



Are Pharmacists Helping or Hurting Patients?

A Look at Buprenorphine/Naloxone in the Treatment of
Opioid Use Disorder

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Objectives

1. Review medication-assisted therapy in the treatment of opioid use disorder (OUD).
2. Examine the benefits and risks associated with the use of buprenorphine in the treatment of OUD.
3. Discuss the barriers patients face when trying to obtain buprenorphine.
4. Discuss the role pharmacists can have in medication-assisted therapy of OUD.



**WE EXIST TO
EMPOWER
WOMEN FOR
LIFETIME
RECOVERY.**

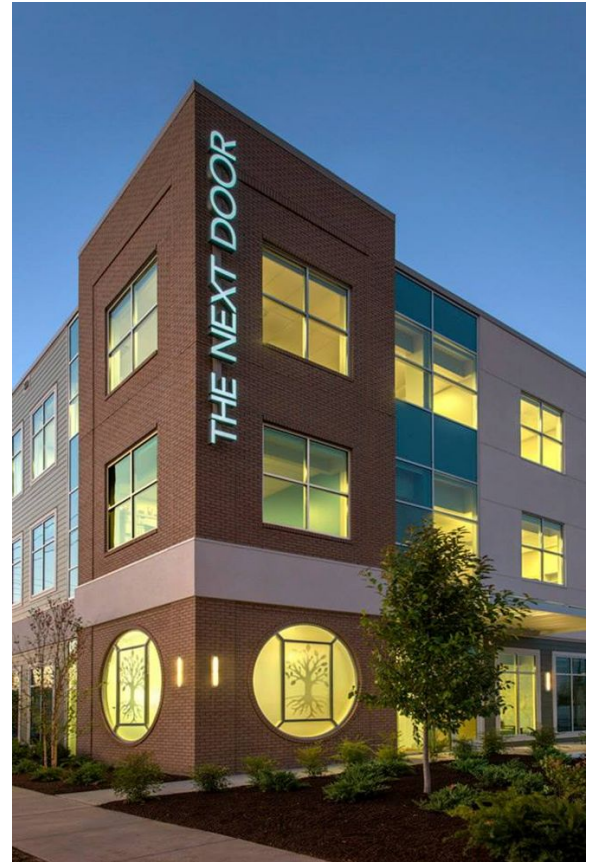


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Background- Substance Use Disorder

- Addiction is a Disease
 - Preventable
 - Treatable
- Factors Increasing Risk
 - Biological, Environmental, Others
- Targets the brain's reward system

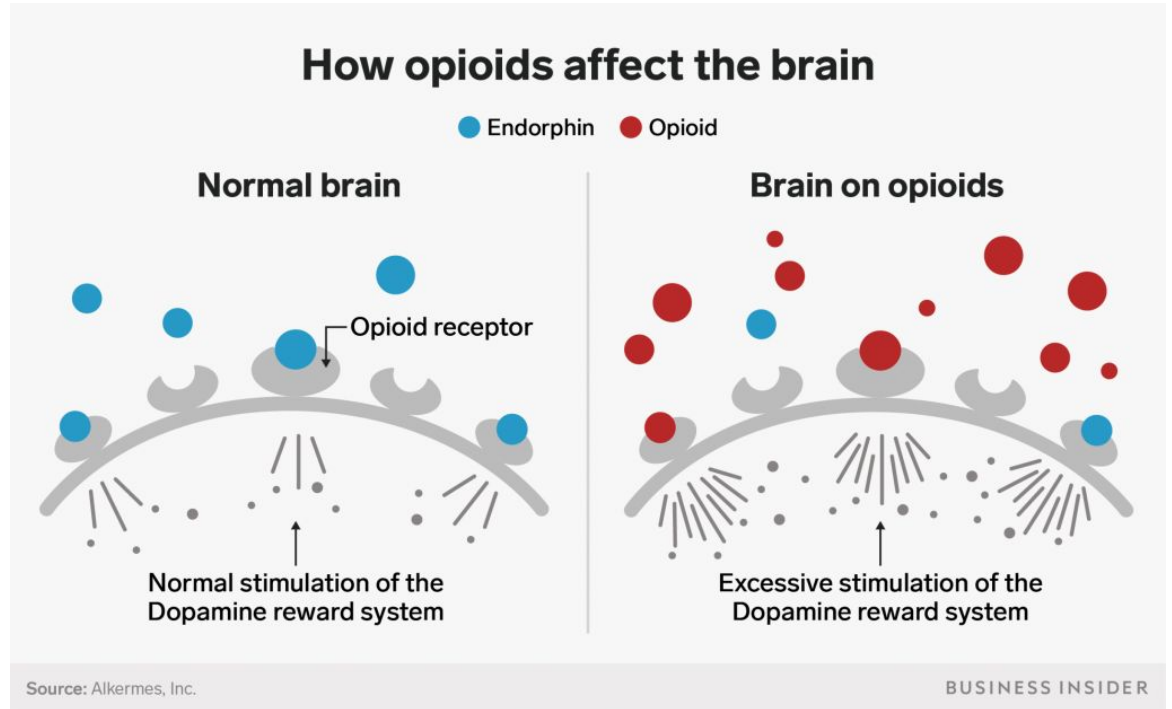


Image Credit: <https://static1.businessinsider.com/image/5b3283e51ae66234008b49b6-2400/the-brain-and-opioid-use-illustration.png>

Impact on the Brain

- Imaging has shown:
 - Opioid dependence causes bilateral volumetric loss in the amygdala
 - Implicated in regulation of affect and impulse control and reward and motivational functions
 - Decreased functional connectivity and ability of axonal pathways to change and dendritic spines begin to disappear
 - Longer use of prescription opioid exposure was associated with greater changes
 - Trouble reasoning and thinking through problems

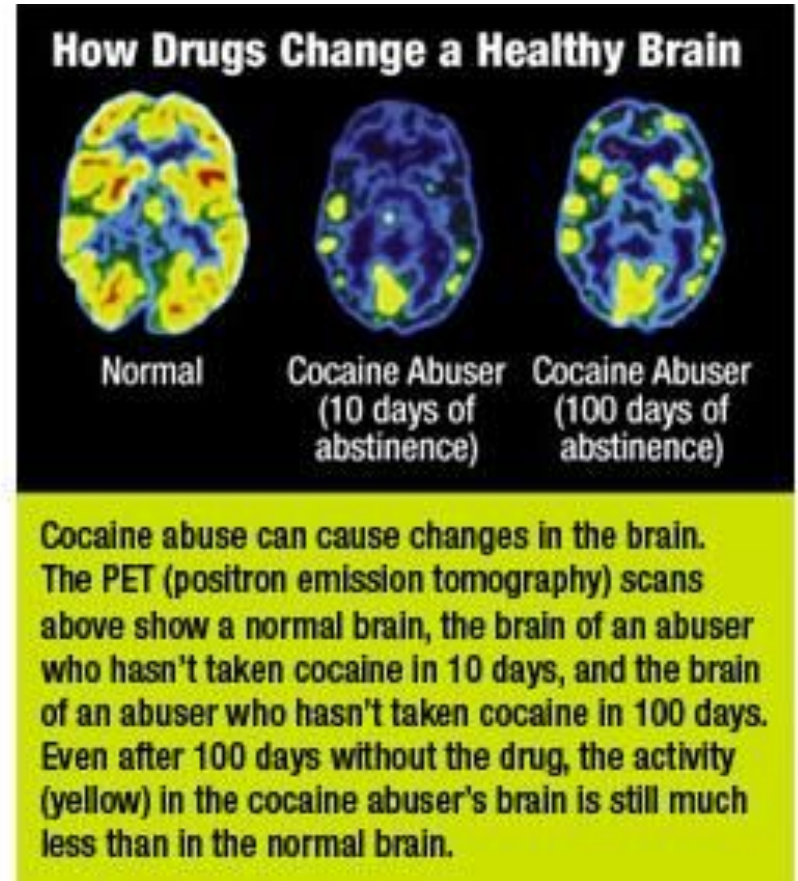


Image credit: <http://headsup.scholastic.com/students/the-science-of-addiction>

Upadhyay J, Maleki N, Potter J, et al. Alterations in brain structure and functional connectivity in prescription opioid-dependent patients. *Brain* 2010;133:2098-2114.

Haydon I. How opioids reshape your brain, and what scientists are learning about addiction. *The Philadelphia Inquirer*. 2018. Available at:

<https://medicalxpress.com/news/2018-08-opioids-reshape-brain-scientists-addiction.html>

Impact on the Brain

Short-Term

- Fatigue
- Numbness (absence of pain)
- Euphoria
- Drowsiness
- Lethargy
- Nausea



Long-Term

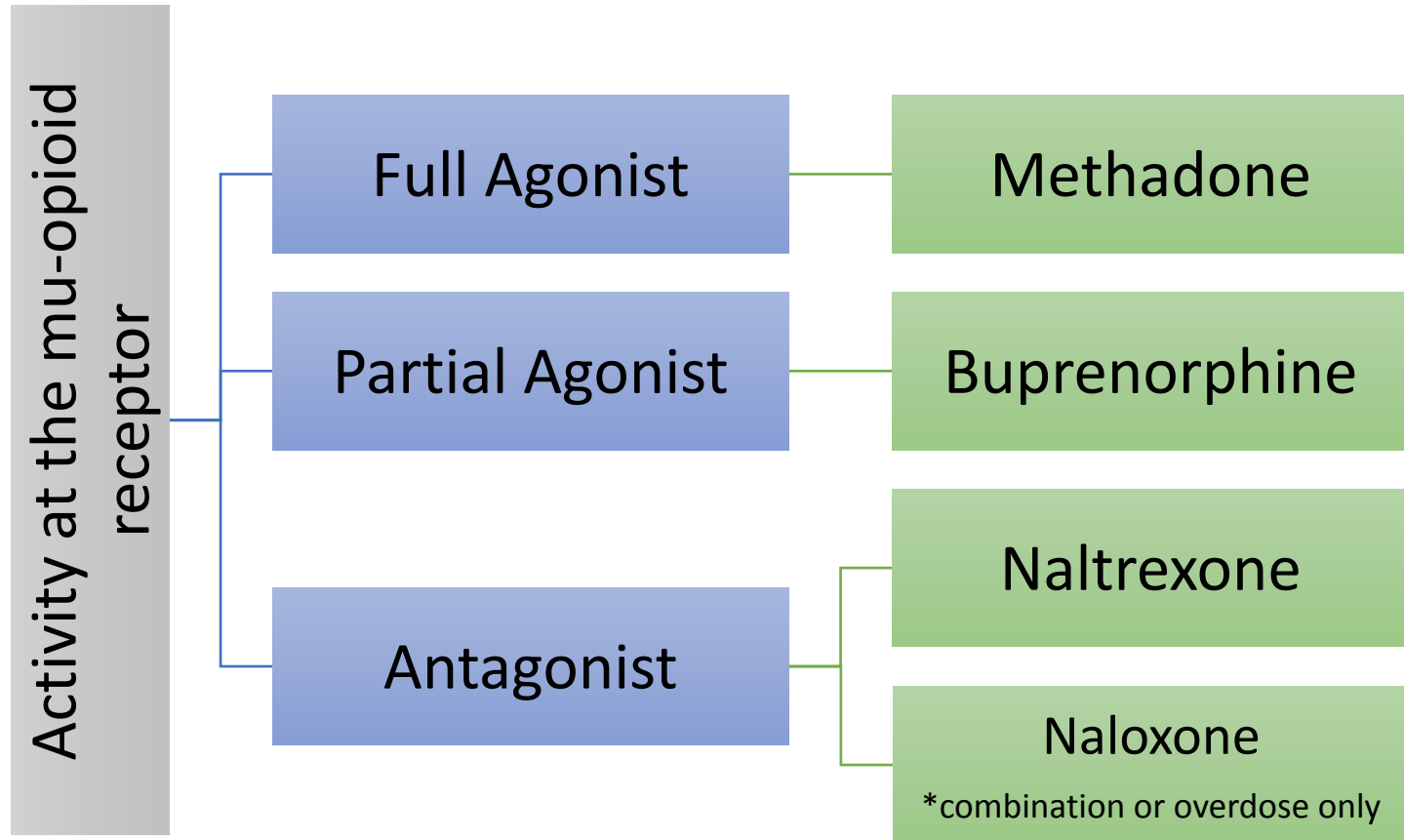
- Irritability
- Hallucinations
- Hypoxia
- Anxiety
- Depression
- Possible Hyperalgesia

Medication-Assisted Therapy

Also known as “MAT”

Use of medications, in combination with counseling and behavioral therapies, to provide a “whole-patient” approach to the treatment of substance use disorders

MAT in Opioid-Use Disorder



Methadone

- Schedule II controlled substance
- Oral dosage form
- Medically supervised withdrawal and maintenance
 - Controls cravings and blunts euphoria from illicit opioids
- Long-acting, usually 24-36 hours
 - Wide individual variability in half-life (8 to 59 hours)
 - Reaches steady state in about 5 days
- Individualized dosing □ begin low dose and gradually increase with daily monitoring over days to weeks
- Therapeutic dose is 80-120 mg daily

Methadone

Common Adverse Effects

- Sweating
- Constipation
- Respiratory depression- especially with alcohol and benzodiazepines

Drug-Drug interactions

- With medications metabolized by CYP3A4, 2B6, 2C19
- Other medications that can cause respiratory depression

Cautions

- Prolonged QT interval
- Hepatic impairment- key role in metabolism
 - Start low and go slow
- Overdose can be fatal

Buprenorphine

- Subutex[®]
 - Buprenorphine sublingual tablets
- Bunavail[®], Suboxone[®], Zubsolv[®]
 - Buprenorphine sublingual tablets, film *with* naloxone
- Typical therapeutic dose orally: 8-16 mg daily
- Probuphine[®]
 - 6 month subcutaneous implant
- Sublocade[®]
 - Monthly abdominal subcutaneous injection
 - Typical therapeutic dose: 100 mg

Buprenorphine

- Schedule III controlled substance
 - Requires a DATA 2000 waiver to prescribe for OUD
<https://www.samhsa.gov/medication-assisted-treatment/become-buprenorphine-waivered-practitioner>
- Medically supervised withdrawal and maintenance
 - Initiate around 12-24 hours after last opioid or can precipitate withdrawal- typically follow COWS score
 - Given with naloxone in maintenance
- Effective/maintenance dose is the dose that prevents withdrawal symptoms and cravings
- Long elimination half-life (24 to 69 hours)

Buprenorphine

Common Adverse Effects

- Nausea, Vomiting, Dizziness, Constipation
- Peripheral edema, sedation
- Mild euphoria

Drug-Drug Interactions

- With CYP450 3A4 enzymes
- Other medications that can cause respiratory depression

Cautions

- Sedative effects (confusion, extreme sleepiness, breathing issues)
 - Especially with benzodiazepines, alcohol, other CNS depressants
- Severe liver impairment- monitor liver
 - Combo product not recommended
 - Mono- product should reduce starting and titration dose by half

Naltrexone

- ReVia® (50 mg oral tablets)
- Vivitrol® (380 mg extended-release injection every 28 days)- IM gluteal

- Antagonist
 - Reduces opioid cravings
 - No euphoria or sedative effects of opioids if patient were to take some

- Prevention of relapse following medically supervised withdrawal

- Not a control substance and not addictive

- Patients need to be opioid free for at least 3-14 days before starting (depending on opioid used) or precipitate withdrawal

Naltrexone

Common Adverse Effects

- Nausea, vomiting, anxiety, insomnia, suicidality, anorexia, fatigue
- Injection site reactions: pain, swelling, cellulitis, abscess, necrosis (surgical intervention)

Drug-Drug Interactions

- Minimal

Cautions

- Risk of overdose
- Hepatotoxicity- increase in liver enzymes; monitor
 - Can cause hepatic injury; can cause further injury in patients with liver dysfunction
 - No dose adjustment with mild/moderate impairment
- Depression/ Suicidality- monitor for symptoms

Comparing MAT Benefits

Table 3. Summary of benefits of treatment by medication^{12,21,22,25-31}

	Buprenorphine	Methadone	Naltrexone XR
Reduced mortality (primarily by opioid overdose)	✓	✓	?
Treatment retention	✓	✓	✓
Reduced illicit opioid use	✓	✓	✓
Reduced opioid cravings	✓	✓	✓
Improved patient health and well-being	✓	✓	?

✓: benefit of treatment; ?: neutral or no effect

Diving Deeper into the Use of Buprenorphine in the Treatment of OUD

Buprenorphine- Risks

Diversion

- Availability on streets and in prisons without a prescription
 - Biggest risk factor: Inability to access treatment
- Diversion goes down with access
- Most often used for therapeutic purposes:
 - reduce withdrawal, reduce heroin use, prevent cravings, save money

Misuse

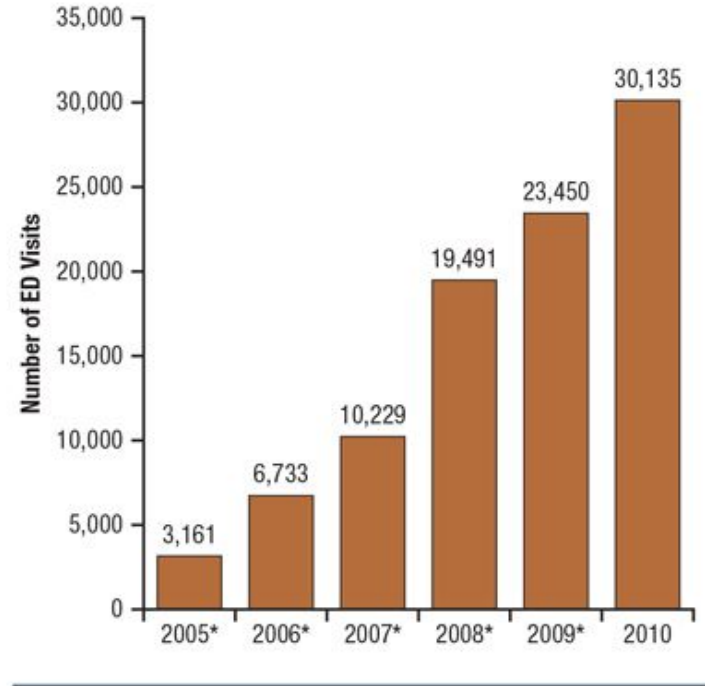
- Taking more than prescribed
 - Overdose risk increase if taken with benzodiazepines or alcohol
- Taking it for euphoria (estimated only 8-25% of people use for this reason)

Medical Complications

- IV use
 - Infectious endocarditis
 - Cutaneous abscesses
 - Osteoarticular infections
 - Meningitis
 - Retinitis
- Emergency Room Visits...

Emergency Department Visits for Buprenorphine

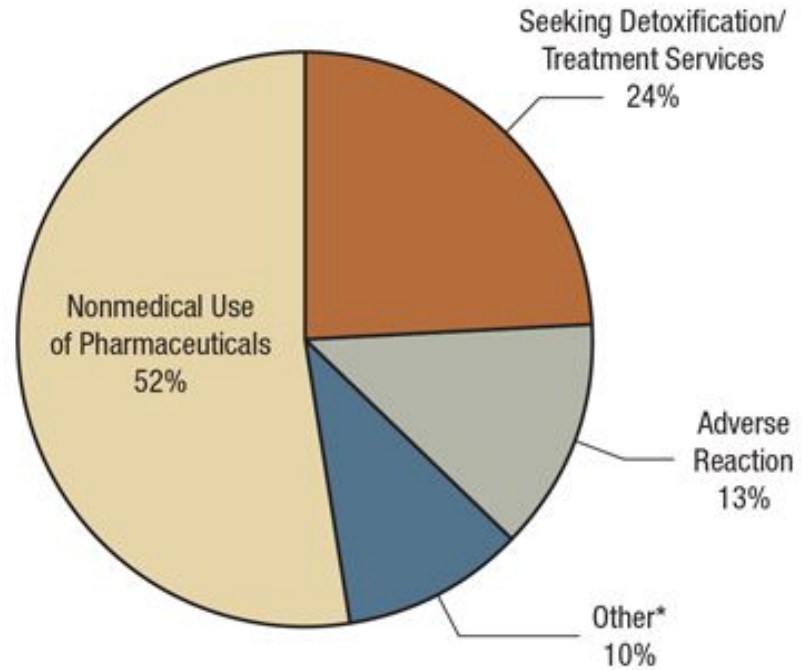
- ED Visits Increased from 2005 to 2010
- FDA approved buprenorphine for use in opioid use disorder in 2002
- From 2005 to 2010:
 - Increase in availability of buprenorphine by certified physicians- 3-fold increase
 - Increase in number of patients who received- 8 fold increase
 - Increase in number of treatment facilities-231% increase



* The estimate was statistically significantly different from the estimate for 2010 at the .05 level.

Source: 2005 to 2010 SAMHSA Drug Abuse Warning Network (DAWN).

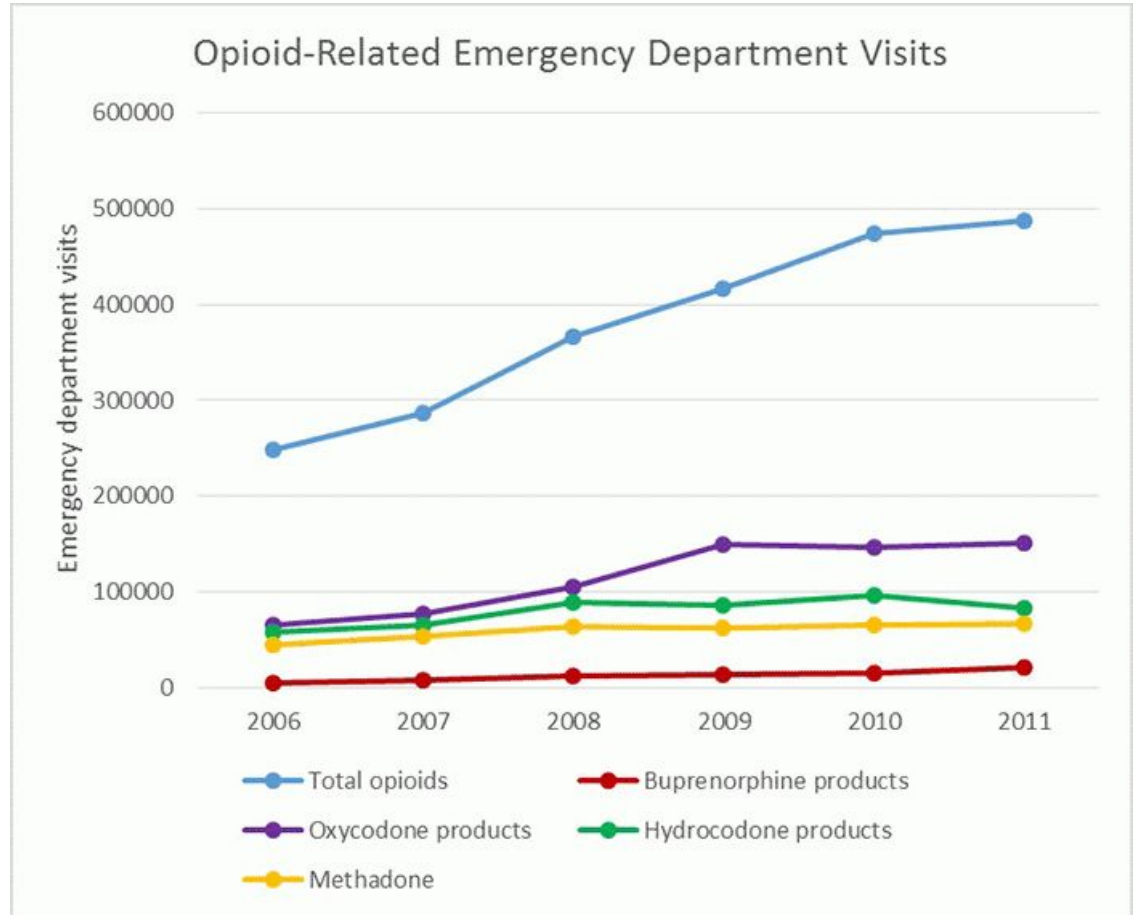
Emergency Department Visits for Buprenorphine- Type of Visit; 2010



* Other types of visits include accidental ingestion and suicide attempts. Because of rounding, percentages do not add to 100.

Source: 2010 SAMHSA Drug Abuse Warning Network (DAWN).

Overall Picture

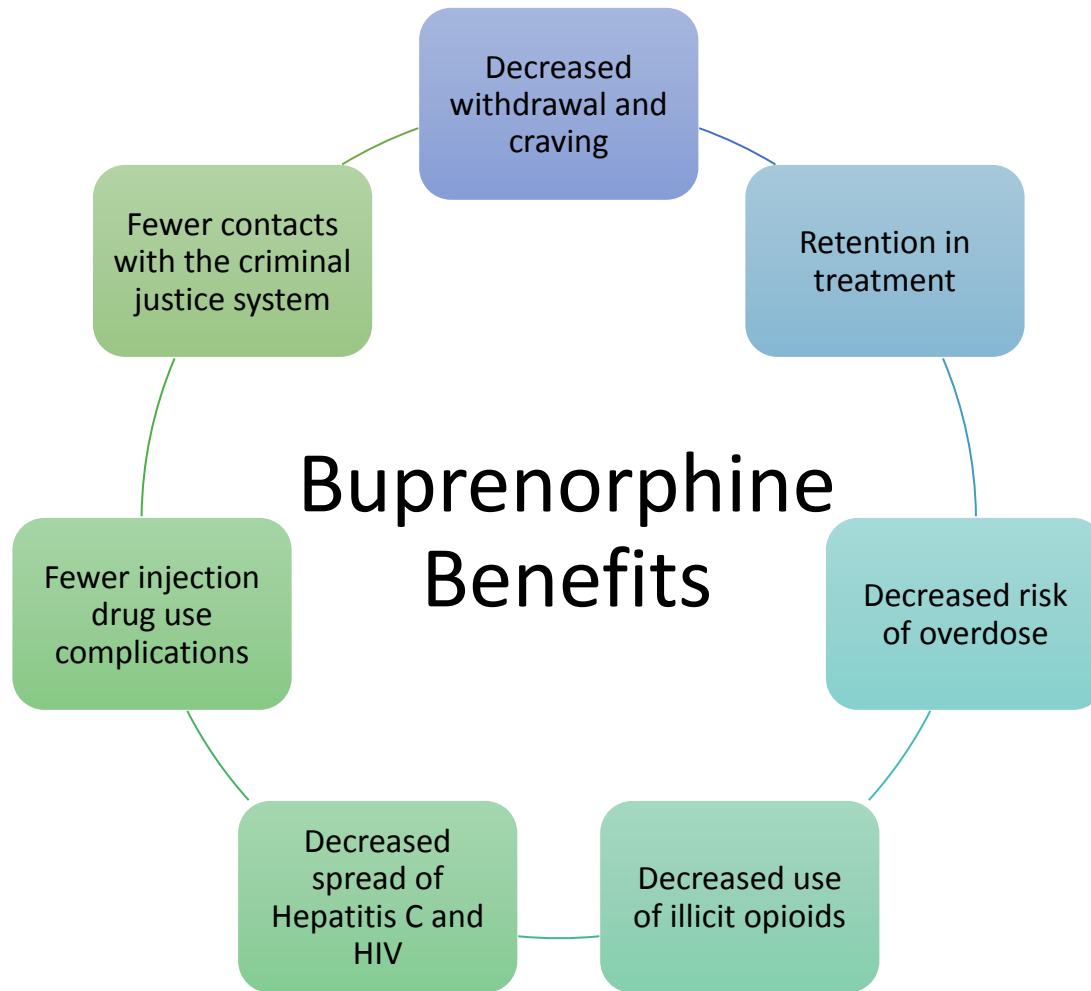


Buprenorphine Diversion- Limited Harm?

- Study by RG Carlson, et al. (2020)
- Demographics of 356 participants:
 - 89% white, 50.3% male, 78.1% at least high school education; Mean age was 39.2 years
 - 25.8% employed; 54.8% considered themselves homeless in past 6 months
 - 27% ($n = 98$) reported overdose (OD) in the previous six months
 - 62.3% reported at least one prior OD
 - 95.5% reported OD due to heroin/non-prescribed fentanyl or non-prescribed opioids
 - Close to 90% reported using non-prescribed buprenorphine for self-treatment of withdrawal symptoms
 - 56.9% reported selling buprenorphine to someone else and 47.9% given buprenorphine prescribed to them to someone else

Buprenorphine Diversion- Limited Harm?

- Results:
 - Greater frequency (mean percentage of days) of non-prescribed buprenorphine use
 - Significantly associated with lower risk of overdose in past 6 months (AOR = 0.81, 95% CI = 0.66, 0.98; $p = .0286$)
- Secondary analyses showed
 - Individuals who used non-prescribed buprenorphine for more than 10 days had 33% lower odds of OD
 - Taking buprenorphine for 2-3 days out of 6 months reduced odds of OD by 20% compared to 1 day
 - Greater frequency of buprenorphine use lower frequency of heroin/fentanyl



Barriers to Buprenorphine- Patient

Acceptance

- Self with having opioid-use disorder and desire for treatment
- Peer acceptance

Induction onto buprenorphine

Insurance coverage

Lack of mental health or psychosocial support- entering back into society

Missing appointments- work/childcare issues

Barriers to Buprenorphine- Patient

Access to a provider

- 60.1% of rural counties in United States lack a physician with a DEA waiver to prescribe
- Research showed waived clinicians who were able to provide care
 - To 275, 100 and 30 patient-clients, showed they prescribed for a median of 101.5 (36.9%), 23.9, or 3.3 (11.3%) patients, respectively, for their patient limit
 - Providers actively prescribing:
 - 38.9% in the 30 patient-clients
 - 2-fold percentage increase over the 30 patient-clients in the 100 or 275 patient-clients

Transportation and travel time

Andrilla CHA, Coulthard C, Larson EH. Barriers Rural Physicians Face Prescribing Buprenorphine for Opioid Use Disorder. *Ann Fam Med*. 2017 Jul;15(4):359-362.

Duncan A, Anderman J, Deseran T, Reynolds I, Stein BD. Monthly Patient Volumes of Buprenorphine-Waivered Clinicians in the US. *JAMA Netw Open*. 2020;3(8):e2014045.

Durkin M. Breaking barriers to buprenorphine. *ACP Internist*. <https://acpinternist.org/archives/2018/09/breaking-barriers-to-buprenorphine.htm>. Published September 1, 2018. Accessed May 13, 2021.

Barriers to Buprenorphine- Prescriber

Insufficient training,
education and
experience

- Inadequate resources

Lack of institutional
support and clinician
peer support

Poor care
coordination

- Lack of time
- Referral for counseling

Reimbursement

- Prior authorizations
- Lifetime limits

Burdensome regulatory
procedures

- Number of patients able to prescribe to
- Waiver training course
- Record Keeping

Provider stigma

Barriers to Buprenorphine- Pharmacists

- Supply policies
 - Drug Enforcement Agency and The SUPPORT for Patients and Communities Act of 2018
 - Requires wholesalers to detect and report suspicious orders of opioids

Wholesalers-
monitor pharmacy
orders and
establish order
thresholds



DEA investigation
if exceed
thresholds



Every prescription
filled closer to this
“cap” and
investigation

- Central Appalachia research
- 12 of 15 pharmacies limit dispensing by refusing new patients, limiting to current patients or refusing to dispense altogether

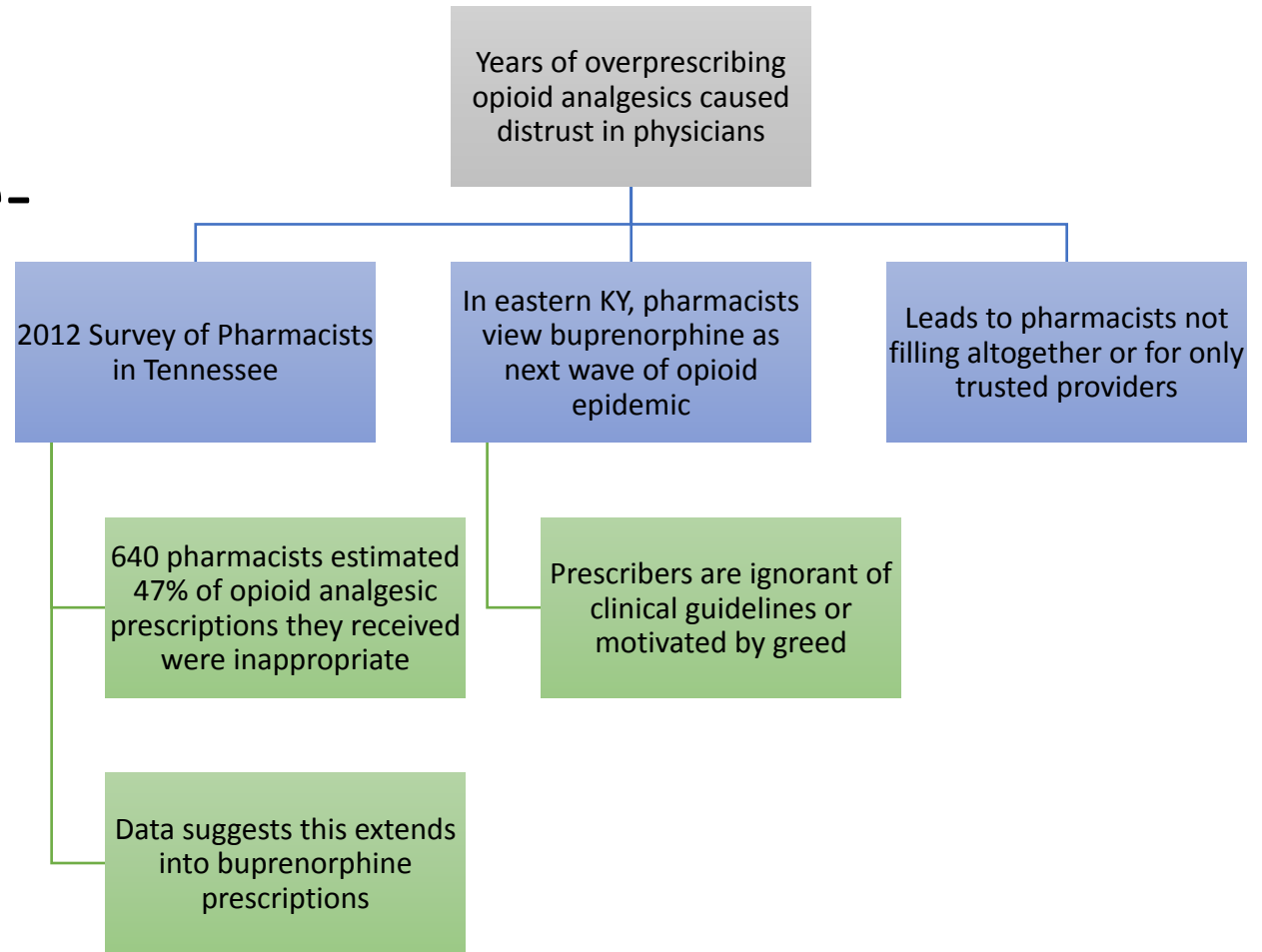


Pharmacists
developed
rationing systems,
turning away new
patients to ensure
consistent supply
available for
current patients,
or refusing to fill

Barriers to Buprenorphine- Pharmacists



Barriers to Buprenorphine-Pharmacists



Hagemeier NE, Murawski MM, Lopez NC, Alamian A, Pack RP. Theoretical exploration of Tennessee community pharmacists' perceptions regarding opioid pain reliever abuse communication. *Res Social Adm Pharm.* 2014;10:562-75.

Cooper HL, Cloud DH, Freeman PR, et al. Buprenorphine dispensing in an epicenter of the U.S. opioid epidemic: a case study of the rural risk environment in Appalachian Kentucky. *Int J Drug Policy.* 2020;85:102701.

Barriers to Buprenorphine- Pharmacists

- Willingness to dispense buprenorphine

Research by Thornton JD, et al. (2016)

- About 80% were pharmacies in West Virginia
- Found 46.7% of pharmacists did not stock buprenorphine and 25.2% did not stock buprenorphine/naloxone
- More likely to fill an opioid analgesic prescription for a patient not living in pharmacy's local area or from out-of-state provider than buprenorphine
- Pharmacists estimated a mean of 23.6 out of 100 patients filling Rx's misuse the medication

Research by Kazerouni NJ, et al. (2021)

- Contacted one independent and one chain in 473 US counties with opioid overdose mortality rates that exceed U.S. average
- Total of 921 pharmacies contacted
 - 467 chain, 454 independent
- Results:
 - 1 in 5 pharmacies (183) indicated they were unable or unwilling to fill a buprenorphine Rx entirely
 - 7% would not disclose availability over the phone
 - Buprenorphine access barriers more common in independent pharmacies and pharmacies located in Southern states
 - 1 in 4 unable or unwilling to dispense

Barriers to Buprenorphine- Pharmacists

Lack of
Education and
Training

Lack of
confidence

Time

Barriers to Buprenorphine- Stigma

Public Opinion

- National public opinion data
 - Negative attitude towards people with OUD > those for other conditions (including mental illness)
- 2016 national survey
 - More than 3/4 of respondents
 - Viewed individuals with OUD as to blame for their substance use
 - Viewed OUD as lacking self-discipline

Misinformation

- Labeling
 - Terminology can increase stigma
- Stereotyping
 - Viewed as criminals
 - Just using to get high or substituting for another drug
 - For personal gain
- Among criminal justice settings, housing sector, child welfare system

Pervasive

- Income
- Education
- Housing status
- Well-being
 - Shame
 - Self-stigma


Moving Forward as Healthcare Professionals-- Addressing Stigma and Improving Treatment Retention

- Addressing Stigma

- Thinking about your own personal beliefs/ stereotypes
- Terminology

- Improve Treatment Retention

- Increased effort and access to:
 - MAT
 - Naloxone distribution

	 Instead of this:	 Consider saying this:
Use person-first language	Mr. X is an opioid addict .	Mr. X is diagnosed with opioid use disorder .
	That Veteran has a drug problem .	That Veteran has problems resulting from use of opioids .
Avoid judgmental terminology	Your urine drug test was clean .	Your urine drug test was negative for illicit substances.
	Your urine drug test was dirty .	Your urine drug test result was positive for (insert drug/ substance name).
	You have to stop your habit of using opioids.	I would like to offer you treatment for opioid use disorder .
Be supportive	There is no cure for your disease.	We have very effective treatments for opioid use disorder. Recovery is achievable.
	I can't help if you choose to keep using opioids.	We understand that no one chooses to develop opioid use disorder . It is a medical disorder that can be managed with treatment.

Moving Forward as Pharmacists- Monitoring for Problematic Opioid Use

- Challenge of balancing legal role to watch for diversion while also providing safe, effective and timely access to treatment
- Screening of individuals for OUD
 - Evidence based approach to identify and reduce risks of problematic use of drugs and alcohol
 - Screening, brief intervention (SBI), with or without Referral to Treatment (SBIRT); starting to use
 - Identify and intervene with unrecognized OUD
 - Study out of North Dakota showed 30% of screened individuals (n=107) were identified as being high risk for overdose and were provided services to reduce risk
- MTM services

Moving Forward as Pharmacists- Role in MAT

Increase access to programs

Patient education

Adoption of legislation to enable pharmacy based opioid addiction treatment distribution

- Study by Wu, et al- 2021
 - 3 office-based buprenorphine treatment clinics (OBBT), 3 community pharmacists with collaborative care model
 - 71 patients; after screening, eligible patient's buprenorphine care transferred from OBBT to community pharmacist for 6 months
 - At end of study, 88.7% treatment retention and 95.3% adherence
 - Opioid-positive drug screens for all collected during six months was 4.9%
 - No safety related events
 - Over 90% of patient endorsed they "were very satisfied with their experience and the quality of treatment offered", treatment transfer was "not difficult at all" and that getting buprenorphine at same place for a visit was "extremely useful/convenient"
 - Positive ratings among physicians/pharmacists

Moving Forward as a Healthcare Community

DEA

- Could have wholesalers remove buprenorphine for OUD from order monitoring systems
- Track it separately from other opioids
- Remove threshold or increase it
- Pharmacies can submit petitions together (to decrease flagging of an individual pharmacy)

Restore trust with
physicians and
pharmacists

- Community forums- increase communication and resolve conflict
- Education

Stigma-reduction

- Contact with people in recovery
- Education at pharmacy, medical, nursing, other healthcare programs

Moving Forward as Christian Healthcare Providers- Loving like Jesus

- Requires person-centered care...a relationship with the patient!
- Whole person approach:
 - Medical
 - Spiritual
 - Psychological
 - Social
 - Vocational
 - Legal

Moving Forward as Christian Healthcare Providers- Loving like Jesus

- Share the Love of Christ and His Redemption
 - I Corinthians 13:13, "So now faith, hope, and love abide, these three; but the greatest of these is love."
 - 1 Peter 4:8, "Above all, love each other deeply, because love covers over a multitude of sins."
 - Mark 2:17– On hearing this, Jesus said to them, "It is not the healthy who need a doctor, but the sick. I have not come to call the righteous, but sinners."
 - Help them heal physically, but also sharing the salvation He provides
 - Jesus is who will truly heal the trauma, pain and shame

Helpful Resources

- Great articles on leveraging pharmacists:
 - Peckham AM, Ball J, Colvard MD, et al. Leveraging pharmacists to maintain and extend buprenorphine supply for opioid use disorder amid COVID-19 pandemic. *American Journal of Health-System Pharmacy*. 2021;78(7):613-618. <https://academic.oup.com/ajhp/article/78/7/613/6067643>
 - DeRonne BM, Wong KR, Shultz E, et al. Implementation of a pharmacist care manager model to expand availability of medications for opioid use disorder. *American Journal of Health-System Pharmacy*. 2021;78(4):354–359. <https://academic.oup.com/ajhp/article/78/4/354/6039310>
- <https://www.pbm.va.gov/academicdetailingservicehome.asp>
- <https://www.va.gov/painmanagement/>
- <https://www.samhsa.gov/medication-assisted-treatment>

Questions?