Abstracts of research articles on
MEDICATION ASSISTED TREATMENT

... more things you should know about
Medication Assisted Treatment for Opioid Addiction.

The full text of several of the articles referenced here can be obtained online by going to PUBMED.GOV and typing the article's title in the search box. A list of these articles (and others) with links to the full text will soon be available on the Stop Stigma Now website (STOPSTIGMANOW.ORG)

MEDICATION ASSISTED TREATMENT FOR OPIOID ADDICTION SAVES LIVES

INTRODUCTION

Though the United States has experienced several opioid misuse epidemics, it is now facing its most deadly opioid crisis. More than two decades ago, this latest opioid epidemic emerged in the U.S. due to increased misuse of prescription opioids, and recently has changed profoundly as heroin and fentanyl (primarily illicitly manufactured) have come to dominate the escalating crisis in terms of higher death rates. Yet, although there has been nearly a 1,000% increase in people with an opioid use disorder (OUD) seeking treatment, most persons addicted to opioids are not in treatment and, among those who are, most are not exposed to the modality with the strongest evidence-base: medication assisted treatment (MAT), also known as medication-based treatment for OUD.

Opioid addiction is a chronic and severe disorder characterized by relapse, especially if not adequately treated. There is substantial data that agonist medications (e.g., methadone and buprenorphine) are the most effective interventions for treating this disorder since maintenance on these medications can effectively reduce/eliminate drug craving, prevent withdrawal, and block the euphoric effects of opioids. In addition to preventing relapse, agonist medications are associated with reductions in criminal behavior, HIV risk behaviors, and overdose deaths. There is also evidence that the opioid antagonist naltrexone, in its extended-release formulation (XR-NTX) [e.g., Vivitrol®], can also effectively treat opioid addiction. There is far less evidence that psychosocial interventions (whether residential or outpatient), without the addition of MAT, can effectively treat opioid addiction. Methadone is a μ-opioid agonist that has been used for more than 50 years to treat opioid addiction. Federal regulations stipulate that methadone maintenance must be administered at a certified opioid treatment program. In 2002, buprenorphine, a partial opioid agonist (often co-formulated with naloxone, an opioid antagonist that precipitates withdrawal if injected) was approved by the FDA to be used in office-based settings to treat OUD. The opioid antagonist naltrexone diminishes the reinforcing effects of opioids by occupying the μ receptors in the brain and, unlike agonist medications, has no addictive potential. Buprenorphine, methadone and naltrexone are examples of MAT and the only medications that are currently approved by the FDA for the treatment OUD.

Unfortunately, there are a number of factors that have prevented the expansion of MAT. Among these factors, as enumerated in a March 2019 news release from the National Academies of Sciences, Engineering and Medicine (NASEM), are:

1. Misunderstanding and stigma toward drug addiction, individuals with OUD, and the medications to treat it.
2. Inadequate education and training of the professionals responsible for working with people with OUD, including treatment providers and law enforcement and other criminal justice personnel.
3. Current regulations around methadone and buprenorphine, such as waiver policies, patient limits, restrictions on treatment settings, and other policies that are not supported by evidence or employed for other medical disorders.
4. A fragmented system of care.

Recognition among professionals, patients, their families and the general population that medications are a first-line treatment for OUD and, as noted in a 2019 NASEM consensus study report, “an integral part of a person’s long-term treatment plan” will go a long way to reducing the harm stemming from our current opioid epidemic.

In an effort to provide education about MAT and the barriers that have diminished its expansion, Stop Stigma Now has begun to identify articles and other documents that describe MAT (including separate articles on the three medications), and factors that have prevented its use among the large number of OUD patients who could benefit from it.

Andrew Rosenblum, PhD
SSN Research Director

ABSTRACTS OF ARTICLES ON MAT AND STIGMA

MAT MEDICATIONS, MAINTENANCE, RECOVERY

Maintenance Medication for Opiate Addiction: The Foundation of Recovery.

Bart G. J Addict Dis. 2012;31(3):207-25.

Illicit use of opiates is the fastest growing substance use problem in the United States, and the main reason for seeking addiction treatment services for illicit drug use throughout the world. It is associated with significant morbidity and mortality related to human immunodeficiency virus, hepatitis C, and overdose. Treatment for opiate addiction requires long-term management. Behavioral interventions alone have extremely poor outcomes, with more than 80% of patients returning to drug use. Similarly poor results are seen with medication-assisted detoxification. This article provides a topical review of the three medications approved by the Food and Drug Administration for long-term treatment of opiate dependence: the opioid-agonist methadone, the partial opioid-agonist buprenorphine, and the opioid-antagonist naltrexone. Basic mechanisms of action and treatment outcomes are described for each medication. Results indicate that maintenance medication provides the best opportunity for patients to achieve recovery from opiate addiction. Extensive literature and systematic reviews show that maintenance treatment with either methadone orbuprenorphine is associated with retention in treatment, reduction in illicit opiate use, decreased craving, and improved social function. Oral naltrexone is ineffective in treating opiate addiction, but recent studies using extended-release naltrexone injections have shown promise. Although no direct comparisons between extended-release naltrexone injections and either methadone or buprenorphine exist, indirect comparison of retention shows inferior outcome compared with methadone and buprenorphine. Further work is needed to directly compare each medication and determine individual factors that can assist in medication selection. Until such time, selection of medication should be based on informed choice following a discussion of outcomes, risks, and benefits of each medication.

Buprenorphine Treatment for Opioid Use Disorder: An Overview.

Shulman M, Wai JM,, Nunes EV. CNS Drugs. 2019 Jun;33(6):567-580.

Opioid use disorder affects over 26 million individuals worldwide. There are currently three World Health Organization-recommended and US Food and Drug Administration-approved medication treatments for opioid use disorder: the full opioid agonist methadone, the opioid partial agonist buprenorphine, and the opioid receptor antagonist naltrexone. We provide a review of the use of buprenorphine for the treatment of opioid use disorder and discuss the barriers, challenges, risks, and efficacy of buprenorphine treatment vs. other treatments. Although evidence from numerous studies has shown buprenorphine to be effective for the treatment of opioid use disorder, a majority of patients with opioid use disorder do not receive buprenorphine, or any other medical treatment. We review the different formulations of buprenorphine, including newer long-acting injectable formulations that may decrease the risk of diversion and improve adherence.

Extended-Release Injectable Naltrexone for Opioid Use Disorder: A Systematic Review.

Jarvis BP, Holtyn AF, Subramaniam S, et al. Addiction. 2018 Jul;113(7):1188-1209.

AIMS: To review systematically the published literature on extended-release naltrexone (XR-NTX, Vivitrol®), marketed as a once-per-month injection product to treat opioid use disorder. We addressed the following questions: (1) how successful is induction on XR-NTX; (2) what are adherence rates to XR-NTX; and (3) does XR-NTX decrease opioid use? Factors associated with these outcomes as well as overdose rates were examined.

METHODS: We searched PubMed and used Google Scholar for forward citation searches of peer-reviewed papers from January 2006 to June 2017. Studies that included individuals seeking treatment for opioid use disorder who were offered XR-NTX were included.

RESULTS: We identified and included 34 studies. Pooled estimates showed that XR-NTX induction success was lower in studies that included individuals that required opioid detoxification [62.6%, 95% confidence interval (CI) = 54.5-70.0%] compared with studies that included individuals already detoxified from opioids (85.0%, 95% CI = 78.0-90.1%); 44.2% (95% CI = 33.1-55.9%) of individuals took all scheduled injections of XR-NTX, which were usually six or fewer. Adherence was higher in prospective investigational studies (i.e. studies conducted in a research context according to a study protocol) compared to retrospective studies of medical records taken from routine care (6-month rates: 46.7%, 95% CI = 34.5-59.2% versus 10.5%, 95% CI = 4.6-22.4%, respectively). Compared with referral to treatment, XR-NTX reduced opioid use in adults under criminal justice supervision and when administered to inmates before release. XR-NTX reduced opioid use compared with placebo in Russian adults, but this effect was confounded by differential retention between study groups. XR-NTX showed similar efficacy to buprenorphine when randomization occurred after detoxification, but was inferior to buprenorphine when randomization occurred prior to detoxification.

CONCLUSIONS: Many individuals intending to start extended-release naltrexone (XR-NTX) do not and most who do start XR-NTX discontinue treatment prematurely, two factors that limit its clinical utility significantly. XR-NTX appears to decrease opioid use but there are few experimental demonstrations of this effect.

Leaving Methadone Treatment: Lessons Learned, Lessons Forgotten, Lessons Ignored.

Magura S & Rosenblum A. Mt Sinai J Med. 2001 Jan;68(1):62-74.

Despite the demonstrated benefits of methadone maintenance, there have been concerns about the ethics, necessity and expense of maintaining addicts on methadone indefinitely. The inability of many patients to achieve normative levels of psychosocial functioning with methadone, combined with widely held attitudes favoring drug abstinence over replacement medication, has led to attempts to promote time-limited methadone treatment. This paper reviews the published research literature on post-discharge outcomes of patients exiting from extended methadone detoxification, "abstinence-oriented" methadone programs, and regular methadone maintenance programs. Virtually all of these studies document high rates of relapse to opioid use after methadone treatment is discontinued. Most of the patients studied left treatment without meeting clinical criteria for detoxification, although high relapse rates were also reported for patients who indicated by greatly increased death rates following discharge. Until more is learned about how to improve post-detoxification outcomes for methadone patients, treatment providers and regulatory/funding agencies should be very cautious about imposing disincentives and structural barriers that discourage or impede long-term opiate replacement therapy.

Medication-Assisted Recovery from Opioid Addiction: Historical and Contemporary Perspectives.

White WL. J Addict Dis. 2012;31(3):199-206.

Recovery is being used as a conceptual fulcrum for the redesign of addiction treatment and related support services in the United States. Efforts by policy, research, and clinical leaders to define recovery and calls for assertive models of long-term recovery management raise critical questions about how transformation efforts of recovery-focused systems will affect the pharmacotherapeutic treatment of opioid addiction and the status of patients participating in such treatment. This article highlights recent work advocating a recovery-oriented approach to medication-assisted treatment.

STIGMA

Messages About Methadone and Buprenorphine in Reality Television: A Content Analysis of Celebrity Rehab With Dr. Drew.

Roose R, Fuentes L, Cheema M. Subst Use Misuse. 2012 Aug; 47(10):1117-24.

Medication-assisted treatment for opioid dependence is safe and effective, yet negative perceptions about methadone and buprenorphine may discourage patients from entering treatment. One source of information that may influence viewers' perceptions is television. We performed a content analysis of a popular reality television program on addiction treatment. Although many patients had histories of opioid use, there were no positive messages about methadone or buprenorphine. The two main messages were that they (1) are primarily drugs of abuse, and (2) not acceptable treatment options. These messages reinforce negative stereotypes and may perpetuate stigma. There were multiple missed opportunities to provide evidence-based information.

Pharmacotherapy of Opioid Addiction: "Putting a Real Face on a False Demon."

Salsitz E, Wiegand T. J Med Toxicol. 2016 Mar;12(1):58-63.

Methadone maintenance therapy (MMT), a pharmacological treatment for opioid use disorder for the past 50 years, continues to remain controversial. Despite consistent and overwhelming evidence confirming the effectiveness and safety of MMT, misconceptions and myths persist regarding its legitimacy as a treatment for opioid addiction. This often results in the underutilization and limited availability of this treatment modality. Despite successful outcomes, the controversial nature of MMT, and the stigma experienced by the patients on methadone, has been a particularly difficult obstacle to overcome. We present the history of MMT, review the evidence for its efficacy in the treatment of opioid dependence, and explore the origins of the stigma and misconceptions related to MMT.

Long-Acting Opioid-Agonists in the Treatment of Heroin Addiction: Why Should We Call Them "Substitution"?

Gerra G1, Maremmani I, Capovani B, Somaini L, Berterame S, Tomas-Rossello J, Saenz E, Busse A, Kleber H. Subst Use Misuse. 2009;44(5):663-71.

Many studies have documented the safety, efficacy, and effectiveness of long-acting opioids (L-AOs), such as methadone and buprenorphine, in the treatment of heroin addiction. This article reviews the pharmacological differences between L-AO medications and short-acting opioids (heroin) in terms of reinforcing properties, pharmacokinetics, effects on the endocrine and immune systems. Given their specific pharmacological profile, L-AOs contribute to control addictive behavior, reduce craving, and restore the balance of disrupted endocrine function. The use of the term "substitution," referring to the fact that methadone or buprenorphine replace heroin in binding to brain opioid receptors, has been generalized to consider L-AOs as simple replacement of street drugs, thus contributing to the widespread misunderstanding of this treatment approach.

Drug Addiction Stigma in the Context of Methadone Maintenance Therapy: An Investigation into Understudied Sources of Stigma.

Earnshaw V, Smith L, Copenhaver M. Int J Ment Health Addict. 2013 Feb 1; 11(1):110-122.

Experiences of stigma from others among people with a history of drug addiction are understudied in comparison to the strength of stigma associated with drug addiction. Work that has studied these experiences has primarily focused on stigma experienced from healthcare workers specifically even though stigma is often experienced from other sources as well. Because stigma has important implications for the mental health and recovery efforts of people in treatment, it is critical to better understand these experiences of stigma. Therefore, we characterize drug addiction stigma from multiple sources using qualitative methodology to advance understandings of how drug addiction stigma is experienced among methadone maintenance therapy patients and from whom. Results demonstrate that methadone maintenance therapy patients experience prejudice, stereotypes, and discrimination from friends and family, coworkers and employers, healthcare workers, and others. Discussion highlights similarities and differences in stigma experienced from these sources.

Does it Matter How We Refer to Individuals With Substance-Related Conditions? A Randomized Study of Two Commonly Used Terms.

Kelly JF, Westerhoff CM. Int J Drug Policy. 2010 May;21(3):202-7.

OBJECTIVE: Stigma is a frequently cited barrier to help-seeking for many with substance-related conditions. Common ways of describing individuals with such problems may perpetuate or diminish stigmatizing attitudes yet little research exists to inform this debate. We sought to determine whether referring to an individual as *"a substance abuser"* vs. *"having a substance use disorder"* evokes different judgments about behavioral self-regulation, social threat, and treatment vs. punishment.

METHOD: A randomized, between-subjects, cross-sectional design was utilized. Participants were asked to read a vignette containing one of the two terms and to rate their agreement with a number of related statements. Clinicians (N=516) attending two mental health conferences (63% female, 81% white, M age 51; 65% doctoral-level) completed the study (71% response rate). A Likert-scaled questionnaire with three subscales ["perpetrator-punishment" (alpha=.80); "social threat" (alpha=.86); "victim-treatment" (alpha=.64)] assessed the perceived causes of the problem, whether the character was a social threat, able to regulate substance use, and should receive therapeutic vs. punitive action.

RESULTS: No differences were detected between groups on the social threat or victim-treatment subscales. However, a difference was detected on the perpetrator-punishment scale. Compared to those in the *"substance use disorder"* condition, those in the *"substance abuser"* condition agreed more with the notion that the character was personally culpable and that punitive measures should be taken.

CONCLUSIONS: Even among highly trained mental health professionals, exposure to these two commonly used terms evokes systematically different judgments. The commonly used *"substance abuser"* term may perpetuate stigmatizing attitudes.

Stigma, Discrimination, Treatment Effectiveness, and Policy: Public Views About Drug Addiction and Mental Illness.

Barry CL, McGinty EE, Pescosolido BA, Goldman HH. Psychia Serv. 2014 Oct;65(10):1269-72.

OBJECTIVE: Public attitudes about drug addiction and mental illness were compared.

METHODS: A Web-based national survey (N=709) was conducted to compare attitudes about stigma, discrimination, treatment effectiveness, and policy support in regard to drug addiction and mental illness.

RESULTS: Respondents held significantly more negative views toward persons with drug addiction. More respondents were unwilling to have a person with drug addiction marry into their family or work closely with them. Respondents were more willing to accept discriminatory practices against persons with drug addiction, more skeptical about the effectiveness of treatments, and more likely to oppose policies aimed at helping them.

CONCLUSIONS: Drug addiction is often treated as a subcategory of mental illness, and insurance plans group them together under the rubric of "behavioral health." Given starkly different public views about drug addiction and mental illness, advocates may need to adopt differing approaches to reducing stigma and advancing public policy.

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www.stopstigmanow.org

2 WASHINGTON SQUARE SUITE #2A LARCHMONT, NY 10538

914 318 4442
STOPSTIGMANOW.ORG