The Impact of Emergency Department Opioid Prescribing Guidelines on Emergency Physician Behaviour and Incidence of Overdose in the Saskatoon Health Region: A Retrospective Interrupted Time-Series Analysis

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Research funding was provided by an internal grant from the University of Saskatchewan College of Medicine Dean's Project fund awarded to Mr. Elder

Competing interests: Dr. Luke Terrett is the lead author and creator of the Saskatoon Health Region emergency department restricted medications prescribing guidelines. He receives no additional funding for his role in their development nor implementation.

Abstract (250 Words):

Background: Deaths related to opioid overdoses have been increasing in North America. The emergency department (ED) has been blamed as a driver of this epidemic. Recent studies in the United States have looked at implementing an opioid prescribing guideline in the ED with success at decreasing total number of prescriptions, though fail to show a reduction in total morphine equivalents prescribed, nor a change in overdose rates.

Methods: We performed a retrospective interrupted time-series analysis of 32 ED physician prescriber habits through quantification of the opioids prescribed per hour worked, and per patient seen, pre- and post- implementation of a restricted medications prescribing guideline. Additionally, overdose data was pulled from local overdose surveillance groups to determine if there were any change in overdose rates.

Results: We found a 31.1% decrease in opioids prescribed ($p = 0.0005$). Over the same period, we found no change in the EMS naloxone usage, and an insignificant increase in the amount of naloxone dispensed by ED pharmacies. Finally, there was no decrease in the number of overdoses in the region following implementation.

Interpretation: A restricted medications prescribing guideline in a Canadian ED setting decreased the quantity of opioids prescribed. Findings also suggest that the ED is unlikely the source of opioids used in acute overdose, though we cannot rule out ED opioid prescriptions as being a risk factor for developing addiction. Future studies are needed to look at the long-term effects of restricted medications prescribing guidelines on rates of addiction and overdose in the community.

Introduction:

Deaths related to opioid overdoses have increased significantly in North America over the past decade with a worrying trend(1,2). During a ten month period in British Columbia, from January 2016 to October 2016, there were 374 fentanyl related overdose deaths, an increase of 194% from the same period in 2015(3). Acute care centers and emergency departments have been proposed as potential drivers of this epidemic(4–7), including a recent longitudinal study in Ontario where patients receiving opioid prescriptions in the emergency department (ED) had a higher risk of admission for opioid toxicity over two years(5). The number of opioids prescribed for adults in ED visits has risen dramatically over the periods of 2001-2010 and continues to trend upward(8). The increase in opioid prescriptions has been attributed to numerous factors including: aggressive marketing by pharmaceutical companies, the desire to minimize acute and chronic pain, and a lack of discussion between prescribers and patients on the risk of addiction associated with opioids(9–11). As such, clinical policies have been created to target opioid prescribing in American EDs(4,12–14). Though these policies have been successful at decreasing the number of prescriptions, they have failed to investigate if the decreased prescription volume results in a decrease in opioid abuse in the community, and have not been shown to be effective in a Canadian healthcare system.

This epidemic has resulted in provincial and national changes in prescribing policy and a shift in attitude of both the general public and the medical community on the risks associated with these medications. Recently, the College of Family Physicians of Canada released updated guidelines to educate physicians opioid prescriptions(15). These guidelines are meant to assist physicians with their prescribing habits and combat the opioid epidemic. Although these guidelines provide broad recommendations on prescribing, they are not universally applicable.

With its high patient volume and lack of a pre-existing patient-provider relationship, the ED has been identified as a possible location where opioid use disorders may develop, with upwards of 29% of opioid abusers having been initially exposed in the ED(5–7).

In September 2016, the Saskatoon Health Region (SHR) ED updated their restricted medications prescribing policies. In this study, we sought to demonstrate whether a departmental guideline would result in a reduction in opioid prescriptions and total morphine equivalents (TMEs) prescribed in a Canadian setting, with secondary objectives of trending local overdoses to find if the ED was a major source of opioids used in overdose.

Methods:

This study was deemed exempt from ethics review by the University of Saskatchewan and the Saskatoon Health Region research ethics boards (REB BIO#17-118), and the SQUIRE reporting guidelines for quality improvement projects was used (16).

In September 2016, the Department of Emergency Medicine in the SHR implemented a restricted medication prescribing guideline to help decrease high-abuse medication prescribing from the ED. This guideline sought to encourage physicians to: review the patient's prescription history looking for misuse, abuse and diversion when requesting these medications, encourage the physician to contact the patient's primary care provider, limit the amount of medication prescribed to the next business day, and reinforce the necessity of a single outpatient prescriber to the patient. A detailed version of the current SHR restricted medications prescribing guidelines can be found in Appendix A.

A retrospective interrupted time-series analysis between the dates of November 1, 2015 to April 30, 2016 (pre-guidelines) and November 1, 2016 to April 30, 2017 (post-guidelines) was

conducted on the ED staff physicians in the SHR using provincial prescription monitoring. Physicians were included if they held part-time or full-time positions with the Department of Emergency Medicine throughout the entire study period. The prescription histories of the 32 ED physicians were provided through the College of Physicians and Surgeons of Saskatchewan Prescription Review Program. The amount of hydromorphone immediate release (IR), hydromorphone extended release (ER), morphine IR, morphine sustained released (SR), acetaminophen with codeine and caffeine, acetaminophen with oxycodone, and fentanyl patches prescribed by individual physicians was totalled and evaluated between the pre- and post-implementation study periods. All the medications were converted to TMEs using the conversion ratios from the College of Family Physicians of Canada's 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain to allow for comparison between formulations(15). The number of hours worked and patients seen for each physician was provided to the Prescription Review Program who returned the anonymized data found in Appendix B. Since fentanyl patches were infrequently prescribed and were likely a refill on a chronic prescription until a primary care provider could be seen, this data was removed for the overall analysis as it could skew the data. TMEs prescribed was then normalized by total hours worked and total patients seen for each physician in order to compare prescribing rates between physicians.

Student's paired two-tailed T-tests were performed on the prescriber populations for both individual drug formulations and the combined TME, for pre- and post-guideline time periods.

Additionally, naloxone usage data was collected from the only pre-hospital EMS provider and the ED pharmacies in the SHR over the same period.

Finally, the SHR Public Health Observatory (PHO) Sentinel Opioid Overdose Surveillance Group began collecting data prospectively in May 2017. Ambulance, police and

pharmacy data is mailed weekly to the PHO. Uncoded "real-time" ED data is received electronically as part of the public health surveillance mandate based on triage complaints and ED physician diagnosis. ED data was analyzed retrospectively from 2016 for historical trends. Coded data (based on nationally recommended Tcodes and F11) is received three to six months after the fact and compliments the "real-time" uncoded ED data. Uncoded ED Overdose High Risk/Unknown Substance roughly corresponds with the coded ED data, and has therefore been found useful as a good proxy measure of overdose occurrence. Some overdose incidents are missed by the category Overdose High Risk Substance, therefore the broader category, ED Substance Misuse (which includes the subcategory Overdose High Risk/Unknown Substance) has been found to be a useful indicator. Coded opioid overdose deaths that arrived in the ED were augmented by ambulance deaths where naloxone was administered, as overdose deaths that occur in the community were not captured by overdose deaths in ED.

Results:

The average TMEs prescribed per hour and per patient seen decreased significantly. The mean TME of each type of narcotic prescription, as well as combined TME of all restricted medications prescribed in the SHR EDs before and after the implementation of the restricted medication prescribing guidelines, is presented normalized per hour worked and per patient seen in Tables 1 and 2 respectively. Specifically, the average TMEs prescribed per hour decreased 28.5% from 18.31 mg MEQ/hour to 13.22 mg MEQ/hour ($p = 0.0001$), and the average TMEs prescribed per patient seen decreased 31.1% from 10.36 mg MEQ/patient to 7.14 mg MEQ/patient ($p = 0.0005$). When looking at each type of narcotic prescribed, hydromorphone IR

reached statistical significance with a decrease in the average TMEs prescribed per hour by 31.2% from 12.44 mg MEQ/hour to 8.56 mg MEQ/hour ($p = 0.0002$), and a decrease in the average TMEs prescribed per patient seen by 32.5% from 6.84 mg MEQ/patient to 4.62 mg MEQ/patient ($p = 0.0002$). The other specific types of restricted medications prescribed failed to reach statistical significance. The raw pre- and post- implementation prescriber prescription data can be found in Appendix B.

The individual prescriber distribution of TMEs prescribed pre- and post- implementation is represented by boxplot in Figure 1, with the distributions by specific restricted medications in Appendix C. Overall, we found decreased variation between the physicians, with a decrease in the median, the mean, and the 3rd quartiles.

Pre-hospital and ED usage of naloxone is shown in Table 3. The number of patients treated with naloxone pre- and post- implementation of the guidelines was unchanged at 39 patients each. The number of 2mg/2ml vials of naloxone dispensed by the regions 3 hospitals increased from 164 to 174.

SHR Public Health Observatory Sentinel Opioid Overdose Surveillance Group data is shown in Figure 2. There was no significant decrease in opioid overdoses or high-risk substances presenting to the SHR EDs in the time since implementation of the restricted medications prescription guideline, though this data is limited due to a lack of data prior to guideline implementation.

Interpretation

We found the implementation of a restricted medication prescribing guideline in a Canadian ED resulted in a decrease in TMEs prescribed of 31.1%, with a significant reduction in

the main opioid prescribed from our EDs (Hydromorphone IR, 32.5%). Over the same study period, we found no change in the EMS usage of naloxone, and an insignificant increase in the amount of naloxone dispensed by ED pharmacies. Finally, even though there was a 31.1% reduction in TMEs prescribed through the EDs, the number of overdoses in the health region, including opioid coded overdoses following CIHI recommendations, did not decrease over the study period nor the months following.

Similar studies have been conducted in the United States, though these studies looked only at a specific ICD-9 diagnosis or excluded some ED providers. Moreover, these studies only looked at the number of prescriptions and not the quantity of TMEs prescribed(4,14). Neither study has looked at the impact of a restricted medication prescribing guideline on the incidence of overdose in the community. Weiner *et al.* found that ED specific guidelines reduced the number of opioid prescriptions being issued by emergency department physicians by 12%, with a decrease being found across all specific opioids(4). The major additions in that study as compared to the national guidelines included the following: encouraging patients to have a sole provider for these medications, not routinely providing prescriptions for lost, stolen or destroyed medications, consulting the patient's primary care provider before re-issuing a prescription, limiting prescriptions to a 3-day supply or enough time for the patient to contact their primary provider, and educating the patient on the addictive nature of opioid medications. The new SHR ED restricted medication prescribing guidelines used similar recommendations, and found a reduction of 31.1% in TMEs prescribed, with the only specific opioid to have a significant reduction in prescribing rates being hydromorphone IR. This is likely due to variances in local practice wherein hydromorphone IR makes up 66% of all opioid prescriptions from the ED. Finally, our study failed to demonstrate meaningful impact on reducing opioid-related overdoses

in the community. The reasoning for this could be two-fold. First, patients overdosing on opioids are acquiring their narcotics from sources other than the ED. Secondly, the initiation of opioids in the ED has been implicated as a risk factor for ongoing opioid addiction and overdose(4–7). With our 31.1% reduction on TMEs prescribed, the effects of reducing the number of patients exposed to the risk of opioid addiction could take several years to decades to surface.

Our study has several limitations. First, we are unable to know if the restricted medications prescribing guideline was the sole driver of practice change. Local and national attitudes and culture have been slowly shifting and these could account for some of the change in prescription habits. Additionally, changes in the accessibility of primary care providers could confound the study results. Second, in our current study we are unable to comment on the appropriateness of the opioid prescriptions provided. Third, the coding of ED data in our health region is through the ED physician's ICD-9/ICD-10 discharge diagnosis on the electronic chart. As the exact drug overdosed on, or even diagnosis, is often unclear at the time of discharge or admission to hospital from the ED, the ED physician's discharge diagnosis is often vague making ED overdoses difficult to extract for ongoing surveillance of overdose. Additional ED data is pulled through the broad category selected at triage, which may miss some overdoses, especially where respiratory distress is designated the most urgent complaint. Fourth, this study was performed in an ED setting and may not be generalizable to other outpatient or inpatient settings. Finally, the ED pharmacy restock of naloxone does not necessarily relate directly to naloxone usage. Vials may have expired, been opened and not used, broken, or been transferred to other units in the hospital.

Conclusion:

This study represents the first report demonstrating an impact of restricted medication prescribing guidelines on TMEs prescribed, with a reduction of 31.1% per patient seen. To our knowledge, this study also represents the first evaluation of ED specific opioid prescribing guidelines in Canada. Our findings indicate that an ED specific restricted medication prescribing guideline significantly decreases the TMEs of opioids prescribed out of the emergency department in a Canadian setting. Future studies are needed to look at the impact of expanding restricted medication prescribing guidelines to other specialties and settings. Additionally, the long-term effects of a restricted medications prescribing guideline on the incidence of opioid addiction and misuse on the community will need to be studied further.

Acknowledgements:

The authors would like to thank Leah Heilman for sharing SHR pharmacy data, Tim Hillier with Medavie Ambulance Service for providing EMS data, Liisa Scherban with the College of Physicians and Surgeons Prescription Review Program for extracting provider prescription data, and Judith Wright with the Public Health Observatory SHR Sentinel Opioid Overdose Surveillance group for sharing local overdose data.

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Table 1: Pre vs Post Morphine Equivalents Prescribed per Hour Worked

	Pre-Guideline		Post-Guideline			
	Average (mg MEQ/Hour)	Median (mg MEQ/Hour)	Average (mg MEQ/Hour)	Median (mg MEQ/Hour)	Average Reduction (mg MEQ/Hour)	P-Value
Hydromorphone IR	12.44	10.91	8.56	6.59	-3.88	0.0002
Hydromorphone ER	1.66	0.63	0.98	0.00	-0.68	0.0925
Morphine IR	0.85	0.54	0.72	0.42	-0.12	0.4432
Morphine SR	0.65	0.00	0.26	0.00	-0.39	0.3255
Oxycodone + Acetaminophen Tabs	0.07	0.00	0.08	0.00	0.01	0.8238
Acetaminophen + Caffeine + Codeine Tabs	2.84	2.08	2.62	1.72	-0.22	0.5635
Total Morphine Equivalents	**18.51**	**16.07**	**13.22**	**11.22**	**-5.28**	**0.0001**

Table 2: Pre vs Post Morphine Equivalents Prescribed per Patient Seen

	Pre-Guideline		Post-Guideline			
	Average (mg MEQ/Patient)	Median (mg MEQ/Patient)	Average (mg MEQ/Patient)	Median (mg MEQ/Patient)	Average Reduction (mg MEQ/Patient)	*p* - Value
Hydromorphone IR	6.84	6.24	4.62	4.14	-2.22	0.0002
Hydromorphone ER	1.00	0.32	0.53	0.00	-0.47	0.0794
Morphine IR	0.46	0.28	0.40	0.24	-0.06	0.5075
Morphine SR	0.36	0.00	0.16	0.00	-0.21	0.3824
Oxycodone + Acetaminophen Tabs	0.06	0.00	0.04	0.00	-0.01	0.7765
Acetaminophen + Caffeine + Codeine Tabs	1.65	1.25	1.39	0.99	-0.26	0.2063
Total Morphine Equivalents	**10.36**	**8.86**	**7.14**	**6.18**	**-3.22**	**0.0005**

Table 3: Naloxone Dispensed in Saskatoon Health Region by EMS and ED Pharmacy

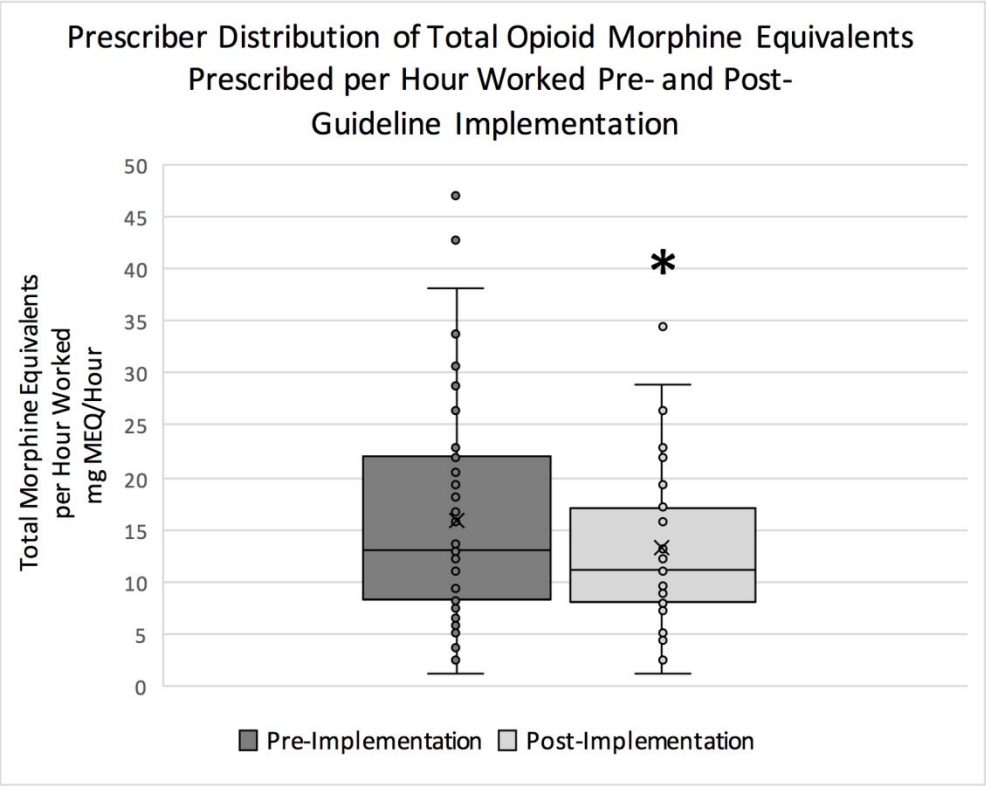
Pre-Hospital Naloxone Given by EMS

Pre-Guideline		Post-Guideline	
Number of Patients Treated	Naloxone (mg)	Number of Patients Treated	Naloxone (mg)
39	23.4	39	34.5

Naloxone Vials (2mg/2ml) Dispensed to EDs

Pre-Guideline		Post-Guideline	
Hospital ED	Number of Vials	Hospital ED	Number of Vials
1	10	1	1
2	111	2	134
3	43	3	39
Total:	**164**		**174**

Figure 1: Prescriber Distribution of TMEs Prescribed per Hour Worked and Patient Seen



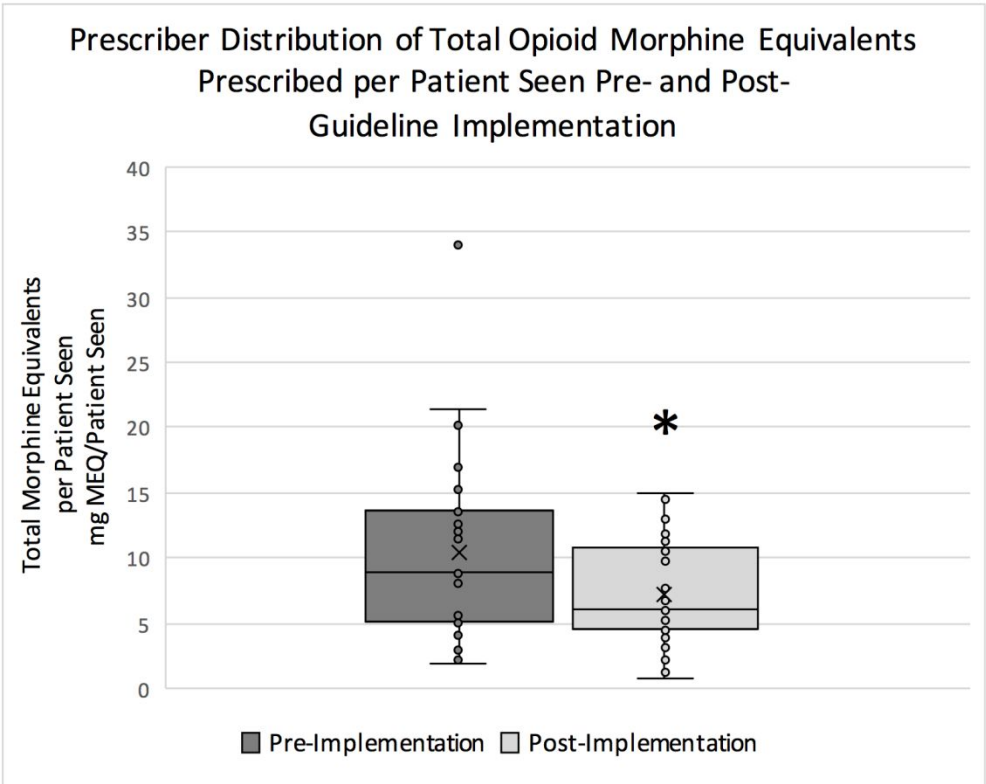
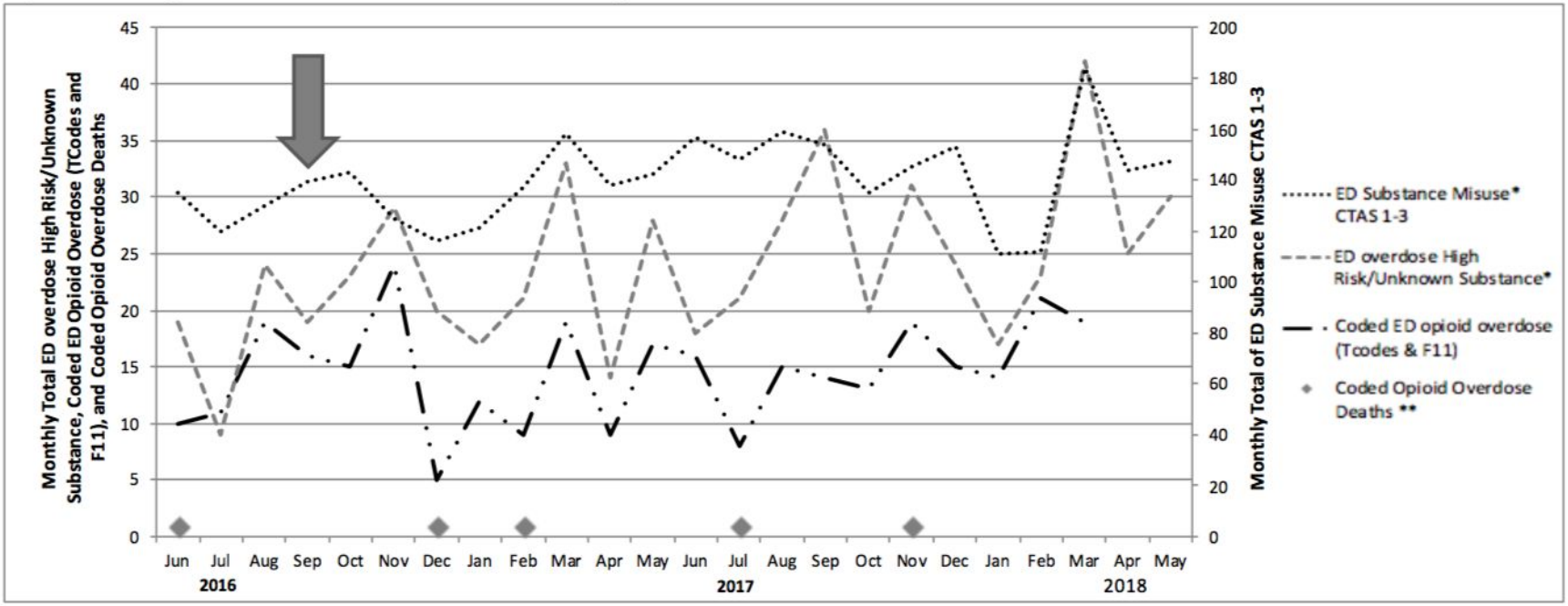


Figure 1: Boxplots of prescriber distribution of TME of hydromorphone IR, hydromorphone ER, morphine IR, morphine SR, acetaminophen with hydrocodone, and acetaminophen with codeine and caffeine prescribed per hour worked and per patient seen in SHR EDs before and after the implementation of restricted medication prescribing guidelines. N=32. * *p*-value < 0.0005. MEQ = morphine equivalents.

Figure 2: Sentinel Opioid Overdose Surveillance Data from June 2016 - May 2018



Arrow denotes implementation of restricted medications prescription guideline.
*Uncoded ED data, complaint category Substance Misuse includes high risk substance/ unknown substance.
**Coded opioid overdose deaths include deaths occurring in hospital only, not community.

Saskatoon Health Region Restricted Medication Prescribing Guidelines

Emergency Department Controlled Substances Prescribing Guideline

Applies to Schedule I-IV Substances of the Controlled Drugs and Substances Act (S.C. 1996, c. 19)

(Opioids, Benzodiazepines, Barbiturates, Marijuana, Stimulants)

1) **Population**
    a. Patients on long-term therapy (> 6 months) who present to the ED requesting a refill for any reason (including theft, lost prescription, ran out of medications, etc).
2) **Single provider**
    a. The patient needs a single prescriber (e.g. family physician).
    b. The ED is not an appropriate/safe place for patients to receive their prescriptions for controlled substances.
    c. If the patient does not have a family physician, unfortunately they are not suitable candidates for long-term therapy with these medications.
3) **PIP review**
    a. A detailed review of the patient's PIP will be performed looking for red flags for misuse/abuse/diversion. These include the following:
        i. Multiple prescribers
        ii. Filling prescriptions at multiple pharmacies
        iii. Frequent early refills
        iv. Escalating dosage
4) **Urine Drug Screen (optional)**
    a. A urine drug screen can be performed in the ED to help the family physician with further decision making in the outpatient setting but should not delay disposition or the decision to prescribe in the ED.
5) **Contact family Physician & Pharmacist**
    a. The ED physician should attempt to contact the family physician & dispensing pharmacy.
    b. A copy of the ED report will be sent to the family physician.
6) **Amount Prescribed**
    a. If the ED physician feels it is appropriate to prescribe to the patient, the amount should be limited until the next business day.
    b. This is regardless of whether the patient reports their family physician is on vacation or unable to see them for 2 weeks.
7) **Dose prescribed**
    a. An amount that the ED physician is comfortable with in the context of the patient's illness.
    b. This may be significantly lower than what the patient is currently receiving.
8) **One-Time Prescription**
    a. This is a one-time prescription regardless of whether the medications have been lost, stolen, or the patient has run out.

b. This will apply across all EDs in the health region.

9) Education regarding appropriate use of opioids and restricted medications

a. The patient needs a single prescriber for these medications.
b. The patient is a partner in their healthcare plan.:
    i. They need to ensure that their meds are not lost/stolen and they do not run out.
    ii. They are responsible for coordinating with their family physician to ensure that they have enough medications to cover vacations or travel.

10) Documentation in the Electronic Medical Record (Sunrise Clinical Manager)

a. This will allow other ED physicians to provide a consistent approach.

Appendix B: Pre-Intervention Opioid Prescriptions (November 1, 2015 - April 30, 2016)

Physician Number	Hours Worked	Patients Seen	Fentanyl patch (mg MEQ*)	Hydromorphone IR (mg MEQ*)	Hydromorphone ER (mg MEQ*)	Morphine IR (mg)	Morphine SR (mg)	Oxycodone + Acetaminophen Tabs (mg MEQ*)	Acetaminophen + Caffeine + Codeine Tabs (mg MEQ*)	Total Morphine Eq. Prescribed
1	523.75	846	12500	6310	1185	834	0	0	3397	24226
2	472.00	694	0	4775	1020	250	0	0	180	6225
3	561.75	780	0	7340	0	500	0	0	2304	10144
4	504.75	1001	0	9600	840	150	0	0	3060	13650
5	774.25	1548	0	22135	2025	0	0	75	1980	26215
6	500.25	976	0	2525	630	1025	0	0	855	5035
7	598.00	1264	0	16070	4860	275	0	225	4073	25503
8	358.50	627	0	4065	0	325	0	0	1395	5785
9	613.25	990	0	9020	2160	200	0	150	1931	13461
10	767.50	1528	0	5855	0	0	0	0	405	6260
11	583.75	1282	125000	5400	450	3070	2970	0	3501	140391
12	531.00	1047	0	2710	120	300	120	0	279	3529
13	604.00	966	0	4875	2700	400	0	0	270	8245
14	760.25	1365	10000	8550	4260	1250	300	0	1197	25557
15	587.50	974	0	8190	1740	0	5450	0	1557	16937
16	656.75	1092	0	6995	0	0	0	0	2003	8998
17	340.50	687	0	8335	0	300	0	0	1791	10426
18	502.00	1162	0	9650	0	300	0	0	3375	13375
19	195.00	372	0	500	0	100	0	0	135	735
20	378.75	866	0	2010	180	0	0	0	392	2582
21	530.50	1049	0	1950	720	3075	0	0	2745	8490
22	370.00	604	0	2430	0	200	0	0	360	2990
23	966.50	2125	0	43830	600	180	0	0	720	45330
24	136.00	244	0	1050	315	0	0	0	0	1365
25	711.75	1039	0	8400	450	620	1040	0	2682	13192
26	558.00	1050	0	2250	0	0	0	0	90	2340
27	530.25	1303	0	5925	150	0	0	0	810	6885
28	610.00	944	0	5465	270	345	900	0	1283	8263
29	399.00	698	0	1900	0	0	0	0	450	2350
30	319.50	665	0	4140	0	300	900	0	0	5340
31	836.00	937	0	15610	6240	640	100	1305	8046	31941
32	381.50	643	0	1525	1440	100	0	0	783	3843
Total	**17162.50**	**31368**	**147500**	**239385**	**32355**	**14739**	**11780**	**1755**	**52049**	**499608**

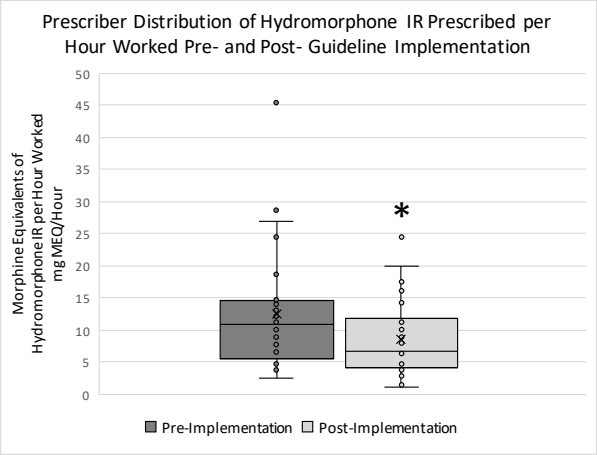
*Calculated in milligrams of Morphine Equivalents

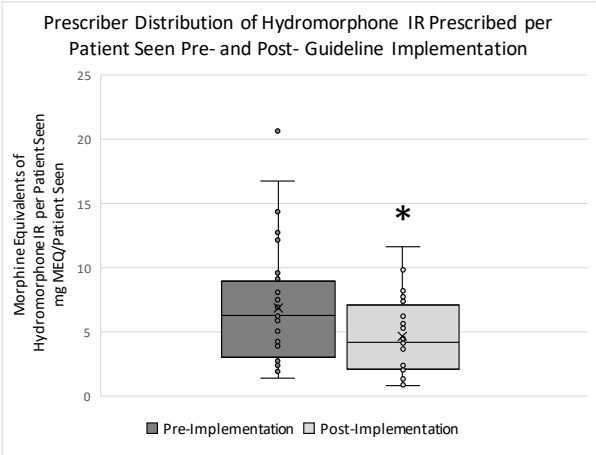
Appendix B: Post-Intervention Opioid Prescriptions (November 1, 2016 - April 30, 2017)

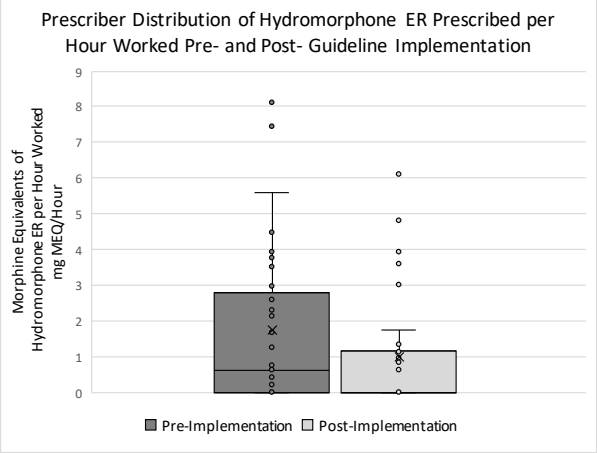
Physician Number	Hours Worked	Patients Seen	Fentanyl patch (mg MEQ*)	Hydromorphone		Morphine		Oxycodone + Acetaminophen Tabs (mg MEQ*)	Acetaminophen + Caffeine + Codeine Tabs (mg MEQ*)	Total Morphine Eq. Prescribed
				IR (mg MEQ*)	ER (mg MEQ*)	IR (mg)	SR (mg)			
1	525.75	778		6240	2070	200	0	0	1625	10135
2	361.75	580	0	2300	0	200	0	0	225	2725
3	401.25	586	0	2600	0	0	0	0	1166	3766
4	546.50	1073	25000	2700	0	300	0	0	1845	29845
5	750.00	1534	0	14975	480	341	0	0	1440	17236
6	544.25	1111	0	2605	540	350	0	0	5040	8535
7	554.75	1134	0	9335	2010	550	620	0	2273	14788
8	358.00	639	0	1315	0	75	0	0	1481	2871
9	517.25	791	100000	5800	900	500	0	150	1035	108385
10	757.50	1590	0	6700	0	0	0	450	90	7240
11	629.25	1320	12500	3200	420	2400	0	0	2070	20590
12	420.25	736	0	715	45	1220	200	0	180	2360
13	500.00	724	0	7065	420	400	0	0	756	8641
14	735.00	1307	0	6840	0	245	300	0	810	8195
15	546.75	937	0	1830	2640	200	0	0	63	4733
16	583.25	969	30000	3765	675	700	0	0	1440	36580
17	265.75	525	0	4300	1620	300	0	0	1440	7660
18	235.75	528	0	2800	0	0	0	225	2160	5185
19	166.25	298	0	250	0	100	0	0	50	400
20	311.25	691	0	1475	0	0	0	0	135	1610
21	496.50	986	0	1415	0	1675	0	0	1215	4305
22	343.75	521	0	3250	0	0	0	0	945	4195
23	783.25	1662	0	19235	900	0	0	150	360	20645
24	87.25	136	0	100	0	0	0	0	0	100
25	791.25	1159	0	6375	840	850	300	0	4226	12591
26	536.00	1022	0	2050	0	100	0	0	158	2308
27	530.50	1202	0	5375	720	100	0	0	743	6938
28	552.25	874	0	3560	0	715	0	225	68	4568
29	410.00	753	0	2745	0	125	0	0	64	2934
30	272.00	576	0	3225	0	0	0	0	198	3423
31	993.25	2272	17500	17455	3000	300	0	255	13122	51632
32	309.75	481	0	620	0	175	1820	0	378	2993
Total	**15816.25**	**29495**	**185000**	**152215**	**17280**	**12121**	**3240**	**1455**	**46801**	**418112**

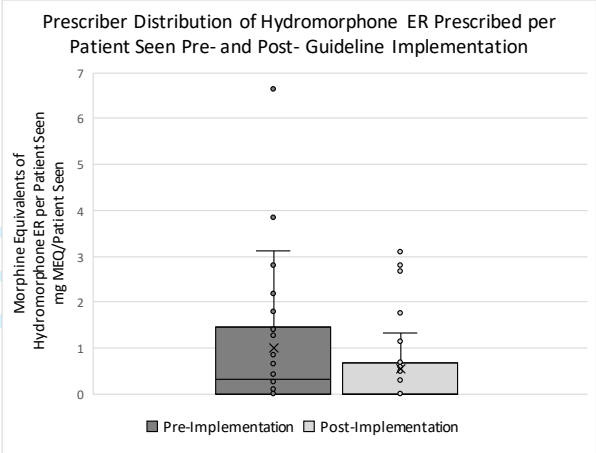
*Calculated in milligrams of Morphine Equivalents

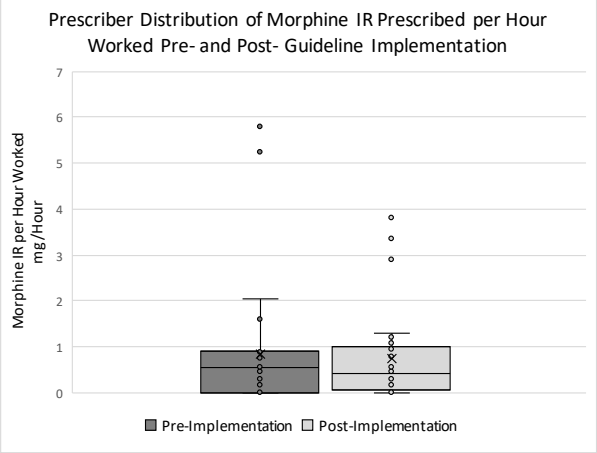
Appendix C: Prescriber Distribution of individual Restricted Medications Prescribed per Hour Worked and Patient Seen

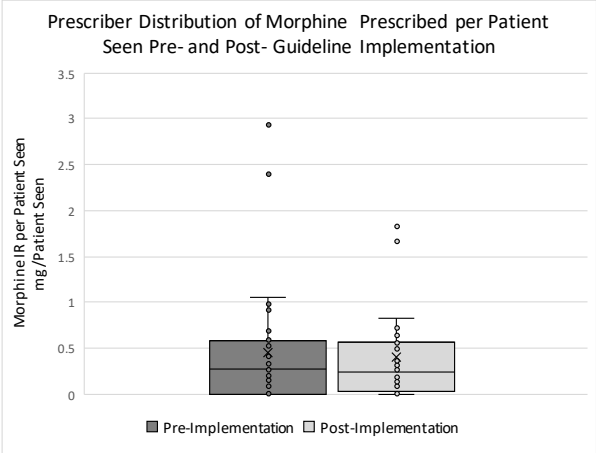


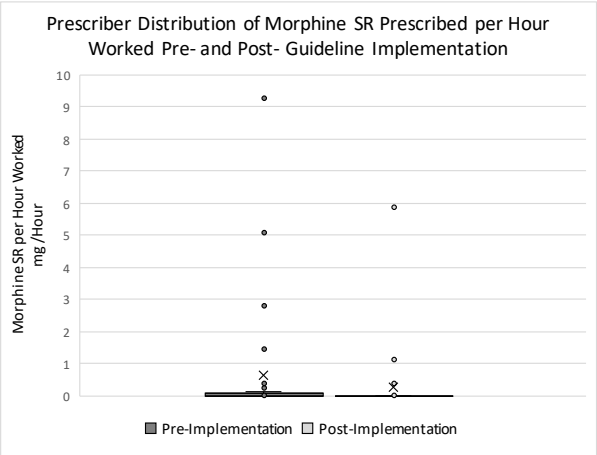


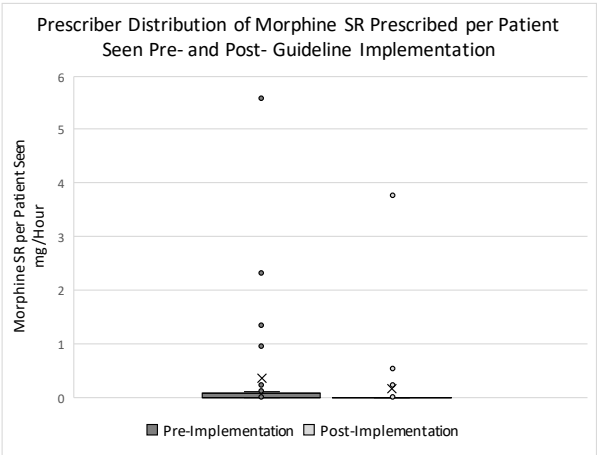


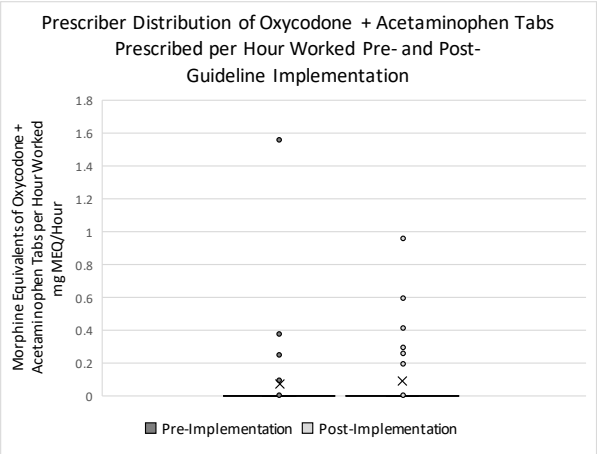


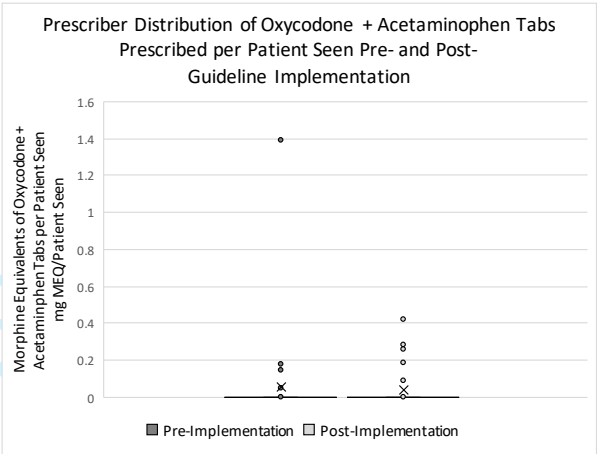


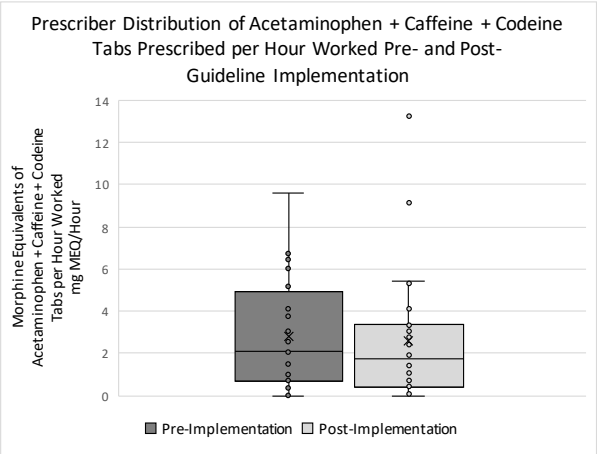


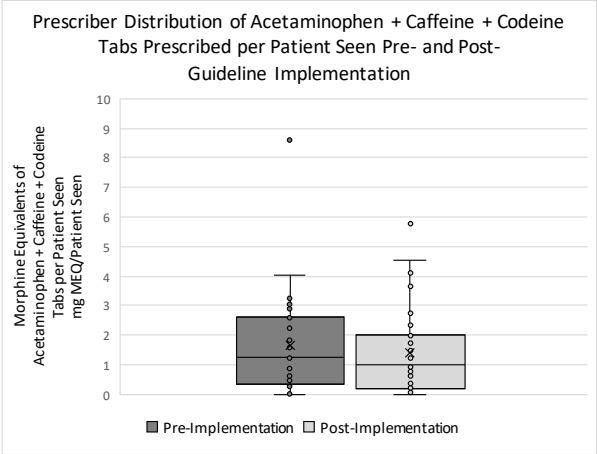












*** Denotes Statistical Significance $p < 0.0005$**