Benzodiazepines: Pharmacology to Co-Prescribing Risks and Concerns

Opioids and Benzodiazepines: An Overview of the Clinical Issues in Pain Management

Elinore F. McCance-Katz, MD, PhD
Chief Medical Officer, RI Department of Behavioral Health,
Developmental Disabilities, and Hospitals | Providence, RI

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Disclaimer
This educational program is designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation.
Learning Objectives
At the conclusion of this session, attendees should be able to:
• Describe the context of the current epidemic of opioid misuse in the US
• Describe the clinical use of Benzodiazepines
• Describe the clinical challenges in Opioid/Benzodiazepine use
• Describe treatment modalities for OUD

Target Audience
Physicians, physician assistants, advanced practice pharmacists, APRNs, residents, & fellows who prescribe controlled substances.

CME Accreditation
This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Warren Alpert Medical School of Brown University and the Rhode Island Department of Health Academic Center. The Warren Alpert Medical School is accredited by the ACCME to provide continuing medical education for physicians.

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Rhode Island Specific: This program qualifies for 1.0 hours CME Credit in Risk Management and Opioid Pain Management/Chronic Pain Management, two of the required areas of section 6.0, 6.2.1 RI CME relicensure requirements.

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Elinore F. McCance-Katz, MD, PhD (Speaker)
Nancy A. DeNuccio* Owner, Narragansett Consultant Coordinator, Narragansett Prevention Partnership Narragansett, RI
Traci C. Green, PhD, MSc* Associate Professor of Epidemiology and Emergency Medicine (Research) | Warren Alpert Medical School Rhode Island Hospital | Providence, RI
Angela Mulholland, BSN* Staff Physician, Interventional Pain Management St. James Hospital | Fall River, MA
Marcia Sullivan, BS* Director, Continuing Medical Education Warren Alpert Medical School | Providence, RI

* Indicates members of the Planning Committee

Elisabeth T. Kretchman, CPS® Associate Administrator of Substance Abuse Prevention & Treatment | Behavioral Healthcare, Division of Behavioral Healthcare (BHDDH) | Department of Health | Providence, RI
James V. McDonald, MD, MPH* (Course Director) Director, RI Board of Medical Licensure & Discipline | Department of Health | Providence, RI
Leigh A. Reposa, MSW, LICSW* Program Manager | Rhode Island Youth Suicide Prevention Program | Warwick, RI
Maria Sullivan, BS* Director, Prescription Drug Overdose Prevention Education & Outreach | Division of Community Health & Equity | Department of Health | Providence, RI
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Elinore F. McCance-Katz MD, PhD
Chief Medical Officer
Rhode Island Department of Behavioral Health, Developmental Disabilities and Hospitals
Elinore.mccancekatz@bhddh.ri.gov
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Disclosures
None

Pain and Addiction: Overview

• Historical Information: Context for the current epidemic of opioid misuse in the U.S
• Benzodiazepines: Clinical use
• Clinical Challenges in Opioid/Benzodiazepine Use
• Treatment Modalities for OUD
We have historically had a history of undertreatment of pain in the U.S.

- Late 19th and early 20th century: high rates of morphine use and addiction
- Source of morphine: doctors
- Early 20th century: criminalization of addiction
- Harrison Act (1914): prohibition on prescription of narcotics (opiates) to addicts
- Result: Physicians underprescribed opioids even in clear cases of chronic, severe pain

How did we get to the current epidemic of prescription opioid abuse?

- Since 1990s: Opposing issues: Pain treatment community began stressing need to address undertreatment of pain vs. large increases in diversion and abuse of prescription opioids observed concomitantly
- New thinking in Pain Medicine which recommended applying the same principles as for treating cancer pain to that of treating chronic, non-malignant pain
- Belief (but no evidence) that those with pain were less likely to abuse opioids; i.e.: at less risk for abuse/addiction

How did we get to the current epidemic of prescription opioid abuse?

- Joint Commission: Pain Management Standards Jan 1, 2001
- Development of new, potent opioid therapies for moderate to severe pain
- In May 2007, Purdue Frederick, a subsidiary of Norwalk, Conn.-based Purdue Pharma L.P., pleaded guilty to felony misbranding of Oxycontin related to its addictive risks as part of a settlement with federal prosecutors. $634.5 million in fines paid by Purdue
Prevalence of Recurrent and Persistent Pain in the US

- Estimated 100 million Americans have pain
- 1 in 4 Americans suffer from recurrent pain (day-long bout of pain/month)
- 1 in 10 Americans report having persistent pain of at least one year’s duration
- 1 in 5 individuals over the age of 65 report pain persisting for more than 24 hours in the preceding month
- 6 in 10 report pain persisting > 1 year
- 2 out of 3 US armed forces veterans report having persistent pain attributable to military service
- 1 in 10 take prescription medicine to manage pain


The Problem of Pain

- Costs US economy estimated $560-635 billion/year
  - Healthcare
  - Welfare & disability payments
  - Lost tax revenue
  - Lost productivity (work absence)
- Most common reason for medical appointments (63% of pain sufferers seek treatment)
- Push toward opioid maintenance therapy in non-malignant pain


Why are Opioids so Widely Misused?

- Misperceptions about their safety. Because these medications are prescribed by doctors, many assume that they are safe to take under any circumstances.
- Varied motivations for their abuse. Underlying reasons include: to get high; to counter anxiety, pain, or sleep problems.
Past Month Nonmedical Use of Types of Psychotherapeutic Drugs among Persons Aged 12 or Older: 2002-2013

Difference between the estimate and the 2013 estimate is statistically significant at the .05 level.

Source Where Pain Relievers Were Obtained for Most Recent Nonmedical Use among Past Year Users Aged 12 or Older: 2013

DRUG OVERDOSE-RELATED DEATHS: A PREVENTABLE PUBLIC HEALTH ISSUE

- Since 2009 drug overdose deaths are leading cause of injury death in the U.S. — more than even car crashes
- Majority of drug overdose-related deaths are caused by prescription opioids and heroin
- 1999 to 2010: Opioid prescribing quadrupled
- 1999 to 2013: Rate for drug poisoning deaths involving opioid analgesics nearly quadrupled*
- 2015: Opioid analgesic-related deaths: 18,893; heroin-related deaths: 10,574

*Most frequently involved in deaths: oxycodone, hydrocodone, methadone, in combination w/alcohol or other drugs, most often benzodiazepines
Unintended Consequences: Prescription Pain Medication Use

- Random sample of 154,684 veterans found fatal opioid overdose to be directly associated with morphine equivalents/d
- 50-99 mg/d conferred greater risk:
- Review of 607,156; 498 individuals 15-64y prescribed an opioid v. 1714 matched controls. Opioid dose directly related to deaths:
  - 50-99 mg morphine equivalent/d OR: 1.92, 100-199 mg/d, OR: 2.04, > 200 mg/d. OR: 2.88 (Gomes, et al. 2011)
- Review of 9940 records from a health maintenance organization:
  - Those receiving 50-99 mg/morphine equivalent/d had 1.7 fold increase in overdose risk, 0.7% death rate, those receiving 100 mg/d or more had 8 fold overdose risk and 1.8% annual death rate (Dunn et al. 2010)

Why Are Greater Numbers of Opioids Being Prescribed?

Model Policy for the Use of Controlled Substances for the Treatment of Pain*

- Pain management integral to medical practice
- Opioids may be necessary
- Physicians will not be sanctioned for prescribing opioids for legitimate medical purposes
- Undertreatment of pain will be considered a deviation from the standard of care
- Use of opioids for purposes other than analgesia threaten individuals and society
- Physicians have a responsibility to minimize abuse and diversion

*Federation of State Medical Boards, 2003
Modifications to FSMB Guidelines - July 2013

- Greater discussion of lack of adequate evidence as to safety and long term effectiveness and safety of long-term opioid therapy
- Emphasizes professional and ethical responsibility of physicians to appropriately assess and manage pain as well as relative level of risk for misuse and addiction, monitor for aberrant behaviors and intervene as appropriate

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Pain: Real to Patients but Subjective to Physicians

- Physical (discomfort sensation) and psychological components (anxiety/depression) with overlapping treatments

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Psychosocial Aspects of Pain

- Physiological and anatomical pathways for pain are the same in humans
- Physical findings on examination can be the same for two people
- However, the perception of pain may be quite different in these two people and responses to pain may be quite different; one may resolve while the other transitions to chronicity
Psychosocial Aspects of Pain

• Consider psychosocial contributors:
  • Psychiatric comorbidities: depression, anxiety
  • Non-organic signs: Widespread pain at multiple sites; somatization
  • Demographic variables: age, gender, weight, education status, smoking status, SES
  • Work factors: worker’s comp, satisfaction at job, physical demands
  • Maladaptive coping strategies: those who have greater fear, who catastrophize (overly focus on pain and negative thoughts regarding ability to cope) may experience pain as more severe; avoid activity that may worsen pain leading to greater disability
• Psychosocial factors are most strongly correlated with low back pain outcomes
  – Chou and McCarberg, 2011

BZDs: Clinical Uses

• Panic Disorder
• Generalized Anxiety Disorder
• OCD, PTSD, Social AD: BZD not shown to be effective
• Used as adjunctive treatments in affective disorders, psychotic disorders
• Pain

BZDs: Mechanism of Action

• GABA-A binding permits chloride influx
• Resulting cell hyperpolarization; decreased excitation
• Receptor subtypes (all BZD bind with greater or lesser affinity)
  • Alpha 1-sedative
  • Alpha 2- anxiolytic
  • Alpha 1, 2, 3- anticonvulsant
Benzodiazepines: Misuse and Abuse

- 2012:
- Anxiolytics, sedatives, and hypnotics (drugs to treat anxiety and insomnia) were found in 33.9 percent of visits related to nonmedical use of pharmaceuticals.
- Benzodiazepines were involved in 28.7 percent of ED visits, with alprazolam (e.g., Xanax) indicated in about a third (9.9%) of such visits.
- 2013: 1.7 million misusers of BZDs

Are BZD Effective Clinically?

- Yes, with short term use (sleep 3-14 days, anxiety < 4 mos)—but most are long term users:
- Almost 90% of anxiolytics/tranquilizers and > 80% of hypnotics sold in U.S. were consumed by those reporting use > 4 months
- Continuous users account for about 70% of anxiolytic and 60% of hypnotic drug sales
- Tranquilizers: anxiolytics e.g.: diazepam, alprazolam, meprobamate, muscle relaxers (e.g.: Flexeril)
- Hypnotics: BZD generally used as sedatives rather than anxiolytics: temazepam, flurazepam, triazepam

Institute of Medicine

Does Long-Term Use Promote Anxiety?

- Long term BZ users may have less anxiety after discontinuation
- And less anxiety than continuous users
- Some chronic BZD users may be maintained to prevent rebound anxiety or withdrawal resulting from chronic use and physiological dependence rather than reducing anxiety

What about Effectiveness in Chronic Pain Management?

- Mixed Results:
  - Single study (n=100): alprazolam 1.5 mg/d; no other interventions
  - At 12 weeks: 83 showed improvement
  - 5 discontinued due to side effects
  - Mean pain score (0-5 scale) decreased 3.6 to 2.2

What about Effectiveness in Pain Management?

- Other studies show no benefit or worsened condition:
  - In mice: midazolam reduced morphine analgesia; blocked by flumazenil
  - Hot plate tests: midazolam and diazepam associated with reduced morphine analgesia
  - Pre-op diazepam followed by post op flumazenil decreased morphine requirements
  - Pakulska W, Czarnecka E: E Pharmazie 2001 56: 89.

What about Effectiveness in Pain Management?

- Human studies:
  - Acute lumbar disc prolapse with sciatica
  - N=60 PT/NSAIDS x 7 d +/- PL v diazepam
  - Day 7 PL: Reduction of distance referred pain (p=0.05)
  - Hospital LOS: PL 8 d v Diazepam 10 d p=0.008
  - Probability of 50% pain reduction: Twice as high in placebo patients (p<0.0015)
What about Effectiveness in Pain Management?

Cochrane Review of BZD for LBP (8 studies)
Acute: 1 high quality trial: diazepam = PLA
1 low quality found diazepam > PLA
Chronic LBP:
2 High quality trials
Tetraezepam increased odds of not experiencing pain relief or global improvement
Lower quality trial: diazepam of no benefit
Chou and Huffman Ann Int Med 2007; 147:505

What about Effectiveness in Pain Management?

- 114 chronic pain patients
- 38% taking > 1 BZD
- 14%: 1-2 y, 46% > 2 years
- 58% concomitant opioids
- 86% using all or in part for sleep
- No difference in sleep problems between those taking BZD or not
- No signs of excessive intake, but only one person willing to stop

What about Effectiveness in Pain Management?

- Study of BZD use in patients on long term opioids for chronic pain (n=1,220)
- 33%: BZD use in past month; 17% daily use
- BZD use associated with:
  - Greater pain severity, pain interference in life, lower feelings of self efficacy regarding pain
  - Being prescribed higher risk opioid doses (>200 MED)
  - Using antidepressant or antipsychotic medication
  - Illicit substance use, alcohol use disorder
  - Greater mental health comorbidity
  - Greater past month use of emergency healthcare: ambulance/accident/emergency services
Pain and Benzodiazepines

- BZD used heavily in chronic pain
- Addiction uncommon
- Evidence:
  - Acute Benefit: small
  - Chronic Benefit: None
- But use tends to be chronic
- Risks: drug interactions, impairment/accidents, rebound anxiety related to withdrawal as chronicity of use increases

Physical Dependence and Rebound

- Up to 40% have difficulty tapering after regular treatment for > 4 months
- Difficult to taper due to withdrawal and rebound
- Duration is more important than dose in difficulty with tapering

Benzodiazepines and Cognition

- Some case reports of depression with BZD use
- Meta-analysis of 13 studies
  - Cognitive impairment with long-term use 9.9 y (1-34 y) mean dose: 17.2 mg diazepam daily, participant age: 48 y (21-75 y):
    - Significant impairment relative to non-BZD users in all areas of cognition:
      - General Intelligence
      - Memory
      - Psychomotor speed
      - Visuospatial capabilities
      - Concentration
      - Motor Performance
      - Reasoning
    - Long-term cognitive effects following withdrawal:
      - 13 studies/age: 47 y, years of BZD use: 10 (1-29 y); 3 mos post withdrawal: still significant impairment on concentration, general intelligence, problem solving, psychomotor speed;
      - Memory, sensory processing, verbal reasoning, motor performance no longer impaired

Baker MD et al. CNS Drugs 2004 18(1): 37-48
BZD and Opioids: Toxicity

- Respiratory Depression: mediated via EAA (glutamate); this function depressed by mu agonists
- Inhibition also mediated by GABA
- Combined effects of opioids and BZD (or alcohol which also acts on GABA) can be lethal
- Toxicities and deaths:
  - Methadone: 52% of deaths had BZD present as well
  - Overall 17% of opioid related deaths had BZD present
  Maxwell and McCance-Katz, 2010

Pain Patients: Who Gets BZDs?

- History of abuse/dependence: alcohol or BZD
- Chronic medical or psychiatric illness
- Personality disorders (borderline, dependent)
- Chronic dysphoria
- Chronic insomnia


Pain Patients: Who Gets BZDs?

- Highest risk patients get the most meds:
- Kaiser NCA 4 million CNMP patients:
- Long term opioid use by drug or alcohol diagnosis:
  - Individuals with SUDS more likely to:
    - Get Schedule II drugs
    - Larger number of days supplies
    - Twice the rate of concurrent sedative-hypnotics
    - More likely to have > 180 days of use
    - Same patterns for those with opioid use disorders vs. those without opioid use disorders

**Benzodiazepines Predict Opioid Use**

Follow up study examining relationship of previous BZD prescription to later opioid prescription (n=17,074)
Odds ratio for moderate-high prescription frequency (>12 prescriptions during 3 yr study period) of opioids 4-7 years after BZD use 3 years earlier: 7.7; controlling for musculoskeletal pain, alcohol use, smoking status and SES: 3.3


**High Dose Opioids Predict BZD Use**

- N=478 veterans with CNMP
- Taking ≥ 180 mg/d morphine sulphate (MS) daily
- Vs
- No opioids (n=500)
- High dose MS patients: more likely to have > 4 pain diagnoses
- Higher rates of psychiatric, medical and SUDs
- 32% of high dose MS: receiving concurrent BZD


**Summary: BZD**

- BZD use disorders are a small portion of addictive disorders in U.S.
- Many using BZD have h/o addiction (alcohol, cocaine, opioids)
- BZD do not help pain; increase impairment
- Patients generally don’t take huge amounts of BZD, but they cannot stop them easily
- Are they addicted: Tolerance, withdrawal, inability to stop, but limited misuse; consequences are the impairment related to chronic use
What Can We/Should We Do?

- The highest risk patients get the most drug
- Taper
- Use alternative sleep/anxiety medications
- Consider anticonvulsants:
  - Gabapentin, valproate, pregabalin, carbamazepine
- Norwegian study: 2004-7 use of gabapentin or pregabalin: 15-29% able to stop BZDs
  
  Bramness JG et al. Basic Clin Pharmacol Toxicol, 2010

Alternatives

- Anxiety: beta blockers, anticonvulsants, buspirone, SSRIs, SNRIs
- Depression: SNRIs, SSRIs
- Analgesics: NSAIDs, local anesthetics, topicals, opioids

Are BZD Reinforcing?

- Animal studies vary by route of administration:
  - Oral: not reinforcing in 8/18 studies
  - IV: reinforcing
  - Humans without anxiety issues: NOT reinforcing
  - Moderate social drinkers (not with AUD): BZD are reinforcing
  
  Griffiths and Wooters, Psychopharmacology 134 (1) 1-37, 1997
Are BZD Reinforcing?

- Street information indicates BZD are reinforcing/abused
  - Significant street value of diazepam/clonazepam Many report getting ‘high’ with these drugs
  - Heroin/methadone users: use to enhance opioid ‘high’
  - Alcoholics: may use to relieve withdrawal, anxiety, insomnia

Preferred Drugs on the Street

- Short acting with rapid onset
- Highly lipophilic: crosses blood brain barrier rapidly
- Short half life, high potency
  - Alprazolam, lorazepam
- Clonazepam: long half life, high potency
  - Widely abused on the street
  - Perceived as ‘safe’

Potency: the relationship between the therapeutic effect of a drug and the dose necessary to achieve that effect.

Treatments for Pain: There are Many Aside from Opioids
Treatments for Pain: There are Many Aside from Opioids

- Depression common: screen (e.g.: BDI, PHQ-9)
- Treating depression can be helpful in treating pain
- Antidepressants commonly used in pain management; mixed reviews on benefit
- Low dose TCAs (e.g.: amitriptyline): Headache, neuropathy, chronic low back pain
- Note: SSRIs not useful for pain; venlafaxine or duloxetine useful for pain and depression
- Best and most effective use of antidepressants in pain management is to treat depression which may result in improved pain control

Evaluation of Pain

- Ask the patient about their pain—set aside longer visit for eval.
- How is the pain experienced physically: how/when it started, location, character, better/worse, lowest/highest during day on scale of 0-10, usual severity of pain on a typical day, what’s been tried, what’s helped or not
- Effect on sleep, mood, ability to work, effect on personal life
- Litigation related to condition?
- Expectations of pain medication(s) on analgesia or recovered function?

Evaluation of Pain

- Associated experiences: nausea, fatigue, depression, anxiety—may offer other ancillary treatments
- Use/abuse of illicit substances
- Stress at home/on job
- Lack of physical activity
- Obesity
Evaluation of Pain

- Screening patients for drug abuse/addiction:
- No group/population or setting definitively identified as likely to abuse
- However, the most reliable predictors of future abuse are family history of or individual history of a substance use disorder
- Screen all patients: “universal precautions” including urine drug screen and check Prescription Monitoring Program if considering opioids
- Some patients may resent this approach; important to explain that:
  - SUDs are common; use of drugs with abuse liability may raise risk; SUDs are treatable and patients will benefit from treatment; all patients are screened in same manner

Opioid Risk Tool (ORT)

- Administration
  - On initial visit
  - Prior to opioid therapy
- Scoring
  - 0-3: low risk (6%)
  - 4-7: moderate risk (28%)
  - >8: high risk (> 90%)

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Scoring totals


Evaluation of Pain

- Screening for Substance Misuse/Abuse:
- CAGE or DAST
- Single question screeners:
  - In the past year, how many times have you had 5 (for women, 4) or more drinks in one day?
    - 84% sensitive, 78% specific for hazardous drinking
    - 88% sensitive, 67% specific for current AUD
- How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?
Evaluation of Pain

- Physical examination required
- Diagnostic testing necessary
- Assessing Risk/Benefit
  - Uncontrolled pain can exacerbate other medical and psychiatric conditions including suicidality;
  - In deciding whether/how to treat the patient:
    - Consider risk of treatment vs. risk of not treating
- This does not mean that all pain must be treated with opioids—consider other options
- But all patients deserve to have their pain evaluated

Opioids for Pain Management

- Chronic opioids for non-malignant pain presents many potential problems:
  - Lack of evidence for efficacy, particularly with high dose opioid therapy
  - Syndrome of rebound pain/hyperalgesic states produced by opioid use
  - Withdrawal syndromes masquerading as “pain”
  - Opioid adverse events: QT prolongation, Torsades de Pointes (methadone; possibly buprenorphine per FDA approved language on buprenorphine pain formulation recently approved)
  - Rate of addiction and misuse may be underestimated; recent literature estimates: 4-26% have OUD; of those without OUD 10% misuse

Considerations with Chronic Opioid Therapy

- Best Practices
  - Thorough history and physical examination; get old medical records; query previous treatments and responses/check prescription monitoring program records
  - Speak with family/S.O. if available/patient consents
  - Diagnostic work-up
  - Consider non-opioid options (especially in those with substance abuse history)
  - Consider Risk/Benefit of chronic opioid therapy
  - Reassess frequently and modify treatment plan as indicated
  - Documentation
Treatment Agreements

- Components:
  - Informed consent for treatment including Risks/Benefits
  - Controlled substances to be prescribed by only one doctor/clinician and obtained from one pharmacy
  - Notify patient that record of controlled substance prescriptions will be obtained through state prescription monitoring program
  - Notify patient of need to abstain from illicit substances and excessive alcohol use due to concerns about drug-drug interactions

Assessing Risk/Benefit of Chronic Opioid Therapy: Can Misuse be Predicted?

- History of drug/alcohol abuse
  - Cigarette smoking
  - Opioid abuse
  - Binge alcohol use
  - Marijuana use
  - Cocaine use
  - Benzodiazepine use (Skurtveit S, et al. Pain Medicine, 2010)

- Family History of drug/alcohol abuse

- Men > Women
- 18-34 years old
- Mood disorder
- Psychotropic use
- Unemployed or out of school
- Fair to poor health
- History of violence (Catalano RF et al., 2011)
Considerations with Chronic Opioid Therapy

Check urine drug screen initially and periodically:
- Illicit drug use highly correlated with opioid abuse/addiction
- Confirm use of the drug you're prescribing
- Point of Service vs. Clinical Lab (GC/MS confirmation)
- Pill Counts

Periodic review:
- Evidence of analgesia
- Treat side effects
- Enhanced social/employment functioning
- Overall improved quality of life

Consultation
- Pain specialists
- Psychiatrist (co-occurring mental illness is common)
- Addiction specialist

Non-Opioid Pain Management Strategies Should be Required with Opioid Therapy

- Non-opioid medication options: NSAIDS, anticonvulsants, muscle relaxants, duloxetine, venlafaxine may have a role
- Psychosocial support, cognitive-behavioral therapy
- Physical therapy
- Management of insomnia, anxiety (non-BZD), depression (co-occurring mental disorders common and large role for psychiatry in assessment/management of chronic pain)
- Acupuncture

Identification of Prescription Narcotic Abusers

- Deterioration in home/work
- Resistance to changes in therapy
- Use of drug by injection or nasal route
- Early refills
- Lost/stolen prescriptions
- Doctor shopping (check PMP)
- Prescription forgery
- Abuse of other substances
- Frequent ED visits
- Unauthorized dose increases
- Seeks specific drug
- Nonmedical use
- Refuses UDS/referral to specialist
Identification of Prescription Narcotic Abusers

- Important to recognize that not all aberrant behaviors are equal
  - E.g.: running out of medication a day or two early is not the same as prescription forgery
  - Important to try to assess the underlying cause of the aberrant behavior—is the pain under-treated; is there a co-occurring mental disorder (depression/anxiety), are there other signs of misuse occurring
  - Try to address the individual patient needs; educate patient regarding use of medications; try other approaches to pain management when indicated; if behaviors are sociopathic enforce treatment agreement which gives a means by which to stop prescribing/refer out

Approaching Patient with Aberrant Medication-Taking Behavior

- Take non-judgmental stance
- Use open-ended questions
- State your concerns about the behavior
- Approach as if they have a relative contraindication to controlled drugs (if not absolute contraindication)
- Take pressure off yourself by referring to clinic policies

What to do if Your Patient Develops a Substance Use Disorder with Prescribed Opioids

- Therapeutic Options:
- Combination of medication treatment plus psychosocial psychotherapeutic interventions:
  - Inpatient (usually medical withdrawal; short term pharmacotherapy) followed by:
  - Residential/intensive outpatient
  - Individual/Group Drug Counseling
- Medication Treatments (Short or Long Term)
  - Naltrexone
  - Methadone maintenance (especially if ongoing opioid analgesia needed) (methadone for opioid dependence can only be prescribed from a licensed narcotic treatment program)
  - Buprenorphine (need waiver for prescribing from office-based practice for treatment of opioid dependence)

Passik SD, Kirsh KL. J Supportive Oncology, 2005.
Clinical Support Systems
Sponsored by Center for Substance Abuse Treatment/SAMHSA

PCSS-O Training
Educational Resources for Providers of Opioid Medications

Ask a clinical question...
- Get a response from an expert PCSS mentor
- (855) 227-2776 (Opioids)

From www.PCSS-O.org
- download clinical tools, helpful forms and concise guidances (like FAQs) on specific questions regarding opioid dependence, use of buprenorphine, safe/effective use of opioids; information on training and peer support

Why is All of This Important?
- Pain is common; costly and deserves treatment
- Opioid use disorders affect significant numbers; prescription opioid analgesic abuse is major opioid problem at present
- Toxicities are most often a result of multiple drug ingestion with opioids/benzodiazepines a significant problem
- It is possible to treat pain effectively, to screen for opioid and other substance use disorders, and to treat those disorders should they arise

References
- Institute of Medicine Report from the Committee on Advancing Pain Research, Care, and Education: Relieving Pain in America. A Blueprint for Transforming Prevention, Care, Education and Research. The National Academies Press, 2011.
Obtain Credits/Certificate

Please complete the Post-Test and Survey upon conclusion. A passing score of 75% is required for credit.

If necessary, please see detailed instructions emailed to you by the CME Office.

Questions or Comments? Contact us at CME@Brown.Edu