



Minnesota Board of Pharmacy

Report to the Legislature: Evaluation of Opiate Product Registration Fee & Increased Licensure Fees on Opiate Prescribing and Treating Chronic or Intractable Pain

Prepared By:

Hannah Frey, Prescription Monitoring Program Data Analyst
Dr. Brock Reed, Controlled Substance Reporting Section Director

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Cost of Report

MN Stats. §3.197 states that a “report to the legislature must contain, at the beginning of the report, the cost of preparing the reporting, including any costs incurred by another agency or another level of government”. The estimated cost of preparing this report was \$17,090.

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Executive Summary

In 2019, Governor Walz signed into law several provisions that created the Opiate Epidemic Response Advisory Council (OERAC), the Opiate Product Registration Fee Program (OPRFP), and the Opiate Epidemic Response Fund (OERF) to assist in the development and implementation of a comprehensive and effective statewide effort to address the opioid addiction and overdose epidemic in Minnesota. The legislation enacted during the 2019 Regular Session contained many provisions that impact all licensees and registrants of the Board of Pharmacy (Board). In addition, the application and annual renewal fees for most drug manufacturers, medical gas manufacturers, wholesale drug distributors, and medical gas wholesalers increased by \$5,000 or \$55,000, depending on the licensee, effective July 1, 2019. Additionally, the OPRFP would assess manufacturers surpassing a threshold of two million opiate “units” distributed within or into Minnesota a fee of \$250,000. The resulting revenue from these policies would be deposited into the OERF as a means of funding programs to combat the opioid epidemic. Henceforth, the terms “opiate” and “opioid” will be used interchangeably as Minnesota statute uses the former term to refer to substances chemically defined as opioids.

This report will assist in helping to evaluate whether the opiate registration fee or increased licensure fees established under Minnesota statute sections 151.065 and 151.066 during calendar years 2021, 2022, and 2023 had any substantial qualitative consequences. The purpose of this paper is to answer two questions. One, if the increase in licensure fees and institution of an opiate product registration fee has impacted the prescribing practices of opiates, and two, if there were unintended consequences in the availability of opiates for the treatment of chronic¹ or intractable² pain to the extent that the Board could effectively identify a correlation³.

Introduction

The current opioid epidemic was ignited in the early 1990s with the overprescribing of opioids to treat pain and the lack of resources, knowledge, and evidence-based addiction treatments to counteract this. In Minnesota, the number of Minnesotans who died from an opioid overdose in 2016 was 395, more than six times the number of opioid overdose deaths in 2000⁴. Of these overdose deaths, prescription opioids accounted for the largest number in Minnesota. However, since 2010, heroin and fentanyl-involved deaths have increased across the nation, including Minnesota. This growing epidemic exploded into the public awareness in mass with the arrival of COVID-19. The State of Minnesota is a leader and a partner in addressing the opioid epidemic and works to form new collaborations with partners inside and outside of government.

In 2010, to counter the growing number of overdose deaths, the Minnesota Legislature passed Minnesota Statute 152.126, which mandated the creation of the Prescription Monitoring Program (PMP)⁵. PMPs are secure, electronic databases meant to aid prescribers and pharmacists in clinical decision-making and to help mitigate prescription drug misuse and diversion. The purpose for the establishment of the Minnesota PMP is to promote public health and safety by detecting diversion and misuse of prescriptions for controlled substances as defined in Minnesota Statutes Section 152.126⁶. Pharmacies and prescribers who dispense from their office are required to submit prescription data to the PMP system for all Schedules II, III, IV and V controlled substances, butalbital and gabapentin dispensed in or into Minnesota.

PMPs are among the most promising state-level interventions to improve opioid prescribing, inform clinical practice, and protect patients at risk. Although findings regarding the implementation of PMPs are mixed, evaluations of PMPs have illustrated

¹ Chronic pain is minimally defined by Minnesota Statute in 256B.0638 Opioid Prescribing Improvement Program subd. 4. (iii), which states that chronic pain lasts 45 days after an acute painful event.

² Intractable pain is defined by 152.125 subdivision 1.c.in which there are two criteria that must be met, pain cannot be removed or general consent of the patient and practical acceptance within the medical community.

³ <https://www.revisor.mn.gov/statutes/cite/151.066>.

⁴ https://mn.gov/dhs/assets/federal-opioid-briefing_tcm1053-336378.pdf.

⁵ This protected health information is collected and securely stored as per Minnesota statute 152.126. Minnesota licensed prescribers and pharmacists and their delegated staff may be authorized to access information from the PMP database.

⁶ <https://www.revisor.mn.gov/statutes/cite/152.126>

reductions in opioid prescribing⁷ and rates of opioid-related emergency department visits and inpatient stays⁸. States have implemented a range of ways to make PMPs easier to use and access, and these changes have significant potential for ensuring the utility and promise of PMPs. Today, PMPs are operational in all 50 states, the District of Columbia, Guam, and Puerto Rico.

Despite all the State's efforts, the opioid epidemic boiled over with the arrival of the COVID-19 pandemic. In response to the new surge in opioid overdose deaths, Governor Walz signed into law several provisions in May 2019. The provisions created the Opiate Product Registration Fee (OPRF), increased the Board's licensure fees, established the Opiate Epidemic Response Account, amongst other items. Together, these strategies are aimed to assist in the development and implementation of a comprehensive and effective statewide effort to address the opioid addiction and overdose epidemic in Minnesota.

The Opiate Product Registration Fee Program (OPRFP) is administrated by the Board of Pharmacy to annually collect data from those distributing opioids to Minnesota locations where opioids are dispensed or administered to patients. Each year, the Board analyzes this data to calculate which manufacturers surpassed the two million total opiate units distributed threshold in the previous calendar year and are thus subject to the \$250,000 registration fee.

Additionally, Minnesota Statute section 151.065 was modified to increase licensure fees for most drug manufacturers, medical gas manufacturers, wholesale drug distributors, and medical gas wholesalers. Effective July 1, 2019, these fees were increased by \$5,000 or \$55,000 depending on the license being issued or renewed. As with the Opiate Product Registration fee, the revenue from these increases is deposited into the Opioid Epidemic Response Account established under Minnesota Statute section 256.043.

Prescription Monitoring Program Data

Morphine Milligram Equivalents (MMEs)

When it comes to analyses regarding opioids and pain, many researchers utilize Morphine Milligram Equivalents (MME) to compare opioid doses between substances. Using an MME conversion factor, one can convert a dose of one opioid into the amount of morphine milligrams it is equivalent to. The MME conversion factor is a standard conversion factor developed by the CDC.

The Daily MME metric is used to gauge the overdose potential of the opioids prescribed. Higher dosages of opioids are associated with a higher risk of overdose and death. Calculating the total daily dose of opioids helps identify patients who may benefit from closer monitoring, reduction, or tapering of opioids, co-prescribing of naloxone, or other measures to reduce the risk of overdose. The formula used to calculate the daily MME is Strength per Unit X (Number of Units/ Days Supply) X MME conversion factor = MME/Day. The intended use of MMEs is to help clinicians make safe, appropriate decisions concerning changes to opioid regimens.

Minnesota Morphine Milligram Equivalent Trends

Since 2021, the annual average total MME per prescription has gone from 515.98 +/- 4.15 to 479.99 +/- 4.11 in 2022 to 469.66 +/- 4.15 in 2023. As such, there is a visible decrease in total MMEs yearly. However, looking at the trend from 2021 to 2023 as a whole-time frame instead of individually, the graphs indicate a steady downward trend from 537 MME in 2021 to 467 in 2022 before leveling around 464-475 MME in 2023. Figure 1 visualizes this decreasing trend across three years. A projected leveling of an average total MME is around 469.63 +/-3.97, should trends continue.

However, even before 2021, Minnesota's total and daily MMEs have decreased. The supplementary report provided by Minnesota Management and Budget (MMB) in 2018-2019 reported that Minnesota's average total MME decreased by 7.5% over two years and dropped a further 3.3% from 2019-2020. The trend continued from 2020-2021, with the average total MME

⁷ Bao Y, Pan Y, Taylor A, et al. Prescription Drug Monitoring Programs Are Associated With Sustained Reductions In Opioid Prescribing By Physicians. Health Aff (Millwood). 2016;35(6):1045-1051. doi:10.1377/hlthaff.2015.1673

⁸ Wen H, Hockenberry JM, Jeng PJ, Bao Y. Prescription Drug Monitoring Program Mandates: Impact On Opioid Prescribing And Related Hospital Use. Health Aff (Millwood). 2019 Sep;38(9):1550-1556.

decreasing by 2.7%. The 2018-2019 MMB supplementary Minnesota PMP document also reported that the average daily MME decreased by 6.5%, while from 2019-2020, the average daily MME dropped by 4.0% and 6.7% from 2020-2021.

As such, while the increased licensure and OPR fees might have contributed to the accelerated decline of average total and daily MME trends, they are not the sole variable impacting the declining trend of falling MMEs. The average total MME and average daily MME report consistently continued falling counts across the three reported years (2021-2023) and consistently falling MME numbers before the increased licensure and OPR fees, which support this analysis. Thus, the data shows that increased license and OPR fees on MMEs have limited visible impact on continued average total and daily MME trends in Minnesota.

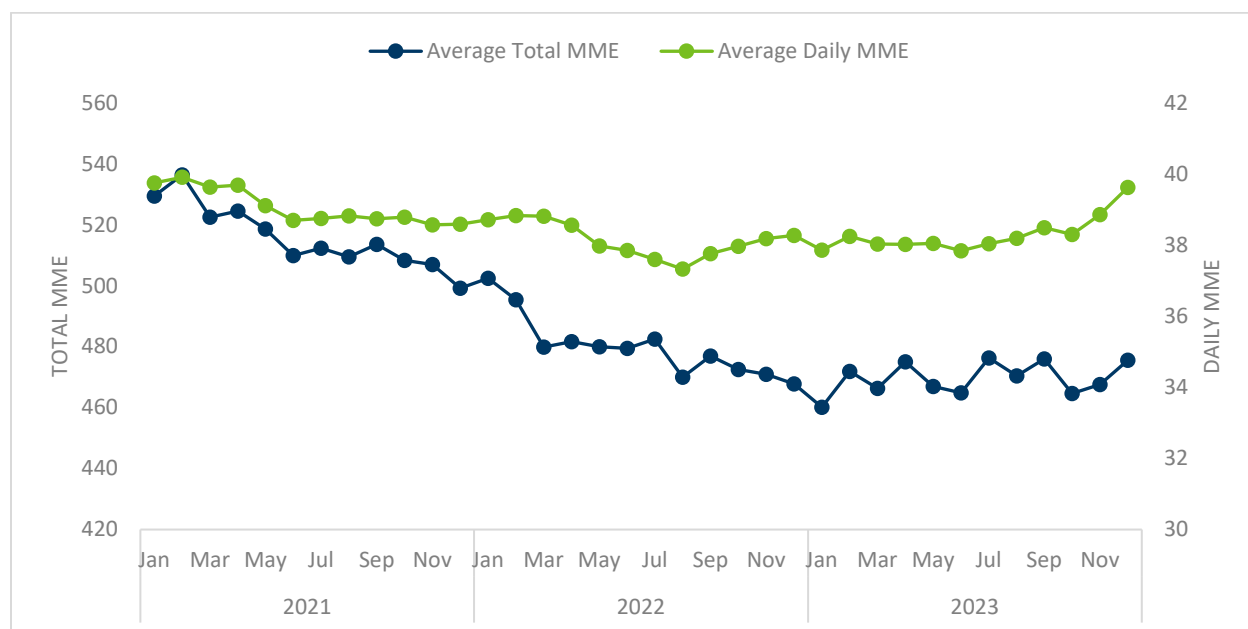


Figure 1: Average total MME per opioid prescription and average daily MME per opioid prescription by month and year.

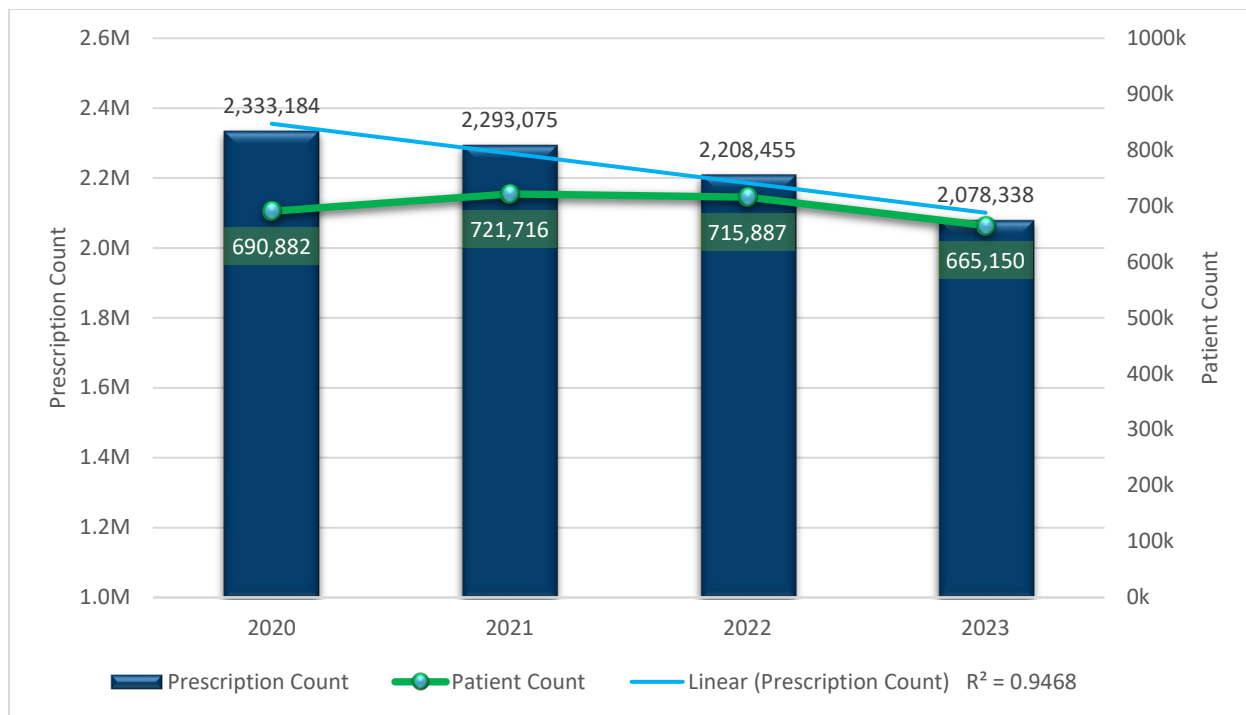


Figure 2: Count of opioid prescriptions issued and the number of unique patients from 2020 to 2023.

Table 1: Average Total MME Per Prescription, 2021-2023

Avg. Total MME						
Month	2021		2022		2023	
	Avg. Total MME	95% CI	Avg. Total MME	95% CI	Avg. Total MME	95% CI
Jan	529.52	4.31	502.51	4.27	460.17	3.99
Feb	536.44	4.43	495.45	4.32	471.87	4.28
Mar	522.57	4.16	479.92	4.02	466.37	4.03
Apr	524.50	4.26	481.71	4.23	475.07	4.28
May	518.62	4.24	480.06	4.06	467.02	4.04
Jun	509.98	4.03	479.44	4.08	464.83	4.03
Jul	512.37	4.14	482.56	4.19	476.29	4.27
Aug	509.50	4.08	470.03	4.02	470.46	4.14
Sep	513.59	4.09	476.93	4.05	476.02	4.23
Oct	508.34	4.10	472.56	4.12	464.67	4.06
Nov	507.02	4.04	470.99	4.03	467.57	4.15
Dec	499.28	3.95	467.81	3.94	475.62	4.33

Table 2: Average Daily MME Per Prescription, 2021-2023

Avg. Daily MME						
Month	2021		2022		2023	
	Avg. Daily MME	95% CI	Avg. Daily MME	95% CI	Avg. Daily MME	95% CI
Jan	39.75	0.21	38.72	0.21	37.86	0.23
Feb	39.91	0.21	38.83	0.24	38.25	0.22
Mar	39.64	0.19	38.81	0.22	38.03	0.20
Apr	39.69	0.20	38.57	0.21	38.03	0.21
May	39.11	0.20	37.98	0.21	38.05	0.21
Jun	38.70	0.19	37.85	0.20	37.85	0.21
Jul	38.76	0.20	37.60	0.20	38.04	0.22
Aug	38.83	0.20	37.33	0.20	38.20	0.21
Sep	38.74	0.20	37.76	0.20	38.49	0.22
Oct	38.79	0.19	37.97	0.21	38.31	0.21
Nov	38.57	0.19	38.18	0.21	38.86	0.22
Dec	38.59	0.19	38.27	0.22	39.62	0.22

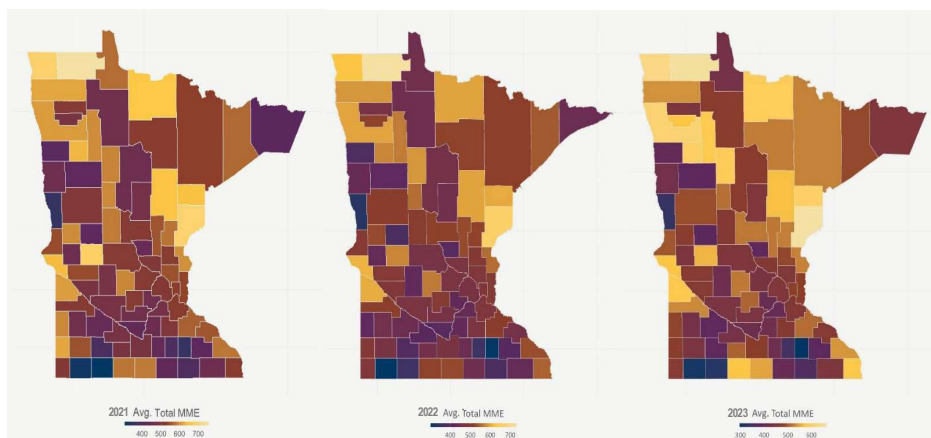


Figure 3: 2021 State Average Total MME by County. A visualization of all 87 counties in Minnesota with their reported average total MME presented on a color scale from blue to red to yellow (low to medium to high). The year 2021 is on the left, the year 2022 is in the middle, and the year 2023 is on the right.

The average total MME numbers per opioid prescription are calculated for each county from 2021 to 2023, shown in Figure 7. In 2021, only 13 counties had average total MME counts higher than 600 average total MME. Of those 13 counties, Roseau County had the highest average total of 755.21 +/-33.31 MME per opioid prescription, while Polk County had the lowest average total of 608.23 +/-14.96 MME per opioid prescription. However, in 2022, the number of counties with an average total MME greater than 600 was six, less than half of the previous year. Of the six counties with an average total higher than 600 MME per opioid prescription, Roseau County had the highest total average with 730.27 +/-32.12 MME, and Carlton County had the lowest total MME with 600.89 +/-14.81. Once again, for 2023, Roseau County had the highest 657.70 +/-27.76 average total MME. The county with the lowest average MME per opioid prescription in 2023 is Mahnommen County at 600.65 ±38.40.

The average total MME amounts decreased for most counties across the state from 2021 to 2023. From 2021 to 2022, all but 12 counties' total MME amounts dropped, while three counties showed no change in MME amounts from 2021 to 2022. Figure 7 shows no regional trend across the state for the average total MME amount per prescription. Additionally, from 2022 to 2023, average total MME county amounts decreased except for 30 counties with increased total MME amounts and nine counties with no change.

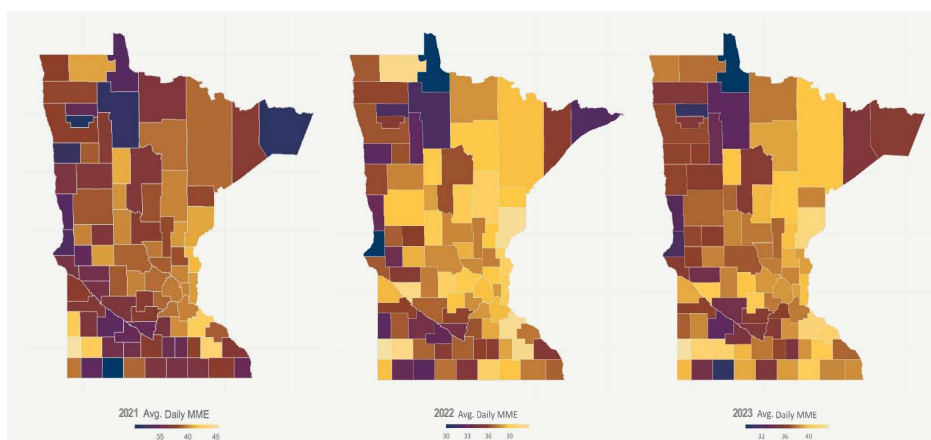


Figure 4: 2021-2023 Minnesota Average Daily MME by County. A visualization of all 87 counties in Minnesota with their reported average daily MME presented on a color scale from blue to red to yellow (low to medium to high). The year 2021 is on the left, the year 2022 is in the middle, and the year 2023 is on the right.

Average Daily MME is the daily dose of opioid for a prescription multiplied by its conversion factor. As shown in Figure 8, the average daily MME per opioid prescription in each county from 2021 to 2024 varied between approximately 28 and 45

MME/day. From 2021 to 2023, Pipestone County had the highest average daily MME at 45.40 +/- 1.87 MME/day in 2021, 41.83 +/- 2.01 MME/day in 2022, 43.42 +/- 2.33 MME/day in 2023. Meanwhile, for 2021, Jackson County had the lowest average daily MME at 30.52 +/- 0.93 MME/day. The lowest average daily MME in 2022 was Traverse County, with 29.98 +/- 1.01 MME/day. In 2023, Lake of the Woods County had the lowest daily MME with 29.31 +/- 0.97 MME/day. Most counties across the state had a decrease in average daily MME from 2021 to 2022. However, from 2022 to 2023, more than half the counties across Minnesota had an increase in average daily MME.

Licensure Fees

Like other health licensing boards, the Board of Pharmacy is a self-funded agency. The mission of the Board of Pharmacy is to promote, preserve, and protect the public health, safety, and welfare by fostering the safe distribution of pharmaceuticals and the provision of quality pharmaceutical care to the citizens of Minnesota. Part of the way in which the Board accomplishes its mission is through the licensing and regulation of pharmacies, manufacturers, wholesale drug distributors, amongst others. Licenses issued by the Minnesota Board of Pharmacy expire annually on a date specified in statute or rule. The first-year licensees and applicants experienced the Board's increase in licensure fees, for the purposes of funding the opioid epidemic response fund, was 2020. Drug manufacturer and wholesaler licenses increased by \$5,000 and a new drug manufacturer category for those producing opiates was created, adding an additional \$50,000 on top of the other fees. When examining the number of license applications received by the Board on a yearly basis, both to renew an existing license as well as to obtain a new license, numbers were steadily increasing year over year until experiencing a sharp drop in 2020 by approximately 40%. While both manufacturer and wholesaler licenses decreased, the latter was responsible for most of the change, as can be seen in Figure 4. It is difficult to directly link this drop to the increased licensure fees due to multiple confounding factors taking place concurrently. The peak of the COVID-19 pandemic took place in 2020 which had a negative effect on many businesses, though the healthcare industry experienced this to a lesser degree than many others. Additionally, other legislative changes meant that numerous pharmacy and manufacturer licensees, previously also holding wholesaler licenses, no longer needed to obtain a separate wholesaler license. While manufacturer licenses eventually recovered and have now surpassed 2019 numbers, the same cannot be said for wholesaler licenses which remain at less than 60% of their 2019 number.

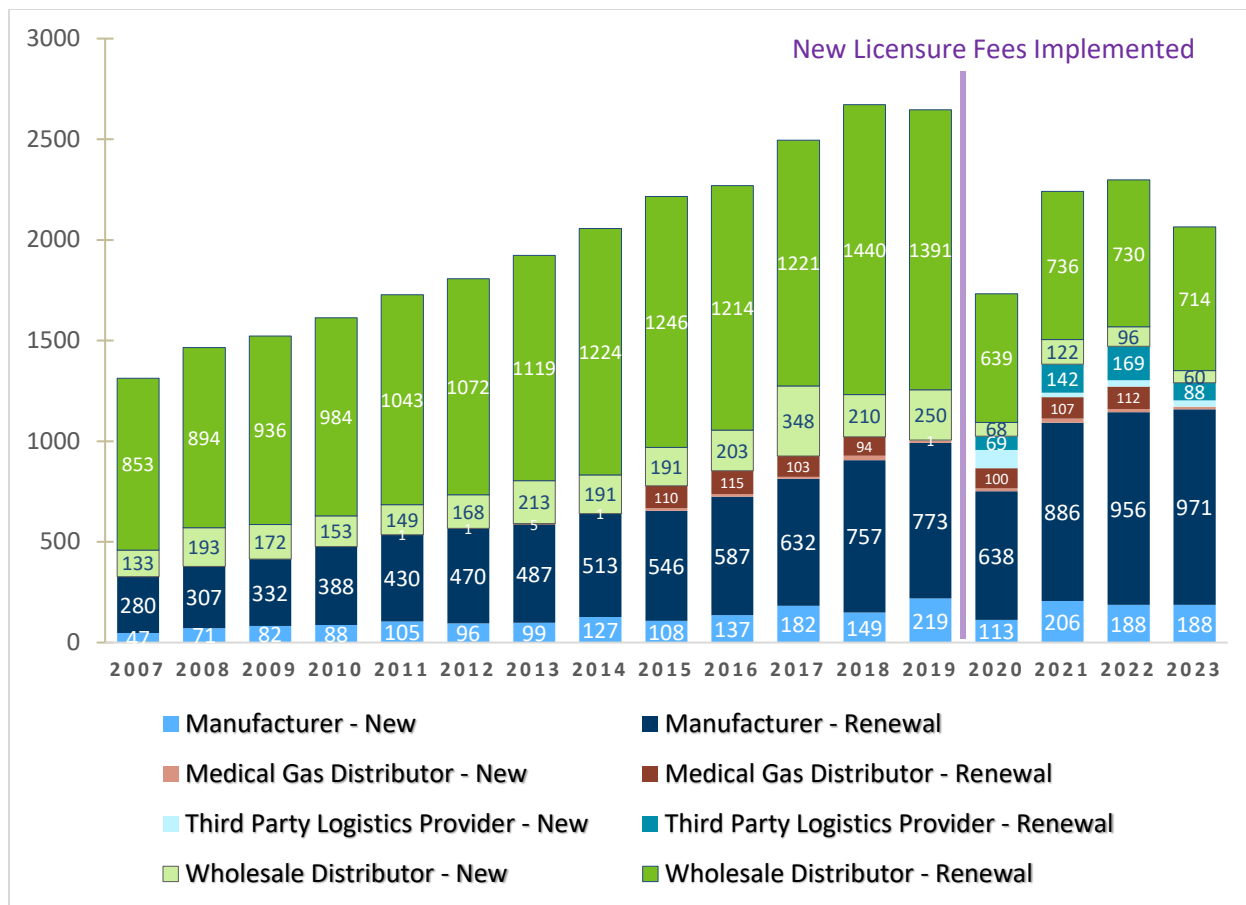


Figure 5: Number of Manufacturer, Wholesaler, Third Party Logistic Provider (3PL), and Medical Gas Distributor applications received by the Minnesota Board of Pharmacy since 2007. Medical Gas Distributor and 3PL licenses began as subtypes of the Wholesaler license prior to reclassification.

Opiate Product Registration Fee Program

Minnesota Statute 151.066 established the Opiate Product Registration Fee Program in 2019 as a means of generating revenue to fund programs combating the opioid epidemic in Minnesota by imposing a \$250,000 fee on manufacturers whose product count exceeded 2,000,000 units in a calendar year. Beginning March 1st of 2020, licensed manufacturers and wholesalers must submit to the Board of Pharmacy their transaction records for opiate products distributed in the previous calendar year to locations in Minnesota legally able to possess medication for the purpose of administering or dispensing to patients. The Board receives these records in the Automation of Reports and Consolidated Orders System (ARCOS) format each year and performs an analysis to calculate the total number of opiate units that were distributed for each manufacturer. By April 1st each year, the Board issues \$250,000 invoices to manufacturers whose total units surpassed a threshold of two million. The number of registration fees assessed has remained relatively stable between 11 to 12 following an initial decrease as can be seen in Table 3.

Table 3: Opiate Product Registration Fees assessed by year.

Year of Opiate Distributions	Number of Manufacturers Assessed \$250,000 OPRF
2019	14
2020 ⁹	11
2021	12
2022	11

As defined in Minnesota Statute 151.066, an opiate unit is the unit of use for the product such that each tablet, mL, gram, syringe, or patch is one unit. For example: both a bottle of 30 tablets and a vial of 30mL would equal 30 opiate units each. Minnesota has seen a decline in the number of opiate units reported as being shipped each year, as seen in Figure 5 below, with a total decrease of approximately 48% from 2020 to 2022. Despite the large reduction in total opiate units, the number of manufacturers with greater than one thousand opiate units distributed experienced only a slight drop from 67 in 2020 to 62 in 2022. The medication which saw the largest drop in total units was tramadol, from 91 million opiate units in 2020 to 28 million opiate units in 2022 as seen in Figure 6. Supplanting tramadol as the top drug by opiate units in 2021 was oxycodone, which increased in total number in 2021 before an overall decrease in 2022. In terms of percentage of total units, the top 5 medications by opiate units were: oxycodone, tramadol, hydrocodone, and fentanyl (see Table 4). It is difficult to translate these findings into a statement concerning the impact on availability of medications for chronic pain patients, however, while tramadol saw a steep decline, it is not typically used in more severe chronic pain such as that often experienced by patients with later-stage cancers.

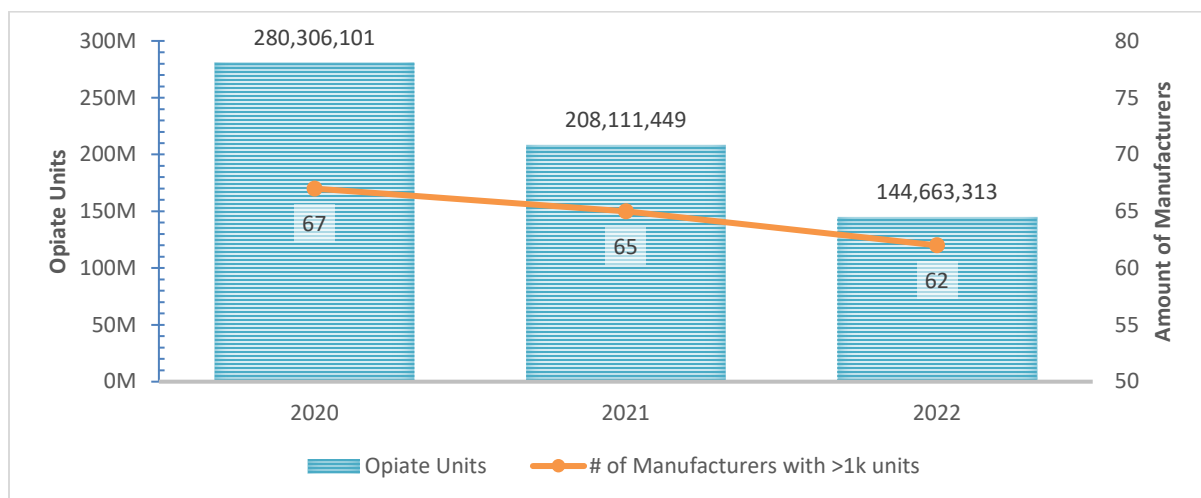


Figure 6: Total calculated opiate units by year and number of manufacturers with greater than 1,000 units.

⁹ Temporary legislation passed to exempt injectable opiate products primarily used in the hospital setting for one year due to the COVID-19 pandemic.

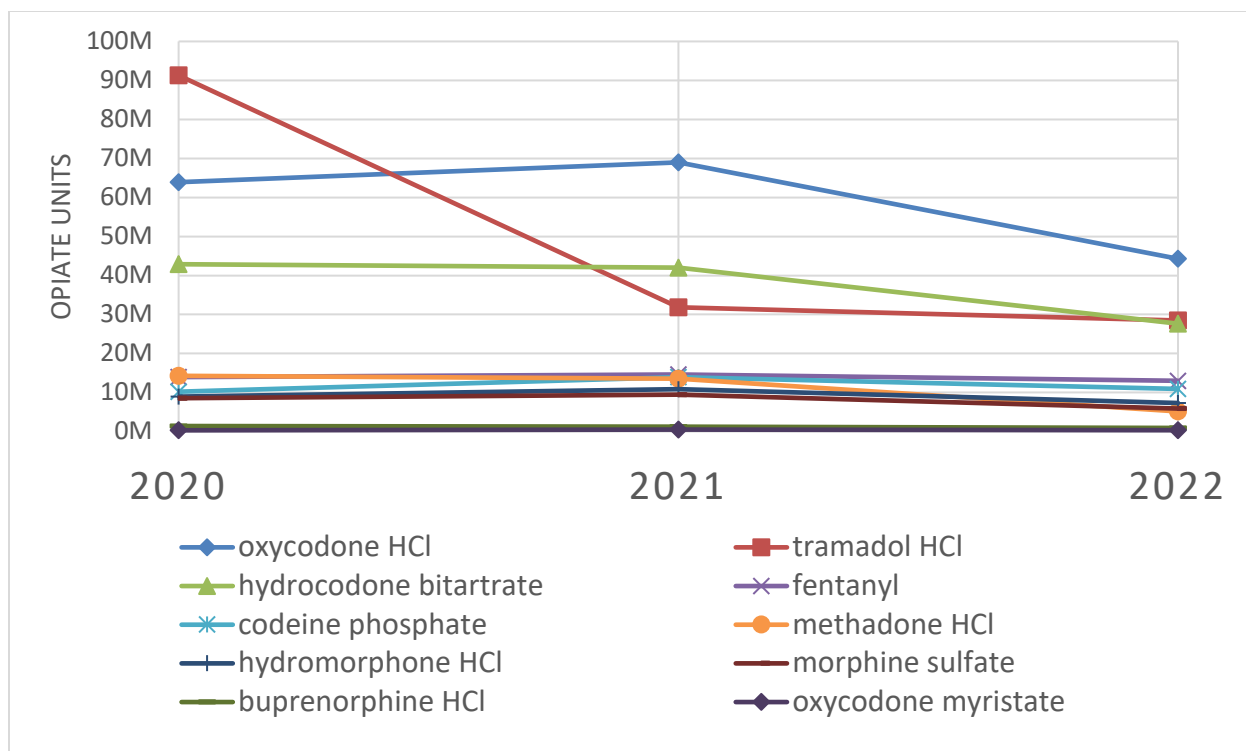


Figure 7: Total opiate units of the top 10 opioids as reported to the OPRFP.

Table 4: Top ten drugs by percentage of total opiate units distributed by distribution year.

Generic Drug Name	2020	2021	2022	2023	Overall
oxycodone HCl	24.9%	33.2%	30.6%	34.3%	29.6%
tramadol HCl	35.5%	15.3%	19.7%	15.6%	23.8%
hydrocodone bitartrate	16.7%	20.2%	19.1%	18.1%	18.4%
fentanyl	5.4%	7.0%	9.0%	13.3%	7.5%
codeine phosphate	4.0%	6.7%	7.5%	6.6%	5.8%
methadone HCl	5.6%	6.5%	3.6%	1.7%	5.0%
hydromorphone HCl	3.5%	5.2%	5.1%	4.8%	4.5%
morphine sulfate	3.3%	4.5%	4.1%	4.0%	3.9%
buprenorphine HCl	0.5%	0.6%	0.6%	0.8%	0.6%
oxycodone myristate	0.1%	0.2%	0.2%	0.2%	0.2%

Limitations

Per Minnesota Statute 152.126, dispensation data in the PMP is only retained for one year and thus historic dispensation data beyond one year has been aggregated and de-identified. As such, this limits the amount of analysis that can be performed to only that which the aggregation allows. For example, finding the total count of opiates and the average total MMEs by AHFS code, NDC, generic name, and label name stop at the county level of the patient, and further details like age, gender, prescriber

type, day supply for each prescription, etc. no longer remain. Historic aggregated dispensation data before 2021 only exists in the form of finalized annual report graphs, tables, maps, and charts. This constraint limits the amount of analysis provided for future reports or addendums to the data that could improve precision and enable further analysis.

Another major limitation is that diagnosis codes are not commonly included on dispensation data reported to the PMP. Since neither diagnosis nor diagnosis code are required to be included on a prescription, pharmacies often do not have this information to report. This severely limits the ability to distinguish between dispensations of opioids for chronic pain versus other indications. Thus, discerning if the increased licensure fees or opiate registration fee had a negative effect on chronic pain patients via analysis of PMP data is markedly impeded.

While manufacturers and wholesalers with Minnesota licenses are statutorily required to submit records of their qualifying opiate distributions to the board, an emerging trend in the business world has added complexity to this. An increasing number of businesses, pharmaceutical manufacturers included, operate primarily virtually in that they have a limited physical presence. A virtual pharmaceutical manufacturer may be the listed owner of the New Drug Application (NDA) or Abbreviated New Drug Application (ANDA) but contract out the actual manufacturing process and never actually physically possess the product they own. The virtual business will also often contract out the shipping and distribution of their product by utilizing businesses called Third-Party Logistics Providers (3PL).

The Board does issue 3PL licenses. However, Minnesota Statute 151.066 does not specifically require 3PLs to report opiate distributions as it does for manufacturers and wholesalers. Some of these virtual entities have expressed resistance when instructed to report their opiate distributions that were conducted via a 3PL as the ARCOS format used to report requires the DEA registration number of the reporter. Since the virtual entity theoretically never has physical possession of the controlled substance, they will often not obtain a DEA registration number and have expressed reluctance to submit a report under the 3PL's DEA. The Board has implemented measures to track 3PL utilization and coordinate 3PL reporting on behalf of virtual manufacturers or wholesalers for the purpose of monitoring opiate distribution reporting compliance, though the possibility exists that some distributions have gone unreported.

Another limitation regarding the data obtained through the OPRFP is that it relies on licensee compliance with the reporting mandate for accurate statistics. The existing statute requires the reporting of opiate distributions but does not require licensees to submit a "zero report" in the event no opiates were distributed during the calendar year. Monitoring reporting compliance is an ongoing effort at the Board, with advances occurring each year, however, one hundred percent reporting compliance is unlikely to have been achieved. The Board is supportive of legislative fixes to better address compliance in reporting.

Conclusion

In conclusion, the final analysis on the impact of increased license fees and opiate fees from 2021 to 2023 on changes of prescribing practices of opiates or unintended consequences on opiate prescription availability for the treatment of chronic or intractable pain remains inconclusive. Analysis shows dispensation data from 2021-2023 reported a weak correlation between the decreasing average total MME and average daily MME per prescription across three years with no visible regional trends, but there is no current way to distinguish between prescriptions intended for chronic pain patients versus those that are not. The overall amount of manufacturer and wholesaler licenses issued did show a drop in numbers initially, however the following two years shows no conclusive trends to support a further increasing, decreasing, or maintaining of license counts. Furthermore, there is a lack of substantial connection between OPR data regarding manufacturers, wholesalers, and 3PLs distributions and provider prescribing practices for treatment of chronic or intractable pain. All data analysis of concern shows various trends that neither prove nor disprove the raised licensure fees and OPRF had an impact on opioid prescribing practices or ability to treat chronic or intractable pain.

Additionally, the various limitations contributed to an inconclusive final analysis. When analyzing whether increased licensure fees and the introduction of the Opiate Product Registration Fee from 2021 to 2023 changed opiate prescribing practices or had unintended consequences on opiate prescription availability for the treatment of chronic or intractable pain, being aware of limitations are integral to the analysis. The major limitation factors that contributed to the inconclusive final analysis were: 1) gaps in oversight of 3PLs and how wholesalers and manufacturers utilize 3PLs 2) no mandatory diagnostic code collection in the Minnesota Prescription Monitoring Program 3) Statute limitations on individual dispensation data retention and 4) what historic aggregated de-identified county level data can be kept. These limitations make performing analysis and conducting reports across time periods over 12 months tenuous and inhibit the accuracy of certain function which are critical for comprehensive and cohesive assessments across departments within the Board of Pharmacy. All these factors indicate either a weak correlation

between increasing licensure and OPR fees, circumstantial factors, or other unaccounted for outside variables exerting influence on the various trends seen across dispensation, licensing, and OPR data.