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Chronic Non-malignant Pain Management Best Practice per Tennessee Guidelines and Federal REMS: *an Interprofessional Perspective*

Off-label uses of medication will be discussed – off-label use will be noted as such

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Meet the Moderator

Howard Teitelbaum, DO, PhD, MPH, FAOCOPM *(dist)*

Dr. Teitelbaum is Professor and Chair of the Department of Preventive and Community Medicine at Lincoln Memorial University-DeBusk College of Osteopathic Medicine and has held academic and administrative posts at several higher education institutions including, the Yale University School of Medicine and Des Moines University College of Osteopathic Medicine. He is the recipient of several teaching awards including induction into the American Osteopathic Association Mentor Hall of Fame and Clinical Professor of the year by the inaugural class at LMU-DCOM.

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Meet the Panel

Mary Beth Babos RPh, BS Pharm, PharmD, CDE

Dr. Babos received her PharmD from Union University – Albany College of Pharmacy and dual MS degrees from the University of Florida in Forensic Toxicology and in Pharmaceutical Chemistry. She is a Certified Diabetes Educator, Certified Anticoagulant Manager, and Board Certified in Pharmacotherapy. She is a clinical pharmacist with over thirty years' practice experience.

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Meet the Panel

Stephanie Hamil, LCSW

Ms. Hamill is a Licensed Clinical Social Worker and has over twenty five years experience in the field of medical social work, primarily working with Home Health and Hospice. She graduated from the University of TN in 1982 with her Master's of Social Work and has been the Executive Director for the past 18 years for Friends of Hospice, a local non-profit organization that provides an annual Camp H.U.G.S. grief camp for children and Serenity House End of Life Care Home. In addition, she has several years experience in private counseling and with Cherokee Health Systems as a Mobile Crisis Counselor.

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Meet the Panel

Sharon N. Duke, D.O., Ph.D., DABAM

Dr. Duke has been a clinical psychologist for 10 years specializing in children and families. She attended medical school at Texas College of Osteopathic Medicine and was the first D.O. to attend the Family Practice/Emergency Medicine residency at Memorial Medical Center in Corpus Christi, Texas. After practicing family medicine and emergency medicine and part-time addiction medicine she decided to shift to full-time addiction recovery, finding generous rewards watching people put their lives together, go to school, find jobs and be involved with their family and community**.** Dr. Duke is a Faculty Member of the American Society of Addiction Medicine (Board Certified in Addiction Medicine) and secretary/treasurer of the Tennessee Society of Addiction Medicine.

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Meet the Panel

Dwan Perry, DO

Dr. Perry is Assistant Professor of Physical Medicine and Rehabilitation (PM&R) and Director of Sports Medicine at Lincoln Memorial University-DeBusk College of Osteopathic Medicine. He received his medical degree from the West Virginia School of Osteopathic Medicine and completed his residency in PM&R at the University of Kentucky Medical Center and Fellowship in Primary Care Sports Medicine at the Edward Via College of Osteopathic Medicine. Dr. Perry has extensive experience in sports and musculoskeletal medicine and is a member of several professional organizations including the American Osteopathic Academy of Sports Medicine, American College of Sports Medicine, and the American Academy of Physical Medicine and Rehabilitation.

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Meet the Panel

Elizabeth Burchette Thompson, DVM

Dr. Thompson is Assistant Professor of Veterinary Science and Dean of the School of Allied Health Sciences at Lincoln Memorial University. She received her DVM from the University of Tennessee, College of Veterinary Medicine after completing undergraduate studies at Lincoln Memorial University. She has over 17 years' practice experience with particular interests in emergency medicine, pharmacology and anesthesia.

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Meet the Panel

Byron E. Turkett, MPAS, PA-C, FCCM

Mr. Turkett is Assistant Professor of Clinical and Didactic Services at Lincoln Memorial University-DeBusk College of Osteopathic Medicine – Physician Assistant (PA) Program. He has over 20 years of professional experience as a Physician Assistant in medical care including emergency medicine, surgery, trauma, neuro-oncology, and international healthcare ministries. Mr. Turkett was the fourth Physician Assistant to be inducted as a Fellow in the American College of Critical Care Medicine in 2011. He was presented the 2006 Faculty Service Award for Teaching by the University of Tennessee, Graduate School of Medicine in 2006 and recognized as PA Preceptor of the Year in 2009 by the South College PA Program.

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Objectives

At the end of the presentation, participants will be able to:

1. Identify key principles of Tennessee Clinical Practice Guidelines for the Management of Chronic Pain and the FDA blueprint for risk evaluation and mitigation strategies related to long acting opioids.
2. Appropriately assess patients for opioid treatment, including long-acting or extended release formulations.
3. Apply best practices during initiation of therapy, dose modification, and discontinuation of opioids, including long-acting or extended release formulations.
4. Appropriately counsel patients about their pain management regimens, including long-acting or extended release opioid formulations.
5. Relate basic pharmacodynamics, pharmacokinetics, and toxicology of opioids to role in treatment, abuse potential, and laboratory test interpretation.
6. Compare and contrast currently available long-acting and extended release opioid formulations, including review of selected product-specific drug information.

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TN Public Chapter 430

Effective October 1 2013

- Chronic pain guidelines
- All prescribers with DEA need 2 hours CME every 2 years
- DEA schedules II-IV only 30 days supply dispensed at a time, no matter how many days supply is ordered

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Purpose of guidelines

- Define appropriate treatment of chronic pain
  - Defined as pain lasting longer than 90 days
- Foster timely and appropriate treatment for pain
- Avoid adverse outcomes
  - Addiction, overdose, neonatal abstinence syndrome (NAS)
- Optimize non-opioid interventions

- Tennessee Clinical Practice guidelines for Outpatient Management of Chronic Non-malignant Pain are NOT applicable to:
  - End of life
  - Emergency department
  - Acute pain management

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Direct quote from guidelines

" Providers still have flexibility to deal with exceptional cases. Occasional deviation from these guidelines for appropriate medical reasons is to be expected and documented."

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Case

JJ is a 48 year old female who has been taking a regimen of long-acting oxycodone with immediate release oxycodone prn breakthrough pain for the last year for chronic back pain. She has never requested early refills, her pill counts have always been accurate, no abnormalities have ever been found on urine drug test or controlled substance database check. Today she requests an increase in dose because her pain is no longer at a tolerable level. What term best describes the most likely underlying cause of her request today?

A. Addiction
B. Allodynia
C. Dependence
D. Hyperalgesia
★ E. Tolerance

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Definitions of common terms

- Abuse – drug use resulting in harm
- Addiction – continued compulsive abuse of drug despite consequences to health, finance, and social life
- Allodynia – perception of pain from non-noxious signal
- CSMD – controlled substance monitoring database
- Dependence – requirement of drug for normal physiologic function due to up-/down- regulation of receptors and/or second messenger systems
- Diversion – selling trading or giving drug to others
- Hyperalgesia – increased amplitude of pain sensation to painful stimulus
- Misuse – taking drug in greater amount/frequency than prescribed
- NAS – neonatal abstinence syndrome
- Non-medical use – use of drug without a prescription or for recreational purpose/non prescribed indication
- REMS = risk evaluation and mitigation strategies are required risk management plans that, pursuant to the Food and Drug Administration Amendments Act of 2007 may be required from drug manufacturers to assure benefits of drug outweigh the risks

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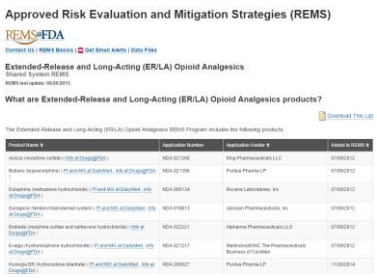
Where to find REMS for specific medications

http://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=RemsDetails.page&REMS=17


Approved Risk Evaluation and Mitigation Strategies (REMS)

REMS@FDA

Extended-Release and Long-Acting (ER/LA) Opioid Analgesics

What are Extended-Release and Long-Acting (ER/LA) Opioid Analgesics products?

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ER and LA opiates in general

- NOT for prn use
- Generally not for opiate naïve individuals
- Generally contain more drug than prompt release products; disruption of controlled release mechanism can lead to life threatening overdose
- Patients and/or caregivers must be counselled appropriately

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THE SCOPE OF THE PROBLEM

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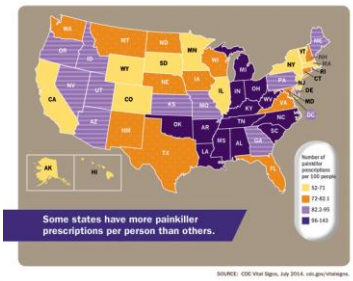
2013 Pain Rx by state



"Nearly 22 times as many prescriptions were written for oxymorphone in Tennessee during 2013 as were written in Minnesota"

http://www.cdc.gov/media/dpk/2014/dpk-vs-opioid-prescribing.html#graphics

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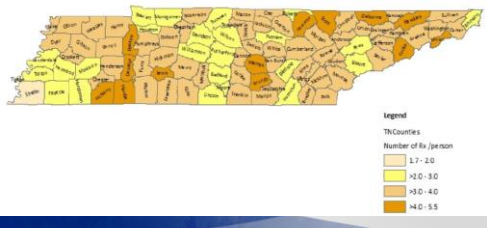
Rate of controlled substance Rx per person 2013

Figure 10. Rate of Prescriptions Dispensed (per capita) Among Tennessee Residents Reported to CSMD, 2013



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Why it matters

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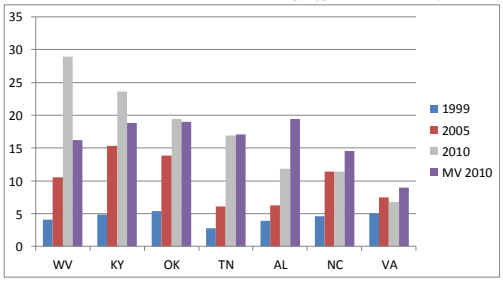
Overdose Mortality (per 100K)



MV = motor vehicle mortality per 100K

http://www.cdc.gov/

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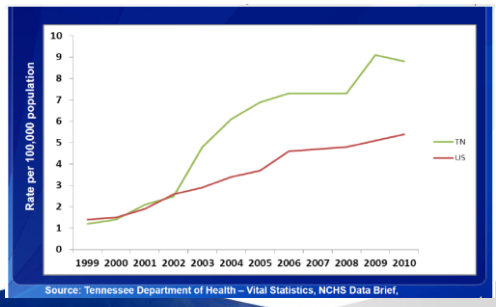
TN versus US Deaths from overdose



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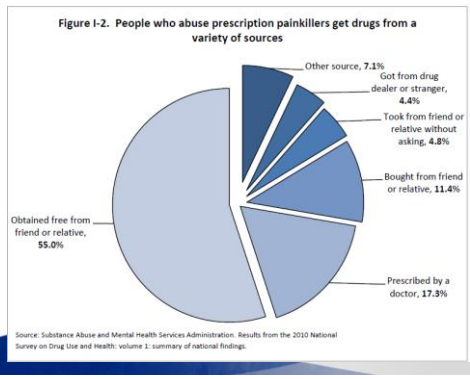

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CDC July 2015

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WHAT CAN BE DONE?

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Trust for America's Health Indicators
1. Prescription drug monitoring program
2. Mandatory use of prescription drug monitoring program
3. Doctor shopping law
4. Support for Substance Abuse Services
5. Prescriber Education Requirement
6. Good Samaritan Law
7. Naloxone Law
8. Physical Exam Requirement
9. ID requirement
10. Pharmacy Lock-In Program

Prescription Drug Abuse: strategies to stop the epidemic 2013
Trust for America's Health funded by Robert Wood Johnson Foundation available at
http://healthyamericans.org/assets/files/TFAH2013RxDrugAbuseRpt16.pdf

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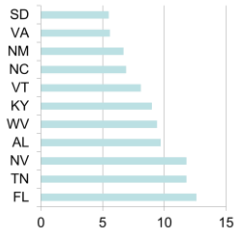
Number of indicators by state

http://media.khi.org/news/documents/2013/10/08/2013DrugAbuseReport.pdf

In 2013, 15.6 Kg of morphine equivalents were dispensed per 10K population in the state of TN according to CSMD



Kg morphine equivalents prescribed per 10K population 2010

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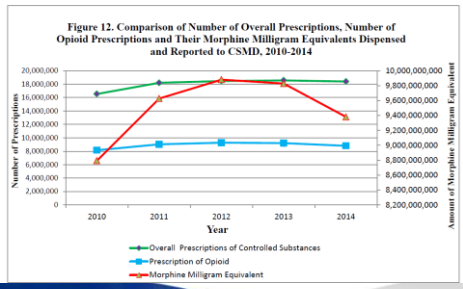
Morphine milligram equiv in TN



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Tennessee Chronic Pain Guidelines

Clinical Practice Guidelines for Outpatient Management of Chronic Non-Malignant Pain

TENNESSEE DEPARTMENT OF HEALTH

THE STATE OF THE STATE OF TENNESSEE

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Table of Contents

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Steps prior to initiating opioid trial

Initial evaluation

- Evaluation and history of pain condition:
  - Nature, intensity, past and current treatments, comorbidity, effect on life function
- Comorbidities should be considered
  - Age, COPD, sleep apnea, diabetes, heart failure, renal/hepatic function, etc.
- Perform initial condition-appropriate physical exam and review of systems
- Review records directly related to chronic pain
- Screen for co-occurring mental health disorders; address them in treatment plan if they exist
- Women with reproductive capacity should be queried about the possibility of pregnancy. Use of long acting contraceptives should be discussed or referral to high-risk OB should be made.

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Steps prior to initiating opioid trial

Establish diagnosis

"There shall be the establishment of current diagnosis that justifies a need for opiate therapy"

Assess for risk of abuse

- Assess risk for misuse, abuse, diversion and addiction using a validated tool
- Check the CSMD
- Obtain a urine drug test (UDT) or compatible oral fluid test

- Make initial assessment about risk of misuse, abuse, addiction, and or diversion

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ASSESSING RISK OF ABUSE AND MENTAL HEALTH

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Risks factors for abuse

- Family history or personal history of addiction
  - Ethanol, cigarettes, illicit drugs, inappropriate use of Rx
- Male sex
- Underlying mental health issues
  - ADD/ADHD, PTSD, etc.
- Youth
  - Peer pressure, lack of family involvement

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Case

A 22 year old female sustained a severe sprain in a fall from a horse. What factor is associated with a higher risk of drug abuse?

- Age
- Female sex
- Concomitant mild head injury
- History of cigarette smoking

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Risk assessment tools

http://www.drugabuse.gov/nidamed-medical-health-professionals/tool-resources-your-practice/screening-assessment-drug-testing-resources/chart-evidence-based-screening-tools-adults

Screening Tool	Substance type		Patient age		How tool is administered	
	Alcohol	Drugs	Adults	Adolescents	Self-administered	Clinician-administered
Prescreen						
NIDA Drug Use Screening Tool: Quick Screen	X	X	X	See APA Adapted NM ASSIST tools	See APA Adapted NM ASSIST tools	X
CRAFFT (Part A)	X	X		X	X	X
Alcohol Use Disorders Identification Test-C (AUDIT-C (PDF, 41KB))	X		X		X	X
Opioid Risk Tool (PDF, 168KB)		X	X		X	
Full Screens						
NIDA Drug Use Screening Tool	X	X	X			X
Alcohol Use Disorders Identification Test (AUDIT (PDF, 233KB))	X		X			X
CAGE-AID (PDF, 659KB)	X	X	X			X
CAGE (PDF, 659KB)	X		X			X
Drug Abuse Screen Test (DAST-10 (PDF, 168KB))		X	X		X	X
CRAFFT	X	X		X	X	X
DAST-20: Adolescent version (PDF, 1.2MB)		X		X	X	X

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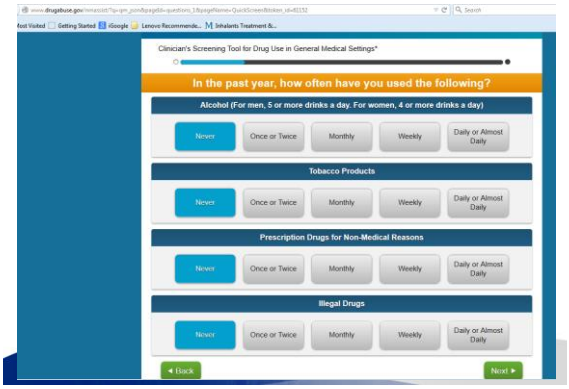

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CHECKING THE CONTROLLED SUBSTANCE MONITORING DATABASE (CSMD)

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When is checking the CSMD* mandated?

- When prescribing a new course of benzodiazepine or opioid intended for a duration of therapy exceeding 7 days
- At least annually when said treatment is continued
- Exceptions:
  - Hospice patients
  - Medication is ordered relative to surgical procedure in licensed healthcare facility
  - Medication is ordered in a non-refillable fashion for a quantity that will not exceed seven days treatment
  - Licensed veterinarians ordering for non-human patients

*CSMD Controlled substance monitoring database

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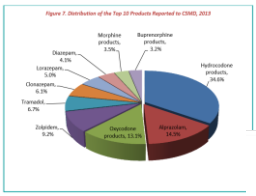
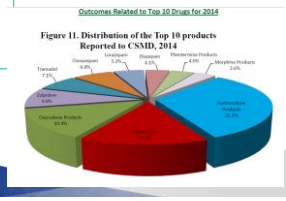
The top 10 2013 and 2014





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When is reporting to CSMD required?

- Any controlled substance dispensed by any licensed provider in or into Tennessee
  - Currently every 7 days
  - Beginning January 1, 2016 will be required daily
- Exceptions to reporting:
  - Medications administered directly to the patient
  - Medication is dispensed subject to reporting under 21 CFR 1304.24 as a registered treatment program
  - Medication is dispensed by licensed healthcare facility in a quantity not intended to exceed 48 hour treatment duration
  - Sample medications
  - Medications dispensed by licensed veterinarians for non-human patients for a quantity of drug not intended to exceed 48 hours treatment duration

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What is the purpose of the CSMD?

- Provide healthcare practitioners with a comprehensive view of patient's controlled substance prescription history
- Assist in research, statistical analysis, criminal investigations, enforcement of state or federal controlled substance laws
- "Education of health care practitioners concerning patients who, by virtue of their conduct in acquiring controlled substances, may require counseling or intervention for substance abuse, by collecting and maintaining data regarding all controlled substances dispensed in this state"
  - TN Clinical Practice Guidelines for Outpatient Management of Chronic Non-malignant Pain V1 2014

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What reports might you receive?

- If you are a "top 50" prescriber, you will get a registered letter
  - For mid-level practitioners, report is also sent to supervising physician
  - Response required within 15 days (Public Chapter 396)
- Clinical Notifications
  - Identifies high risk patients
  - Must be acknowledged within 3 days by clicking on hyperlink or a reminder email will be sent until acknowledgement

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What does high risk mean?

High risk definitions

- Number of pharmacies
  - » Red 4 in 60 days; yellow 3 in 60 days
- Number of prescribers*
  - » Red 4 in 60 days; yellow 3 in 60 days
- MME Morphine milligram equivalents
  - » Red 120 MME, Yellow 90 MME per day
  - » *different providers in same office are counted separately

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Monitoring changes doctor shopping

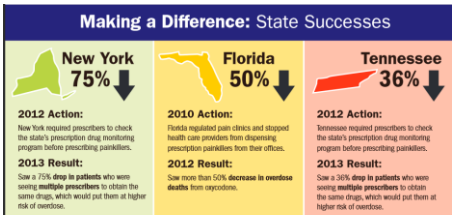

Table 10. Number of Doctor-Pharmacy Shoppers Identified in CSMD by Quarter, 2010 – 2014*

Year	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter	Total	Change (%)
2010	1,695	2,005	2,127	1,830	7,657	-
2011	1,950	2,413	2,515	2,352	9,230	20.5
2012	2,246	2,218	2,261	1,940	8,665	-6.1
2013	1,785	1,533	1,533	1,335	6,186	-28.6
2014	1,374	1,404	1,278	1,307	5,363	-13.3

*5 prescribers or more and 5 pharmacies or more in 3 months

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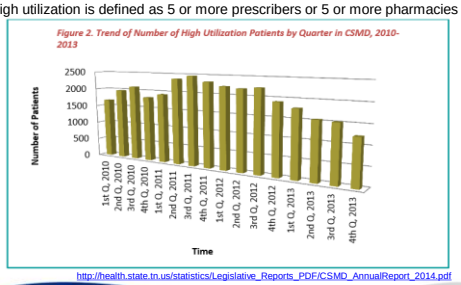
Decline in high-utilization patients

High utilization is defined as 5 or more prescribers or 5 or more pharmacies



http://health.state.tn.us/statistics/Legislative_Reports_PDF/CSMD_AnnualReport_2014.pdf

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Reports you can request

- All Rx against your DEA number
- Controlled substance history of a patient
  - What if you find a doctor shopper?
    - You must report to nearest law enforcement or the Meth and pharmaceutical task force 423-752-1479

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Integration of Resources

CP is a 45 year old male who has been referred to the Physiatrist for management of chronic pain. The CSMD reveals that he has had four different controlled substances prescribed by three different providers in the past two months. What other information can assist in evaluating this patient's risk for abuse?

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UDT

Frequency

- At prescriber's discretion, based on risk
  - Lower risk once or twice per year
  - Moderate 3-4 per year
  - High risk, those receiving over 100mg morphine equivalents per day, aberrant behavior more frequently
- Unannounced
  - Be aware of adulteration
    - pH, creatinine, temperature for validity

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UDT false positives on immunoassay

- Amphetamines
  - Amantadine, bupropion, chlorpromazine, desipramine, fluoxetine, labetalol, methylphenidate, phentermine, phenylephrine, phenylpropanolamine, pseudoephedrine, ranitidine, thioridazine, selegiline, trazodone
- Benzodiazepines
  - Oxaprozin, sertraline
- Cannabinoids
  - Efavirenz, ibuprofen, ketoprofen, naproxen, piroxicam, pantoprazole, sulindac, foods containing hemp
- Cocaine
  - Amoxicillin
- Opiates
  - DM, diphenhydramine, fluoroquinolones, poppy seed, quinine, rifampin, verapamil
- PCP
  - DM, diphenhydramine, ibuprofen, imipramine, ketamine, meperidine, thioridazine, tramadol, venlafaxine

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Human Metabolites

Parent	Metabolite
Codeine	Morphine
Hydrocodone	Hydromorphone
Oxycodone	Oxymorphone
Chlordiazepoxide	Diazepam, oxazepam
Heroin	Morphine
Diazepam	Oxazepam
Methamphetamine	Amphetamine
Primidone	Phenobarbital
Carisoprodol	Meprobamate

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WOMEN'S HEALTH

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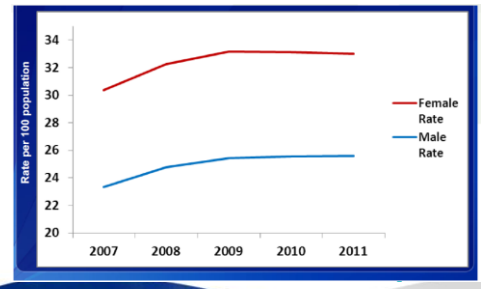
Rate of opioid Rx by gender in TN



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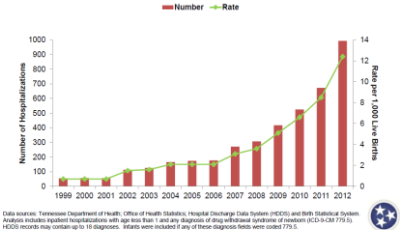
NAS Hospitalizations in TN: 1999-2012



*NAS neonatal abstinence sydrome

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Recent NAS-Related Legislation

- Public Chapter 820 (2014)
  - Allows mother to be charged with misdemeanor if she ***illegally*** uses narcotic during pregnancy ***and if baby is harmed as a result (ex. NAS)***
  - Does **not** require health care providers or hospitals to report to law enforcement
  - Does **not** change requirement to report NAS cases to the Tennessee Department of Health

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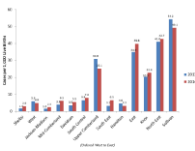
Incidence of NAS in TN by region



County	Region	% of County
Knox	Knox	11.0
Sullivan	Sullivan	7.6
Davidson	Davidson	5.5
Scott	East	4.4
Washington	North East	4.3
Shelby	Shelby	3.8
Greene	North East	3.1
Putnam	Upper Cumberland	3.1
Anderson	East	3.0
Campbell	East	3.0
TOTAL		49.9

Table 4: Top Ten Counties with Highest Percentage of NAS Cases, 2014

County	Region	Rate of Cases (per 1,000 live births)
Grainger	East	91.2
Campbell	East	78.5
Union	East	64.4
Roane	East	63.0
Hawkins	East	61.8
Madison	North East	59.9
Claiborne	East	59.3
Van Buren	Upper Cumberland	50.0
Greene	North East	49.6
Sullivan	Sullivan	49.1

Table 5: Top Ten Counties with Highest Rate of NAS Cases, 2014

Map I-2. Tennessee Department of Health Regions

http://tn.gov/health/cedep/ch/chronic-health/attachments/NAS_Annual_report_2014_FINAL.pdf

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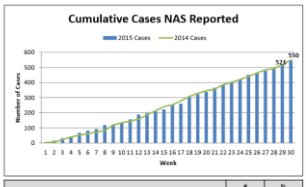
Drug Dependent Newborns (Neonatal Abstinence Syndrome)

Surveillance Summary For the Week of July 26 – August 1, 2015[1]

Reporting Summary (Year-to-date)
Cases Reported: 550
Male: 301
Female: 249
Unique Hospitals Reporting: 45



Maternal County of Residence (By Health Department Region)	# Cases	%Cases[2]
Davidson	34	6.2
East	126	22.9
Hamilton	15	2.7
Jackson/Madison	0	0
Knox	69	12.6
Mid-Cumberland	54	9.8
North East	78	14.2
Shelby	18	3.3
South Central	27	4.9
South East	11	2.0
Sullivan	47	8.6
Upper Cumberland	58	10.6
West	13	2.4
Total	**550**	**100.2**

Source of Maternal Substance (if known)[3]	# Cases[3]	% Cases
Supervised replacement therapy	341	62.0
Supervised pain therapy	58	10.5
Therapy for psychiatric or neurological condition	42	7.6
Prescription substance obtained WITHOUT a prescription	186	33.8
Non-prescription substance	125	22.7
No known exposure but clinical signs consistent with NAS	4	0.7
No response	8	1.5

1. Summary reports are archived weekly at: http://tn.gov/health/article/nas-summary-archive
2. 2. Total percentage may not equal 100.0% due to rounding.
3. Multiple maternal substances may be reported; therefore the total number of cases in this table may not match the total number of cases reported.

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NAS = long term risk of:

- ADD
- Hyperactivity
- Impulse control
- Difficulty transitioning between tasks
- Sleep disorders
- Sensory disorders
- Future addictive behavior

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Case

- A 45 year old male with severe pain from diabetic peripheral neuropathy that has not adequately responded to tricyclic antidepressants, SSRI, or anticonvulsant agents. After initial assessment, he agrees to a trial of opioid.
- T/F The patient should be counseled regarding the risks of opiate adverse effects, risk of addiction, and risk of overdose as they compare to the benefit of achieving goal of complete pain relief

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Final step prior to initiation

Goals for Treatment

- Primary goal should be clinically significant improvement in function
- Treatment plan should include modalities beyond opioids
- The patient should be counselled that the goal of opioid treatment is to help improve function and reduce pain, but NOT to eliminate pain.

"Documentation of this discussion shall be included in the medical record" Chronic Pain Guidelines version 1 p.2

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SUMMARY OF STEPS PRIOR TO INITIATION

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In summary: prior to initiation

- Non-opioid if possible
- Women's issues
  - Counsel about pregnancy
    - Evaluation of newly pregnant (not necessarily related to initiation)
- Document testing in medical record
- No telemedicine
- Assess and address co-morbid mental conditions
- Establish and document current dx that justifies need
- Assess risk for abuse using validated tools
- Check CSMD
- Establish goals, document discussion
  - Plan for opioid and non-opioid
  - Goal to improve function, not eliminate pain

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Upon initiation of opioid

- Initiation presented as therapeutic trial
  - For new patients, you are under no obligation to continue previous therapy without an appropriate diagnosis
- Initiate at lowest dose, titrate up
- Informed consent
  - Risks, benefits, adverse effects, etc.
  - Sample consent in guidelines
- Written treatment agreement
  - Sample agreement in guideline
  - For women, agreement includes notification of prescriber of pregnancy
- Monitor for signs of abuse, misuse, diversion
  - UDT should be done twice a year at minimum
- Women's health issues
  - Pregnancy testing at initiation, discussion of contraception
  - Ask about possibility of pregnancy (and document) at each visit

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Am Fam Physician. 2010 Mar 1;81(5):635-640

Behaviors indicative of misuse

Taking a controlled substance for a long period of time (new patients)

Refusing permission to obtain old records/communicate with previous physicians

Demonstrating reluctance to undergo a comprehensive history, physical examination, or diagnostic testing (especially urine drug screening)

Requesting a specific drug (often because of the higher resale value of a brand name)

Professing multiple allergies to recommended medications

Resisting other treatment options

Other aberrant behavior:

- Issuing threats or displaying anger
- Targeting appointments at the end of the day or during off hours (nights or weekends)
- Giving excessive flattery
- Calling and visiting a physician's associates
- Repeatedly losing a prescription
- Requesting a dose escalation
- Demonstrating noncompliance with prescription instructions
- Demonstrating other evidence of alcohol or illicit drug misuse

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More on initiating opioids

- Maximum of 4 doses of short-acting opioids per day
  - There is no clinically sound reason to place a patient on two different short acting opioids
- Non-pain medicine specialists should not prescribe methadone
- Buprenorphine should not be used PO or SL for chronic pain
- Avoid benzodiazepines
- Document reasons for deviation from guidelines in record
- Single provider and pharmacy best

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Monitoring opioids: 5A's

- Analgesia
- Activity
- Adverse effects
- Aberrant behaviors
- Affect

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Case

The guidelines require that any patient receiving over 200 mg morphine equivalents per day be referred to a pain management specialist. Which daily dose is less than 200mg morphine equivalents daily?

- Fentanyl 75mcg/hr patch
- Hydrocodone ER 100mg po bid
- Hydromorphone ER 32mg po bid
- Oxycodone ER 40mg po bid

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MEDD = morphine equivalent daily dose

Opioid	Appx equianalgesic dose (PO or Transdermal)
Morphine	30mg
Codeine	200mg
Fentanyl TD	12.5mcg/hr
Hydrocodone	30mg
Hydromorphone	7.5mg
Oxycodone	20mg
Oxymorphone	10mg

MEDD for doses on previous slide
Fentanyl 12.5mcg/hr = 418.6 MEDD
Hydrocodone ER 100mg q12hr = 200mg MEDD
Hydromorphone ER 32mg q12hr = 256 MEDD
Oxycodone ER 40mg q12h = 120 MEDD

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Pain Medicine Specialist

TN has set forth two tiers for pain management

- Tier 1 Non-pain medicine specialist: valid TN license, current DEA, Attend CE pertinent to pain management as defined by their governing board
- Tier 2 Pain Management Specialists
  - American Board of Medical Specialties (ABMS) pain management fellowship leading to subspecialty certification in pain medicine
    - Board of anesthesiology
    - Physical Medicine and Rehabilitation
    - Psychiatry and Neurology
  - American Board of Pain Medicine Diplomat status by 7/1/16

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Ongoing Treatment

- Should refer those who require greater than 100 MEDD to pain specialist
- Consult with Pain Medicine Specialist:
  - Treating patients requiring 120 MEDD or more
  - Ongoing therapy of 120 MEDD or more for more than 6 months at least annually
- "Shall" refer if greater than 200 MEDD
- UDT at least twice yearly
- 5 A's
- CSMD at least annually
- Communication with other providers (e.g., ED with primary)
- Discontinue when risk exceed benefits

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BEYOND THE TN GUIDELINES

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Case

A 45 year old male with severe pain from diabetic peripheral neuropathy that has not adequately responded to tricyclic antidepressants, SSRI, or anticonvulsant agents. He has refused previous prescriptions for opioids. After initial assessment, he agrees to a trial of opioid treatment in addition to his current maximal dose of amitriptyline (Elavil) (NOTE: the use of amitriptyline in diabetic peripheral neuropathy is off-label and has not been approved by the FDA). Which option is most appropriate for initiation?

- Fentanyl 25mcg/hr patch with hydrocodone/acetaminophen 10/325 q4h prn breakthrough pain
- ★ Hydromorphone 4mg po q4h prn severe pain
- Meperidine 50mg po q3h prn severe pain
- Oxycontin SR
- Tapentadol 50mg po q12 hours prn severe pain

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Comparison of opioids

"Weak" opioids		
Drug	DEA	Considerations
Buprenorphine	CIII	Partial agonist may ppt withdrawal in dependent patients; Ceiling effect
Butorphanol	CIV	Mixed agonist/antagonist may ppt withdrawal Reduce dose in hepatic/renal impairment; Ceiling effect
Codeine + APAP	CIII	Prodrug with minimal effect; apap limits max dose; caution in hepatically impaired or severe renal impaired
Hydrocodone + APAP	CII	APAP limits upper dose; caution in hepatically impaired
Nalbuphine	N/A	Mixed agonist/antagonist may PPT withdrawal; ceiling effect
Tapentadol	CII	Upper dose limited by toxicity (serotonin syndrome, NE excess)
Tramadol	TN CIV	Upper dose limited by toxicity (serotonin syndrome, NE excess); reduce dose in elderly, renal or hepatic impairment

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Comparison of opioids

"Strong" opioids		
Drug	DEA	Considerations
Fentanyl	CII	NOT FOR OPIATE NAÏVE; transmucosal forms are prompt release that require REMS access enrollment; reduce dose for hepatic and renal impairment
Hydromorphone	CII	Reduce dose in hepatic or renal impairment (though less problematic than others)
Levorphanol	CII	Also NMDA antagonist; reduce dose in renal/hepatic
Meperidine	CII	Evidence that efficacy is less than others; normeperidine (toxic metabolite) limits dose; use with caution if at all in elderly, renal, hepatically impaired
Methadone	CII	NMDA antagonist; some MAO-I activity, reduce dose in renal/hepatic; titration is tricky
Morphine	CII	6-glucuronide is active; 3-glucoronide is neurotoxic- may accumulate in renal impaired; reduce dose in hepatic
Oxycodone	CII	Mfg recommends increase dose, not decrease interval; reduce dose in renal or hepatic impairment
Oxymorphone	CII	Metabolite of oxycodone

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When are ER/LA opiates appropriate at initiation?

- Pain is moderate to severe (generally 4-10 on pain scale)
- Patient has failed to adequately respond to non-pharmacologic and/or non-opiate pharmacologics
- Continuous around-the-clock analgesia will be required for an extended period
  - Still need to cover breakthrough pain
- Potential benefits outweigh risks
- These products are NOT for PRN use and generally should not be initiated until pain is managed with immediate release formulations

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Example of morphine initiation for opiate naïve using delayed release

SR 10-15mg q12h with IR 5mg q 1-4 hr prn breakthrough pain with documentation WHY SR product being used at initiation

- Pain level is 0-3/10 without significant adverse effect: continue to monitor
- Pain is 4-6/10 OR patient uses more than 3 breakthrough doses per day after steady state has been acheived
  - Calculate average daily mg dose
  - Divide this by number of SR doses to be taken daily
  - Round this to an achievable SR dose
  - Add 5-15% of the new total daily dose to breakthrough dose
- Pain is still 7-10/10: consider parenteral or immediate release product for titration

Disease-a-Month 2013; 59:342

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Definition of opiate tolerant per FDA

At least one week of:

- Fentanyl 25mcg/hr transdermal
- Hydrocodone 45mg PO daily
- Hydromorphone 8mg PO daily
- Morphine po 60mg daily
- Oxycodone PO 30mg daily
- Equianalgesic dose of other opioid

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Discontinuing chronic opioids

WHY?

- Patient is not responding despite titration and rotation
- Intolerable side effects that are unmanageable
- Patient is nonadherent or unsafe
  - Unauthorized dose increases
  - Using opioid for unapproved symptom (e.g., anxiety)
  - Sharing medications with others
- Behaviors that suggest abuse or diversion

HOW?

- No evidence based guidelines, but protocols generally range from 10%/week to 25-50% every few days
- Patients on higher doses can generally tolerate more rapid initial taper

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What symptoms of opiate withdrawal?

"Cold Turkey" piloerection /sweating

Dilated pupils

GI cramps and diarrhea

Yawning

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Opiate rotation

WHY?

- Poor response
- Intolerable adverse effects
  - Hyperalgesia?
- Patient desire/need for different formulation (e.g., change of route of administration, change in dose frequency, economics)
- Drug availability
- Change in clinical status
- Concern about abuse or diversion
- Drug interactions
- Tolerance

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Opiate rotation

HOW?

- Calculate approximate total daily equianalgesic dose
- Reduce by 25-50% to allow for incomplete cross-tolerance
- Divide by number of SR doses per day, round to achievable dose
- Add 5-15% per dose for breakthrough pain at appropriate prn inteval
- Titrate up or down

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Equianalgesic Dosing*		
Opioid Agonist	Appx PO Dose	Appx IV Dose
Morphine	30 mg	10 mg
Codeine	130 mg	75 mg
Hydrocodone	30mg	N/A
Hydromorphone	7.5 mg	1.5 mg
Meperidine	300 mg	100 mg
Oxycodone	20mg	N/A
Oxymorphone	6 mg	1.5 mg
Fentanyl		100 micrograms

* Incomplete cross tolerance may occur – when switching opioids, decrease the dose of the new opioid by approximately 25-30%.

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Opiate: important points

- Do not crush, split, chew ER/LA tablets
  - Not for PRN use!
- Do not cut fentanyl patches
  - IV drug abusers have been known to withdraw fentanyl from patch and inject it IV
- Appropriate disposal:
  - Tablets, capsules, liquids mix with noxious substance (e.g., coffee grounds, dishwashing soap) and discard in trash
  - Fentanyl patches should be folded over and immediately flushed or discarded!
- Patients should be made aware of risks of dependence and withdrawal at the start
  - Informed consent/treatment agreement
- Patients and caregivers need to be aware of the risks of CNS depression, especially when multiple agents are used

http://www.ismp.org/nan/files/nan-20120425.pdf

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Opiate interactions

- Drug-disease - COPD, renal impairment, hepatic impairment
- Pharmacogenomic – CYP 2D6 most predominantly, but also CYP 3A4, OATP1B1, UGT, predilection for QTc interval prolongation, etc
- Pharmacodynamic
  - use of multiple CNS depressants
  - Serotoninergic effects
  - QTc prolongation
  - Additive GI effects (obstruction)
- Pharmacokinetic – alterations in clearance with subsequent accumulation

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TN Public Chapter 623

- Allows licensed providers to prescribe naloxone (Narcan) when acting in good faith and exercising reasonable care:
  - For a person at risk of experiencing an opiate related overdose
  - For a family member, friend, or other person in a position to assist a person at risk of experiencing an opiate-related overdose
- IV onset 2 minutes
- Some evidence that Intranasal or IM effective
- Must watch for re-emergence
  - Especially when ER/LA products are used
- Immune from civil liability:
  - Licensed healthcare provider who prescribes or dispenses naloxone
  - Anyone who administers naloxone to the patient at risk

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And after all has been said…

Acts of TN general assembly chapter 327 section 3

•Inadequate treatment of acute and chronic pain originating from cancer or noncancerous conditions is a significant health problem;
•For some patients, pain management is the single most important treatment a physician can provide;
•A patient with severe chronic intractable pain should have access to proper treatment of such pain;
•In the hands of knowledgeable, ethical, and experienced pain management practitioners, opiates administered for severe acute and severe chronic intractable pain can be safe

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TN Acts 2001 chapter 327

- Notwithstanding any other provision of law, a provider may prescribe or administer dangerous drugs or controlled substances to a person in the course of the treatment of a person for intractable pain to provide adequate pain treatment.
- *It is not what you prescribe, but how well you manage the patient's care and document that care in legible form that is important.*

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Please close your video browser to continue to the post-test in the CME activity