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Approved Opioid-Induced Constipation Medication Use in Emergency Department Patients With Opioid-Induced Constipation

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BACKGROUND

- Opioid-induced constipation (OIC), a side effect of opioid treatment, may lead to emergency room visits, which are associated with a significant burden on patients and the healthcare system[1,2]
- Approved medications for OIC (OIC-Rx), such as methylnaltrexone subcutaneous (SC; MNTX; Relistor®), are effective in treating OIC[3] and are often administered in the emergency department (ED) setting[4]
- This effectiveness may translate into reduced healthcare resource utilization (HRU) and cost savings
- However, there is limited evidence available on the impact of OIC-Rx use in the ED on HRU and costs among patients with OIC

OBJECTIVE

- The objectives of this study are to describe and compare patients with OIC receiving and not receiving OIC-Rx (including MNTX) in the ED setting in terms of HRU and costs

STUDY DESIGN

- Retrospective encounter-based analysis of adult patients with OIC with an ED encounter

METHODS

Reweighting approach

- Patient demographics, hospital characteristics, and index ED encounter characteristics were reweighted between the OIC-Rx and No-OIC-Rx cohorts using entropy balancing—a reweighting technique used to reduce selection bias
  - Appropriate reweighting was done for each population, separately (i.e., OIC-Rx overall [and a subset of MNTX only], cancer subsample [and a subset of MNTX only])

Figure 1a. Study design – OIC-Rx cohort

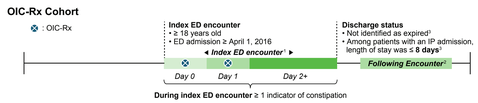
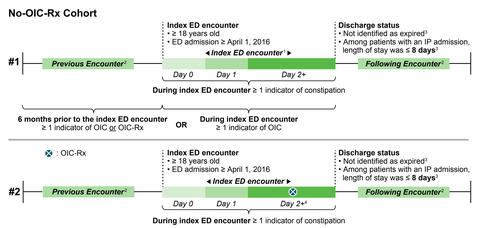


Figure 1b. Study design – No-OIC-Rx cohort



[1] Index ED encounter was randomly selected among all ED encounters that met the study sample selection criteria. [2] Patients may or may not have had other encounters previous to or following the index ED encounter. [3] Patients with a discharge status of expired and patients with an IP admission duration of over 8 days were considered to not be constipation-related encounters. [4] Patients may have received OIC-Rx after being admitted as an inpatient (i.e., not within the ED setting).

Outcomes

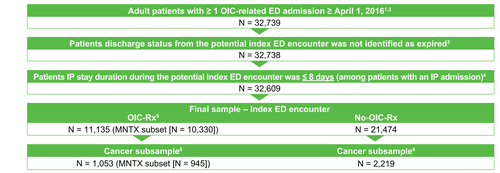
- HRU and costs were compared using weighted logistic regression for binary variables and ordinary least squares (OLS) for continuous variables with random effects at the hospital level (clusters)
- Outcomes were assessed among all patients and a subsample of patients with cancer. Inpatient days prevented and healthcare costs were also assessed among a subset of the OIC-Rx cohort receiving MNTX specifically

RESULTS

Population

- Most OIC-RX patients received a peripherally acting mu opioid receptor antagonist (PAMORA), which was overwhelmingly MNTX injections. Few patients also got chloride channel activators-lubiprostone (for drug-induced constipation)

Figure 2. Sample selection



[1] ED admission was defined as an encounter with admission type of emergency or urgent. [2] OIC-related was defined by having one of the following: i) Principal ICD-10 CM code for constipation; ii) Principal ICD-10 CM code for abdominal pain and a secondary code for constipation; iii) Principal ICD-10 CM code for nausea and vomiting, unspecified and a code for secondary constipation, and one or more of the following: i) Any OIC-Rx use during the index ED encounter or 6 months prior to index; ii) Principal or secondary ICD-10 CM code for opioid abuse/dependency during the index or 6 months prior to index. [3] Discharge status of expired was excluded based on clinical input that patients' death is unlikely to be primarily due to constipation. [4] Inpatient stays for >8 days were excluded based on clinical input that inpatient stays of this duration were unlikely to be primarily due to constipation. [5] 93% of patients received MNTX, 5% received lubiprostone, and 4% received naloxegol. [6] Patients with cancer were identified using ICD-10 CM codes for malignant neoplasms.

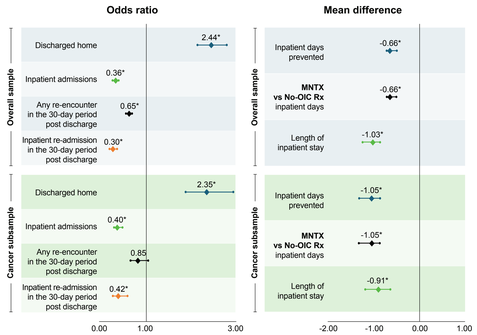
Table 1. Patient demographics and hospital characteristics

	Overall sample[1]			Cancer subsample[2]		
	Before balancing		After balancing	Before balancing		After balancing
	OIC-Rx N=11,135	No-OIC-Rx N=21,474	No-OIC-Rx N=21,474	OIC-Rx N=1,053	No-OIC-Rx N=2,219	No-OIC-Rx N=2,219
Patient demographics						
Age, mean ±SD [median]	58.6 ± 17.5 [60.0]	58.1 ± 18.4 [59.0]	58.6 ± 17.5 [60.0]	63.1 ± 12.8 [64.0]	63.2 ± 14.1 [64.0]	63.1 ± 12.8 [64.0]
Sex, N (%)						
Female	6,730 (60.4%)	13,317 (62.0%)	12,979 (60.4%)	501 (47.6%)	1,202 (54.2%)	1,056 (47.5%)
Race,[2] N (%)						
White	9,122 (81.9%)	16,528 (77.0%)	17,591 (81.9%)	141 (13.4%)	328 (14.8%)	297 (13.4%)
Black	1,347 (12.1%)	3,005 (14.0%)	2,598 (12.1%)	830 (78.8%)	1,661 (74.9%)	1,749 (78.8%)
Other	564 (5.1%)	1,672 (7.8%)	1,088 (5.1%)	73 (6.9%)	192 (8.7%)	154 (6.9%)
Unknown	102 (0.9%)	269 (1.3%)	197 (0.9%)	9 (0.9%)	38 (1.7%)	19 (0.9%)
Primary payer, N (%)						
Medicare	5,766 (51.8%)	11,143 (51.9%)	11,120 (51.8%)	256 (24.3%)	522 (23.5%)	539 (24.3%)
Commercial	2,588 (23.2%)	4,312 (20.1%)	4,991 (23.2%)	173 (16.4%)	374 (16.9%)	365 (16.4%)
Medicaid	2,045 (18.4%)	4,548 (21.2%)	3,944 (18.4%)	561 (53.3%)	1,204 (54.3%)	1,182 (53.3%)
Other	736 (6.6%)	1,471 (6.9%)	1,420 (6.6%)	63 (6.0%)	119 (5.4%)	133 (6.0%)
Hospital characteristics						
Bed size, N (%)						
0-199	3,347 (30.1%)	6,602 (30.7%)	6,454 (30.1%)	250 (23.7%)	548 (24.7%)	526 (23.7%)
200-399	3,619 (32.5%)	7,059 (32.9%)	6,979 (32.5%)	361 (34.3%)	699 (31.5%)	761 (34.3%)
400+	4,169 (37.4%)	7,813 (36.4%)	8,042 (37.4%)	442 (42.0%)	972 (43.8%)	932 (42.0%)
Region, N (%)						
South	4,884 (43.9%)	8,574 (39.9%)	9,420 (43.9%)	415 (39.4%)	922 (41.6%)	875 (39.4%)
Midwest	3,559 (32.0%)	5,085 (23.7%)	6,863 (32.0%)	304 (28.9%)	514 (23.2%)	640 (28.8%)
West	2,254 (20.2%)	5,366 (25.0%)	4,346 (20.2%)	241 (22.9%)	444 (20.0%)	508 (22.9%)
Northeast	438 (3.9%)	2,449 (11.4%)	845 (3.9%)	93 (8.8%)	339 (15.3%)	196 (8.8%)
Quarterly number of ED encounters,[3] N (%)						
0-4,999	1,352 (12.1%)	2,887 (13.4%)	2,607 (12.1%)	98 (9.3%)	281 (12.7%)	207 (9.3%)
5,000-9,999	3,296 (29.6%)	5,823 (27.1%)	6,356 (29.6%)	265 (25.2%)	557 (25.1%)	558 (25.1%)
10,000-14,999	3,853 (34.6%)	6,741 (31.4%)	7,429 (34.6%)	377 (35.8%)	670 (30.2%)	794 (35.8%)
15,000-19,999	1,659 (14.9%)	3,445 (16.0%)	3,199 (14.9%)	206 (19.6%)	392 (17.7%)	434 (19.6%)
20,000+	975 (8.8%)	2,578 (12.0%)	1,883 (8.8%)	107 (10.2%)	319 (14.4%)	227 (10.2%)
Teaching status, N (%)						
Non-teaching	8,150 (73.2%)	13,084 (60.9%)	15,716 (73.2%)	700 (66.5%)	1,206 (54.3%)	1,475 (66.5%)
Teaching	2,985 (26.8%)	8,390 (39.1%)	5,758 (26.8%)	353 (33.5%)	1,013 (45.7%)	744 (33.5%)
Population served, N (%)						
Urban	9,414 (84.5%)	17,794 (82.9%)	18,155 (84.5%)	919 (87.3%)	1,863 (84.0%)	1,937 (87.3%)
Rural	1,721 (15.5%)	3,680 (17.1%)	3,319 (15.5%)	134 (12.7%)	356 (16.0%)	282 (12.7%)
During index ED encounter						
Index encounter year, N (%)						
2016	2,949 (26.5%)	4,920 (22.9%)	5,687 (26.5%)	277 (26.3%)	482 (21.7%)	583 (26.3%)
2017	3,480 (31.3%)	6,688 (31.1%)	6,711 (31.3%)	305 (29.0%)	682 (30.7%)	643 (29.0%)
2018	2,828 (25.4%)	5,967 (27.7%)	5,454 (25.4%)	267 (27.3%)	627 (28.3%)	605 (27.3%)
2019	1,878 (16.9%)	3,899 (18.2%)	3,622 (16.9%)	184 (17.5%)	428 (19.3%)	387 (17.4%)
OIC-related procedure,[4] N (%)						
Abdominal X-ray	5,867 (52.7%)	9,712 (45.2%)	11,314 (52.7%)	556 (52.8%)	1,037 (46.7%)	1,171 (52.8%)
Abdominal CT	3,371 (30.3%)	7,990 (37.2%)	6,501 (30.3%)	405 (38.5%)	925 (41.7%)	853 (38.4%)
Enema	1,848 (16.6%)	3,629 (16.9%)	3,564 (16.6%)	238 (22.6%)	502 (22.6%)	502 (22.6%)
Fecal disimpaction	294 (2.6%)	495 (2.3%)	567 (2.6%)	29 (2.8%)	50 (2.3%)	61 (2.7%)
OIC-related diagnosis,[5] N (%)						
Opioid use	4,121 (37.0%)	10,025 (46.7%)	7,947 (37.0%)	700 (66.5%)	1,615 (72.8%)	1,475 (66.5%)
Opioid abuse/dependence	3,408 (30.6%)	19,886 (92.6%)	6,573 (30.6%)	501 (47.6%)	2,038 (91.8%)	1,056 (47.6%)
Drug-induced constipation	2,894 (26.0%)	7,136 (33.2%)	5,581 (26.0%)	375 (35.6%)	974 (43.9%)	790 (35.6%)
Constipation	**11,135 (100.0%)**	**21,474 (100.0%)**	**21,474 (100.0%)**	**1,053 (100.0%)**	**2,219 (100.0%)**	**2,219 (100.0%)**
OIC-related conditions,[5] N (%)						
Abdominal pain	4,662 (41.9%)	10,418 (48.5%)	8,991 (41.9%)	455 (43.2%)	906 (40.8%)	959 (43.2%)
Nausea/vomiting	961 (8.6%)	2,773 (12.9%)	1,853 (8.6%)	145 (13.8%)	452 (20.4%)	306 (13.8%)
Cancer,[2] N (%)	1,053 (9.5%)	2,219 (10.3%)	2,031 (9.5%)	**1,053 (100.0%)**	**2,219 (100.0%)**	**2,219 (100.0%)**

[1] Overall sample patients index ED encounters occurred within 801 distinct hospitals (MNTX only N=801), cancer subsample patients index ED encounters occurred within 632 distinct hospitals (MNTX only N=628). [2] Other race was defined as having a racial designation of Hispanic or other. [3] Quarterly number of ER encounters were measured during the quarter of the index encounter admission date and were deseasonalized to account for potential variation in the number of ER 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 and conditions were identified using ICD-10 CM codes. [6] Cancer diagnoses were identified using ICD-10 CM codes for malignant neoplasms.

HRU

Figure 3. HRU – OIC-Rx vs No-OIC-Rx

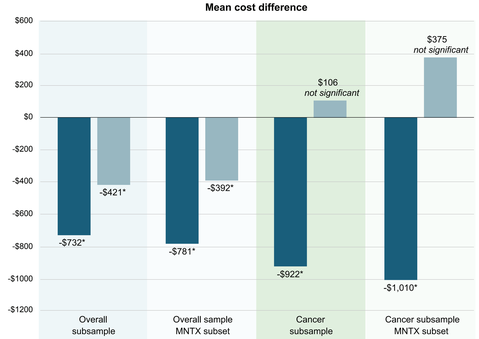


*Significant at the 5% level.

Healthcare costs

- Receiving OIC-Rx during the index ED encounter versus not receiving OIC-Rx resulted in:
  - Overall sample:
    - A **$1,152** reduction in overall costs ($732 reduction in costs per encounter and $421 reduction in costs during the 30-day period post discharge)
      - MNTX vs No-OIC-Rx: A **$1,173** reduction in overall costs ($781 reduction in costs per encounter and $392 reduction in costs during the 30-day period post discharge)
  - Cancer subsample:
    - A **$922** reduction in overall costs ($922 reduction in costs per encounter and a non-significant difference in costs during the 30-day period post discharge)
      - MNTX vs No-OIC-Rx: A **$1,010** reduction in overall costs ($1,010 reduction in costs per encounter and a non-significant difference in costs during the 30-day period post discharge)

Figure 4. Costs – OIC-Rx vs No-OIC-Rx



*Significant at the 5% level.

Economic impact of OIC-Rx simulation

- In a simulated hospital model, an average hospital (35,323 ED encounters annually) with 50 OIC-related ED encounters annually (Table 2) would save from **$236 to $945** and **7 to 29 annual inpatient days** per OIC ED encounter by initiating 25% to 100% of No-OIC-Rx patients on OIC-Rx instead (93% MNTX; Table 3)
  - Initiating 25% to 100% of No-OIC-Rx patients on MNTX instead would save from **$251 to $1,005** and **8 to 31 annual inpatient days** per OIC ED encounter
- In the cancer subsample, an average hospital (47,005 ED encounters annually) with 4 OIC-related ED encounters annually (Table 2) would save **$173 to $692** and **1 to 3 annual inpatient days** per OIC ED encounter by initiating 25% to 100% of No-OIC-Rx patients on OIC-Rx instead (90% MNTX; (Table 3)
  - Initiating 25% to 100% of No-OIC-Rx patients on MNTX instead would save from **$175 to $700** and **1 to 3 annual inpatient days** per OIC ED encounter

Table 2. Characteristics of an average hospital with OIC ED encounters

	All OIC-Rx		MNTX subset	
	Overall sample	Cancer subsample	Overall sample	Cancer subsample
	Hospital N = 675[1]	Hospital N = 341[1]	Hospital N = 611[1]	Hospital N = 320[1]
Average proportion of patients' insurance type among all ED encounters per hospital				
Medicare	53.7%	52.2%	53.4%	52.2%
Medicaid/Uninsured	29.7%	30.1%	29.9%	30.1%
Private/Paying other	16.6%	17.8%	16.7%	17.7%
Average annual number of ED encounters per hospital	35,323	47,005	36,050	46,971
OIC ED encounters	50	4	51	4
OIC ED encounters with OIC-Rx use	9	1	7	1
OIC ED encounters without OIC-Rx use (potential OIC-Rx users)	41	3	44	3
Potential impact of OIC-Rx vs No-OIC-Rx per encounter[2]				
Cost savings	$1,152	$922	$1,173	$1,010
Inpatient days prevented	0.7	1.0	0.7	1.0

[1] For the description of average hospital characteristics, hospitals with only potentially incomplete years of data were excluded. [2] 93% of the OIC-Rx patients in the overall sample and 90% in the cancer subsample of all OIC-Rx patients received MNTX during their index ED encounter.

Table 3. Simulated impact of OIC-Rx for an average hospital with OIC ED encounters

	All OIC-Rx								MNTX subset							
	Overall sample				Cancer subsample				Overall sample				Cancer subsample			
	Hospital N = 675				Hospital N = 341				Hospital N = 611				Hospital N = 320			
Proportion of No-OIC-Rx patients switched to OIC-Rx	100%	75%	50%	25%	100%	75%	50%	25%	100%	75%	50%	25%	100%	75%	50%	25%
Number of patients switched to OIC-Rx	41	31	21	10	3	2	2	1	44	33	22	11	3	2	1	1
Impact of increased OIC-Rx use in the ED																
Per OIC ED encounter cost savings	$945	$708	$472	$236	$692	$519	$356	$173	$1,005	$754	$503	$251	$700	$525	$350	$175
Annual IP days prevented	29	22	14	7	3	2	2	1	31	23	15	8	3	2	1	1

CONCLUSIONS

- **Patients receiving OIC-Rx in the ED are more likely to be discharged home, less likely to be hospitalized, and have a shorter inpatient stay**
  - **Results are largely driven by patients receiving MNTX which represent over 90% of all OIC-Rx patients**
- **Patients receiving OIC-Rx cost $1,152 less (MNTX subset: $1,173; cancer subsample: $922) and save 0.7 inpatient days (MNTX subset: 0.7 inpatient days; cancer subsample: 1.0 inpatient days) per OIC ED encounter than when patients do not receive OIC-Rx in the ED setting**

LIMITATIONS

- The total number of ED OIC encounters may be underestimated in the study database and hospitals included in the database may not be representative of all US hospitals
- Limited clinical information was available and reasons for patients receiving or not receiving OIC-Rx in the ED was not available
- The study database cannot distinguish between patients receiving OIC-Rx in the ED versus during their inpatient admission among patients who were admitted on the same day as their ED encounter, in such case patients were assumed to receive OIC-Rx in the ED setting

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DISCLOSURES

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