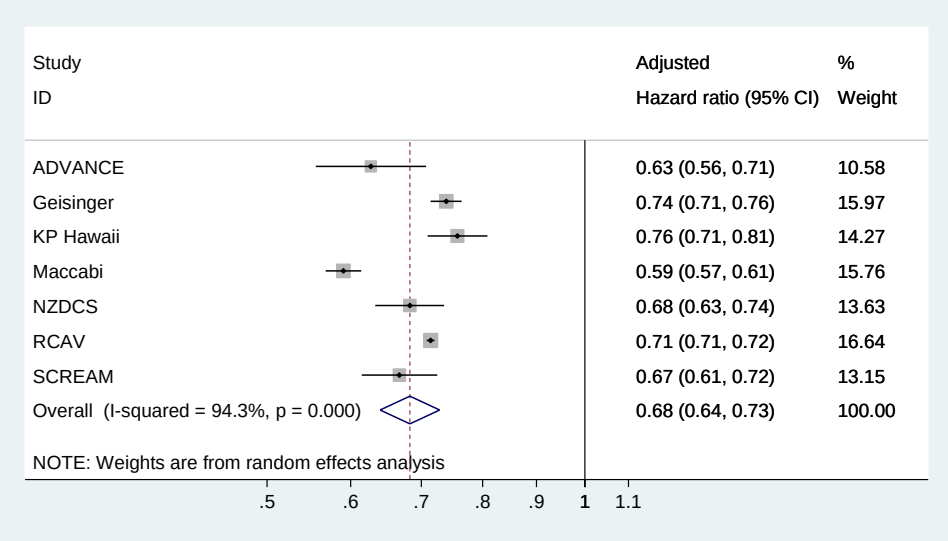
eGFR<60 ml/min/1.73 m^2; diabetes



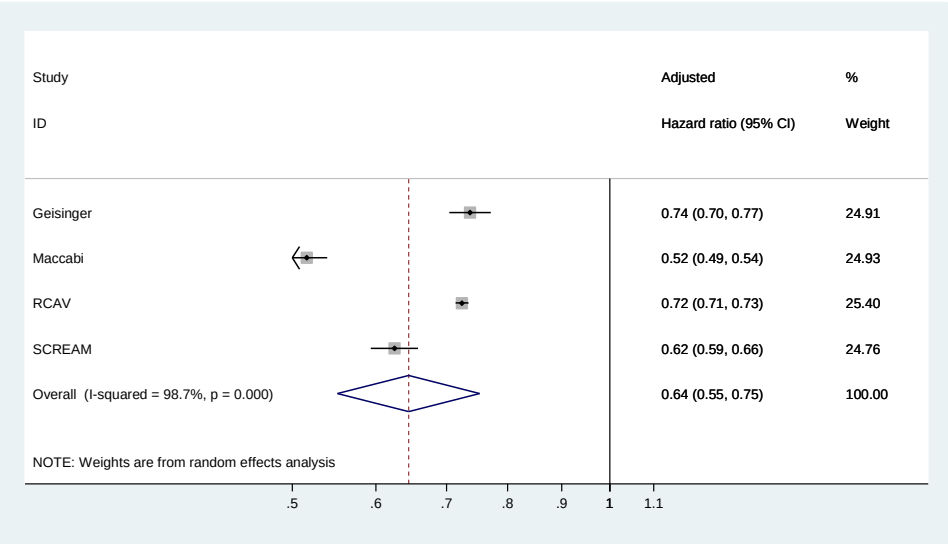
eGFR<60 ml/min/1.73 m^2; no diabetes



eGFR 60+ ml/min/1.73 m^2; diabetes

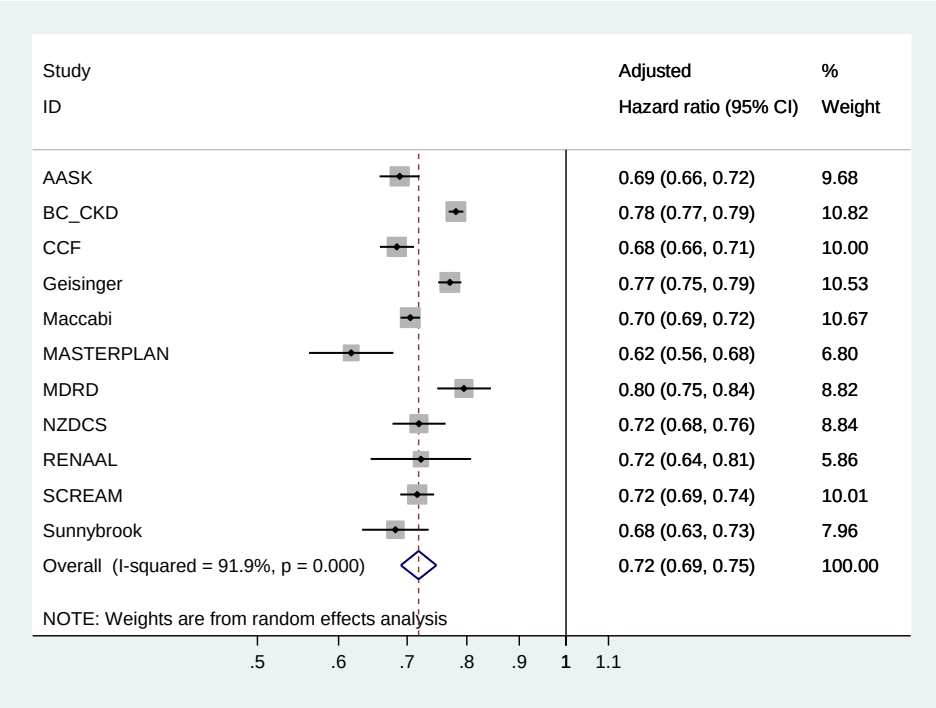


eGFR 60+ ml/min/1.73 m^2; no diabetes

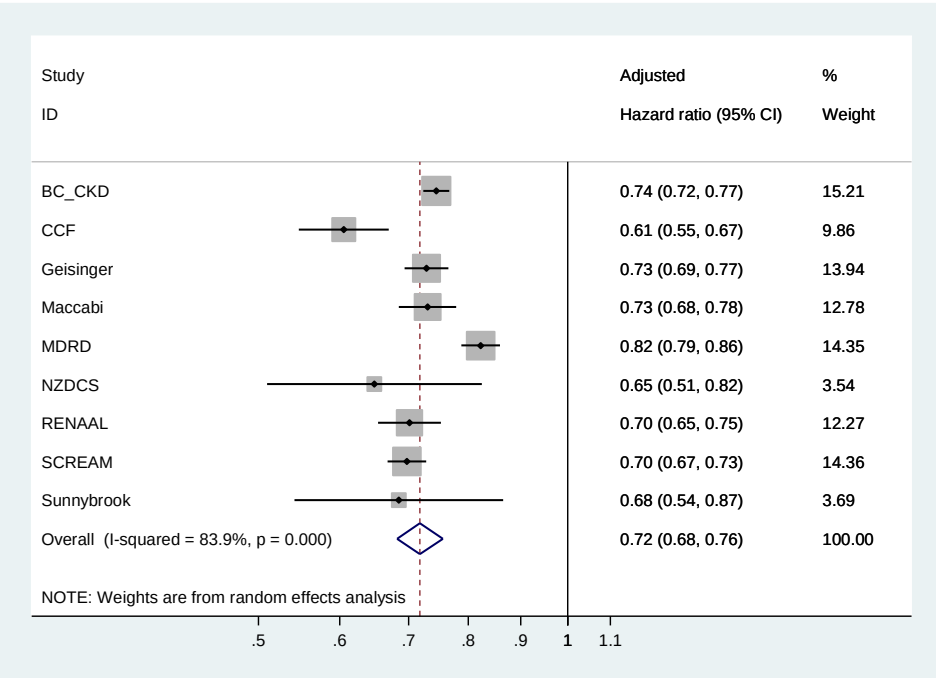


eFigure 5. Forest plot of adjusted hazard ratios for end-stage kidney disease associated with a 0.75 ml/min per 1.73 m^2 per year change in estimated glomerular filtration rate over 2-years estimated using linear mixed models, stratified by baseline estimated glomerular filtration rate and hypertension status

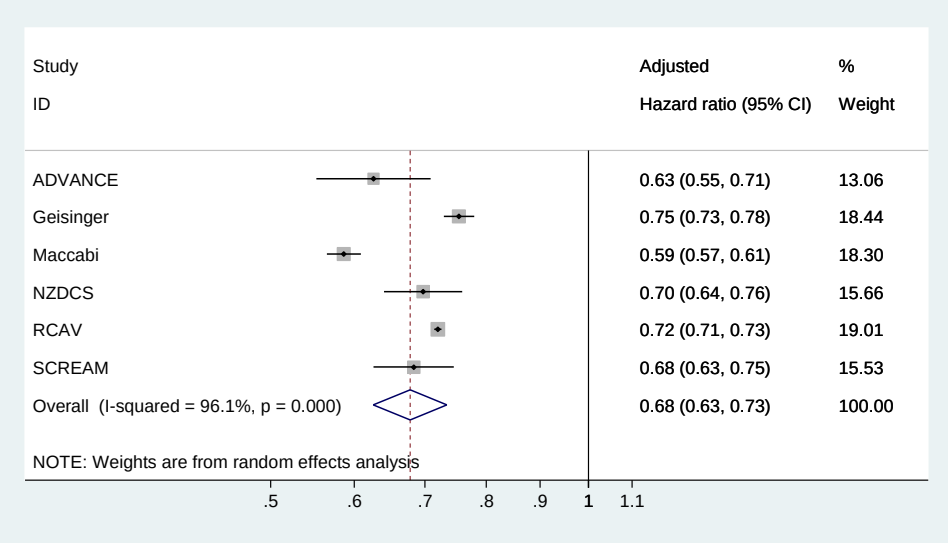
eGFR<60 ml/min/1.73 m^2; hypertension



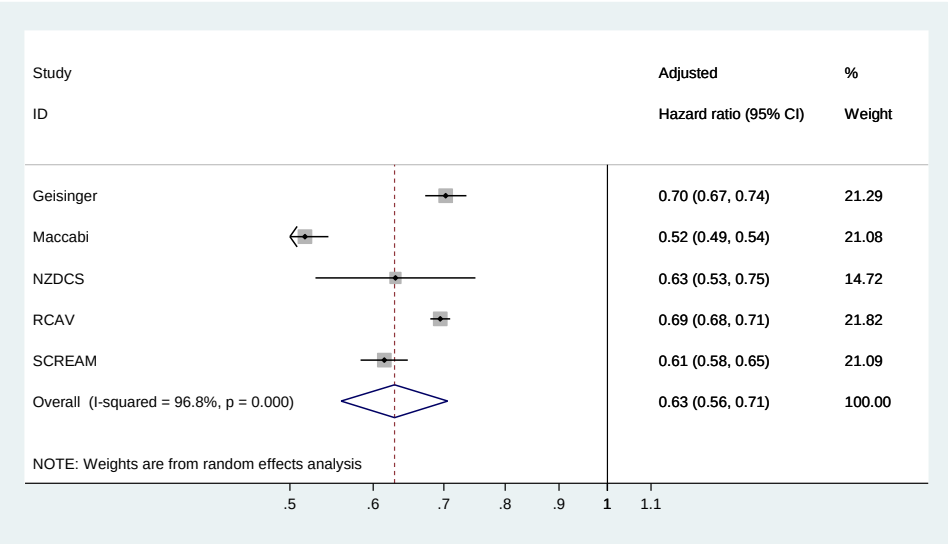
eGFR<60 ml/min/1.73 m^2; no hypertension



eGFR 60+ ml/min/1.73 m^2; hypertension

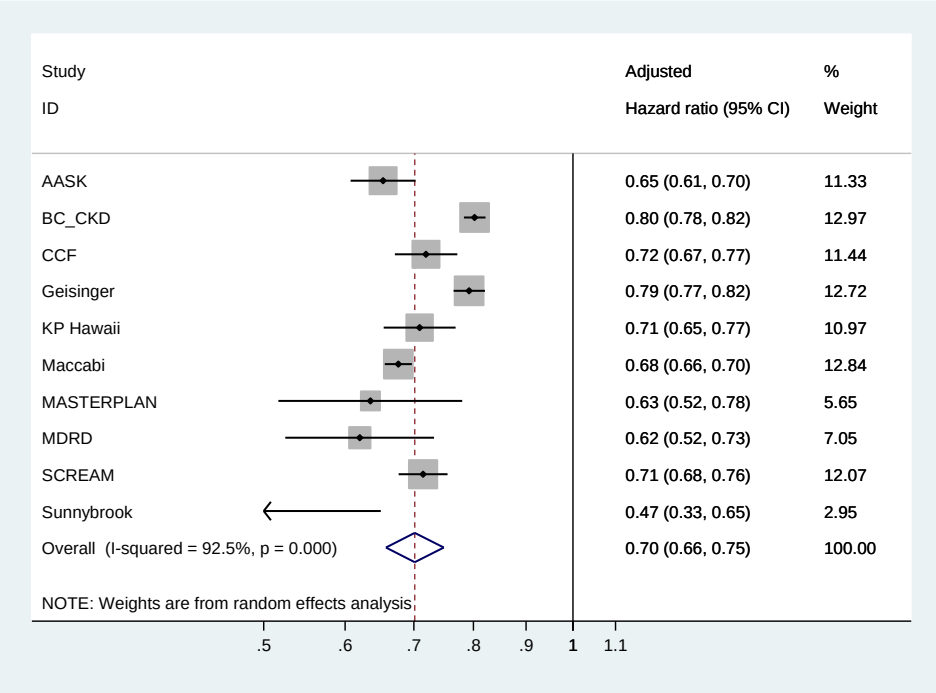


eGFR 60+ ml/min/1.73 m^2; no hypertension

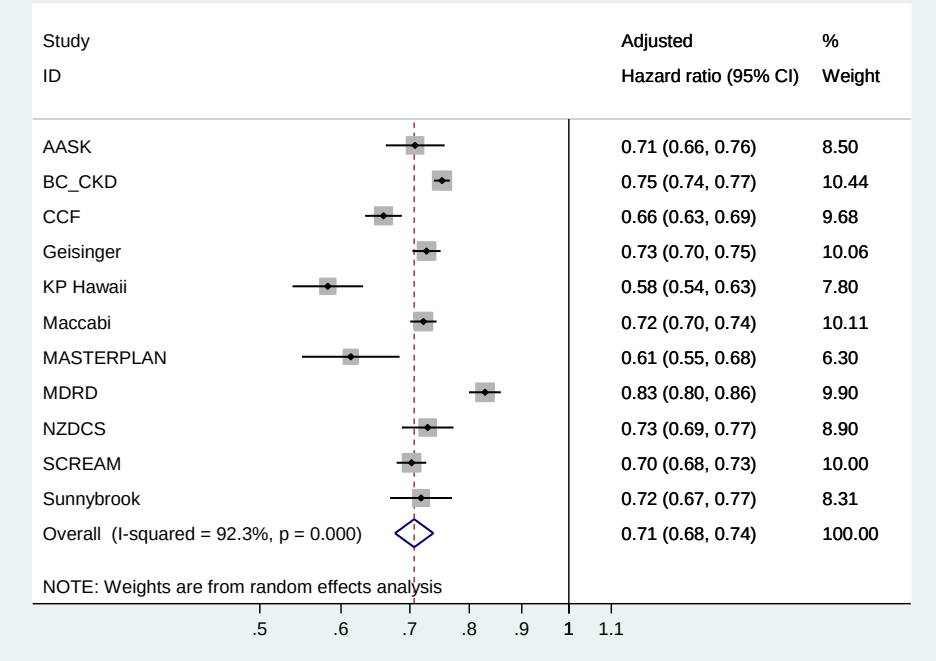


eFigure 6. Forest plot of adjusted hazard ratios for end-stage kidney disease associated with a 0.75 ml/min per 1.73 m^2 per year change in estimated glomerular filtration rate over 2-years estimated using linear mixed models, stratified by baseline estimated glomerular filtration rate and history of cardiovascular disease status

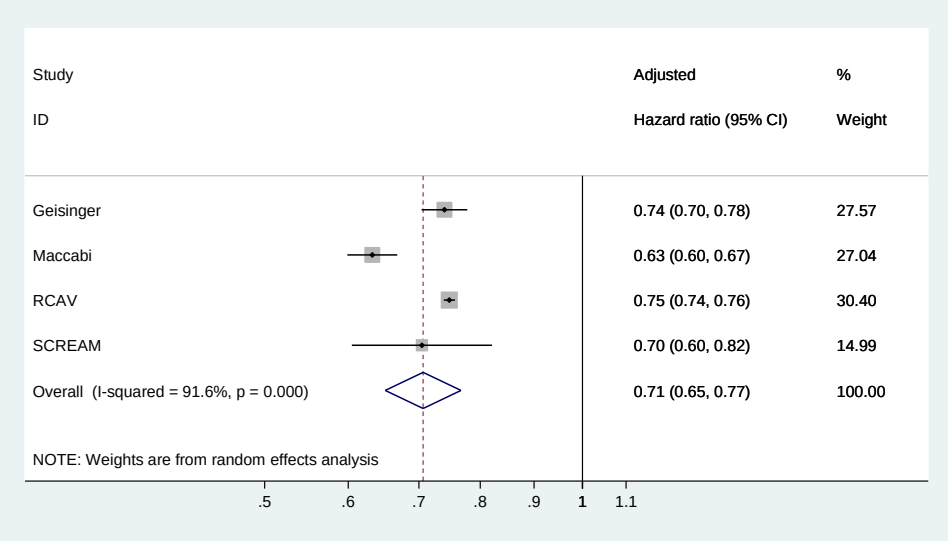
eGFR<60 ml/min/1.73 m^2; history of cardiovascular disease



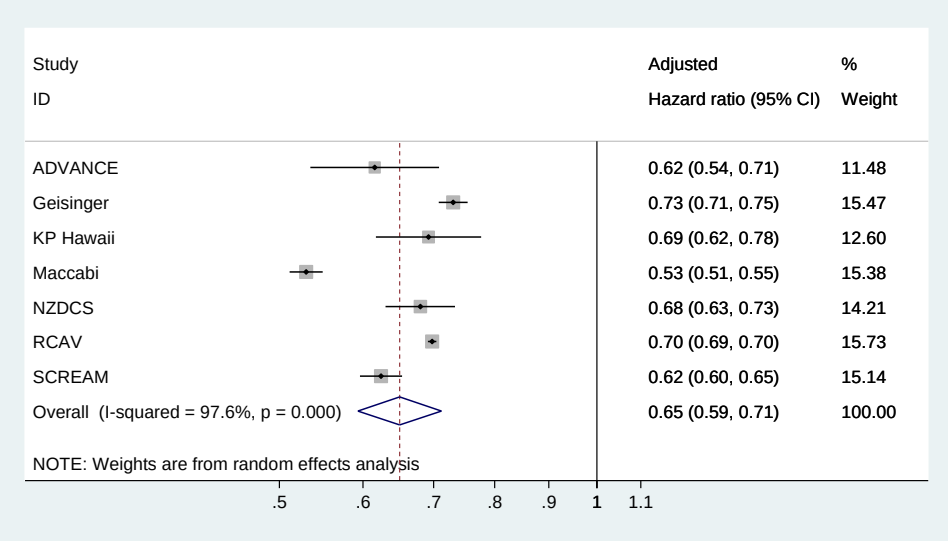
eGFR<60 ml/min/1.73 m^2; no history of cardiovascular disease



eGFR 60+ ml/min/1.73 m^2; history of cardiovascular disease

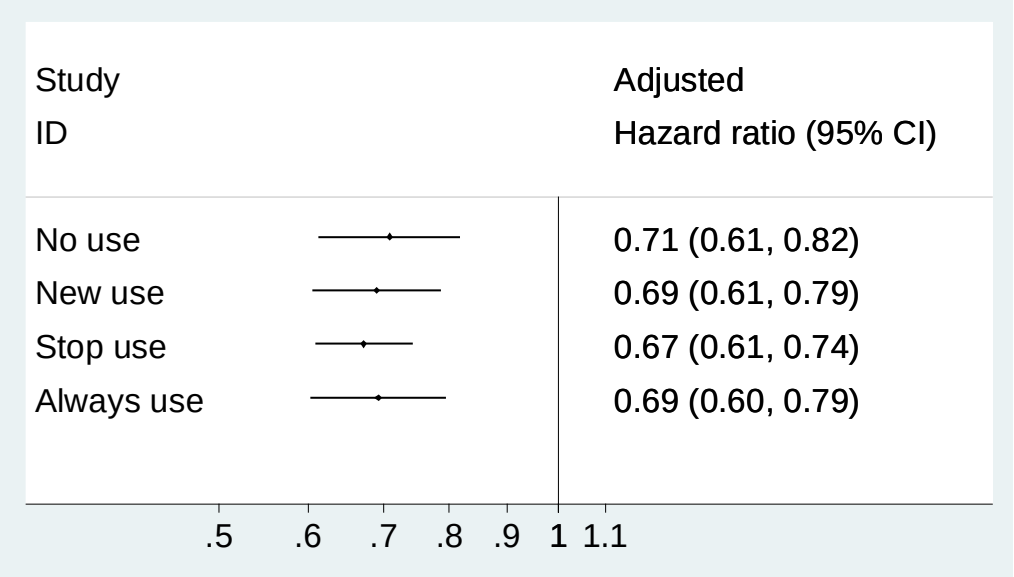


eGFR 60+ ml/min/1.73 m^2; no history of cardiovascular disease

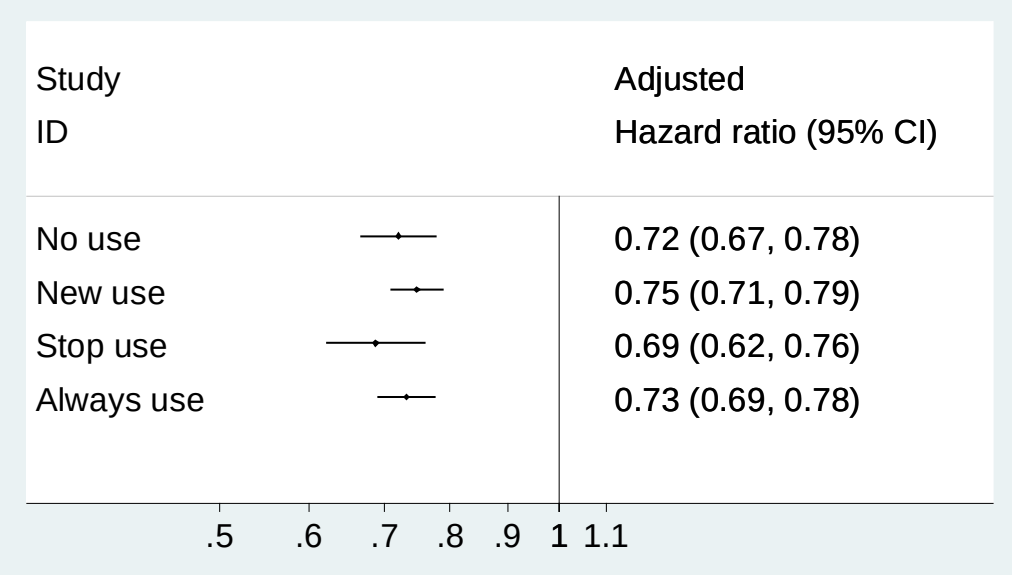


eFigure 7. Adjusted hazard ratios for end-stage kidney disease associated with a 0.75 ml/min/1.73 m^2 per year change eGFR over 2-years estimated using linear mixed models, stratified by baseline estimated glomerular filtration rate and including an interaction term for category of ACE/ARB use at first and last visit (e.g. New use corresponds to no use at the first visit and use at the last visit of the baseline period used to calculate the slope of eGFR decline).

eGFR<60 ml/min/1.73 m^2



eGFR 60+ ml/min/1.73 m^2



References

1. Matsushita, K, van der Velde, M, Astor, BC, Woodward, M, Levey, AS, de Jong, PE, Coresh, J, Gansevoort, RT: Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet,* 375**:** 2073-2081, 2010.
2. Matsushita, K, Mahmoodi, BK, Woodward, M, Emberson, JR, Jafar, TH, Jee, SH, Polkinghorne, KR, Shankar, A, Smith, DH, Tonelli, M, Warnock, DG, Wen, CP, Coresh, J, Gansevoort, RT, Hemmelgarn, BR, Levey, AS: Comparison of risk prediction using the CKD-EPI equation and the MDRD study equation for estimated glomerular filtration rate. *JAMA,* 307**:** 1941-1951, 2012.
3. Hallan, SI, Matsushita, K, Sang, Y, Mahmoodi, BK, Black, C, Ishani, A, Kleefstra, N, Naimark, D, Roderick, P, Tonelli, M, Wetzels, JF, Astor, BC, Gansevoort, RT, Levin, A, Wen, CP, Coresh, J: Age and Association of Kidney Measures With Mortality and End-stage Renal Disease. *JAMA,* 308**:** 2349-2360, 2012.
4. Levey, AS, Coresh, J, Greene, T, Marsh, J, Stevens, LA, Kusek, JW, Van Lente, F, Collaboration, fCKDE: Expressing the Modification of Diet in Renal Disease Study Equation for Estimating Glomerular Filtration Rate with Standardized Serum Creatinine Values. *Clin Chem,* 53**:** 766-772, 2007.
5. Levey, AS, Stevens, LA, Schmid, CH, Zhang, YL, Castro, AF, 3rd, Feldman, HI, Kusek, JW, Eggers, P, Van Lente, F, Greene, T, Coresh, J: A new equation to estimate glomerular filtration rate. *Ann Intern Med,* 150**:** 604-612, 2009.
6. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group: KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney International Supplements,* 3**:** 1-150, 2013.
7. Wright, JT, Jr., Bakris, G, Greene, T, Agodoa, LY, Appel, LJ, Charleston, J, Cheek, D, Douglas-Baltimore, JG, Gassman, J, Glassock, R, Hebert, L, Jamerson, K, Lewis, J, Phillips, RA, Toto, RD, Middleton, JP, Rostand, SG: Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA,* 288**:** 2421-2431, 2002.
8. Patel, A, MacMahon, S, Chalmers, J, Neal, B, Woodward, M, Billot, L, Harrap, S, Poulter, N, Marre, M, Cooper, M, Glasziou, P, Grobbee, DE, Hamet, P, Heller, S, Liu, LS, Mancia, G, Mogensen, CE, Pan, CY, Rodgers, A, Williams, B: Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. *Lancet,* 370**:** 829-840, 2007.
9. Levin, A, Djurdjev, O, Beaulieu, M, Er, L: Variability and risk factors for kidney disease progression and death following attainment of stage 4 CKD in a referred cohort. *Am J Kidney Dis,* 52**:** 661-671, 2008.
10. Schold, JD, Navaneethan, SD, Jolly, SE, Poggio, ED, Arrigain, S, Saupe, W, Jain, A, Sharp, JW, Simon, JF, Schreiber, MJ, Jr., Nally, JV, Jr.: Implications of the CKD-EPI GFR estimation equation in clinical practice. *Clin J Am Soc Nephrol,* 6**:** 497-504, 2011.
11. Perkins, RM, Bucaloiu, ID, Kirchner, HL, Ashouian, N, Hartle, JE, Yahya, T: GFR decline and mortality risk among patients with chronic kidney disease. *Clin J Am Soc Nephrol,* 6**:** 1879-1886, 2011.
12. Lee, BJ, Forbes, K: The role of specialists in managing the health of populations with chronic illness: the example of chronic kidney disease. *BMJ,* 339**:** b2395, 2009.
13. Shalev, V, Chodick, G, Goren, I, Silber, H, Kokia, E, Heymann, AD: The use of an automated patient registry to manage and monitor cardiovascular conditions and related outcomes in a large health organization. *Int J Cardiol,* 152**:** 345-349, 2011.
14. van Zuilen, AD, Bots, ML, Dulger, A, van der Tweel, I, van Buren, M, Ten Dam, MA, Kaasjager, KA, Ligtenberg, G, Sijpkens, YW, Sluiter, HE, van de Ven, PJ, Vervoort, G, Vleming, LJ, Blankestijn, PJ, Wetzels, JF: Multifactorial intervention with nurse practitioners does not change cardiovascular outcomes in patients with chronic kidney disease. *Kidney Int,* 82**:** 710-717, 2012.
15. Klahr, S, Levey, AS, Beck, GJ, Caggiula, AW, Hunsicker, L, Kusek, JW, Striker, G: The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. *N Engl J Med,* 330**:** 877-884, 1994.
16. Elley, CR, Kenealy, T, Robinson, E, Drury, PL: Glycated haemoglobin and cardiovascular outcomes in people with Type 2 diabetes: a large prospective cohort study. *Diabet Med,* 25**:** 1295-1301, 2008.
17. Kovesdy, CP, Norris, KC, Boulware, LE, Lu, JL, Ma, JZ, Streja, E, Molnar, MZ, Kalantar-Zadeh, K: Association of Race With Mortality and Cardiovascular Events in a Large Cohort of US Veterans. *Circulation,* 132**:** 1538-1548, 2015.

18. Brenner, BM, Cooper, ME, de Zeeuw, D, Keane, WF, Mitch, WE, Parving, HH, Remuzzi, G, Snapinn, SM, Zhang, Z, Shahinfar, S: Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med*, 345**:** 861-869, 2001.
19. Gasparini, A, Evans, M, Coresh, J, Grams, ME, Norin, O, Qureshi, AR, Runesson, B, Barany, P, Arnlov, J, Jernberg, T, Wettermark, B, Elinder, CG, Carrero, JJ: Prevalence and recognition of chronic kidney disease in Stockholm healthcare. *Nephrol Dial Transplant*, 31**:** 2086-2094, 2016.
20. Tangri, N, Stevens, LA, Griffith, J, Tighiouart, H, Djurdjev, O, Naimark, D, Levin, A, Levey, AS: A predictive model for progression of chronic kidney disease to kidney failure. *JAMA*, 305**:** 1553-1559, 2011.