

SUDden Impact

Newsletter of the Quality Enhancement Research Initiative—Substance Use Disorder Module

BUPRENORPHINE GAINS FDA APPROVAL

Laura McNicholas, MD

Buprenorphine is a partial agonist of the μ opioid receptor and has been in clinical use as an analgesic since the 1970's under the trade name "Buprenex". As a partial agonist, buprenorphine has a "ceiling effect." In October 2002, the FDA approved buprenorphine, as a sublingual tablet in two forms, for the treatment of opioid dependence. The two forms of buprenorphine are a mono tablet of buprenorphine, 2 mg or 8 mg, and a combination tablet of 2 mg buprenorphine and 0.5 mg naloxone or 8 mg buprenorphine and 2 mg naloxone. The naloxone in the sublingual tablets is not systemically available.

A number of clinical trials have established the effectiveness of buprenorphine for the treatment of heroin addiction. These have included studies that have compared buprenorphine to placebo (Johnson *et al*, 1995; Ling *et al*, 1998), as well as comparisons to methadone (e.g., Johnson *et al*, 1992; Strain *et al*, 1994a, 1994b; Ling *et al*, 1996; Schottenfeld *et al*, 1997; Fischer *et al* 1999; Pani *et al*, 2001; Petitjean *et al* 2001) as well as to methadone and LAAM (Johnson *et al* 2000). Results from the latter studies suggest that buprenorphine is equally effective as moderate doses of

methadone (e.g., 60 mg per day), although it is not clear whether it can be as effective as higher doses of methadone (80-100 mg/day) in patients requiring higher doses of methadone for maintenance therapy. Meta-analysis comparing buprenorphine to methadone (Barnet *et al*, 2001) concluded that buprenorphine was more effective than 20-35 mg of methadone but did not have as robust an effect as 50-80 mg methadone, much the same as the individual studies concluded.

Buprenorphine continued page 4

NIDA Clinical Trials Network: Bridging the gap

George Woody, MD

The NIDA Clinical Trials Network (CTN) was developed in response to a 1996 report from the Institute of Medicine which pointed out that many gaps exist between what research has shown to be effective in treating persons with substance use disorders, and what is actually done. Examples were many and included research findings that professional staff and longer treatments improve outcome but neither are widely available; findings that rapid admission

improves retention but that many waiting lists exist; that a range of approaches are necessary but that most programs rely on 12-step approaches; and many others.

A major recommendation was that NIDA develop a network of clinical research sites where community programs work together with university based researchers to test treatments that appear effective. The idea is much like the QUERI initiative with a focus on testing projects that can improve

the way treatment is delivered in many settings. As of this writing, NIDA has established 17 CTN "Nodes" involving a university based research staff and 5 or more community treatment programs. Protocols have been selected with a special focus on choosing studies that are likely to show positive results and, if so, can be implemented in these real-life settings. Seven protocols have been fielded to date, and results from some should be available in the next year.

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Developing a system to increase use of a smoking cessation telephone Helpline *John Kelly, PhD*

Smoking is the leading preventable cause of death in the United States. In 1999, the standardized prevalence of smoking in the VA was 33% for men and women, versus a 23% rate in the general U.S. population. Telephone counseling is an effective smoking cessation intervention, but a VA guideline implementation study (Project QUITs) has found that referrals to smoking cessation help lines are rare, even with expert recommendations advocating their use. This suggested barriers to external referral were significant, leading to the impetus for the current project.

A SUD QUERI Coordinating Center project will evaluate the impact of a multi-faceted intervention to encourage use of the California Smokers Helpline. The project PI is Scott Sherman, MD, at the VA Greater Los Angeles HCS. John Kelly, Ph.D., is coordinating project activities at a second site, the VA Palo Alto HCS.

The intervention consists of:

- education and training for providers and staff
- specific brochures designed to inform/remind patients, staff and providers about the Helpline
- system change (simplified referral process, basic case management).

The intervention will be implemented at approximately 10 clinics; 6 clinics will serve as comparison sites. The primary outcome will be the proportion of patients contacting the Helpline in each condition. A patient coordinator at each site will monitor and track callers to the Helpline, and assist them receiving prescriptions for smoking cessation medications.

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Intervention Phase of HSR&D Smoking Cessation Project Begins *Melissa Partin, PhD*

Melissa Partin, PhD

The intervention phase of the VA Health Services Research and Development project entitled "Facilitating Implementation of the PHS Smoking Cessation Guideline" started in September, 2002. This project is designed to test a strategy for linking relapsed smokers interested in quitting with appropriate repeat treatment. Thus far, 1,010 subjects from five VA Medical Centers (Seattle, Providence, New Orleans, Salt Lake City, and Denver) have been randomized to either the control or intervention



group. Subject accrual will continue for another few months.

A team of three interviewers at the Minneapolis VA is calling subjects in the intervention group to collect information about their smoking status, intention to quit, and treatment preferences. Information regarding subjects' quit intentions and treatment preferences gathered from these interviews is passed on to primary care providers and smoking cessation treatment coordinators in the form of a computerized progress note. The interviewers have contacted over 300 subjects to date. Preliminary findings from the inter-

views suggest that most (94%) smokers who have recently failed a quit attempt want to try to quit again within six months, and welcome assistance from the VA. 95% of these subjects would like to try the nicotine patch, nicotine gum, and/or bupropion SR (Zyban); 71% are interested in receiving behavioral treatment. Between February and September of 2003, outcome data will be collected and evaluated to determine if this intervention increases the proportion of relapsed smokers who receive repeat smoking cessation treatment.

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Opiate Initiative Project Update

Andrea Postier, MPH

The goal of the OpiATE (Opioid Agonist Therapy Effectiveness) Initiative is to examine the feasibility and effectiveness of implementing four evidence-based practices in opioid agonist therapy (OAT) for opioid dependence. These four target practices include adequate methadone dosing, adequate counseling frequency, subscribing to a maintenance (vs. abstinence) approach to treatment, and use of contingency management (CM). Since October 2002, all clinics are receiving the facilitated quality improvement (QI) intervention. The following is an update regarding QI progress in each of the four practice areas. Both quantitative and qualitative OpiATE Initiative data indicate that meaningful QI efforts are being implemented at all nine clinics.

⇒**Dose:** Data from Month 4 (five months into the project) indicate that,

since baseline, the percent of patients taking at least 60 mg/day of methadone (or its LAAM equivalent) increased at six clinics, remained the same at one clinic, and decreased at two clinics (see Figure 1). Interestingly, the two clinics whose percentage of patients taking at least 60 mg/day of methadone (or its LAAM equivalent) decreased were not yet receiving the intervention at Month 4. Early efforts to increase dose appear to have been effective at clinics receiving the immediate intervention, with only one clinic remaining the same.

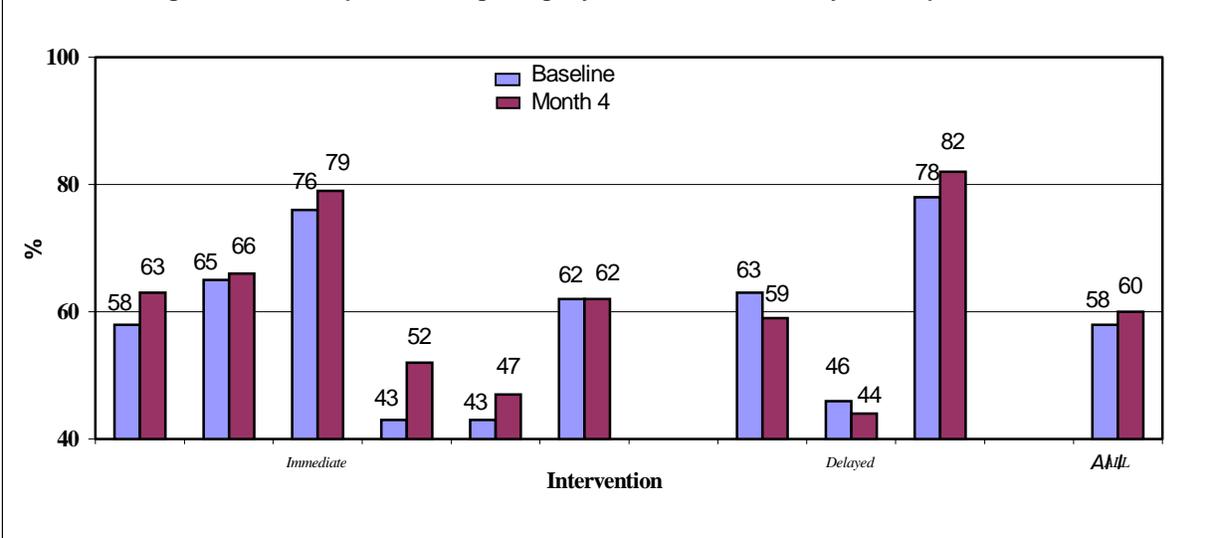
⇒**Counseling Frequency:** At Month 4, eight of nine clinics were meeting the minimum counseling frequency standard of one visit per week in the first month of treatment and one visit per month thereafter. The clinic not meeting the minimum standard has made QI in this area a priority, which

will also provide OpiATE Initiative staff an opportunity to work with this practice area.

⇒**Program Orientation:** At baseline clinic staff were asked to complete the Abstinence Orientation Scale (AOS) (Coplehorn, 1998), which contains items measuring OAT orientation on a scale of one to five. A score greater than three indicates an abstinence orientation and vice versa. At baseline, median clinic-level scores ranged from 1.9 to 3.1 (clinic N=9). Five of nine clinics have completed and returned six-month follow-ups, showing a trend toward decreased median scores.

⇒**Contingency Management:** All nine clinics have received and reviewed the OpiATE Initiative CM materials. Some are already using the sample CM plans and forms as templates for improving their existing CM policies.

Figure 1. Percent of patients taking 60 mg/day or more of methadone by clinic, OpiATE Initiative



QUERI-SUD Module Executive Committee:

Research Coordinator: John Finney, PhD
Clinical Coordinator: Mark Willenbring, MD

SUDDen Impact Staff:

Mark Willenbring, MD (612) 467-3967
mark.willenbring@med.va.gov
Marie Kenny (612) 467-3991
marie.kenny@med.va.gov

Executive Committee Members:

Paul G. Barnett, PhD	Jan Beyer
Brenda Booth, PhD	Katharine A. Bradley, MD, MP
Hildi Hagedorn, PhD	Anne M. Joseph, MD, MPH
John F. Kelly, PhD	Michael Kilfoyle, MD
Dan Kivlahan, PhD	Thomas Kosten, MD
Philip Lavori, PhD	Rudolf Moos, PhD
Dennis Raisch, PhD	Manning Carrington Reid, MD
Kathleen Schutte, PhD	Richard Suchinsky, MD
George Woody, MD	

Translation Coordinators Announce New Survey

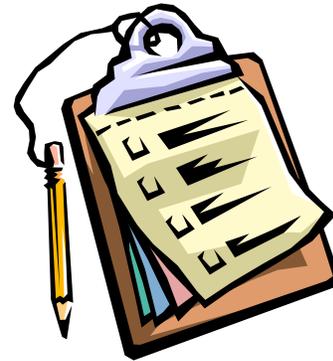
Hildi Hagedorn, PhD and John Kelly, PhD

In addition to continuing direction of the OpiATE Initiative, the QSUD translation coordinators are currently developing a follow-up to the QSUD 2001 Clinical Practice Guideline (CPG) Survey of VA substance use disorder (SUD) treatment program leaders. The 2001 survey assessed program leaders familiarity with CPGs, attitudes toward CPGs, and perceived barriers to implementation of CPGs. Program leaders identified lack of staff skills and knowledge as a major barrier to CPG implementation. Survey results also indicated that staff were perceived by program leaders as either neutral or opposed to CPGs. The follow-up survey will be

directed to line staff. We have randomly selected 50 VA SUD treatment programs for inclusion in the survey. All staff with 20 or more hours devoted to direct clinical services will be asked to complete the survey. The survey will assess staff knowledge, beliefs, and opinions regarding CPGs. It will allow us to compare staff responses to program leaders' beliefs regarding staff knowledge of and acceptance of CPGs as identified in the original survey. The survey will also allow staff to rank order perceived barriers to and methods for improving the implementation of CPGs. The goal of the follow-up survey is to provide further guidance for select-

ing targets and methods for translating evidence-based SUD treatments into clinical practice.

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Buprenorphine from page 1

Buprenorphine's affinity and dissociation profiles on the μ opioid receptors are responsible for important features of its clinical and therapeutic effects. The drug's high affinity for μ opioid receptors is responsible for its ability to compete with full μ agonists, such as heroin, and to block their effects. Buprenorphine has a very slow dissociation rate from the μ opioid receptor and this slow dissociation gives rise to its prolonged therapeutic effects. This slow dissociation of buprenorphine from μ opioid receptors allows the drug to be given as infrequently as three times per week (and there is some evidence to suggest it may be possible to give buprenorphine as infrequently as twice per week). Under the Drug Addiction Treatment Act of 2000, physicians who have notified DHHS and DEA of

their intent to use buprenorphine in office-based settings may treat up to 30 patients at any given time. In order to appropriately notify DHHS and DEA, a physician must qualify to use buprenorphine according to specifics set out in the law. Physicians may qualify to use buprenorphine if s/he is ASAM-certified, has Added Qualifications in Addiction Psychiatry or has taken an approved course on the treatment of opioid dependence and the use of buprenorphine in that treatment; the course must be a minimum of 8 hours. There are also presently two courses offered on-line, one from APA and the other from AAAP that fulfill the course requirement. In addition, under the Act, SAMSHA must produce Clinical Practice Guidelines. At the present time, a revised draft of previously available guidelines is being reviewed for scientific accuracy and completeness, and should be available, a

least as a final draft product, within 2-3 months. Physicians who have taken the training or who otherwise qualify may now send in their notification through the CSAT website. Physicians in licensed Opiate Treatment Programs do not need to notify DHHS/DEA in order to use buprenorphine in the OTP, nor are the OTP's constrained in the number of patients treated with buprenorphine.

At the present time, the cost of buprenorphine as Subutex® (mono) or Suboxone® (combo) is not known. We have been told that the combo product will probably be priced less than the mono product, as it is recommended that the combo product be the primary prescribed entity to decrease diversion to the injection route. It is estimated that a 16 mg dose of sublingual buprenorphine will be less than \$10/patient, but that figure could easily change.

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