Buprenorphine Pharmacotherapy in the Treatment of Opioid Dependence

Summary Prepared by the Committee on the Treatment of Opioid Dependence of CSAM
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Medication Assisted Treatment for opioid addiction

CSAM aligns itself with the NIH consensus statement of 1997, which defines opioid addiction as a chronic disease, and calls for increased access to long-term treatments. [1] The World Health Organization also supports maintenance pharmacotherapy as a way to save lives and prevent HIV transmission among persons who are opioid dependent, and has declared buprenorphine to be an 'essential medication.' [2] Maintenance pharmacotherapy with psychosocial treatment (currently known as Medication-Assisted Treatment or MAT) represents the medical standard of care. Methadone maintenance treatment (MMT) was the first and still the most common form of such treatment in the US.[3]Since 1965 MMT has been shown to reduce mortality, lower criminality, enhance functionality, and to reduce the incidence of seroconversion to HIV.[4-6] The NIH Consensus statement called for increased access to maintenance pharmacotherapy, and reduction in the severely restricting regulations that have governed methadone maintenance. [1] The Institute of Medicine (IOM) 2006 report also promotes integration of substance abuse care across health care settings, including primary care. [7]

Office-based opioid pharmacotherapy using sublingual buprenorphine

A major change enhancing treatment options for opioid dependence was the Drug Addiction Treatment Act of 2000 (DATA 2000), enabling office-based use of certain approved opioids in the treatment of opioid dependence.[8] This law is sometimes nicknamed the 'buprenorphine law', because under its restrictions the only two medications allowed in office-based treatment by qualified physicians are two formulations of sublingual buprenorphine that were approved by the FDA in 2002 for the treatment of opioid dependence, Suboxone® and Subutex®. These medications have been scheduled as three by the DEA because they have a better safety profile in cases of over-dosing than full agonist opioids such as methadone.
Office-based treatment is a major breakthrough in access to care for individuals who find it burdensome or impossible to attend a highly regulated specially-licensed outpatient clinic for their daily dose of methadone. Office-based opioid treatment (OBOT) also holds the promise of integrating health-care needs and thus improving the quality of care. Now, under DATA 2000, opioid-dependent patients may receive opioid pharmacotherapy treatment with their own physician and using sublingual buprenorphine in a familiar setting integrated with their medical and psychiatric care. Instead of daily visits to a specialty clinic, the patient can now fill his or her prescription at a local pharmacy. Not surprisingly, in controlled comparisons of clinic care versus OBOT, the OBOT was significantly better in patient satisfaction.[9] Analyses of the use of office-based sublingual buprenorphine in the US to date show that compared to MMT, buprenorphine treatment reaches patients who are better educated, more likely to be employed, and more likely to have taken prescription opioids as their main drug of abuse when compared to MMT. Addiction treatment professional societies have trained thousands of physicians throughout the country in the office-based treatment using sublingual buprenorphine, and seventy thousand patients have taken advantage of this treatment. [10, 11] Based on these reports of OBOT patient characteristics, it would be expected that private insurance coverage is more likely to be at issue in OBOT than in a more disabled clinic population. Prescription opioid abuse has been on the rise in the US. SAMHSA statistics show that around 5% of Californians over the age of 12 have participated in non-medical use of prescription pain relievers, and estimate that 252,000 persons meet the DSM criteria for abuse/addiction to pain relievers in the Pacific states.[12] This high abuse of pain relievers is also reflected in more ED mentions of problems related to prescription opioids.[13]According to the SAMHSA - sponsored random sampling study of buprenorphine medication-assisted treatment, buprenorphine is indeed used to treat this new group of opioid dependent patients.[11]

Length of treatment in opioid dependence

As with other chronic illness, opioid addiction has a wide range of severity of presentation. Since naturally occurring withdrawal from opioids is not in itself life-threatening, some addicted persons withdraw with no treatment at all, and may remain abstinent for years with ongoing self-help or mutual help meetings. When more severe symptoms are anticipated, patients may choose to undergo a gradual medically supervised withdrawal (MSW) in an inpatient or outpatient setting, followed by full addiction treatment, psychosocial support and monitoring. Many patients and family members still focus on 'detox' or 'rehab' and wish for a quick correction or cure to addictive behavior and dependence. However, the pattern of addiction is chronic. [14, 15]Although safe, forms of medically-supervised withdrawal for opioid dependence, even when enriched with psychosocial services, do not usually result in long-term abstinence, and relapse rates are high.[16, 17] Even when every effort has been made to enhance psychosocial treatment during and after the actual MSW, the drop-out rates and death rates remain high, and outcomes are better on maintenance than other treatments. [18, 19]No matter the method of detoxification, and no matter the criteria for patient selection for detoxification, poor long-term outcomes (40-60% relapse by six months, approaching 90% by 12 months) suggest a chronic disease - perhaps a long lasting abstinence syndrome - that is not being addressed by MSW of any kind. [20][[21] [14, 22] [16, 23] A recent CSAT treatment guide about the use of detoxification treatment in addiction medicine points out that detoxification is successful if it has fostered the patient's involvement in full, long-term treatment.[24] This benefit of maintenance over MSW has been shown for sublingual buprenorphine treatment. In one placebo controlled study retention in treatment was 75% for maintenance, and 0% after a six day detoxification.[25]Because of this high relapse to opioid abuse, addiction specialists recommend that even when MAT is used for medically supervised withdrawal, maintenance be readily available as a backup in case of threatened or actual relapse. [26, 27]

Buprenorphine maintenance treatment (BMT)

Methadone maintenance has been used since 1965, with long-term use conferring lasting and increasing benefit over time. [4, 28] [29, 30]Sublingual buprenorphine was developed in the US for maintenance treatment, and is thought to confer similar benefit with a better safety profile and the possibility of flexible venues for care. In the development of new treatments, controlled trials for 6-12 months with sufficient size are recommended before FDA approval of medications for long-term use, so that problematic side effects and complications would likely surface.[31] Safety and effectiveness for long-term use were shown by the initial US clinical trials of sublingual buprenorphine and buprenorphine/naloxone.[32, 33] Multi-site clinical trials showed comparable effectiveness in MAT with methadone or sublingual buprenorphine. [32-34] These studies showed excellent retention in treatment and reduction in opioid positive urine tests, results comparable to therapeutic doses of methadone maintenance. Extending after the initial clinical trials which led to FDA approval of sublingual buprenorphine in 2002, positive reports from long-term use in office-based and primary care private practice settings of up to four years of maintenance are now seen in the US. [35-37] In addition, later studies have also shown that sublingual buprenorphine is useful in medically supervised withdrawal, although relapse remains high.[38] A consensus panel in 2004 suggested BMT should always be available as backup whenever MSW was offered.[26]

Cost of sublingual buprenorphine treatment for addiction

There are clear cost savings in long-term treatment of opioid addiction. However, comparisons between the cost of methadone treatment to treatment with buprenorphine are difficult at present in the US. The two types of care are generally offered in different venues, by different physicians. The demographics suggest that these may be distinct populations, and that we should be careful in our comparisons. As mentioned above, the patients currently taking advantage of buprenorphine treatment are a different group arriving earlier to care and more likely to be using different opioids from those who are in methadone maintenance. It is thought that perhaps these are patients who would not ever go to a methadone clinic at the early stage in which they present for treatment in the office setting. [39] Neither are patients transferring out of methadone clinics to office-based

care in large numbers. Denial of one type of care over the other may be denying access to care for a distinct group of patients.

The cost-effectiveness of methadone maintenance has been studied and found to be cost-effective.[40] If studied and treated as a chronic condition, cost-effectiveness for MMT and for addiction treatment in general is even higher than when looked at as a single episode. Cost-effectiveness studies support chronic care as more cost-effective than repeated failed attempts at abstinence. [41, 42]Some of the savings are in patient suffering and repeated hospitalizations and emergency department visits for medical co-morbidities [41]. There is additional benefit to society from reduced criminality and increased productive activity. [43] One 2001 analysis of the cost-effectiveness of buprenorphine in the US projected that it would be cost effective if medication cost per day were below fifteen dollars. [44]

Cost-benefit studies have been done specifically looking at sublingual buprenorphine treatment outside the US in health care systems that differ from ours, where the venue is parallel between the two medications. These studies show comparable cost-benefit compared to methadone maintenance over a range of outcomes and in both specialty and primary care settings. They suggest no benefit in transferring from one treatment medication to another. [45, 46]

The place of sublingual buprenorphine in the treatment of opioid addiction

In view of the excellent results shown in controlled trials with sublingual buprenorphine maintenance, this medication is now considered part of the mainstream treatment for opioid dependence. Primary care and office-based settings are now additional venues to the standard care with methadone maintenance. As of this writing, 652 physicians' names and contact information are on the SAMHSA physician locator as offering sublingual buprenorphine treatment in California. Surveys of buprenorphine office-based care show that a distinct group of patients are presenting for care in primary care settings earlier and with less disability. Compared to medically supervised withdrawal or detoxification alone, full maintenance treatment is more effective and reduces overall cost associated with episodic medical care for co-morbidities and of repeated unsuccessful detoxification episodes. In summary, the evidence supports long-term use of medication for patients who are unable to remain relapse-free. Arbitrary limits to length of care or doses of medication are not consistent with current standard of care for the treatment of opioid dependence.

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