**Topic 10: “Treatment Options for Opioid Substance Abuse”**

Comparative effectiveness of medication regimens, intensive counseling, and combined modalities for treatment of opioid substance abuse.

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| Introduction              | **DESCRIPTION OF CONDITION**  
- Opioid dependence occurs when patients are unable to stop using opioids (substances derived from the opium poppy or synthetic versions such as morphine, heroin, and oxycodone).  
- Dependence can be related to use of illicit or prescribed drugs.  
- Opioid prescription painkillers were involved in almost 15,000 deaths in 2008.  

**TREATMENTS**  
- Medication Assisted Treatment (MAT) involves the use of drugs that are longer-acting, but induce less euphoria. This treatment has been shown to be effective in randomized control trials and meta-analyses. Replacement medications include:  
  - **Methadone**  
    - Used to reduce diversion, it is only available in Narcotic Treatment Programs subject to specific licensing and regulations (not available in doctor’s offices)  
  - **Buprenorphine**  
    - Used to reduce diversion and available via doctor’s prescription as long as physician meets specific requirements to dispense  
    - Use is FDA approved only in combination with naloxone  
- **Naltrexone**, though used more often for alcohol dependence, is prescribed for relapse prevention to block the effects of opioids.  
- Counseling is also used to teach skills to reduce cravings, prevent relapse and address related issues (e.g., mental and physical health, socioeconomics, and relationships).  
- Combination MAT and counseling/sober support groups are another option  
- Fewer than 10% of people dependent on opioids in the U.S. receive MAT treatment due to lack of access.  
- Detoxification programs are not covered in this brief.  |
| Relevance to patient-centered outcomes | - The most relevant patient-centered outcome is quality of life. New research that identified the most effective ways to allow access to treatments for opioid addiction, with minimal relapse rates, could drastically improve the quality of life for addicts as well as their families, employers, and society as a whole.  |
| Burden on Society            | **PREVALENCE AND SUB-POPULATIONS**  
- About 4.5% of US adults (14.1 million) reported non-medical use of prescription opioids in the past year in a national survey; of these, about 13% (1.84 million) met the criteria for opioid dependence.  
- Some sub-populations are at increased risk:  |

*PCORI Topic Brief: Assessment of Prevention, Diagnosis, and Treatment Options*
### Criteria

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<tr>
<td>o People with low incomes&lt;sup&gt;8&lt;/sup&gt;</td>
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<td>o People on Medicaid (in Washington State, one study found 45% of people who died from prescription painkiller overdoses were enrolled in Medicaid)&lt;sup&gt;9&lt;/sup&gt;</td>
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<td>o People with mental illness and/or addiction to other substances (e.g., alcohol)&lt;sup&gt;8&lt;/sup&gt;</td>
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<td>o Residents of the Southwestern U.S. and the Appalachian region&lt;sup&gt;1&lt;/sup&gt;</td>
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**INCIDENCE**

- Incidence is rising dramatically: in 2002, 1.9 million Americans ≥12 years reported initiating use of nonmedical prescription pain relievers, but by 2011, this had risen to 11.1 million.<sup>10</sup>

### Effects on patients’ quality of life, productivity, functional capacity, mortality, and use of health services

**QUALITY OF LIFE/FUNCTIONAL CAPACITY/MORTALITY**

- A recent meta-analysis found that 32% of people using opioids for nonmedical reasons had comorbid mental health symptoms.<sup>11</sup>
  - 17% had comorbid depression
  - 16% had comorbid anxiety
  - 48% reported chronic pain
- Patients with opioid addictions are generally unable to maintain employment and personal relationships.<sup>12</sup>
- Opioid-related fatalities have increased dramatically in past ten years;<sup>13</sup> in 2008, opioids contributed to approximately 5 out of 100,000 deaths in the U.S.<sup>14</sup>
- Opioid overdose is the second leading cause of accidental death in U.S.<sup>4</sup>

**USE OF HEALTH SERVICES/PRODUCTIVITY**

- Recent study found that healthcare utilization costs in opioid users were >5 times higher than non-users ($2138/month vs. $408/month)<sup>15</sup>
- Societal costs were estimated to be $55.7 billion in 2007.<sup>12</sup>
  - $25.6 billion from lost earnings from reduced productivity/early death
  - $25.0 billion from health care costs (medical/prescription costs)
  - $5.1 billion from criminal justice costs (prison/police costs)

### How strongly does the overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?

**FACTORS IN FAVOR**

- Moderate to high number of Americans affected (n=1.84 million)<sup>7</sup>
- Chronic/long-term condition
- High economic burden, especially for serious patient outcomes (e.g., overdose)<sup>12</sup>
- Many patients have chronic pain

**FACTOR AGAINST**

- Even if most effective treatment methods identified, lack of access to treatment might limit use
- Social stigma against persons with substance-abuse problems

### Options for Addressing the Issue

**Based on recent systematic reviews, what is known about the relative benefits and harms of available management**

- Many (approximately 18) Cochrane reviews synthesize evidence for various treatments for opioid addiction.
- Three Cochrane Systematic Reviews<sup>16-18</sup> and an American Society of Addiction Medicine<sup>19</sup> consensus panel concluded psychosocial counseling in addition to pharmacological treatments is the most effective way to treat opioid dependence.
  - Psychosocial counseling alone was not effective.<sup>16-18</sup>
- One systematic review found that buprenorphine can be used for maintenance
### Criteria | Brief Description
--- | ---
Options? & treatment due to its lower abuse potential, but three Cochrane reviews suggested it may be less effective than methadone delivered at adequate dosages; the National Institute for Health and Care Excellence (NICE) guidelines recommend use of methadone as a first choice. A recent meta-analysis of 18 randomized control trials concluded that doses >60 mg/day and individualized doses of methadone are associated with better retention compared to doses <60 mg/day or fixed-dose strategies. The U.S. Department of Veteran’s Affairs/U.S. Department of Defense and the World Federation of Societies of Biological Psychiatry recommend methadone or a combination of buprenorphine and naloxone as first-line treatment. A Cochrane review found that heavy sedation upon commencement of naltrexone maintenance treatment does not confer additional benefits compared to light sedation and might lead to life threatening adverse effects and greater costs. Another recent Cochrane review suggested that prescribing heroin along with flexible doses of methadone could decrease heroin use among long-term, treatment refractory opioid users compared to methadone alone. Evidence shows heroin prescriptions might reduce involvement in criminal activity, incarceration, mortality, and increase retention in treatment programs. Two Cochrane reviews found insufficient evidence on effectiveness of detoxification and maintenance treatments for adolescents who were dependent on opioids. Three other Cochrane reviews found insufficient evidence regarding the effectiveness of sustained-release naltrexone, oral naltrexone, and oral morphine.

### What could new research contribute to achieving better patient-centered outcomes?
- Comparative effectiveness of long-term outcomes of MAT.
- Comparative effectiveness of long-term maintenance therapy plus different types of psychosocial therapy (e.g., cognitive behavioral therapy, 12-step programs, group therapy, family therapy)
- Comparative effectiveness of different maintenance therapies in terms of treatment of non-cancer chronic pain in patients with opioid addictions.
- Comparative effectiveness of different treatment plans among adolescents addicted to opioids.
- Patient preferences for alternative treatment strategies including site of care (i.e., clinic vs. doctors office)

### Have recent innovations made research on this topic especially compelling?
- Use of clonidine off-label (currently used to mitigate withdrawal symptoms) for maintenance therapy

### How widely does care now vary?
- Because of high prevalence of relapse, most patients require many episodes of treatment or ongoing treatment
- Type of treatment depends on many factors, including prior treatment history, medical and/or mental health co-morbidities, co-occurring alcohol and/or other drug use,
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<td>Care varies greatly and is dependent upon the availability of Narcotic Treatment Programs, insurance status, and other factors.</td>
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| How likely is it that new CER on this topic would provide better information to guide clinical decision making? | • CER that identified sub-populations that would benefit from certain treatment regimens would improve clinical decision-making.  
• CER that improved access to treatment and reduced relapse rates would also provide valuable information that would impact clinical decisions. |

**Potential for New Information to Improve Care and Patient-Centered Outcomes**

What are the facilitators and barriers that would affect the implementation of new findings in practice?

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<th>BARRIERS</th>
<th>FACILITATORS</th>
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| Access to treatment is limited.                                          | • Under the Affordable Care Act, all health insurance plans sold on Health Insurance Exchanges or provided by Medicaid must include services for substance abuse. However, for states that are opting out of Medicaid expansion, people with incomes <133% of federal poverty level will not have access to treatment.  
• Private insurance generally covers treatment.  
• Medicaid generally covers treatment.  
• In some counties, public health departments provide vouchers for entry into MAT programs. |
| Methadone, regulated by the Drug Enforcement Administration, is only available in federal and state-licensed Narcotic Treatment Programs, so not available through general practitioners in the U.S. as it is in Canada and many other countries.  
Physicians who want to prescribe buprenorphine must meet requirements outlined in Drug Abuse Treatment Act of 2000 or take 8-hour training course; also physicians are limited to 30 buprenorphine patients in their first year and 100 patients in subsequent years. | • Medicare Part A pays for inpatient substance abuse care.  
• Medicare Part B pays for outpatient substance abuse treatment services, but methadone is not covered when delivered on an outpatient basis. |

How likely is it that the results of new research on this topic would be implemented right away?

• Somewhat likely that new research would be implemented right away; however, the major issue is access to treatment  
• Research on novel drug regimens or novel uses for existing drugs will take time to reach patients, given the need for FDA approval and the typical pace of diffusion for...
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<td>• Research on improved access to care and retention in treatment would likely be readily implemented.</td>
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<td>Would new information from CER on this topic remain current for several years or would it be rendered obsolete quickly by subsequent studies?</td>
<td>• New information from CER on opioid dependence would likely remain current for several years.</td>
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CER = comparative effectiveness research; FDA = U.S. Food and Drug Administration; MAT = medication assisted treatment; NICE = National Institute for Health and Care Excellence
References for Topic 10: “Treatment Options for Opioid Substance Abuse”


