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Utilizing Buprenorphine in Pain Management

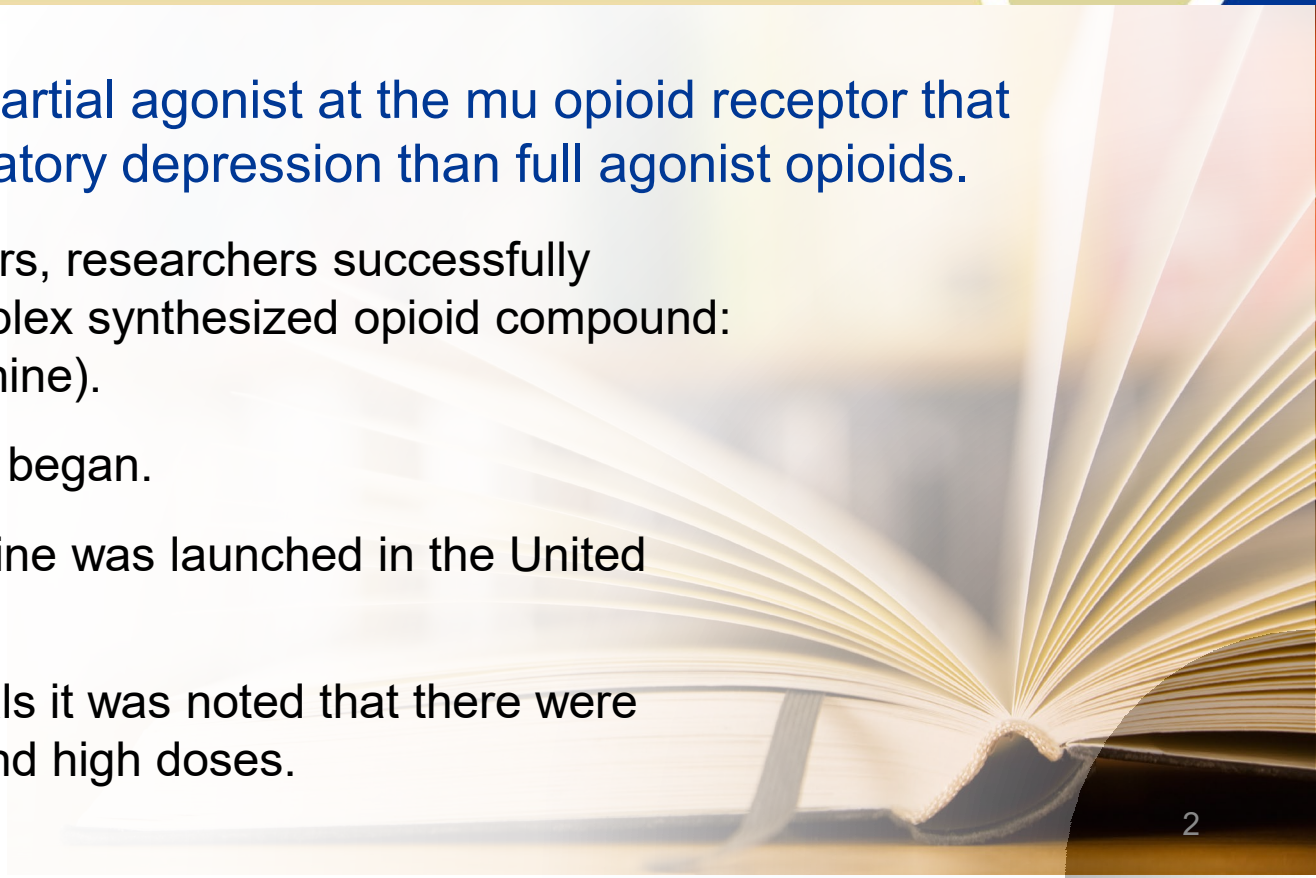
A BRIEF OVERVIEW

June 21, 2023

A Short History

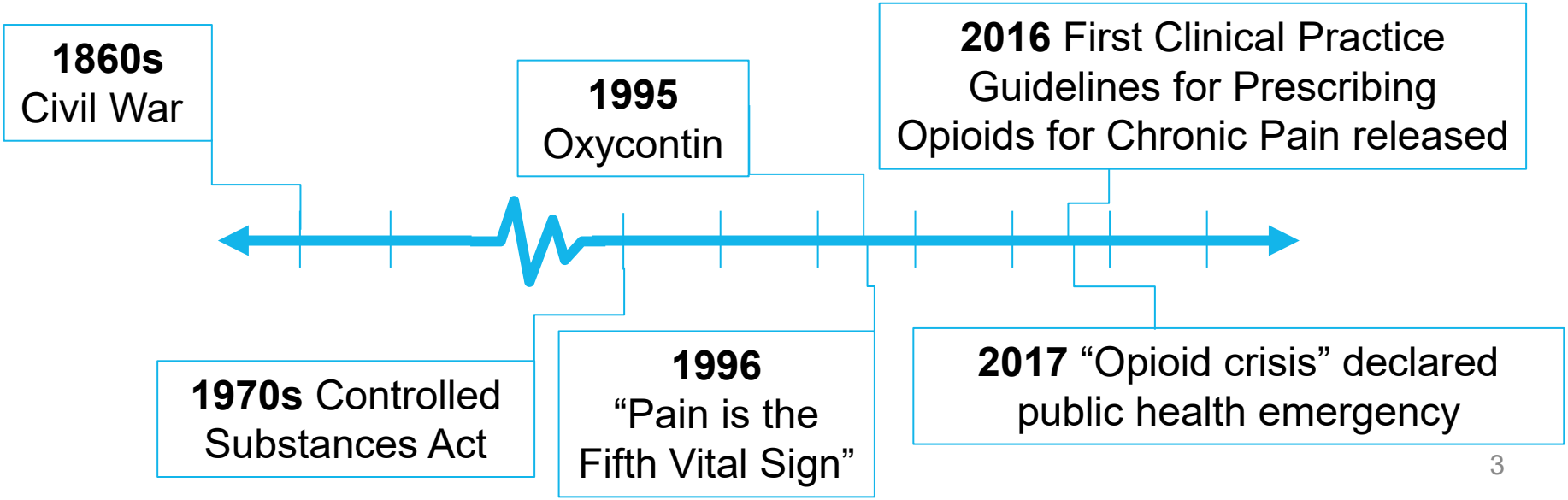
Buprenorphine: a partial agonist at the mu opioid receptor that produces less respiratory depression than full agonist opioids.

- In **1969**, after 10 years, researchers successfully created a more complex synthesized opioid compound: RC6029 (buprenorphine).
- In **1971** human trials began.
- By **1978** buprenorphine was launched in the United Kingdom.
- In buprenorphine trials it was noted that there were effects at both low and high doses.



Managing Chronic Pain:
Where We Have Been

- Over **27% of the population** suffers from chronic pain.
- **Since around 2100 BC** people have used opioids for pain management.



Managing Chronic Pain:
Where We Are Going

2016 Centers for Disease Control and Prevention (CDC) Guidelines changed:

- Prescribing habits
- Opioids were harder to prescribe
- Many prescribers moved away from treating chronic pain

Patients are still in pain… so what now?

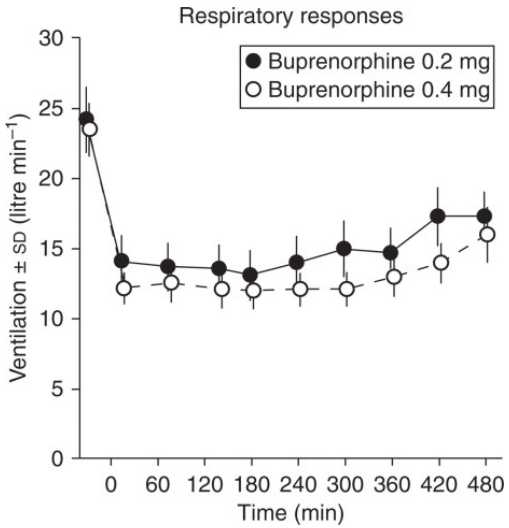
- Using opioids while minimizing risk
- Non-pharmacologic pain management

Why consider buprenorphine for pain management?

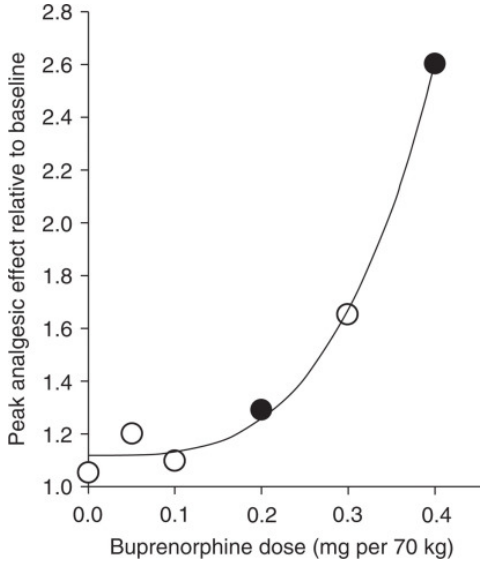
1. Managing chronic pain that does not respond to other treatment
2. Buprenorphine offers harm reduction as a partial opioid agonist tightly bound to the mu receptors
3. Support in guidelines and op-ed by experts
   - 2022 VA guidelines indicate “For patients receiving daily opioids for the treatment of chronic pain, we suggest the use of buprenorphine instead of full agonist opioids due to lower risk of overdose and misuse.”

Ceiling Effect of Buprenorphine

Ceiling effect on respiratory depression



Benefit to analgesia continues with dose increases



Dahan A, Yassen A, Romberg R, et al. Buprenorphine induces ceiling in respiratory depression but not in analgesia. Br J Anaesth 2006;96(5):627–32. https://pubmed.ncbi.nlm.nih.gov/16547090/

Options Available

Buprenex® Injection

- Initial U.S. Food and Drug Administration (FDA) approval in 1985
- Indicated for moderate to severe pain management

Butrans® Transdermal Patch

- Initial FDA approval in 2010
- Indicated for moderate to severe chronic pain

Belbuca® Buccal Film

- Initial FDA approval in 2015
- Indicated for around-the-clock, long-term opioid treatment for pain management

Buprenorphine Agents Indicated for Pain Management

Buprenex® Injection 0.3mg/ml ampules

- Intramuscular (IM) or Intravenous (IV) Injection only
- Dosing: 1 ml (may repeat once, then 1 ml every 6 to 8 hours)

Butrans® Transdermal Patch

- Change patch and rotate placement every seven days
- Available as 5mcg/hour, 7.5mcg/hour, 10mcg/hour, 15mcg/hour and 20mcg/hour

Previous Opioid Analgesic Daily Dose (Oral Morphine Equivalent)	<30 mg	30-80 mg
Recommended BUTRANS Starting Dose	**5 mcg/hour**	**10 mcg/hour**

https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=794aa355-66de-41b8-aedf-f2c40f6bc664&type=display

Buprenorphine Agents Indicated for Pain Management (Continued)

Belbuca® Buccal Film

- One film buccally twice a day
- Available as 75mcg, 150mcg, 300mcg, 450mcg, 600mcg, 750mcg and 900mcg

Table 1: Initial BELBUCA Dose Based on Prior Opioid Expressed as Oral Morphine Sulfate Equivalents

Prior Daily Dose of Opioid Analgesic Before Taper to 30 mg Oral MSE	Initial BELBUCA Dose
Less than 30 mg oral MSE	BELBUCA 75 mcg once daily or every 12 hours
30 mg to 89 mg oral MSE	BELBUCA 150 mcg every 12 hours
90 mg to 160 mg oral MSE	BELBUCA 300 mcg every 12 hours
Greater than 160 mg oral MSE	Consider alternate analgesic

BELBUCA doses of 600 mcg, 750 mcg, and 900 mcg are only for use following titration from lower doses of BELBUCA. Individual titration should proceed in increments of 150 mcg every 12 hours, no more frequently than every 4 days.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/207932s002lbl.pdf

What is slowing the use of buprenorphine for pain?

- Only low-dose agents are FDA-approved
- Lack of dependable morphine equivalence resources
- Lack of awareness on variety of buprenorphine agents available for chronic pain management
- Prescriber and patient discomfort with variety of dosage forms
- Patient push back

Adding Buprenorphine to Treatment Options

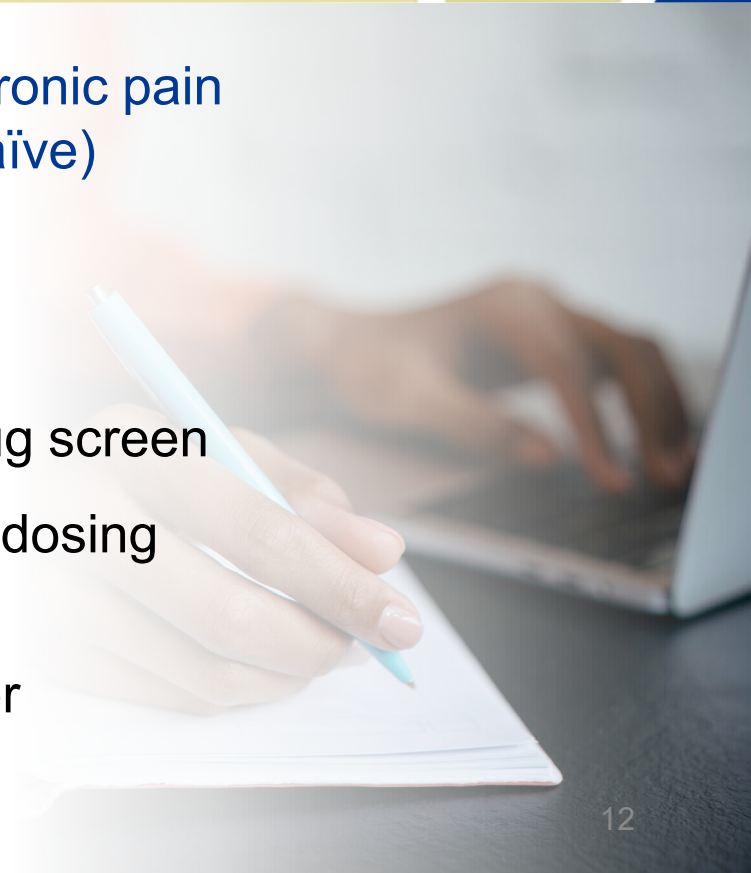
The 12 CDC Clinical Practice Guideline Recommendations from 2022 are grouped into four areas of consideration:

1. **Determining whether or not to initiate opioids for pain**
2. **Selecting opioids and determining opioid dosages**
3. **Deciding duration of initial opioid prescription and conducting follow-up**
4. **Assessing risk and addressing potential harms of opioid use**

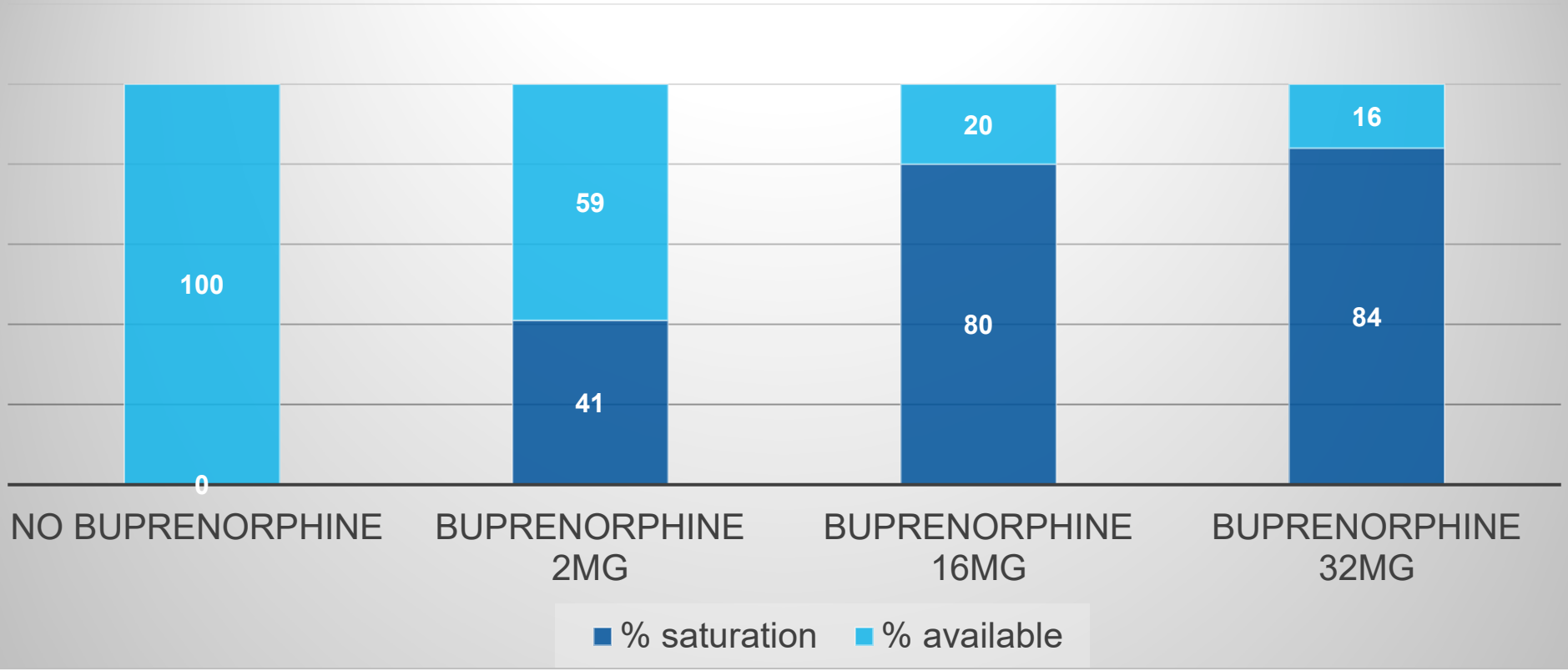
Adding Buprenorphine to Treatment Options (continued)

Decision made to begin buprenorphine for chronic pain in patient not chronically on opioids (opioid naïve)

- Check insurance
- Know cost per month
- Check state drug registry and consider drug screen
- Labels for Butrans® and Belbuca® provide dosing guidelines
- Full agonist opioids can be used with either Butrans® or Belbuca®

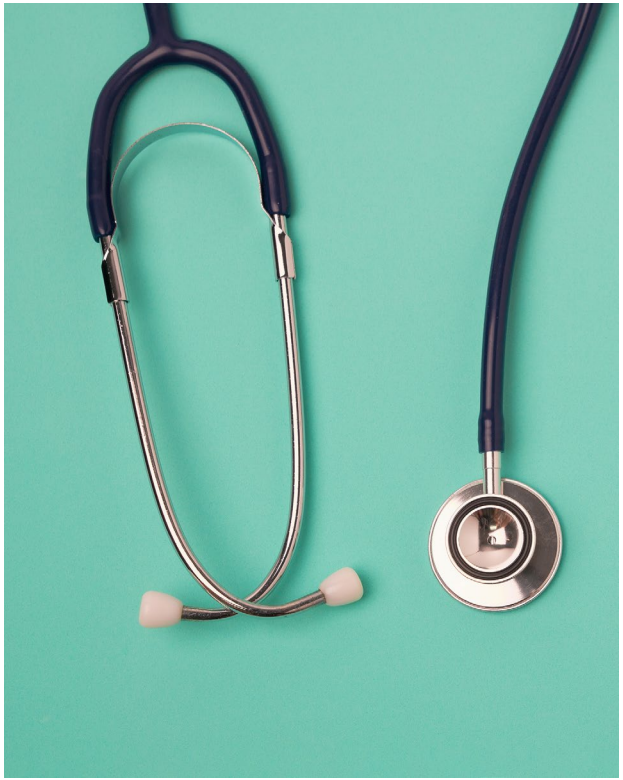


Mu-Opioid Receptor Availability



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):2000–9

Adding Full Mu-Agonist Opioids



- Only available data is for 2mg to 32mg buprenorphine
- Microgram buprenorphine doses are effective for analgesia and leave receptor site vacancy
- Microgram to milligram equivalency has not been established
- Buprenorphine to morphine equivalency has not been established
- Risk of respiratory depression increases with the addition of other central nervous system (CNS) active agents

Reminders

Buprenorphine is still an opioid.

Become familiar with the warnings for buprenorphine.

Be sure to train the patient on naloxone use.

Switching Patient from Full Agonist Opioid to Buprenorphine

- Make same considerations for cost and insurance as for opioid naïve patient
- Labels for Butrans® and Belbuca® give dosing guidelines for transition
- If patient is being transitioned because they may have opioid use disorder (OUD):
  - Refer patient for OUD evaluation (if needed)
  - Remember OUD and chronic pain are not mutually exclusive
  - If patient has OUD, consider buprenorphine sublingual products

Buprenorphine for OUD: Sublingual films and tablets

Buprenorphine/naloxone and buprenorphine monotherapy sublingual agents:

- FDA approved Suboxone® and Subutex® in 2002
- Indicated only for maintenance treatment
- X-waiver requirement in effect (with several modifications) until eliminated in January 2023
- Off-label prescribing is allowed with U.S. Drug Enforcement Administration (DEA) license but needs to be specified for pain

Buprenorphine for OUD: Long-acting injections

Sublocade® (available since 2017): a long-acting buprenorphine formulation for injection by a healthcare professional.

Brixaldi® (approved in May 2023 and available in September 2023): a subcutaneous injection offering more flexibility.

Pain Management for OUD

1. Co-occurring OUD and chronic pain

- Use buprenorphine
- Divide dosage for use up to four times per day for better pain relief
- Consider opioid treatment program (e.g., methadone program) if pain cannot be managed

Pain Management for OUD (continued)

2. Emergent pain in patients with OUD

- Coordination between buprenorphine prescriber and pain management prescriber
- Continue buprenorphine with option to increase dosage **or** add short active full agonist opioid with high binding affinity (e.g., hydromorphone, fentanyl) for short time to current buprenorphine regimen.

Stigma: Language Matters

- Feeling stigmatized may impede a patient's desire to seek treatment.
- Stigmatizing language may reflect belief drug addiction is a moral failing, not a disease.
- Fight OUD stigma to help people feel like their life is worth saving.

OUD Stigma Resources

National Institute on Drug Abuse:
Addressing Stigma and Health Disparities

CDC:
Stigma Reduction

National Center on Substance Abuse and Child Welfare:
Disrupting Stigma: How Understanding, Empathy, and Connection Can Improve Outcomes for Families Affected by Substance Use and Mental Disorders

Mountain Pacific:
Stigmas Surrounding Opioid Use Disorder Webinar | Slides

In Summary…

- Become familiar with buprenorphine products before prescribing.
- Harm reduction comes first.
- Prescribe naloxone.
- Refer patients for OUD evaluation, if needed.
- Be aware of the stigma that could be in the language you use.
- Make sure to check your sources and their date of publication.
- Being in an opioid crisis, the landscape can change rapidly!

Questions?

Resources

General information:

Providers Clinical Support System: pcssnow.org

American Academy of Pain Management: painmed.org

American Society of Addiction Medicine: asam.org

Substance Abuse and Mental Health Services Administration (SAMHSA): https://www.samhsa.gov/practitioner-training

Specific articles:

Understanding Buprenorphine for Use in Chronic Pain: Expert Opinion; *Pain Medicine, 21(4), 2020, 714–723 doi: 10.1093/pm/pnz356*

A Narrative Pharmacological Review of Buprenorphine: A Unique Opioid for the Treatment of Chronic Pain; *Pain Ther (2020) 9:41–54 https://doi.org/10.1007/s40122-019-00143-6*

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8163969/

https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOpioidsCPG.pdf

https://downloads.asam.org/sitefinity-production-blobs/docs/default-source/guidelines/npg-jam-supplement.pdf?sfvrsn=a00a52c2_4

https://www.asam.org/education

https://www.suboxone.com/

https://butrans.com/

https://www.belbuca.com/hcp

https://www.cdc.gov/opioids/healthcare-professionals/prescribing/guideline/at-a-glance.html

THANK YOU!

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