Opioid-induced constipation: cost impact of approved medications in the emergency department

SUPPLEMENTARY MATERIAL

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Supplementary Table S1. Variables used for reweighting (entropy balancing)

Patient characteristics	**Age**
	Age (continuous)
	Under 45
	45-64
	65-74
	75-84
	85+
	Sex
	Female
	Male
	Unknown
	Race
	White
	Black
	Other
	Unknown
	Ethnicity
	Not Hispanic
	Hispanic
	Unknown
	Primary payer
	Medicare
	Commercial
	Medicaid
	Other
	Point of origin
	Non-healthcare facility
	Clinic
	Transfer from another healthcare facility
	Transfer from SNF or ICF
	Unknown
Hospital characteristics	**Cost type**
	Relative value units
	Medicare cost to charge ratio
	Bed size
	0-99
	100-199
	200-299
	300-399
	400-499
	500+
	Region

	South
	Midwest
	West
	Northeast
	Quarterly number of ED encounter
	0-4,999
	5,000-9,999
	10,000-14,999
	15,000-19,999
	20,000-24,999
	25,000-29,000
	30,000+
	Teaching status
	Non-teaching
	Teaching
	Population served
	Urban
	Rural
Index ED encounter characteristics	**Index encounter quarter**
	2016 Q2
	2016 Q3
	2016 Q4
	2017 Q1
	2017 Q2
	2017 Q3
	2017 Q4
	2018 Q1
	2018 Q2
	2018 Q3
	2018 Q4
	2019 Q1
	2019 Q2
	2019 Q3
	OIC-related procedure
	Abdominal X-ray
	Abdominal CT
	Enema
	Fecal disimpaction
	OIC-related diagnosis
	Opioid use
	Opioid abuse/dependence
	Drug induced constipation
	Constipation
	OIC-related conditions
	Abdominal pain

	Nausea/vomiting
	Cancer

Cancer subsample analyses

Patient characteristics (**Supplementary Table S2**), HRU (**Supplementary Table S3**), and healthcare cost findings (**Supplementary Table S4**) in the cancer subsample were consistent with the overall population.

Supplementary Table S2. Patient and hospital characteristics – Cancer subsample

	Cancer subsample					
	Before balancing				After balancing	
	OIC-Rx N = 1,053		No OIC-Rx N = 2,219		No OIC-Rx N = 2,219	
Patient demographics[1]						
Age, years; mean ± SD [median]	63.1 ± 12.8 [64.0]		63.2 ± 14.1 [64.0]		63.1 ± 12.8 [64.0]	
Sex, N (%)						
Female	501	(47.6%)	1,202	(54.2%)	1,056	(47.6%)
Race[2], N (%)						
White	830	(78.8%)	1,661	(74.9%)	1,749	(78.8%)
Black	141	(13.4%)	328	(14.8%)	297	(13.4%)
Other	73	(6.9%)	192	(8.7%)	154	(6.9%)
Unknown	9	(0.9%)	38	(1.7%)	19	(0.9%)
Primary payer, N (%)						
Medicare	561	(53.3%)	1,204	(54.3%)	1,182	(53.3%)
Commercial	256	(24.3%)	522	(23.5%)	539	(24.3%)
Medicaid	173	(16.4%)	374	(16.9%)	365	(16.4%)
Other	63	(6.0%)	119	(5.4%)	133	(6.0%)
Hospital characteristics[1]						
Bed size, N (%)						
0-199	250	(23.7%)	548	(24.7%)	526	(23.7%)
200-399	361	(34.3%)	699	(31.5%)	761	(34.3%)
400+	442	(42.0%)	972	(43.8%)	932	(42.0%)
Region, N (%)						
South	415	(39.4%)	922	(41.6%)	875	(39.4%)
Midwest	304	(28.9%)	514	(23.2%)	640	(28.8%)
West	241	(22.9%)	444	(20.0%)	508	(22.9%)
Northeast	93	(8.8%)	339	(15.3%)	196	(8.8%)
Quarterly number of ED encounters[3], N (%)						
0-4,999	98	(9.3%)	281	(12.7%)	207	(9.3%)
5,000-9,999	265	(25.2%)	557	(25.1%)	558	(25.1%)
10,000-14,999	377	(35.8%)	670	(30.2%)	794	(35.8%)
15,000-19,999	206	(19.6%)	392	(17.7%)	434	(19.6%)
20,000+	107	(10.2%)	319	(14.4%)	227	(10.2%)
Teaching status, N (%)						
Non-teaching	700	(66.5%)	1,206	(54.3%)	1,475	(66.5%)

Teaching	353	(33.5%)	1,013	(45.7%)	744	(33.5%)
Population served, N (%)						
Urban	919	(87.3%)	1,863	(84.0%)	1,937	(87.3%)
Rural	134	(12.7%)	356	(16.0%)	282	(12.7%)
During the ED index encounter[1]						
Index encounter year, N (%)						
2016	277	(26.3%)	482	(21.7%)	583	(26.3%)
2017	305	(29.0%)	682	(30.7%)	643	(29.0%)
2018	287	(27.3%)	627	(28.3%)	605	(27.3%)
2019	184	(17.5%)	428	(19.3%)	387	(17.4%)
OIC-related procedure[4], N (%)						
Abdominal X-ray	556	(52.8%)	1,037	(46.7%)	1,171	(52.8%)
Abdominal CT	405	(38.5%)	925	(41.7%)	853	(38.4%)
Enema	238	(22.6%)	502	(22.6%)	502	(22.6%)
Fecal disimpaction	29	(2.8%)	50	(2.3%)	61	(2.7%)
OIC-related diagnosis[5], N (%)						
Opioid use	700	(66.5%)	1,615	(72.8%)	1,475	(66.5%)
Opioid abuse/dependence	501	(47.6%)	2,038	(91.8%)	1,056	(47.6%)
Drug induced constipation	375	(35.6%)	974	(43.9%)	790	(35.6%)
Constipation	**1,053**	**(100.0%)**	**2,219**	**(100.0%)**	**2,219**	**(100.0%)**
OIC-related conditions[5], N (%)						
Abdominal pain	455	(43.2%)	906	(40.8%)	959	(43.2%)
Nausea/vomiting	145	(13.8%)	452	(20.4%)	306	(13.8%)
Cancer[6], N (%)	**1,053**	**(100.0%)**	**2,219**	**(100.0%)**	**2,219**	**(100.0%)**

Abbreviations: *CT: computed tomography; ED: emergency department, OIC: opioid-induced constipation; SD: standard deviation*

Notes:
[1] All characteristics were included in reweighting.
[2] Other race was defined as having a racial designation of Hispanic or other.
[3] Quarterly number of ED encounters were measured during the quarter of the index encounter admission date and were deseasonalised to account for potential variation in the number of ED encounters over time.
[4] OIC-related procedures were identified using ICD-10-PCS codes, CPT codes, standard charge master descriptions, and description used in the hospital's billing system.
[5] OIC-related diagnoses were identified using ICD-10 CM codes.
[6] Cancer diagnoses were identified using ICD-10 CM codes for malignant neoplasms.

Supplementary Table S3. Healthcare resource utilization for the OIC-Rx and No OIC-Rx cohorts – Cancer subsample

	OIC-Rx N = 11,135	No OIC-Rx N = 21,474	OIC-Rx vs. No OIC-Rx		
			OR/Mean difference[1]	[95% CI]	P-value
During ED encounter					
Inpatient days[2], days, mean ± SD [median]	0.8 ± 1.5 [0.0]	1.9 ± 2.6 [1.0]	-1.05	[-1.28, -0.82]	< 0.001*
Methylnaltrexone SC only[3]	0.8 ± 1.5 [0.0]	1.9 ± 2.6 [1.0]	-1.05	[-1.29, -0.81]	< 0.001*
Length of inpatient stay[2], days, mean ± SD [median]	2.7 ± 1.6 [2.0]	3.7 ± 2.1 [3.0]	-0.91	[-1.19, -64]	< 0.001*
Discharged home from ED, N (%)	707 (67.1%)	1,032 (46.5%)	2.35	[1.89, 2.93]	< 0.001*
During 30-day post-discharge period					
Any re-encounter, N (%)	566 (53.8%)	1,284 (57.9%)	0.85	[0.68, 1.06]	0.147

** Significant at the 5% level*

Abbreviations: *CI: confidence interval; ED: emergency department; OIC: opioid-induced constipation; OR: odds ratio; SD: standardized difference*

Notes:

[1] Odds ratios, 95% CIs, and p-values were estimated for binary variables using weighted logistic regressions. An odds ratio < 1 indicates a lower odds of OIC-Rx having the outcome than No OIC-Rx. Mean difference, 95% CIs, and p-value were estimated for continuous variables using weighted ordinary least squares regression models. A mean difference < 0 indicates fewer inpatient days on average in OIC-Rx compared to No-OIC-Rx. Standard errors were estimated with robust standard errors using a random effect at the hospital level (clusters).

[2] Inpatient days was calculated among all patients in the cohort and length of inpatient stay was calculated among those with an inpatient stay as the difference between discharge date and admit date plus 1 day.

[3] Among patients in the OIC-Rx cohort who received methylnaltrexone SC specifically.

Supplementary Table S4. Mean reduction in healthcare costs per OIC ED encounter in the OIC-Rx cohort compared to patients in the No OIC-Rx cohort – Cancer subsample

	OIC-Rx vs. No OIC-Rx		
	Overall	**Commercial[1]**	**Medicare/Medicaid[2]**
During ED encounter cost, ($), mean	-922	-1370	-778
Methylnaltrexone SC only[3]	-1010	-1395	-883

Percé, Quebec, Canada

Abbreviations: *ED: emergency department; OIC: opioid-induced constipation*

Notes:

[1] Commercial includes workers compensation, direct employer contract, other government payors, and other.

[2] Medicare/Medicare includes charity, indigent, and self-pay.

[3] Among patients in the OIC-Rx cohort who received methylnaltrexone SC specifically.