

Supplemental Content 1**Table.** MedDRA classes and their frequencies

	MedDRA ID	MedDRA Class	Occurrences	%
1	10017947	Gastrointestinal disorders	236	52.6
2	10040785	Skin and subcutaneous tissue disorders	116	25.8
3	10037175	Psychiatric disorders	77	17.1
4	10029205	Nervous system disorders	65	14.5
5	10021428	Vascular disorders	32	7.1
6	10007541	Cardiac disorders	30	6.7
7	10047065	Immune system disorders	27	6.0
8	10018065	General disorders and administration site conditions	23	5.1
9	10038738	Ear and labyrinth disorders	17	3.8
10	10013993	Respiratory, thoracic and mediastinal disorders	15	3.3
11	10027433	Metabolism and nutrition disorders	3	0.7
12	10028395	Renal and urinary disorders	3	0.7
13	10038359	Musculoskeletal and connective tissue disorders	2	0.4
14	10015919	Eye disorders	1	0.2
15	10019805	Hepatobiliary disorders	1	0.2
16	10005329	Blood and lymphatic system disorders	1	0.2

Notes: “Occurrences” refers to the number of patients who reported the MedDRA class to at least one opioid. “%” refers to the proportion of patients who reported the MedDRA class among the 449 patients who reported at least one MedDRA class.

Supplemental Content 2**Table. Ingredients and RxNorm codes of opioid medications included in the study**

Opioid	RxNorm code	Ingredient name
Codeine	821601	Acetaminophen/Aspirin/Caffeine/Codeine
Codeine	689552	Acetaminophen/Aspirin/Caffeine/Codeine/salicylamide
Codeine	689555	Acetaminophen/Aspirin/Codeine
Codeine	689561	Acetaminophen/butalbital/Caffeine/Codeine
Codeine	689563	Acetaminophen/butalbital/Codeine
Codeine	814657	Acetaminophen/Caffeine/Codeine
Codeine	817430	Acetaminophen/Caffeine/Codeine/Meprobamate
Codeine	689568	Acetaminophen/Caffeine/Codeine/salicylamide
Codeine	817579	Acetaminophen/Codeine
Codeine	817356	Acetaminophen/Codeine/Ibuprofen
Codeine	1007238	Aconite/Codeine/Erysimum preparation
Codeine	690996	Aluminum Hydroxide/Aspirin/Codeine/Magnesium Hydroxide
Codeine	214237	anhydrous calcium iodide/Codeine
Codeine	214160	Aspirin/butalbital/Caffeine/Codeine
Codeine	689511	Aspirin/Caffeine/Codeine
Codeine	689522	Aspirin/Carisoprodol/Codeine
Codeine	135095	Aspirin/Codeine
Codeine	1008493	Benzoate/Codeine
Codeine	1008060	Butalbital/Caffeine/Codeine
Codeine	691032	Calcium iodide/Codeine
Codeine	2670	Codeine
Codeine	1008110	Codeine/Diclofenac
Codeine	1008954	Codeine/Erysimum preparation
Codeine	1007477	Codeine/Ethylmorphine
Codeine	710303	Codeine/Ibuprofen
Codeine	214443	Codeine/iodinated glycerol
Codeine	729517	Codeine/Kaolin
Codeine	690089	Codeine/Papaverine
Codeine	1007293	Codeine/Potassium
Codeine	690096	Codeine/potassium citrate
Codeine	1007204	Codeine/propyphenazone
Codeine	690101	Codeine/Pyrimidine
Codeine	689569	Acetaminophen/Caffeine/dihydrocodeine
Codeine	151196	Acetaminophen/dihydrocodeine
Codeine	689783	Acetaminophen/dihydrocodeine/salicylamide
Codeine	689512	Aspirin/Caffeine/dihydrocodeine
Codeine	23088	Dihydrocodeine
Oxycodone	214183	Acetaminophen/Oxycodone
Oxycodone	214256	Aspirin/Oxycodone
Oxycodone	484259	Ibuprofen/Oxycodone
Oxycodone	1545902	Naloxone/Oxycodone
Oxycodone	7804	Oxycodone
Hydrocodone	689553	Acetaminophen/Aspirin/Caffeine/Hydrocodone
Hydrocodone	689562	Acetaminophen/butalbital/Caffeine/Hydrocodone
Hydrocodone	214182	Acetaminophen/Hydrocodone
Hydrocodone	689515	Aspirin/Caffeine/Hydrocodone
Hydrocodone	214253	Aspirin/Hydrocodone
Hydrocodone	5489	Hydrocodone
Hydrocodone	214627	Hydrocodone/Ibuprofen
Tramadol	352362	Acetaminophen/Tramadol
Tramadol	10689	Tramadol

Supplemental Content 3

Table. Sex differences in the risk of having a note in the allergy section indicating adverse reactions to opioids (men as reference group) among participants in the RIGHT study prescribed an opioid between 1/1/2004 and 12/31/2017 (n = 8,457) or not prescribed an opioid in the study timeframe but having a note in the allergy section indicating adverse reactions to an opioid (n = 128)

Characteristic	Total (events / observations)	Sex		Un-Adjusted OR (95% CI)	Adjusted OR* (95% CI)	P-value†
		Men (ref)	Women			
Adverse reactions to any opioid	1119 / 8585‡	266 / 3350 (7.9%)	853 / 5235 (16.3%)	2.3 [2 - 2.6]	2.3 [2 - 2.6]	< 0.001
Adverse reactions by opioid						
Codeine	653 / 2094	125 / 628 (19.9%)	528 / 1466 (36%)	2.3 [1.8 - 2.8]	2.3 [1.8 - 2.8]	< 0.001
Tramadol	191 / 3782	42 / 1443 (2.9%)	149 / 2339 (6.4%)	2.3 [1.6 - 3.2]	2.3 [1.6 - 3.2]	< 0.001
Hydrocodone	116 / 4069	36 / 1566 (2.3%)	80 / 2503 (3.2%)	1.4 [0.9 - 2.1]	1.4 [0.9 - 2.1]	0.105
Oxycodone	372 / 6573	102 / 2614 (3.9%)	270 / 3959 (6.8%)	1.8 [1.4 - 2.3]	1.8 [1.4 - 2.3]	< 0.001
Adverse reactions to an opioid by MedDRA class§						
Gastrointestinal	631	116 (3.5%)	515 (9.8%)	3 [2.5 - 3.7]	3 [2.5 - 3.7]	< 0.001
Skin and subcutaneous tissue	271	65 (1.9%)	206 (3.9%)	2.1 [1.6 - 2.7]	2.1 [1.6 - 2.7]	< 0.001
Psychiatric	168	73 (2.2%)	95 (1.8%)	0.8 [0.6 - 1.1]	0.8 [0.6 - 1.1]	0.234
Nervous system	154	37 (1.1%)	117 (2.2%)	2 [1.4 - 3]	2 [1.4 - 3]	< 0.001

*Adjusted for race and ethnicity

† P-values for multivariable (adjusted) models; $\alpha = 0.0125$ (Bonferroni correction) for the analyses by opioid and by MedDRA class

‡ 128 participants were not prescribed an opioid in the study coverage but had a note indicating adverse reactions to an opioid

§ Among those who were prescribed an opioid and/or reported at least one adverse reaction to an opioid (men, n = 3350; women, n = 5235).