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The role of MOUDs in Managing comorbid OUD & Chronic Pain

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Disclosures

- I have the following relationships to disclose:
  - None

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Substance Use Disorder ↔ Chronic Non-Cancer Pain

- CNCP is common among those treated for SUD
- SUD is common among those treated for CNCP
- Among lifetime SUD, lifetime CP prevalence >50%
  - Those in tx for SUD, CP prevalence as high as 75%
- Overall prevalence of current SUD among CNCP 3-48%
  - Lifetime prevalence of any SUD if have CNCP 16-74%

John WS, Wu LT. Chronic non-cancer pain among adults with substance use disorders: Prevalence, characteristics, and association with opioid overdose and healthcare utilization. Drug Alcohol Depend. 2020;209:107902.
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SUD ↔ CNCP

- Substance use as coping response to pain-related symptoms
- Substance use related injury leading to chronic pain conditions
- Diathesis-stress model
  - “Semi-dormant characteristics of the individual before the onset of chronic pain that are then activated and exacerbated by the stress of this chronic condition, eventually resulting in diagnosable psychopathology.”

Alford DP, German JS, Samet JH, Cheng DM, Lloyd-Travaglini CA, Saitz R. Primary Care Patients with Drug Use Report Chronic Pain and Self-Medicate with Alcohol and Other Drugs. J Gen Intern Med. 2016 May;31(5):486-91.
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Ilgen MA, Perron B, Czyz EK, McCammon RJ, Trafton J. The timing of onset of pain and substance use disorders. Am J Addict. 2010 Sep-Oct;19(5):409-15.

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SUD ↔ CNCP

- In 200 patients with CLBP, SUD preceded the onset of chronic pain
- In 421 patients with CLBP, no correlation between premorbid psychopathology and chronic pain disability
- In patients CLBP and SUD, SUD preceded LBP in 77% of patients with current and 63% with lifetime substance use disorders

Polatin PB, Kinney RK, Gatchel RJ, Lillo E, Mayer TG. Psychiatric illness and chronic low-back pain. The mind and the spine--which goes first? Spine. 1993 Jan;18(1):66-71.
Gatchel RJ, Polatin PB, Mayer TG. The dominant role of psychosocial risk factors in the development of chronic low back pain disability. Spine. 1995 Dec 15;20(24):2702-9.
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Medications for OUD

- FDA approved MOUDs
  - Methadone
  - Buprenorphine
  - Naltrexone

https://www.samhsa.gov/medication-assisted-treatment/treatment#medications-used-in-mat

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OUD: Methadone (PO)

- Doses of from 80-100mg/day have significant advantages, compared to lower doses, in reducing illicit opioid use and in retaining patients in treatment
- For most patients, a stable dose ranges from 80-120mg/day

Medications for Opioid Use Disorder: For Healthcare and Addiction Professionals, Policymakers, Patients, and Families [Internet]. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2018. (Treatment Improvement Protocol (TIP) Series, No. 63.) Chapter 3B: Methadone. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535269/
Saxon AJ, Hser YI, Woody G, Ling W. Medication-assisted treatment for opioid addiction: methadone and buprenorphine. J Food Drug Anal. 2013 Dec;21(4):S69-S72.
Strain EC, Bigelow GE, Liebson IA, Stitzer ML. Moderate- vs high-dose methadone in the treatment of opioid dependence: a randomized trial. JAMA. 1999 Mar 17;281(11):1000-5.

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OUD: Buprenorphine (SL, buccal, SQ, SD)

- Final stabilization doses of buprenorphine range from 2-32mg/day
- Average dose, 16mg/day
  - 24mg/day, most common maximum dose
- New implantable and injectable formulations

Saxon AJ, Hser YI, Woody G, Ling W. Medication-assisted treatment for opioid addiction: methadone and buprenorphine. J Food Drug Anal. 2013 Dec;21(4):S69-S72.
Oesterle TS, Thusius NJ, Rummans TA, Gold MS. Medication-Assisted Treatment for Opioid-Use Disorder. Mayo Clin Proc. 2019 10;94(10):2072-2086.

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OUD: Naltrexone (PO, IM)

- Common dose is 50mg/day

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Managing CNCP in patients with OUD

- Multi-disciplinary care teams
- Stepped care models
- Therapies
  - Non-pharmacologic tx
  - Non-opioid pharmacologic tx
  - MOUDs

Clark MR, Stoller KB, Brooner RK. Assessment and management of chronic pain in individuals seeking treatment for opioid dependence disorder. Can J Psychiatry. 2008 Aug;53(8):496-508.
Ballantyne JC, LaForge KS. Opioid dependence and addiction during opioid treatment of chronic pain. Pain. 2007;129:235–255.
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Speed TJ, Parekh V, Coe W, Antoine D. Comorbid chronic pain and opioid use disorder: literature review and potential treatment innovations. Int Rev Psychiatry. 2018 10;30(5):136-146.

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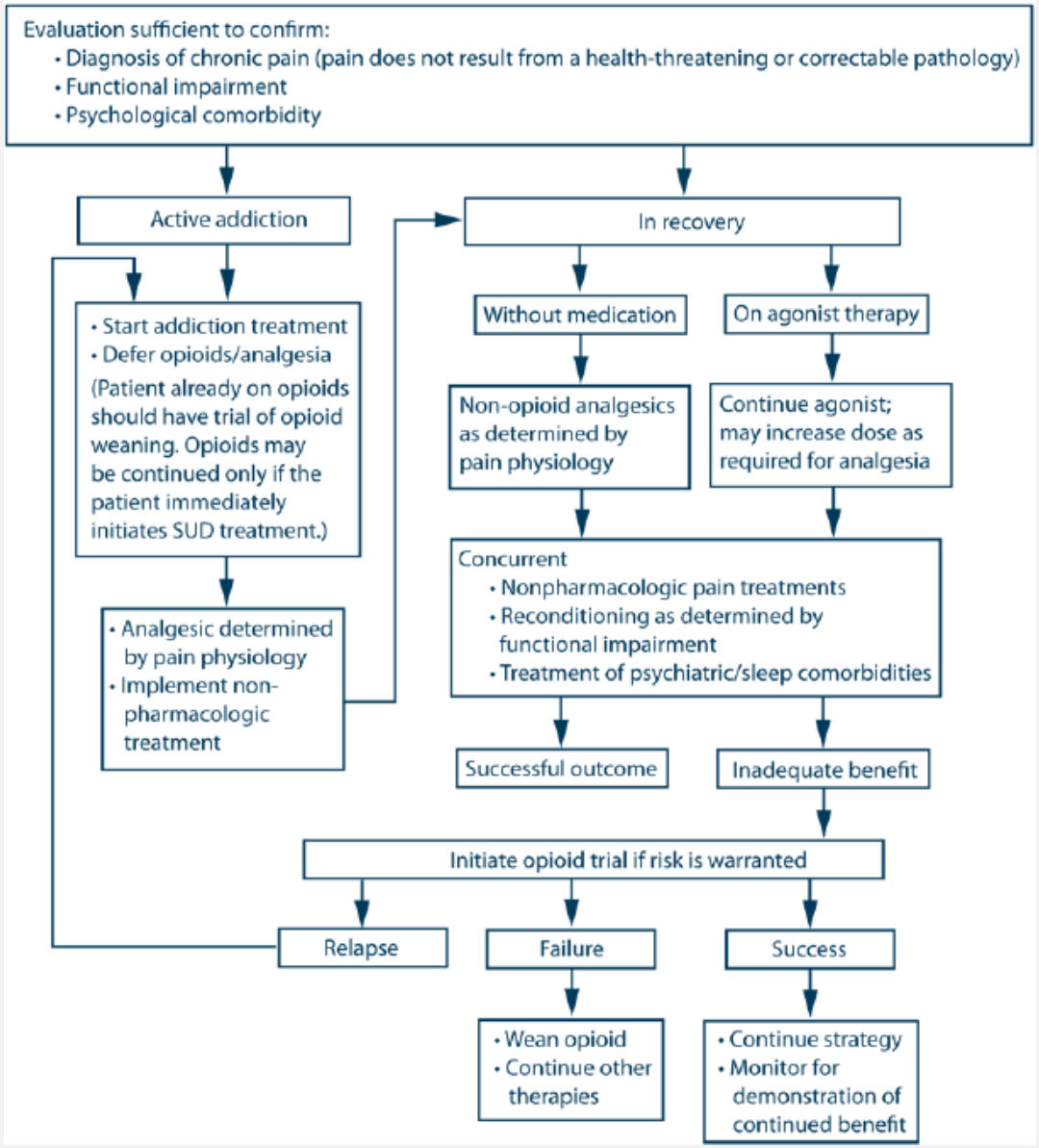
Managing CNCP & SUD



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CNCP & OUD: Non-opioid Analgesics

Medication	Notes
Acetaminophen	Potentiates analgesia
NSAIDS	Relieve numerous types of pain, especially bone, dental, and inflammatory, and enhance opioid analgesia
SNRIs	Relieve migraine, fibromyalgia, low back pain
Tricyclic antidepressants	Efficacy in migraine prophylaxis, fibromyalgia, many neuropathic pains, vulvodynia, and functional bowel disorders
Anticonvulsants	Some efficacy for fibromyalgia, migraine prophylaxis, and neuropathic pain
Topical analgesics	Work locally
Antipsychotics	To abort migraine/cluster headache only
Muscle relaxants	Not recommended (acute period?)
Benzodiazepine	Not recommended
Cannabinoids	Not recommended

Center for Substance Abuse Treatment. Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); 2012. (Treatment Improvement Protocol (TIP) Series, No. 54.) 3, Chronic Pain Management. Available from: https://www.ncbi.nlm.nih.gov/books/NBK92054/

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CNCP & OUD: MOUDs

- *Very little data available*
- Higher doses may be required
- Shorter dosing intervals
  - Methadone (PO): BID-TID-QID dosing
  - Buprenorphine (buccal, SL): TID dosing
- Naltrexone: Not used, lacks analgesia
- Other opioids: Should be used with extreme caution

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MOUDs: Efficacy for CNCP & OUD

- Buprenorphine meta-analysis
  - Beneficial effect on pain intensity overall
  - Small mean effect size in patients with comorbid chronic pain and OUD
  - Moderate-to-large effect size in chronic pain patients without OUD

- Buprenorphine vs methadone therapy
  - Both appear to improve chronic pain

Lazaridou A, Paschali M, Edwards RR, Gilligan C. Is Buprenorphine Effective for Chronic Pain? A Systematic Review and Meta-analysis. Pain Med. 2020 Apr 24
Shulman M, Luo S, Campbell ANC, et al. Secondary Analysis of Pain Outcomes in a Large Pragmatic Randomized Trial of Buprenorphine/Naloxone Versus Methadone for Opioid Use Disorder. J Addict Med. 2020 Feb 7.
Cote J, Montgomery L. Sublingual buprenorphine as an analgesic in chronic pain: a systematic review. Pain Med. 2014 Jul;15(7):1171-8.
Chou R, Ballantyne J, Lembke A. Rethinking Opioid Dose Tapering, Prescription Opioid Dependence, and Indications for Buprenorphine. Ann Intern Med. 2019 Sep 17;171(6):427-429.

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Other Pharmacologic Agents?

- Ibogaine – psychoactive indole alkaloid investigated as potential agent to treat opioid addiction
  - Lacks data
  - Concerns about serious side effects

Koenig X, Hilber K. The anti-addiction drug ibogaine and the heart: a delicate relation. Version 2. Molecules. 2015 Jan 29;20(2):2208-28.

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Thank You

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TABLE. Comparison

Parameter (characteristic)	Buprenorphine	Methadone	Naltrexone
Pharmacologic action	Partial agonist at the μ-opioid receptors and an antagonist at κ-opioid receptors	Full opioid agonist	Full opioid antagonist
FDA-approved clinical indication	Opioid-use disorder, pain	Opioid-use disorder, pain	Opioid-use disorder, alcohol-use disorder
Route of administration	Buccal film, subcutaneous extended-release injection, subdermal implant, transdermal patch	Oral, parenteral	Oral, intramuscular
Therapeutic dose	Orally: 8 to 16 (max 24) mg; subcutaneously monthly: 100 mg to 300 mg; subdermal implant: 74.2 mg every 6 months; transdermal patch: maximum 20 μg/h; replace every 7 days	80 mg to 120 mg daily	Orally: 50 mg daily or 100 mg orally every other day; or 150 mg orally every third day
Frequency of administration	Orally: daily, every other day, 3 times a week; subcutaneously: monthly; patch: weekly; implant: every 6 months	Daily	Orally: daily, every other day or every third day; intramuscularly: monthly
Protein binding	96%	85% to 90%	21%
Bioavailability	Buccal film: 46% to 65%; transdermal: 15%	Oral: 36% to 100%	5% to 40%
Half-life elimination	Buccal film, subdermal implant; transdermal patch: 24 to 48 hours; subcutaneous extended-release injection: 43 to 60 days	8 to 59 hours	4 to 13 hours
Onset of action	10 to 30 min	30 to 60 min	Up to 3 day; following 100-mg oral doses for 3 days (96% on day 1, 87% on day 2, 46% on day 3)
Duration of action	6 hours	5 to 8 hours	50 mg: 24 hours; 100 mg: 48 hours; 150 mg: 72 hours; intramuscularly: 4 weeks

Adapted from *Medications for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series 63.*[108]

Oesterle TS, Thusius NJ, Rummans TA, Gold MS. Medication-Assisted Treatment for Opioid-Use Disorder. Mayo Clin Proc. 2019 10;94(10):2072-2086.

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Principles of chronic opioid maintenance for pain

- First try aggressive rehabilitative approach that may utilize opioids, but aims to restore function and reduce reliance on medications.
- Consider longer term treatment a serious undertaking that will require the commitment of both physician and patient.
- Ensure that other treatment options have been maximized.
- Consider opioid therapy as an adjunct; sole opioid therapy is rarely successful.
- Use goal directed therapy; set limits and goals and agree these.
- Use of a written agreement, contract or consent is helpful for setting out terms of treatment, terms for discontinuing treatment, and a clear statement of likely benefits and risks.
- Unless pain is occasional, base regime on long-acting opioids, and avoid breakthrough medication.
- Ensure careful and regular follow-up.
- Monitoring of opioid use is helpful using pharmacy databases, pill-counting or urine toxicology.
- Be prepared to wean and discontinue if treatment goals are not met.
- Maintain good documentation.

Ballantyne JC, LaForge KS. Opioid dependence and addiction during opioid treatment of chronic pain. Pain. 2007;129(3):235-255.