

Supplementary Information

Acute kidney injury in patients with non-valvular atrial fibrillation treated with rivaroxaban or warfarin: a population-based study from the United Kingdom

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AKI, acute kidney injury

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Supplementary Table 1. Read codes for AKI.

Read code	Description
K04..00	Acute renal failure
K040.00	Acute renal tubular necrosis
K041.00	Acute renal cortical necrosis
K042.00	Acute renal medullary necrosis
K043.00	Acute drug-induced renal failure
K044.00	Acute renal fail urin obstruct
K04y.00	Other acute renal failure
K04z.00	Acute renal failure NOS
Kyu2000	[X]Other acute renal failure
G500400	Acute pericarditis - uraemic
K101000	Acute pyelonephritis without medullary necrosis
K101100	Acute pyelonephritis with medullary necrosis
K04..11	ARF - Acute renal failure
K04..12	Acute kidney injury
K043000	Acute renal failure due to ACE inhibitor
K043100	Acute renal failure induced by aminoglycoside
K043300	Acute renal failure induced by cyclosporin A
K043400	Acute renal failure induced by non-steroid anti-inflamm drug
K045.00	Acute renal failure due to non-traumatic rhabdomyolysis
K046.00	Acute renal failure induced by toxin
K04B.00	Acute renal failure due to traumatic rhabdomyolysis
K04C.00	Acute kidney injury stage 1
K04D.00	Acute kidney injury stage 2
K04E.00	Acute kidney injury stage 3

Supplementary Table 2. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function: on-treatment analysis.

Baseline eGFR	Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
AKI Method A						
Any eGFR	Warfarin (N=7129)	11,201.1	75	67.0	1.0 (ref)	
	Rivaroxaban (N=6436)	9019.2	70	77.6	1.18 (0.85–1.65)	0.33
eGFR >50mL/min/1.73m ²	Warfarin (N=6043)	9621.0	48	49.9	1.0 (ref)	
	Rivaroxaban (N=5547)	7847.6	46	58.6	1.16 (0.77–1.76)	0.48
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1086)	1580.1	27	170.9	1.0 (ref)	
	Rivaroxaban (N=889)	1171.7	24	204.8	1.15 (0.64–2.06)	0.64
AKI Method B						
Any eGFR	Warfarin (N=7129)	11,022.7	278	252.2	1.0 (ref)	
	Rivaroxaban (N=6436)	8918.1	175	196.2	0.76 (0.62–0.92)	<0.01
eGFR >50mL/min/1.73m ²	Warfarin (N=6043)	9484.6	206	217.2	1.0 (ref)	
	Rivaroxaban (N=5547)	7760.2	133	171.4	0.74 (0.59–0.92)	0.01
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1086)	1538.1	72	468.1	1.0 (ref)	
	Rivaroxaban (N=889)	1157.9	42	362.7	0.81 (0.54–1.20)	0.28

Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, polymedication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA2DS2VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

Supplementary Table 3. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function: as-treated analysis.

Baseline eGFR	Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
AKI Method A						
Any eGFR	Warfarin (N=7230)	14903.4	104	69.8	1.0 (ref)	
	Rivaroxaban (N=7045)	12,064.0	93	77.1	1.13 (0.85–1.50)	0.4
eGFR >50 mL/min/1.73m ²	Warfarin (N=6124)	12,806.7	67	52.32	1.0 (ref)	
	Rivaroxaban (N=6081)	10,567.3	62	58.67	1.12 (0.79–1.58)	0.54
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1106)	2096.7	37	176.5	1.0 (ref)	
	Rivaroxaban (N=964)	1496.7	31	207.1	1.14 (0.69–1.87)	0.61
AKI Method B						
Any eGFR	Warfarin (N=7225)	14,580.6	345	236.6	1.0 (ref)	
	Rivaroxaban (N=7020)	11,861.3	216	182.1	0.77 (0.65–0.91)	<0.01
eGFR >50 mL/min/1.73m ²	Warfarin (N=6119)	12,563.2	259	206.2	1.0 (ref)	
	Rivaroxaban (N=6057)	10,390.5	167	160.7	0.76 (0.63–0.93)	0.01
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1106)	2017.5	86	426.3	1.0 (ref)	
	Rivaroxaban (N=963)	1470.9	49	333.1	0.82 (0.57–1.18)	0.28

Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, poly medication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

Supplementary Table 4. Incidence rate per 10,000 person-years of severe AKI (using AKI Method B – see footnote) and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function (intention-to-treat analysis).

Baseline eGFR	Cohort	Person-years	Incident severe AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
Any eGFR	Warfarin (N=7129)	19,492.2	104	53.4	1.0 (ref)	
	Rivaroxaban (N=6436)	13,686.8	54	39.5	0.74 (0.53–1.04)	0.08
eGFR >50mL/min/1.73m ²	Warfarin (N=6043)	16,946.4	78	46.0	1.0 (ref)	
	Rivaroxaban (N=5547)	11,963.1	38	31.8	0.68 (0.46–1.01)	0.06
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1086)	2545.8	26	102.1	1.0 (ref)	
	Rivaroxaban (N=889)	1723.6	16	92.8	0.95 (0.50–1.82)	0.88

Note: Method B was based on the Aberdeen algorithm. Severe AKI was defined as stage 2 or 3 AKI.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, poly medication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

Supplementary Table 5. Incidence rate per 10,000 person-years of severe AKI (using AKI Method B – see footnote) and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function (on-treatment analysis).

Baseline eGFR	Cohort	Person-years	Incident severe AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
Any eGFR	Warfarin (N=7129)	11,022.7	63	57.2	1.0 (ref)	
	Rivaroxaban (N=6436)	8918.1	40	44.9	0.81 (0.54–1.21)	0.30
eGFR >50mL/min/1.73m ²	Warfarin (N=6043)	9484.6	45	47.5	1.0 (ref)	
	Rivaroxaban (N=5547)	7760.2	26	33.5	0.68 (0.41–1.11)	0.13
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1086)	1538.1	18	117.0	1.0 (ref)	
	Rivaroxaban (N=889)	1157.9	14	120.9	1.10 (0.53–2.29)	0.79

Note: Method B was based on the Aberdeen algorithm. Severe AKI was defined as stage 2 or 3 AKI.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, poly medication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

Supplementary Table 6. Incidence rate per 10,000 person-years of severe AKI (using AKI Method B – see footnote) and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function (as-treated analysis).

Baseline eGFR	Cohort	Person-years	Incident severe AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
Any eGFR	Warfarin (N=7225)	14,580.6	76	52.12	1.0 (ref)	
	Rivaroxaban (N=7020)	11,861.3	49	41.31	0.82 (0.57–1.18)	0.29
eGFR >50mL/min/1.73m ²	Warfarin (N=6119)	12,563.2	52	41.39	1.0 (ref)	
	Rivaroxaban (N=6057)	10,390.5	35	33.68	0.82 (0.53–1.27)	0.38
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1106)	2017.5	24	118.96	1.0 (ref)	
	Rivaroxaban (N=963)	1470.9	14	95.18	0.85 (0.43–1.69)	0.65

Note: Method B was based on the Aberdeen algorithm. Severe AKI was defined as stage 2 or 3 AKI.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, poly medication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

Supplementary Table 7. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, stratified by baseline renal function (intention-to-treat analysis): Fine and Gray models.

Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	SHR* (95% CI)	p value
AKI Method A					
Warfarin (N=7129)	20,027.6	136	67.9	1.00 (ref)	
Rivaroxaban (N=6436)	13,917.5	113	81.2	1.15 (0.89–1.47)	0.29
AKI Method B (any AKI)					
Warfarin (N=7129)	19,492.2	457	234.5	1.00 (ref)	
Rivaroxaban (N=6436)	13,686.8	266	194.4	0.77 (0.66–0.89)	<0.01
AKI Method B (severe AKI)					
Warfarin (N=7129)	19,492.2	104	53.4	1.00 (ref)	
Rivaroxaban (N=6436)	13,686.8	54	39.5	0.72 (0.51–1.00)	0.05

Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm. Severe AKI was defined as stage 2 or 3 AKI. (stage 1 was included as a competing risk).

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, poly medication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; SHR, sub-distribution hazard ratio; PCP; primary care practitioner

Supplementary Table 8. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function: more stringent method B criteria (intention-to-treat analysis).

Baseline eGFR	Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
AKI algorithm (meeting criterion 2 or 3)[†]						
Any eGFR	Warfarin (N=7129)	20,134.2	60	29.8	1.0 (ref)	
	Rivaroxaban (N=6436)	14,029.4	21	15.0	0.50 (0.30–0.84)	0.01
eGFR >50	Warfarin (N=6043)	17,455.3	38	21.8	1.0 (ref)	
	Rivaroxaban (N=5547)	12,236.7	15	12.3	0.53 (0.28–1.00)	0.05
eGFR ≤50	Warfarin (N=1086)	2678.8	22	82.1	1.0 (ref)	
	Rivaroxaban (N=889)	1792.7	6	33.5	0.36 (0.14–0.97)	0.04
AKI algorithm (meeting criterion 3)[‡]						
Any eGFR	Warfarin (N=7129)	20,159.0	37	18.4	1.0 (ref)	
	Rivaroxaban (N=6436)	14,041.6	11	7.8	0.41 (0.20–0.84)	0.01
eGFR >50	Warfarin (N=6043)	17,478.0	19	10.9	1.0 (ref)	
	Rivaroxaban (N=5547)	12,243.7	9	7.3	0.70 (0.29–1.67)	0.42
eGFR ≤50	Warfarin (N=1086)	2681.1	18	67.1	1.0 (ref)	
	Rivaroxaban (N=889)	1797.9	2	11.1	0.15 (0.03–0.71)	0.02

Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, polymedication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

[†]Serum creatinine ≥1.5 times higher than the lowest creatinine within 7 days (criterion 2) or serum creatinine >26 µmol/L higher than the lowest creatinine within 48 hours (criterion 3).

[‡]Serum creatinine >26 µmol/L higher than the lowest creatinine within 48 hours (criterion 3).

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

Supplementary Table 9. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function (using 60 mL/min/1.73m² as the cut-off) (intention-to-treat analysis).

Baseline eGFR	Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
AKI Method A						
Any eGFR	Warfarin (N=7129)	20,028	136	67.91	1.0 (ref)	
	Rivaroxaban (N=6436)	13,917	113	81.19	1.19 (0.92–1.54)	0.18
eGFR >60 mL/min/1.73m ²	Warfarin (N=4921)	14,338	66	46.0	1.0 (ref)	
	Rivaroxaban (N=4537)	10,051	47	46.8	0.98 (0.67–1.44)	0.91
eGFR ≤60 mL/min/1.73m ²	Warfarin (N=2208)	5690	70	123.0	1.0 (ref)	
	Rivaroxaban (N=1899)	3866	66	170.7	1.39 (0.98–1.97)	0.06
AKI Method B						
Any eGFR	Warfarin (N=7129)	19,492	457	234.45	1.0 (ref)	
	Rivaroxaban (N=6436)	13,687	266	194.35	0.80 (0.68–0.93)	0.00
eGFR >60 mL/min/1.73m ²	Warfarin (N=4921)	13,986	270	193.1	1.0 (ref)	
	Rivaroxaban (N=4537)	9893	154	155.7	0.75 (0.61–0.92)	<0.01
eGFR ≤60 mL/min/1.73m ²	Warfarin (N=2208)	5507	187	339.6	1.0 (ref)	
	Rivaroxaban (N=1899)	3793	112	295.3	0.86 (0.67–1.09)	0.21

Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, polymedication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

Supplementary Table 10. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function: inverse propensity score weighting analysis (intention-to-treat analysis).

Baseline eGFR	Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
AKI Method A						
Any eGFR	Warfarin (N=7128)	19,907	133	66.7	1.0 (ref)	
	Rivaroxaban (N=6437)	14,062	113	80.1	1.19 (0.92–1.54)	0.17
eGFR >50 mL/min/1.73m ²	Warfarin (N=6093)	17,391	93	53.4	1.0 (ref)	
	Rivaroxaban (N=5499)	12,158	72	59.2	1.12 (0.82–1.53)	0.49
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1035)	2516	40	159.2	1.0 (ref)	
	Rivaroxaban (N=938)	1903	41	213.5	1.32 (0.85–2.05)	0.22
AKI Method B						
Any eGFR	Warfarin (N=7128)	19,397	441	227.6	1.0 (ref)	
	Rivaroxaban (N=6437)	13,822	273	197.4	0.82 (0.70–0.96)	0.01
eGFR >50 mL/min/1.73m ²	Warfarin (N=6093)	16,981	344	202.6	1.0 (ref)	
	Rivaroxaban (N=5499)	11,964	209	174.3	0.81 (0.68–0.97)	0.02
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1035)	2416	97	402.7	1.0 (ref)	
	Rivaroxaban (N=938)	1858	64	346.1	0.83 (0.60–1.16)	0.27

Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, polymedication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

Supplementary Table 11. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function: with further adjustment for cerebrovascular events, infection in the previous year, antineoplastic agents, NSAIDs, diuretics, angiotensin receptor blockers and ACE inhibitors (intention-to-treat analysis).

Baseline eGFR	Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
AKI Method A						
Any eGFR	Warfarin (N=7129)	20028	136	67.9	1.0 (ref)	0.19
	Rivaroxaban (N=6436)	13917	113	81.2	1.18 (0.92–1.53)	0.19
eGFR >50 mL/min/1.73m ²	Warfarin (N=6043)	17367	93	53.6	1.0 (ref)	
	Rivaroxaban (N=5547)	12155	74	60.9	1.13 (0.82–1.54)	0.46
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1086)	2661	43	161.6	1.0 (ref)	
	Rivaroxaban (N=889)	1762	39	221.3	1.3 (0.81–2.07)	0.28
AKI Method B						
Any eGFR	Warfarin (N=7129)	19492	457	234.5	1.0 (ref)	
	Rivaroxaban (N=6436)	13687	266	194.4	0.8 (0.69–0.94)	0.01
eGFR >50 mL/min/1.73m ²	Warfarin (N=6043)	16946	349	205.9	1.0 (ref)	
	Rivaroxaban (N=5547)	11963	208	173.9	0.79 (0.67–0.95)	0.01
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1086)	2546	108	424.2	1.0 (ref)	
	Rivaroxaban (N=889)	1724	58	336.5	0.81 (0.58–1.12)	0.2

Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, polymedication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure, liver disease, cerebrovascular events, infection in the previous year, antineoplastic agents, NSAIDs, diuretics, angiotensin receptor blockers and ACE inhibitors, frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives).

ACE, angiotensin-converting enzyme; AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; NSAID, non-steroidal anti-inflammatory drug; PCP; primary care practitioner

Supplementary Table 12. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function, **restricted to patients with heart failure** (intention-to-treat analysis).

Baseline eGFR	Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
AKI Method A						
Any eGFR	Warfarin (N=901)	2269	35	154.3	1.0 (ref)	0.42
	Rivaroxaban (N=720)	1460	19	130.1	0.78 (0.43–1.41)	
eGFR >50 mL/min/1.73m ²	Warfarin (N=661)	1760	20	113.6	1.0 (ref)	0.52
	Rivaroxaban (N=570)	1193	13	109.0	0.78 (0.36–1.69)	
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=240)	509	15	294.9	1.0 (ref)	0.46
	Rivaroxaban (N=150)	267	6	224.7	0.59 (0.14–2.44)	
AKI Method B						
Any eGFR	Warfarin (N=901)	2142	108	504.3	1.0 (ref)	0.46
	Rivaroxaban (N=720)	1389	67	482.2	0.89 (0.65–1.22)	
eGFR >50 mL/min/1.73m ²	Warfarin (N=661)	1655	76	459.1	1.0 (ref)	0.54
	Rivaroxaban (N=570)	1138	52	457.1	0.89 (0.62–1.29)	
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=240)	486	32	658.3	1.0 (ref)	0.95
	Rivaroxaban (N=150)	252	15	595.8	0.98 (0.48–1.98)	

Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, polymedication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

Supplementary Table 13. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function, **restricted to patients with diabetes mellitus** (intention-to-treat analysis).

Baseline eGFR	Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
AKI Method A						
Any eGFR	Warfarin (N=1601)	4327	47	108.6	1.0 (ref)	
	Rivaroxaban (N=1375)	2959	38	128.4	1.32 (0.85–2.06)	0.22
eGFR >50 mL/min/1.73m ²	Warfarin (N=1247)	3476	32	92.1	1.0 (ref)	
	Rivaroxaban (N=1123)	2430	27	111.1	1.35 (0.79–2.30)	0.27
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=354)	850	15	176.4	1.0 (ref)	
	Rivaroxaban (N=252)	529	11	208.0	1.61 (0.63–4.11)	0.32
AKI Method B						
Any eGFR	Warfarin (N=1601)	4095	187	456.6	1.0 (ref)	
	Rivaroxaban (N=1375)	2871	93	323.9	0.70 (0.54–0.90)	0.01
eGFR >50 mL/min/1.73m ²	Warfarin (N=1247)	3310	135	407.9	1.0 (ref)	
	Rivaroxaban (N=1123)	2376	65	273.6	0.63 (0.46–0.85)	<0.01
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=354)	785	52	662.2	1.0 (ref)	
	Rivaroxaban (N=252)	495	28	565.4	0.94 (0.57–1.55)	0.8

Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, poly medication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner

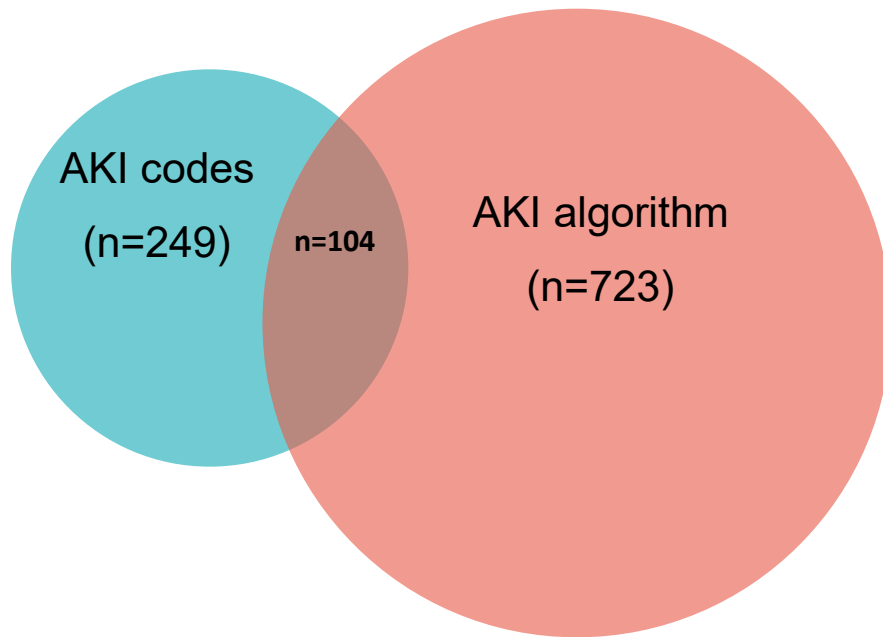
Supplementary Table 14. Incidence rate per 10,000 person-years of AKI and HR (95% CI) comparing AKI in the rivaroxaban vs. warfarin cohorts, overall and stratified by baseline renal function, **restricted to patients with patients aged >65 years** (intention-to-treat analysis).

Baseline eGFR	Cohort	Person-years	Incident AKI cases (N)	Incidence rate per 10,000 person-years	HR* (95% CI)	p value
AKI Method A						
Any eGFR	Warfarin (N=5951)	16,362	126	77.0	1.0 (ref)	
	Rivaroxaban (N=5239)	11,150	100	89.7	1.13 (0.86–1.48)	0.38
eGFR >50 mL/min/1.73m ²	Warfarin (N=4902)	13,815	85	61.5	1.0 (ref)	
	Rivaroxaban (N=4369)	9428	62	65.8	1.02 (0.73–1.43)	0.89
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=1049)	2547	41	161.0	1.0 (ref)	
	Rivaroxaban (N=870)	1722	38	220.7	1.28 (0.81–2.05)	0.29
AKI Method B						
Any eGFR	Warfarin (N=XXX)	15,899	410	257.9	1.0 (ref)	
	Rivaroxaban (N=XXX)	10,955	232	211.8	0.78 (0.66–0.92)	<0.01
eGFR >50 mL/min/1.73m ²	Warfarin (N=XXX)	13,466	305	226.5	1.0 (ref)	
	Rivaroxaban (N=XXX)	9275	174	187.6	0.76 (0.63–0.92)	0.01
eGFR ≤50 mL/min/1.73m ²	Warfarin (N=XXX)	2433	105	431.5	1.0 (ref)	
	Rivaroxaban (N=XXX)	1680	58	345.3	0.82 (0.59–1.15)	0.25

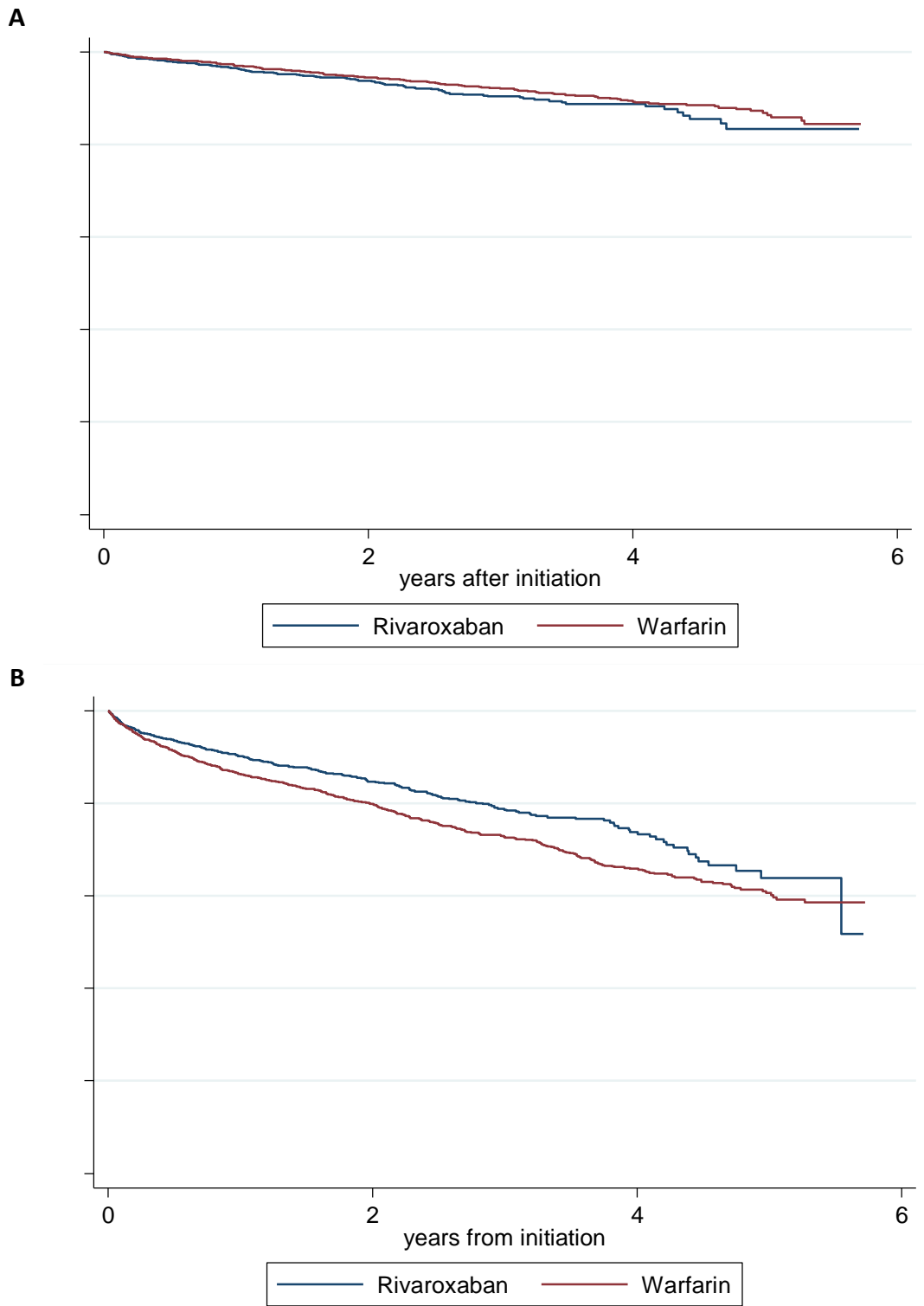
Note: Method A was based on Read codes, and Method B was based on the Aberdeen algorithm.

*Adjusted for age, sex, baseline eGFR (both as categorical and continuous variables), number of previous eGFR measurements at baseline, Townsend index, poly medication, smoking, body mass index, use of health services in the year before baseline (PCP visits, referrals and hospitalizations), comorbidity (ischemic heart disease, cancer, diabetes, heart failure and liver disease), frailty, CHA₂DS₂VASc score, and use of antiplatelets/anti-infectives.

AKI, acute kidney injury; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; PCP; primary care practitioner



Supplementary Figure 1. AKI cases identified by the two case identification definitions.
AKI, acute kidney injury



Supplementary Figure 2. Kaplan–Meier plots showing time to AKI using **(A)** Method A, and **(B)** Method B.