Opioids, Naloxone, and Buprenorphine-Key Updates in Tennessee

Sarah T. Melton, PharmD, BCPP, BCACP, FASCP
Professor of Pharmacy Practice
ETSU Center of Excellence for HIV/AIDS
January 26, 2017

BILL GATTON
COLLEGE *of* PHARMACY
EAST TENNESSEE STATE UNIVERSITY

Opening Discussion

- What are the most common dilemmas you encounter in practice that deal with opioid prescribing, a patient with opioid use disorder, medication assisted treatment, or provision of naloxone?
- How are the patient populations with HIV and Hepatitis C especially complicated when dealing with these issues?

Learning Objectives

- Describe the scope and epidemiology of the opioid public health emergency in Tennessee and on the national level
- Discuss the diagnostic criteria for opioid use disorder (OUD)
- Compare the different medications used to treat OUD and opioid overdose
- Interpret recent updated prescribing guidelines in Tennessee related to the treatment of OUD, chronic pain, and co-prescribing of naloxone
- Explain methods of educating patients with substance use disorders (SUD) and ways of decreasing stigma.

Describe the scope and epidemiology of the opioid public health emergency in Tennessee and on the national level

Public Health Emergency

- October 26, 2017 – National level
- *"We're losing 144 people a day to drug overdoses. That's like a plane crash every single day in America for an entire year. Or, put another way, it's like losing a sold-out Yankee Stadium all in one second."*

Jessica Nickel, president, and CEO of the Addiction Policy Forum

Prescription Opioid Use Among Subgroups

- Older adults (aged 40 years and older) are more likely to use prescription opioids than adults aged 20 – 39
- Women are more likely to use prescription opioids than men
- Non-Hispanic whites are more likely to use prescription opioids than Hispanics
  - No significant differences in prescription opioid use between non-Hispanic whites and non-Hispanic blacks

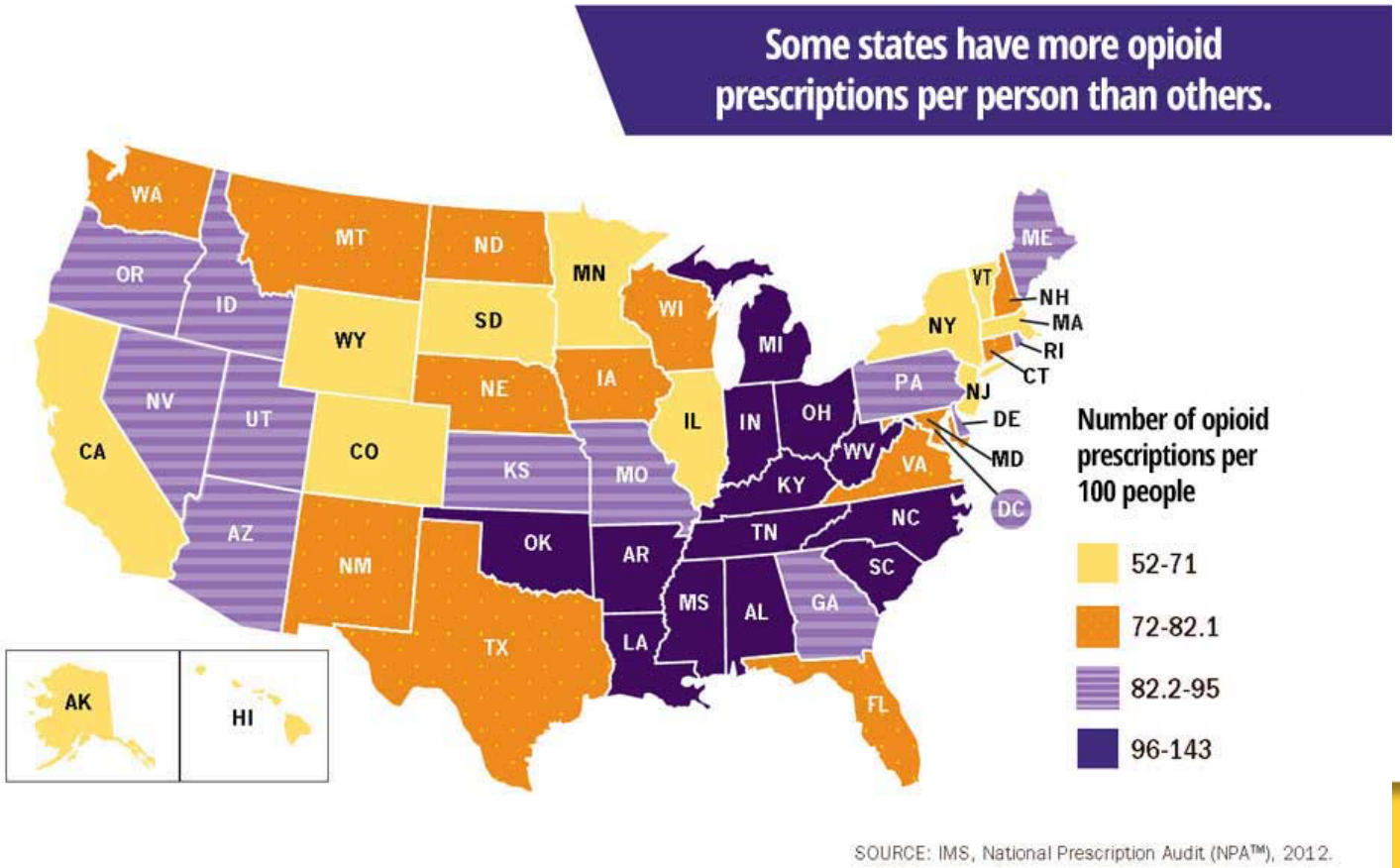
https://www.cdc.gov/drugoverdose/data/prescribing.html

Current Trends: National

- According to the International Narcotics Control Board, in 2013, the US held 99% of global stock of hydrocodone which accounted for 49 tons[1]
- Every day, over 1,000 people are treated in emergency departments for misusing prescription opioids[2]
- Approximately 20.8 million people aged 12 and older had a substance use disorder, including both alcohol and illicit drugs[2]

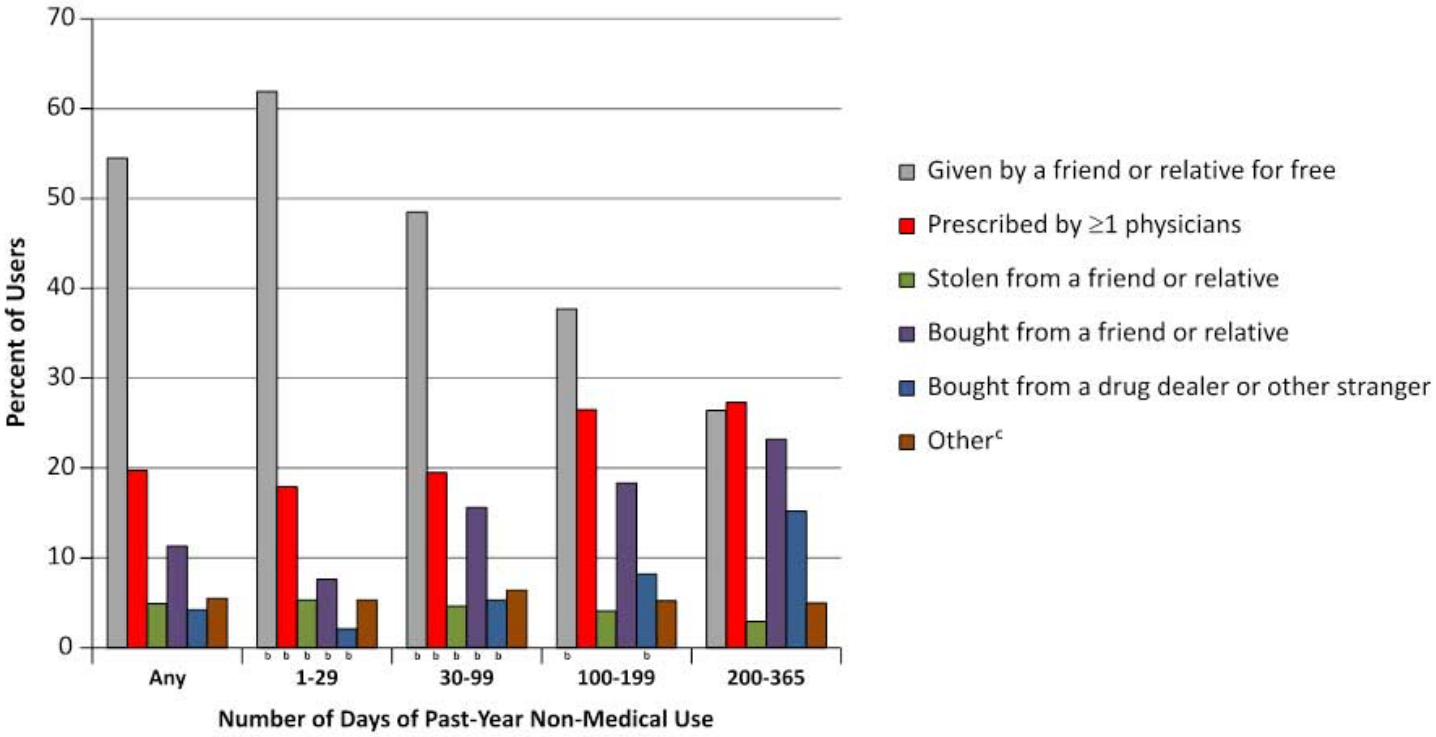
1. International Narcotics Control Board-Availability of Internationally Controlled Drugs - https://www.incb.org/incb/en/publications/incb-publications.html
2. Results From the 2015 National Survey on Drug Use and Health https://www.samhsa.gov/data/

Number of Opioid Prescriptions/100 People



https://www.cdc.gov/drugoverdose/data/prescribing.html

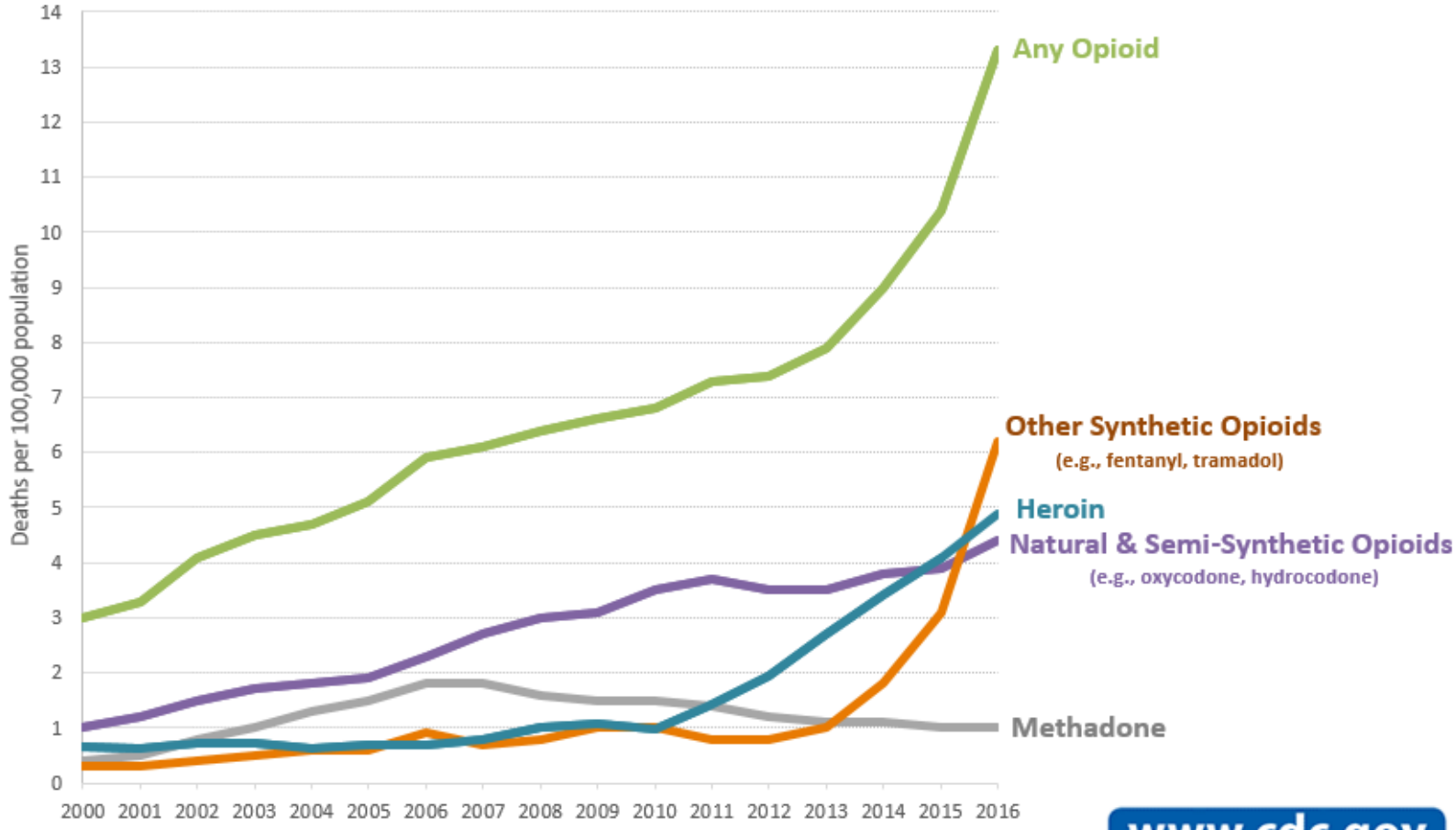
Sources of Prescription Opioids Among Past-Year Non-Medical Users[a]



[a] Obtained from the US National Survey on Drug Use and Health, 2008 through 2011.[5]
[b] Estimate is statistically significantly different from that for highest-frequency users (200-365 days) ($P < .05$).
[c] Includes written fake prescriptions and those opioids stolen from a physician's office, clinic, hospital, or pharmacy; purchases on the Internet; and obtained some other way.

SOURCE: Jones C, Paulozzi L, Mack K. Sources of prescription opioid pain relievers by frequency of past-year nonmedical use: United States, 2008–2011. JAMA Int Med 2014; 174(5):802-803.

Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2016



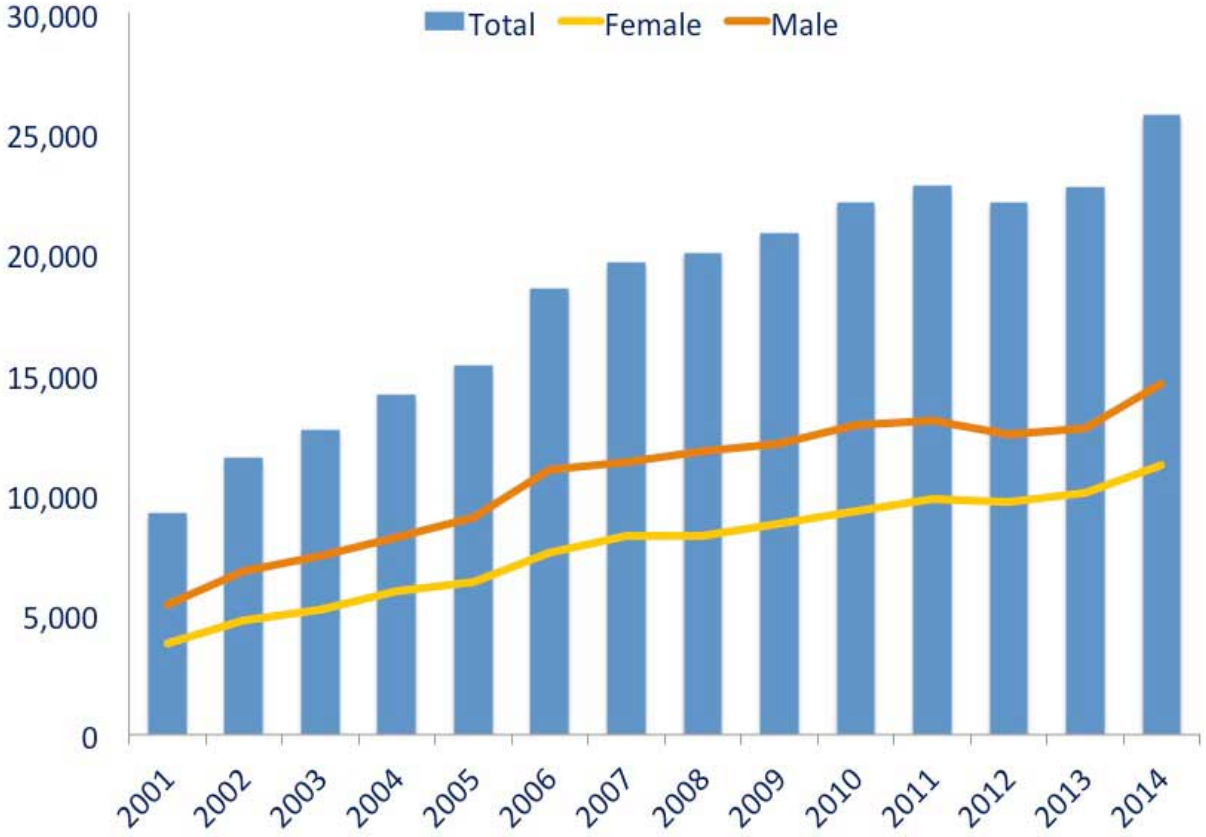
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Ser vices, CDC; 2016. https://wonder.cdc.gov/.

www.cdc.gov
Your Source for Credible Health Information

National Institute on Drug Abuse

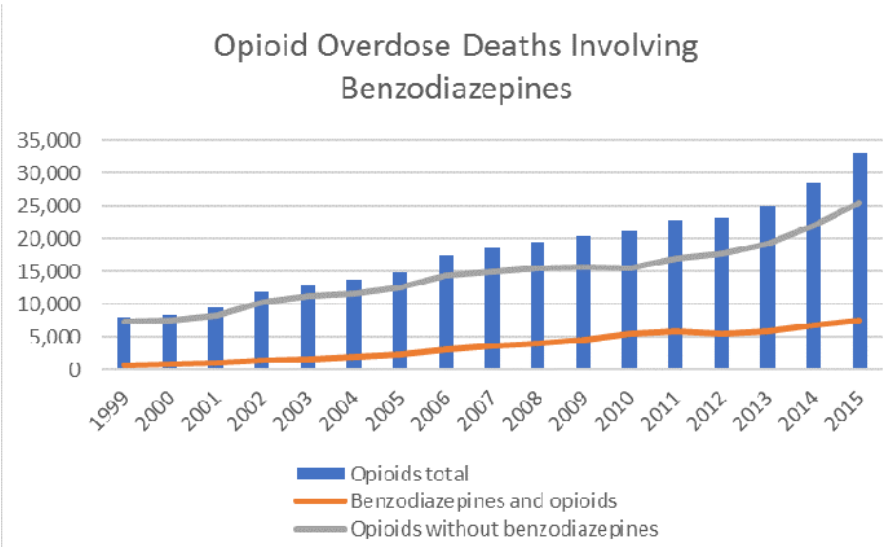
National Overdose Deaths

Number of Deaths from Prescription Drugs



Source: National Center for Health Statistics, CDC Wonder

Benzodiazepines with opioids



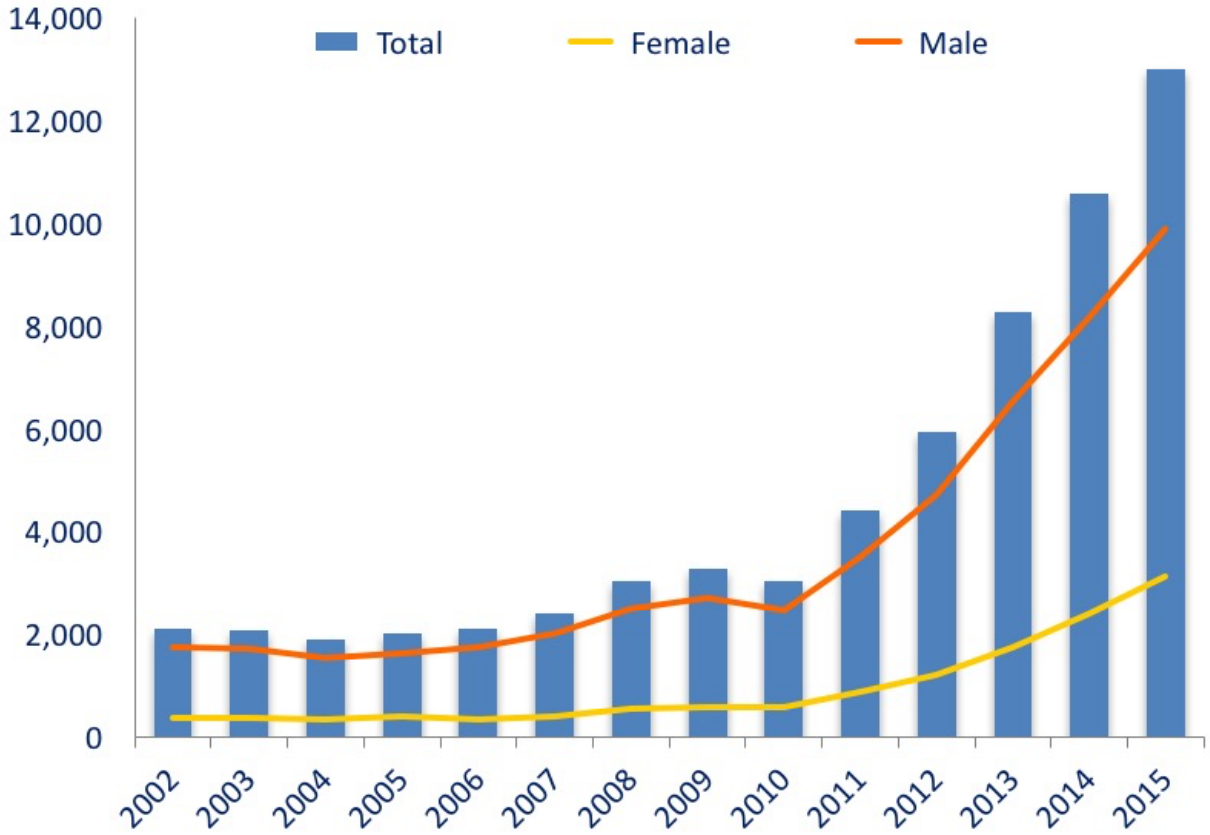
- Number of American adults filling a benzodiazepine prescription is increasing as is quantity filled
- 30% of overdose deaths are associated with benzodiazepines
- FDA black box warning

Bachhuber MA, et al. Increasing Benzodiazepine Prescriptions and Overdose Mortality in the United States, 1996–2013. *American Journal of Public Health*. 2016;106(4):686-688. doi:10.2105/AJPH.2016.303061.

NIH National Institute on Drug Abuse

National Overdose Deaths

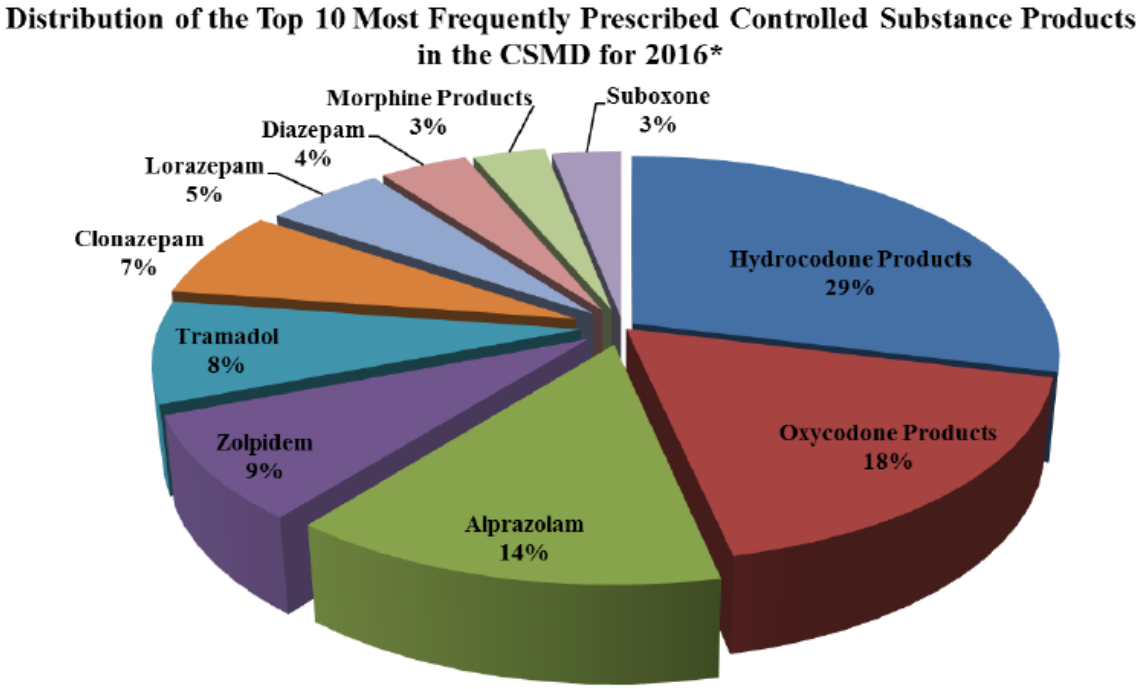
Number of Deaths Involving Heroin



Source: National Center for Health Statistics, CDC Wonder

Current Trends: TN

Distribution of the Top 10 Most Frequently Prescribed Controlled Substance Products in the CSMD for 2016



* Including all dispensers who reported to the CSMD in 2016.

Adapted from the CSMD 2017 Report to the 110th General Assembly, TDH, CSMD Advisory Committee

TN Department of Health | Office of Informatics & Analytics

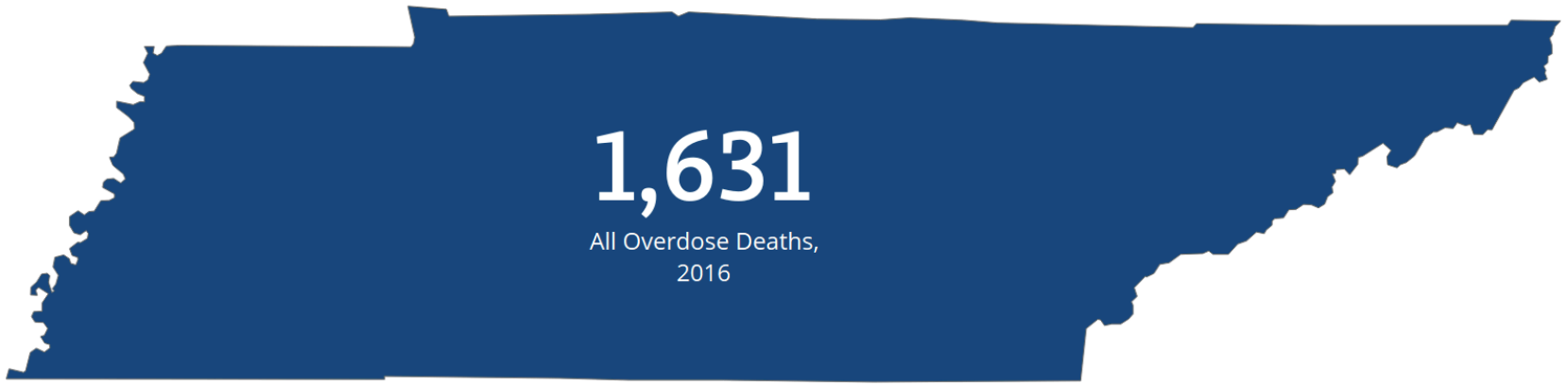
Tennessee Drug Overdose Data

1,186
Opioid Overdose Deaths, 2016

13,034
Nonfatal Overdose Outpatient Visits, 2015

7,092
Nonfatal Overdose Inpatient Stays, 2015

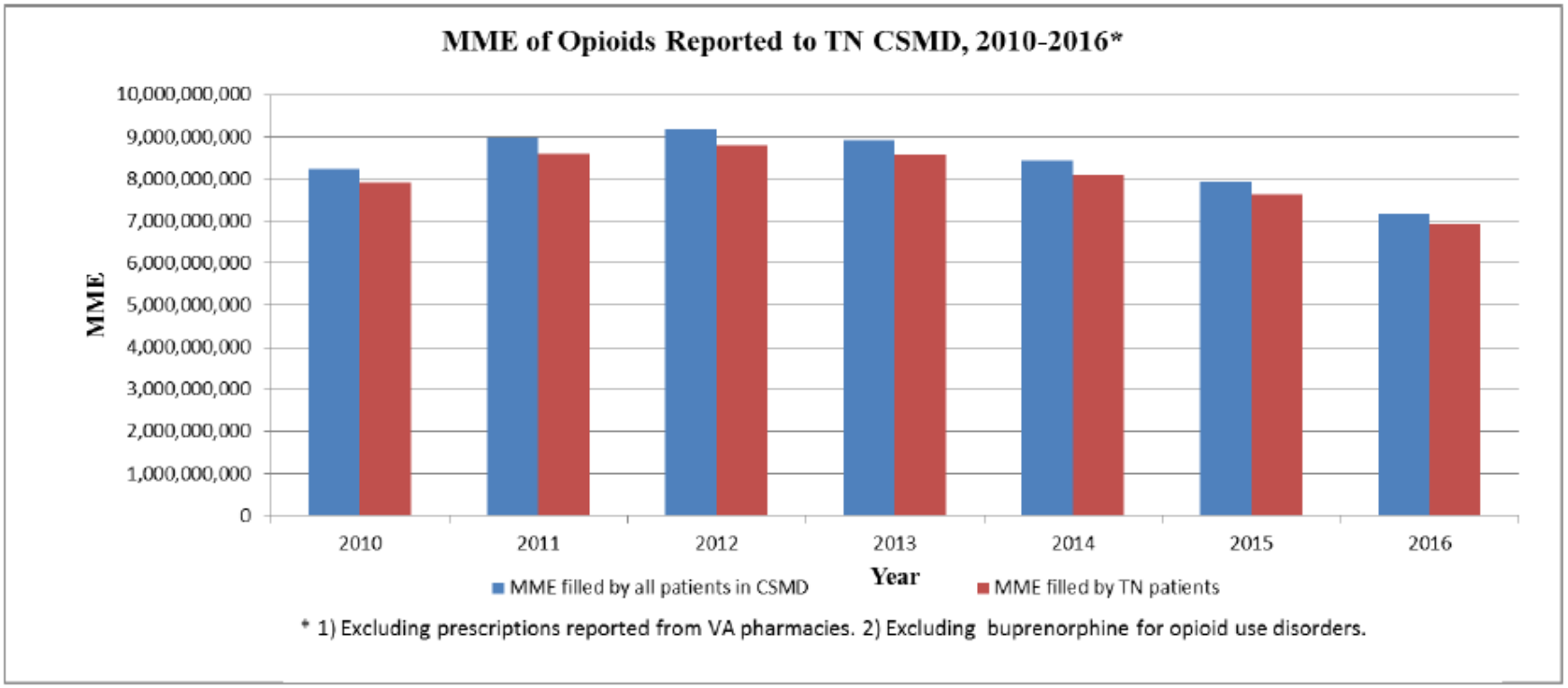
7,636,112
Painkiller Prescriptions, 2016



https://www.tn.gov/health/health-program-areas/pdo/pdo/data-dashboard.html

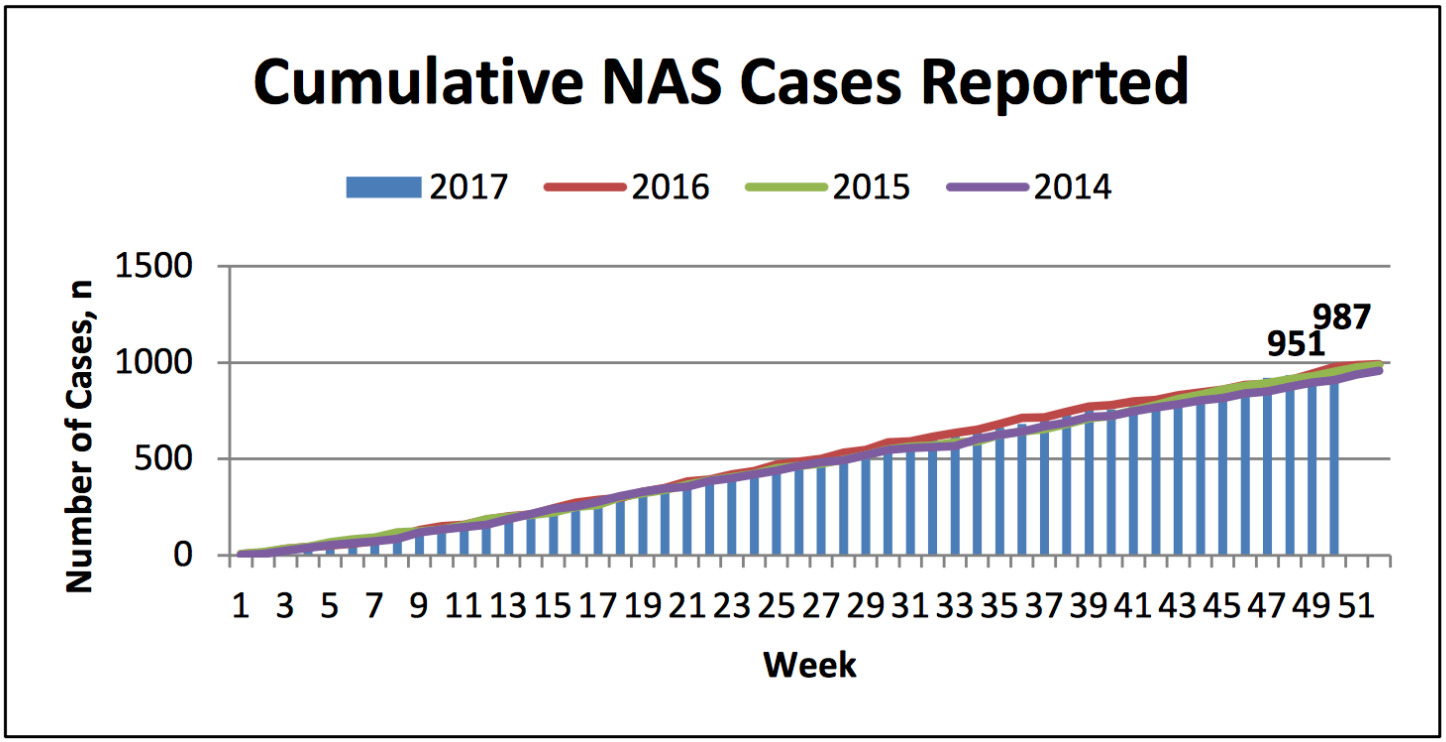
Current Trends: TN

MME of Opioids Reported to TN CSMD, 2010-2016*



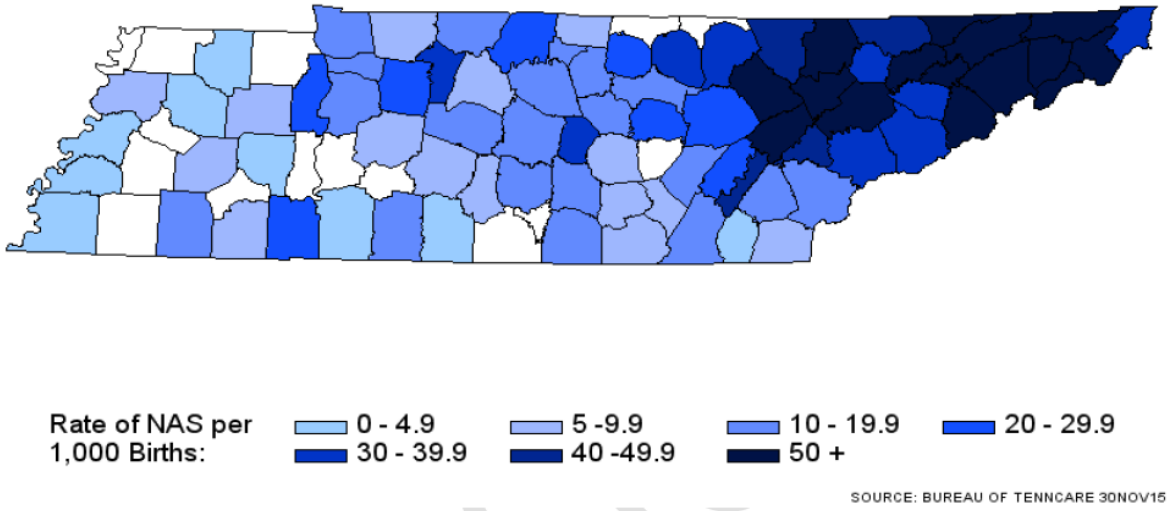
Adapted from the CSMD 2017 Report to the 110th General Assembly, TDH, CSMD Advisory Committee

Neonatal Abstinence Syndrome 2017



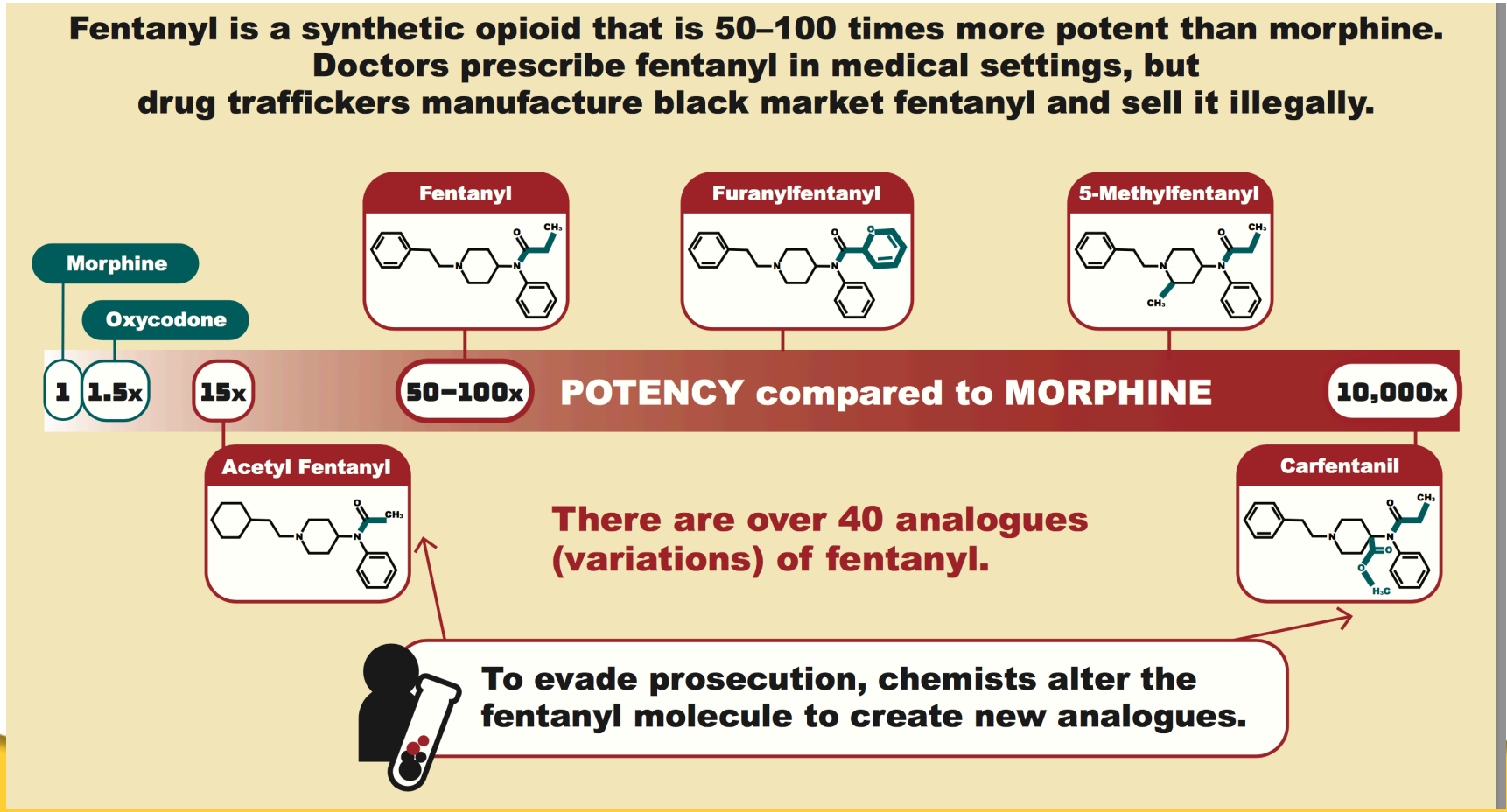
Current Trends in TN: NAS

Map 1: Incidence of NAS among TennCare recipients - 2014 data



SOURCE: BUREAU OF TENNCARE 30NOV15

Fentanyl and Analogues



http://www.safemedicines.org/wp-content/uploads/2017/03/Fentanyl101-infographic-4p.pdf

Fentanyl and Tennessee

Photo Courtesy of Tennessee Bureau of Investigation.

- Public health and safety advisory issued in 2017
- Law enforcement officials have made several kilo-plus size seizures of fentanyl analogues across Tennessee in forms such as heroin and counterfeit versions of popular opioids
- Law enforcement advised to use extreme caution when encountering and unknown substance
- From 2013 to 2015 in Tennessee, the appearance of fentanyl in drugs associated with overdose deaths has more than doubled, from 5 percent in 2013 to 12 percent in 2015

https://www.tn.gov/content/dam/tn/health/healthprofboards/Fentanyl_Public_Health_Advisory.pdf

Lethal Doses

http://www.usfra.org/m/group/discussion?id=916090%3ATopic%3A248658

Lethal Dose of Carfentanil

http://www.usfra.org/m/group/discussion?id=916090%3ATopic%3A248658

Current Trends in TN: Fentanyl

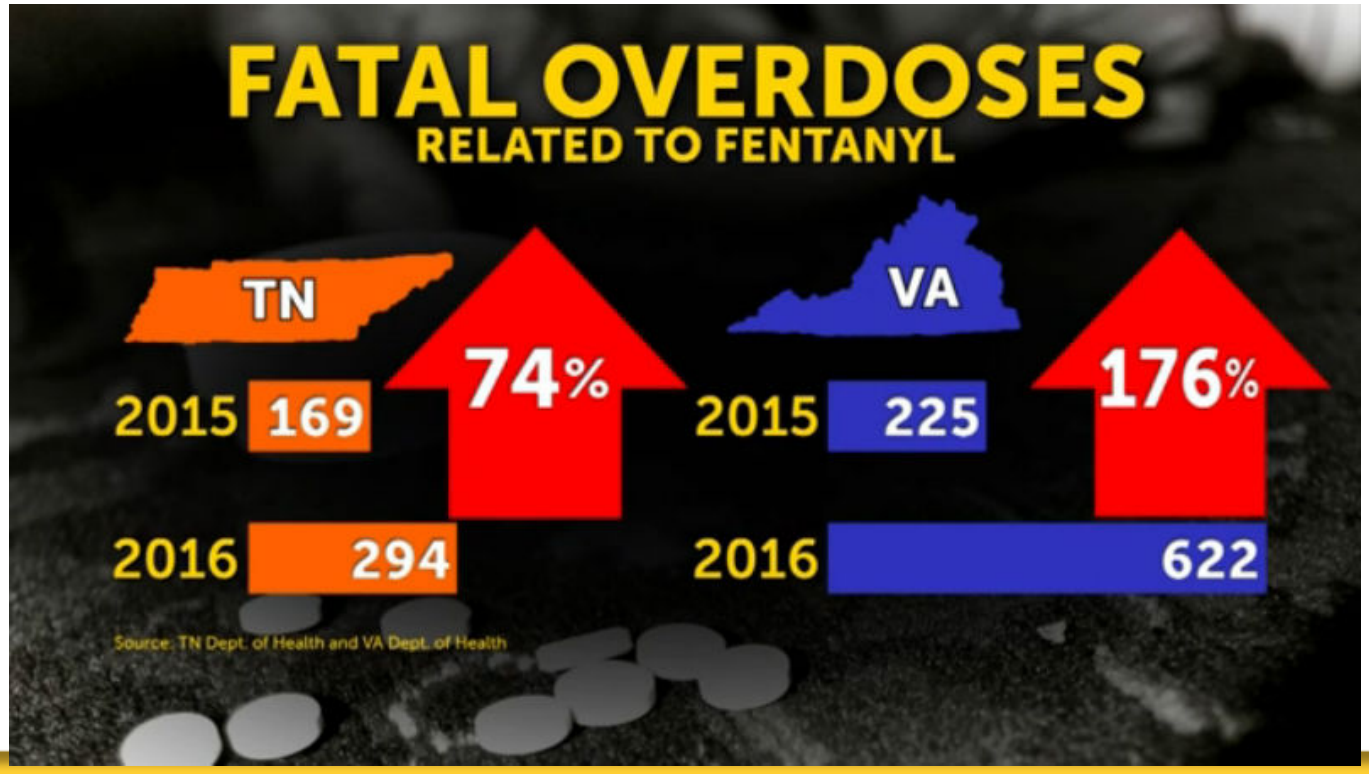
(Courtesy: 24th Judicial District Drug Task Force)

Mobile Pharmaceutical Plant

Fentanyl Test Strips

http://www.wbur.org/commonhealth/2017/05/11/fentanyl-test-strips

Fentanyl



http://wjhl.com/2017/11/20/dangerous-drug-fentanyl-on-rise-in-tennessee/

Discuss the diagnostic criteria for opioid use disorder (OUD)

Diagnosis of Opioid Use Disorder

- Opioids taken in larger amounts or over a longer period than was intended
- Persistent desire or unsuccessful efforts to cut down or control opioid use
- A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects
- Craving, or a strong desire or urge to use opioids
- Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home
- Continued use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids
- Important social, occupational, or recreational activities are given up or reduced
- Recurrent use in situations in which it is physically hazardous
- Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
- Tolerance
- Withdrawal

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Preventing OUD

- Prescription drug monitoring programs
- State prescription drug laws
- Formulary management strategies in insurance programs, such as prior authorization, quantity limits, and drug utilization review
- Academic detailing to educate providers about opioid prescribing guidelines and facilitating conversations with patients about the risks and benefits of pain treatment options

https://www.cdc.gov/drugoverdose/prevention/opioid-use-disorder.html

Preventing OUD

- Quality improvement programs in health care systems to increase implementation of recommended prescribing practices
- Patient education on the safe storage and disposal of prescription opioids
- Improve awareness and share resources about the risks of prescription opioids, and the cost of overdose on patients and families.

https://www.cdc.gov/drugoverdose/prevention/opioid-use-disorder.html

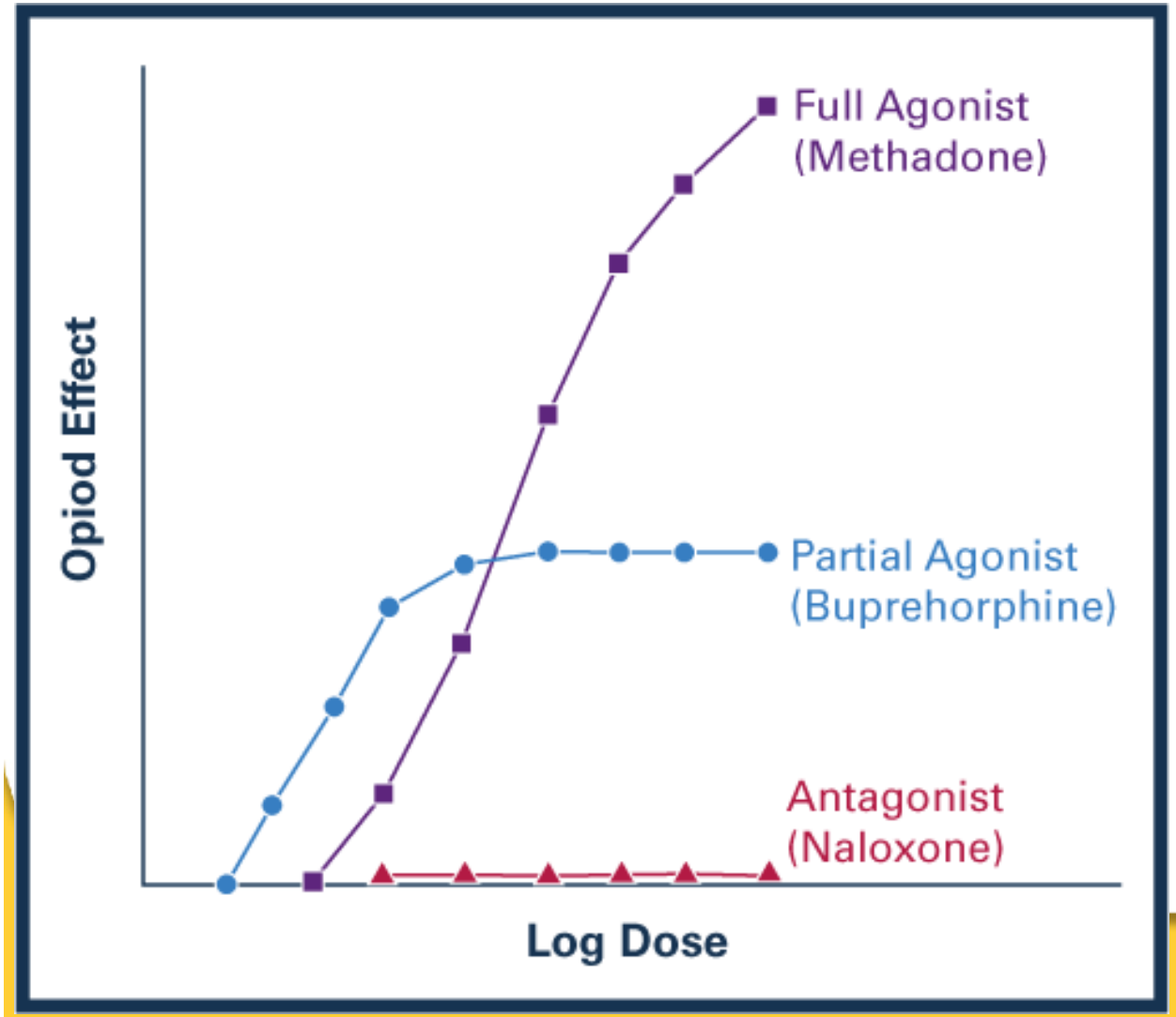
Types of Treatment Available

- Long-term residential treatment
- Short-term residential treatment
- Outpatient treatment
- Medication-Assisted Treatment (MAT)

Compare the different medications used to treat OUD and opioid overdose

Medication-Assisted Treatment

- Methadone
- Naltrexone
- Buprenorphine



Comparison of Agents

http://depts.washington.edu/hivaids/spop/case2/discussion.html

Common Misconceptions with MAT

Myth: Maintenance opioid agonists provide adequate analgesia

- Analgesic properties of methadone/buprenorphine
  - Dosed every 24 hours
  - Suppress cravings and opioid withdrawal for 24 to 48 hours
  - Provide analgesia for 4 to 8 hours per dose
    - Period of even partial pain relief with these medications is small
- Opioid tolerance
  - Reason why patients derive little pain relief from maintenance opioids
  - Patients often require higher and more frequent doses of analgesics to achieve adequate pain control
- Opioid-induced hyperalgesia
  - Altered pain perception that increases pain sensitivity

Common Misconceptions with MAT

Myth: Maintenance opioid agonists is just "switching addictions" and patient should not be on them long term

- Research on maintenance treatment demonstrated
  - Normal function
  - No euphoric, tranquilizing, or analgesic effects
  - No change in tolerance levels over time
  - Effectiveness when administered orally
  - Relief for opioid craving
  - Minimal side effects
- Research on forced tapering demonstrated
  - Significant rate of relapse
  - Increased risk for drug overdose

Methadone

- Full opioid agonist
- Generally dosed daily
  - Average dose of 80-120 mg per day
- Drug of choice in pregnant women needing opioid addiction treatment, according to current guidelines
- Only available for addiction treatment in an Opioid Treatment Program (“Methadone Clinic”). Includes strict State and Federal requirements regarding clinic attendance, counseling, and drug screens.
- Cost: approximately $16/day

Naltrexone

- Full opioid antagonist
  - Blocks the euphoric effect of alcohol and any effect of opioids
  - No abuse potential
- Approved to treat alcoholism since 1995
  - Reduces number of heavy-drinking days
  - May prevent a misstep from becoming a relapse
- Monthly IM injection may improve patient adherence but at a cost
  ~$1,200 per injection
- Anyone authorized to prescribe can prescribe since not a controlled substance.
- Covered by TennCare

Naltrexone

- Available in 50mg tablets (ReVia®) or 380mg IM injection (Vivitrol®)
- Black box warning regarding hepatotoxicity
- Precipitates withdrawal unless abstinent >7days, 10 days for long acting opioids
- Must educate patient regarding the loss of tolerance while being treated with naltrexone
- A relapse with an opioid dose familiar to patient prior to naltrexone may result in overdose and death when taken near end of dosing schedule

Buprenorphine

- First drug for office-based opioid treatment (OBOT) under DATA 2000 regulations (Allows prescriber to prescribe CIII-CV substances approved for addiction)
- Obtain DEA waiver, waiver ID is same as DEA # but begins with an “X”
- Providers now may now provide care for up to 275 patients

Buprenorphine

- MOA
  - Partial agonist mu-opioid receptor, antagonist at kappa-opioid receptor
  - “Ceiling effect” limits effects of subsequently used opioids, considered safer in overdose and milder withdrawal symptoms
- Drug Interactions
  - Primarily metabolized by CYP3A4
  - Ceiling effect can be negated by concurrent benzodiazepine or alcohol use
- Dosing
  - 4 mg-24 mg/day(per labeling) with usual maximal dose of 16 mg/day; most patients require much less

Characteristics of Preferred MAT Buprenorphine Providers?

http://www.johnsoncitypress.com/Health-Care/2017/09/01/Local-doctors-organizations-say-Suboxone-billboard-increases-stigma-calls-for-its-removal

Characteristics of Preferred MAT Buprenorphine Providers

- Accept insurance!
- Buprenorphine waivered prescriber co-located with licensed behavioral health specialist
- Monoproduct is only used in pregnant women or in transition from methadone, and rarely with naloxone intolerance
- Maximum daily dose of 16 mg

http://www.dmas.virginia.gov/Content_pgs/bh-cred.aspx

Characteristics of Preferred MAT Buprenorphine Providers

- No tolerance for use of other opioids, including tramadol, sedative hypnotics, carisoprodol, or benzodiazepines except for those already taking for 3 months during a relapse or taper plan
- Medication for other physical or mental health disorders must be provided onsite or by referral
- Screening for HIV, Hep B and C, and tuberculosis at baseline and then annually

Interpret recent updated prescribing guidelines in Tennessee related to the treatment of OUD, chronic pain, and co-prescribing of naloxone

Buprenorphine Treatment Guidelines

Tennessee Nonresidential
Buprenorphine Treatment Guidelines

TN Department of Mental Health & Substance Abuse Services

TN Department of Health

- Informed consent
- Controlled Substance Database review
- Pregnancy/neonatal abstinence/contraception
- Benzodiazepines
- Monoproduct (5% rule)
- Physical exam
- HIV, Hep C, TB, STI screening
- Adverse Childhood Experiences Scale (ACES)
- Counseling
- Frequency of visits
- Urine drug toxicology

https://www.tn.gov/content/dam/tn/health/documents/2018%20Buprenorphine%20Tx%20Guidelines.PDF

Buprenorphine Dispensing

- Build relationships with clinicians and prescribers at local clinics
  - Lock-in patients to one pharmacy
  - Notify clinics if you notice patient attempting to fill early on a regular basis
- PMP checks to assess adherence with treatment
- Although buprenorphine with naloxone is an abuse deterrent formulation, it can still be misused and should be dispensed with equal due diligence as the formulation with buprenorphine alone

Buprenorphine Deaths

- TDH found a total of 67 deaths associated with buprenorphine in 2016
  - Most combined with benzodiazepines, alcohol, gabapentin, etc.
- Buprenorphine alone can sometimes lead to death
  - 10 Tennesseans only had buprenorphine present when they died between 2013 and 2016
- Virginia shows similar data

https://www.tn.gov/health/news/2018/1/8/tdh-finds-some-overdose-deaths-associated-with-buprenorphine.html

Common Risks for Opioid Overdose

Abstinence

- Release from incarceration
- Relapse
- Completion of detoxification

Chronic Medical Illness

- Lung, liver, and renal compromise

Mixing Substances/Polypharmacy

- Alcohol, benzodiazepines, other respiratory depressants

Previous Overdose

Depression

Opioid Dose and Change in Formulation

History of Addiction

Social Isolation and Using Alone

Naloxone Online Continuing Education

Volunteer to Save a Life

Tennessee Overdose Education and Naloxone Distribution

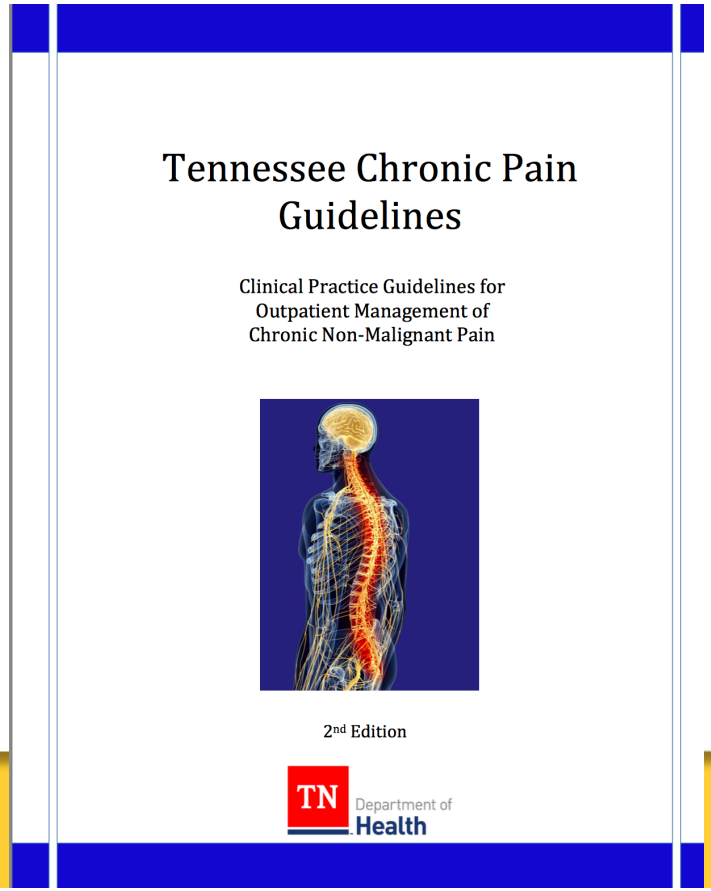
https://www.etsu.edu/com/cme/vtsalem.php

BILL GATTON COLLEGE *of* PHARMACY
EAST TENNESSEE STATE UNIVERSITY

TN Prescription Safety Act of 2016

- **Reauthorizes the TN Prescription Safety Act of 2012**
- **All healthcare practitioners** who prescribe or dispense controlled substances in practice providing direct care to patients in Tennessee by prescribing or dispensing on more than fifteen (15) days in a calendar year shall be registered in the controlled substance database.
- **All healthcare practitioners** are required to check before prescribing or dispensing an opioid or benzodiazepine to a human patient as a new episode of treatment – and at least annually when said controlled substance remains a part of the treatment.
- **All practice sites** that prescribe or dispense or dispense controlled substance must provide electronic access to the Controlled Substance Monitoring Database. Violation is $100 per day.

Chronic Pain Guidelines



- Any prescriber deviating from these guidelines needs to document why in the patient's medical record
- If a licensing board investigates a prescriber for inappropriate prescribing of controlled substances, the first thing the investigator looks for is documentation of the reason for the deviation in a medical record

https://www.tn.gov/content/dam/tn/health/healthprofboards/ChronicPainGuidelines.pdf

Chronic Pain Guidelines

- The treatment plan should establish realistic goals for pain and function
- For acute pain, limit to 7 days maximum; must document rationale in chart if greater amount is written
- (PCP) Start with immediate-release opioid therapy for chronic pain
- CSMD should be reviewed to determine whether the patient is receiving opioid dosages or dangerous combinations

https://www.tnmed.org/tma/News_and_Media/News/Tennessee_Chronic_Pain_Guidelines_Updated.aspx

Chronic Pain Guidelines

- Evidence-based treatment for patients with opioid use disorder be used and in some cases referral to an addiction specialist may be appropriate
- Medication Assisted Treatment Program Appendix-
  paragraph discusses the new law regarding licensure of nonresidential office-based opioid treatment facilities
- Pregnant women: appropriate discontinuation has been shown to be safe for fetus during pregnancy. However, unintended consequences from tapering may outweigh benefits.
- Expanded appendices on risk evaluation tools, urine drug testing, and non-opioid therapies

https://www.tnmed.org/tma/News_and_Media/News/Tennessee_Chronic_Pain_Guidelines_Updated.aspx

Explain methods of educating patients with substance use disorders (SUD) and ways of decreasing stigma

Educating Patients with SUD

- Discuss in a quiet, private location
- Avoid stigmatizing words
- Ask about illicit and non-illicit substance use for a full medication history
- Encourage patient to use the same pharmacy and prescriber
- Keep in mind that drug-seeking behavior is generally a sign of untreated SUD – relationship is with the drug
- Do not avoid or refuse to fill without discussion with the patient and provider to clarify your concerns

Decreasing Stigma

- Offering compassionate support
- Displaying kindness to people in vulnerable situations
- Listening while withholding judgment
- Seeing a person for who they are, not what drugs they use
- Doing your research; learning about substance use disorders and appropriate treatment
- Treating people with substance use disorders with dignity and respect
- Avoid pejorative titles/language
- Replacing negative attitudes with evidence-based facts
- Speaking up when you see someone mistreated because of their drug use

https://drugabuse.com/library/addiction-stigma/

Syringe Services Program

- PUBLIC CHAPTER NO.413 (May 2017)
- Approval by the Tennessee Department of Health
- Disposal of used needles and hypodermic syringes;
- Provide needles, hypodermic syringes, and other injection supplies at no cost and in quantities sufficient to ensure that needles, hypodermic syringes, and other injection supplies are not shared or reused
  - Strive for one-to-one syringe exchanges
  - No public funds may be used to purchase needles, hypodermic syringes, or other injection supplies
- Reasonable and adequate security

Syringe Services Program

- Educational material
  - Overdose prevention
  - Prevention of HIV, AIDS, and viral hepatitis transmission
  - Drug abuse prevention
  - Treatment for mental illness and substance use
- Access to naloxone
- Personal consultations concerning mental health or addiction treatment
- NOTE: An exchange cannot be established within two thousand feet (2,000') of any school or public park

Questions and Discussion

https://www.tennessean.com/topic/1325c3b8-e264-4502-8869-93a98af26257/tn-opioid-crisis/