Aligning Buprenorphine Treatment for Opioid Use Disorder with Updated National Practice Guidelines

Marco Cunicelli, DO
Family Physician, Family Medicine Residency Program
Penn Medicine Lancaster General Health

Jon Lepley, DO
Medical Director, Addiction Medicine
Penn Medicine Lancaster General Health


Cunicelli


Lepley

Earlier this year, the Centers for Disease Control and Prevention (CDC) reported that deaths from unintentional drug poisonings in the United States exceeded 100,000 in 2021.[1] This is the largest number of overdose deaths ever recorded in a one-year period in this country. Further analysis of the data reveals that more than 75% of these overdose deaths were due to opioids.

Lancaster County has not been shielded from this national epidemic of opioid-related overdose deaths. During the 2020 calendar year, our county saw 143 deaths from unintentional drug poisonings, and opioids were implicated in 89% of those deaths.[2] The broad consensus is that untreated, or inadequately treated, opioid use disorder (OUD) is a major factor underlying this crisis.

Our colleague Tara Tawil, MD, described the evolution of this epidemic over the past 30 years in the pages of this journal in 2019.[3] In that article, which serves as useful background for this manuscript, Tawil also described treatment options for OUD, the emergence of buprenorphine in 2002, and efforts to increase prescribing of buprenorphine within the Penn Medicine Lancaster General Health network of primary care practices. Buprenorphine is a medication approved by the Food and Drug Administration (FDA) to treat OUD; the provision of the medication is associated with substantial reductions in all-cause mortality and opioid overdose deaths.[4,5]

In 2020, the American Society of Addiction Medicine (ASAM) released a focused update to their National Practice Guideline (NPG) for the treatment of OUD.[6] The release of this document was overshadowed by the COVID-19 pandemic and likely escaped the attention of many providers of buprenorphine treatment. These guidelines contain new recommendations and substantial revisions pertaining to buprenorphine initiation and medication management. The goal of this article is to highlight specific changes outlined in the ASAM NPG pertaining to buprenorphine treatment and how these may help improve the robust OUD treatment norms that already exist in our community.

THE ROLE OF PSYCHOSOCIAL ASSESSMENTS AND TREATMENT

> Comprehensive assessment of the patient is critical for treatment planning. However, completion of all assessments should not delay or preclude initiating pharmacotherapy for opioid use disorder. If not completed before initiating treatment, assessments should be completed soon thereafter.[7]

> Patients' psychosocial needs should be assessed, and patients should be offered or referred to psychosocial treatment based on their individual needs. However, a patient's decision to decline psychosocial treatment or the absence of available psychosocial treatment should not preclude or delay pharmacotherapy, with appropriate medication management.[7]

These two statements stand in stark contrast to prior guidance, which recommended a comprehensive assessment at the first visit followed by assimilation of this data to determine whether pharmacotherapy is appropriate.[8] Components of this initial assessment consisted of:

- comprehensive medical history with laboratory assessment including screening for infectious diseases,
- assessment for psychiatric disorders,
- evaluation of past and current use of all substances, and
- identification of social and environmental factors that could pose barriers to participation in treatment.[8]

Adherence to such guidance precluded prompt initiation of buprenorphine and implied justification for withholding medication from some individuals seeking treatment. The erstwhile guidelines described addiction as a "bio-psycho-social-spiritual illness"[8] and

clearly undervalued the merit of medication relative to psychosocial interventions. In the face of that background, some buprenorphine prescribers still require patients to have an intake assessment and ongoing involvement with a detached counseling provider or recovery support organization as a condition to receiving an initial and ongoing prescription for buprenorphine. This process risks gatekeeping a medication that, if expedited, may save lives.

The ASAM NPG focused update clearly recognizes the merits of affording treatment-seeking individuals prompt and ongoing access to medication like buprenorphine. That approach recognizes the lifesaving qualities associated with providing opioid-agonist treatment for OUD[4] and the superiority of these medications over other treatment pathways.[9] Psychosocial interventions can have a role in successful treatment, but there is no counseling modality that works for every patient.[10] Medication is now recognized as an effective standalone treatment for OUD.[11]

Physicians and advanced practice providers can offer buprenorphine to patients with OUD who desire treatment and provide informed consent,[7] a process that can occur in the first interaction without jeopardizing treatment retention.[12] Comprehensive assessments can take place at follow-up visits, and the treatment plan can be adjusted accordingly. All patients should be offered psychosocial treatment to give them the best chance to succeed, but buprenorphine should not be delayed, withheld, or removed from individuals who do not participate in psychosocial treatments.

PRESCRIBING NALOXONE TO ALL PATIENTS WITH OPIOID USE DISORDER

> Naloxone, for the reversal of opioid overdose, should be provided to patients being treated for, or with a history of, opioid use disorder. Patients and family members/significant others should be trained in the use of naloxone in overdose.[7]

Naloxone is a medication that rapidly reverses the effects of opioids and has long been a tool of health care providers and first responders to revive an individual on the cusp of death from opioid overdose. Although traditionally a parenteral drug, naloxone can be prescribed as an intranasal formulation, which lends itself to administration by a layperson.[13]

Prompt administration of naloxone in the face of respiratory depression and apnea due to opioid overdose can prevent irreversible brain injury or death, and it should be administered without hesitation when an opioid overdose is suspected.[14]

The nidus for the updated ASAM NPG in 2020 is the recent unprecedented rise in deaths due to unintentional opioid overdose. The new recommendation to prescribe naloxone to all patients with OUD exemplifies the focus on prevention of death as the foremost goal of treatment.

Nearly half of all opioid overdose deaths involve the presence of bystanders,[15] and this recommendation recognizes that naloxone possession and administration should not be confined solely to first responders who encounter the scene of overdose after critical time has passed. Widespread dissemination of naloxone to the public is likely to be the most effective public health intervention to reduce opioid-related deaths over the next decade.[16]

Fig. 1. A combination of buprenorphine and naloxone can be administered sublingually via tablet (8 mg, both sides shown, top) or film (8 mg shown, bottom). *Photos via Wikimedia Commons, CC BY-SA 4.0: tablet by Supertheman, film by Sintegral.*

Regarding the concern that dissemination of naloxone may make use of riskier opioids more appealing by reducing the potential for negative consequences,[17] recent history suggests otherwise. From 2016 to 2019, naloxone dispensing in the United States increased more than six-fold.[18] Yet, rates of opioid misuse declined substantially in all age categories — most dramatically among people under the age of 25 — over the same timeframe.[19] Intranasal naloxone should be prescribed alongside buprenorphine liberally and without compunction.

MEDICATION MANAGEMENT WITH BUPRENORPHINE

> Following initiation, buprenorphine dose should be titrated to alleviate symptoms. To be effective, buprenorphine dose should be sufficient to enable patients to discontinue illicit opioid use. Evidence suggests that 16 mg per day or more may be more effective than lower doses.[7]

The more senior author of this paper has consistently observed that many clinicians consider transmucosal buprenorphine doses of 16 mg per day to be a maximum dose, a rationale based in part on results of "receptor saturation studies." These studies purportedly show that a 16 mg buprenorphine dose provides nearly complete blockade of mu-opioid receptors. Several neuroimaging studies utilize positron emission tomography paired with radiolabeled tracers to describe correlations between serum buprenorphine levels and receptor availability,[20-22] but none corroborate that doses above 16 mg lack additional benefit.[23]

A full narrative of buprenorphine activity at all opioid receptors (mu, kappa, delta, and ORL-1) is beyond the scope of this article, but basic neurobiology informs us that receptor occupancy is a dynamic process wherein ligand binding exists in a state of flux between association and dissociation from the receptor. This introduces tremendous potential for heterogeneity in responses outside of the controlled setting of a research lab.

Further, there is no standard operational definition for mu-opioid blockade and there is no defined threshold of opioid receptor occupancy that correlates with clinically meaningful effects such as withdrawal suppression and attenuation of effects of illicit opioid use.[23] Neuroimaging studies serve as an important foundation for further research, but studies that describe clinically meaningful outcomes in real-world settings are far more valuable.

An appraisal of the history of methadone maintenance in the United States informs us that a similar wariness to escalate dosage above an arbitrary and suboptimal dosage cap was commonplace for its first 20 years post-FDA approval[24] despite evidence that higher doses are more effective.[25,26] The practice of capping buprenorphine dose at a fixed limit of 16 mg per day for all patients may be a sociologic phenomenon reflecting prescriber hesitation that is common to other forms of opioid substitution treatment, but it is not rooted in traditional application of principles of evidence-based medicine.

The ASAM NPG now validates that transmucosal buprenorphine doses above 16 mg per day are associated with clinically meaningful patient-oriented outcomes when compared to lower doses. Daily buprenorphine doses of 16 mg or greater are often necessary to effectively suppress illicit opioid use based on placebo-controlled trials,[27] and higher buprenorphine doses are clearly associated with better treatment retention.[28,29]

BUPRENORPHINE AND PREGNANCY

> A medical examination and psychosocial assessment are recommended when evaluating pregnant women for opioid use disorder. However, completion of all assessments should not delay or preclude initiating pharmacotherapy for opioid use disorder. If not completed before initiating treatment, assessments should be completed as soon as possible thereafter.[7]

Pregnant females are as affected by OUD as non-pregnant individuals,[30] and there is broad consensus that the life-saving benefits of buprenorphine for treating OUD extend to pregnant females and the unborn child. Clinicians should work to decrease barriers to care for this highly vulnerable subset of the population. For example, residential treatment programs may reconsider policies that delay admission to pregnant patients until completion of an ultrasound to assess gestational age.

Buprenorphine induction in the pregnant patient is essentially the same as buprenorphine induction for non-pregnant individuals. Care is taken to avoid precipitated withdrawal, and thorough instructions for starting the medication must be reviewed and understood by the patient. Home induction is feasible and does not appear to be inferior to medically supervised induction,[31,32] and this finding likely extends to pregnant females.[33]

A prevalent practice pattern that demands pregnant females complete an ultrasound before receiving pharmacotherapy and withholds the opportunity to undertake a home buprenorphine induction with informed consent is unwarranted.

> Naloxone should be used in the case of maternal overdose to save the woman's life and can be used in the combination buprenorphine/naloxone product for opioid use disorder treatment as the naloxone is minimally absorbed when taken as prescribed.[7]

Buprenorphine for the treatment of OUD became widely available in Europe in the mid-1990s.[34] When the medication became available in the United States for the treatment of OUD, buprenorphine was combined with naloxone in a 4:1 ratio to deter misuse of the product (see Fig. 1).[35] This combination of buprenorphine/naloxone became the dominant formulation for treatment of OUD in the United States.[36]

Owing to the existence of more robust experience with buprenorphine mono-product during pregnancy in Europe, a common practice pattern emerged wherein patients stabilized on buprenorphine/naloxone combination product were reflexively switched to buprenorphine upon learning of a pregnancy.

Sufficient data has emerged over the course of the past 20 years to reasonably ascertain that maternal and neonatal outcomes with buprenorphine/naloxone are not significantly different from other forms of opioid agonist treatment, including buprenorphine monotherapy.[37] Switching a pregnant female to a buprenorphine formulation that may be more prone to misuse appears to be unwarranted, thus patients who are stable on buprenorphine/naloxone treatment may continue the medication if they become pregnant.

BUPRENORPHINE AND PAIN MANAGEMENT

The addition of a short-acting full agonist opioid to the patient's regular dose of buprenorphine can be effective for the management of severe acute pain in supervised settings, such as during hospitalization. The dose of additional full agonist opioid analgesic is anticipated to be higher than the typical dose necessary to achieve adequate analgesia in opioid-naive individuals.[7]

Buprenorphine is a partial opioid agonist with a strong affinity for the mu-opioid receptor and long duration of action (see Fig. 2). These characteristics, which make it an attractive treatment option for helping a person reduce or eliminate unsafe opioid use, raise concern that the medication could block the effects of other opioid agonists that are administered to treat severe pain.

In 2004, just two years after FDA approval of buprenorphine for treatment of opioid use disorder, the U.S. Center for Substance Abuse Treatment (CSAT) provided guidance that recommended discontinuation of buprenorphine well in advance of anticipated surgery.[38,39] These CSAT guidelines, based on very limited experience, exerted long-lasting influence on practice norms, and we continue to witness inappropriate buprenorphine discontinuation in hospitalized patients and prior to surgery.

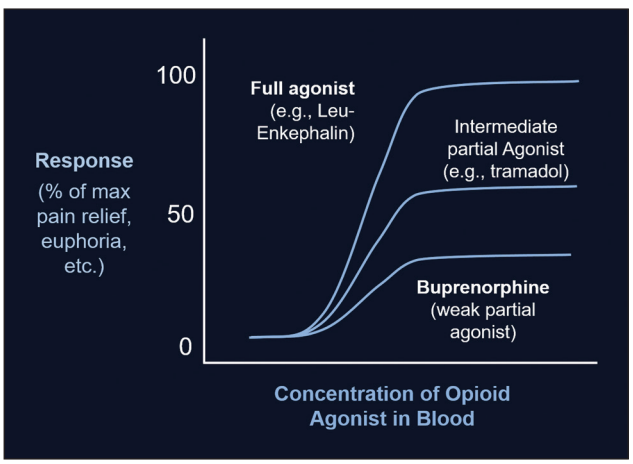

Fig. 2. This graph demonstrates how buprenorphine is a partial agonist of the mu-opioid receptor. This means that when the dose is escalated (moving to the right on the x-axis), there will be a ceiling effect for all the responses related to activation of the mu-opioid receptor. This includes euphoria, analgesia (pain relief), and respiratory depression.

Graph by Vanwa71, via Wikimedia Commons, CC BY-SA 4.0.

Buprenorphine should be continued during the perioperative period of surgery, whether planned or otherwise, and during virtually all episodes of acute pain during hospitalization. Buprenorphine discontinuation is associated with increased all-cause mortality[4] and high rates of adverse events requiring acute care.[40]

Patients are particularly at risk for drug-related overdose deaths after hospital discharge,[41] and an episode of hospitalization for any reason is a very inopportune time to discontinue buprenorphine treatment. Furthermore, post-operative pain management is likely to be more challenging when buprenorphine is discontinued because patients will require significantly more opioid analgesics after surgery.[42]

Multi-modal analgesia and non-opioid pain management interventions should still be utilized first line, although a full discussion of pain management for patients taking buprenorphine is beyond the scope of this article. Yet, we support and encourage the principle that buprenorphine should almost always be continued during hospitalization at a dose that suppresses opioid withdrawal symptoms and preserves treatment retention. For persistent moderate to severe pain in the face of conservative modalities, additional opioid analgesics can be administered and the dose adjusted to achieve the desired effect in hospital-based settings.

BUPRENORPHINE IN JAILS AND PRISONS

All FDA-approved medications for the treatment of opioid use disorder should be available to individuals receiving health care within the criminal justice system.[7]

As of 2017, fewer than 1% of jails and prisons in the United States offered access to buprenorphine treatment,[43] although we have known for at least 15 years that nearly 20% of individuals who enter the correctional system report regular use of opioids.[44] Release from these institutions is associated with 129-fold increased risk of death from drug overdose.[45]

Negative attitudes among correctional staff toward buprenorphine treatment[46,47] likely play a role in restrictions, but the relatively large number of individuals with problematic opioid use within these institutions may pose a more taxing barrier to implementation of this recommendation. National estimates indicate that fewer than 5% of people in the

community misuse opioids and less than 1% have an opioid use disorder.[19] However, most of these individuals report involvement with the criminal justice system,[48] and periods of incarceration are common.[49] Jails and prisons often become repositories which house a high concentration of individuals with opioid use disorder. During the final six months of 2021, more than 20% of all individuals entering Lancaster County Prison required treatment for opioid withdrawal.[50] This disparity in disease burden highlights a need to direct more resources toward treatment of opioid use disorder in correctional settings.

In a recent survey of 23 state prison systems most heavily impacted by opioid overdose deaths (Pennsylvania among them), lack of funds for medication provision was the most frequently cited barrier to providing medication for opioid use disorder.[51] The Social Security Amendments of 1965 prohibit states and counties from using federal Medicaid funds to provide health care to incarcerated individuals. Local governments bear the cost of providing medical care to incarcerated individuals in non-federal prisons. Legislative reform of this decades-old provision could substantially improve the health of incarcerated people[52] and allow for more strategic allocation of federal health care dollars to fund buprenorphine treatment in jails and prisons.

We agree that all medications for opioid use disorder should be available in correctional institutions. Such measures clearly have potential to produce a sizable reduction in fatal overdose associated with community reentry.[53,54] Practical implementation of this recommendation requires increasing subsidies for medication treatment in carceral settings and offering alternatives to incarceration for individuals with opioid use disorder.

CONCLUSION

The 2020 focused update of the ASAM NPG for the treatment of OUD reflects a shift toward prioritization of access to treatment and recognition that medication can be an effective standalone intervention. We should eliminate fragmented and cumbersome intake processes for treatment-seeking individuals to avoid delays in implementation of potentially life-saving medication. Further, psychosocial interventions and recovery support services should not be compulsory nor a condition for receiving medication.

Once initiated, medical management of buprenorphine should be guided by studies that describe clinically meaningful patient-oriented outcomes, and providers should recognize that some patients will do better with higher doses of buprenorphine. Take-home naloxone should be co-prescribed liberally and without hesitation or fear that it will cultivate further opioid misuse. These principles extend to special populations such as pregnant patients, people with acute pain, and those involved in the criminal justice system.

We have an excellent foundation of primary care practices in our community providing buprenorphine treatment to combat our current epidemic of opioid-related overdose deaths. The next stage to winning that fight involves changing prevalent practice norms in the face of new information and aligning buprenorphine treatment of opioid use disorder with these updated national practice guidelines.

REFERENCES

1. Ahmad FB, Cisewski JA, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2022. Accessed June 28, 2022. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm
2. Pennsylvania Office of Drug Surveillance and Misuse Prevention (ODSMP) – Drug Overdose Surveillance Interactive Data Report. Accessed June 28, 2022. https://public.tableau.com/app/profile/pennsylvania.pdmp/viz/PennsylvaniaODSMPDrugOverdoseSurveillanceInteractiveDataReport/Contents
3. Tawil T. Reducing overdose deaths in Lancaster County: the rise of an epidemic, and LGH's response. *JLGH.* 2019;14(3):68-75.
4. Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ.* 2017;357:j1550.
5. Larochelle MR, Bernson D, Land T, et al. Medication for opioid use disorder after nonfatal opioid overdose and association with mortality: a cohort study. *Ann Intern Med.* 2018;169(3):137-145.
6. Crotty K, Freedman KI, Kampman KM. Executive summary of the focused update of the ASAM national practice guideline for the treatment of opioid use disorder. *J Addict Med.* 2020;14(2):99-112.
7. The ASAM national practice guideline for the treatment of opioid use disorder: 2020 focused update [published correction appears in J Addict Med. 2020;14(3):267]. *J Addict Med.* 2020;14(2S Suppl 1):1-91.
8. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) national practice guideline for the use of medications in the treatment of addiction involving opioid use. *J Addict Med.* 2015;9(5):358-367.
9. Wakeman SE, Larochelle MR, Ameli O, et al. Comparative effectiveness of different treatment pathways for opioid use disorder. *JAMA Netw Open.* 2020;3(2):e1920622.
10. Dugosh K, Abraham A, Seymour B, McLoyd K, Chalk M, Festinger D. A systematic review on the use of psychosocial interventions in conjunction with medications for the treatment of opioid addiction. *J Addict Med.* 2016;10(2):93-103.
11. Friedmann PD, Schwartz RP. Just call it "treatment." *Addict Sci Clin Pract.* 2012;7(1):10.
12. Jakubowski A, Lu T, DiRenno F, et al. Same-day vs. delayed buprenorphine prescribing and patient retention in an office-based buprenorphine treatment program. *J Subst Abuse Treat.* 2020;119:108140.
13. Ortega R, Nozari A, Baker W, Surani S, Edwards M. Intranasal naloxone administration. *N Engl J Med.* 2021;384(12):e44.
14. Boyer EW. Management of opioid analgesic overdose. *N Engl J Med.* 2012;367(2):146-155.
15. Mattson CL, O'Donnell J, Kariisa M, Seth P, Scholl L, Gladden RM. Opportunities to prevent overdose deaths involving prescription and illicit opioids, 11 states, July 2016–June 2017. *MMWR.* 2018;67(34):945–951.

16. Rao IJ, Humphreys K, Brandeau ML. Effectiveness of policies for addressing the U.S. opioid epidemic: a model-based analysis from the Stanford-Lancet Commission on the North American Opioid Crisis. *Lancet Reg Health Am.* 2021;3:100031.
17. Frank RG, Humphreys K, Pollack HA. Does naloxone availability increase opioid abuse? The case for skepticism. *Health Affairs.* 2018. Accessed March 3, 2022. https://www.healthaffairs.org/do/10.1377/hblog20180316.599095/full/
18. Guy GP Jr, Khushalani JS, Jackson H, Sims RSC, Arifkhanova A. Trends in state-level pharmacy-based naloxone dispensing rates, 2012-2019. *Am J Prev Med.* 2021;61(6):e289-e295.
19. Han B. *Key substance use and mental health indicators in the United States: results from the 2019 National Survey on Drug Use and Health.* Rockville, MD: Substance Abuse and Mental Health Services Administration; 2020.
20. Zubieta J, Greenwald MK, Lombardi U, et al. Buprenorphine-induced changes in mu-opioid receptor availability in male heroin-dependent volunteers: a preliminary study. *Neuropsychopharmacology.* 2000;23(3):326-334.
21. Greenwald MK, Johanson CE, Moody DE, et al. Effects of buprenorphine maintenance dose on mu-opioid receptor availability, plasma concentrations, and antagonist blockade in heroin-dependent volunteers. *Neuropsychopharmacology.* 2003;28(11):2000-2009.
22. Greenwald M, Johanson CE, Bueller J, et al. Buprenorphine duration of action: mu-opioid receptor availability and pharmacokinetic and behavioral indices. *Biol Psychiatry.* 2007;61(1):101-110.
23. Greenwald MK, Comer SD, Fiellin DA. Buprenorphine maintenance and mu-opioid receptor availability in the treatment of opioid use disorder: implications for clinical use and policy. *Drug Alcohol Depend.* 2014;144:1-11.
24. U.S. General Accounting Office. *Methadone maintenance: some treatment programs are not effective; greater federal oversight needed.* Washington, DC: U.S. General Accounting Office; 1990.
25. Strain EC, Stitzer ML, Liebson IA, Bigelow GE. Dose-response effects of methadone in the treatment of opioid dependence. *Ann Intern Med.*1993;119:23-27.
26. Strain EC, Bigelow GE, Liebson IA, Stitzer ML. Moderate- vs. high-dose methadone in the treatment of opioid dependence: a randomized trial. *JAMA.* 1999;281(11):1000-1005.
27. Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev.* 2014;(2):CD002207.
28. Hser YI, Saxon AJ, Huang D, et al. Treatment retention among patients randomized to buprenorphine/naloxone compared to methadone in a multi-site trial. *Addiction.* 2014;109(1):79-87.
29. Fareed A, Vayalapalli S, Casarella J, Drexler K. Effect of buprenorphine dose on treatment outcome. *J Addict Dis.* 2012;31(1):8-18.
30. Committee opinion no. 711: opioid use and opioid use disorder in pregnancy. *Obstet Gynecol.* 2017;130(2):e81-e94.
31. Lee JD, Grossman E, DiRocco D, Gourevitch MN. Home buprenorphine/naloxone induction in primary care. *J Gen Intern Med.* 2009;24(2):226-232.
32. Sohler NL, Li X, Kunins HV, et al. Home- versus office-based buprenorphine inductions for opioid-dependent patients. *J Subst Abuse Treat.* 2010;38(2):153-159.
33. Kelly JC, Raghuraman N, Stout MJ, et al. Home induction of buprenorphine for treatment of opioid use disorder in pregnancy. *Obstet Gynecol.* 2021;138(4):655-659.
34. European Monitoring Centre for Drugs and Drug Addiction. 2005 annual report. Accessed March 13, 2022. https://www.emcdda.europa.eu/publications/selected-issues/buprenorphine_en
35. Chiang CN, Hawks RL. Pharmacokinetics of the combination tablet of buprenorphine and naloxone. *Drug Alcohol Depend.* 2003;70(2 Suppl):S39-S47.
36. Jones HE. Practical considerations for the clinical use of buprenorphine. *Sci Pract Perspect.* 2004;2(2):4-20.
37. Link HM, Jones H, Miller L, Kaltenbach K, Seligman N. Buprenorphine-naloxone use in pregnancy: a systematic review and metaanalysis. *Am J Obstet Gynecol MFM.* 2020;2(3):100179.
38. Lembke A, Ottestad E, Schmiesing C. Patients maintained on buprenorphine for opioid use disorder should continue buprenorphine through the perioperative period. *Pain Med.* 2019;20(3):425-428.
39. Haber LA, DeFries T, Martin M. Things We Do for No Reason™: discontinuing buprenorphine when treating acute pain. *J Hosp Med.* 2019;14(10):633-635.
40. Williams AR, Samples H, Crystal S, Olfson M. Acute care, prescription opioid use, and overdose following discontinuation of long-term buprenorphine treatment for opioid use disorder. *Am J Psychiatry.* 2020;177(2):117-124.
41. White SR, Bird SM, Merrall EL, Hutchinson SJ. Drugs-related death soon after hospital-discharge among drug treatment clients in Scotland: record linkage, validation, and investigation of risk-factors. *PLoS One.* 2015;10(11):e0141073.
42. Macintyre PE, Russell RA, Usher KA, Gaughwin M, Huxtable CA. Pain relief and opioid requirements in the first 24 hours after surgery in patients taking buprenorphine and methadone opioid substitution therapy. *Anaesth Intensive Care.* 2013;41(2):222-230.
43. Williams T. Opioid users are filling jails. Why don't jails treat them? *The New York Times.* August 4, 2017. Accessed June 6, 2022. https://www.nytimes.com/2017/08/04/us/heroin-addiction-jails-methadone-suboxone-treatment.html
44. Bronson J, Stroop J, Zimmer S, Berzofsky M. Drug use, dependence, and abuse among state prisoners and jail inmates, 2007-2009. Washington, DC: Bureau of Justice Statistics, U.S. Department of Justice. 2017. Accessed June 6, 2022. https://bjs.ojp.gov/content/pub/pdf/dudaspji0709.pdf
45. Binswanger IA, Stern MF, Deyo RA, et al. Release from prison — a high risk of death for former inmates [published correction appears in N Engl J Med. 2007;356(5):536]. *N Engl J Med.* 2007;356(2):157-165.
46. Nunn A, Zaller N, Dickman S, Trimbur C, Nijhawan A, Rich JD. Methadone and buprenorphine prescribing and referral practices in U.S. prison systems: results from a nationwide survey [published correction appears in Drug Alcohol Depend. 2011;113(2-3):252]. *Drug Alcohol Depend.* 2009;105(1-2):83-88.
47. Friedmann PD, Hoskinson R, Gordon M, et al. Medication-assisted treatment in criminal justice agencies affiliated with the criminal justice-drug abuse treatment studies (CJ-DATS): availability, barriers, and intentions. *Subst Abus.* 2012;33(1):9-18.
48. Winkelman TN, Chang VW, Binswanger IA. Health, polysubstance use, and criminal justice involvement among adults with varying levels of opioid use. *JAMA Netw Open.* 2018;1(3):e180558.
49. Boutwell AE, Nijhawan A, Zaller N, Rich JD. Arrested on heroin: a national opportunity. *J Opioid Manag.* 2007;3(6):328-332.
50. Lancaster Prison Board. Meeting minutes. February 17, 2022. Accessed June 26, 2022. http://www.co.lancaster.pa.us
51. Scott CK, Dennis ML, Grella CE, Mischel AF, Carnevale J. The impact of the opioid crisis on U.S. state prison systems. *Health Justice.* 2021;9(1):17.
52. Khatri UG, Winkelman TNA. Strengthening the Medicaid Reentry Act — supporting the health of people who are incarcerated. *N Engl J Med.* 2022;386(16):1488-1490.
53. Green TC, Clarke J, Brinkley-Rubinstein L, et al. Postincarceration fatal overdoses after implementing medications for addiction treatment in a statewide correctional system. *JAMA Psychiatry.* 2018;75(4):405-407.
54. Marsden J, Stillwell G, Jones H, et al. Does exposure to opioid substitution treatment in prison reduce the risk of death after release? A national prospective observational study in England. *Addiction.* 2017;112(8):1408-1418.

Marco Cunicelli, DO
Family Medicine Residency Program
Penn Medicine Lancaster General Health
540 N. Duke St.
Lancaster, PA 17602
717-544-4950
Marco.Cunicelli@pennmedicine.upenn.edu

Jon Lepley, DO
Addiction Medicine
Penn Medicine Lancaster General Health Physicians
609 N. Cherry St.
Lancaster, PA 17602
717-544-2120
Jon.Lepley@pennmedicine.upenn.edu