Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

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eMethods

We used sub-distribution hazard and standard hazard regression (Cox regression) to model the association between eGFR and risks of kidney failure and death, stratified by age (65-69, 70-74, 75-79, and ≥80 years). We estimated stratified sub-distributional hazard ratios using Cox regression weighted for the probability of censoring. To obtain individual record weights, we first restructured the data in an expanded risk set and calculated time-dependent probability of censoring weights for study participants who experienced a competing event (i.e., death as a competing event for the kidney failure analysis and kidney failure for mortality). These individuals have a weight of 1 in the analysis until they experience the competing event, after which they are kept in the risk set, but their weight decreases. The decrease is based on the conditional probability of being censored, which we estimated using a non-parametric (Kaplan–Meier) estimate of the censoring distribution. The weights only change at times when there is a failure for the event of interest and the value of censoring distribution has changed. Similar to the Fine and Gray model this method requires to model each sub-distribution hazard separately, although it is computationally faster and relaxes the assumption of common censoring distribution of the Fine and Gray model. We used the multistate package in R for theses analyses.

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eTable 1. Baseline characteristics, captured in the fixed-threshold CKD cohort

Characteristics	Same day (N=37,018)	Earlier[a] (N=16,157)	Later[a] (N=731)	Only (N=72,703)	Only[b] (N=523)
Male	17,069 (46.1)	7,377 (45.7)	376 (51.4)	32,548 (44.8)	216 (41.3)
First age[c], y	60 (18-105)	76 (53-101)	37 (18-51)	75 (55-105)	41 (19-52)
18-39	749 (2.0)	−	545 (74.6)	−	224 (42.8)
40-64	30,142 (81.4)	290 (1.8)	186 (25.4)	2,429 (3.3)	299 (57.2)
≥65	6,127 (16.6)	15,867 (98.2)	−	70,274 (96.7)	−
Index age[d], y	61 (18-106)	77 (65-102)	37 (19-51)	76 (65-107)	42 (19-54)
18-39	677 (1.8)	−	504 (68.9)	−	203 (38.8)
40-64	29,777 (80.4)	−	227 (31.1)	−	320 (61.2)
≥65	6,564 (17.7)	16,157 (100)	−	72,703 (100)	−
First eGFR[c]	53.5 (15.0-59)	53.3 (16.3-59)	55.0 (16.8-59)	55.6 (15.0-59)	55.8 (15.4-59)
60-74	−	−	−	−	−
45-59	27,222 (73.5)	14,435 (89.3)	647 (88.5)	68,455 (94.2)	486 (92.9)
15-44	9,796 (26.5)	1,722 (10.7)	84 (11.5)	4,248 (5.8)	37 (7.1)
Index eGFR[d]	51.7 (15-59)	48.9 (15.1-59)	52.3 (15.7-59)	54.5 (15.1-59)	54.5 (15.3-59)
60-74	−	−	−	−	−
45-59	24,869 (67.2)	10,991 (68.0)	561 (76.7)	66,870 (92.0)	458 (87.6)
15-44	12,149 (32.8)	5,166 (32.0)	170 (23.3)	5,833 (8.0)	65 (12.4)
Albuminuria[e]					
Unmeasured	2,091 (5.6)	1,002 (6.2)	19 (2.6)	3,373 (4.6)	18 (3.4)
Normal/mild	25,471 (68.8)	10,949 (67.8)	324 (44.3)	58,557 (80.5)	301 (57.6)
Moderate	5,310 (14.3)	2,860 (17.7)	113 (15.5)	8,514 (11.7)	84 (16.1)
Severe	4,146 (11.2)	1,346 (8.3)	275 (37.6)	2,259 (3.1)	120 (22.9)
CVDM[f]					
Neither	20,128 (54.4)	5,857 (36.3)	499 (68.3)	36,093 (49.6)	370 (70.8)
CV only	4,882 (13.2)	3,766 (23.3)	44 (6.0)	16,299 (22.4)	34 (6.5)
DM only	7,801 (21.1)	3,500 (21.7)	153 (20.9)	12,034 (16.6)	98 (18.7)
Both	4,207 (11.4)	3,034 (18.8)	35 (4.8)	8,277 (11.4)	21 (4.0)

Values are median (range) or number (%). Percentages do not add to 100% because of rounding.
[a]Earlier/later: the fixed eGFR threshold algorithm identified the study participants at an earlier or later date, as compared to the age-adapted algorithm.
[b]Captured by the fixed-threshold algorithm only during the accrual period and by the age-adapted algorithm before the study start date (April 1, 2009).
[c]First age and first eGFR refer to the values at the beginning of the qualifying period. eGFR: estimated glomerular filtration rate (mL/min/1.73 m^2).
[d]Last age (baseline age) and last eGFR (index eGFR) refer to the values at the end of the qualifying period (study entry or index date).
[e]Albuminuria was categorized as normal or mild, moderate, severe, or unmeasured based on the most recent outpatient values, with the following types of measurement in descending order of preference: albumin-to-creatinine ratio (<30, 30 to 300, or >300 mg/g), protein-to-creatinine ratio (<150, 150 to 500, or >500 mg/g), and urine dipstick protein (negative or trace, 1+, or ≥2+).
[f]CVDM: presence of cardiovascular disease (CV: congestive heart failure, myocardial infarction, peripheral vascular disease, or stroke) or diabetes mellitus (DM) at baseline.

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eTable 2. Baseline characteristics, captured in the age-adapted CKD cohort

Characteristics	Same day (N=37,018)	Later[a] (N=16,157)	Earlier[a] (N=731)	Only (N=7,817)	Only[b] (N=19,486)
Male	17,069 (46.1)	7,377 (45.7)	376 (51.4)	3,636 (46.5)	8,169 (41.9)
First age[c], y	60 (18-105)	79 (65-106)	34 (18-39)	34 (18-39)	82 (65-109)
18-39	749 (2.0)	−	731 (100)	7,817 (100)	−
40-64	30,142 (81.4)	−	−	−	−
≥65	6,127 (16.6)	16,157 (100)	−	−	19,486 (100)
Index age[d], y	61 (18-106)	80 (65-106)	36 (19-51)	36 (18-51)	83 (66-111)
18-39	677 (1.8)	−	651 (89.1)	7,635 (97.7)	−
40-64	29,777 (80.4)	−	80 (10.9)	182 (2.3)	−
≥65	6,564 (17.7)	16,157 (100)	−	−	19,486 (100)
First eGFR[c]	53.4 (15.0-74)	40.6 (15.3-44)	66.9 (36.3-74)	70.4 (16.1-74)	41.0 (15.2-44)
60-74	47 (0.1)	−	631 (86.3)	7,322 (93.7)	−
45-59	26,719 (72.2)	−	94 (12.9)	454 (5.8)	−
15-44	10,252 (27.7)	16,157 (100)	6 (0.8)	41 (0.5)	19,486 (100)
Index eGFR[d]	51.7 (15-59)	39.0 (15-44)	59.1 (16.8-74)	69.6 (18.6-74)	39.6 (15.0-44)
60-74	−	−	338 (46.2)	7,070 (90.4)	−
45-59	24,869 (67.2)	−	332 (45.4)	699 (8.9)	−
15-44	12,149 (32.8)	16,157 (100)	61 (8.3)	48 (0.6)	19,486 (100)
Albuminuria[e]					
Unmeasured	2,091 (5.6)	505 (3.1)	43 (5.9)	695 (8.9)	649 (3.3)
Normal/mild	25,471 (68.8)	10,663 (66.0)	322 (44.0)	6,291 (80.5)	13,756 (70.6)
Moderate	5,310 (14.3)	3,373 (20.9)	113 (15.5)	529 (6.8)	3,717 (19.1)
Severe	4,146 (11.2)	1,616 (10.0)	253 (34.6)	302 (3.9)	1,364 (7.0)
CVDM[f]					
Neither	20,128 (54.4)	4,493 (27.8)	514 (70.3)	7,251 (92.8)	6,243 (32.0)
CV only	4,882 (13.2)	4,523 (28.0)	35 (4.8)	194 (2.5)	6,154 (31.6)
DM only	7,801 (21.1)	3,156 (19.5)	157 (21.5)	335 (4.3)	3,043 (15.6)
Both	4,207 (11.4)	3,985 (24.7)	25 (3.4)	37 (0.5)	4,046 (20.8)

Values are median (range) or number (%). Percentages do not add to 100% because of rounding.
[a]Earlier/later: the age-adapted algorithm identified the study participants at an earlier or later date, as compared to the fixed eGFR threshold algorithm.
[b]Captured by the age-adapted algorithm only during the accrual period and by the fixed-threshold algorithm before the study start date (April 1, 2009).
[c]First age and first eGFR refer to the values at the beginning of the qualifying period. eGFR: estimated glomerular filtration rate (mL/min/1.73 m^2).
[d]Last age (baseline age) and last eGFR (index eGFR) refer to the values at the end of the qualifying period (study entry or index date).
[e]Albuminuria was categorized as normal or mild, moderate, severe, or unmeasured based on the most recent outpatient values, with the following types of measurement in descending order of preference: albumin-to-creatinine ratio (<30, 30 to 300, or >300 mg/g), protein-to-creatinine ratio (<150, 150 to 500, or >500 mg/g), and urine dipstick protein (negative or trace, 1+, or ≥2+).
[f]CVDM: presence of cardiovascular disease (CV: congestive heart failure, myocardial infarction, peripheral vascular disease, or stroke) or diabetes mellitus (DM) at baseline.

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eTable 3. Baseline characteristics of people aged ≥65 years with normal/mild albuminuria, by index eGFR

Characteristics	eGFR 45-59[a] (N=54,342)	eGFR 60-89[b] (N=90,393)
Male	23,473 (43.2)	42,529 (47.1)
Index age, y		
Median (IQR)	76 (71-82)	70 (67-75)
65-69	11,469 (21.1)	43,643 (48.3)
70-74	12,880 (23.7)	25,778 (28.5)
75-79	12,009 (22.1)	11,484 (12.7)
≥80	17,984 (33.1)	9,488 (10.5)
Index eGFR		
Median (IQR)	55.2 (51.8-57.8)	80.5 (71.5-86.7)
45-59	54,342 (100)	-
60-74	-	30,398 (33.6)
75-89	-	59,995 (66.4)
Albuminuria[c]		
Normal/mild	54,342 (100)	90,393 (100)
CVDM[d]		
Neither	29,148 (53.6)	62,991 (69.7)
CV only	11,978 (22.0)	11,120 (12.3)
DM only	8,364 (15.4)	12,422 (13.7)
Both	4,852 (8.9)	3,860 (4.3)

Values are number (%), otherwise stated. Percentages do not add to 100% because of rounding.
CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate (mL/min/1.73 m^2); IQR: inter-quartile range.
[a]Incident CKD cases identified only by the fixed-eGFR-threshold definition
[b]Non-CKD controls.
[c]Albuminuria normal or mild was defined based on the most recent outpatient values prior to cohort entry, with the following types of measurement in descending order of preference: albumin-to-creatinine ratio (<30 mg/g), protein-to-creatinine ratio (<150 mg/g), and urine dipstick protein (negative or trace).
[d]CVDM: presence of cardiovascular disease (CV: congestive heart failure, myocardial infarction, peripheral vascular disease, or stroke) or diabetes mellitus (DM) at baseline.

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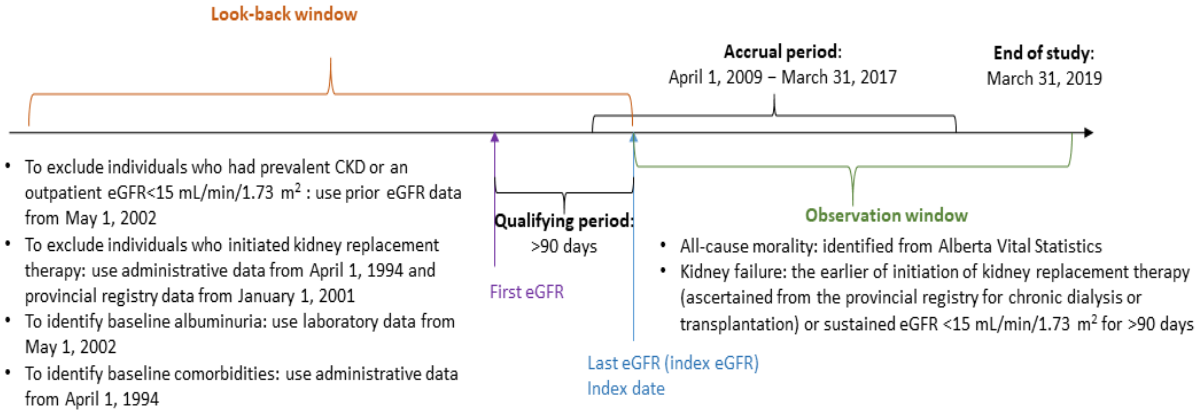
eFigure 1. Study design and data sources



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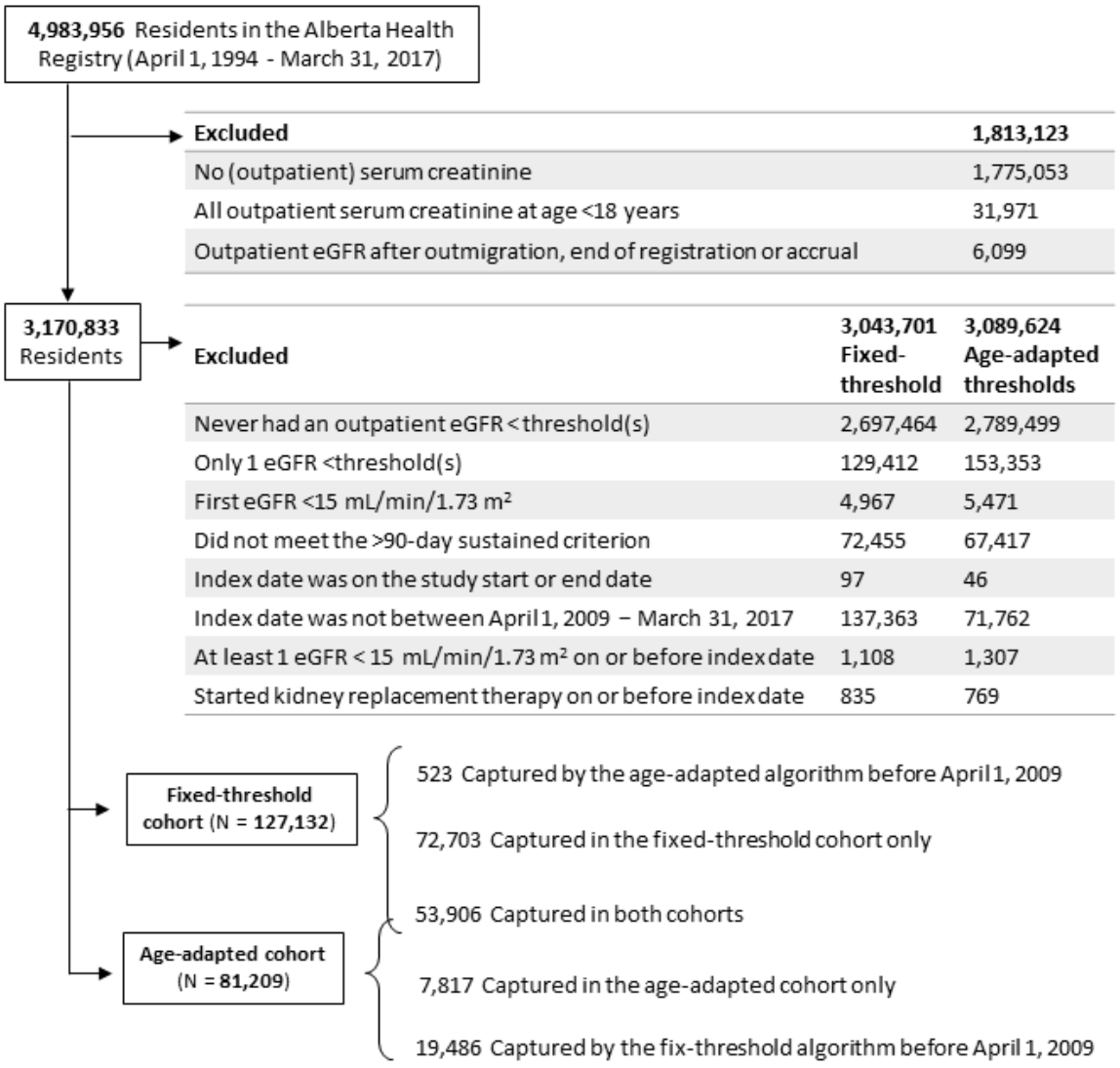
eFigure 2. Cohort formation for two eGFR-based CKD cohorts



Legend: Algorithms to identify CKD, defined by sustained eGFR below a fixed or age-adapted eGFR threshold for >3 months.

The Alberta population registry started in 1994. Serum creatinine data started on May 1, 2002, with nearly complete coverage (~98% of the Alberta population) from July 1, 2003 and complete coverage from January 1, 2005. About 1/3 of the population (n=1,573,084) who never had an eGFR measurement largely comprises people who were in the registry before the study start date (April 1, 2009). We considered all the available information preceding Apr 1, 2009 (look-back window for eGFR measurements and other data) to minimize the inclusion of prevalent cases in the incident CKD cohorts between Apr 1, 2009 and Mar 31, 2017.

Of note, Alberta residents who did not have an outpatient serum creatinine measurement comprised 18.5% of those who were registered for at least 1 fiscal year between Apr 1, 2009 and Mar 31, 2017. Most of these people without a creatinine measure (~85%) were younger than 40 years, an expected figure considering that a screening test for serum creatinine is not recommended under 40 years of age in the absence of clinical indications.

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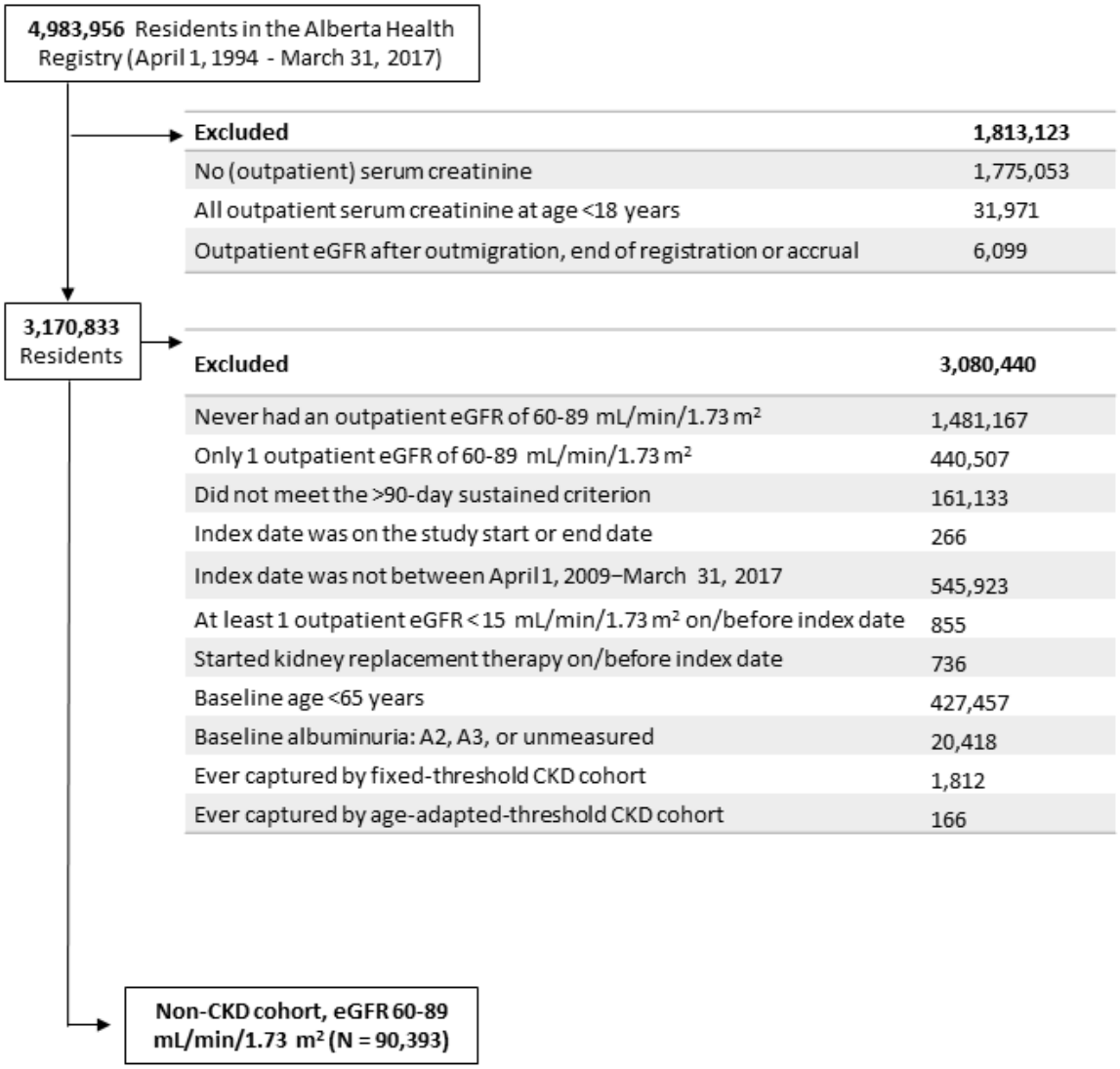
eFigure 3. Cohort formation for non-CKD controls



Legend: Algorithms to identify a non-CKD cohort with sustained eGFR of 60-89 mL/min/1.73 m^2 for >3 months, age ≥65 years and normal/mild albuminuria at baseline, without prior entry into the fixed and age-adapted cohorts.

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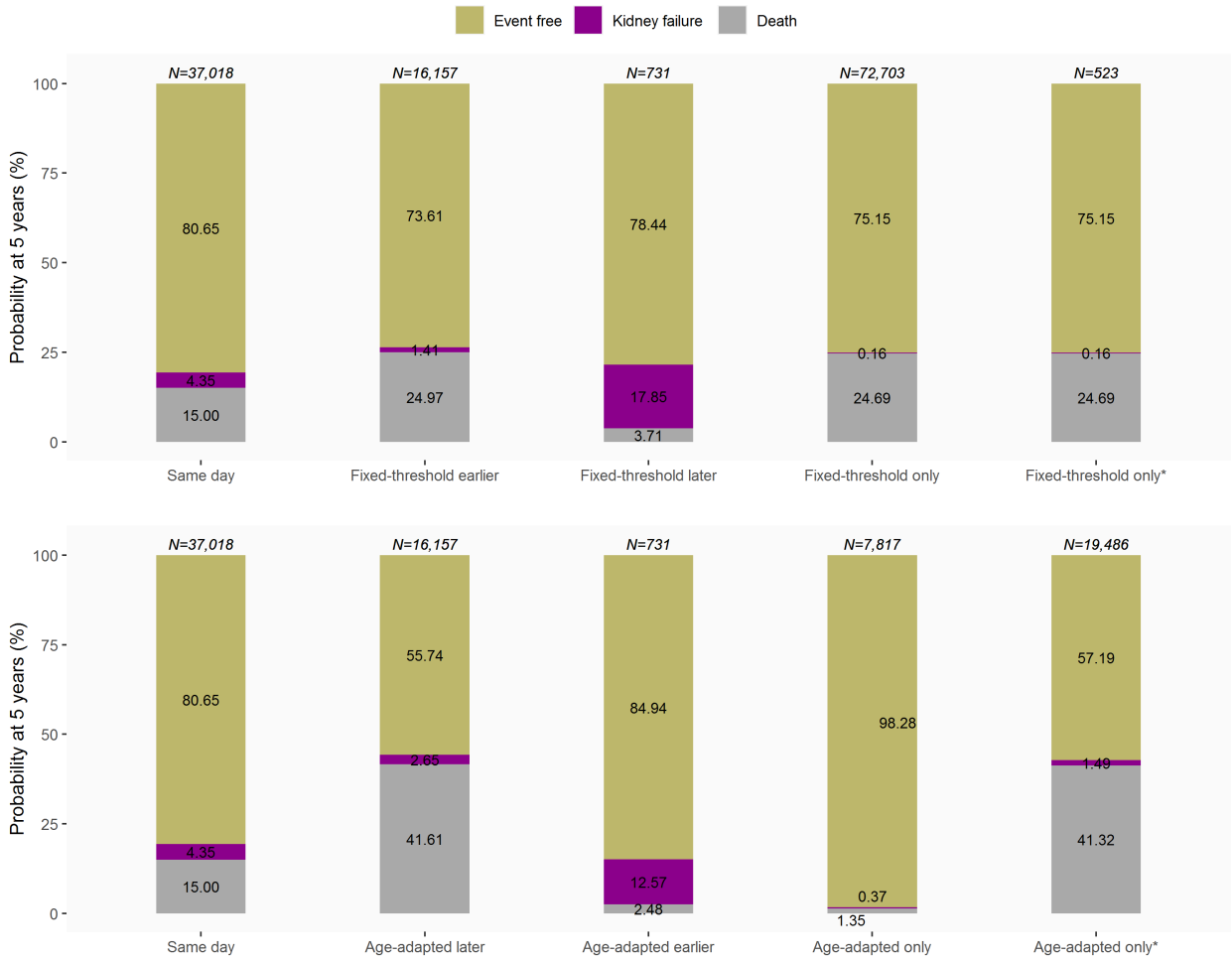
eFigure 4. Risks of kidney failure and death at 5 years, in subgroups defined by the agreement between the fixed and age-adapted eGFR threshold for CKD



Legend: Risks were estimated from entry in each of the two cohorts (fixed-threshold, top; age-adapted, bottom).
Earlier/later: one algorithm identified the study participants earlier or later than the other algorithm.
*Captured by one algorithm only during the accrual period but captured by the other algorithm before the study start date (April 1, 2009).

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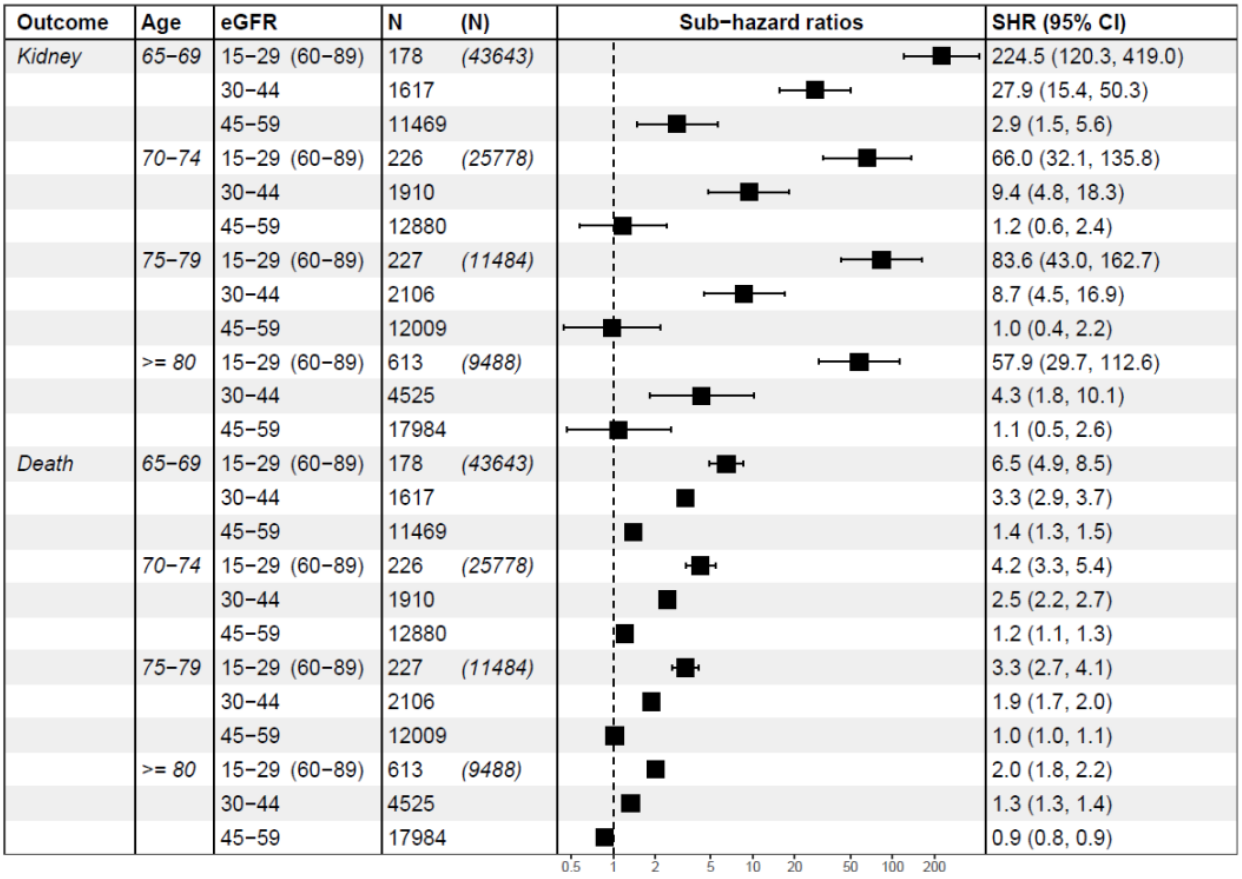
eFigure 5. Sub-distribution hazard model



Legend: Analyses were restricted to people aged ≥65 years with normal/mild albuminuria. Outcomes were kidney failure and death. Age in years. eGFR (estimated glomerular filtration rate in mL/min/1.73 m^2) indicates the level of comparison vs. an eGFR of 60-89 mL/min/1.73 m^2 (reference category). CKD was defined using the fixed-threshold approach. Study participants were assigned to each eGFR category based on the index eGFR at cohort entry. People without CKD were defined using sustained eGFR 60-89 mL/min/1.73 m^2 for >3 months. N indicates the number of individuals defined by age and index eGFR. SHR indicates sub-hazard ratio; CI indicates confidence interval.

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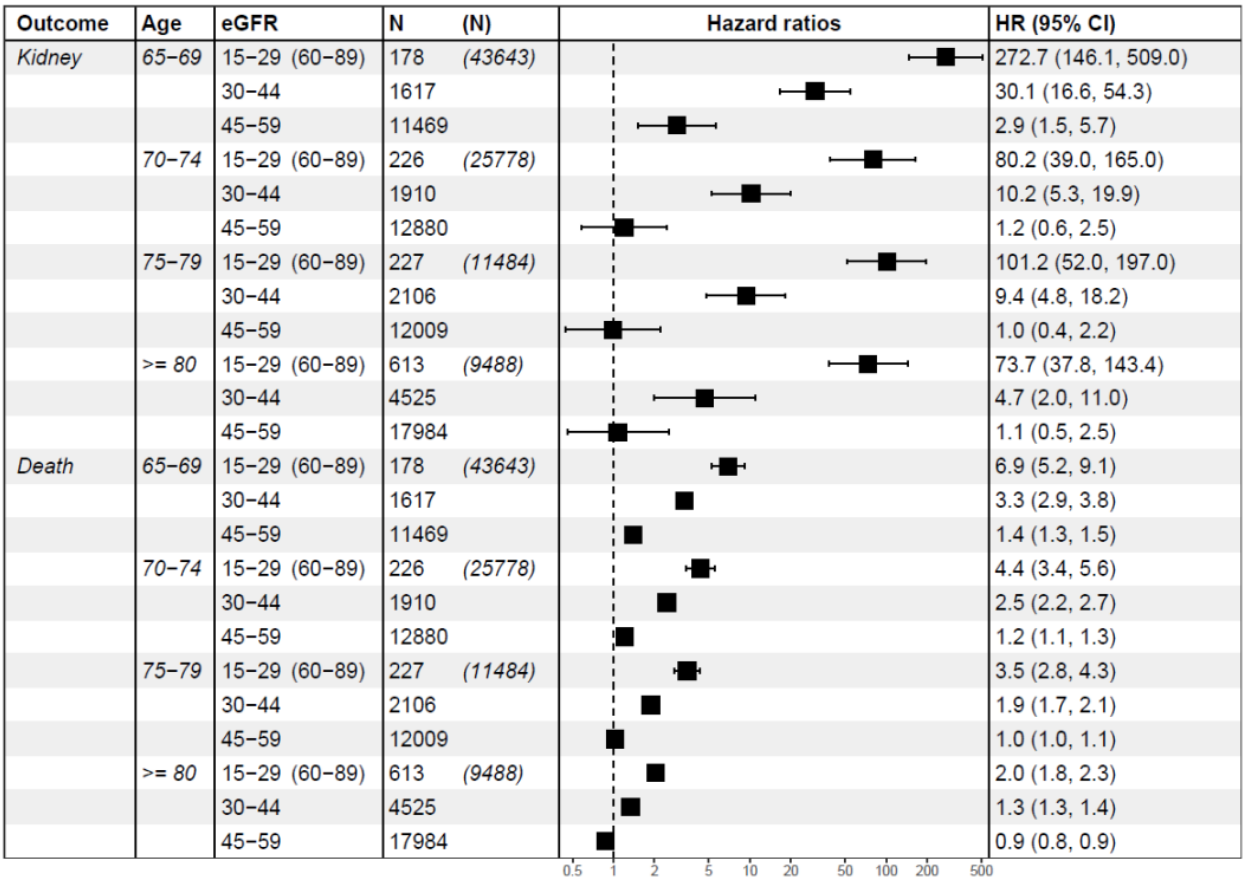
eFigure 6. Hazard model



Legend: Analyses were restricted to people aged ≥65 years with normal/mild albuminuria. Outcomes were kidney failure and death. Age in years. eGFR (estimated glomerular filtration rate in mL/min/1.73 m^2) indicates the level of comparison vs. an eGFR of 60-89 mL/min/1.73 m^2 (reference category). CKD was defined using the fixed-threshold approach. Study participants were assigned to each eGFR category based on the index eGFR at cohort entry. People without CKD were defined using sustained eGFR 60-89 mL/min/1.73 m^2 for >3 months. N indicates the number of individuals defined by age and index eGFR. HR indicates hazard ratio; CI indicates confidence interval.

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