TITLE

Epidemiology of Prescription Opioid Use among Metis in Manitoba

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ABSTRACT

Background: Canada is in the midst of an opioid crisis. Indigenous people, and specifically First Nations people, are among the populations hardest hit by opioid-related harms. However, to date there is no information available about opioid use in Metis populations in Canada. Without this evidence, Metis leadership are excluded from planning and implementing harm-reduction strategies in their communities. To address this knowledge gap, we examined the epidemiology and patterns of prescription opioid dispensations among Manitoba Metis.

Methods: We conducted a population-based, retrospective longitudinal study for fiscal years 2006/07-2017/18 using administrative data from the Manitoba Population Research Data Repository. Age- and sex-adjusted rates of prescription opioid dispensations were compared between Metis and All Other Manitobans (AOM).

Results: Betwen 2006-2018, the number of prescription opioid dispensations decreased among Metis (5.2%) and AOM (12.0%); the difference in this decrease between Metis and AOM was not significant (p=0.4927). The mean number of days a person used a prescription opioid increased from 78 to 116 (48%) for Metis and 65 to 89 (37%) for AOM; the increase among Metis was significantly greater than among AOM (p<0.0001). The use of highly potent opioids (e.g., fentanyl) trended upwards in both groups.

Interpretation: While the number of opioid prescriptions dispensed in Manitoba appears to be declining, use of stronger opioids and the duration of use is rising, particularly among Metis but also among AOM, likely contributing to opioid-related harms. The trend toward greater use of potent opioids is a concern for all Manitobans, but disproportionately affects Metis populations.

INTRODUCTION

The opioid crisis in Canada is well-documented (1–3). Recent estimates of harms associated with opioid use show a 55% increase in opioid-related deaths from 2016-2018, with a total of 4,382 deaths in 2018 (4), and hospitalizations due to opioid poisonings climbed by 5% from 2016-2018, with 17.6 per 100,000 people hospitalized in 2018 (1,4). The highly addictive nature of opioids, together with the inappropriate prescribing practices often applied to them, are major contributors to the worsening opioid crisis (5).

Certain Canadian populations are at high risk of being negatively impacted by prescribed opioids. Indigenous people have been shown to have higher rates of hospitalizations from opioid poisonings than other Canadians (1). However, to date there have been no studies examining the impact of the opioid crisis among Metis specifically. Metis people are descendants of First Nations and European settlers who once governed a distinct nation in the northwest part of the continent. Canadian colonial laws and policies dispossessed the Metis of their lands and subjected them to many other damaging injustices. Despite these challenges, they remain resilient and resourceful, celebrating a rich cultural and social history (6), and they maintain their rights to self-determination and self-government.

Metis leaders consider the health and well-being of their people to be a top priority, but the lack of Metis-specific data on health issues like the opioid crisis act as a barrier to implementing effective public health harm-reduction and intervention strategies in their communities. In this study, researchers at the Manitoba Metis Federation (MMF) and the University of Manitoba have partnered to examine the epidemiology of the opioid crisis and to document patterns of prescription opioid use among Manitoba Metis.

METHODS

Study Design

We conducted a longitudinal, population-based, retrospective administrative data study of prescription opioid dispensations in the province of Manitoba. We compared the rate of opioid dispensations and the dose of opioid-associated morphine equivalents among Metis people and All Other Manitobans (AOM) in fiscal years 2006/07 and 2017/18, and examined trends in the dose of morphine equivalents over time from 2006/07 to 2017/18 by age, sex, income level, urbanicity, number of comorbidities and opioid type. Opioid-associated morphine equivalents,

the cumulative intake of an opioid drug over a 24-hour period, allow for a standardized comparison of different types of opioids with different potency levels.

Data Source

The data were derived from the Manitoba Population Research Data Repository at the Manitoba Centre for Health Policy (MCHP), University of Manitoba. The Repository comprises over 90 databases that can be linked at the individual- and family-levels across databases and over time. It includes de-identified records for virtually every contact Manitobans make with the health care system as well as information on prescription drug dispensations from community pharmacies for >99% of Manitoba residents, including members of the Metis Nation. **Appendix Table 1** provides a description of the databases used in the study.

Study Cohort

The cohort included all people living in Manitoba at some point between 2006/07 and 2017/18 who were registered for health insurance. We excluded children under the age of ten. With permission from the MMF, we identified citizens of the Metis Nation by linking the Manitoba Metis Registry to the Repository at MCHP. The comparison group comprised All Other Manitobans (AOM), which included non-Indigenous residents of Manitoba as well as Inuit, First Nations and other individuals who were not in the Metis Registry (**Figure 1**).

Measures

To examine how prescription opioid dispensations have changed over the last 15 years, we calculated the rate of dispensations per 1,000 person-years, mean number of days individuals had an opioid prescription, mean morphine equivalents per user, and mean morphine equivalents per day among Metis and AOM in 2006/07 and 2017/18 with a 180 day washout period for each newly dispensed prescription. We also tested time trends in mean morphine evivalents per user among Metis and AOM (2006/07 to 2017/18); these were stratified by age, sex, urbanicity, number of comorbidities, income quintile and opioid type. Comorbidities were assessed using the Elixhauser Comorbidity Index, which categorizes patient comorbidities based on 31 different sets of International Classification of Diseases (ICD) diagnosis codes (7,8).

Statistical Analysis

Longitudinal time trend analyses were used to determine if the time trends were statistically significant. The t-statistic of each group's slope coefficient and its associated p-value were

tested at p=0.05 to indicate whether the estimated slope was different from zero. All analyses were done using SAS Version 9.4.

Ethics

The study was approved by the University of Manitoba Human Research Ethics Board (HS22883 – H2019:218), and the MMF provided a letter of support. The Health Information Privacy Committee (HIPC) of the Manitoba Government also reviewed and approved the study (HIPC No. 2019/20-16).

RESULTS

Study Cohort Characteristics

Socio-demographic characteristics (age, sex, income, physical and mental health comorbidities) of Metis people and AOM are presented in **Table 1**, with additional data on the Elixhauser comorbidity groupings presented in **Appendix Table 2**. While many of the two groups' characteristics were similar, AOM were more likely than Metis to live in urban areas and be in the wealthiest income quintiles. Compared to AOM, a higher proportion of Metis had been diagnosed with a mental health disorder, such as a mood/anxiety disorder and/or a substance use disorder, within the past five years.

Prescription Opioid Dispensations

Comparisons of key indicators of prescription opioid dispensations between Metis and AOM in 2006/07 and 2017/18 are presented in **Table 2**, and the same indicators are shown stratified by opioid type in **Appendix Table 3**. Between 2006 and 2018, the rate of prescription opioid dispensations among Metis and AOM decreased by 5.2% and 12.0%, respectively. However, the mean number of days for which individuals were dispensed prescription opioids increased by 48% among Metis and 37% among AOM. Mean morphine equivalents (i.e., the potency of prescribed opioids) per user also increased (by 23% among Metis and by 16% among AOM), as did mean morphine equivalents per day (by 14% among Metis and 21% among AOM).

Time Trends in Opioid-Associated Morphine Equivalents

Figure 2 presents time trends in morphine equivalents (ME) per user, stratified by age, number of comorbidities, income quintile and opioid type; **Appendix Figure 1** shows these trends stratified by sex and urbanicity. Metis and AOM in the 45-54 year-old and 55-64 year-old groups had the highest mean ME per user, while individuals under 25 years had the lowest (**Figure 2a**). Metis and AOM living with three or more comorbidities had a higher mean ME per user than those living with two or fewer comorbidities (**Figure 2b)**; however, since 2016, mean ME per

user has decreased among AOM (but not Metis) living with three or more comoribidities. There was substantial variation in ME per user by income quintile (**Figure 2c**); among AOM, an inverse gradient between mean ME and income quintile was evident, i.e., individuals living in the poorest income quintiles (Q1 and Q2) had the highest mean ME per user and vice versa, whereas among Metis, only those in the wealthiest income quintile (Q5) had a substantially lower ME per user until it began to climb in 2014.

Among both Metis and AOM, hydromorphone and morphine were the opioids contributing the highest mean ME per user, but the ME per user associated with these drugs have been slowly decreasing over the past decade, while ME per user from codeine and fentanyl have gradually increased (**Figure 2d**). The ME per user from oxycodone and tramadol have also increased, although this trend is not obvious in **Figure 2d** and can be better seen in **Appendix Table 3**. Lastly, we examined the time trend of mean ME per user in the wealthiest income quintile alone because of the increasing ME per user of some opioid types and the upward trend among Q5 Metis opioid users. Among Metis in Q5, there was a steep upward trend in ME per user from morphine from about 2013-2018 (**Figure 2e**), even though it declined among Metis overall. The increase in ME per user from oxycodone was also evident in this higher income group. Among AOM in Q5, the ME per user from oxycodone also increased but there was no corresponding rise in ME from morphine.

INTERPRETATION

In Manitoba, the rate of prescription opioid dispensations among Metis and AOM has declined since 2007/08, but other measures of prescription opioid use point to the potential for increasing opioid-related harms, particularly among Metis. The duration of opioid prescriptions and the use of higher potency opioids have increased substantially in the last 15 years, leading to higher doses (higher morphine equivalents per user) being consumed by Manitobans. A large proportion of Manitobans with an opioid prescription are older (45-64 yrs) and are experiencing multiple health challenges concurrent with using opioids. And while we generally observed an inverse relationship between mean morphine equivalents per user and income level, prescription opioid dispensations among Metis in the wealthiest quintile are on the rise.

The overall decline of prescription opioid dispensations in Manitoba is in contrast to growing opioid use in many other parts of Canada (2,3,9), including British Columbia, Alberta, Yukon, and Northwest Territories (2). However, the increasing duration of opioid prescriptions and prescribing of highly potent opioids (e.g., fentanyl and oxycodone) in Manitoba is concerning. In

British Columbia, longer duration of prescription opioid therapy and increased use of fentanyl, oxycodone and hydromorphone are also becoming more prevalent (10). Prescribing of high-dose and high-potency opioids has been shown to be strongly associated with opioid-related mortality (11). Our study also corroborates the finding that growing opioid use is not limited to illegal or street drug procurement (2). In Manitoba, the rate of opioid-related overdose among individuals with an active opioid prescription is 62.9%, while the rate of intentional overdose is 35.9%, and the prevalence of prescribing prior to an opioid-related hospitalization (52.2%) is among the highest in the country (3).

Our findings highlight the disproportionate burden of opioid-related harms in Indigenous communities in Canada. Our findings show that compared to other Manitobans, Metis had consistently higher rates of prescription opioid dispensations, were more likely to have a longer opioid prescription, and morphine equivalents per user were higher. Other Canadian research has shown that the age-standardized rate of opioid-related hospitalizations among Metis is more than three times higher than among other people living in Canada (34.3 vs 10.9 per 100,000 person-years) (1). The reasons for this discrepancy are related to the determinants of Indigenous health, among which a history of colonization and racism directed towards Metis has resulted in numerous harms that have made it challenging for Metis to access appropriate mental health supports and harm reduction treatments (12,13). Income, another critical determinant of health, likely also plays an important role in opioid-related harms among Metis and other Canadians. Our finding of an inverse income gradient in prescription opioid dispensations aligns with other Canadian studies showing that those living in lower income neighbourhoods tend to have higher rates of prescription opioid dispensations and are at higher risk for an opioid-related event, such as hospitalization (2,3,10). Additionally, the higher burden of comorbidities and the potentially higher prevalence of chronic pain among older individuals (Metis and AOM) may help to explain their disproportionate use of prescription opioids.

This study highlights the gravity of the opioid crisis in Manitoba, particularly among the Metis. The findings presented here provide critical information for Metis health leadership to plan interventions and advocate for better resources and supports for individuals at risk of opioid-related harms. The research team is currently working with the MMF to integrate the study findings into the current health policy landscape and develop Metis-specific strategies to eliminate the burden of the opioid crisis in Manitoba. Future research will explore in more detail the patterns of health and social outcomes associated with prescription opioid use and delve into physician prescribing practices. It would also be valuable to examine the epidemiology of

pain-related disease and the various biological, psychological or socio-cultural mechanisms that drive people to seek health care for pain management.

A number of study limitations should be taken into consideration. The use of an administrative data repository as our main data source meant that we used opioid prescription dispensations as a proxy for opioid use; we did not have any information on whether dispensed opioids were taken as directed. As well, we examined prescription opioid dispensations only and were unable to investigate harms from opioid procurement by other means (e.g., black market, sharing, etc.).

Although Canada is facing a national opioid crisis, opioid-related harms disproportionately affect Metis populations in Manitoba, especially older individuals, those living in lower income neighbourhoods, and those living with multiple comorbidities. While rates of prescription opioid dispensations in the province are declining, other measures of harm have increased substantially. This study highlights the urgent need for better resources and the political will to tackle the Manitoba opioid crisis for once and for all.

Acknowledgements

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Funding Statement

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Data Sharing Statement

Data used in this study were derived from administrative health and social data as a secondary use. The data were provided to the Manitoba Centre for Health Policy (MCHP) under specific data sharing agreements only for approved use at MCHP. The original source data is not owned by the researchers or MCHP and as such cannot be provided to a public repository. The original data source and approval for use have been noted in the acknowledgments of the article. Where necessary, source data specific to this article or project may be reviewed at MCHP with the consent of the original data providers, along with the required privacy and ethical review bodies.

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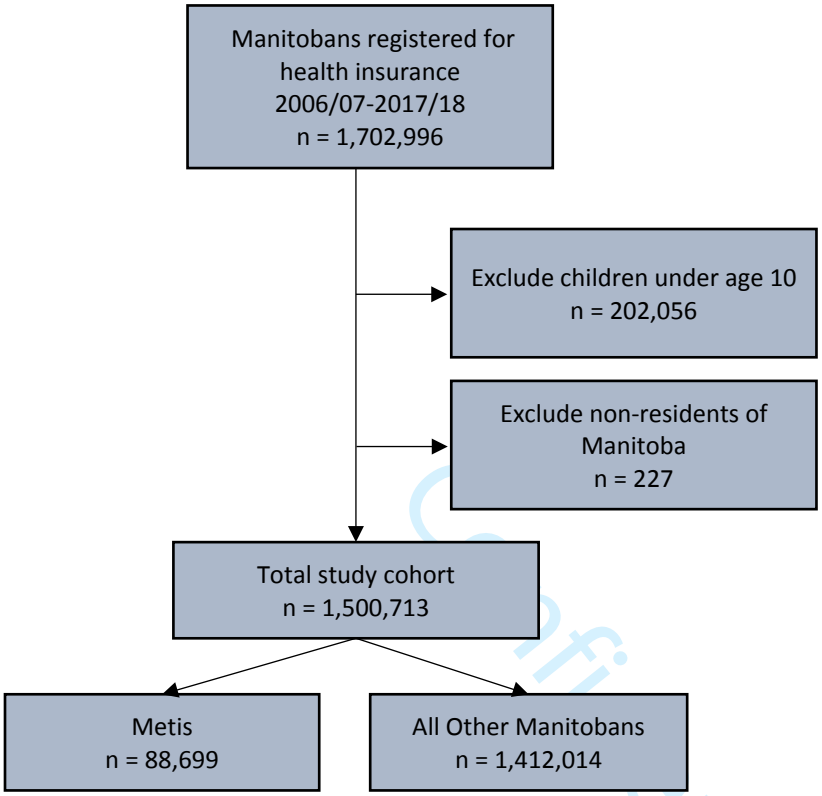
http://www.mmf.mb.ca/docs/metis_health_status_report.pdf

Figure 1. Study Cohort



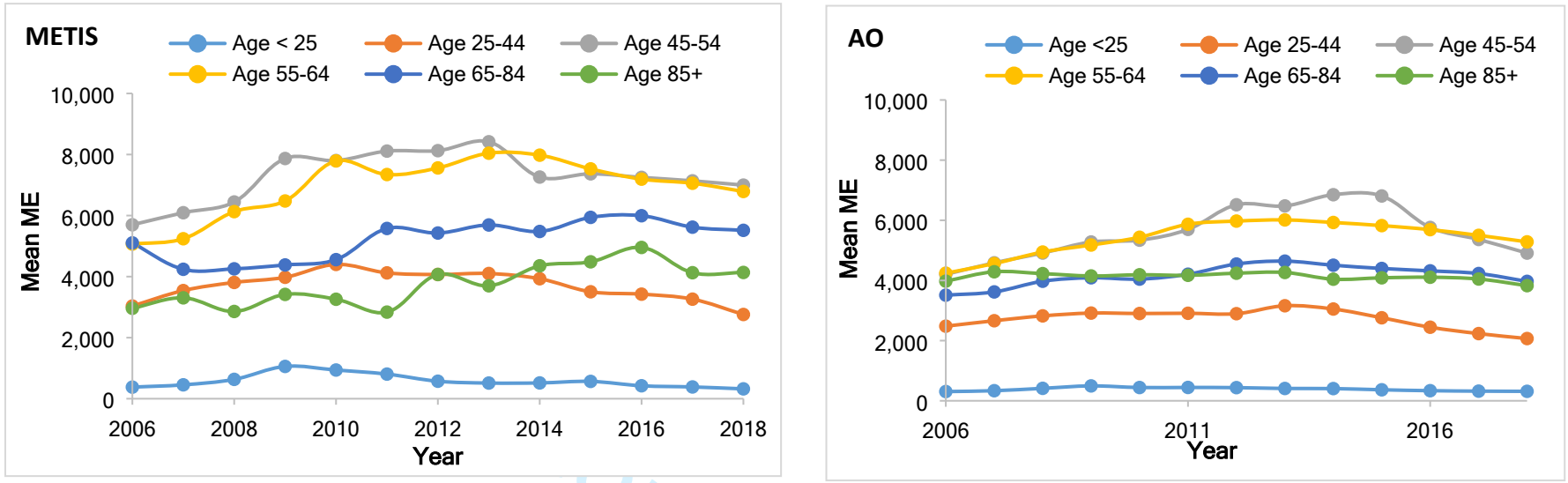


Figure 2a. Trends in Prescription Opioid Morphine Equivalents among Metis and AOM – by Age

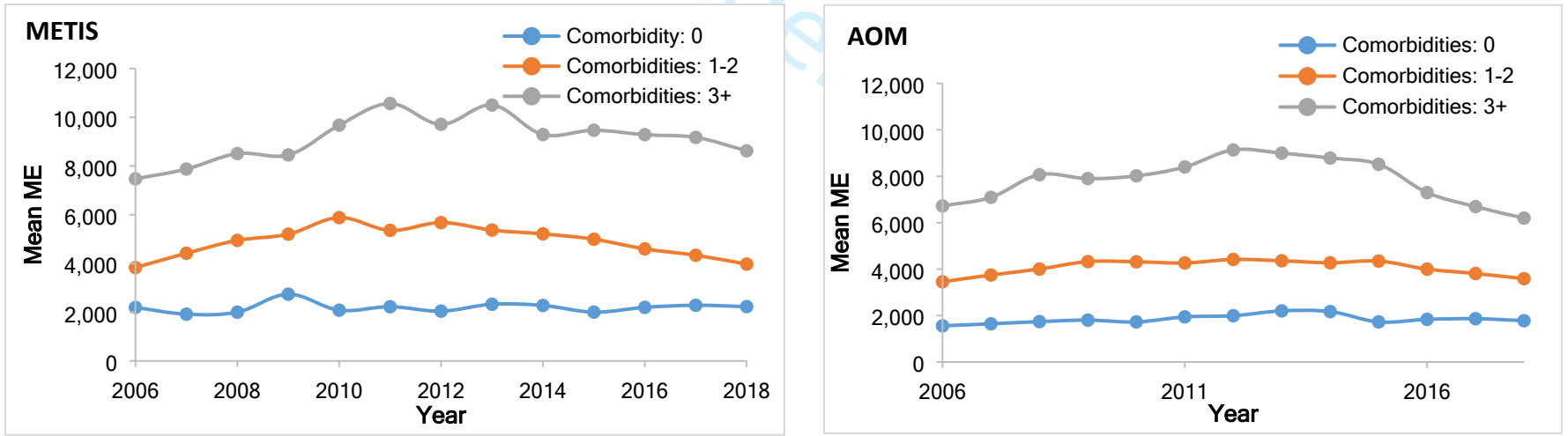


Figure 2b. Trends in Prescription Opioid Morphine Equivalents among Metis and AOM – by Number of Comorbidities

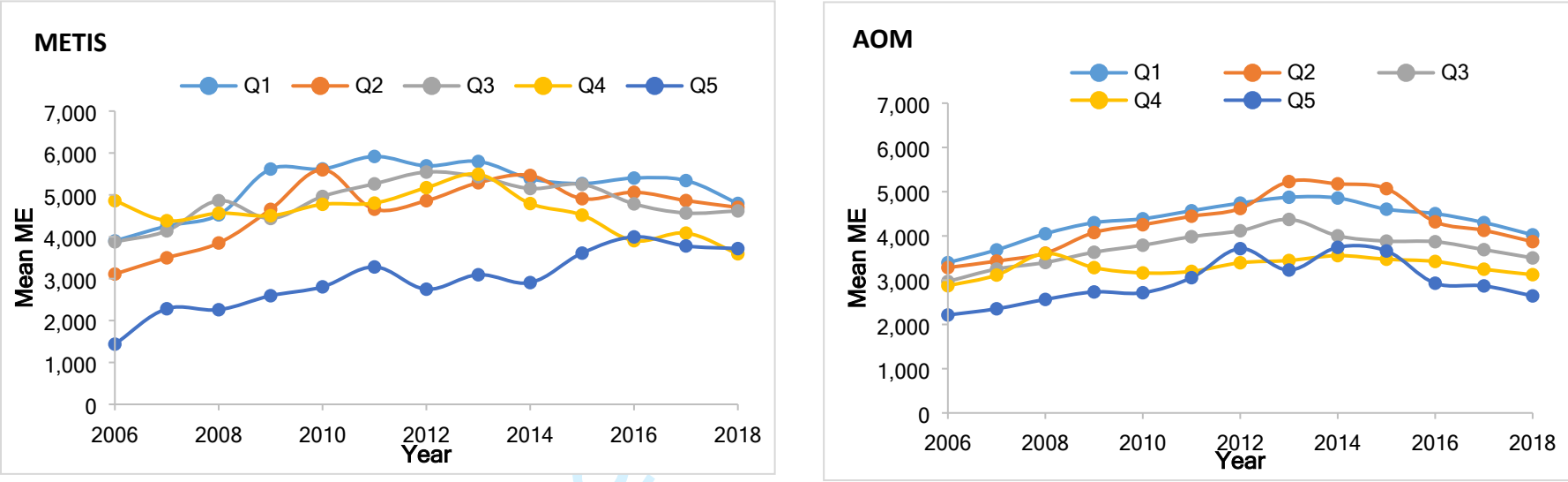


Figure 2c. Trends in Prescription Opioid Morphine Equivalents among Metis and AOM – by Income Quintile

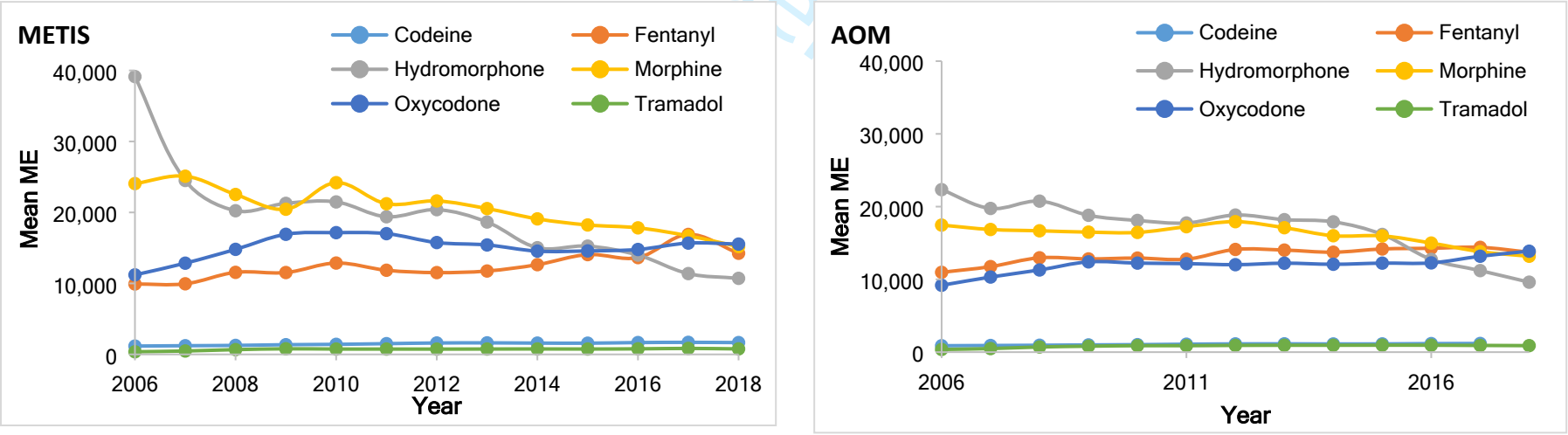


Figure 2d. Trends in Prescription Opioid Morphine Equivalents among Metis and AOM – by Opioid Type

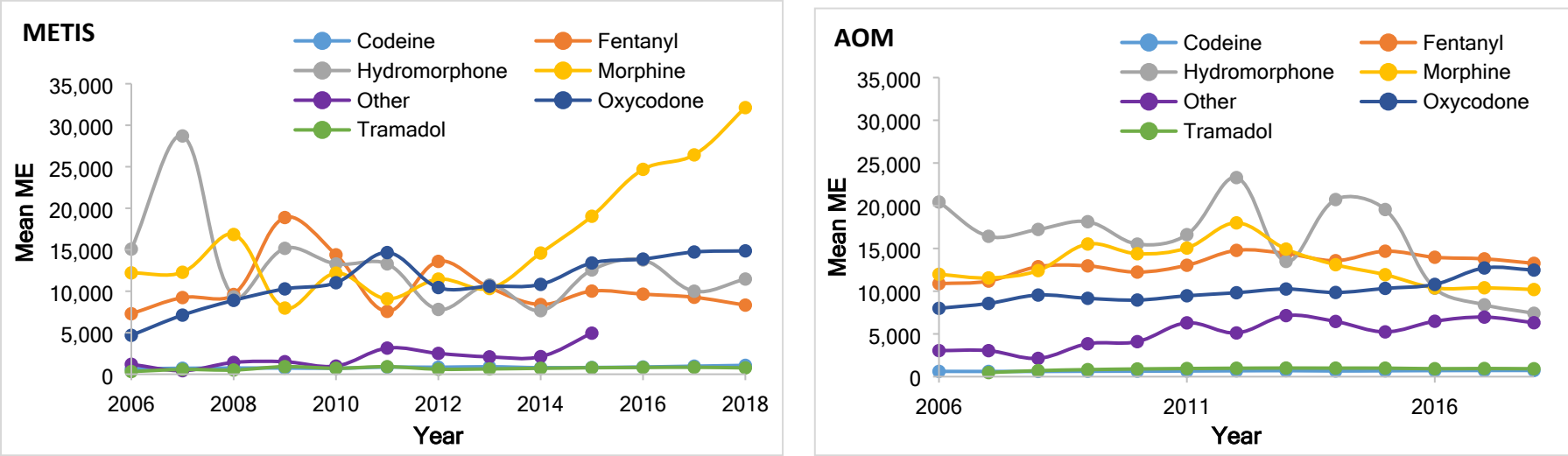


Figure 2e. Trends in Prescription Opioid Morphine Equivalents among Metis and AOM in Income Quintile 5 Only – by Opioid Type

Table 1. Study Cohort Characteristics (2006 and 2018)

	2006				2018			
	Metis		All Other Manitobans		Metis		All Other Manitobans	
	N	%	N	%	N	%	N	%
Total	68,200	100.00	965,868	100.00	76,755	100.00	1,117,854	100.00
Sex								
Male	33,241	48.74	473,525	49.03	37,456	48.80	552,842	49.46
Female	34,959	51.26	492,343	50.97	39,299	51.20	565,012	50.54
Age								
85+	438	0.64	23,858	2.47	1024	1.33	29,088	2.60
65 - 84	6,217	9.12	130,945	13.56	9,962	12.98	175,697	15.72
55 - 64	7,332	10.75	121,290	12.56	9,037	11.77	166,096	14.86
45 - 54	9,817	14.39	166,199	17.21	9,815	12.79	160,239	14.33
25 - 44	22,234	32.60	295,192	30.56	25,110	32.71	349,715	31.28
< 25	22,162	32.50	228,384	23.65	21,807	28.41	237,019	21.20
Income Quintile								
Q1	16,653	24.42	182,958	18.94	18,411	23.99	212,822	19.04
Q2	13,848	20.30	190,642	19.74	16,022	20.87	220,666	19.74
Q3	13,117	19.23	193,081	19.99	15,848	20.65	225,411	20.16
Q4	13,275	19.46	192,468	19.93	14,341	18.68	224,349	20.07
Q5	10,979	16.10	197,764	20.48	11,259	14.67	225,654	20.19
Not found	328	0.48	8,955	0.93	874	1.14	8,952	0.80
Urbanicity								
Unknown	328	0.48	8,955	0.93	874	1.14	8,952	0.80
Urban	31,732	46.53	597,919	61.90	35,304	46.00	702,640	62.86
Rural	36,140	52.99	358,994	37.17	40,577	52.87	406,262	36.34
Elixhauser Comorbidity Index								
0	40,613	59.50	571,893	59.20	40,580	52.90	610,471	54.60
1-2	24,146	35.40	347,053	35.93	29,042	37.84	415,535	37.17
3+	3,441	5.05	46,922	4.86	7,133	9.29	91,848	8.22
Mental Health								
Any mental disorder diagnosis	17,264	25.31	208,418	21.58	22,541	29.37	255,088	22.82
Mood/anxiety disorder diagnosis	14,263	20.91	175,948	18.22	19,693	25.66	226,396	20.25

Personality disorder diagnosis	628	0.92	7,400	0.77	907	1.18	7,887	0.71
Psychotic disorder diagnosis	855	1.25	15,230	1.58	1,261	1.64	15,358	1.37
Suicide attempts	335	0.49	2,514	0.26	296	0.39	2,024	0.18
Substance use disorder diagnosis	4,935	7.24	43,496	4.50	5,505	7.17	44,463	3.98

"Any mental disorder" comprises personality, psychotic, and mood and anxiety disorders. All indicators in the mental health category are measured over 5 years (2012/13-2017/18).

Table 2. Relative Difference in Prescription Opioid Dispensations between Metis and All Other Manitobans

	Metis			All Other Manitobans			Metis vs AOM
	2006	2018	% Diff	2006	2018	% Diff	p-value (% Diff)
Rate of opioid dispensations/ 1,000 person-years	200.6	190.1	-5.2	149.9	131.9	-12.0	0.4927
Mean number of days/user	78	116	47.7	65	89	36.9	<0.0001
Mean morphine equivalents/user	3,616	4,438	22.7	3,032	3,511	15.8	0.2712
Mean morphine equivalents/day	278	316	13.6	204	247	21.2	0.8909

Appendix Table 1. Repository Databases Used in this Study

Database	Description
Manitoba Health Insurance Registry	Demographic information on Manitoba residents registered for universal healthcare.
Manitoba Metis Registry	A registry of Metis citizens living in Manitoba.
Vital Statistics	Mortality records and causes of death.
Hospital Discharge Abstract Database	Demographic and clinical information on hospitalized patients, including information on births and birth outcomes.
Medical Services	Claims for physician visits in offices, hospitals and outpatient departments, fee-for-service components for tests such as lab and x-ray procedures performed in offices and hospitals, and payments for on-call agreements.
Drug Program Information Network	Data on prescriptions dispensed from community pharmacies (but not pharmacies in hospitals or nursing homes/personal care homes).
Canada Census	Small geographical area-level data from the Canada Census, used to create the Socioeconomic Factor Index 2 (SEFI 2)*, an index of socio-economic status.

*Chateau D, Metge C, Prior H, Soodeen RA. 2012. Learning from the census: The Socio-Economic Factor Index (SEFI) and health outcomes in Manitoba. Can J Public Health 103(8 Suppl 2): S23-7.

Appendix Table 2: Study Cohort Characteristics – Elixhauser Comorbidity Groups

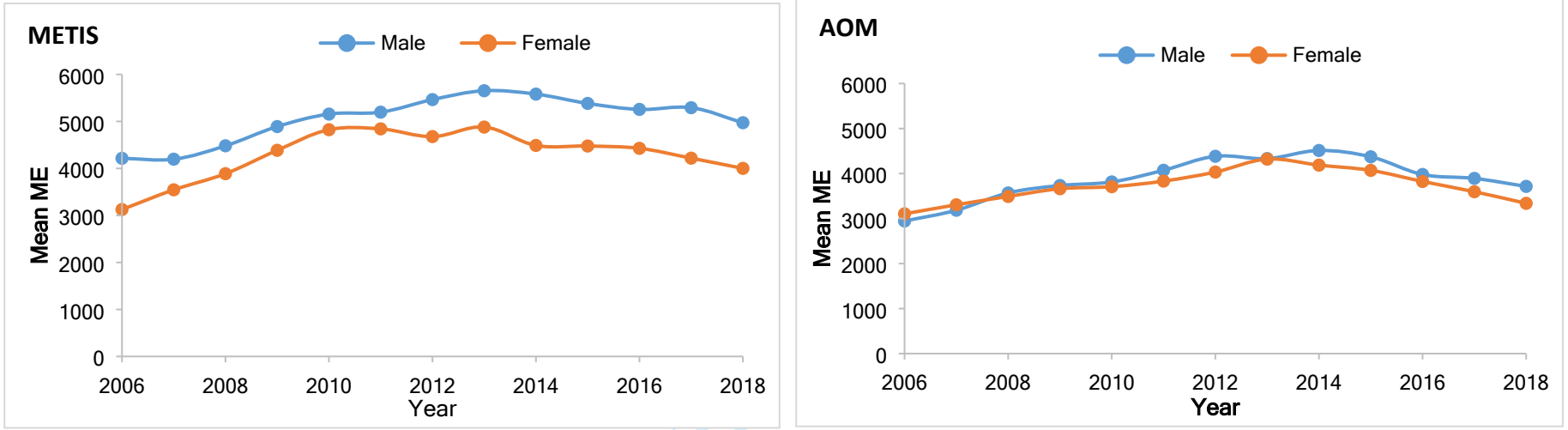
	2006				2018			
	Metis		All Other Manitobans		Metis		All Other Manitobans	
	N	%	N	%	N	%	N	%
1. Congestive Heart Failure	580	0.85	10,428	1.08	756	0.98	12,228	1.09
2. Cardiac Arrhythmia	820	1.20	16,956	1.76	1,347	1.75	23,214	2.08
3. Valvular Disease	224	0.33	4,101	0.42	339	0.44	5,524	0.49
4. Pulmonary Circulation Disorders	58	0.09	1,040	0.11	136	0.18	1,774	0.16
5. Peripheral Vascular Disorders	439	0.64	6,806	0.70	627	0.82	9048	0.81
6. Hypertension w/o complications	6,967	10.22	126,272	13.07	12,649	16.48	205,780	18.41
7. Hypertension with complications	96	0.14	1,579	0.16	52	0.07	1,019	0.09
8. Paralysis	140	0.21	2,115	0.22	150	0.20	2075	0.19
9. Other Neurological Disorders	676	0.99	12,009	1.24	1,229	1.60	17,842	1.60
10. Chronic Pulmonary Disease	6,988	10.25	81,496	8.44	6,617	8.62	78,476	7.02
11. Diabetes w/o complications	3,949	5.79	51,370	5.32	6,567	8.56	87,302	7.81
12. Diabetes with complications	146	0.21	1,730	0.18	730	0.95	8,141	0.73
13. Hypothyroidism	1,339	1.96	20,366	2.11	2,604	3.39	44,087	3.94
14. Renal Failure	292	0.43	5,238	0.54	458	0.60	7,149	0.64
15. Liver Disease	508	0.74	6,259	0.65	948	1.24	13,364	1.20
16. Peptic Ulcer Disease excluding bleeding	418	0.61	4,384	0.45	191	0.25	2,918	0.26
17. HIV/AIDS	20	0.03	275	0.03	85	0.11	1,088	0.10
18. Lymphoma	107	0.16	2,037	0.21	149	0.19	2,666	0.24
19. Metastatic Cancer	78	0.11	1,258	0.13	122	0.16	1,779	0.16
20. Solid Tumor without Metastasis	1,063	1.56	21,088	2.18	1,459	1.90	26,090	2.33
21. Rheumatoid Arthritis/Collagen	5,196	7.62	70,155	7.26	7,195	9.37	97,829	8.75
22. Coagulopathy	214	0.31	3,384	0.35	280	0.36	4,819	0.43
23. Obesity	937	1.37	9,888	1.02	1,640	2.14	18,284	1.64
24. Weight Loss	32	0.05	553	0.06	64	0.08	986	0.09

25. Fluid and Electrolyte Disorders	264	0.39	4,357	0.45	452	0.59	6,683	0.60
26. Blood Loss Anemia	23	0.03	325	0.03	10	0.01	129	0.01
27. Deficiency Anemia	518	0.76	8,262	0.86	1,822	2.37	27,501	2.46
28. Alcohol Abuse	415	0.61	4,272	0.44	369	0.48	3,549	0.32
29. Drug Abuse	917	1.34	7,786	0.81	1,624	2.12	11,188	1.00
30. Psychoses	412	0.60	7,670	0.79	889	1.16	11,312	1.01
31. Depression	9,068	13.30	114,807	11.89	13,322	17.36	154,743	13.84

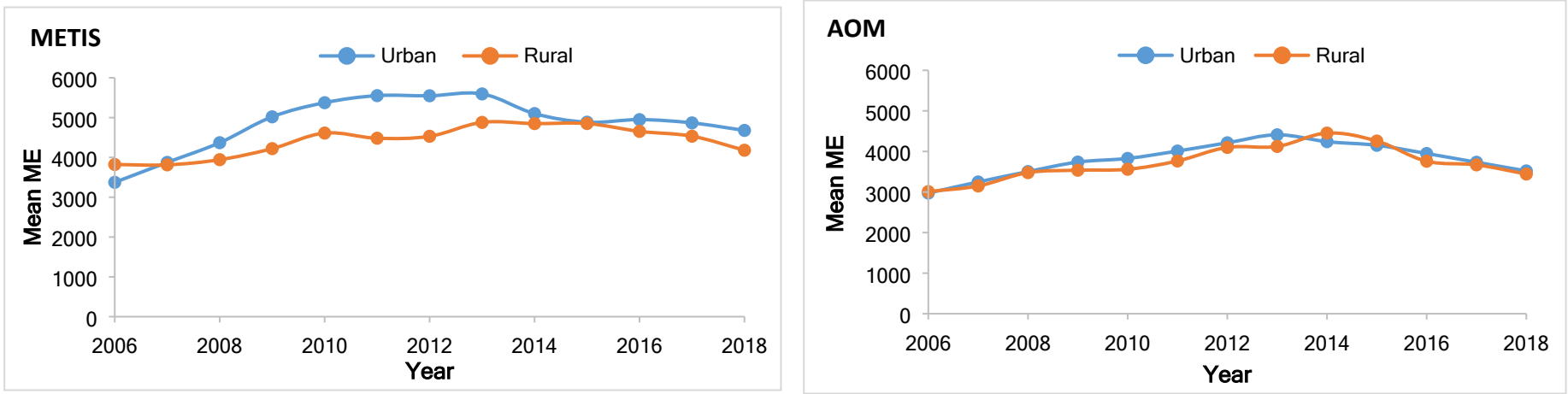
Appendix Table 3. Relative Difference in Prescription Opioid Dispensations between Metis and AOM – by Opioid Type

	Metis			All Other Manitobans			Metis			All Other Manitobans		
	Rate of prescription opioid dispensations per 1,000 person-years						Mean number of days per user					
Opioid Type	**2006**	**2018**	**% Diff**	**2006**	**2018**	**% Diff**	**2006**	**2018**	**% Diff**	**2006**	**2018**	**% Diff**
Codeine	183.8	152.3	-17.2	136.3	102.1	-25.1	58	87	50.4	43	62	44.2
Fentanyl	3.6	1.6	-54.6	2.5	1.2	-53.1	192	256	33.1	231	245	6.3
Hydromorphone	3.5	14.6	314.9	3.3	11.7	251.4	169	116	-31.1	166	116	-30.1
Morphine	6.0	5.3	-12.5	4.6	3.1	-31.8	174	163	-6.4	162	161	-1.1
Oxycodone	17.5	17.1	-2.3	12.1	8.1	-32.7	146	244	67.1	121	210	73.6
Tramadol	5.0	24.3	385.8	4.8	21.2	339.9	20	45	129.0	23	51	123.5
Other	2.6	0.5	-81.7	1.2	0.3	-76.4	76	217	184.6	73	193	163.3
TOTAL	**200.6**	**190.1**	**-5.2**	**149.9**	**131.9**	**-12.0**	**78**	**116**	**47.7**	**65**	**89**	**36.9**
	Mean morphine equivalents per user						Mean morphine equivalents per day					
Opioid Type	**2006**	**2018**	**% Diff**	**2006**	**2018**	**% Diff**	**2006**	**2018**	**% Diff**	**2006**	**2018**	**% Diff**
Codeine	1,172	1,663	41.8	880	1,193	35.5	91	112	23.2	75	87	15.2
Fentanyl	9,917	14,245	43.6	10,968	13,733	25.2	434	936	115.8	587	721	22.7
Hydromorphone	39,136	10,711	-72.6	22,336	9,615	-57.0	3,655	982	-73.1	1,517	746	-50.8
Morphine	24,060	15,182	-36.9	17,462	13,179	-24.5	1,766	1,258	-28.8	1,082	1042	-3.7
Oxycodone	11,202	15,539	38.7	9,188	13,873	51.0	734	951	29.5	496	855	72.3
Tramadol	366	773	111.2	365	893	144.3	45	56	23.4	42	58	37.2
Other	4,105	24,325	492.6	3,709	6,366	71.6	982	1,500	52.9	442	382	-13.5
TOTAL	**3,616**	**4,438**	**22.7**	**3,032**	**3,511**	**15.8**	**278**	**316**	**13.6**	**204**	**247**	**21.2**

"Other" opioids include meperidine, buprenorphine, butorphanol, pentazocine, sufentanil, tapentadol, dextropropoxyphene and opium.



Appendix Figure 1a. Trends in Prescription Opioid Morphine Equivalents among Metis and AOM – by Sex



Appendix Figure 1b. Trends in Prescription Opioid Morphine Equivalents among Metis and AOM – by Urbanicity

The RECORD statement – checklist of items extended from the STROBE statement that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	1a. Abstract 1b. Abstract	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	1.1 Abstract 1.2 Title and Abstract 1.3 Title and abstract
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	pp. 3		
Objectives	3	State specific objectives, including any prespecified hypotheses	pp. 3		
Methods					
Study Design	4	Present key elements of study design early in the paper	p. 4, "Study Design"		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p. 4, "Study Cohort"		
Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the	6a. p. 4, "Study Cohort"	RECORD 6.1: The methods of study population selection (such as codes or	6.1 p. 4, "Study Cohort" and

		sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case	6b. p. 4, "Study Cohort"	algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	"Data Source" 6.2 p. 4, "Study Cohort" and "Data Source" 6.3 Figure 1.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	p. 5-6 under "Measures".	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	7.1 p. 4, "Measures"
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Data sources and measures are described on p. 4 under "Data Source" and "Measures".		
Bias	9	Describe any efforts to address potential sources of bias	We included a number of explanatory variables in our		

			linear trend model to account for differences among study subjects – pp. 4-5 under "Statistical Analyses".		
Study size	10	Explain how the study size was arrived at	p. 4, "Study Cohort" and Figure 1		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	pp. 4-5, "Statistical Analyses"		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses	pp. 4-5, "Statistical Analyses"		
Data access and cleaning methods				RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study	12. 1 Data sources and access to the data are described on

				population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	pp.4 under "Data Source" 12.2 Data quality assessment and cleaning procedures occur for all datasets at MCHP and are not part of this study. See cited validation studies for more detail.
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	pp. 4 under "Data Source"
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram	Not applicable for this retrospective analysis where our cohort includes only individuals who could be followed for the entire study period.	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	p. 4, "Study Cohort" and Figure 1
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data	Table 1 & 2 and p. 5		

		for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures	Table 2-3, Figures 2-3, and pp. 5-6		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Table 2-3, Figures 2-3, and pp. 5-6		
Other analyses	17	Report other analyses done - e.g., analyses of subgroups and interactions, and sensitivity analyses	n/a		
Discussion					
Key results	18	Summarise key results with reference to study objectives	p. 6		
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and	p. 8	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include	p. 8

		magnitude of any potential bias		discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p. 7		
Generalisability	21	Discuss the generalisability (external validity) of the study results	p. 7-8		
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p. 9		
Accessibility of protocol, raw data, and programming code				RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	n/a