Approaches to Opioid Prescribing with High-Risk Behavior and Opioid Use Disorder in Oncology

Taylor Butler, PharmD, BCOP, BCPS
Clinical Pharmacy Specialist
Vanderbilt-Ingram Cancer Center

TOPA

1

Disclosures

- Dr. Butler has no relevant financial relationships with ineligible companies to disclose.

TOPA

2

Objectives

- List strengths and weaknesses of monitoring oncology patients initiated on opioid therapy
- Select analgesic options appropriate for individuals with high-risk opioid behaviors
- Discuss how to empathize and approach patients with concerning behavior

TOPA

3

Oncology Pain

- Pain from cancer and/or its treatments
- Incidence
  - Active Treatment: 55%
  - Metastatic Disease: 66.4%
  - Survivorship: 39.3%
- Cancer Pain Management
  - Moderate to severe pain – utilize opioid therapy

Source: Copenhaver DJ et al. Fundamentals of Cancer Pain Management 2021.; NCCN 2023.

TOPA

4

Oncology Pain

- Importance of Pain Management
  - Quality of life
  - Eligibility for treatment
  - Cancer Outcomes??

Source: Butler TW. HOPA News 2023.

TOPA

5

Tennessee (TN) Chronic Pain Guidelines

- Experts in the state of TN released a clinical practice guideline for the outpatient management of chronic ***non-malignant*** pain
  - Published in January 2020
- The guideline reviews many aspects of outpatient pain management including risk assessment, disposal, dosing, tapering, etc.

Tennessee laws reference following the Tennessee Chronic Pain Guidelines

Source: TN Dept of Health, 2020.

6

Centers for Disease Control and Prevention (CDC) Opioid Prescribing Guidelines

- CDC noted issues with opioid prescribing and wanted to review the available evidence to examine benefit and risk
  - Released in 2016, updated in 2022
- Systematic review developed to answer common questions and concerns, including benefit, opioid monitoring, risk considerations, etc.

Source: Dowell D. MMWR Recomm Rep 2022.

7

Opioid Monitoring

8

Opioid Monitoring Tools

- These are the tools that are available to monitor patients on opioid therapy
  - Office visits
  - Controlled Substance Monitoring Database
  - Drug Screens
  - Opioid Risk Assessments
  - Pill and Patch Counts

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

9

Office Visits

- Office visits are utilized for history and physical assessments

Office Visits
TN Pain Guidelines - No formal recommendation
CDC Opioid Therapy Guidelines - Clinicians should regularly reassess all patients receiving long-term opioid therapy, including patients who are new to the clinician but on long-term opioid therapy, with a suggested interval of every 3 months or more frequently for most patients.

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

10

Office Visits

- Strengths
  - Physical assessment of pain
  - Develop a relationship
- Weaknesses
  - Patient logistics
  - Scheduling
- Tips – think of the significance of bringing the patient into clinic

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

11

Controlled Substance Monitoring Database (CSMD)

- CSMD is where every opioid *filled* is documented

CSMD
TN Pain Guidelines - Clinicians should review the patient's history of controlled substance prescriptions using the Controlled Substance Monitoring Database (CSMD) data to determine whether the patients receiving opioid dosages or potentially dangerous combinations
CDC Opioid Therapy Guidelines - Ideally, PDMP data should be reviewed before every opioid prescription for acute, subacute, or chronic pain. This practice is recommended in all jurisdictions where PDMP availability and access policies, as well as clinical practice settings, make it practicable (e.g., clinician and delegate access permitted).

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

12

CSMD

- Strengths
  - Evidence of prescription fills
  - Limits doctor shopping
  - Helps with refill dates
- Weaknesses
  - Prescription reporting errors
  - Does not connect with all other states
- Tips – most patients who violate are unaware of consent so always educate well

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

13

Drug Screens

- Collecting blood, urine, or hair to test concentrations of drug in the body
  - Randomized preferred over planned schedule

Drug Screens
TN Pain Guidelines - Providers must continually monitor the patient for signs of abuse, misuse or diversion. A urine drug screen (or a comparable oral fluids screen or test) should be done twice a year at a minimum
CDC Opioid Therapy Guidelines - When prescribing opioids for subacute or chronic pain, clinicians should consider the benefits and risks of toxicology testing to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

14

Drug Screens

- Types of Drug Screens
  - Immunoassay – uses antibodies to detect the presence of selected drugs and/or their metabolites based on a predetermined cutoff threshold
  - Chromatography – detects the presence of specific drugs and/or metabolites
    - GC/MS – gas chromatography/mass spectrometry
    - LC/MS/MS – liquid chromatography/tandem mass spectrometry
    - High-performance liquid chromatography

Source: Raouf M et al. Fed Pract 2018.

15

Drug Screens

- Strengths
  - Objective evidence that patient is utilizing their medications
- Weaknesses
  - Sensitivity/specificity issues
  - Expensive
  - Patient can manipulate results
- Tips – get to know your toxicologist

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.; Raouf M et al. Fed Pract 2018.

16

Opioid Risk Assessments

- Multiple risk assessments have been created to help evaluate patient risk for aberrant behavior

Drug Screens
TN Pain Guidelines - The prescriber shall assess the patient's risk for misuse, abuse, diversion, and addiction using a validated risk assessment tool prior to initiating opioid therapy
CDC Opioid Therapy Guidelines - Clinicians should ask patients about their drug and alcohol use and use validated tools or consult with behavioral specialists to screen for and assess mental health and substance use disorders.

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

17

Opioid Risk Tool

Item	Female Score	Male Score
Family History of substance abuse - Alcohol - Illegal Drugs - Prescription Drugs	 1 2 4	 3 3 4
Personal history of substance abuse - Alcohol - Illegal Drugs - Prescription Drugs	 3 4 5	 3 4 5
Age (if 16-45)	1	1
History of preadolescent sexual abuse	3	0
Psychological disease - Attention deficit disorder, obsessive-compulsive disorder, bipolar, schizophrenia - Depression	 2 1	 2 1
Low risk = 0-3; Moderate risk = 4-7; High risk = >8		

Source: Webster LR et al. Pain Med 2005.

18

Opioid Risk Assessments

- Strengths
  - Easy to administer
  - Screens and identifies risk factors to consider
- Weaknesses
  - Limited data on application in clinical practice and patient outcomes
  - Based on patient reporting
- Tips – unsure of the utility

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

TOPA Tennessee Oncology Pharmacists Association

19

Pill and Patch Counts

- A randomized count of medications in between visits to determine utilization
- No formal recommendations provided per the state of Tennessee or CDC

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

TOPA Tennessee Oncology Pharmacists Association

20

Pill and Patch Counts

- Strengths
  - Ensure that patient is not using too much medications or diverting medications
- Weaknesses
  - Borrow medication
  - Logistical issues
  - Staffing issues
- Tips – really think through the logistics, candidates, etc. prior to instituting

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

TOPA Tennessee Oncology Pharmacists Association

21

Which of the following statements are true?

Opioid risk assessments were developed to exclude patients from opioid therapy — 0%

Immunoassays are more specific urine drug screenings than mass spectrometry — 0%

CSMD may have reporting errors — 0%

Pill and patch counts will always catch overuse and diversion — 0%

Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

23

Managing Cancer Pain with Co-morbid Opioid Use Disorder

24

Opioid Use Disorder

- Qualitative interviews conducted by Wood et al of oncology providers indicated that the majority did not view opioid misuse as a problem
- Evidence exists that cancer patients are a statistically significant higher risk to have drug use disorder (Adjusted Odds Ratio = 1.64; 95% CI = 1.13-3.39)
  - Prevalence is unknown but has been reported up to 23.5%

Source: Wood T et al. JOP 2023; Mallet J et al. Eur J Cancer 2018.; Preux C et al. J Clin Med 2022.

25

Opioid Use Disorder

- Opioid use disorder may effect outcomes in cancer patients
  - Increase in distress, morbidity, and mortality (including opioid-related deaths)

Source: American Psychatric Association, 2022.; Yennurajalingham S et al. JAMA Oncol 2021.; Preux C et al. J Clin Med 2022.

26

Opioid Use Disorder

- A problematic pattern of opioid use leading to clinically significant impairment or distress

DSM-V Criteria for Opioid Use Disorder	
Opioids are often taken in larger amounts or over a longer period of time than was intended.	Important social, occupational, or recreational activities are given up or reduced because of opioid use.
There is a persistent desire or unsuccessful efforts to cut down or control opioid use.	Recurrent opioid use in situations in which it is physically hazardous.
Continued opioid use despite having persistent or recurrent social or interpersonal problems caused by or exacerbated by the effects of opioids.	Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that's likely to have been caused or exacerbated by the substance.
Craving, or a strong desire or urge to use opioids.	Tolerance as either need increased amount for desired effect or a diminished effect with the same amount
Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.	Withdrawal as either opioid withdrawal syndrome or the same or similar substance is taken to relieve symptoms
A great deal of time is spent in activities to obtain the opioid, use the opioid, or recover from its effects.	
Mild = 2-3 symptoms; Moderate = 4-5 symptoms; Severe = 6+ symptoms; *Source: American Psychiatric Association 2013*	

27

Guidance on Opioid Management for Opioid Misuse or Use Disorder

- The authors recruited participants from various addiction and palliative care organizations to administer cases and examine using the Delphi model.
- Goal to provide guidance on 3 common clinical scenarios in cancer-pain management

Recruited: N=129 → Participated: N=120 → Completed all material: N=84

Source: Jones KF et al. JAMA Oncol 2023.

28

Cases – *Jones et al.*

- Man in his 50s with advanced cancer on active cancer treatment and comorbid pain from cancer and/or its treatment. Noted to be maximized on alternative analgesics and provided appropriate opioid education

Source: Jones KF et al. JAMA Oncol 2023.

29

Case #1 – *Jones et al.*

- Patient has recent history of opioid use disorder and not currently on OUD treatment or opioids for pain management

Source: Jones KF et al. JAMA Oncol 2023.

30

Case #2 – *Jones et al.*

- Patient has no history of OUD. He repeatedly takes more opioids than prescribed for pain. Urine drug screens negative.

Source: Jones KF et al. JAMA Oncol 2023.

31

Case #3 – *Jones et al.*

- Patient has no history of OUD. He is prescribed opioids and tests positive for unprescribed benzodiazepines.

Source: Jones KF et al. JAMA Oncol 2023.

32

Evaluating Benefit vs. Risk

Benefit

- Work fast and well acutely
- No ceiling effect
- No deleterious effect on organ function
- May improve performance status
- May improve quality of life
- Patient satisfaction?

Risk

- Risk of substance use disorder relapse
- May increase risk of mortality
- Diversion
- Frequent monitoring

33

Evaluating Benefit vs. Risk

Benefit

- Have these medications been helpful?
- Has he had any side effects?
- Alternatives trialed?
- What type of cancer treatment?
- How aggressive is the disease?
- What support services are available?

Risk

- When was last illicit use?
- Any concerning prescription patterns?
- What was the drug of choice?
- Was the last drug screen appropriate?

Can we mitigate risk?

34

Fentanyl

- Convert opioids to fentanyl patches alone
  - No fentanyl transmucosal products
- Patch counts
- Difficult to abuse
  - A case report of fentanyl patch abuse

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.; Guan W et al. Prim Care Companion CNS Disord 2011.

35

Buprenorphine

- Partial Opioid Agonist
  - May include opioid antagonist (naloxone)
- FDA approved for Opioid Use Disorder and Pain
  - Available as a sublingual film, sublingual tablet, injectable, and transdermal patch
- Per the state of Tennessee, buprenorphine products must be used for FDA-approved indications

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

36

Buprenorphine Considerations

- Highest affinity to the opioid receptor
  - Clinical Significance → Blocks illicit substances; may displace current full opioid agonist
- Analgesic activity is shorter than suppression of opioid withdrawal
  - Clinical Significance → Once daily dosing insufficient
- Dose correlates with receptor saturation
  - Clinical significance → there are still some opioid receptors available if need supplementation with full opioid agonist

Buprenorphine	2 mg	16 mg	32 mg
μ-Opioid Receptors Available	59%	8-15%	2-6%

Source: Alford DP et al. Ann Intern Med 2007.

37

Buprenorphine Considerations

- Buprenorphine films
  - Opioid naïve or <30 MME/day – 75 mcg film daily or every 12 hours
  - 30-89 MME/day – 150 mcg film every 12 hours
  - 90-160 MME/day – 300 mcg film every 12 hours
  - Maximum dose is 900 mcg every 12 hours
- Buprenorphine patches
  - Opioid naïve or <30 MME/day – initiate patch at 5 mcg/hr; change patch every 7 days
  - 30-80 MME – initiate patch at 10 mcg/hr, change patch every 7 days
  - Maximum dose is 20 mcg/hr patch
- Note – recommended to taper prior to initiation if above MME range

Source: Belbuca [package insert], 2015.; Butrans [package insert], 2019.

38

Methadone

- Full opioid agonist
  - Alternative mechanism of antagonizing NMDA
  - Limited to no euphoria
- Available as oral and injectable
- Per Federal Law, must be prescribed by a methadone clinic for opioid use disorder

Source: Davis MP. Ann Palliat Med 2020.; TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

39

Methadone

- Methadone clinic
  - Strengths
    - Supervised administration
    - May provide support services
    - Patient may not be allowed a home supply
  - Weaknesses
    - Logistics of daily visits
    - Analgesia does not last 24 hours
    - May not change dose for pain report

Source: TN Dept of Health, 2020.; Dowell D. MMWR Recomm Rep 2022.

40

Case #1 – *Jones et al.*

- Patient has recent history of opioid use disorder and not currently on OUD treatment or opioids for pain management
  - Initiate buprenorphine standard induction therapy
  - Prognosis may factor into deciding to utilize full opioid agonist
    - Increased monitoring (possibly weekly)
    - Consider fentanyl patches alone

Source: Jones KF et al. JAMA Oncol 2023.

41

Case #2 – *Jones et al.*

- Patient has no history of OUD. He repeatedly takes more opioids than prescribed for pain. Urine drug screens negative.
  - Increased monitoring
  - Consider
    - Caution on opioid dose escalations
    - Buprenorphine products
  - Do not taper opioid doses

Source: Jones KF et al. JAMA Oncol 2023.

42

Case #3 – *Jones et al.*

- Patient has no history of OUD. He is prescribed opioids and tests positive for unprescribed benzodiazepines.
  - Increased monitoring
  - Do not taper opioids or transition to buprenorphine products

Source: Jones KF et al. JAMA Oncol 2023.

43

Other Support/Resources

- Addiction Medicine
- 12 Step Programs
- Support Groups
- Maximize non-opioid analgesics

Source: CDC 2020

TOPA Tennessee Oncology Pharmacists Association

44

A 55 yo M pt with a hx of substance use disorder presents to the cancer clinic with pancreatic adenocarcinoma. He is having sever pain related to his mass. Currently on buprenorphine/naloxone 16 mg daily. What would be the next step to manage his pain?

Discontinue buprenorphine/naloxone and start oxycodone 5 mg every 4 hours as needed	0%
Start oxycodone 5 mg every 4 hours as needed	0%
Start gabapentin 300 mg every 8 hours	0%
Increase buprenorphine to 32 mg daily	0%

Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

46

Approaching Aberrant Behavior

47

Aberrant Behavior

- Opioid misuse – may be intentional or unintentional

Aberrant Behavior per Webster et al.	
Used additional prescribed opioids	Using nonprescribed opioids
Forged prescription	Sold prescription
Seeking euphoria from opioids	Using opioids for nonmedical uses
Overdose	Injected drugs
Abnormal drug screen	Doctor shopping
Alcohol abuse	Unauthorized ER visits
Resisted alternatives	Lost or stolen prescriptions
Missing appointments	Requesting early refills

Source: Webster LR et al. Pain Med 2005.

TOPA Tennessee Oncology Pharmacists Association

48

Empathy

Empathy: Talking to Patients About Substance Use Disorder	
Ask permission and provide options	Let them know that you care and want to partner with them in getting any help they need.
Normalize the conversation	Tell them that discomfort is normal and they are not alone.
Be transparent	Explain that it is important to ask specific questions to make sure they are safe
Work collaboratively with patients	Remind your patients that recovery is possible and a variety of resources are available
Address confidentiality concerns honestly	Tell patients your respect their privacy and will comply with protections required by law
Establish trust and show empathy	Active listening, non-judgmental language, respect patient, address their disorder as a disease

Source: CDC 2022.

49

Evaluating Benefit vs. Risk

Benefit

- Have these medications been helpful?
- Has he had any side effects?
- Alternatives trialed?
- What type of cancer treatment?
- How aggressive is the disease?
- What support services are available?

Risk

- When was last illicit use?
- Any concerning prescription patterns?
- What was the drug of choice?
- Was the last drug screen appropriate?

TOPA Tennessee Oncology Pharmacists Association

50

De-Stigmatizing Addiction

Preferred Language	Non-preferred language
Substance use disorder (or with the substance, e.g. opioid use disorder) Unhealthy/risky use Non-medical use	Substance abuse or drug problem
Addiction	Dependence (correctly separate the two terms)
Person with substance use disorder, person with…	Addict, alcoholic, IV drug user, drug-seeker, abuser
Person in recovery	Former addict, clean
Substance present (or not) in drug screen	Dirty or clean urine
Medications for opioid use disorder Medications for addiction treatment	Opioid replacement therapy Medication-assisted treatment
Undertreated pain	Pseudoaddiction
Using opioids for non-pain symptoms	Chemical coping
Opioids or any scheduled substance	Narcotics

Source: Ho J et al. Fast Facts #429 2021.

51

Case #1 – *Jones et al.*

- Patient has recent history of opioid use disorder and not currently on OUD treatment or opioids for pain management

Ask permission and provide options	"I see you were recently diagnosed with opioid use disorder. May I ask you a few personal questions?"
Normalize the conversation	"I know this conversation may be awkward, that is normal."
Be transparent	"I need you to be specific so it can help us come up with the best plan to manage your pain."
Work collaboratively with patients	"I just want the best outcome from you. It can be hard to manage pain and opioid use disorder. Let's see if we can find what works for you."
Address confidentiality concerns honestly	"I will never disclose any of your information without your consent."
Establish trust and show empathy	"Thank you for sharing that information with me. That is very hard and this is a challenging situation. I am here to help walk you through it."

Source: Jones KF et al. JAMA Oncol 2023.; CDC 2022.

52

A patient presents with a urine drug screen positive for benzoylecgonine and his prescribed opioids. What would be an appropriate approach to this patient?

Confront the patient about drug use and that they can never have pain medicines 0%

Discharge the patient from clinic 0%

Offer active listening about the results, supportive services, and develop an appropriate safe analgesic plan 0%

Ignore the results and continue to prescribe as is 0%

Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

54

Conclusion

- Opioid monitoring is a vital part of prescribing opioids
- Patients with comorbid opioid use disorder have tools to manage their pain with or without opioid therapy
- Provider-patient relationship is an important aspect and there are ways

TOPA
Tennessee Oncology Pharmacists Association

55

References

- Alford DP, Compton P, and Samet JH. Acute Pain Management for Patients Receiving Maintenance Methadone or Buprenorphine Therapy. Ann Intern Med 2006; 144(2): 127-34.
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Washington DC. American Psychiatric Association 2013: 541.
- Belbuca (buprenorphine) [package insert]. Malvern, PA: Endo Pharmaceuticals, Inc. 2015.
- Butrans (buprenorphine) [package insert]. Stamford, CT: Purdue Pharma L.P. 2019.
- Butler TW. Importance of Cancer Pain Management. HOPA News 2023; 20(2): 3-5.
- Centers for Disease Control and Prevention. Empathy: Talking to Patients About Substance Use Disorder. Updated 7/7/2022. Accessed on 10/6/2023. < https://www.cdc.gov/opioids/addiction-medicine/conversation-starters/talking-to-patients.html>
- Centers for Disease Control and Prevention. Opioids Help and Resources. Updated 1/28/2020. Accessed on 10/6/2023. < https://www.cdc.gov/opioids/addiction-medicine/conversation-starters/talking-to-patients.html>
- Copenhaver DJ, Huang M, Singh J, and Fishman SM. History and Epidemiology of Cancer Pain. Fundamentals of Cancer Pain Management 2021; CTAR (82): 3-15.
- Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. MMWR Recomm Rep 2022;71(No. RR-3):1–95.
- Greenwald MK, Johanson CE, Moody DE, et al. Effects of Buprenorphine Maintenance Dose on μ-Opioid Receptor Availability, Plasma Concentrations, and Antagonist Blockade in Heroin-Dependent Volunteers. Neuropsychopharmacology 2003; 28: 2000-9.

56

References

- Guan W, Schneider R, and Patterson J. "I Am in Pain!"—A Case Report of Illicit Use of Transdermal Fentanyl Patches. Prim Care Companion CNS Disord 2011; 13(5): PCC. 11101196.
- Ho J, Jones KF, Sager Z, Wakeman S, and Merlin JS. De-stigmatizing the language of addiction. Fast Fact #429. Palliative Care Network of Wisconsin. Accessed on 10/6/2023. < https://www.mypcnow.org/fast-fact/de-stigmatizing-the-language-of-addiction/>
- Preux C, Bertin M, Tarot A, et al. Prevalence of Opioid Use Disorder among Patients with Cancer-Related Pain: A Systematic Review. J Clin Med. 2022;11.
- Raouf M, Bettinger JJ, and Fudin J. A Practical Guide to Urine Drug Monitoring. Fed Pract 2018; 35(4): 38-44.
- TN Dept of Health. Tennessee Chronic Pain Guidelines. 3-TR Edition: 1-76.
- Webster LR and Webster RM. Predicting Aberrant Behaviors in Opioid-Treated Patients: Preliminary Validation of the Opioid Risk Tool. Pain Med 2005; 6(6): 432-42.
- Wood T, Cheung W, Ruether D, et al. Safe Prescribing Practices: Clinicians' Views on Prescribing Opioids to Patients With Early-Stage Cancer. JCO Oncol Pract 2023; 19(7): 456-64.
- Yennurajalingam S, Arthur J, Reddy S, et al. Frequency of and Factors Associated With Nonmedical Opioid Use Behavior Among Patients With Cancer Receiving Opioids for Cancer Pain. JAMA Oncol. 2021;7:404-411.

57