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Show Me the Money: Economic Evaluations of Opioid Use Disorder Interventions

Opioid misuse has reached epidemic proportions in the United States. According to the [Centers for Disease Control and Prevention \(CDC\)](#), in 2014 more than 18,900 people died from an overdose of prescription pain relievers and 10,575 people died from an overdose of heroin, which amounts to 78 Americans dying from opioid overdose each day. The societal costs associated with opioid misuse may be as high as [\\$92 billion annually](#), when health care, labor, and criminal justice costs are taken into account.

The Administration's [proposed budget](#) for 2017 includes more than \$1 billion for fighting this epidemic, with \$920 million to support cooperative agreements with states to expand access to medication-assisted treatment for opioid use disorders. While the final budgeted amount will be a product of negotiations with Congress, there is bipartisan support for significant sums devoted to treatment. Policymakers now face the key question of how best to spend this money, considering treatments that are both clinically and cost effective. This Issue Brief discusses treatments for opioid use disorders and summarizes a new systematic review of economic evaluations of these interventions.

Upfront: Only 10% of individuals with an opioid use disorder receive any therapy at all

In a comprehensive [literature review](#), Murphy and Polsky (2016) summarized 49 studies from 2007 through 2015 that included an economic evaluation of an opioid use disorder intervention. Their findings come with an important caveat, because only 10% of individuals with an opioid use disorder receive any therapy at all. They note that the existing economic literature does not answer a simple yet fundamental question: what is the cost effectiveness of just offering effective opioid use disorder therapy? It could be that expanding access to different kinds of treatment brings more people into treatment itself, which may be a cost effective strategy. This is important to keep in mind because most economic evaluations have compared alternative therapies, as opposed to evaluating the impact of making any treatment available to the 90% of patients with an opioid use disorder who are not currently in treatment.

THIS ISSUE BRIEF DISCUSSES
TREATMENTS FOR OPIOID USE
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DESPITE HIGHER OUTPATIENT
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Opioid use disorder therapies: What's effective

Effective interventions for opioid use disorders are available and fall into two broad categories: psychosocial and pharmacological. Psychosocial therapies include cognitive behavioral therapies, relapse prevention, contingency management (reinforcing desired behaviors and not reinforcing undesired behaviors), and motivational enhancement. These therapies can be used by themselves or in combination with pharmacological therapy.

Pharmacotherapies vary in the degree to which they mimic, or block, the euphoric effects of opioids. Methadone, a long-acting opioid, activates opioid receptors in the brain, reducing pain, cravings, and withdrawal symptoms without producing the full euphoric effects of illicit or prescription opioids. Buprenorphine, a partial opioid agonist, activates opioid receptors in the brain to a lesser extent, which minimizes the symptoms of withdrawal and cravings. Maintenance therapy with methadone or buprenorphine is widely regarded as an effective form of therapy. Both can also be used to assist with short-term detoxification (medically-supervised withdrawal). Because they are controlled substances with the potential for abuse, they are highly regulated. Although not commonly used in the United States, injectable heroin is another form of pharmacotherapy used in Canada and the United Kingdom for opiate dependent persons who do not benefit from or cannot tolerate other opiate replacement treatments.

In contrast, antagonists, such as naloxone and naltrexone, block opioid brain receptors and have the advantage of being non-narcotic and non-addictive. Because antagonists block these receptors, they can cause withdrawal symptoms if taken by an individual physically dependent on opioids. Naloxone is used as a rescue medication for opioid overdose and is not used alone in the treatment of opioid dependence. Naloxone is typically combined with buprenorphine to reduce the likelihood that buprenorphine will be diverted (illicit drugs being used for illicit purposes) or misused.

Providers have varying abilities to prescribe these pharmacotherapies to treat opioid use disorder. Buprenorphine is only available by specially trained and licensed physicians and methadone is only available at specialty clinics. In contrast, naloxone and naltrexone can be prescribed by any provider who is licensed to prescribe medications. Additionally, naloxone can be administered by non-medical personnel and, in some states, is available at pharmacies without a prescription.

Given that policymakers must make decisions on how to allocate scarce resources, evidence of effectiveness for the treatment of opioid use disorder is not enough—nor should it be. Economic evaluations can provide evidence to help guide decisions to allocate public resources efficiently and effectively.

New systematic review finds pharmacotherapy is associated with lower total health care costs

In their review, Murphy and Polsky found that 30% of the studies focused on comparing health care use and costs associated with different kinds of treatments.

EVIDENCE THAT MMT IS
ECONOMICALLY
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BMT IS LIMITED BUT
PROMISING.

Overall, they found that in spite of higher outpatient or prescription costs, pharmacotherapy for opioid use disorders is associated with lower total health care costs, primarily due to lower utilization of high-cost services such as emergency department (ED) visits and inpatient care.

- A study comparing health plan beneficiaries on MMT with those receiving non-methadone outpatient treatment found that patients on MMT had lower health care costs (\$7,163 in 2004 USD) than patients with two or more non-methadone outpatient visits (\$14,157) and patients with zero or one non-methadone outpatient visits (\$18,684). The relatively low cost for MMT patients was due to fewer ED and primary care visits, and fewer inpatient stays.

Studies comparing different pharmacotherapies show that methadone maintenance therapy (MMT) patients tend to use more health care resources and have higher health care costs than patients receiving buprenorphine-naloxone maintenance therapy (BMT), at least in the short-term (six months).

- One study also showed at six months post treatment, MMT patients were significantly more expensive than patients being treated with oral naltrexone and extended-release naltrexone.
- A number of studies compared total health care costs of different BMT approaches and dosage forms. Patients receiving BMT and psychosocial therapy had similar costs to those receiving psychosocial therapy only, and lower costs than those receiving little or no treatment. Other studies found lower costs associated with buprenorphine-naloxone film versus tablets, and improved retention in treatment for high-dose versus low-dose buprenorphine-naloxone patients, with no increase in total health care costs.

MMT and BMT are cost effective by US standards for treatments, although evidence for BMT and naltrexone is more limited

Policymakers are keenly interested in cost offsets, in terms of both health care and criminal justice-related costs, but also want to know what these scarce resources are buying in terms of outcomes. Murphy and Polsky reviewed 30 studies that addressed both the costs and benefits of pharmacotherapy. A key challenge in translating cost-benefit and cost-effectiveness research for policymakers is how to standardize outcomes, which can encompass abstinence rates, opioid-free days, quality of life measures, and benefit-cost ratios. The most frequently used measure is the quality-adjusted life-year (QALY), which standardizes outcomes across conditions and treatments. A traditional, though informal, US threshold for a cost effective intervention has been \$50,000 per QALY gained, although \$100,000/QALY has become more accepted recently.

By the \$50,000 per QALY standard, multiple studies found that MMT and BMT would be considered cost effective relative to no pharmacotherapy. However, other studies calculated much smaller incremental cost-effectiveness gains. Relative to MMT, extended-release naltrexone had a cost-effectiveness ratio of \$72 (in 2014 USD) per opioid free day. Relative to naltrexone, BMT had cost-effectiveness ratios less than \$50 (in 2004 USD) for a host of primary outcomes, including heroin abstinence and days to relapse. But the authors stress that there are no accepted standards upon which to judge these alternate values.

THE AUTHORS FIND THAT THE ECONOMIC EVIDENCE ON BMT AND NALTREXONE TREATMENTS IS LIMITED. HOWEVER, THE RESULTS ARE PROMISING FOR BMT, AS WELL AS FOR CONTINGENCY MANAGEMENT APPROACHES AND CERTAIN THERAPY IMPLEMENTATION STRATEGIES.

MMT may be more cost effective than BMT, but both are better than no pharmacotherapy

Twelve studies focused on MMT, relative to residential therapy or outpatient non-pharmacological treatments, and two others assessed MMT or BMT relative to an outpatient non-pharmacological alternative. Several studies compared MMT with other pharmacological therapies, including injectable heroin and naltrexone.

- Cost-effectiveness and cost-benefit studies comparing MMT and BMT generally favored MMT, but both are cost effective relative to no treatment or drug-free treatment. A study of Medicaid patients found that those receiving either BMT or MMT were 50% less likely to relapse than those receiving behavioral treatments only. MMT and BMT patients had mean monthly health care costs that were \$184-\$191 less than those receiving behavioral treatment only.
- In one study using modeling to predict cost-effectiveness, extended-release naltrexone was predicted to be more effective, and also more costly, than MMT and BMT.
- Overall, abstinence rates were statistically similar for BMT and MMT, but MMT was less expensive. MMT had better six-month patient retention rates than BMT, but BMT was more effective in terms of detox rates. MMT was more cost effective than BMT in terms of opioid-free days.
- In one Canadian study injectable heroin was found to be more cost effective than MMT, but a UK study found that injectable heroin was slightly less cost effective than injectable methadone. Of note, the savings attributed to injectable treatments were associated with the criminal justice system; injectable forms of both heroin and methadone were cost ineffective from the National Health Service perspective.
- In studies comparing BMT with no treatment, short-term detoxification, and naltrexone alone, the results generally favored BMT.

Limited cost-effectiveness evidence on contingency management, other implementation strategies

Two studies looked at the cost effectiveness of contingency management (CM) with prizes or vouchers as an add-on to usual treatment for patients with opioid use disorders. Both used the longest duration of abstinence and the number of negative urine samples as outcome measures, and calculated incremental cost effectiveness as \$212 per week of abstinence and \$156 per negative urine sample. Murphy and Polsky stress that there are no generally-accepted cost-effectiveness thresholds for outcomes of this sort. A [recent article](#) by the same authors assessed an internet-delivered CM intervention for substance use disorders, and found that it was likely cost-effective based on the clinical outcome of abstinence.

A few studies looked at the cost effectiveness of implementation strategies. One study found unobserved dosing of BMT was more advantageous than observed dosing, because it was found to be less expensive with no significant differences in days of heroin use, quality of life, or psychological state. Another study found MMT programs that were highly concordant with clinical practice guidelines were more expensive, on average, than less concordant programs but were more effective with regard to therapy sessions completed, abstinence and quality-of-life scores.

MORE RESEARCH IS NEEDED
TO BETTER EVALUATE THE
RELATIVE COST EFFECTIVENESS
OF THESE COMMON OPIOID USE
DISORDER THERAPIES.

Conclusion

The latest systematic review reveals strong evidence that MMT is an economically advantageous form of treatment for opioid use disorders. The authors find that the economic evidence on BMT and naltrexone or extended-release naltrexone treatments is limited. However, the results are promising for BMT, as well as for contingency management approaches and certain therapy implementation strategies. Much more research is needed to better evaluate the relative cost effectiveness of these common opioid use disorder therapies. Evaluations directly comparing MMT to other pharmacological treatments and analyses assessing treatment versus no treatment are needed. As policymakers and practitioners grapple with the fallout of the opioid epidemic, these economic evaluations are critical in a time where limited resources must be stretched over a large, and growing population. Researchers, in turn, may need to hear from policymakers about the cost-effectiveness measures most likely to be useful in the policymaking process.

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About LDI: Since 1967, the Leonard Davis Institute of Health Economics (LDI) has been the leading university institute dedicated to data-driven, policy-focused research that improves our nation's health and health care. Originally founded to bridge the gap between scholars in business (Wharton) and medicine at the University of Pennsylvania, LDI now connects all of Penn's schools and the Children's Hospital of Philadelphia through its more than 200 Senior Fellows. For additional information on this Issue Brief or LDI, contact Janet Weiner (email: weinerja@mail.med.upenn.edu; 215-573-9374).

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About CHERISH: The Center for Health Economics of Treatment Interventions for Substance Use Disorders, HCV, and HIV (CHERISH) is a multi-institutional Center of Excellence, funded by the National Institute on Drug Abuse. The Center's mission is to develop and disseminate health economic research on healthcare utilization, health outcomes, and health-related behaviors that informs substance use disorder treatment policy and HCV and HIV care of substance users. The Center is a collaboration among Weill Cornell Medicine, Boston Medical Center, the University of Pennsylvania, and the University of Miami Miller School of Medicine. For additional information on this Issue Brief or CHERISH, contact Julia Mitchell (email: julia.mitchell@cherishresearch.org; 215-573-4599).

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