Effective Strategies for the Non-Adherent Buprenorphine Patient: Rational Monitoring and Contingency

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Disclosures/Conflicts of interest

The speakers and planners of this webinar have no relevant financial relationships to disclose

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Ted's Story

- 29 y.o. man presents to our clinic for ongoing buprenorphine-naloxone management, 12 mg/ daily, which has helped him "stay clean for 2 years." He recently moved to the Bay Area for a new job in a local hospital, seeking a "fresh start".

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Ted's Story

- Based on self-reported history, we diagnose the following:
  - Opioid use disorder (hx of IV heroin use)
  - Cocaine use disorder (crack)
  - Cannabis/nicotine use disorder
  - Alcohol use disorder
  - Anxiety disorder, NOS

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Ted's Story

- In addition to prescribing bup 12 mg/daily, per Ted, his prior doctor was prescribing clonazepam 4 mg/daily and alprazolam 4 mg/daily. Without benzos, Ted reports he becomes suicidal.
- Soc Hx: Patient living with his friend, who is also in recovery, and got Ted his new job. He commutes 2 hours each way by bus to his job. He works the night shift.

5

How will we manage Ted's benzodiazepines, which put him at increased risk for accidental overdose, especially given his reluctance to make changes?

6

Is Ted telling the truth about his current substance use?

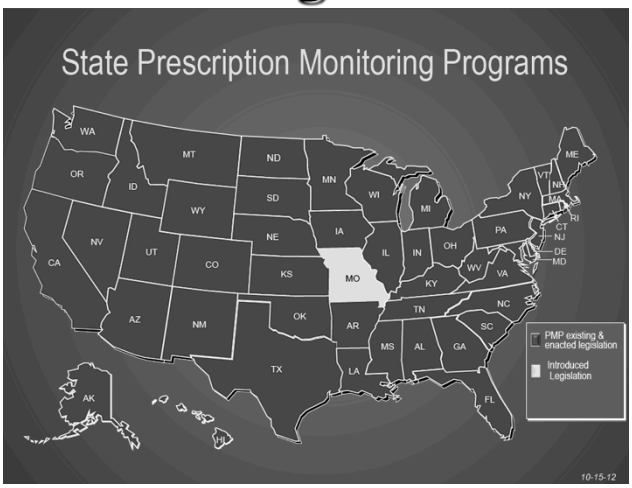
7

Without objective data, it is impossible to know.

What to do?!

8

Prescription Drug Monitoring Program



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PDMP

Prescription Drug Transaction Details :

Number of Records: 37 **Start Date: 10/22/2013** **End Date: 10/22/2014**

Date Filled	First Name	Last Name	DOB	Address	Drug Name	Form	Str	Qty	PHY Name	PHY#	Dr.'s DEA #	Dr.'s Name	RX#	Refill#
10/22/2013					ZOLPIDEM TARTRATE	TAB	10 MG	45						2
10/30/2013					ZOLPIDEM TARTRATE	TAB	10 MG	45						2
11/01/2013					ZOLPIDEM TARTRATE	TAB	10 MG	30						0
11/01/2013					ZOLPIDEM TARTRATE	TAB	10 MG	30						1
11/01/2013					LORAZEPAM	TAB	0.5 MG	60						1
11/01/2013					ZOLPIDEM TARTRATE	TAB	10 MG	60						1
11/05/2013					ZOLPIDEM TARTRATE	TAB	10 MG	30						0
11/05/2013					ZOLPIDEM TARTRATE	TAB	10 MG	30						0
11/08/2013					ZOLPIDEM TARTRATE	TAB	10 MG	60						1
11/09/2013					ZOLPIDEM TARTRATE	TAB	10 MG	30						0
11/10/2013					ZOLPIDEM TARTRATE	TAB	10 MG	30						0
11/11/2013					ZOLPIDEM TARTRATE	TAB	10 MG	30						2
11/11/2013					ZOLPIDEM TARTRATE	TAB	10 MG	30						0

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Urine Drug Screen

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Why Test?

- Diagnosis – substance abuse and dependence
- Pain management – monitoring compliance and detecting addiction
- Accountability - improves outcomes
- Documentation of recovery - advocacy
- Detection of relapse – early intervention
- Prevention – deterrence – in schools, homes, etc
- Detection of Diversion – important to the DEA when they visit

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Two basic types of tests

- Screening – highly sensitive but not so specific
  - Immunoassay – lab based or Point of Care Test
  - ELISA, EMIT, DRI – cross reactivity
  - "Presumptive positive"
- Confirmation – highly specific but not easily automated
  - GC/MS
  - LC/MS/MS
- Best used together – screening and if positive then do confirmation for that analyte

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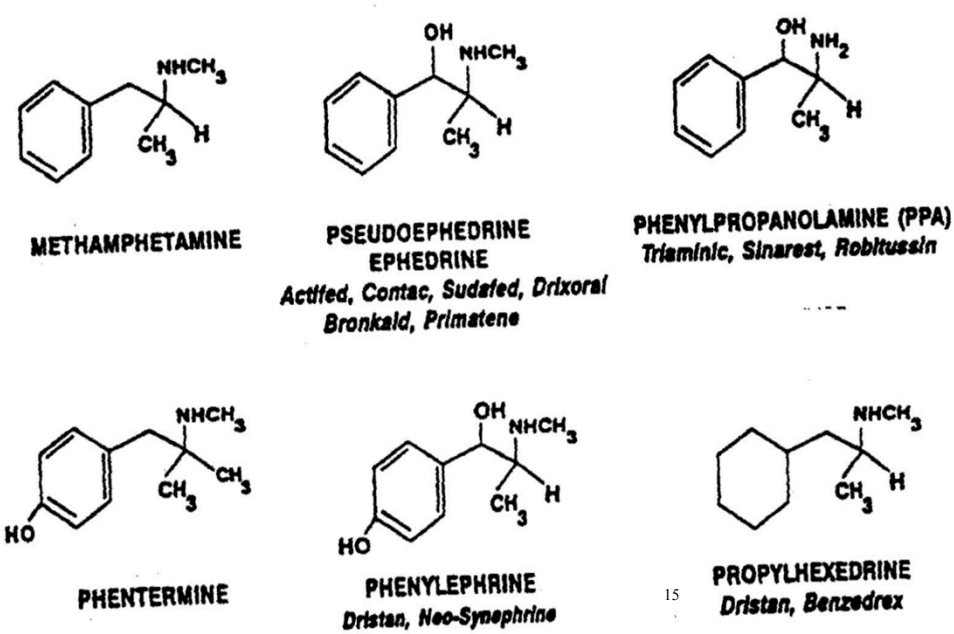

Panels

- POCT – 12 panel - limited – "CLIA waived"
- Immunoassay screening by laboratory – extensive panels available - over 125 immunoassay kits now available
- Selecting a drug test panel
  - NIDA 5 – profoundly inadequate today
  - Must include typical drugs of abuse
  - Any other particular drugs of possible concern
    - e.g. buprenorphine, methadone, dextromethorphan, ketamine, etc.

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Window of Detection

Table 1. Approximate windows of detection of drugs in urine

Drug	General detection time in urine
Amphetamines	Up to 3 days
THCA (depending on the grade and frequency of marijuana use) – Single use – Chronic use	 – 1 to 3 days – Up to 30 days
Cocaine – BEG after cocaine use	Hours – 2 to 4 days
Opiates (morphine, codeine) – Heroin – 6-MAM	2 to 3 days – 3 to 5 minutes – 25 to 30 minutes
Methadone – EDDP (methadone metabolite)	Up to 3 days – Up to 6 days
Benzodiazepines (depending on specific agent and quantity used)	Days to weeks

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Cutoffs

Table 3. Initial and confirmatory cutoff concentrations[a] used for federally regulated testing (effective October 1, 2010])[20]

Initial test analyte	Initial test cutoff	Confirmatory test analyte	Confirmatory test cutoff
Marijuana/metabolites	50 ng/mL	THCA	15 ng/mL
Cocaine/metabolites	300 ng/mL	BEG	150 ng/mL
Opiate/metabolites • Codeine/morphine[b] • 6-MAM	2000 ng/mL 10 ng/mL	Codeine Morphine 6-MAM	2000 ng/mL 2000 ng/mL 10 ng/mL
PCP	25 ng/mL	PCP	25 ng/mL
Amphetamines • Amphetamine/methamphetamine[c] • MDMA	500 ng/mL 500 ng/mL	Amphetamine Methamphetamine[d] MDMA MDA MDEA	250 ng/mL 250 ng/mL 250 ng/mL 250 ng/mL 250 ng/mL

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Ethylglucuronide (EtG)

Formation

- via conjugation of ethanol with activated glucuronic acid in the presence of membrane bound mitochondrial UDP glucuronyl transferase (UGT)

Stephan Seidl et al.

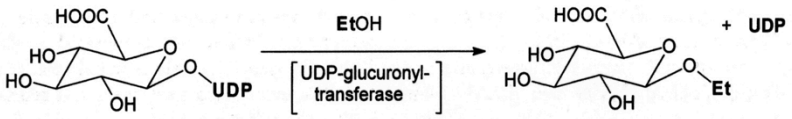

Figure 1. *Formation of ethyl glucuronide (EtG) by conjugation of UDP-glucuronic acid and ethanol.*

Seidl S, Wurst FM, Skipper GE, Alt A, Addiction Biol 6, 2001

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Ted's UDS is positive for BZDs, bup, cannabis, and cocaine; PDMP negative.

20

After UDS results, Ted admits he drank to blackout on Saturday night and "probably used cocaine … that's what I do."

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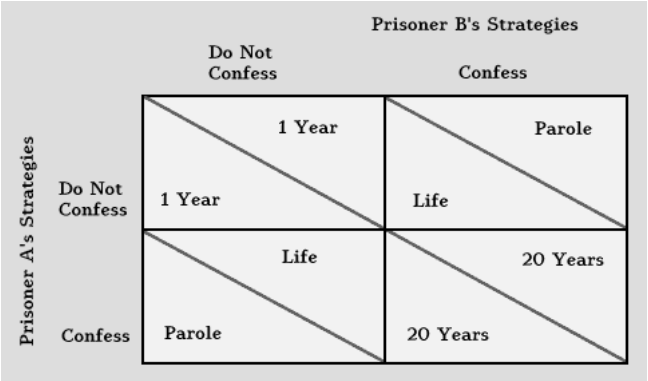
The *Prisoner's Dilemma*



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Axelrod's computer simulation competition

- Strategies that did poorly?
  - "Nasty" strategies
  - "Always nice"
- The winning strategy?
  - Just four lines of BASIC
  - "Tit for tat"

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How to Play *Tit-for-Tat*?

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Tit for Tat: cooperate, then repeat opponent's last move

- Doctor
  - Cooperate →
  - Cooperate →
  - Cooperate →
  - Defect →
  - Defect →
  - Cooperate →
- Patient
  - Cooperate
  - Cooperate
  - Defect
  - Defect
  - Cooperate
  - Cooperate

25

Respond to aberrant behavior with *Tit for Tat*

- Limit prescriptions to 1-2 weeks
- Increase visits
- Reduce the dose by 10%
- Get urine tox screens *before* prescribing
- Get family involved
- Refer to a higher level of care (e.g. methadone maintenance … Dr. Scott Steiger pearl)

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Evidence for *Tit for Tat*?

- See the contingency management literature
- Contingency management
  - Punishment certainty > punishment severity
  - Immediate punishment > delayed punishment
  - Punishment = transgression
  - Rewards for good behavior
- South Dakota's "24/7 Sobriety Program" reduced both repeat DUI and domestic violence arrests at the county level (www.rand.org)

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Tit for Tat a better alternative to:

- Enabling

- Retaliation

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Back to Ted's Case

Ted's UDS is positive for BZDs, bup, cannabis, and cocaine; PDMP negative.

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Visit #0: Using *Tit for Tat*, what is the best next step?

A. Tell Ted you can't treat him because he lied about his drug use and you can't work with a liar

B. Give Ted an Rx for a month's worth of buprenorphine 12 mg/day, Clonazepam 4 mg/day, and Alprazolam 4 mg/day, RTC 1 month

C. Give Ted an Rx for a month's worth of bup 12 mg/day but no benzos, RTC 1 week

D. Do not give Ted prescriptions before confirming with prior prescriber and setting the terms of your relationship ("contract")

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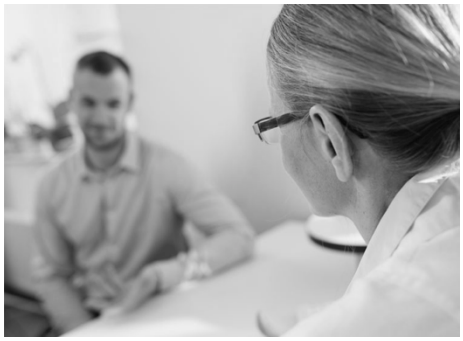
Answer = "D"

- Do not give Ted prescriptions before confirming with prior prescriber and setting the terms of your relationship ("contract")



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What Did We Do? Treatment Plan Visit #0

- No prescriptions until after confirming with previous provider about hx and Rx
- Previous provider not aware of binge alcohol, cocaine, or cannabis use; no UDS/PDMP; but confirms bup and clon doses. Alpraz only 2mg.
- "Controlled Substance Contract": No EtOH, no other opioids, no illicits, no cannabis, nicotine okay, AA/NA, weekly UDS/PDMP/pill counts
- Rx'd one week of meds, Alprazolam only 2mg daily as per provider

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Ted's Level of Satisfaction with his Care after Visit #0

- 2 out of 10.

33

Visit #1 (1 week after initial visit)

- UDS negative except benzos and bup
- PDMP negative for aberrant behavior
- Pill count consistent with prescribing
- Tolerating alprazolam 2 mg daily

34

Visit #1: Using *Tit for Tat*, what is the best next step?

A. Tell Ted he's doing great and Rx a month's worth of the same meds, RTC 1 month

C. Rx a week of meds, but this time cut out the alprazolam, RTC 1 week

D. Tell Ted you talked with a colleague and you now feel Ted is too high risk; Rx 2 weeks of meds at the same doses and give other names for F/U

E. Rx another week of meds, except lower alprazolam to 1.5mg daily.

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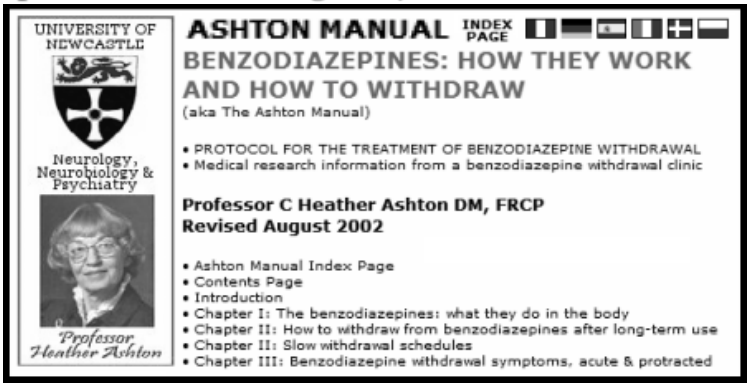
Answer = "E"

- Rx another week of meds, except lower alprazolam to 1.5mg daily



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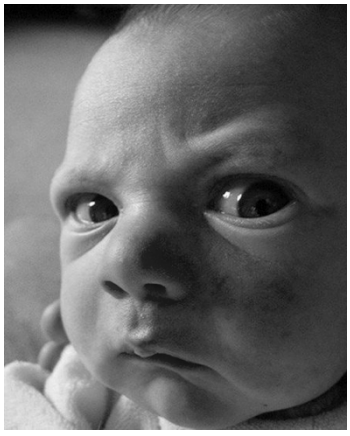
What Did We Do? Treatment Plan Visit #1

- Rx'd another week of meds, except lowered alprazolam to 1.5mg daily.

37

Ted's level of satisfaction with his care after visit #1

- 1 out of 10.



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Visit #2 (2 weeks after initial visit)

- UDS positive for benzos, bup, cocaine, and cannabis; PDMP negative.
- Pill count shows no remaining pills
- Roomate using cocaine in the home
- Ted talks about burden of working the night shift, no money, long commute, uncertain housing, difficult roommate, struggling to keep his job

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Visit #2: Using *Tit for Tat*, what is the best next step?

A. Re-visit the terms of the original agreement, and reduce the daily bup dose to 8mg daily as a response to non-adherence; Rx 1 week meds

B. Re-visit the terms of the original agreement and emphasize the importance of following the contract, but make no changes; Rx 1 week meds

C. Tell Ted that since he broke the contract, you can no longer treat him, and refer him to a methadone clinic

40

Answer = "A"

- Re-visit the terms of the original agreement, and reduce the daily bup dose to 8mg daily as a response to non-adherence; Rx 1 week meds

41

What Did We do? Treatment Plan Visit #2

- Re-explained contract and Rx'd week of meds; same doses.
- No *Tit for Tat*. Why?
  - *Tit for Tat* has room for forgiveness
  - We thought we were alliance building
  - Issues of the working poor: money, transportation, time, other pressures
- However, I'm not sure we did Ted any favors…

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The Poor and Under-Educated Treated Differently

- People receiving Medicaid are prescribed painkillers)
- at 2x rate of non-Medicaid patients
- and die from prescription overdoses at 6x the rate
- Mack K, Zhang K, Paulozzi L, Jones C. Prescription practices involving opioid analgesics among Americans with Medicaid, 2010. J Health Care Poor Underserved. 2015;26(1):182–198
- Reasons for these differences?
- Provider factors
- Patient factors

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Ted's level of satisfaction with his care after visit #2

- 5 out of 10.

44

Visit #3 (3 weeks after initial visit)

- Patient did not show for his appointment.
- Make up appointment same day in the afternoon, or else no Rx
- At make up appointment, UDS positive for benzos, bup, cocaine, cannabis
- PDMP negative; didn't bring meds for pill count
- States "I feel terrible." And says he gets suicidal or relapses to heroin if alprazolam lowered further

45

Visit #3: Using *Tit for Tat*, what is the best next step?

A. Re-visit the terms of the original agreement, and reduce the daily bup dose to 8mg daily as a response to non-adherence; Rx 1 week meds

B. Re-visit the terms of the original agreement and emphasize the importance of following the contract, but make no changes; Rx 1 week meds

C. Tell Ted that since he broke the contract, you can no longer treat him, and refer him to a methadone clinic

46

Answer = "A"

- Re-visit the terms of the original agreement, and reduce the daily bup dose to 8mg daily as a response to non-adherence; Rx 1 week meds

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What Did We Do? Treatment Plan Visit #3

- **Alprazolam continued at 1.5 mg daily, despite veiled threats. SI assessed and not active. Patient able to contract "for safety"**
- **Patient told if UDS positive next week for cocaine or other illicits, we will reduce the buprenorphine dose further and continue reducing at each visit until UDS adhering to treatment.**
- **We agree cannabis use would not qualify as non-adherence.**

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Ted's level of satisfaction with his care after visit #3

- 0 out of 10.

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Turned a Corner

50

Visit #4 (4 weeks after initial visit)

- UDS positive for benzos, bup, and cannabis; PDMP negative.

51

Visit #4: Using *Tit for Tat*, what is the best next step?

A. Re-visit the terms of the original agreement, and further reduce the daily bup dose to 4mg daily; Rx 1 week meds

B. Re-visit the terms of the original agreement and emphasize the importance of following the contract, but make no changes; Rx 1 week meds

C. Re-visit the terms of the original agreement and emphasize the importance of following the contract; increase bup back up to 12 mg/daily; Rx 1 week meds

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Answer = "C"

- Re-visit the terms of the original agreement and emphasize the importance of following the contract; increase bup back up to 12 mg/daily; Rx 1 week meds
- Reward course correction

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What Did We Do? Treatment Plan Visit #4

- **Increased buprenorphine back to 12mg/day continued alprazolam at 1.5 mg daily**
- **Patient recommitted to the contract**
- **Started looking for new housing options to get away from cocaine-using roommate**

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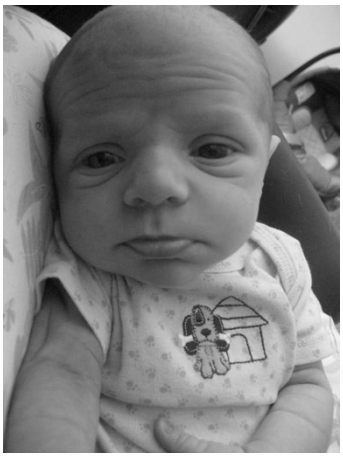
Ted's level of satisfaction with his care after visit #4

- 2 out of 10.



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It's a Dance…

And you're teaching your patient the steps

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Ted Today!

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Don't Forget Naloxone!

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Department of Health and Human Services
Substance Abuse and Mental Health Services Administration
Center for Substance Abuse Prevention

Medical Review Officer Manual

for

Federal Agency Workplace Drug Testing Programs

EFFECTIVE MAY 31, 2014

Note: This manual applies to federal agency drug testing programs that come under Executive Order 12564 dated September 15, 1986, section 503 of Public Law 100-71, 5 U.S.C. section 7301 note dated July 11, 1987, and the Department of Health and Human Services Mandatory Guidelines for Federal Workplace Drug Testing Programs (73 FR 71858) dated November 25, 2008 (effective October 1, 2010).

This manual does not apply to specimens submitted for testing under U.S. Department of Transportation (DOT) Procedures for Transportation Workplace Drug and Alcohol Testing Programs (49 CFR Part 40).

The current version of this manual and other information including MRO Case Studies are available on the SAMHSA website. The website (currently under construction) is available at:

http://beta.samhsa.gov/workplace.

Previous Versions of this Manual are Obsolete

Medical Review Officer Manual published by SAMHSA

Medical Review Officer Handbook by Theodore Shultz - Available on Amazon

Consider becoming a certified Medical Review Officer by taking a weekend course and passing an exam offered by AAMRO or MROCC. (Available to any licensed physician.)

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Weighing the Risks and Benefits of Chronic Opioid Therapy

ANNA LEMBKE, MD; KEITH HUMPHREYS, PhD; and JORDAN NEWMARK, MD
Stanford University School of Medicine, Stanford, California

Evidence supports the use of opioids for treating acute pain. However, the evidence is limited for the use of chronic opioid therapy for chronic pain. Furthermore, the risks of chronic therapy are significant and may outweigh any potential benefits. When considering chronic opioid therapy, physicians should weigh the risks against any possible benefits throughout the therapy, including assessing for the risks of opioid misuse, opioid use disorder, and overdose. When initiating opioid therapy, physicians should consider buprenorphine for patients at risk of opioid misuse, opioid use disorder, and overdose. If and when opioid misuse is detected, opioids do not necessarily need to be discontinued, but misuse should be noted on the problem list and interventions should be performed to change the patient's behavior. If aberrant behavior continues, opioid use disorder should be diagnosed and treated accordingly. When patients are discontinuing opioid therapy, the dosage should be decreased slowly, especially in those who have intolerable withdrawal. It is not unreasonable for discontinuation of chronic opioid therapy to take many months. Benzodiazepines should not be coprescribed during chronic opioid therapy or when tapering, because some patients may develop cross-dependence. For patients at risk of overdose, naloxone should be offered to the patient and to others who may be in a position to witness and reverse opioid overdose. (*Am Fam Physician*. 2016;93(12):982-990. Copyright © 2016 American Academy of Family Physicians.)

▶ See related Editorials on pages 970 and 975, and Practice Guideline on page 1042.

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 976.

Author disclosure: No relevant financial affiliations.

▶ Patient information: A handout on this topic, written by the authors of this article, is available at http://www.aafp.org/afp/2016/0615/p982-s1.html.

Opioid analgesics have historically been prescribed for acute trauma, perioperative care, cancer pain, and pain associated with life-limiting illness. Over the past several decades, opioids have been increasingly dispensed chronically for many nonacute conditions. More than one-half of patients who receive continuous opioid therapy for 90 days are still receiving opioids more than four years later.[1] By sheer volume, family physicians prescribe more opioid analgesics than any other subspecialists.[2]

The benefit of short-term opioid therapy is supported by multiple clinical trials.[3] However, the benefit of opioids for managing chronic pain is limited. Chronic visceral or central pain syndromes (e.g., abdominal or pelvic pain, irritable bowel syndrome, fibromyalgia, headache, neuropathic pain) may be especially unresponsive to long-term opioid therapy. Furthermore, the risks associated with chronic opioid therapy increase in a dose-dependent manner.[4]

Nonetheless, chronic opioid therapy benefits some patients with chronic pain. The American Academy of Family Physicians urges physicians "to individualize therapy based on a review of the patient's potential risks, benefits, side effects, and functional assessments, and to monitor ongoing therapy accordingly."[5] This review explores how to assess and mitigate risks when initiating, continuing, and discontinuing chronic opioid therapy. For terms and definitions, see *Table 1*.[6-8]

Risk Assessment When Initiating Chronic Opioid Therapy

Patients for whom chronic opioid therapy is being considered should be screened for risks and contraindications. Overdose is a key risk. Patients at increased risk of overdose include those with medical comorbidities (e.g., sleep apnea, lung disease, heart failure)[9]; those receiving benzodiazepines or other sedative-hypnotics[8,10]; those with problematic alcohol use; and those with psychiatric comorbidities (e.g., depression).

OPIOID MISUSE/OPIOID USE DISORDER

Opioid misuse and opioid use disorder are other key risk factors. Patients for whom chronic opioid therapy is being considered should be evaluated for these conditions.

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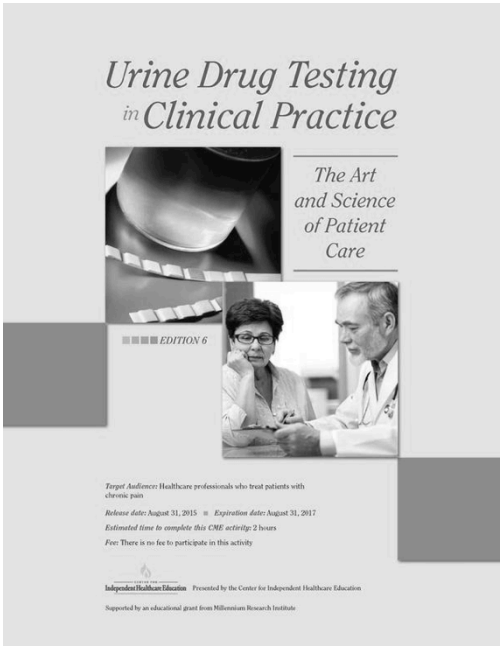

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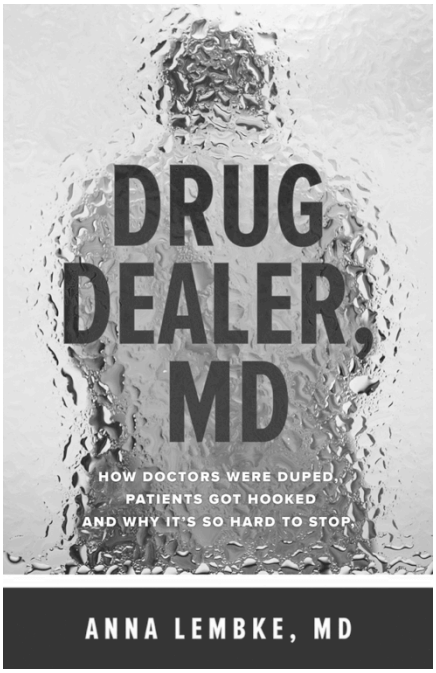

More information regarding

Drug Dealer, MD: How Doctors Were Duped, Patients Got Hooked, And Why It's So Hard to Stop

will be sent in a follow-up email.

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Thanks for listening! Questions?

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CSAM

California Society of Addiction Medicine (CSAM)

Treating Addiction in the Primary Care Safety Net (TAPC)

Soraya Azari, MD
Christina Fritsch, MD
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Jean Marsters, MD
Scott Steiger, MD
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NEXT WEBINAR Friday, 02/24/2017:

Psychological Approaches to Pain Management for the Primary Care Provider meeting

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Friday, 05/19/2017

Friday, 06/23/2017

Friday, 07/28/2017

Friday, 08/18/2017*

Friday, 09/22/2017

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You can view our previous webinars:

- ✓ ***"Expanding Access to Medication Assisted Treatment Utilizing Nurse Care Managers"***
- ✓ ***"Patient Confidentiality and Medication-Assisted Treatment in California Primary Care Settings"***
- ✓ ***"Office-Based Buprenorphine: Patient Selection, Induction, and Management"***

✓ for a small fee for CME/CEU on the CSAM Education Center at:
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OR

Free on the CHCF TAPC Program Resource Page at:
https://tapcprogram.com/

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After the webinar ends, stay online and you will be automatically transferred to a site where, after you answer a brief quiz and evaluation, you will be sent a certificate by email. The link to the quiz/evaluation/CME site will be sent to you about 1 hour after the conference.

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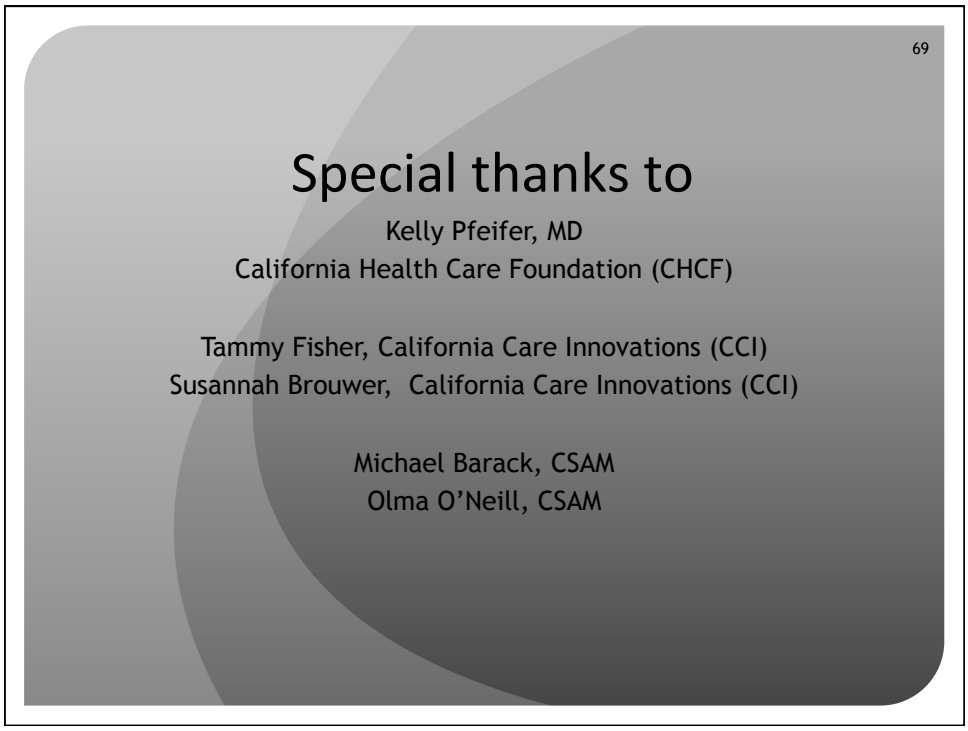
Save the date!

CSAM Addiction Medicine Review Course
and Board Exam Preparation
August 24 – August 27, 2017
Hilton San Francisco Union Square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