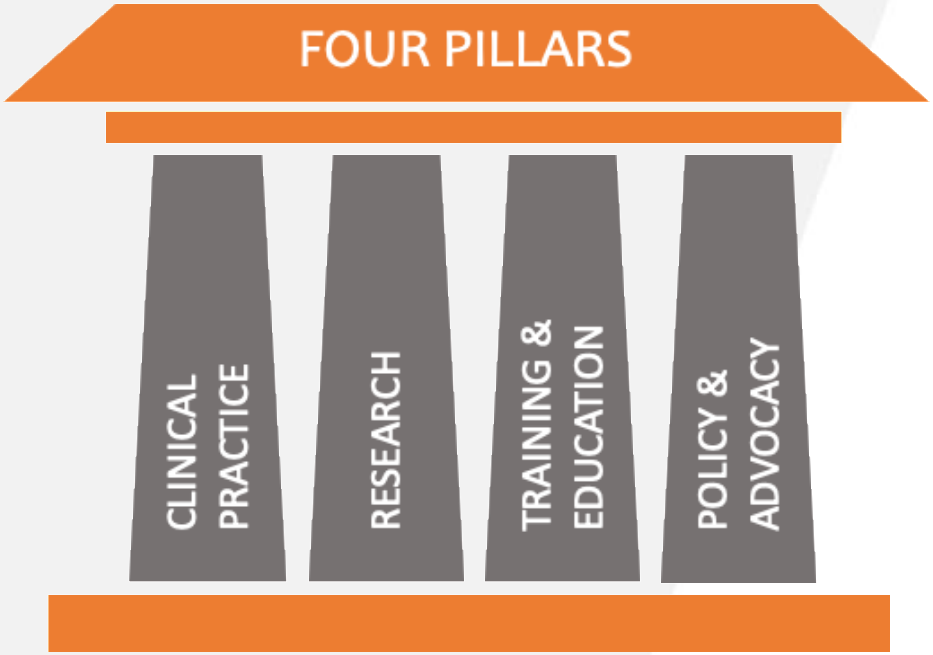
Current Research and Activities

National Center for
WELLNESS & RECOVERY
OKLAHOMA STATE UNIVERSITY

Dr. Don Kyle, Adjunct Professor of Pharmacology
and Physiology, OSU Center for Health Sciences

National Center for Wellness & Recovery



MISSION

"To inspire hope and to develop innovative, science-driven treatment interventions to improve the lives of those afflicted by pain and substance use disorders"

Ending Addiction and Managing Pain

- Discovery and approval of new, non-addictive, pain medications has been disappointing.
  - Pain perception is subjective
  - Placebo effects are common
  - Translation from animal models to human has been poor
- Addiction mechanisms are not well understood.
  - Genetic pre-disposition
  - Childhood trauma
  - Environmental factors
- To end the opioid crisis, scientific research aimed at discovering alternatives to opioids and elucidating the mechanisms of addiction is required.
  - Pain and addiction biomarkers are urgently needed
  - New molecular approaches for treating pain are of premiere importance
  - More options for MAT and reversal of overdose are crucial

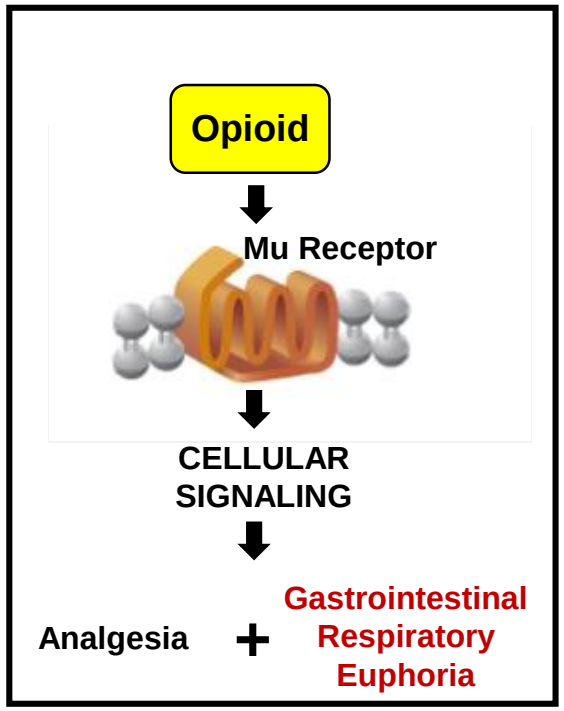
Biomarker Research

- NCWR has unique access to nearly 50,000 bio-samples from consenting patients.
  - Samples obtained from ~2003-2015 in over 30 clinical protocols
  - Tested drugs include opioids and non-opioids (time-course)
  - Blood, DNA, and RNA are cross-referenced to non-confidential patient records
  - Planning is underway to extend this research asset by collecting additional bio-samples during MAT in the future
- Research strategies and identification of collaborators and scientific advisors in progress.
  - Internal assessments of existing and future NCWR core competencies
  - Data mining and visualization tools are under consideration
  - Complementary industrial and academic partners enhance and accelerate NCWR's mission
- Successful research will have broad and significant medical impact.
  - Translational bio-markers will stimulate new research for opioid alternatives
  - Pain bio-marker would supplement self-report measures in clinical trials, improving trial outcomes
  - Predictive bio-markers for risk and/or onset of addiction would benefit patients and physicians

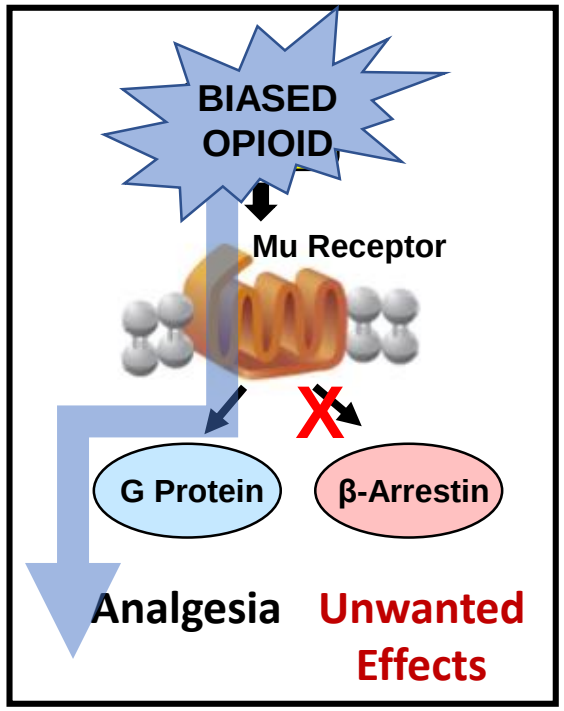
Pain Research

1800-1965	1970-2020
PIONEERING OPIOID CHEMISTRY Morphine, oxycodone, fentanyl, buprenorphine	PIONEERING OPIOID BIOLOGY Mu receptor, enkephalin, cell signaling, biotech

Opioid Pharmacology

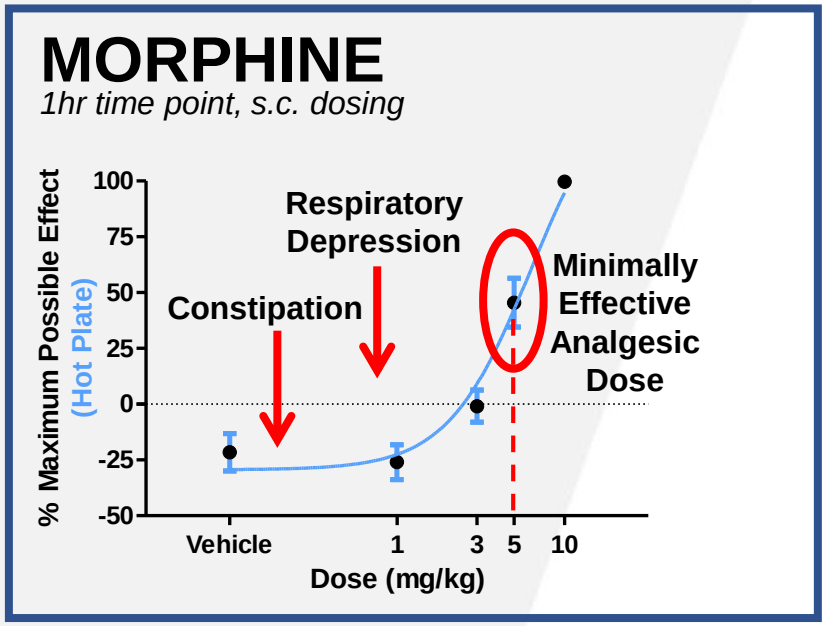


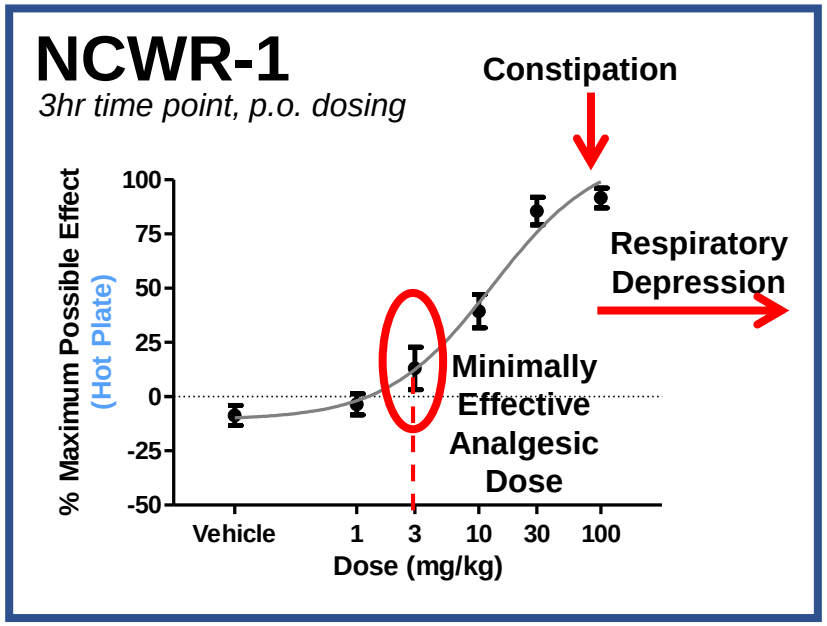
New Opioid Pharmacology



- The discovery of opioid drug molecules does not overlap in time with the discoveries about their mechanism.
  - It has always been presumed that opioid analgesia and unwanted effects are inseparable.
- Unpublished, "biased opioid" research molecules at NCWR show analgesic efficacy with reductions in unwanted effects in animal models.
  - Molecules in this collection may also lead to new MAT treatment options
- NCWR is well positioned to advance the science in this area and make new discoveries that will benefit patients.

NCWR-1: A Novel Pre-Clinical Research Molecule with Biased Mu Receptor Signaling

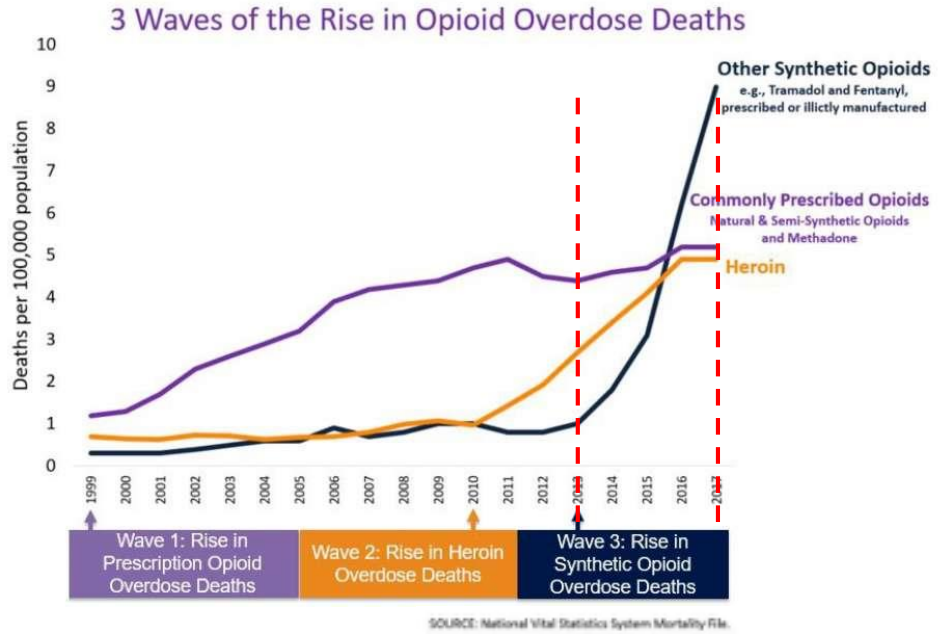




- The onset of important opioid side-effects differ significantly between morphine and NCWR-1 in animal models, despite both being mu receptor agonists.

Fighting the Emerging Fentanyl Crisis

- The 3rd wave of the opioid crisis is fueled by fentanyl
- Fentanyl is particularly dangerous
  - Mu receptor affinity and duration of action exceed naloxone
  - "Designer" analogs of fentanyl are evasive to law enforcement
  - Inexpensive to prepare without need of opium poppies
  - Blended into other drugs of abuse without knowledge of the end-user.



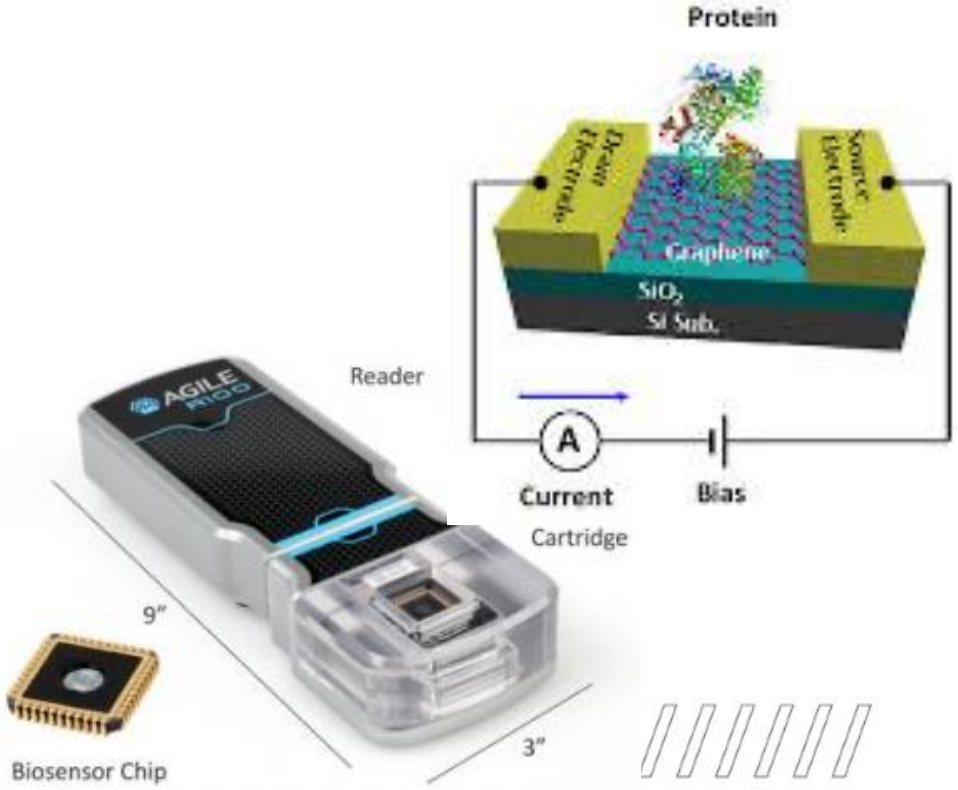
	Affinity	Potency	Efficacy	CNS Penetration	Duration
Molecule	Mu Opioid Receptor			Lipophilicity	Half-Life
	K_i (nM)	GTPγS EC_{50} (nM)	GTPγS E_{MAX} (%)	AlogP	Hours
Fentanyl	2.7	133	88	4.05	4-8
Naloxone	8.8	>20000	0	2.1	0.5 – 1.5

- Research molecules at the NCWR have profiles that may lead to effective alternative treatments for fentanyl overdose
  - Higher affinity to mu opioid receptor
  - High CNS penetration
  - Long duration of action

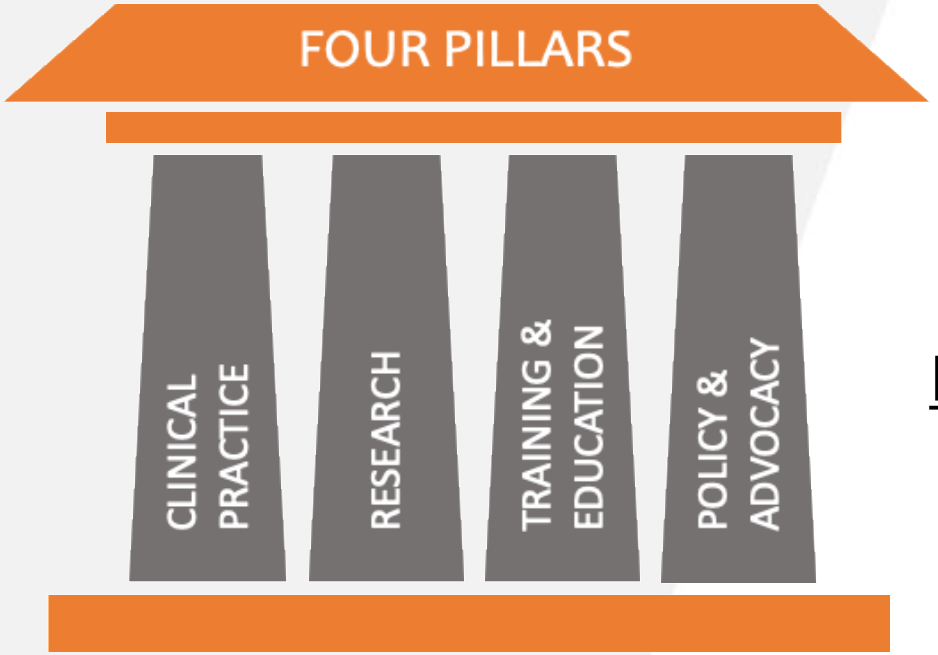
“Fighting Fire-With Fire”: Research Agreements in Progress with Industry

Oral thin film formulation

High-sensitivity fentanyl bio-sensor



National Center for Wellness & Recovery



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Presentation Summary

- Biomarker research for pain and addiction
- Novel mechanisms for pain and MAT treatment
- New molecules, delivery systems, and analytical tools to combat the emerging fentanyl crisis

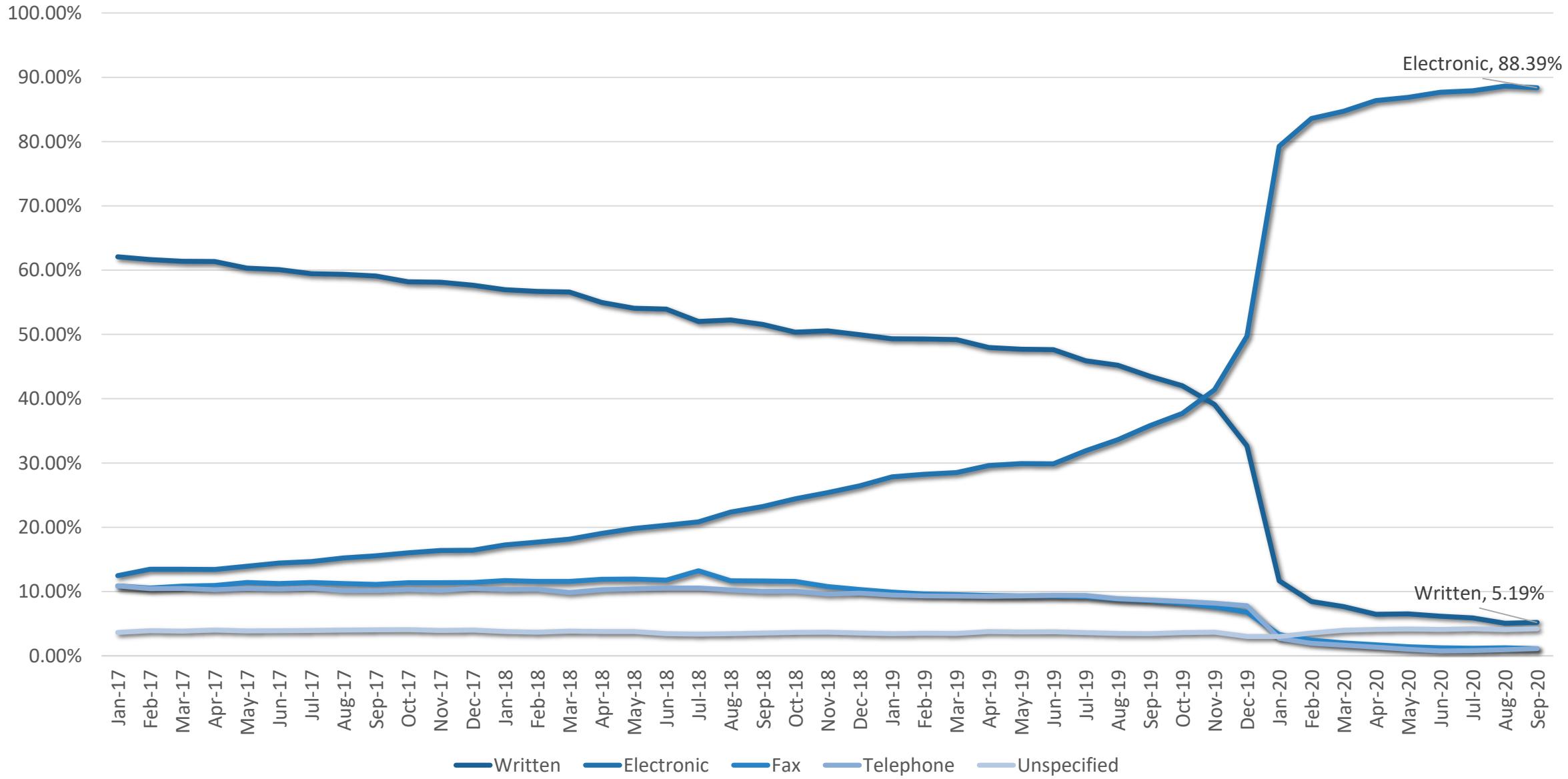
Oklahoma Bureau of Narcotics

SEPTEMBER 10, 2020

Integration and E-prescribing

- STATUS OF INTEGRATION
  - 139 ENTITIES IN THE PROCESS OF INTEGRATING
  - OVER 5,300 PRESCRIBERS BEING INTEGRATED
- STATUS OF ELECTRONIC PRESCRIBING
  - 88% OF PRESCRIPTIONS ARE SUBMITTED ELECTRONICALLY
  - 5.19% OF PRESCRIPTIONS ARE WRITTEN

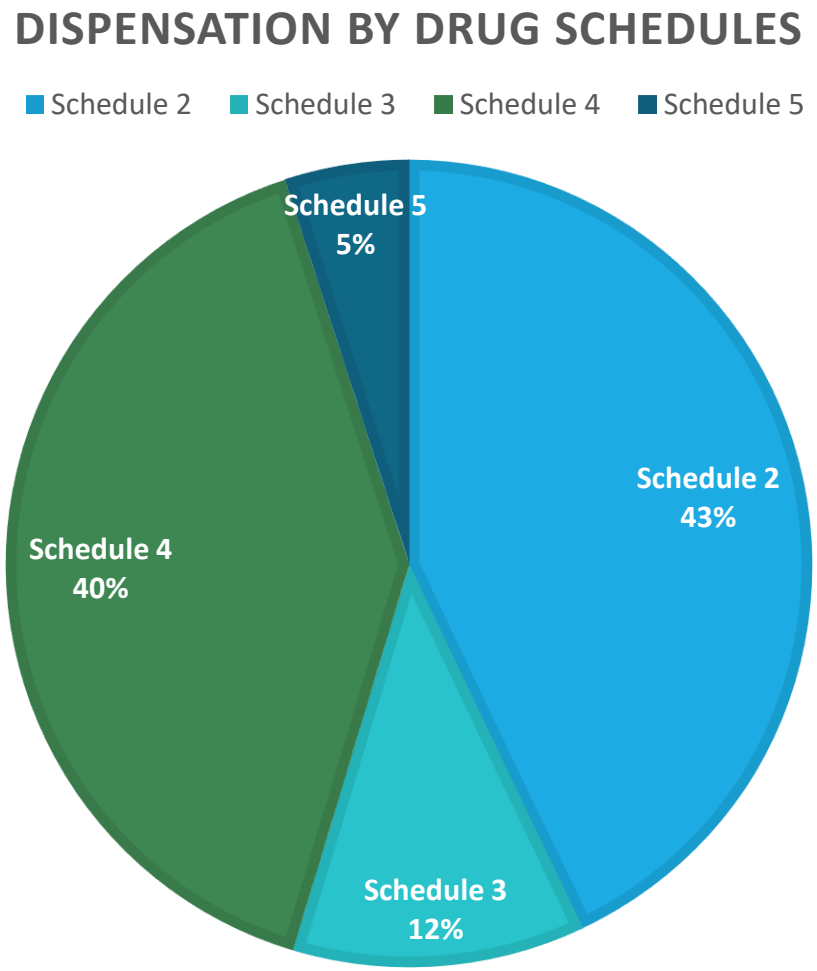
Prescription Submission Type



PMP Statistics

2020 year to date		
Opioids	2,416,694	45.3%
Non-Opioid	2,917,528	54.7%
Total	5,334,222	100%

2020 year to date		
HYDROCODONE	977,142	18.3%
OXYCODONE	485,807	9.1%
TRAMADOL	391,994	7.3%
ALPRAZOLAM	384,804	7.2%
ZOLPIDEM	312,827	5.9%
Total	2,552,574	47.8%



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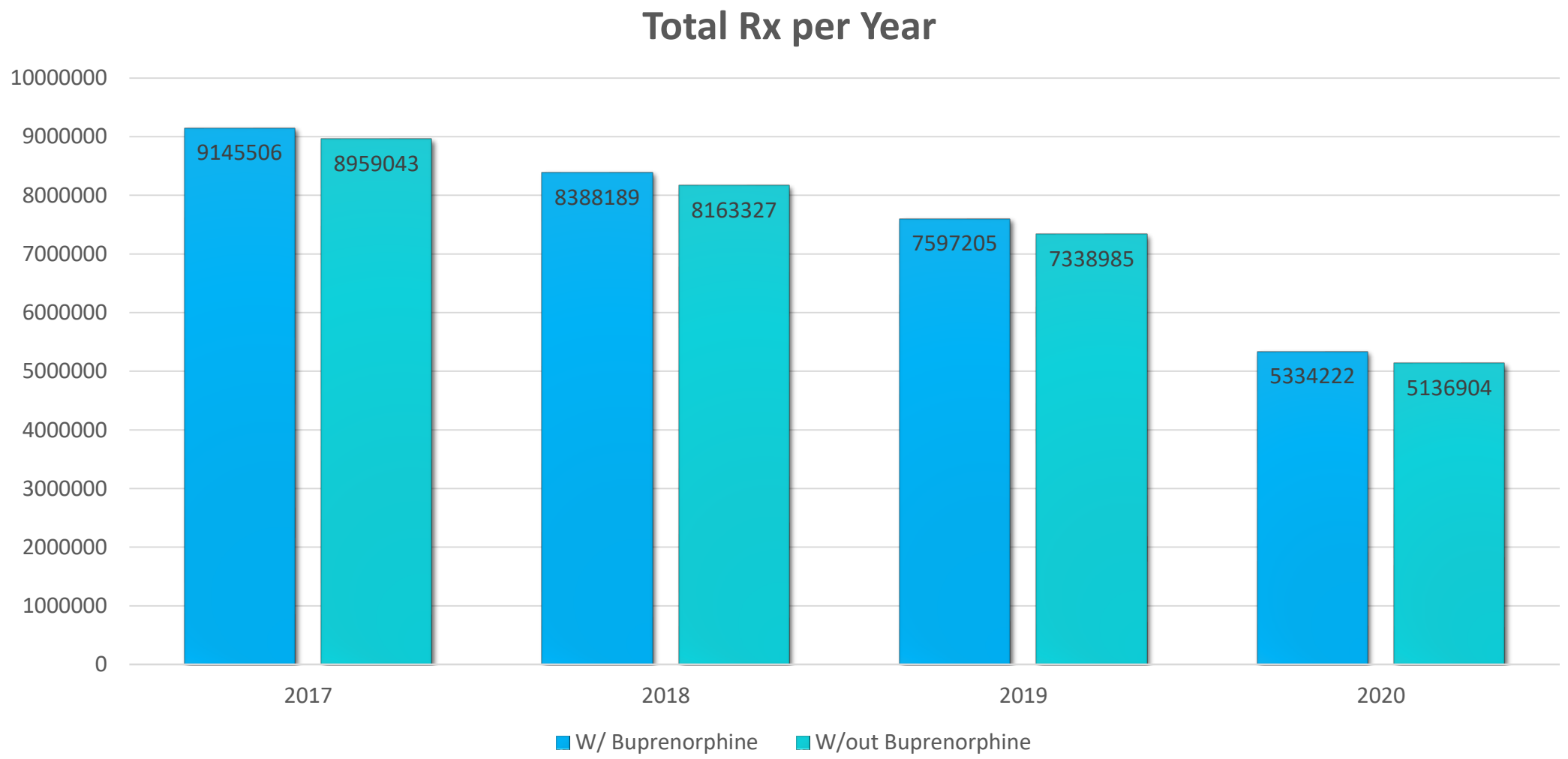
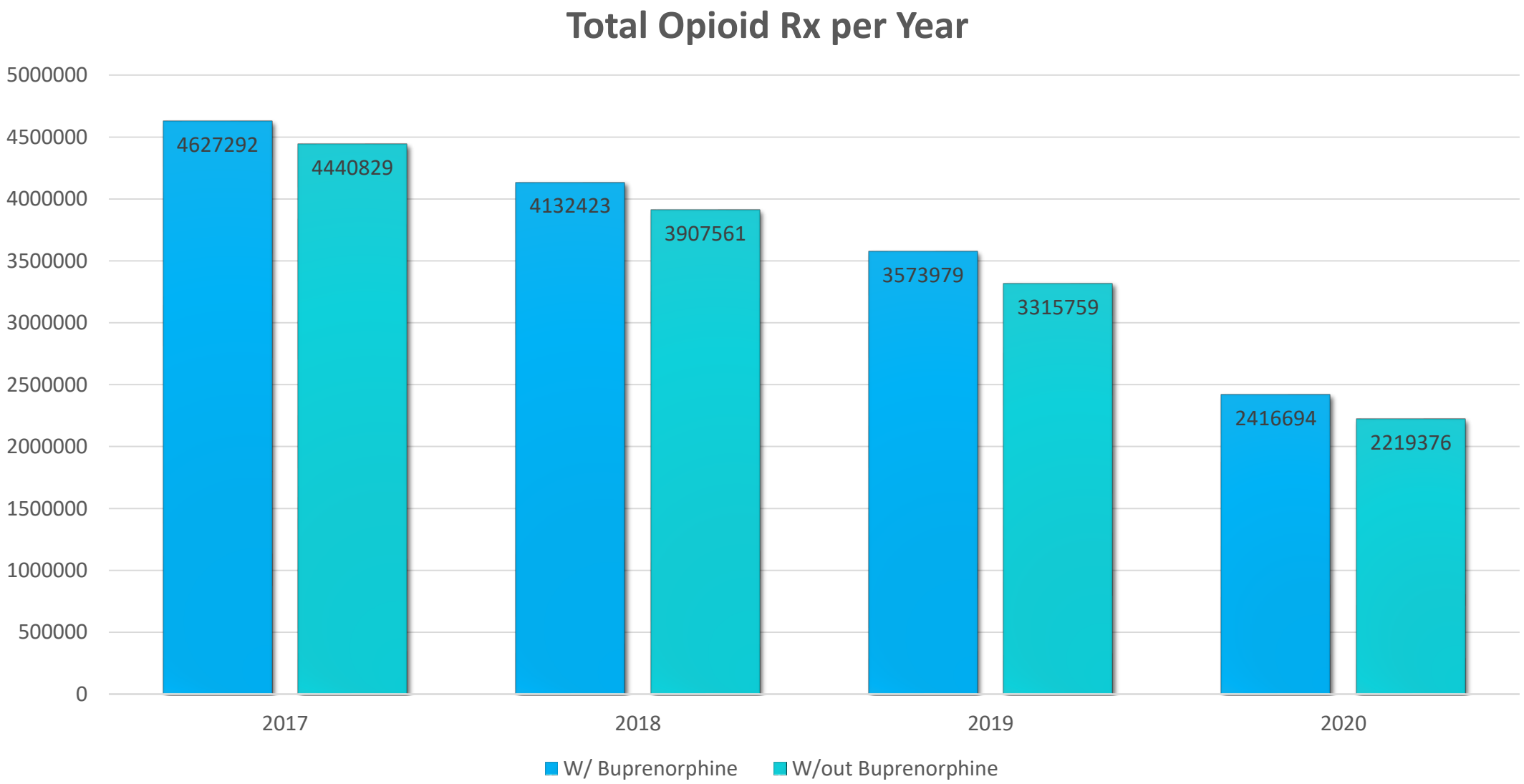


Opioid Statistics



Disclaimer

- All data was pulled September 9, 2020.
- Data is labeled by whether it includes Buprenorphine.
- Data is entered by the pharmacy and errors could occur.

LEGISLATIVE UPDATE 9/10/20

Deputy Attorney General Lori Carter

HOUSE BILLS

- **HB4138** by **Representative Kevin Wallace and Senator Roger Thompson**
- Creates the Opioid Abatement Revolving Fund and the Opioid Abatement Board to disperse opioid grant awards to political subdivisions for the purpose of abating the opioid crisis in Oklahoma
- Signed by the Governor on **May 21, 2020/effective date August 28, 2020**

- **HB4140** by **Representative Kevin Wallace and Senator Roger Thompson**
- Appropriates $10.22 million from the Opioid Lawsuit Settlement Fund to the Oklahoma Opioid Abatement Revolving Fund, as created by HB4138
- Signed by the Governor on **May 21, 2020/effective date August 28, 2020**

SENATE BILLS

- **SB1718** by **Senator John M. Montgomery and Representative Jon Echols**
  - Parity legislation - It requires benefits for mental health conditions and substance use disorders be equal to benefits for treatment of all other conditions and shall be subject to the same preauthorization and utilization review mechanisms and other terms and conditions as all other physical diseases and disorders.
  - Requires health insurers to meet federal parity guidelines
  - Requires insurers to file an annual report with the Insurance Commissioner to demonstrate compliance with state and federal parity laws
  - Requires Insurance Commissioner to enforce the parity laws and shall post online redacted reports submitted and identify noncompliant insurers
  - Status: Signed by the Governor **May 19, 2020/effective Nov. 1, 2020**

- **SB1915** by **Senator Kim David and Representative John Pfeiffer**
  - Amends the Physician Assistant Act to provide for physician "delegation" instead of "supervision" and authorizes physician assistants to provide health care services, provided a practice agreement with an allopathic or osteopathic physician or physicians is in place
  - P.A. is to be considered the primary care provider and services must be reimbursed the same as if a physician had ordered or provided them
  - Status: Signed by the Governor **May 21, 2020/effective Aug. 28, 2020**

INTERIM STUDIES & NEXT SESSION

- **IS20-023** by Representative Cindy Munson
  - Will look at the availability of over-the-counter loperamide (Imodium) – opioid-based
  - September 15, 2020 in Room 206, 9am-11am

- **Sickle Cell Anemia bill**

OTHER UPDATES

- **Opioid Overdose Fatality Review Board**
  - Virtual Meeting October 16, 2020 at 1:00pm

- **OSU Center for Wellness and Recovery**
  - State of Addiction Virtual Conference September 9-11, 2020

NEXT MEETING

- **Oklahoma Commission on Opioid Abuse**
  - November 10, 2020 (possibly virtual) at 1:30pm Attorney General's Office
  - Final Report Due: **December 31, 2020**