

Figure S1. Forest plots of adjusted risk ratio (RR) of hospitalization comparing those participants with time-updated (A) opioid and (B) NSAID use in the past versus none, stratified by key demographic and case-mix subgroups and adjusted for all other covariates in primary analysis.

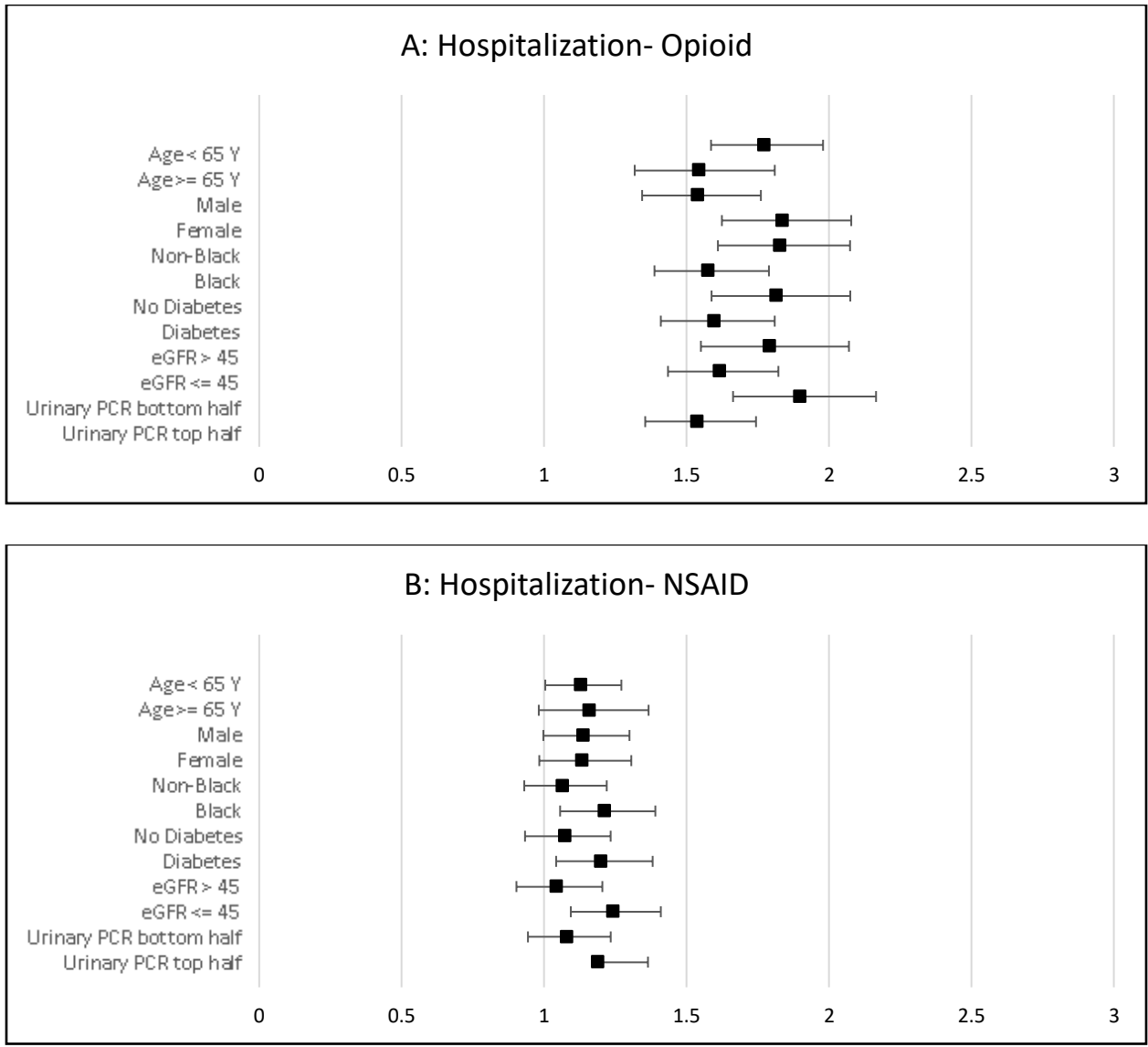


Table S1 Forest plot point estimates and confidence intervals

50% GFR Reduction or ESKD	NSAID			OPIOD		
	Estimate	Lower	Upper	Estimate	Lower	Upper
Age < 65 Y	1.0376	0.8331	1.2922	1.1756	0.949	1.4562
Age >= 65 Y	1.107	0.7831	1.5648	1.4613	1.0375	2.0582
Male	1.108	0.8546	1.4365	1.2715	0.9734	1.6608
Female	1.0061	0.7699	1.3148	1.2434	0.981	1.576
Non-Black	0.8337	0.6367	1.0915	1.1523	0.879	1.5106
Black	1.309	1.0119	1.6932	1.3486	1.0677	1.7033
No Diabetes	0.8553	0.6283	1.1643	1.1679	0.8702	1.5675
Diabetes	1.206	0.9566	1.5205	1.2982	1.0367	1.6258
eGFR > 45	1.1717	0.8549	1.6057	1.1029	0.755	1.6111
eGFR <= 45	0.9961	0.7963	1.2462	1.3255	1.0886	1.6139
Urinary PCR bottom half	0.9075	0.6025	1.3669	1.3348	0.8545	2.085
Urinary PCR top half	1.1028	0.8948	1.359	1.2378	1.02	1.502
ESKD	NSAID			OPIOD		
	Estimate	Lower	Upper	Estimate	Lower	Upper
Age < 65 Y	0.8559	0.6567	1.1155	1.0348	0.8129	1.3173
Age >= 65 Y	0.9954	0.6572	1.5077	1.3123	0.916	1.8801
Male	1.2097	0.9066	1.6141	1.0275	0.7692	1.3725
Female	0.6267	0.446	0.8804	1.2451	0.9459	1.639
Non-Black	0.7836	0.5642	1.0884	1.0386	0.7717	1.3978
Black	1.0178	0.7471	1.3866	1.188	0.9098	1.5511
No Diabetes	0.8453	0.5807	1.2305	1.0281	0.7319	1.4444
Diabetes	0.9327	0.709	1.2269	1.1634	0.9072	1.492
eGFR > 45	1.3781	0.8859	2.1438	0.7902	0.457	1.3663
eGFR <= 45	0.7727	0.5981	0.9983	1.2032	0.972	1.4893
Urinary PCR bottom half	0.5203	0.2821	0.9598	1.4369	0.8459	2.4409
Urinary PCR top half	1.0003	0.7859	1.2732	1.0675	0.8634	1.3199
DEATH	NSAID			OPIOD		
	Estimate	Lower	Upper	Estimate	Lower	Upper
Age < 65 Y	0.8812	0.62	1.2525	1.6471	1.1739	2.311
Age >= 65 Y	0.8073	0.5345	1.2193	1.3957	0.9519	2.0465
Male	0.7689	0.528	1.1197	1.3097	0.9122	1.8803
Female	0.9333	0.6207	1.4035	1.7721	1.2265	2.5603
Non-Black	0.9458	0.6658	1.3435	1.6926	1.2138	2.3603
Black	0.6732	0.4404	1.0291	1.2373	0.8378	1.8272
No Diabetes	0.7082	0.469	1.0695	1.3287	0.8849	1.9951
Diabetes	0.9619	0.6696	1.3817	1.6436	1.1939	2.2627
eGFR > 45	0.771	0.5182	1.1471	1.5927	1.0604	2.3923
eGFR <= 45	0.8949	0.617	1.2978	1.4576	1.0536	2.0165
Urinary PCR bottom half	0.6664	0.4647	0.9557	1.4303	1.0008	2.0441
Urinary PCR top half	1.0906	0.7292	1.6311	1.5715	1.0929	2.2597
HOSPITALIZATION	NSAID			OPIOD		
	Estimate	Lower	Upper	Estimate	Lower	Upper
Age < 65 Y	1.1299	1.0042	1.2713	1.7717	1.586	1.9793
Age >= 65 Y	1.1582	0.9814	1.3668	1.5445	1.3181	1.8098
Male	1.1386	0.9974	1.2997	1.5386	1.3442	1.761
Female	1.1332	0.9832	1.3061	1.8372	1.6242	2.0782
Non-Black	1.0654	0.9304	1.2199	1.8274	1.6102	2.074
Black	1.212	1.0563	1.3906	1.5756	1.3875	1.7893

No Diabetes	1.0728	0.933	1.2336	1.8151	1.5879	2.0749
Diabetes	1.1998	1.0423	1.3811	1.5972	1.4097	1.8096
eGFR > 45	1.0429	0.9029	1.2046	1.7916	1.5505	2.0702
eGFR ≤ 45	1.2418	1.0939	1.4097	1.6172	1.435	1.8225
Urinary PCR bottom half	1.0789	0.9434	1.2339	1.8978	1.6633	2.1653
Urinary PCR top half	1.1887	1.0353	1.3647	1.5372	1.355	1.7439

Table S2 Hazard and rate ratios and corresponding E-values for each analgesic and associated outcomes

Outcome	Analgesic	Full cohort		Analgesic	Sub-cohort	
		HR* (95% CI)	E-value (CI)		c	HR* (95% CI)
ESKD/50% eGFR Reduction	Opioid	1.4(1.2, 1.7)	2.2 (1.7)	Opioid	1.6 (1.3, 2.0)	2.6 (1.9)
	NSAID	1.2 (1.0, 1.5)	1.7 (1)	NSAID	1.1 (0.9, 1.4)	1.4 (1)
ESKD	Opioid	1.4 (1.1, 1.7)	2.2 (1.4)	Opioid	1.5 (1.2, 2.0)	2.4 (1.7)
	NSAID	1.1 (0.8, 1.3)	1.4 (1)	NSAID	1.0 (0.7, 1.3)	1 (1)
Pre-ESKD Death	Opioid	1.5 (1.2, 2.0)	2.4 (1.7)	Opioid	1.6 (1.1, 2.2)	2.6 (1.4)
	NSAID	0.9 (0.7, 1.1)	1	NSAID	1.2 (0.8, 1.7)	1.7 (1)
Hospitalization	Opioid	1.7 (1.6, 1.9)	2.8 (2.6)	Opioid	1.7 (1.5, 1.9)	2.8 (2.4)
	NSAID	1.1 (1.0, 1.3)	1.4 (1)	NSAID	1.1 (0.9, 1.3)	1.4 (1)

*Note: Hazard ratio except for hospitalization which is a rate ratio

a) full cohort (number of visits =24552 for ESKD/halving of eGFR, 24838 for other outcomes) and b) a sub-cohort comprised of those cohort participants who ever used non-opioid analgesics or tramadol (number of visits =13663 for ESKD/halving of eGFR, 13859 for other outcomes)