VA PRACTICE Matters

FEBRUARY 2001 VOL. 6 ISSUE 2

Effective Treatment for Opioid Dependence

- *As many as 900,000 Americans are dependent on heroin or other illicit opioids.*
- *VA is the largest provider of substance abuse treatment in the world, and treated almost 30,000 opioid-dependent patients in 1999.*
- *The majority of heroin users administer drugs intravenously. In the U.S., injection drug use is responsible for 24% of new HIV infections among men and 47% among women. Up to 90% of intravenous drug users contract Hepatitis C.*
- *Opioid agonist treatment (OAT) with methadone or L-alpha acetyl methadol (LAAM) is an effective treatment that reduces substance use, HIV transmission, criminal behavior, and mortality.*
- *Many opioid dependent individuals who could benefit from OAT never receive it because ideological and practical factors have limited access to this form of care.*
- *VA research shows that methadone maintenance is extremely cost-effective. It has a cost-effectiveness ratio of $6,000 per quality-adjusted life year gained, far less than other widely-available medical treatments.*

MDRC
MANAGEMENT DECISION AND RESEARCH CENTER
VA HSR&D
Health Services Research & Development Service

A publication of the Management Decision and Research Center
A program within the Department of Veterans Affairs Health Services Research and Development Service

BACKGROUND

Opioid dependence remains a serious health problem across the U.S. In addition to high rates of death from direct causes (3–8 percent per year, mainly from overdose and trauma), opioid dependent individuals are at high risk for HIV (5-40 percent prevalence in major cities), Hepatitis C, and soft-tissue infection (Holmberg, 1996; Austin et al, 2000).

Despite these grim statistics, there is a reason for hope: an effective treatment exists. Opioid agonist treatment (OAT) reduces opioid use, crime, unemployment, opioid-related mortality, and the spread of infectious diseases, and improves patients' quality of life (Ball & Ross, 1991; Glanz et al., 1997; Ling et al., 1976; Marsch, 1998; McLellan et al., 1993; Newman & Whitehill, 1979; Sees et al., 2000; Zaric et al., 2000). Yet less than 20% of opioid dependent individuals are receiving treatment (NIH consensus statement, 1997).

Access to high-quality OAT is extremely limited. VA operates only 31 opioid agonist treatment clinics, and most of these are unable to keep up with treatment demand in their local area. Some VISNs have no OAT services at all despite significant heroin use in their catchment area. Finally, some VA OAT clinics do not adhere to treatment practices that have been demonstrated to produce the best outcomes (Hamilton & Humphreys, 1996). Expanding and optimizing opioid agonist treatment should decrease the suffering and economic burden associated with opiate dependence.

TREATMENT

Treatment for opioid dependence is directed at decreasing morbidity and mortality, and improving quality of life. In addition to reducing drug use, specific treatment goals include: reducing the prevalence of HIV transmission, hepatitis and soft-tissue infections; improving psychological, emotional and physical well-being; increasing employment and social stability; and reducing criminality.

Available therapies

Two major types of OAT are practiced: maintenance and medically-managed withdrawal (O'Connor & Fiellin, 2000). Maintenance treatment involves long-term (i.e., from six months to indefinite) administration of methadone or LAAM (levo alpha acetyl methadol) with the aim of eliminating withdrawal symptoms and drug-craving and blocking the effects of illicit opioids. Methadone is typically dispensed daily, whereas LAAM is dispensed less frequently because of its longer duration of effect (48-72 hours). Both medications are oral opioid substitutes. Optimally, maintenance treatment is given in conjunction with psychosocial services and is continued for an indefinite period. By contrast, medically-managed withdrawal is a short-term pharmacological treatment with or without additional psychosocial services, and is intended to minimize withdrawal symptoms associated with cessation of drug use and to stabilize the patient psychologically. Clinical studies have demonstrated that maintenance OAT is significantly safer and more effective than medically-managed withdrawal (Newman & Whitehill, 1979; Sees et al, 2000).

The preponderance of evidence shows that OAT is the most effective treatment for most opioid dependent patients, and care that follows treatment guidelines produces better results. For example, for most patients, treatment with 60-100 mg/day of methadone more effectively blocks craving and withdrawal symptoms and reduces illicit opiate use than does treatment with lower doses (Ling et al, 1976; Strain et al, 1999).

Moreover, the effectiveness of methadone is significantly improved when the medication is supplemented with psychosocial services (McLellan et al, 1993). Perhaps most importantly, trials show that patients should have the option of continuing in OAT indefinitely. Discontinuation of treatment, even after years of successful abstinence from illicit opioids, leads to increased incidence of relapse to heroin use (Greenfield, 1999). Even though it must be provided long-term, OAT is a highly cost-effective intervention, as detailed below.

Benefits of treatment

Numerous benefits of OAT have been documented. Proper maintenance treatment has consistently been shown to sharply reduce the use of heroin and, more variably, other drugs of abuse. Treatment reduces high-risk injection practices, as well as mortality (1 – 2 percent annual death rate

Continued on page 4

EXPERT OPINION

Science continues to provide an ever-increasing array of tools with which to combat addiction. In the past 25 years, a variety of effective medications and behavioral therapies have been developed for treating substance dependence, particularly heroin addiction. Well-known medications such as LAAM and methadone, for example, occupy the same brain receptors as heroin and eliminate withdrawal symptoms that often accompany the sudden cessation of drug use. When administered in adequate doses, these medications stabilize the patient's brain, allowing them to function normally and to perform mental or physical tasks without impairment. When medications such as these are coupled with behavioral treatments, patients are able to lead productive lives.

Unfortunately, although these treatments have been determined to be safe, effective, and cost effective, they are not nearly as widely used as they should be. One set of impediments is the broad misunderstanding about these agonist medications – the belief that they are simply substitutes for heroin. This of course runs counter to our understanding that methadone and LAAM actually stabilize the brain of a heroin addict. Moreover, there are strict state and federal regulations that control the use of these medications, frequently making it difficult for the estimated 900,000 individuals in need of opiate treatment to receive it. This point was made strongly by the 1997 NIH Consensus Development Conference on the Effective Medical Treatment of Opiate Addiction. A positive note in this treatment gap scenario is the fact that Congress has just recently passed legislation that will allow qualifying physicians to dispense or prescribe in their offices several of the pending new medications for heroin addiction. These new medications, such as buprenorphine and buprenorphine/naloxone, have been shown to have a higher safety and lower diversion potential than other available treatments. Patients enrolled in clinical trials with these products have also reported that the withdrawal syndrome associated with buprenorphine is minimal. Once these medications are approved by the Food and Drug Administration, the fact that qualified physicians will be able to prescribe them from their offices should greatly expand the diversity of the anti-addiction clinical toolbox and thus provide expanded treatment options for the diverse opiate addict patient population.

Alan I. Leshner, Ph.D.
Director, National Institute on Drug Abuse

RECOMMENDATIONS

- To enhance patient outcomes, OAT clinics should more consistently follow clinical practice guidelines. Treatment that complies with guidelines, which specify that the dose be sufficient to prevent withdrawal and craving (generally equivalent to at least 60 mg/day methadone; LAAM is given at 1.2 to 1.3 times the methadone dose every other day), has been shown to be most effective. Appropriate psychosocial services would enhance patient outcomes and should be continued as needed. Higher methadone/LAAM doses, more extensive psychosocial services, and continuance of treatment have been demonstrated to optimize outcome.

- Access to OAT should be improved by expanding existing programs and by establishing new programs in locations where treatment is not yet available.

- The implementation and facilitation of new therapies, including buprenorphine and other office-based opioid agonist treatments, should be seriously considered as they become available.

TREATMENT

Continued from page 2

for patients in treatment versus 2-8 percent for those not in treatment). Further, opioid maintenance patients typically experience increased psychosocial stability, increased income, and improved quality of life.

OAT also has significant benefits to the general population. Opioid agonist treatment reduces the spread of HIV to the general population, and saves societal resources by reducing criminal behavior and unemployment among patients. Cost-benefit research indicates that, collectively, such benefits to society at large are sufficient to fully justify the cost of providing OAT to opiate dependent individuals (Zaric et al, 2000).

Barriers to treatment access

Despite the large body of evidence supporting the effectiveness of OAT, this treatment is not available to many opioid-dependent individuals. Neither VA nor non-VA programs can fully accommodate the demand for treatment; there are many long waiting lists and few openings. Travel distance to clinics compounds these limitations on access to care because OAT patients typically attend clinics 3-7 days a week.

New developments in treatment

Several new opioid agonist treatments have been developed to improve access, outcome, and flexibility in therapy. Buprenorphine, both alone and in combination with naloxone, is in trials as an alternative to methadone and LAAM. The pharmacological properties of this medication confer several potential advantages over methadone: it has reduced potential for overdose, morbidity and mortality, abuse, and diversion to illicit sale, and may decrease the dysphoria associated with opioid withdrawal (Ling et al, 1996, O'Connor & Fiellin, 2000). When approved by the FDA, this form of OAT could be given to large numbers of patients.

To increase its accessibility, buprenorphine will be available through primary care practices as well as OAT clinics. Primary care-based methadone maintenance may also one day be available; the Substance Abuse and Mental Health Services Administration is currently piloting and evaluating such a program in San Francisco. Although the exact number of Americans who would seek some form of OAT through a primary care provider is unknown, the experience of other nations that offer OAT in this fashion (e.g., Germany) suggests than many individuals would prefer to receive treatment in this fashion.

ACKNOWLEDGEMENTS:

This issue of *VA Practice Matters* on Effective Treatment for Opioid Dependence was written by: Jodie Trafton, Ph.D., Director of the QUERI Multi-site Opiate Substitution Treatment Study; Paul Barnett, Ph.D., Director of the Health Economics Resource Center; John Finney, Ph.D., Project Director of the QUERI Substance Abuse Module; Rudolf Moos, Ph.D. Research Coordinator for the QUERI Substance Abuse Module; Mark Willenbring, M.D., Clinical Coordinator for the QUERI Substance Abuse Module, and Keith Humphreys, Ph.D., Associate Director of the Program Evaluation and Resource Center. Other contributors included QUERI Substance Abuse Module Executive Committee Members Thomas Kosten, M.D., Dan Kivlahan, Ph.D., Dennis Raisch, Ph.D., Richard Suchinsky, M.D., and George Woody, M.D. Eric C. Strain, MD, Johns Hopkins University School of Medicine, and Laura F. McNicholas, MD, PhD, Philadelphia VA Medical Center and the University of Pennsylvania, served as reviewers. The issue was edited by Geraldine McGlynn, M.Ed. and Diane Hanks, MA, of VA's Management Decision and Research Center.

VA Practice Matters is a publication for VA decision makers and practitioners that summarizes the results of important research to help inform policy and to promote the application of research for improved health care delivery and decision making within VA. It is produced by HSR&D's Information Dissemination Program in collaboration with topic experts in the field. For more information or to provide us with your suggestions, please contact:

Information Dissemination Program
Management Decision and Research Center (152-M)
VA Boston Health Care System
150 South Huntington Avenue
Boston, MA 02130
Phone: (617) 278-4433
FAX: (617) 278-4438

Email: geraldine.mcglynn@med.va.gov

VA Practice Matters is also available on the VA R&D internet at www.va.gov/resdev/prt, and on our Fax on Demand system by dialing (617) 278-4492 and following the voice prompts.

Evidence Chart

Study	*Participants* *Per group*	*Intervention*	*Outcome*
MAINTENANCE VS. WITHDRAWAL Newman & Whitehill. Lancet 1979: 485-8	n=50 patients with heroin addiction	Methadone maintenance (100 mg) vs. methadone dose-reduction (decreased by 1 mg/day from 60 mg start)	After 32 weeks, 72% of maintenance patients were still in treatment, but only 10% of the dose-reducing group remained. Only the maintenance group showed reductions in heroin use.
MAINTENANCE VS. WITHDRAWAL Sees et al. JAMA 2000; 283: 1303-10	n=88-91 patients with opioid dependence	Ongoing psychosocial services with methadone as a maintenance vs. detoxification treatment.	Methadone maintenance patients stayed in treatment longer and showed greater opioid abstinence than medically-managed withdrawal patients. ($p<0.01$).
DOSE Ling et al. Arch Gen Psychiatry 1976; 33: 709-20	n=142-146 VA patients with opioid dependence	LAAM (80 mg) vs. Low (50 mg) vs. High (100 mg) dose methadone	High dose methadone patients had the best retention in treatment. Both LAAM and high dose methadone groups had better global drug use outcomes than the low dose methadone group ($P<0.005$).
DOSE Strain et al. JAMA 1999; 281: 1000-5	n=95-97 patients with opioid dependence	Low (40-50 mg) vs. High (80-100 mg) dose methadone	Both groups decreased illicit opioid use; high dose had significantly greater reductions in opioid use ($p=0.01$)
PSYCHOSOCIAL SERVICES McLellan et al. JAMA 1993; 269: 1953-9	n=32-35 patients with opioid dependence	Methadone prescription only vs. with standard psychosocial services vs. with enhanced psychosocial services	All treatments decreased illicit drug use. Increases in services led to a greater percentage of patients showing heroin abstinence ($p<.01$). The enhanced service group had better employment, alcohol use, and legal outcomes ($p<0.05$).
COST-EFFECTIVENESS Barnett. Addiction, 1999; 94: 479-88	N/A	Cost-effectiveness analysis to compare methadone maintenance treatment to standard care	Methadone maintenance treatment has an incremental cost-effectiveness ratio of less than $6,000/quality adjusted life year, well below the $50, 000 standard for cost-effectiveness.

REFERENCES

Austin GE, Jensen B, Leete J, De L'Aune W, Bhatnagar J, Racine M, Braun JE. Prevalence of hepatitis C virus seropositivity among hospitalized US veterans. *American Journal of Medical Science* 2000; 319:353-9.

Ball JC, Ross A. The effectiveness of methadone maintenance treatment. New York: Springer Verlag, 1991.

Barnett P. The cost-effectiveness of methadone maintenance as a health care intervention. *Addiction* 1999; 94: 479-488.

Greenfield L. Methadone treatment outcomes in the National Treatment Improvement Evaluation Study (NTIES). Bethesda, MD: Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, 1999.

Glanz M, Klawansky S, McAullipe W, Chalmers T. Methadone vs. L-alpha acetyl methadol (LAAM) in the treatment of opiate addiction: A meta-analysis of randomized controlled trials. *American Journal of Addiction* 1997; 6: 339-349.

Hamilton EG, Humphreys, K. Outpatient methadone services in the Department of Veterans Affairs. Palo Alto, CA: Department of Veterans Affairs, Program Evaluation and Resource Center, 1996.

Holmberg SD. The estimated prevalence and incidence of HIV in 96 large US metropolitan areas. *American Journal of Public Health* 1996;86: 642-654.

Ling W, Charuvastra C, Kaim SC, Klett CJ. Methadyl acetate and methadone as maintenance treatment for heroin addicts: A Veterans Administration cooperative study. *Archives of General Psychiatry* 1976; 33: 709-720.

Ling W, Wesson DR, Charuvastra C, Klett CJ. A controlled trial comparing buprenorphine and methadone maintenance in opioid dependence. *Archives of General Psychiatry* 1996; 53:401-7

Marsch LA. The efficacy of methadone maintenance interventions in reducing illicit opioid use, HIV risk behavior, and criminality: A meta-analysis. *Addiction* 1998; 93: 515-532.

McLellan AT, Arndt IO, Metzger DS, Woody GE, O'Brien CP. The effects of psychosocial services in substance abuse treatment. *Journal of the American Medical Association* 1993; 269:1953-1959.

Newman RG, Whitehill WB. Double-blind comparisons of methadone and placebo maintenance treatments of narcotic addicts. *The Lancet* 1979; 8141: 485-488.

NIH Consensus Conference. Effective medical treatment of opioid addiction. National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction. *Journal of the American Medical Association* 1998; 280: 1936-43.

O'Connor PG, Fiellin DA Pharmacological Treatment of Heroin-Dependent Patients. *Annals of Internal Medicine* 2000; 133: 40-54.

Sees KL, Delucchi KL, Masson C, Rosen A, Clark HW, Robillard H, Banys P, Hall S. Methadone maintenance versus 180-day psychosocially enriched detoxification for treatment of opioid dependence: A randomized controlled trial. *Journal of the American Medical Association* 2000; 283: 1303-1310.

Strain EC, Bigelow GE, Liebson IA, Stitzer ML. Moderate- vs. high-dose methadone in the treatment of opioid dependence: a randomized trial. *Journal of the American Medical Association* 1999; 281:1000-5.

Zaric GS, Barnett P, Brandeau M. HIV transmission and the cost-effectiveness of methadone maintenance. *American Journal of Public Health* 2000; 90: 1100-1111.