ADDICTION TREATMENT

Forum

THE QUARTERLY NEWSLETTER FOR CLINICAL HEALTH CARE PROFESSIONALS ON ADDICTION TREATMENT

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Are buprenorphine and LAAM improvements over methadone? Are the newer agents safe alternatives?

IN THIS ISSUE

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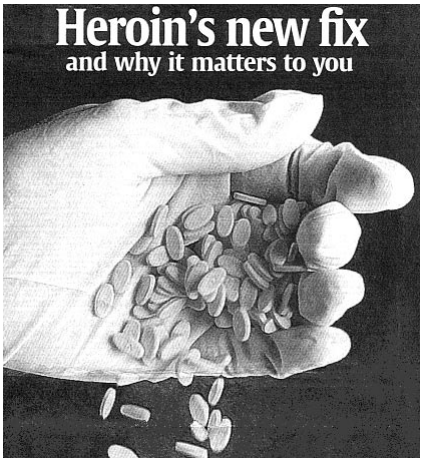
Clinical Concepts

How Safe Are Methadone, LAAM, Buprenorphine?

Alternatives Praised

Newer medications have been proposed as superior alternatives to methadone in the treatment of opioid dependency. This especially came to light in "Heroin's new fix," a cover story in the May 31, 2000 edition of *USA Today*, the largest daily circulation U.S. newspaper. The article began, "New drugs, younger addicts fuel push to shift treatment from methadone clinics."



Source: USA Today

The news article quoted scientists and health officials as claiming newer opioid agonists could reduce methadone's role as well as that of methadone maintenance treatment (MMT) clinics. In particular, buprenorphine was portrayed as a "cutting-edge" medication, effective and safe, and destined to move addiction treatment into doctors' offices nationwide. Additionally, a combination buprenorphine-naloxone

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MMT & Beyond

Office-Based Methadone Prescribing

In 1997, NIDA funded a 3-year research project on "Office-Based Methadone Prescribing" at Montefiore and Beth Israel Medical Centers, and the Albert Einstein College of Medicine. Following is a report from project director Ellen L. Tuchman, CSW, PhD (cand) and principal investigator Ernest Drucker, PhD.

More than 30 years since its inception, most methadone maintenance treatment (MMT) in the U.S. continues to be delivered only through clinics that are heavily regulated. After years of MMT, patients may still be attending the clinic 4 to 5 times per week, even though they are making every effort to avoid being in places that have any association with drugs or their previous lifestyle.

Methadone for addiction treatment remains a medication that cannot be prescribed by physicians outside of MMT programs. Furthermore, many MMT patients do not receive primary medical care and, if they do, that care is often divorced from their treatment for addiction.

The goal of our study was to explore the possibility of extending options available for methadone treatment by determining the safety, practicality, and efficacy of a primary care model for prescribing methadone.

Study Design

We enrolled 151 women in a randomized trial comparing "Office-Based Prescribing" (OBP) with usual care in MMT clinics. Fifty-three (53) patients were assigned to OBP (the experimental group) and 100 were followed as con-

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Events to Note

For additional postings & information, see: www.atforum.com

JULY 2001
Summit for Clinical Excellence
July 26-29, 2001
San Francisco, California
Contact: 480-563-1192

AUGUST 2001
New England Adv. School of Addiction Studies
August 21-24, 2001
Waterville Valley, New Hampshire
Contact: neias@neias.org; www.neias.org

SEPTEMBER 2001
14th Ann. Prevention Research Conf.
September 9-12, 2001
Charlotte, North Carolina
Contact: 405-325-1447, scarlson@ou.edu

OCTOBER 2001
American Methadone Treatment Assn.
October 7-10, 2001
St. Louis, Missouri
Contact: 856-423-7222 x360; www.americanmethadone.org

Amer. Public Health Assn. Ann. Mtg.
October 21-25, 2001
Atlanta, Georgia
Contact: 202-777-2479; lynn.schoen@apha.org

Amer. Academy Child/Adolescent Psychiatry Annual Mtg.
October 23-28, 2001
Honolulu, Hawaii
Contact: 202-966-7300; meetings@aacap.org; www.aacap.org

NOVEMBER 2001
ASAM State of the Art Course
November 1-3, 2001
Washington, DC
Contact: 301-656-3920; www.asam.org

ASAM Forensics in Addiction Medicine Workshop
November 29, 2001
Washington, DC
Contact: 301-656-3920; www.asam.org

LATER 2001...
American Psychological Society
June 14-17, 2001
Toronto, Ontario, Canada
Contact: 202-783-2077

American Methadone Treatment Assn.
October 7-10, 2001
St. Louis, MO
Contact: 856-423-7222 ext. 360; www.americanmethadone.org

[To post your announcement in A.T.Forum and /or our Web site, fax the information to: 847/413-0526 or submit it via e-mail from www.atforum.com]

A.T.F.

Straight Talk... from the Editor

Where's the Evidence?!

Evidence-based addiction medicine is a tough taskmaster.

It commands: "Your experience, opinions, and speculations are of limited use. Where's the research evidence to support your claims?"

We're reminded of the boisterous elderly lady (Clara Peller was her name) in TV commercials for a fast food hamburger chain some years ago. "Where's the beef?!" she protested with a look of disgust as she examined her anemic-looking sandwich.

Like the meat in Clara's sandwich, evidence is the substance of science.

Credible evidence is rarely served up in quickly digested nuggets.

Beefier Articles

Perhaps long-time readers of *AT Forum* have noticed some of our articles have grown a bit longer and more complicated in the interest of providing more substance. Such is the case with this issue's research into the safety of medications for opioid addiction.

We started with an analysis of adverse events reported to the FDA regarding methadone, LAAM, and buprenorphine during a several-year period. Plus, we scoured the research literature to see if there was supporting evidence for our findings.

The results were surprising, although methadone clearly retained its position as the "gold standard."

A summary of our report without documentation and as few intruding numbers as possible is in this edition of AT Forum. The full report is available by request (see the feedback card) and at our Web site – www.atforum.com. But, we must advise readers that there's a lot of "beef" in the full report – it's long and complex.

Credible evidence is rarely served up in quickly digested nuggets.

Slicing Through SPAM

At the other end of the evidence spectrum, this edition also has an article presenting "voices of dissent" – those self-proclaimed experts who argue against the concept of addiction as a disease and downplay the role of medical treatments in recovery. These folks appear to be unhindered by a careful examination of scientific evidence.

We hesitated to devote space to such ideologies, lest anyone think we endorse them. Yet, it is vital that everyone in the addiction treatment field is aware of these viewpoints, for they are a prime breeding ground for what Carlton Erickson, PhD has called SPAM – Stigma, Prejudice and Misunderstanding – surrounding drug addiction and its treatment.

Scientific evidence can slice through SPAM; however, we must be willing to search out and examine it. Indeed, the answer to "Where's the evidence?" is: "It's there if we look for it, and more is becoming available every day."

AT Forum will continue to search on your behalf and hopefully present our discoveries in ways that are easily understood and usable in everyday practice. Let us know how we're doing.

Survey – MMT Attitudes?

As usual, we want to know what our readers think about addiction and methadone treatment. Please respond to the following statements:

1. An MMT patient who continues to use heroin should be given higher doses of methadone. ____ agree; ___ disagree.
2. Complete abstinence from illicit drugs is essential for recovery in MMT. ____ agree; ___ disagree.
3. Many patients need to be maintained on methadone indefinitely. ____ agree; ___ disagree.

   Are you responding as a ____ staff member; or, ___ patient.

There are several ways to respond: **A.** Provide your answers on the postage-free feedback card in this issue; **B.** Write or fax us [see info below]; or **C.** Visit our Web site to respond online. As always, your ***written comments*** are important to help us discuss the results in our next issue.

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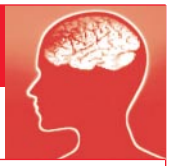

Part 8: Voices of Dissent

"Though dissenters seem to question everything in sight,
they are actually bundles of dusty answers and never conceived a new question." - Eric Hoffer

Despite all that medical science has uncovered about the nature of substance dependence, Eliot Gardner, PhD – senior research scientist at NIDA's Intramural Research Program, Washington, DC – observes that some authorities still argue against the concept of addiction as a disease. Others claim drug and alcohol addictions are under purely voluntary control and many people can abstain at will or naturally grow out of their addictions.[1]

These claims may breed prejudice and stigma surrounding addiction and its treatment, and clinicians, counselors, and patients need to be aware of them. While not endorsing such viewpoints, this article presents some of those voices of dissent.

Some [authorities] frequently conceive of drug or alcohol dependence as a self-inflicted disease of the will or moral flaw.

No Pain, No Gain

Behavioral healthcare consultant Harold Sloves comments, "Some government leaders, public health officials, members of the medical community, and the public at large frequently conceive of drug or alcohol dependence as a self-inflicted disease of the will or moral flaw."[2]

Particularly concerning methadone maintenance therapy, Sloves proposes that science still needs to overcome the social stigma and negative perceptions of addiction. There are many who regard methadone maintenance "as an ineffective narcotic substitution and believe that a drug-free state is the only valid treatment goal. There seems to be something of a 'no pain, no gain' viewpoint at work here."

Part of the problem, according to Sloves, is that substance abuse treatment has historically emphasized a psychosocial model, rather than a medical one. The antidote to this has been advances of the past two decades in documenting the neurobiology of opioid dependence. "Whatever social conditions might lead to opiate exposure," he writes, "opiate dependence is in fact a brain-related disorder, with the requisite characteristics of a medical illness that can be treated. Furthermore, the safety and efficacy of narcotic agonist (methadone) maintenance treatment has been unequivocally established."

Yet, those advances of science often seem ignored.

Addiction a Way of Life

Possibly the most prolific and vocal critic of the addiction-as-disease concept has been Stanton Peele, a social psychologist who taught organizational behavior at Harvard Business School and, more recently, entered the practice of law.[3]

Peele has published 7 addiction-related books, beginning with *Love and Addiction* in 1975. He is adamant that addiction is not a disease and does not believe that any drug is inherently addictive.

He concedes that addiction is all in the mind, but claims it has nothing to do with neurobiological functioning – it cannot be defined biologically, and has nothing to do with brain chemistry.[4]

"People become addicted to a wide range of involvements" in addition to drugs, he asserts.[4] "Anything we do can be addictive or not addictive." His concept embraces a wide range of addictions to other people, pets, sex, gambling, shopping, eating, psychotherapy, and even education (the "PhD syndrome").

"Addiction is not an aberration from our way of life," Peele proposes. "Addiction is our way of life."[4]

In fact, he argues, because people become addicted to so many things in life "it proves that addiction is not caused by chemical or biological forces and it is not a special disease state." He claims that the problem with disease theories of science is that "they avoid the work of understanding why people drink and smoke in favor of simply declaring these activities to be addictions, as in the statement 'he drinks so much because he's an alcoholic.'"[5]

Peele further asserts that drug withdrawal symptoms are a function of social settings that nurture their expression. The addict's response to withdrawal – the agony, the intense craving – is a cultural creation fostered by "inflammatory literature" such as Nelson Algren's book *The Man With The Golden Arm*.[4]

Peele states that "Addiction is nothing more than a way of coping with life, of attaining feelings and rewards people feel they cannot achieve in any other way."[6] People become addicted to drugs, as well as other experiences, because they like the psychoactive effects, the way it changes their sensations, the experience itself. For example, when cocaine produces a feeling of exhilaration it is the feeling to which the person becomes addicted. "No other explanation – about supposed chemical bondings or inbred biological deficiencies – is required," he claims.[5]

Peele rejects the notion of people saddled indefinitely with addictive lifestyles or personalities. "This can never account for the fact that so many people – most people – outgrow their addictions."[5] This "maturing out" or natural remission from addiction is central to much of Peele's arguments.

Those who do not outgrow their addiction have succumbed to self-fulfilling prophesies of disease, he believes. "[T]he readier people are to decide that their behavior is a symptom of an irreversible addictive disease, the more readily they fall into a disease state."[5]

Philosophically, Peele argues that "[a]ddiction is caused by environmental factors – more common in our time than any other – which are destructive of the wholeness of the individual."[4] "As such, addiction is no more a treatable medical problem than is unemployment…." The remedy for addiction, he proposes, is for people to have the resources, values, and environments necessary for living productive lives.[6]

The Power of Choice

In a recent book, psychologist Jeffery Schaler echoes the sen-

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While wailing about insufficient science in the addiction treatment and mental health fields, the voices of dissent do nothing to advance scientific knowledge.

timents of Peele and others by proclaiming in the title *Addiction is a Choice*.[7] He argues that society has erred by caving in to the AA vision that addiction is a disease, that addicts cannot help themselves, and that they need a Higher Power to be saved.

Schaler proposes that rather than being a disease, drug addiction is a scapegoated behavior, a victim of bad science and misguided policy, incorrectly identified as a physical or mental illness. People use drugs, he argues, as a way of avoiding and coping with certain existential experiences.

However, drug addicts do not want to do what's necessary to change their experience, he says. Drug use and addiction have less to do with what drugs do to the body than with the motivations and choices behind drug taking.

Like other voices of dissent, such as Peele, Schaler draws primarily upon a chorus of like-minded authors – Thomas Szasz, John Stuart Mill, Malcolm X, and others – rather than scientific research to support his speculative intellectual arguments.

Medicinal Manipulation

Others also contend that the disease model of mental illness and addiction prevails despite a lack of supporting scientific evidence. Psychologist Les Ruthven observes, "The [disease model] is very appealing because it gives society hope that a simple chemical is the answer to a variety of complex clinical problems… such as alcohol abuse, suicide, and violence."[8]

Addiction as disease, Ruthven laments, suggests to patients that their behaviors and symptoms are beyond their control. The concept reduces complex situations to simple solutions – i.e., taking pills to adjust brain chemistry. To many psychologists, he says, the notion of manipulating brain chemistry as a solution for mental disorders is at best naïve.

Ruthven suspects that many persons are being overdiagnosed with certain disorders because physicians believe there are effective medications to treat them. This, he believes, has happened with ADD or ADHD and bipolar disorder. "We have no pill for hysteria or for any other personality disorders and, as a result, they are underdiagnosed and the core problems of these patients are being neglected," he claims.

He observes that psychiatric treatment today focuses on medication and manipulation of medication when the patient is doing poorly. And, while psychiatry has been moving more toward a disease model, general medicine is moving in the opposite direction of a holistic model addressing the whole person in order to improve health outcomes.

Enticing Webs

By his own admission, Peele is an outsider who developed his views without actually working in the addiction field. His writings favor references to history and the musings of social philosophers, rather than scientific clinical studies. For Peele, it appears addiction is in the mind, rather than in brain chemistry, and it is the human intellect that harbors the solutions.

Unfortunately, experience over the years has demonstrated that intelligence is not a particularly potent tool for personal recovery. An addict is no more likely to simply think his/her way into sobriety than the "Just say 'no'" slogan of the 1980s could stem the rising tide of substance abuse in the first place.

In Schaler's perspective, people have the right to make their own choices, including destroying themselves with drugs. A civilized society has no right to coerce people into any kind of treatment program against their will, he believes.

The scholarly arguments of dissenting voices may spin enticing webs for some. Such activist ideologies also may sell books by rehashing old questions; however, they do nothing to help the thousands of addicts right now shivering on street corners as they anxiously await their drug dealers. While wailing about insufficient science in the addiction treatment and mental health fields, the voices of dissent do nothing to advance scientific knowledge. Their proclamations are a reminder that it is relatively easy to criticize or raise doubts; it is much more painstaking to arrive at valid and workable answers.

1. Gardner EL. The neurobiology and genetics of addiction: implications of the "Reward Deficiency Syndrome" for therapeutic strategies in chemical dependency. In: Elster J, ed. *Addiction: Entries and Exits*. New York: Russel Sage Foundation;1999:57-119.
2. Sloves H. Drug treatment for drug addiction: surmounting the barriers. *Behavioral Health Management*. 2000(July/August):42-46.
3. For an online overview of Stanton Peele's philosophies and writing see: www.peele.net.
4. Peele S, Brodsky A. Addiction is a social disease. *Addictions*. 1976 (Winter):2-21.
5. Peele S. *Diseasing of America*.
6. What is addiction and how do people get it. Lexington, MA; Lexington Books/Jossey-Bass: 1989, 1995. Peele S. *Cures depend on attitude, not programs*. Los Angeles Times. March 14, 1990.
7. Schaler JA. *Addiction is a Choice*. Chicago, IL: Open Court; 2000.
8. Ruthven L. Has the medication revolution gone too far? In: *2000 Behavioral Healthcare Sourcebook*. Providence, RI: Manisses Communications Group; 2000:58-63.

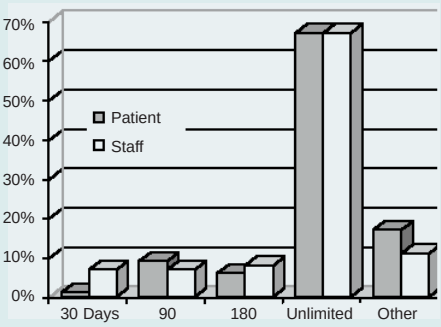
MSW Limits & Reasons

The Fall 2000 edition of *AT Forum* (Vol. 9, No. 4) observed that the term "detox," or detoxifying patients who have been on methadone for some time, is an incorrect expression as well as a misdirected outlook on the process. More appropriate, would be the concept of therapeutic tapering or dose reductions of methadone over time under close medical supervision – i.e., medically supervised withdrawal or MSW.

However, the question remains, how long should this process take? Readers were asked to share their opinions on time limits, and also reasons for withdrawing patients from methadone in the first place.

Unlimited MSW Time Favored

During a several month-period readers submitted responses via feedback cards or at the *AT Forum* Web site (www.ATForum.com). There were 281 survey responses: 145 from healthcare staff (e.g., physicians, nurses, counselors); 136 from patients. These are summarized in the graph.



Staff and patients were in strong agreement (67% of each group) that an unlimited amount of time should be allowed for very gradual methadone reductions. It is interesting to observe that small and roughly equivalent proportions of each group believed that 90 or 180 days would be adequate time. And about 7% of staff felt that a mere 30 days could be sufficient.

"Other" responses included 60 days, 45 days, and other time periods mostly falling below 180 days. In total, 67% favored unlimited time, while roughly 23% considered 180 days or less as adequate.

A Range of Reasons

As for the reasons behind MSW, many healthcare workers' responses focused on what might most appropriately be called "administrative" reasons. These included failure to follow clinic policies or procedures; to free-up slots for new patients; request of legal authorities or pending incarceration; and, of course, failure to pay.

Patients, on the other hand, seemed more centered on "performance" issues: e.g., continual abuse of illicit substances; fighting in the clinic or not abiding by rules; to be free of stigma and frequent clinic attendance.

Both groups did list medical or recovery-related rationales: e.g., to overcome long-term dependency and become drug-fee; social and psychological readiness; methadone interactions with other medications. Many readers noted that the best reason is a patient's personal decision, without coercion, and in consultation with caring medical staff.

Why Is MSW Necessary At All?

For many patients, their motivation for MSW apparently is to escape an unbearable situation that they believe has them "chained" to a methadone clinic for a lifetime. This seems to reflect ongoing problems with clinic operations, inadequate funding, and rigid regulations; rather than medical appropriateness or psychosocial readiness for MSW.

The comments of one patient summarized many responses: "A patient should never be forced into [MSW] and there should be encouragement to permanently stay on methadone maintenance. If a patient really wants to attempt withdrawal, he/she should be informed of all pertinent information, including relapse rates."

"There should not be a time limit placed on withdrawal. Pushing a time limit is playing with that patient's very life. Nonpayment of fees should not force withdrawal – the patient might be referred to another facility. Even prisoners should be allowed to stay on methadone maintenance. If they are offered MSW, then the time limit should be between the prisoner and medical staff."

Finally, a concerned parent provided an insightful argument: "I am the mother of a heroin addict who is on methadone and I believe that patients should be treated for as long as necessary and not be given any specific time limit to withdraw from methadone. Diabetics are not kicked off insulin because they can't live a totally 'clean' life. 'Detoxing' patients prematurely or against their will is Nazi-like treatment that has no place in an ethical medical setting."

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product was mentioned as being under investigation. LAAM, approved by the FDA in 1993, also was cited as a newer alternative to methadone.

Are buprenorphine and LAAM improvements over methadone, the foremost or "gold standard" opioid agonist for the treatment of opioid dependency since its introduction in the mid-1960s?

Even more important, are the newer agents really safe alternatives?

Unexpected Findings

To examine these safety issues, AT Forum analyzed adverse event reports concerning methadone, LAAM, and buprenorphine that were submitted to the U.S. Food & Drug Administration during a 3-year period, November 1997 to November 2000. A medical literature search also was conducted to identify published evidence supporting or opposing the findings.

Adverse events (AEs) associated with drugs are unanticipated reactions or consequences that are considered medically harmful to the patient, or a female patient's unborn baby. Sometimes they are called drug "side effects," although these generally tend to be less severe.

During the 3-year period, there were 170 AE reports submitted for methadone, 40 for LAAM, and 178 for buprenorphine. Compared with methadone, for which the AE reports represented only 0.03% of all methadone-treated persons during the 3 years, there were an unexpectedly high number of AEs associated with LAAM and buprenorphine.

This considers that, in the U.S., persons on methadone outnumbered LAAM patients by 45 to 1 so, proportionately, there should only have been about 4 reports for LAAM. And, since buprenorphine was not yet FDA-approved and still under study for opioid-dependency therapy in even fewer patients than for LAAM, the 178 AEs for buprenorphine seem extremely high and of concern.

Buprenorphine-treated patients were significantly younger than those receiving either LAAM or methadone. Younger patients have been suggested as a primary target population for buprenorphine (as also noted in the news articles mentioned above). It might be expected that such patients,

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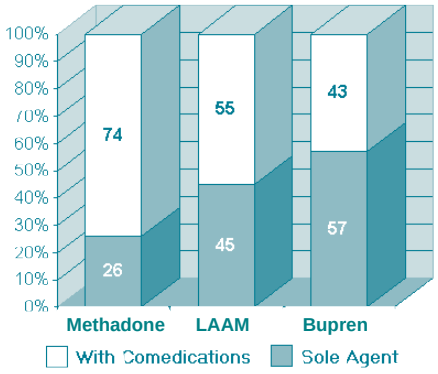
generally with addictions of less longevity and severity, might be healthier and would potentially experience fewer adverse events with buprenorphine. This was not evident.

Comedication Effects

The AE reports noted whether methadone, LAAM, or buprenorphine was the only drug – the "sole agent" – involved, or if the patient also was taking other drugs, "comedications." Only about a quarter (26%) of total AEs associated with methadone involved the drug as a sole agent, suggesting that interactions with other drugs play the major role in adverse reactions with methadone.

Compared with methadone, more than twice as many buprenorphine AEs occurred with the drug by itself (57%), possibly suggesting a more harmful effect of buprenorphine. Similarly, 45% of LAAM-related AEs were as a sole agent. ***See Figure 1.***

Figure 1. AEs With/Without Comedications



From this information, it appears that methadone, by itself, is by far the safest of the 3 medications. Furthermore, these findings suggest that the vast majority of AEs associated with methadone might be avoided by more careful prescribing of any comedications used in a particular patient's treatment.

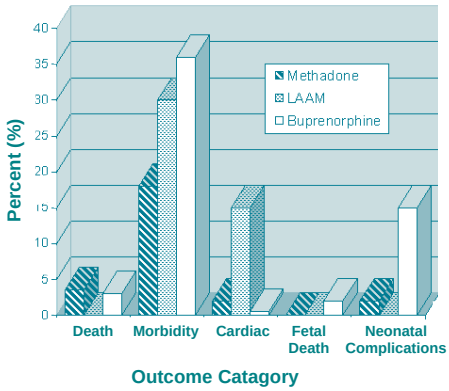
Troublesome Trends

The best indication of a drug's accountability in producing AEs might be in viewing it as a sole agent, unaffected by interactions with other drugs, prescribed or illicit.

Looking at each medication as a sole agent, FDA AE reports were further organized into several categories more clearly describing what happened – i.e., outcomes – as a result of drug effects. The outcomes included death, morbidity (which includes reactions often requiring emergency care or hospitalization), and cardiac-related effects (such as irregular heartbeat or heart attack). Additionally, as a result of the mother's exposure to the drug, some AEs reported fetal death or neonatal complications (e.g., abstinence syndrome in the newborn, tremor, or problems feeding or breathing).

The trends are summarized and displayed in ***Figure 2.***

Figure 2. AE Outcome Trends - Sole Agent



Deaths

Patient deaths were roughly equal for methadone and buprenorphine; however, this may be misleading, considering the much greater number of patients treated each year with methadone. Also, due to a number of factors, there have been questions about the accuracy of deaths attributed solely to methadone in the past and most reports indicate other causes or medications were present. Long-term studies of MMT patients have found no deaths directly caused by methadone.

A single death with LAAM in the FDA AE reports was in association with benzodiazepines. Similarly, there have been a number of deaths reported in the literature with buprenorphine in combination with benzodiazepines.

Morbidity

A considerably higher frequency of morbidity was reported for LAAM and buprenorphine than for methadone. In fact, there were twice as many hospitalizations, emergency care situations, and other reactions requiring treatment for buprenorphine as for methadone.

An important concern is that twice as many buprenorphine AEs in this category were due to patients dissolving tablets in liquid for IV injection, rather than sublingual administration (dissolving tablets under the tongue) as prescribed. Reactions specifically associated with IV abuse of buprenorphine involved injection site complications, such as blood vessel inflammation or clots, abscesses, edema, and pain.

This IV abuse potential of buprenorphine has been widely reported in the literature, along with a black market for the drug in countries where it has been available. This has raised concerns about the liberal prescription of take-home buprenorphine tablets, and it is uncertain that a buprenorphine-naloxone combination product in development would resolve the problem.

Cardiac Related

FDA-reported cardiac-related events were minimal for methadone and buprenorphine, but disproportionately much greater for LAAM. Due to concerns about cases of life-threatening heart rhythm disturbances, European authorities recently advised against using LAAM.

There were only 4 cases of heart disturbances associated with methadone. Practitioners in the field have noted that most such events in methadone patients might be traced back to preexisting medical conditions or an inherited tendency to develop heart problems.

A single cardiac-related event was reported for buprenorphine as a sole agent and it is possible that this might be a safety advantage of the medication. Further research in this area concerning all 3 opioid agonist medications seems appropriate.

Fetal Deaths/Neonatal Complications

Surprisingly, there were unusually high percentages of fetal deaths and neonatal complications associated with buprenorphine. This is a particular concern because the medication has been proposed for major use in younger addicts, which would include women of prime child-bearing age.

There were 4 deaths and 27 neonatal complication cases reported with buprenorphine, or proportionately 9 times more neonatal complications than with methadone. There has been relatively little research into the safety of buprenorphine during pregnancy and further investigations of this issue seem needed.

There were no fetal deaths and only 3 complications in newborns associated with methadone as a sole agent, which was noteworthy considering the very large numbers of women maintained on methadone each year. LAAM has been prohibited in pregnancy since its FDA approval, so there were no reports of fetal or neonatal AEs with this medication as a sole agent.

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Research Limitations

AEs reported to the FDA for methadone, LAAM, and buprenorphine might have been just the tip of the iceberg. Some have suggested that, in general, only 1% of all serious adverse reactions to drugs are reported to the FDA. Adjusting for this, however, it still would have resulted in only a very small percentage of all persons on methadone experiencing reactions to the drug during the 3-year period; for LAAM it would have been a third (33%) of all patients, and possibly much greater for buprenorphine.

Furthermore, the FDA reports do not provide information regarding illness prior to drug administration, so there is no way of knowing the relative impact of a patient's medical history. Substance dependent persons, especially older patients, often have multiple physical problems and symptoms that might make accurate reporting difficult.

Finally, AE reports sent to the FDA might be characterized as a collection of anecdotal cases. Still, in lieu of a better information-gathering system, such accounts do often carry considerable weight, as in the European warnings about LAAM mentioned above.

Methadone Still "Gold Standard"

In its approximately 35-year history as the "gold standard" treatment for opioid dependency, methadone has proved to be a safe medication. In the millions of patients treated during that time, extending more than 20 years in some patients, severe adverse reactions requiring emergency care or hospitalization have been relatively rare.

Medication side effects have been more common during the early days of MMT and easily managed. Women stabilized on methadone generally have more healthful pregnancies and healthier newborns than would be observed without such therapy.

Recently noted concerns about LAAM affecting heart health may limit its use to only special cases in which risks are overshadowed by specific advantages, such as its longer action permitting less-frequent dosing.

Buprenorphine and a buprenorphine-naloxone combination may offer advantages in carefully selected patients. However, risks of potential IV abuse must be considered and possible hazards of buprenorphine in pregnancy need to be better understood.

Robert Newman, MD, president emeritus of Continuum Health Partners, New York, and a leader in the addiction treatment field, has observed that there is no reason to believe that buprenorphine will be superior to methadone maintenance or other modalities for treating opioid dependence.

One major proposed advantage of buprenorphine would be its widespread and easy accessibility to patients in community-based medical practices. However, there do not appear to be any research-proven safety advantages that make buprenorphine better suited to this treatment approach than methadone. As Newman stressed, the same rationale for permitting buprenorphine to be prescribed by all licensed practitioners applies equally well to methadone.

Certainly, if multiple agents were available for opioid-dependency treatment, patients could benefit; just as multiple forms of antibiotics offer advantages in treating infection. However, patient safety should remain a prime concern.

Full Report Available: This research was sponsored by an educational grant from Mallinckrodt Inc., a manufacturer of methadone. The complete report, including 80 resource references, is available by checking the appropriate box and mailing the feedback card in this issue. It is also readily available in electronic format at <www.ATForum.com> under the "Current/Past Issues" tab, at the bottom of the contents page in the "Unpublished Reports" section.

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trols at their MMT clinics. Only women were included in this preliminary study to simplify the research design and reduce costs. In a subsequent stage men will be included.

To be eligible for the study, patients had to be on a stable dose of methadone for at least 6 months and at a reduced pickup schedule of 5 times or less per week. Patients with an existing primary care physician were excluded, so as not to interrupt already established medical care relationships.

The experimental and control groups were demographically equivalent. Average age and time in MMT for all subjects was roughly 41 years and 13 years, respectively. On average, the women were attending their clinics 3 to 4 days per week for methadone dosing at the start of the study. Methadone dispensing for both groups of patients continued to take place at participating MMT program clinics.

The objective of this study was to demonstrate equivalence: i.e., that the OBP patients would do as well as the MMT clinic controls. Two treatment outcomes were examined: retention and illicit drug use.

Results

Twelve medical practitioners were recruited from primary care community practices and health clinics at Montefiore and Beth Israel Medical Centers. Physicians were trained in all aspects of methadone treatment.

Prescribing authority over methadone dosage and pickup schedules for the 53 OBP patients was then transferred to participating practitioners. OBP patients made monthly visits to these primary care providers, who could alter dosages and pickup schedules within the practice guidelines and regulations operative in the MMT programs. All OBP patients continued to attend their MMT clinics for regular methadone dispensing, urine tests, and ancillary clinic services.

For ***treatment retention***, with 12-months follow-up, 5.7% of OBP patients left treatment compared with 6.1% of MMT patients.

For ***use of illicit drugs***, with 12-months follow-up, 82.3% of the women in OBP vs 71.1% of the women in MMTP had not used heroin or cocaine. We defined "illicit use" as two or more positive urine screens.

Differences between groups for retention and illicit drug use were not statistically significant, demonstrating that office-based physicians apparently can safely manage methadone prescribing for stable patients. However, to be of practical significance and to help increase total MMT capacity, office-based prescribing must be coupled with community pharmacy dispensing of methadone.

Integrating Community Pharmacy Dispensing

During the next 4 years our research will be expanded under a new NIDA grant, "Office Based Prescribing and Community

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Pharmacy Dispensing of Methadone."

We have worked with the Pharmacists Society of the State of New York to identify and recruit 4 well-regarded community pharmacies that have agreed to participate in the study. All are already serving many methadone patients' general pharmacy needs and have submitted required applications for appropriate licensing to administer methadone.

Participating pharmacies are open at least 6 days and for an average of 70 hours per week. The pharmacist will obtain methadone on a weekly basis and be responsible for preparing observed and take-home doses.

Twenty-five (25) current study patients, who completed at least one year with an office-based prescribing physician, will be eligible for the new pharmacy program. Patients will select one of the participating pharmacies, which will serve as a "medication unit."

Each patient will have a case manager – a social worker who coordinates care and provides all required psychosocial services, and all documentation required by state and federal rules. The women will see this case manager at least once each month and as needed.

Patients will begin receiving medication at the pharmacy at their current dosage and pickup schedule. As is the case in MMT clinics, doses administered at the pharmacy will be observed. Participating pharmacies will have a private consultation area where these doses will be administered.

Expanded Spectrum of Care

MMT clinics are invaluable for those who first enter treatment, for those who continue abusing heroin and other drugs, and for those who need more intensive psychosocial services and other care.

At the other end of the spectrum, for the most stable patients, we already have medical methadone maintenance. These patients are seen by their physicians monthly and given up to 30 days of take-home methadone at the office visit. This is appropriate for only a small percentage of patients.

OBP and pharmacy methadone dispensing could serve a larger percentage of MMT patients, and would open significant space in existing clinics for new patients. Plus, there are many cities in the US (and 8 states) where there is no methadone treatment or not enough slots in existing methadone clinics for those who want treatment.

Other patients also could benefit. Travel, illness, and disabilities prevent many from remaining in MMT clinics. Working patients sometimes fear their jobs are in jeopardy because MMT clinic hours conflict with work schedules. Women with young children may lack the finances or social support for childcare so that they can attend the clinic. And some stable patients simply no longer need all the structure and support services of a clinic setting.

In one model proposed by the American Methadone Treatment Association, the MMT clinic is seen as the hub of all treatment. Patients in hub clinics would be able to move fluidly from the clinic to an office-based provider with community pharmacy dispensing, and perhaps then to medical maintenance. However, there would always be an option to return to the MMT clinic during a period of instability or relapse.

If this model is to be effective in expanding access to care and maintaining quality, it is imperative that MMT program staff develop the ability to work well with outside physicians and pharmacists. In the next phase of our project we hope to demonstrate the feasibility of this transition, and document the effects on patients and the responses of providers to this new model of care.

This report is based on a poster presentation at the College on Problems of Drug Dependency, (CPDD), in San Juan, Puerto Rico, June 2000. Office Based Methadone Prescribing in Primary Care Practice: Results of a Randomized Trial of Feasibility and Efficacy. E. Drucker, D. Hartel, E. Tuchman, K. Bonuck, P. Vavaglakis, J. Garfield, and W. McCarthy.

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