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Supplemental Materials

Associations of opioid prescriptions with death and hospitalization across the spectrum of estimated GFR

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Supplemental Table 1. ICD Codes.

Outcome/Covariate	ICD codes
Non-pathologic Fracture	733.0x, M81.x
Overdose	965.0x, E850.1, E850.2, E950.0, E980.0
Incident Diabetes Mellitus	250, E10, E11, E13
Coronary Artery Disease	410, I21, I22, 36.1, 0210, 0211, 0212, 0213
Cardiovascular Disease	428, I50
Peripheral Arterial Disease	440.x, 443.9, 38.18, 39.50, 39.2x, 84.1, I70.2, I70.92, I73.9, 031x
Major Depressive Disorder	293.83, 296.x, 298.0, 300.4, 301.1x, 307.44, 309, 311, F06.30, F32, F33, F31.x, F34.x, F51.1x, F43.2, F93.0, F94.8, F43.8
Osteoporosis	733.0, M81

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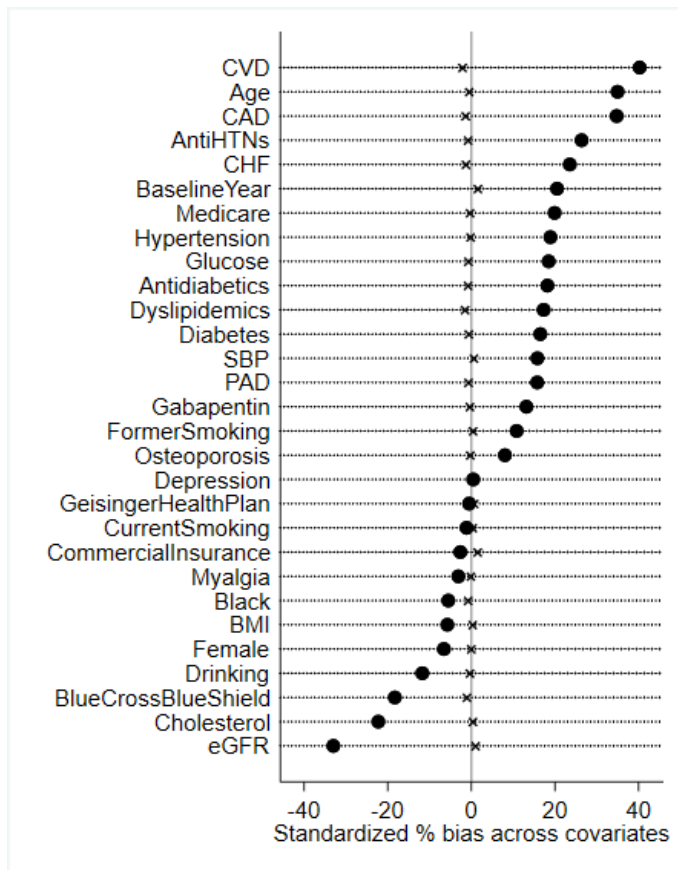
Supplemental Table 2. Population Characteristics at the Time of First Prescription for Opioids versus Gabapentinoids Analysis (Before and After Propensity-Matching).

Covariables	Before Propensity-Matching			After Propensity-Matching		
	People Prescribed Opioids	People Prescribed Gabapentinoids	Standardized Mean Difference	People Prescribed Opioids	People Prescribed Gabapentinoids	Standardized Mean Difference
	N = 53,351	N = 6,089		N = 7,512	N = 3,756	
Age, mean (SD)	55 (17)	56 (16)	-7	54 (16)	55 (16)	-5
Female, N (%)	30,023 (56%)	3535 (58%)	-4	4403 (59%)	2230 (59%)	-2
Black race, N (%)	1582 (3%)	208 (3%)	-3	100 (1%)	50 (1%)	0
Baseline eGFR, ml/min/1.73m ² , mean (SD)	87.5 (23.9)	86.2 (23.0)	6	89.9 (20.4)	89.3 (19.7)	3
Body mass index, kg/m ² , mean (SD)	31.2 (7.8)	31.2 (7.6)	1	31.0 (7.5)	31.0 (7.4)	0
Systolic blood pressure, mmHg, mean (SD)	127.3 (17.7)	125.3 (16.7)	11	125.7 (16.6)	125.9 (16.4)	-1
Total cholesterol, mmol/L, mean (SD)	185.2 (40.9)	187.1 (43.7)	-4	187.4 (31.8)	186.6 (32.8)	2
Random glucose, mmol/L, mean (SD)	105.8 (32.6)	113.3 (41.9)	-20	105.5 (31.0)	105.3 (29.8)	1
Alcohol consumption, N (%)	22,881 (47%)	2352 (43%)	8	3559 (47%)	1761 (47%)	1
Current cigarette use, N (%)	11,244 (21%)	1572 (26%)	-11	1836 (24%)	873 (23%)	3
Former cigarette use, N (%)	16,239 (30%)	1716 (28%)	5	2271 (30%)	1128 (30%)	0
Antihypertensive prescription, N (%)	27,335 (51%)	3459 (57%)	-11	3848 (51%)	1920 (51%)	0
Antidyslipidemic prescription, N (%)	19,332 (36%)	2617 (43%)	-14	2810 (37%)	1391 (37%)	1
Antidiabetic prescription, N (%)	9240 (17%)	1737 (29%)	-27	1292 (17%)	652 (17%)	0
Coronary artery disease, N (%)	6813 (13%)	671 (11%)	5	793 (11%)	404 (11%)	-1
Congestive heart failure, N (%)	1882 (4%)	132 (2%)	8	145 (2%)	57 (2%)	3
Cardiovascular disease, N (%)	3171 (6%)	340 (6%)	2	1228 (16%)	595 (16%)	1
Peripheral artery disease, N (%)	1370 (3%)	188 (3%)	-3	194 (3%)	83 (2%)	2
Major Depressive Disorder, N (%)	9319 (17%)	1143 (19%)	-3	1422 (19%)	664 (18%)	3
Diabetes, N (%)	5225 (10%)	756 (12%)	-8	721 (10%)	365 (10%)	0
Hypertension, N (%)	14,376 (27%)	1529 (25%)	4	1904 (25%)	970 (26%)	-1
Osteoporosis, N (%)	3508 (7%)	362 (6%)	3	468 (6%)	247 (7%)	-1
Myalgias, N (%)	3593 (7%)	585 (10%)	-11	412 (5%)	206 (5%)	0
Amputations, N (%)	84 (0%)	8 (0%)	1	7 (0%)	2 (0%)	1

Abbreviations: eGFR - estimated glomerular filtration rate; % reflect column-wise percentages

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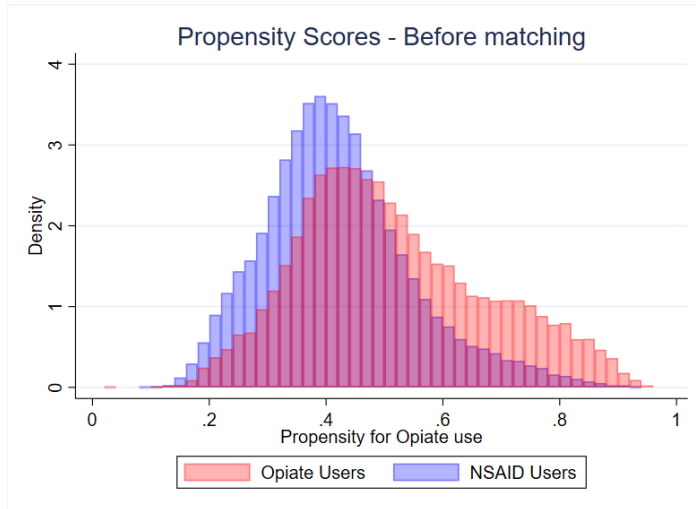
Supplemental Figure 1. Propensity-matching for Opioid versus NSAIDs Analysis. Before propensity matching, the median (IQR) propensity score for opioids and NSAIDs were 0.72 [0.63-0.80] and 0.34 [0.28-0.39], respectively. After propensity matching, the median (IQR) propensity score for opioids and NSAIDs were 0.45 [0.38-0.53] and 0.45 [0.38-0.53], respectively. Values <10% indicate a negligible difference between groups.



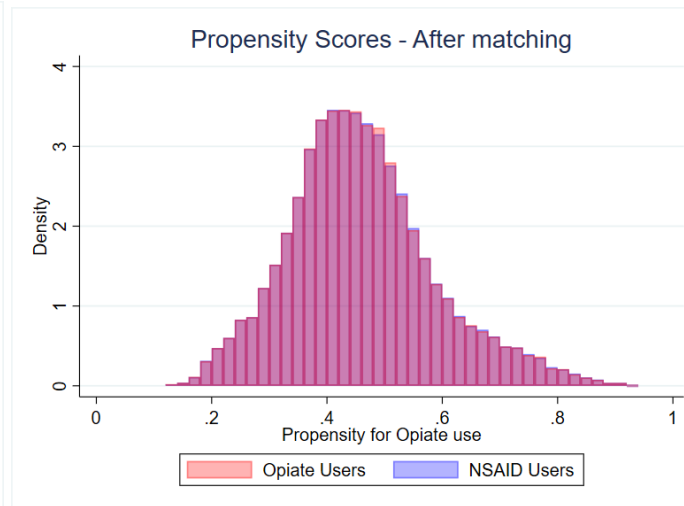
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Supplemental Figure 2. Distribution of Propensity Scores for Opioid Prescription in the Opioid versus NSAID Analysis (Before and After Matching).

A)

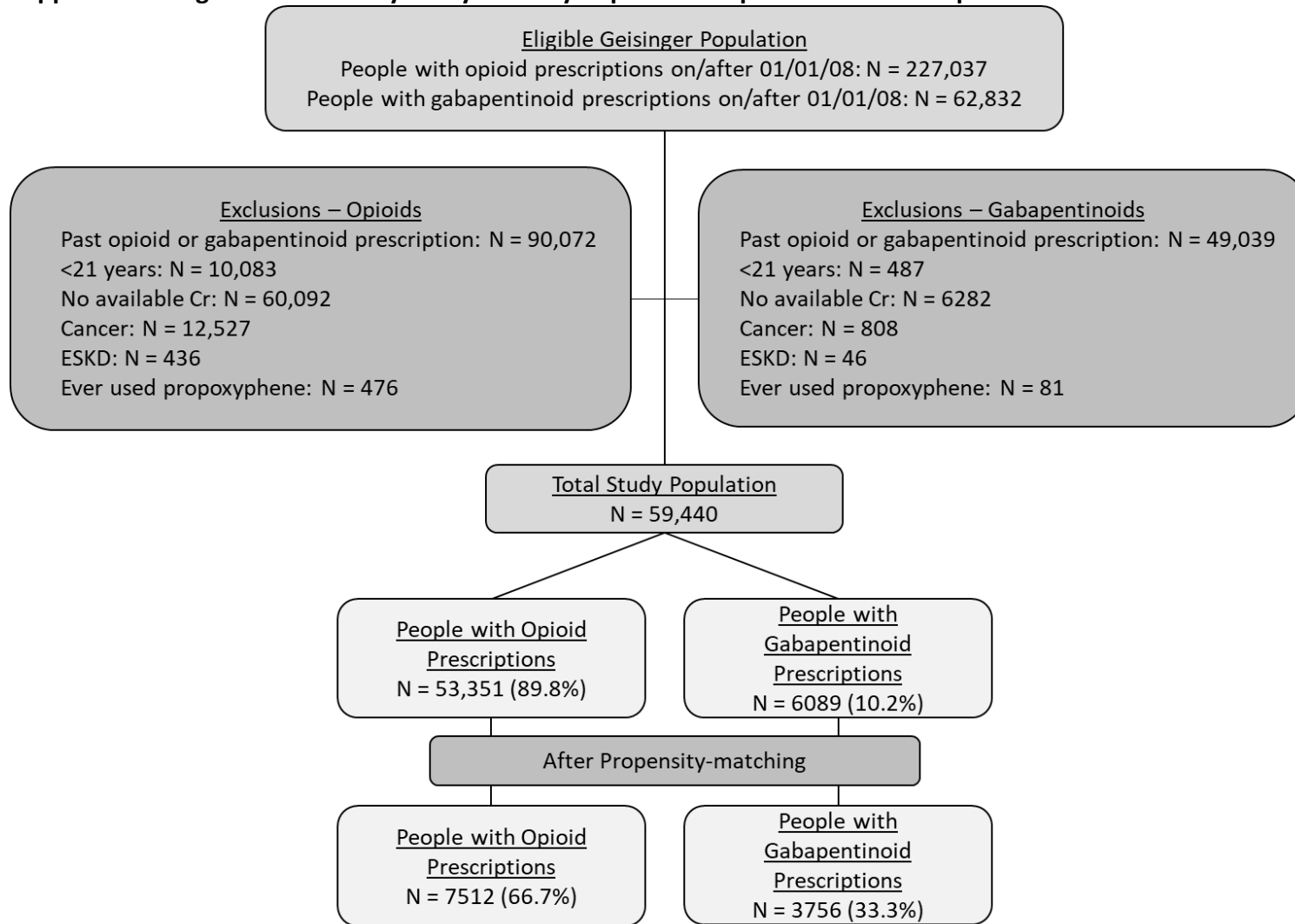


B)



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Supplemental Figure 3. Sensitivity Analysis Study Population: Opioids versus Gabapentinoids.

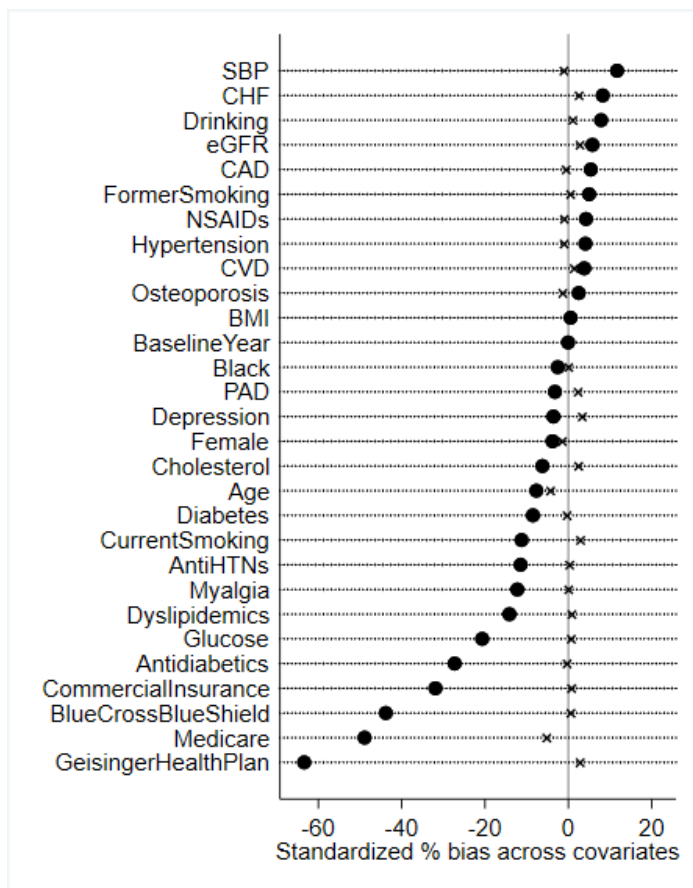


Abbreviations: Cr – creatinine, ESKD – end stage kidney disease

2:1 Matching was used because of the relatively few numbers of patients receiving gabapentinoids.

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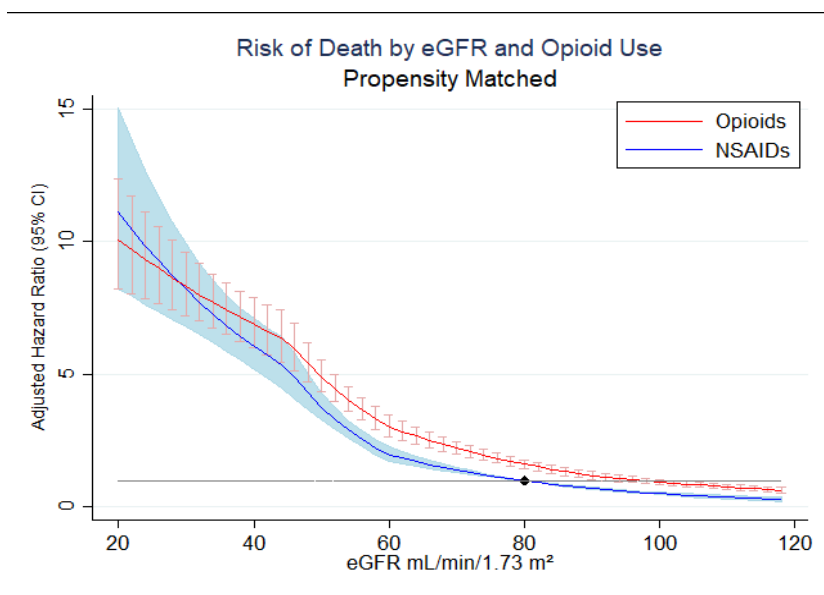
Supplemental Figure 4. Propensity-matching for Opioid versus Gabapentinoid Analysis. Before propensity matching, the median (IQR) propensity score for opioids and gabapentinoids were 0.90 [0.88-0.92] and 0.84 [0.79-0.89], respectively. After propensity matching, the median (IQR) propensity score for opioids and gabapentinoids were 0.90 [0.88-0.92] and 0.90 [0.88-0.92], respectively. Values <10% indicate a negligible difference between groups.



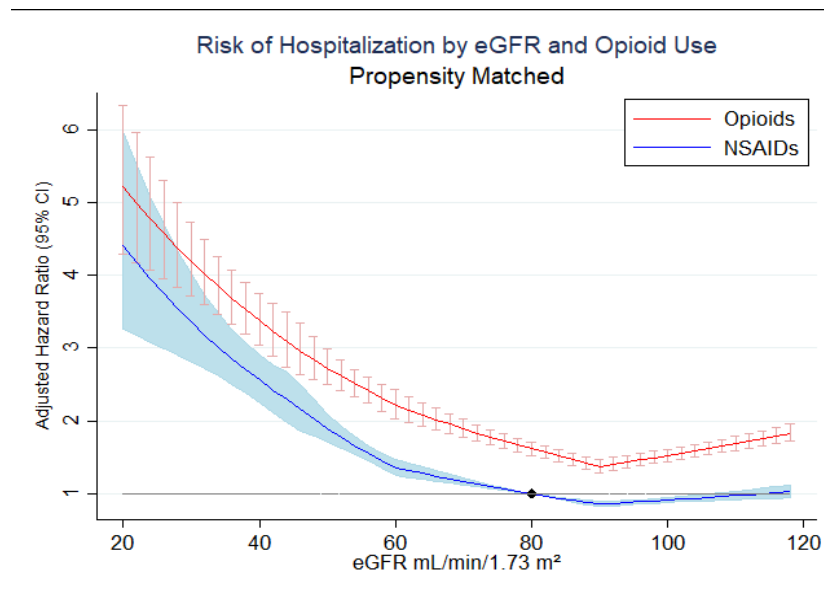
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Supplemental Figure 5. Sensitivity Analysis: Using Initial Prescription Status and eGFR. A) Adjusted hazard ratios for death and B) hospitalization in those with opioids prescriptions (red line), and NSAID prescriptions (blue line) compared to a reference group of individuals with an NSAID prescription and eGFR 80 ml/min/1.73m².

A)



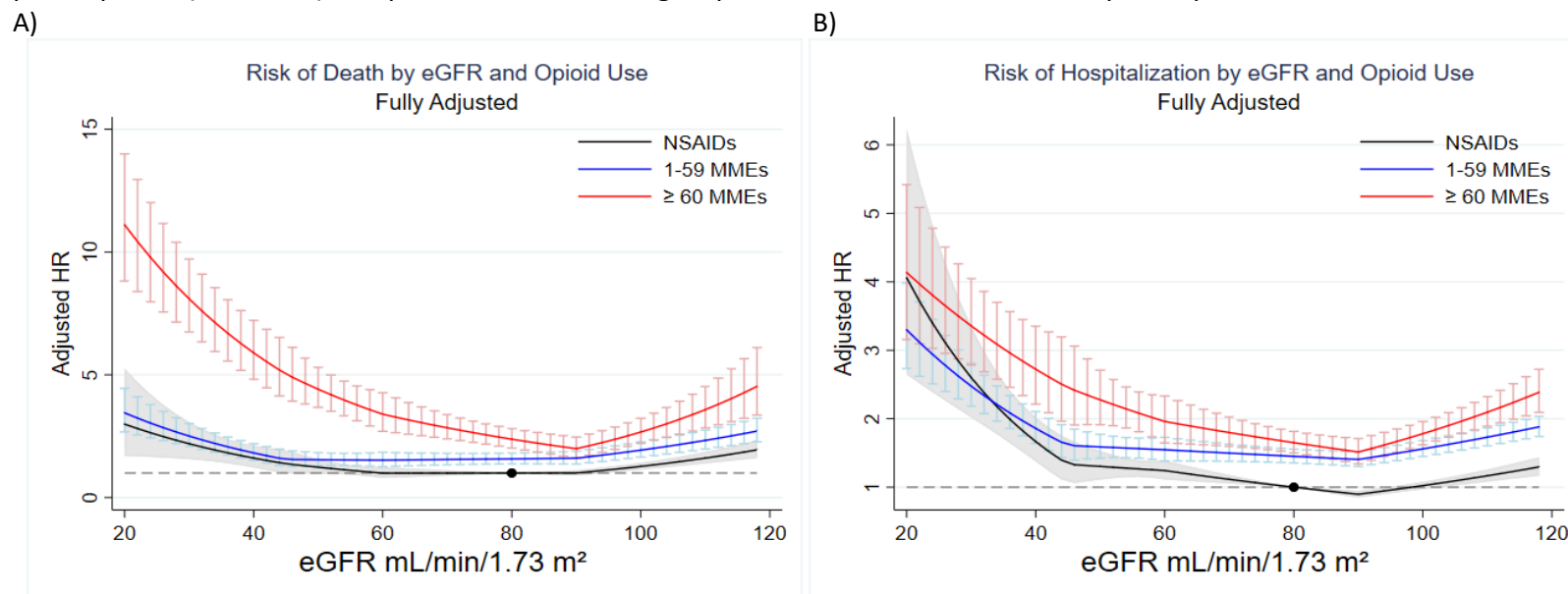
B)



Abbreviations: eGFR - estimated glomerular filtration rate

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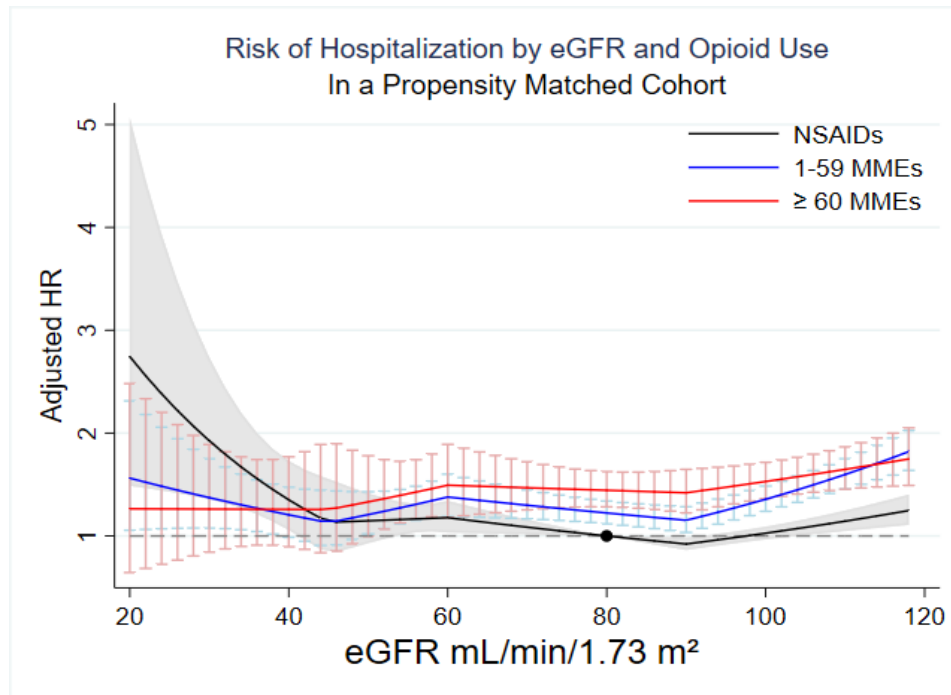
Supplemental Figure 6. Sensitivity Analysis: Fully Adjusted Opioids versus NSAIDs. A) Adjusted hazard ratios for death and B) hospitalization in those with ≥ 60 oral morphine milligram equivalents (MME) (red line), 1-59 MMEs (blue line), and NSAID prescriptions (black line) compared to a reference group of individuals with an NSAID prescription and eGFR 80 ml/min/1.73m².



Abbreviations: eGFR - estimated glomerular filtration rate

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Supplemental Figure 7. Sensitivity Analysis: Competing Risk Analysis for Hospitalizations. Adjusted hazard ratios for hospitalization in those with ≥ 60 mg oral morphine equivalents (red line), 1-59 mg oral morphine equivalents (blue line), and NSAID prescriptions (black line) compared to a reference group of individuals with an NSAID prescription and eGFR 80 ml/min/1.73m².

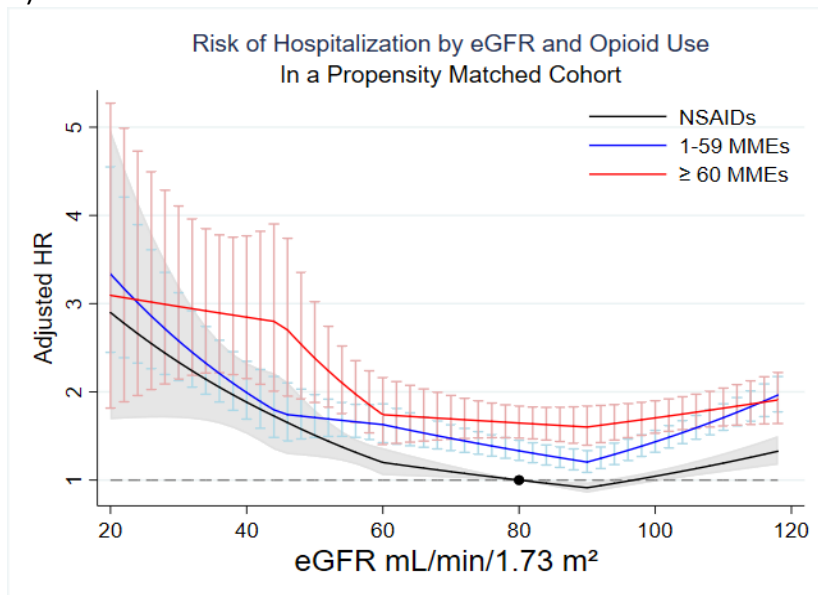


Abbreviations: eGFR - estimated glomerular filtration rate

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Supplemental Figure 8. Sensitivity Analysis: Risk of Hospitalization Censoring on Last Clinic Visit. A) Adjusted hazard ratios for hospitalization in those with ≥ 60 oral morphine milligram equivalents (MMEs) (red line), 1-59 MMEs (blue line), and NSAID prescriptions (black line) compared to a reference group of individuals with an NSAID prescription and eGFR 80 ml/min/1.73m². B) Adjusted hazard ratios for hospitalization in those with ≥ 60 oral morphine milligram equivalents (MMEs) (red line), 1-59 MMEs (blue line), and gabapentinoid prescriptions (black line) compared to a reference group of individuals with a gabapentinoid prescription and eGFR 80 ml/min/1.73m².

A)



B)

