

Supplemental Material

Supplemental Table 1. Missing values of potassium and estimated glomerular filtration rate (eGFR)

Variable	Missing	Total	Percent Missing
egfr0	0	8,399	0
egfr2	257	8,399	3.06
egfr4	345	8,399	4.11
egfr8	353	8,399	4.2
egfr16	505	8,399	6.01
egfr32	863	8,399	10.28
egfr48	1,214	8,399	14.45
egfr64	1,778	8,399	21.17
egfr80	3,087	8,399	36.75
egfr96	4,124	8,399	49.1
egfr112	5,017	8,399	59.73
egfr128	5,894	8,399	70.18
egfr144	6,767	8,399	80.57
egfr160	7,604	8,399	90.53
egfr176	8,183	8,399	97.43
egfr192	8,376	8,399	99.73
k0	176	8,399	2.1
k2	245	8,399	2.92
k4	336	8,399	4
k8	359	8,399	4.27
k16	520	8,399	6.19
k32	889	8,399	10.58
k48	1,252	8,399	14.91
k64	1,798	8,399	21.41
k80	3,101	8,399	36.92
k96	4,145	8,399	49.35
k112	5,031	8,399	59.9
k128	5,902	8,399	70.27
k144	6,775	8,399	80.66
k160	7,608	8,399	90.58
k176	8,183	8,399	97.43
k192	8,376	8,399	99.73

Supplemental Table 2. Potassium changes from randomization to 2 months and subsequent outcomes

ΔK+ (mmol/L)	Events, n. (%)	Inc. rate, per 100py	Landmark model	P-value
Primary outcome				
HypoK-HypoK	111 (33.2)	16.7	1.57 (1.28-1.95)	<0.001
HypoK-NormoK	140 (28.3)	14	1.26 (1.05-1.51)	0.015
NormoK-NormoK	1022 (21.2)	10.3	Referent	-
HyperK-NormoK	43 (23.2)	11.7	1.01 (0.74-1.38)	0.94
HyperK-HyperK	93 (25.6)	12.9	1.16 (0.93-1.45)	0.19
HF hospitalization				
HypoK-HypoK	77 (23.1)	11.0	1.81 (1.39-2.34)	<0.001
HypoK-NormoK	88 (17.8)	8.3	1.33 (1.05-1.70)	0.019
NormoK-NormoK	612 (12.7)	6.0	Referent	-
HyperK-NormoK	26 (14.1)	7.0	0.98 (0.66-1.47)	0.94
HyperK-HyperK	54 (14.8)	7.0	1.09 (0.81-1.48)	0.56
CV death				
HypoK-HypoK	67 (20.1)	9.8	1.61 (1.25-2.09)	<0.001
HypoK-NormoK	84 (17.0)	8.1	1.23 (0.97-1.55)	0.081
NormoK-NormoK	608 (12.6)	6	Referent	-
HyperK-NormoK	25 (13.5)	6.5	1.00 (0.67-1.50)	0.99
HyperK-HyperK	62 (17.0)	8.6	1.32 (1.01-1.72)	0.041
All-cause death				
HypoK-HypoK	78 (23.4)	11.5	1.56 (1.23-1.97)	<0.001
HypoK-NormoK	96 (19.4)	9.3	1.15 (0.92-1.42)	0.22
NormoK-NormoK	750 (15.6)	7.4	Referent	-
HyperK-NormoK	36 (19.5)	9.3	1.15 (0.82-1.61)	0.42
HyperK-HyperK	71 (19.5)	9.8	1.22 (0.95-1.57)	0.11
Sudden death				
HypoK-HypoK	25 (7.5)	3.7	1.10 (0.73-1.66)	0.66
HypoK-NormoK	39 (7.9)	3.8	1.07 (0.77-1.50)	0.68
NormoK-NormoK	302 (6.3)	3	Referent	-
HyperK-NormoK	12 (6.5)	3.1	1.09 (0.61-1.96)	0.81
HyperK-HyperK	25 (6.9)	3.5	1.15 (0.76-1.75)	0.51
Pump failure death				
HypoK-HypoK	25 (7.5)	3.7	2.55 (1.66-3.92)	<0.001
HypoK-NormoK	23 (4.7)	2.2	1.37 (0.88-2.14)	0.6
NormoK-NormoK	163 (3.4)	1.6	Referent	-
HyperK-NormoK	6 (3.2)	1.6	0.77 (0.34-1.74)	0.52
HyperK-HyperK	22 (6.0)	3.0	1.68 (1.07-2.64)	0.024
Non-CV death				
HypoK-HypoK	11 (3.3)	1.6	1.30 (0.70-2.42)	0.41
HypoK-NormoK	12 (2.4)	1.2	0.77 (0.42-1.43)	0.42
NormoK-NormoK	142 (3.0)	1.4	Referent	-

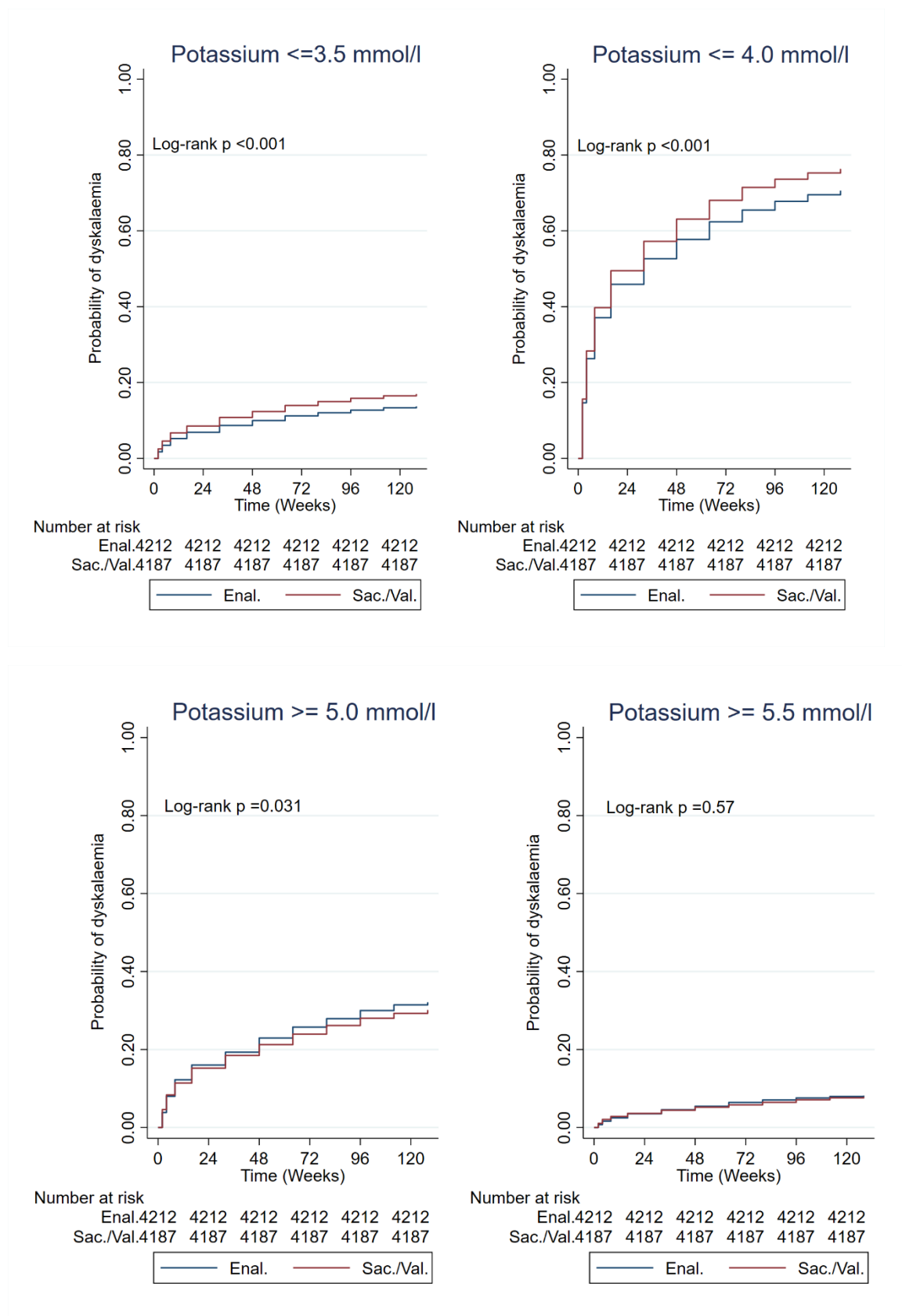
HyperK-NormoK	11 (6.0)	2.9	1.73 (0.93-3.22)	0.084
HyperK-HyperK	9 (2.5)	1.2	0.82 (0.42-1.62)	0.58

Legend: Δ , delta potassium from randomization to 2 months; CV, cardiovascular; HF, heart failure.

HypoK =hypokalemia defined as $K^+ < 4$ mmol/L.

HyperK =hyperkalemia defined as $K^+ > 5$ mmol/L

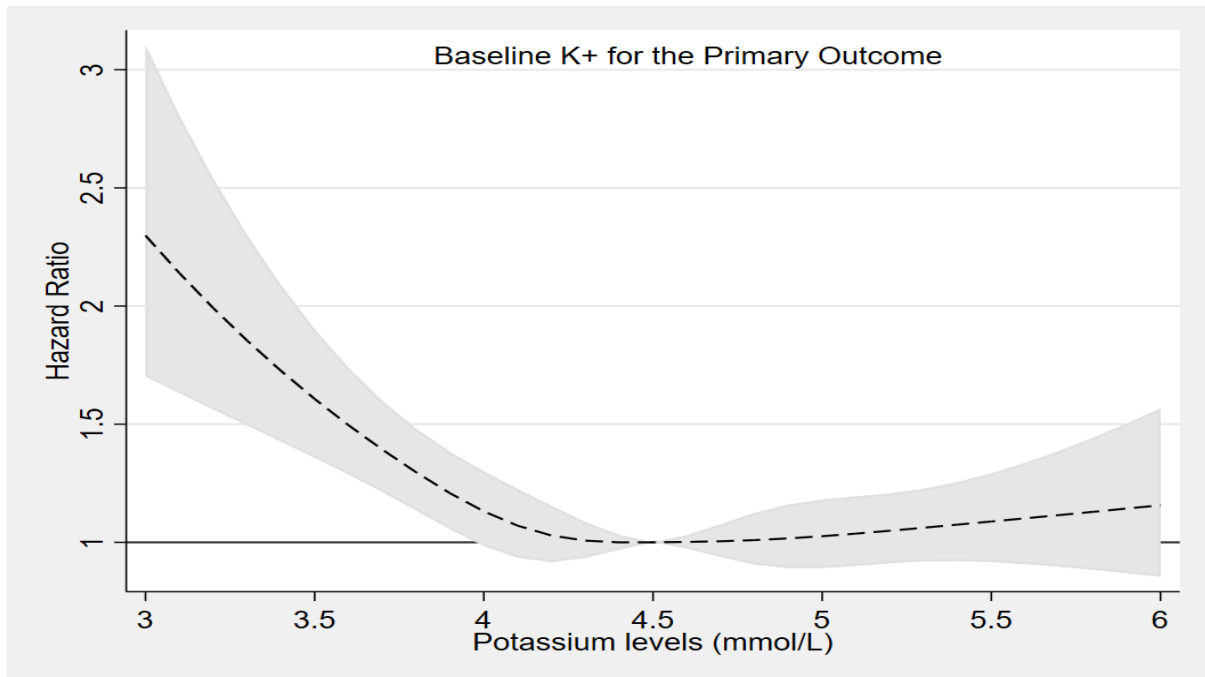
Supplemental Figure 1. Incidence of both hypo- and hyperkalemia throughout the follow-up and by randomized treatment group in the PARADIGM-HF trial



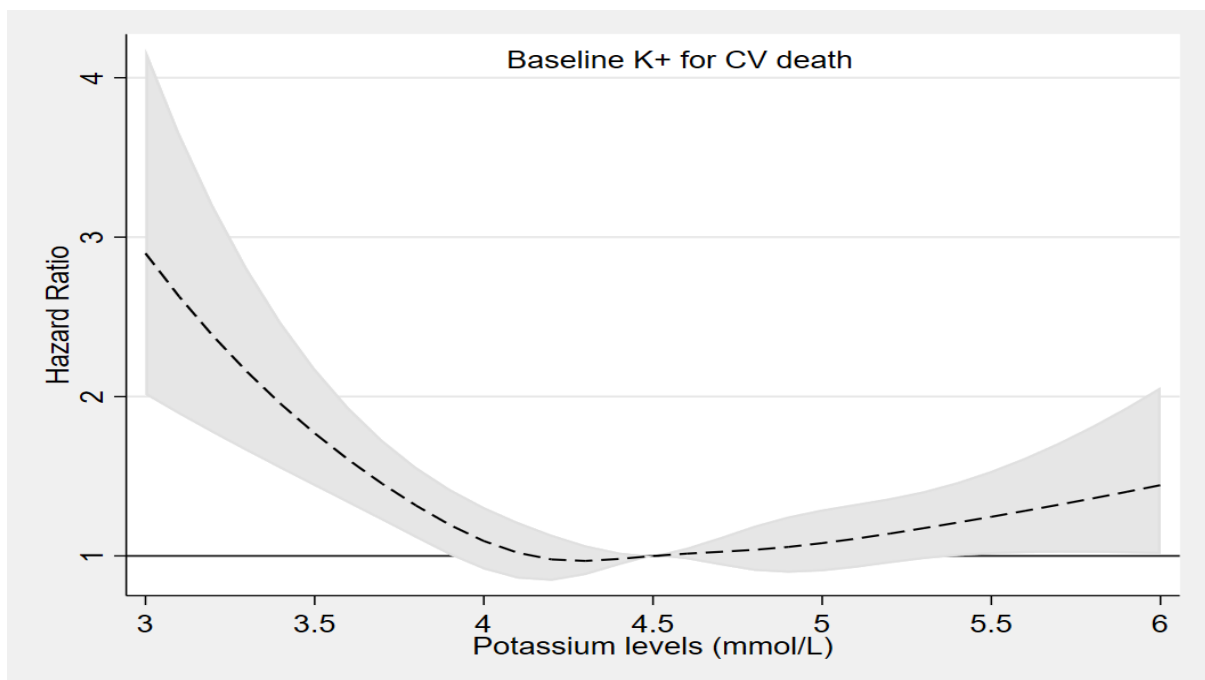
Legend: Enal., enalapril; Sac./Val., sacubitril/valsartan.

Supplemental Figure 2. Baseline potassium and subsequent outcomes

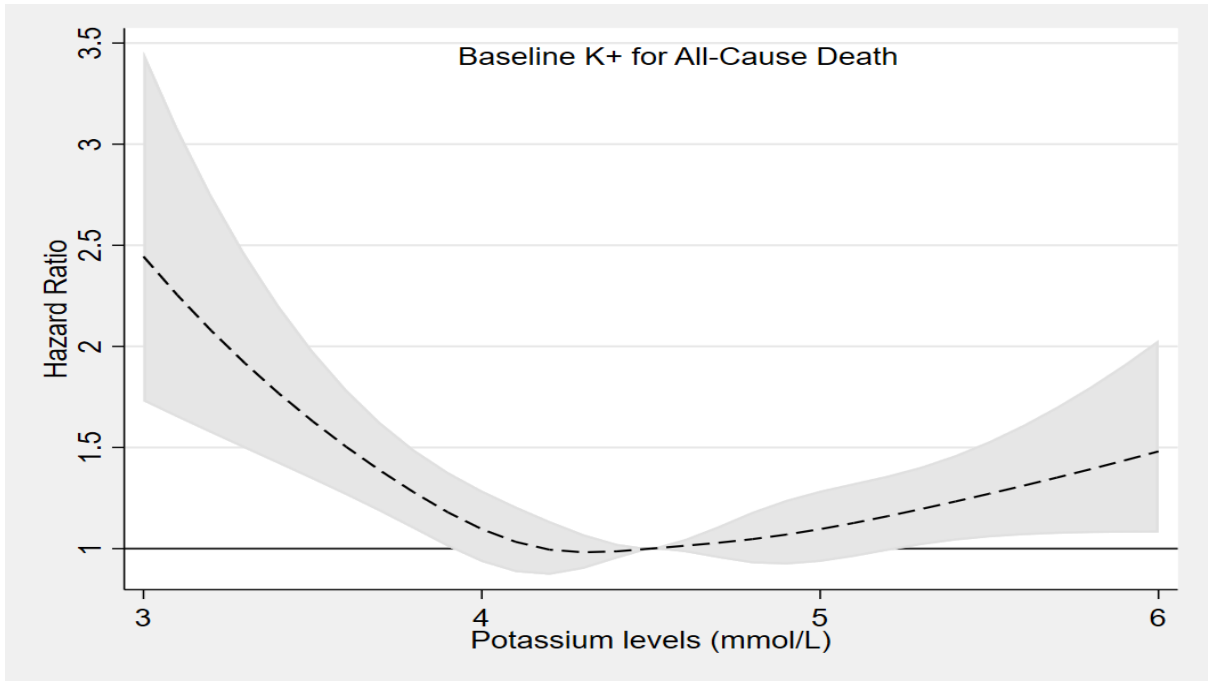
(A)



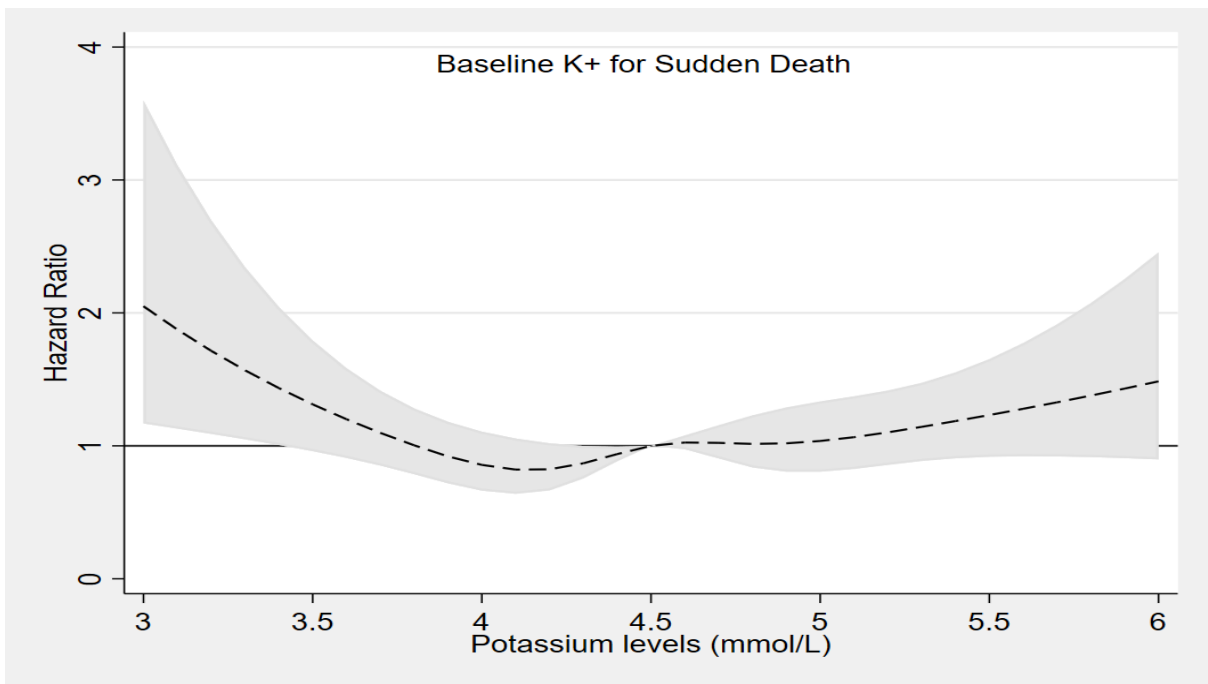
(B)



(C)

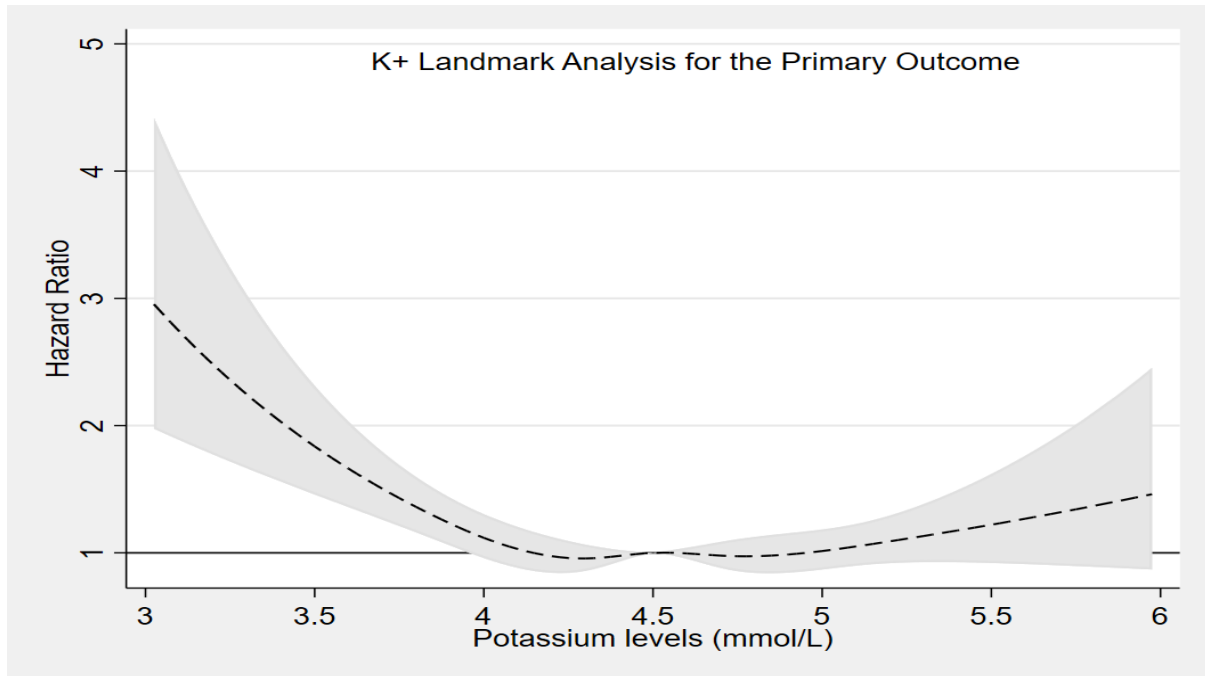


(D)

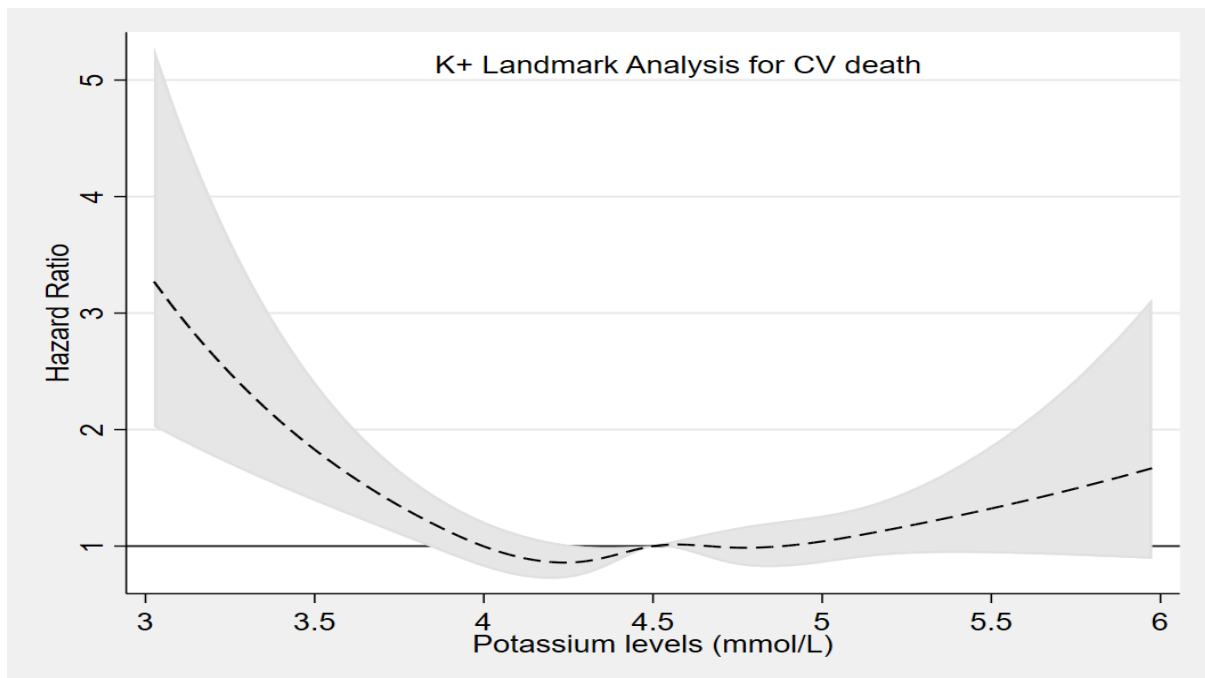


Supplemental Figure 3. Landmark (2-month) analysis and subsequent outcomes

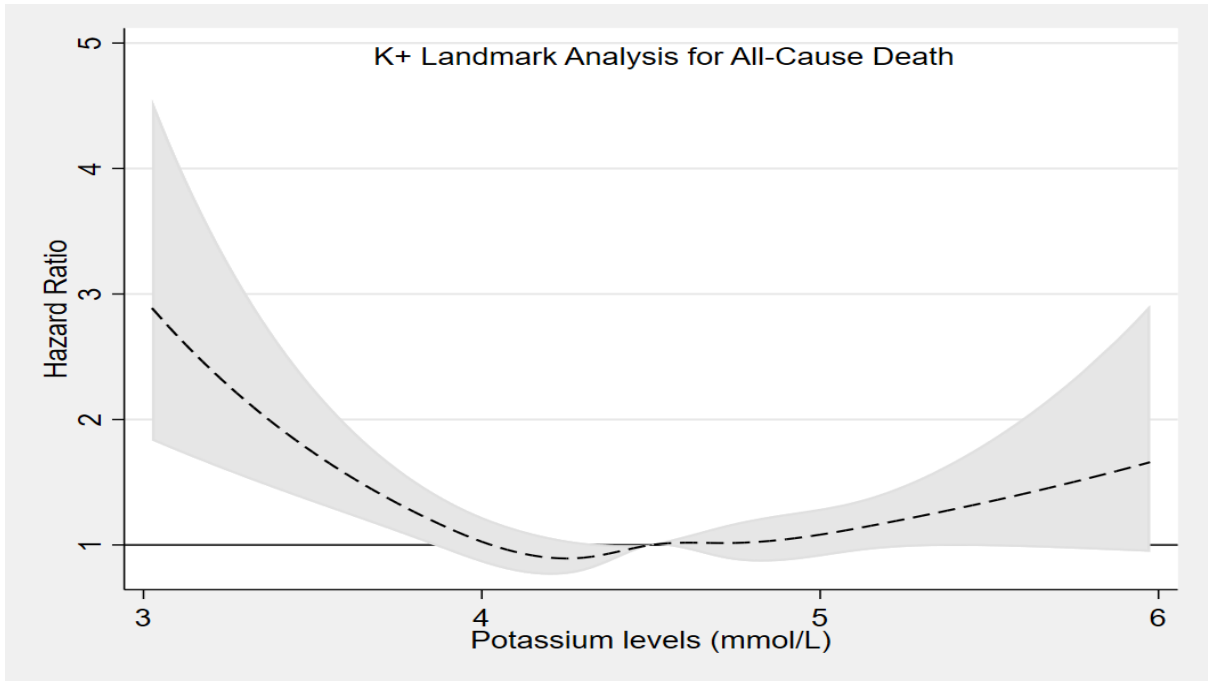
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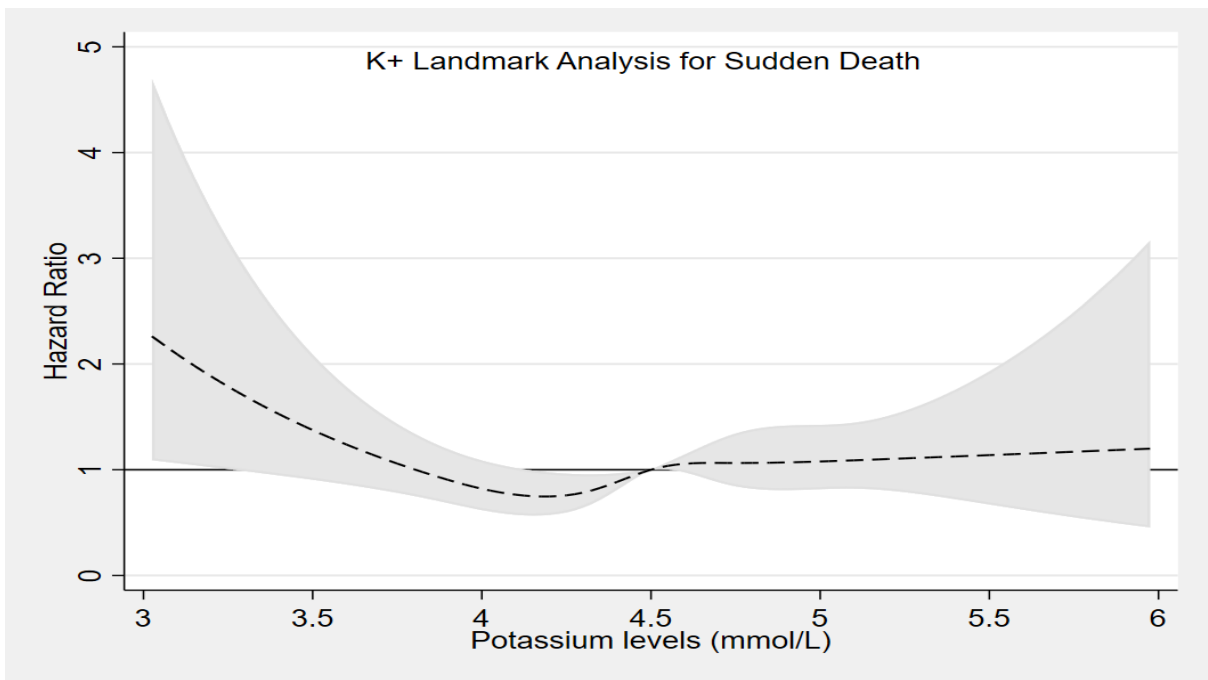
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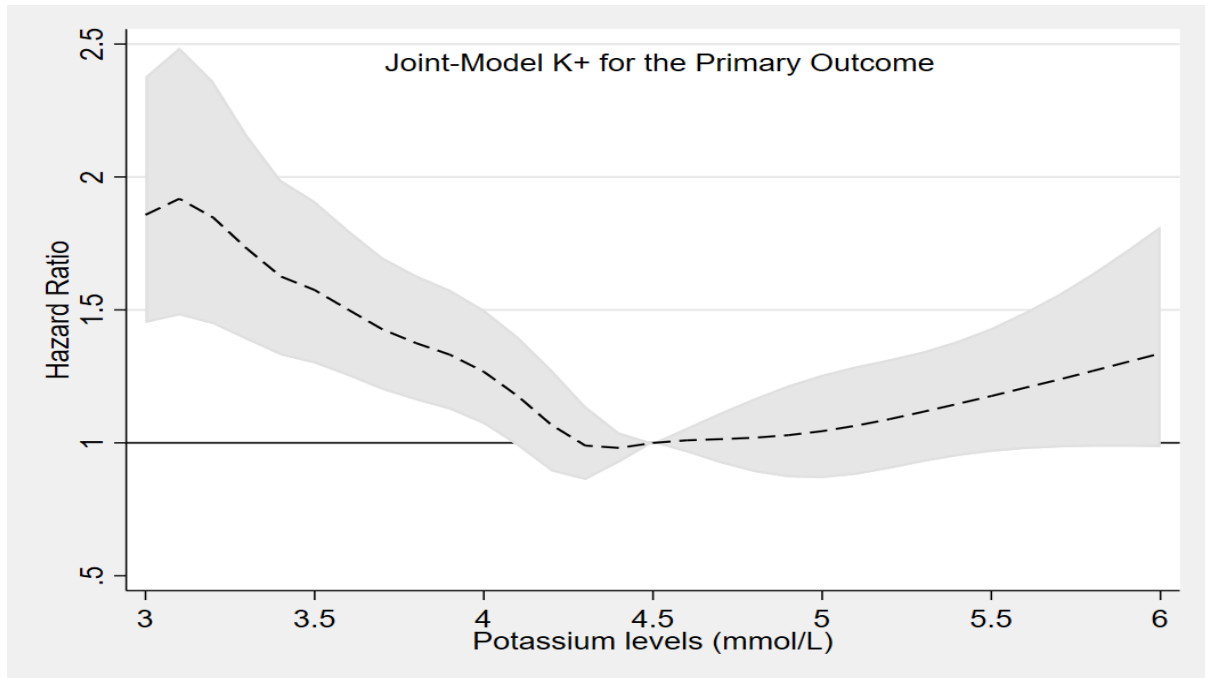


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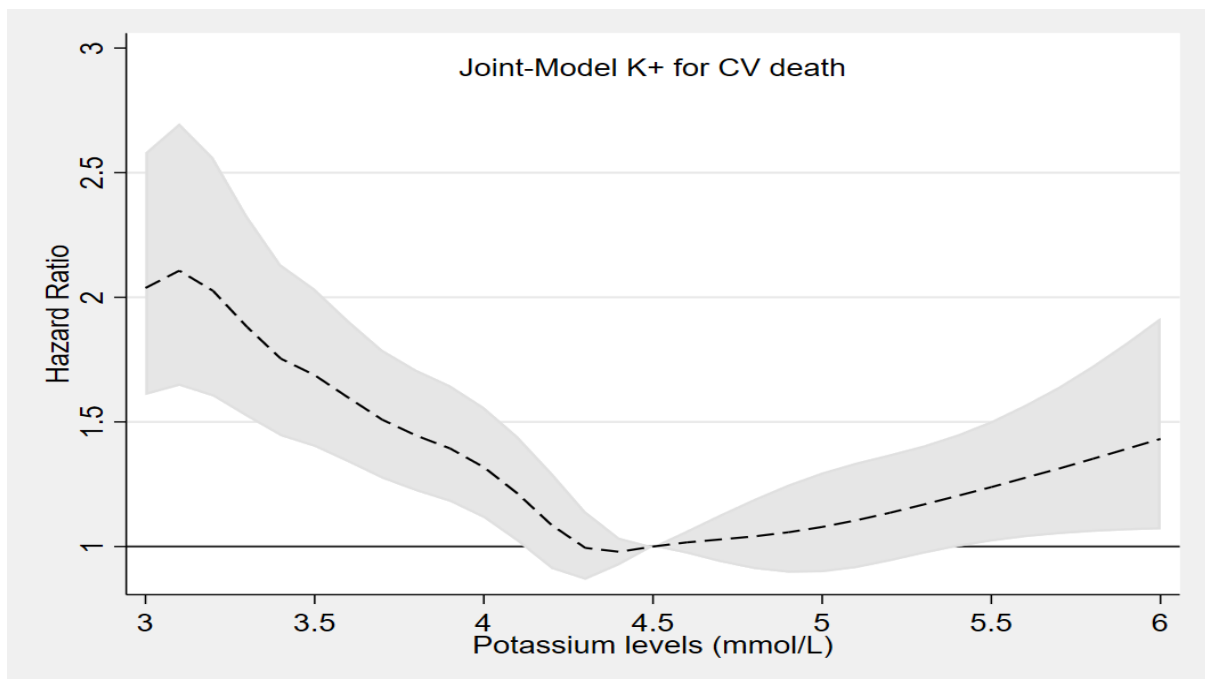


Supplemental Figure 4. Joint-model for potassium and subsequent outcomes

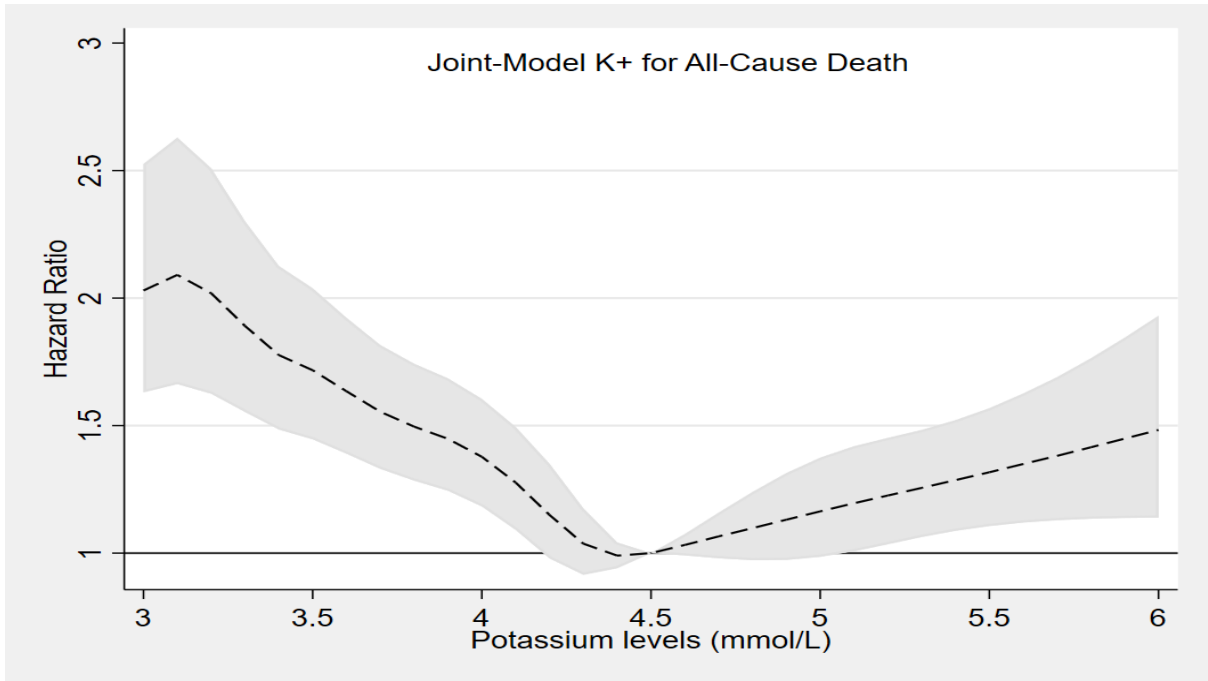
(A)



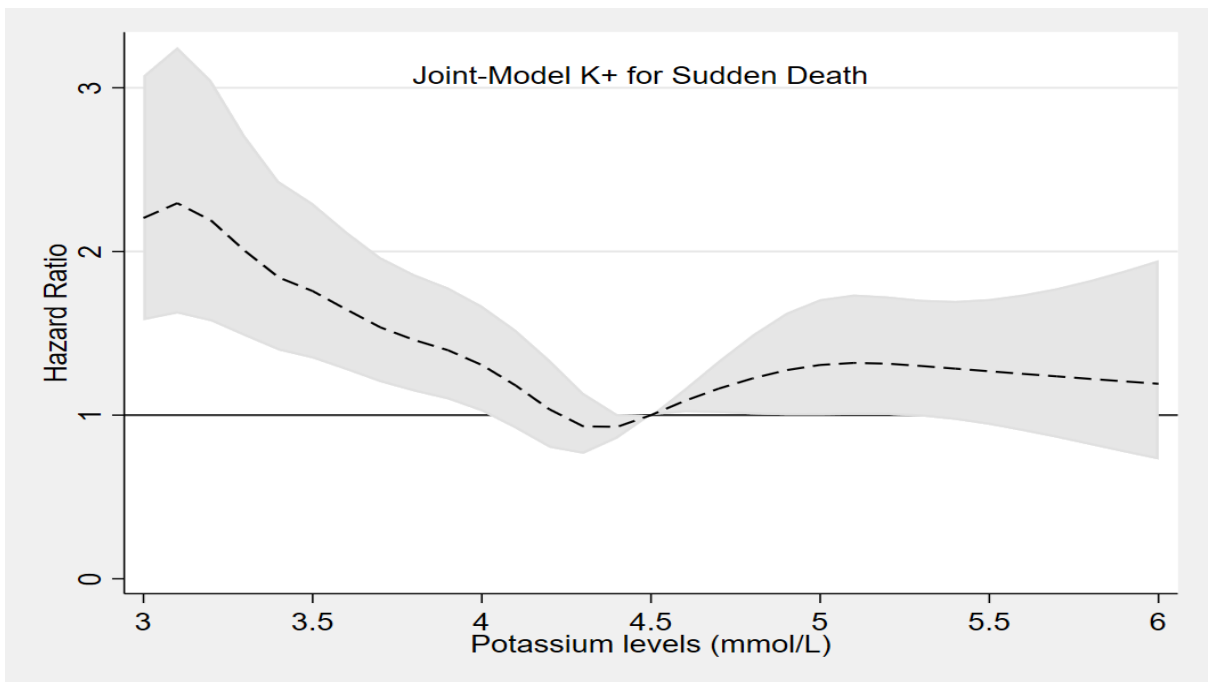
(B)



(C)



(D)



Supplemental Figure 5. E-value (and corresponding HR) needed to offset the association of hypokalemia (≤ 3.5 mmol/l) with the study primary outcome

