Buprenorphine: "Field Trials" of a New Drug

Michael Agar
Philippe Bourgois
John French
Owen Murdoch

Buprenorphine is being introduced as a new treatment drug for narcotics addiction in the United States. The authors were asked by the National Institute on Drug Abuse to conduct a field trial to determine if buprenorphine might play a role in street markets. Because no street use of the drug existed in the United States, the authors used three sources of information: (a) "street readings" of clinical studies, (b) Internet discussion lists, and (c) research in other countries. By using an emergent style of analysis that relies on replication of patterns across disparate data sources, it was determined that buprenorphine has desirable characteristics from a street addict point of view. An evaluation of the field trial 5 years later evaluates its accuracy.

Buprenorphine is a new treatment drug for heroin addicts in the United States. Like methadone, it is an opioid *agonist*; that is, it satisfies the craving for a narcotic and prevents the withdrawal syndrome. Unlike methadone, it is also an *antagonist*; that is, it reacts against opiates and precipitates withdrawal. According to Navaratnam (1995), the agonist effect operates up to a certain dosage level, at which point the antagonist effect begins to operate.

We were asked by the National Institute on Drug Abuse to find out if buprenorphine currently played any role in U.S. street drug markets. From the medical and legal points of view, the question was one of what these fields call the "abuse liability" of a proposed treatment drug. Would the new treatment medication also turn into a hot street commodity, as it happened with methadone in the 1970s? Few programs used buprenorphine at the time of the study in 1996, so it played no street role in the United States, at least not among numerous different networks in San Francisco, Baltimore, and Newark. Because few users existed in the United States, we decided to experiment with the idea of a "field trial" for the drug, as opposed to the traditional notion of a "clinical trial." The "field" concept was borrowed from

AUTHORS' NOTE: Report prepared under National Institute on Drug Abuse Medications Development Division Purchase Order 263-MD-523831 and National Institute on Drug Abuse Division of Epidemiology and Prevention Research Contract No. NO1DA-3-5201 (CEWG)—State and Local Epidemiology Planning and Information Development. Please address correspondence to Michael Agar, P.O. Box 5804, Takoma Park, MD 20913; email: magar@anth.umd.edu.

QUALITATIVE HEALTH RESEARCH, Vol. 11 No. 1, January 2001 69-84

cultural anthropology with its emphasis on fieldwork, although field here is used differently from that traditional term. The logic of the field trial runs like this:

1. The field is expanded from a focus on a particular human group to *any* information available on the topic of interest, whether in the United States or in other countries, whether presented in media or a conversation, whether scholarly or popular in nature.
2. The field contains examples of use that vary in set and setting. The researcher's problem is to locate and organize set/setting information that is already available along the lines of the concept of the "natural experiment."
3. Analysis features emergent search for pattern, a style that is traditional in anthropology but also found in such areas as complexity theory (Waldorf, 1992) and marketing research (Michman, 1994). Validity derives from replication of patterns across disparate sources.
4. The analysis is anchored in a particular perspective from which the patterns are evaluated. In this case, the perspective will be that of urban American street addicts, a population with which we have decades of collective experience.

Our goal, then, is to present a field trial designed to forecast whether buprenorphine might play a role as a street narcotic in the United States and to estimate the chances that this situation might come about. To accomplish this goal, we will review a variety of different field sources and look for emergent patterns that replicate across this material from a street addict point of view. Our model of that point of view is derived from prior ethnographic work.

BUPRENORPHINE

Buprenorphine does have a history in the United States as a medication with a corresponding literature that evaluates it. This professional literature will be examined with a different filter snapped over the lens to give it a "street reading." How would this literature make buprenorphine sound if one were an opiate addict looking to buy it in a street market? Even in the technical literature, buprenorphine clearly has some desirable characteristics from this point of view. From various online literature abstracts, we learn that buprenorphine compares favorably with morphine in the management of postoperative pain. In fact, the literature suggests longer lasting and more moderate effects.

A clinical study of 6 men with histories of opioid use also adds credibility to the hypothesis (Pickworth, Johnson, Holicky, & Cone, 1993). Those who received intravenous buprenorphine rather than a placebo reported increased positive responses to a "feel drug" question and higher scores on scales of liking, good effects, euphoria, and apathetic sedation. The authors concluded that buprenorphine has substantial abuse liability when administered intravenously.

Another study, meant to test comparative effects of sublingual versus subcutaneous use, reported varying degrees of euphoria and little dysphoria and sedation from buprenorphine, also noting that "subject liking" was reported by both subjects and observers (Jasinski, Fudala, & Johnson, 1989). And finally, in what must be one of the first clinical studies of the drug (Jasinski, Pevnick, & Griffith, 1978), buprenorphine is described as having potential as a treatment drug because it is acceptable to addicts, has prolonged action, and produces a low level of physical dependence

such that addicts may easily detoxify. Such reasons are, of course, also the reasons why buprenorphine would be of interest from a street point of view as well.

Buprenorphine appears, hypothetically, as a longer, gentler "high" when compared to morphine. Returning to the abstracts, we learn that buprenorphine also has some history as an experimental drug for the treatment of opioid addiction in the United States. The effects of buprenorphine were evaluated using a rapid dose-induction procedure among 19 heroin-dependent men (Johnson, Cone, Henningfield, & Fudala, 1989). During the first 4 days of transition from heroin to buprenorphine, patients reported significantly elevated ratings of good effects, feelings of overall well-being, and decreased ratings of overall sickness. Euphoria increased and dysphoria and sedation decreased after buprenorphine administration.

A second study by the same team added that buprenorphine offered greater control of opioid withdrawal symptoms and that between-dose intervals of 48 hours could be tolerated (Fudala, Jaffe, Dax, & Johnson, 1990). In a later study (Johnson, Jaffe, & Fudala, 1992), 8 mg of buprenorphine per day compared favorably with 60 mg of methadone in treating illicit opioid use and maintaining patients in treatment. Yet another study showed that buprenorphine doses of 2 mg/day compared favorably with 30 mg/day of methadone in a heroin detoxification program (Bickel et al., 1988).

The effects of buprenorphine versus placebo on patterns of operant acquisition of heroin and money were studied in 10 male volunteers with a history of heroin addiction (Mello, Mendelson, & Kuehnle, 1982). Subjects were maintained on 8 mg/day of buprenorphine for 10 days during which they could earn money ($1.50) or heroin (7 or 13.5 mg/injection IV) by responding on a second order schedule of reinforcement for approximately 90 minutes. Buprenorphine subjects took only between 2% and 31% of the total amount of heroin available, whereas placebo subjects took between 93% and 100%.

These studies confirm that buprenorphine might serve as a desirable substitute for heroin. But would it? This is a difficult question to answer when talking about the United States because the drug is not available. In other countries, though, buprenorphine has a different history. By scanning international studies where buprenorphine is available, we might get some clues about what could happen in the United States. What follows is a brief review of some samples of international research on buprenorphine that we found in the abstracts.

Fifty known drug addicts (median age 28.6 years) admitted to a Marseille Hospital in France between June and October 1992 were examined (Arditti et al., 1992). Buprenorphine was identified in urine in 9 (18%) of them. In another study in Scotland, the effects of prescribing restrictions on the incidence of buprenorphine hydrochloride (Temgesic) are reported (Stewart, 1991). Three months after the restrictions were imposed, the rate of abuse dropped but then rose again over the next 8 months to nearly prerestriction values. Furthermore, as buprenorphine use declined, other opiate use doubled. The restrictions resulted in only a temporary drop in the availability of the drug.

In a second study from Scotland, researchers reported that 51% of opioid misusers in 1988 and 70% in 1990 were receiving prescribed opioids before assessment (Griffin, Peters, & Reid, 1993.) They report that, in the prior month, injectable opioids such as Temgesic (buprenorphine) were significantly more common in 1988 than in 1990. Although there are some indications of street use of buprenorphine in

England, the reports are less compelling. One article (Strang, 1991), for instance, describes a pattern of use in which sublingual tablets are crushed and the resulting powder inhaled. In another study, a description of 150 drug users in a London general practice indicates only 5 cases of reported buprenorphine use as opposed to 121 cases of reported heroin use (Cohen et al., 1992).

Another study from Finland (Hakkarainen & Hoikkala, 1992) reports on a policy debate over buprenorphine. During the 1980s, increasing Temgesic abuse was noted, and the drug was classified under the narcotics legislation. The status of that classification is under review. Barcelona also reported problem use of buprenorphine (San, Torrens, Castillo, Porta, & De La Torre, 1993). In studies carried out in 1988 and 1990, illicit use at some time was reported by 66% (1988) and 71% (1990) of patients in treatment, with respectively 5.9% and 6.1% actually testing positive for the drug. More than 70% of those with buprenorphine experience reported intravenous use. Australia also showed concerns about buprenorphine. One case study describes an intravenous buprenorphine addict with a history of injecting 4.5 mg/day for a period of 2 months (Quigley, Bredemeyer, & Seow, 1984). Other articles discuss general policy issues around the control of buprenorphine and its potential liabilities (Lebedevs, 1985; Wodak, 1984).

In a presentation at the 1995 College of Problems on Drug Dependence meeting, Kumar, Mandell, Shakuntala, and Daniels (1995) offered a poster session on buprenorphine use in Madras, India. Among 250 injecting drug users recruited in an HIV outreach, 96% had used buprenorphine—74% in the previous 30 days—and 44% were DSM III-defined buprenorphine dependent at the time of the interview.

Dr. Kumar was fortuitously encountered by the senior author at a conference. He described the history of buprenorphine use in detail. The upshot was that a dramatic increase in heroin availability created a population of addicts in the 1980s, but later political events and harsher laws resulted in a heroin shortage. Buprenorphine, manufactured locally in Tamilnadu State, provided an alternative for addicts, and its use rose dramatically. One unfortunate consequence of the shift was that buprenorphine—available in ampules—was injected, whereas heroin had been smoked. When heroin did return to the street market, addicts carried the new practice of injecting with them, with obvious increases in HIV risk.

Information on Bangladesh is contained in a report by Ahmed and Ara (1995). Their interviews with 30 addicts in treatment reveal the establishment of buprenorphine as a street drug, beginning in 1992, in response to declining quality and increasing cost in the heroin market. All 30 used buprenorphine daily and praised it for staving off withdrawal, pleasurable effects, and ease of use—it must be injected less frequently than heroin and its availability in ampules makes for simpler preparation.

These studies do not directly answer our question of whether buprenorphine might become a commodity with competitive value in the U.S. street market. But they do show that buprenorphine has appeared as a street drug in several other countries—France, Finland, Scotland, England, Spain, Australia, India, Bangladesh—to one degree or another. The studies support the hypothesis that buprenorphine is actively sought out and that it is something that addicts in street settings are motivated to obtain. This positive view of buprenorphine's effects held by heroin addicts suggests a potentially successful street "product." Other studies—international and U.S. based—add to the possibility of success by showing how buprenorphine interacts with other street drugs in ways similar to heroin and methadone.

In Scotland, researchers reported that 727 new needle-exchange clients (93% of the total) completed an intake questionnaire in 1992 (Gruer, Cameron, & Elliott, 1993). The most common drugs injected were heroin, buprenorphine (Temgesic), and temazepam, injected by 61%, 45%, and 28%, respectively. Most clients regularly used at least two drugs, typically heroin or buprenorphine and a benzodiazepine. Another study of a 13-week detoxification program using buprenorphine and behavioral therapy reported that 89% tested positive for benzodiazapenes and 63% for cocaine at least once during the program (Bickel, Amass, Higgins, Badger, & Esch, 1997).

From a *Scientific American* article comes a report of buprenorphine featuring both its agonist and antagonist effects (Holloway, 1991). The article notes that Jack H. Mendelson, who had recently completed a study of 12 heroin and cocaine users taking buprenorphine, suggested that high doses of buprenorphine might enhance cocaine's effects. Mendelson's concerns are supported by a clinical study from the Connecticut Mental Health Center (Rosen, Pearsall, McDougle, Price, & Kosten, 1993). In a double-blind study of 5 cocaine- and heroin-dependent patients who had been drug free for at least 36 hours, it was found that subject ratings of cocaine's pleasurable effects as well as pulse increases resulting from cocaine use were both enhanced by buprenorphine. In his dissertation on cocaine use, Erin Brown (1993) notes that the effect of cocaine was "potentiated" by coadministration of buprenorphine and that the two drugs can act together in a synergistic manner.

These studies echo two common patterns of polydrug use among heroin addicts in the United States. According to the first one, a mix of heroin and cocaine called a "speedball" is used; in the second pattern, the effects of either heroin or methadone are boosted with benzodiazapines. The sources just cited suggest that buprenorphine fits such patterns in the same way.

The literature shows that buprenorphine's effects are desirable from a street addict's point of view, it has already appeared as a street drug in several countries, and it mixes with benzodiazapines and cocaine in ways already established in street patterns of heroin and methadone use. In addition, we asked about buprenorphine on an illicit drug listserve as another source of information for this field trial.

John French logged onto a drug discussion group on the Internet and asked about buprenorphine. The three elaborate comments he received in reply echoed the themes in the literature.

1. You can think of buprenorphine as providing opiate replacement therapy similar to methadone maintenance, but with a somewhat more interesting drug. Buprenorphine is a mixed opioid agonist/antagonist, meaning that it has some effects that are like morphine and heroin, and others that block the actions of the drug. It also seems to bind to opiate receptors in the body for a very long time, so its effects are very long lasting. Basically, buprenorphine is enough like heroin that it doesn't seem to induce a withdrawal syndrome in someone who is already addicted to morphine, methadone or heroin. Buprenorphine is also "enough" like heroin that it seems to have a mild euphoric effect, at least at low doses, so there's a bit of an incentive for former addicts to use it. Buprenorphine is not very addictive on its own (though it has seen some recreational use in areas where it's freely available). It also blocks the effects of other opiates like heroin almost completely, so someone shooting up with heroin while taking buprenorphine wouldn't achieve the high they expected.
2. In places like Scotland where the heroin supply is erratic, there is a greater reliance upon various pills. Temgesic grew in popularity because for a while, the medical profession thought that they had little potential for misuse. In fact, because they were

designed to dissolve by being placed under the tongue, it was discovered that they were quite a reasonable tablet to inject as they were not laden with chalk. The strange thing about Temgesic is that they are an opiate antagonist. This means that if you've got a smack habit and you do some Temgesic, you'll end up in withdrawal. On the other hand, if you don't have a habit at all, they have an opiate-like effect. They have become popular with injectors who lack access to "real" injectable opiates in places like the Outer Hebrides.

3. There are some trials in the US at the moment I believe. I am working as a physician at a Dutch methadone programme. I started to prescribe Buprenorphine nearly a year ago in some cases: people who want to stop using opiates (it's easier to quit with buprenorphine than with methadone) and who don't want to use any other opiates (it's not working well together with other opiates). My clients (that's what patients are called) are mostly very satisfied. It is a synthetic opiate partly agonist/antagonist. It's used as a pain-killer in Holland. It must be available in the US, too.

Thus, Internet comments from those knowledgeable about buprenorphine dovetail with the reported results, suggested hypotheses, and research questions based on materials in the literature. If we summarize the different sources of information reviewed in this section, we get the following field trial results for buprenorphine:

1. Buprenorphine has characteristics that compare favorably with the desirable characteristics of morphine, methadone, and heroin. Furthermore, buprenorphine may have fewer undesirable characteristics than those drugs.
2. There are indications that buprenorphine use lends itself to polydrug use in ways similar to heroin and methadone.
3. Buprenorphine can play a role in "habit management"; that is, in situations in which a preferred narcotic is not available, buprenorphine can be used to stave off withdrawal and provide an agonist effect.
4. Buprenorphine may be the preferred narcotic in locations where heroin is not available.
5. Buprenorphine might have characteristics that lead it to become a preferred narcotic in its own right, even in a market that offers several available options.

At the end of this review, we can say that it is clear that buprenorphine has a potential role to play in the streets. We can forecast a "possible world" within which buprenorphine would find a street market in the United States. In fact, we can give an optimistic street reading on buprenorphine based on what we learned, a provisional but plausible one, given the material at hand: "Buprenorphine is a nice mellow high and it lasts a long time. It's easy to kick, it makes a good speedball, and you can boost it with benzodiazapines."

The results of this field trial are clear. Could buprenorphine possibly develop into a street drug in the United States? Yes, it could. We return to this question and the subjunctive verb *could* in the conclusion.

THE ANTAGONIST MIX

After this field trial began, we learned that a focus on buprenorphine alone would no longer answer the question about potential street use. Even as we did this study, interest in the United States was shifting from buprenorphine as a stand-alone treatment to a mix of buprenorphine and *naloxone*, a narcotic antagonist. Even though buprenorphine already has an antagonist effect, that effect—as we have seen—clearly

does not discourage street use. Naloxone, supposedly, would beef up the antagonist and make the drug less attractive in the streets. However, such a strategy would also make it less attractive with respective implications for recruitment and retention in treatment.

Dr. John Mendelson, who was cited earlier in the literature review, showed us the results of a new study in which buprenorphine was compared with a buprenorphine/naloxone mix during an interview with Agar and Bourgois. According to evaluations obtained from 10 subjects, buprenorphine alone was a desirable drug with a high street value. But the high user ratings of buprenorphine alone plunged when naloxone was added. The potential problem with the buprenorphine/naloxone mix lies in the classic problem with antagonists in the past. Their history shows that the few patients who succeed tend to be of higher socioeconomic status with a prior commitment to quit their narcotics addiction. It is no surprise that most addicts, when offered something that will make them sick and will never get them high, do not find the offer attractive.

Nonetheless, the focus in future U.S. clinical trials apparently will be on buprenorphine/naloxone mixes. In an interview with Agar, Dr. Richard Resnick pointed out that the addition of naloxone to buprenorphine is meant to prevent its diversion into the streets. The sublingual dose of naloxone will not affect the buprenorphine, but an individual who is addicted to heroin will feel the effects of withdrawal. The new mixture will also offer commercial and marketing advantages from the manufacturer's point of view.

We wonder if possible strategies could be developed in the streets to manage the antagonist component of the new buprenorphine/naloxone mix. Numerous shifts in street pharmacology over the years have been observed as users have changed drugs, modes of preparation, perception of effects, and styles of use. Both Mendelson and Resnick, in interviews with us, argue that this will not occur. However, it will be an important exercise to monitor the "street trials" that will follow the clinical trials if and when buprenorphine/naloxone becomes a widely used treatment modality.

THE STREET/TREATMENT BOUNDARY

We would like to make it clear that we came to this study neither to praise nor to bury buprenorphine. Our judgment at the end of this field trial is that buprenorphine alone appears to be a worthwhile alternative treatment modality to methadone, at least worthy of further study. However, buprenorphine alone will likely lend itself to street use, as methadone did when it was introduced in the 1970s.

Mendelson, in an interview with Agar and Bourgois, pointed out possible advantages of the shift to buprenorphine: (a) Buprenorphine does not have the negative or "loser" image that methadone has acquired over the years; (b) one cannot overdose on buprenorphine, although frankly we are still wondering about agonist/antagonist interactions in the context of the normal polydrug street environment; (c) buprenorphine is not as euphoric as methadone, although again the same thing was said of methadone when it was first introduced, and the literature reviewed earlier sometimes suggests the contrary; and (d) with its longer acting effects, buprenorphine

will be cheaper to administer, requiring a visit to a clinic site every few days instead of daily.

Resnick, who has experimented with buprenorphine as a treatment modality for some time, argues that the drug has other advantages as well (Resnick & Falk, 1987; Resnick et al., 1992; Resnick, Resnick, & Galanter, 1991). Stressing the diversity of the addict population, Resnick finds that buprenorphine may appeal to addicts who will not enter the health care system via methadone treatment or therapeutic communities and who are not motivated to use a narcotic antagonist. Such addicts show a higher level of psychosocial functioning when compared to nonresponders in his studies. Buprenorphine proves useful in detoxification as well, he adds.

But how do we reconcile an interest in buprenorphine as an alternative treatment for heroin addiction—something clearly supported by our two interviewees and three of the four authors of this article—with our field trial results that show buprenorphine's possible future as a street drug? Based on our collective experience with methadone maintenance over the years, we would argue that it is not a matter of reconciling a contradiction. Instead, it is a matter of accepting that you cannot have one without the other. An effective maintenance drug will always be interesting to the streets as well.

When methadone was first proposed as a maintenance drug in the 1960s, it initiated an experiment that had not been tried for decades. Since the closing of the U.S. morphine clinics in the 1920s, if one wanted treatment, one had to eliminate physical dependence right at the beginning. Treatment started only after detoxification. Relapse rates after such treatment were uniformly high. With methadone maintenance, things changed. Now an addict could enter treatment without first kicking the habit. In fact, by some program philosophies, one would never have to kick the habit.

In other words, methadone clouded the boundary between treatment and the streets more than ever before. Now treatment included taking an opiate, rather than requiring that opiate use cease before treatment started. Methadone accommodated an addict's world and, compared to any other drug-free treatment, made it easier for him or her to experiment with a "patient" role. Treatment evaluations showed a higher retention rate for methadone compared with drug-free modalities. But then, the other side of the story is this: If a treatment modality accommodates the street world, then the street world can incorporate the treatment modality. Historically, we saw this happen with methadone, as a "medication" from the clinical point of view also became a commodity in the street markets (Agar, 1977; Agar & Stephens, 1975; Preble & Miller, 1977).

When the boundary between street and treatment turns fluid and fuzzy as it did with methadone, the treatment drug is no longer either "medication" or "dope." It is both. Buprenorphine is another chemical move in this treatment game. With its widespread use as a treatment drug in the United States, it will probably develop a street market here as well. In the next section, in which we discuss in more detail the current buprenorphine situation in France, we will see that it has, in fact, become an exceptionally popular street drug in that country and that it is injected rather than used sublingually as originally intended.

Interesting and problematic will be the development of buprenorphine/naloxone mixes. Efforts to use naloxone to build a wall against street use may, by this logic, recruit fewer addicts and resemble the limited role that antagonists alone

have always played. The paradox, again, is this: A medication with powerful and effective outreach and recruitment into treatment is also a drug with a role to play in street markets. With apologies to Gunnar Myrdal, we might call this the "American treatment dilemma" and simply close by hoping that our field trial clarifies its inevitable and enduring presence.

A YEAR-2000 UPDATE

Roughly 5 years have passed since we conducted the research on which this article is based. Since that time, needless to say, the buprenorphine story has continued. In this brief update, we first look at some of the recent literature to check whether the field trial holds up. We searched MedLine with key words *buprenorphine*, *human*, and *abuse* and came up with about 80 abstracts since 1995. After a brief review of this literature, we will take a look at the current situation in France, where the liberalization of prescription laws for sublingual buprenorphine in 1996 increased the street market noticeably. In fact, underground economy sales are so robust that the street price of buprenorphine is actually cheaper than the pharmacy price. Finally, we will briefly look at how buprenorphine has become more of a newsworthy topic in the United States. In general, our review of this new material will show that, with a few minor exceptions, the field trial of 5 years ago was accurate.

In recent years, the professional literature has continued to grow, with many reports evaluating buprenorphine—often by comparison with methadone—and concluding that the new drug does indeed have a role to play in the treatment of heroin addiction (see, for example, O'Connor et al., 1996, 1998; Petry, Bickel, & Badger, 1999). Some studies now discuss a lower retention rate for buprenorphine when compared to methadone (Eder et al., 1998; Fischer et al., 1999). There is more recognition of the drug's abuse liability, although articles still neglect street views of buprenorphine, and street voices commenting on the drug are absent.

Earlier we argued that one signal of buprenorphine's desirability from a street point of view was its ability to mix with other drugs in ways similar to heroin and methadone. By and large, this statement is still supported (see, for example, Schottenfeld, Pakes, & Kosten, 1998). However, the recent literature is more equivocal on the mix of buprenorphine and cocaine. In one comparison of methadone and buprenorphine, it is reported that the buprenorphine treatment sample produced fewer cocaine-positive urines, although the difference was not statistically significant (Eder et al., 1998). Another study concludes that buprenorphine may be more effective than methadone for controlling cocaine abuse (Foltin & Fischman, 1996). On the other hand, a third study questions the claim that buprenorphine reduces cocaine use more than methadone does (Schottenfeld, Pakes, Oliveto, Ziedonis, & Kosten, 1997).

Clearly, the jury is still out on the mix of cocaine and buprenorphine. This contrasts with our statements that cocaine mixed well with the drug. However, the ability of buprenorphine to blend in with benzodiazapines has held up (Eder et al., 1998). A comparison of buprenorphine and methadone patients showed no difference in use of benzodiazapines or alcohol (Schottenfeld et al., 1998). In the French case discussed below, one article actually reports several deaths caused by

buprenorphine/benzodiazapine mixes (Tracqui, Kintz, & Ludes, 1998), and another suggests that the two drugs are sometimes coprescribed by physicians (Seyer, Dif, Balthazard, & Sciortino, 1998). Ethnographers and outreach workers present the mixing of buprenorphine and benzodiazepines—especially Rohypnol—as a matter of street-based common sense (Kempfer, 1998a, 1998b; A. Lovell, personal communication, May 29, 2000.).

Another part of the field trial based on the 1996 research focused on the future of buprenorphine/naloxone mixes. Several research articles report on this mix during the past 5 years, and the news is pretty much as we forecast earlier. Mendelson, whom we interviewed for the original research, reported that a buprenorphine/naloxone combination precipitated withdrawal and was unpleasant and that half the subjects could not distinguish between naloxone alone and the mix during the first hour of the experiment (Mendelson, Jones, Welm, Brown, & Batki, 1997). Another study reports that the mix produced opiate withdrawal, and it suggests explicitly that this will reduce buprenorphine's street value (Nath, 1999). These studies describe such outcomes as an advantage, a way to reduce the abuse liability of buprenorphine. In our field trial, we argued that, from a street perspective, the mix would reduce interest in buprenorphine/naloxone in the street markets, but it would also reduce interest in the mix as a treatment drug. Indications in the recent literature suggest that our argument, based on the earlier research, still holds up.

In the 1996 research, we scanned international studies of buprenorphine to see if it had become a street drug in the countries where it was more available. The studies we located suggested that it had, and this conclusion led us to strengthen our forecast for the future street role of buprenorphine in the United States. For this update, Bourgois, whose professional contacts and language abilities made a look at recent developments in France possible, contacted colleagues and looked at some literature. Fortuitously, Anne Lovell, an anthropologist with the University of Toulouse and researcher with INSERM (the French equivalent of the National Institutes of Health), contacted Agar on another matter as we were revising this article, and her detailed suggestions and advice made much of our summary possible.

The street history of buprenorphine in Europe—especially France—teaches us a great deal about the potential appeal of the drug among street addicts. It was initially developed as an injectable painkiller in the United Kingdom in 1978 under the trade name Temgesic and was soon marketed throughout most of Europe. In France, it became relatively widely available in 1987 but solely in injectable form. By 1990, its distribution was curtailed due to reports of street abuse, and the injectable form was limited to hospital pharmacies. In 1996, it became widely available through unrestricted medical prescription from general practitioners in a sublingually administered form known under the trademark Subutex intended exclusively as a substitute treatment for heroin addiction. By the year 2000, approximately 58,000 addicts were officially on Subutex maintenance compared to only 7,000 on methadone. France was the only European country where buprenorphine was so widely and systematically used in drug treatment (C. Carrandie, personal communication, May 24, 2000; Kempfer, 1998/1999; Lert et al., 1998).

According to ethnographers and outreach workers, a significant number of French maintenance patients resell their prescribed sublingual doses on the street

where they are dissolved into syringes by street addicts for injection. Unfortunately, this particular form of sublingual buprenorphine rapidly deteriorates veins and causes especially virulent abscessing when injected (Kempfer, 1998b, 2000; A. Lovell, personal communication, May 29, 2000). The lack of an ecstatic rush effect from buprenorphine exacerbates its deleterious effects on the veins of street injectors as it often provokes a cycle of compulsive repeat injection in a search for the elusive rush. As with methadone in the United States, the frustrating euphorigenic effects of buprenorphine lead to the phenomenon of low-status, multiple-substance abusers who combine alcohol and benzodiazepines with the treatment drug to try to "boost" its effects (Bourgois, 2000; Kempfer, 2000).

Perhaps the exceptional frequency with which street-based addicts inject sublingual buprenorphine in France can be explained by street market fluxes in heroin availability. In the late 1990s, street injectors in the Goutte d'Or neighborhood of Paris told Bourgois that they were forced to inject Subutex because of the poor quality of heroin in street markets. Indeed, the artificially low price of Subutex on Paris streets, approximately 10 francs for an 8 mg dose compared to 100 to 200 francs for the standard street dose of heroin, may explain the frequency with which street-based heroin addicts were injecting (Kempfer, 2000). A French outreach worker reports that buprenorphine is sold at below pharmacy cost on the street because dealers access the drug for free as indigent patients by presenting themselves for treatment to a half-dozen doctors simultaneously (Kempfer, 2000). An ethnographer based in Marseilles confirms that Subutex is an inexpensive alternative to heroin for street addicts and that it is sometimes called a poor man's heroin (A. Lovell, personal communication, May 29, 2000.). Nevertheless, it is widely used on the streets of both cities. In a study of street-recruited heroin injectors in Marseilles, 23% were current Subutex injectors (Lovell, in press). Treatment centers in Paris similarly report detoxing addicts who are exclusively injectors of Subutex (C. Carrandie, personal communication, May 24, 2000). Outreach workers and ethnographers also report that some younger addicts have exclusively had careers of Subutex injection (see also Kempfer, 2000), and even nonaddicts will use Subutex as an occasional party drug (A. Lovell, personal communication, May 29, 2000.). Of course, a silent majority of French addicts do use buprenorphine to "normalize" and mainstream their lifestyles, as it was intended (Lovell, in press).

The French scenario of a relatively high street demand for buprenorphine among injectors may be somewhat specific to the culture of French substance abuse, which revolves especially intensively around needle use. This is suggested, for example, by the fact that a disproportionately high number of crack users in the Goutte d'Or neighborhood that Bourgois visited in the late 1990s insisted on injecting crack instead of smoking it (Kempfer, 1998b; Lefort, 1998). The easy accessibility of buprenorphine by general practitioner prescription in France also contrasts dramatically with the extremely limited access of addicts to methadone maintenance. And finally, buprenorphine in France does *not* have the antagonist mixed in, as the United States now plans to do. If it did, injection of the sublingual dose would precipitate withdrawal.

The French case shows—with more depth than the earlier review of the international literature allowed—how treatment policy, market conditions, and cultural

dynamics might combine to enable a flourishing buprenorphine street scene to develop. Another interesting change since the earlier research is the degree to which buprenorphine has become more of a public topic in the United States, although we anticipated this from the reaction with which an earlier draft of this article was greeted by the original sponsors, who saw undesired qualifications around the development of a promising new treatment drug. However, the senior author was contacted in early 2000 by the Center for Substance Abuse Treatment of the U.S. Public Health Service. They had obtained an earlier version of this article and asked if they might use it in their role to regulate buprenorphine-based treatment. We sent them the manuscript and asked for information that we might use as part of the revision in this update section. Unfortunately, they did not respond.

Buprenorphine has also become "news" for the general public, if a recent article in *USA Today* is any indication (Leinwand, 2000). A front-page feature is titled "Heroin's New Fix and Why It Matters to You." The feature is rather elaborate, but part of it discusses buprenorphine, which is one example of a new treatment that is "far more difficult to abuse than methadone because they are much less addictive" (Leinwand, 2000, p. 1). According to the article, a drug called Suboxone is near FDA approval—it is a mix of buprenorphine and naloxone. They note that another pill, this one only containing buprenorphine, has already been given to addicts in France. A physician and drug expert is quoted as saying buprenorphine has been a "huge success. People can function totally normally and be very alert if it's properly dosed" (Leinwand, 2000, p. 2). Along with the report on the new treatment drugs, buprenorphine key among them, the article talks about how doctors will be able to prescribe it out of their office so that clinics will not have to be set up in neighborhoods. Congress and the Drug Enforcement Agency, says the article, are in support of the change in treatment drug and prescription practice. However, there are some concerns in law enforcement that the take-home medication will appear in street markets.

We leave it to the reader, based on the material in this article, to sort through the *USA Today* feature. It seems striking that the use of buprenorphine for heroin addict treatment now warrants a feature in a widely read national newspaper. Five years ago, few people had even heard of the drug, including us when we were first contacted about this project, and many of our colleagues in the drug field. Clearly, buprenorphine will now be tried in the United States, so the acid test for our field trial and this update are now at hand. We see no reason to change our forecast. If buprenorphine alone is used, a street market will develop. If heavy doses of antagonist are mixed with buprenorphine, the mix will enjoy less success in enrolling or holding people in treatment.

At the same time, we feel that maintenance of physically dependent persons is a valuable and humane harm-reduction strategy. The fact that an attractive maintenance drug has some street value has to be accepted as part of the deal. Given that framework, buprenorphine with or without the naloxone mix, as many researchers we reviewed and interviewed for this article have said, offers an interesting new alternative to methadone that deserves a chance. It is good to remember our French colleague, cited earlier, who said that a "silent majority" of addicts used buprenorphine to buy some time to change their lives. However, buprenorphine—like methadone before it—is no "magic bullet." Unrealistic expectations for success that neglect

the realities and needs of the streets only yield surprises that could have been anticipated.

CONCLUSIONS

Does buprenorphine possibly have a future in the U.S. street markets? Possibly, without a doubt; probably, it depends.

It depends, first of all, on the results of the street trials that will inevitably follow the clinical trials, whereby *street trials* we mean actual experiments with the drug conducted by users themselves. Navaratnam (1995), cited earlier in this article, outlined a picture of buprenorphine's rising and falling effects in an interview. Over much of the curve, cocaine or benzodiazipines might be used to boost the effects without triggering the antagonist. As the curve falls, an addict could use heroin or methadone without fear of pushing the curve into the zone where the antagonist effect begins. His scenario outlined a hypothetical street trial outcome.

It also depends on the way buprenorphine is introduced. The addition of naloxone to the treatment drug increases the antagonist effect. It remains to be seen how this would effect treatment efficacy and street interest. Our prediction is that the mix will be of less interest in the streets, and it will not draw people into treatment as effectively, except for the highly motivated or those fleeing the stigma and/or inaccessibility of methadone. We could be wrong. Buprenorphine might offer enough to satisfy an addict's craving, whereas the stronger antagonist might deter use of illicit street narcotics. And we might be twice wrong if street trials develop polydrug strategies to enhance the agonist and reduce the antagonist effect, even with the added naloxone, although the experts we interviewed argue that this will not be the case.

And it depends, finally, on market conditions. Methadone was introduced at the time of the Nixon-era crackdown on the Turkey-Lebanon-France-U.S. pipeline that had delivered heroin to the United States for years. Sharp reductions in quantity and quality of heroin together with rapid increases in methadone availability led to a shift that placed methadone in a key role in the street markets. Buprenorphine's fate will also depend on market conditions, as the example of France showed so well.

Our summary reflects a forecasting effort that departs from traditional clinical trials in several ways. We consulted disparate data from the field and developed scenarios based on conditions that make outcomes more or less probable. Forecasting is different from traditional science, as recent work shows all too well (Sherden, 1998). At the same time, the forecast is useful in outlining alternative scenarios—we now know something about what might happen and the conditions that are likely to make a difference. We move into the future with an outline map rather than no map at all. Field trials, drawing on multidisciplinary and multimethodology sources from epidemiology to ethnography and from treatment research and medical anthropology to the field of jurisprudence research, clearly offer an alternative and important understanding of drugs and their future that other approaches do not provide. And with the opportunity to evaluate the mid-1990s field trial 5 years later, we can say that, in this case, the field trial worked relatively well.

REFERENCES

Agar, M. (1977). Going through the changes: Methadone in New York. *Human Organization*, *36*, 291-295.

Agar, M., & Stephens, R. (1975). The methadone street scene: The addict's view. *Psychiatry*, *38*, 381-387.

Ahmed, S. K., & Ara, N. (1995). *Patterns and trends of buprenorphine abuse: An ethnographic study*. Report prepared for the Community Epidemiology Work Group, National Institute of Drug Abuse, Washington, DC. Manuscript submitted for publication.

Arditti, J., Bourdon, J. H., Jean, P., Landi, H., Nasset, D., Jouglard, J., & Thirion, X. (1992). Buprenorphine abuse in a group of 50 drug-use abusers admitted to Marseille hospital. *Thérapie*, *47*, 561-562.

Bickel, W. K., Amass, L., Higgins, S. T., Badger, G., & Esch, R. A. (1997). Effects of adding behavioral treatment to opiate detoxification with buprenorphine. *Journal of Consulting and Clinical Psychology*, *65*(5), 803-810.

Bickel, W. K., Stitzer, M. L., Bigelow, G. E., Liebson, I. A., Jasinski, D. R., & Johnson, R. E. (1988). Clinical trial of buprenorphine: Comparison with methadone in the detoxification of heroin addicts. *Clinical Pharmacology and Therapeutics*, *43*, 72-78.

Bourgois, P. (2000). Disciplining addictions: The bio-politics of methadone and heroin in the United States. *Culture, Medicine and Psychiatry*, *24*(2), 165-195.

Brown, E. (1993). *Investigations of the neurobiological and behavioral actions of cocaine*. Unpublished doctoral dissertation, University of British Columbia.

Cohen, J., Schamroth, A., Nazareth, I., Johnson, M., Thomson, D., & Graham, S. (1992). Problem drug use in a central London general practice. *British Medical Journal*, *304*, 1158-1160.

Eder, H., Fischer, G., Gombas, W., Jagsch, R., Stuhlinger, G., & Kasper, S. (1998). Comparison of buprenorphine and methadone maintenance in opiate addicts. *European Addiction Research*, *4*, 3-7.

Fischer, G., Gombas, W., Eder, H., Jagsch, R., Peternell, A., Stuhlinger, G., Pezawas, L., Aschauer, H. N., & Kasper, S. (1999). Buprenorphine versus methadone maintenance for the treatment of opioid dependence. *Addiction*, *94*, 1337-1347.

Foltin, R. W., & Fischman, M. W. (1996). Effects of methadone or buprenorphine maintenance on the subjective and reinforcing effects of intravenous cocaine in humans. *Journal of Pharmacology and Experimental Therapeutics*, *278*, 153-164.

Fudala, P. J., Jaffe, J. H., Dax, E. M., & Johnson, R. E. (1990). Use of buprenorphine in the treatment of opioid addiction: Part 2. Physiologic and behavioral effects of daily and alternate-day administration and abrupt withdrawal. *Clinical Pharmacology and Therapeutics*, *47*, 525-534.

Griffin, S., Peters, A., & Reid, M. (1993). Drug misusers in Lothian: Changes in injecting habits. *British Medical Journal*, *306*(6879), 693.

Gruer, L., Cameron, J., & Elliott, L. (1993). Building a city wide service for exchanging needles and syringes. *British Medical Journal*, *306*(6889), 1394.

Hakkarainen, P., & Hoikkala, T. (1992). Temgesic: Gullible doctors, drug addicts in disguise. *Nordisk Alkohol Tidskrift*, *9*(5), 261-274.

Holloway, M. (1991). Rx for addiction. *Scientific American*, *264*(3), 94.

Jasinski, D. R., Fudala, P. J., & Johnson, R. E. (1989). Sublingual versus subcutaneous buprenorphine in opiate abusers. *Clinical Pharmacology and Therapeutics*, *45*, 513-519.

Jasinski, D. R., Pevnick, J. S., & Griffith, J. D. (1978). Human pharmacology and abuse potential of the analgesic buprenorphine. *Archives of General Psychiatry*, *35*, 501-516.

Johnson, R. E., Cone, E. J., Henningfield, J. E., & Fudala, P. J. (1989). Use of buprenorphine in the treatment of opiate addiction: Part 1. Physiologic and behavioral effects during a rapid dose induction. *Clinical Pharmacology and Therapeutics*, *46*, 335-343.

Johnson, R. E., Jaffe, J. H., & Fudala, P. J. (1992). Controlled trial of buprenorphine treatment for opioid dependence. *Journal of the American Medical Association*, *267*, 2750-2755.

Kempfer, J. (1998a). De l'Ortenal à l'Artane: Les detournements de médicaments et leurs consequences [From Ortenal to Artane: The consequences of the black market in medicines]. *Interdépendance Journal de SOS Drogues International*, *31*, no pagination.

Kempfer, J. (1998b). La vie à Paris avec drogues mais sans toit [Living in Paris with drugs, but without shelter]. *SWAPS*, *7*, 2-4.

Kempfer, J. (1998/1999). Subutex: Au commencement était le Temgesic et celui-ci était injectable [Subutex: In the beginning there was Temgesic and it was injectable]. *SWAPS*, *10*, 6-7.

Kempfer, J. (2000). "Des produits utilisés par les usagers de drogues du centre de Paris [Some products consumed by drug users in the center of Paris]. Excerpted in 1998 report to the AUDVIH (Aide aux Usagers de Drogues confrontés au VIH). Paris: Association AIDES Ile de France.

Kumar, M. S., Mandell, W., Shakuntala, S., & Daniels, D. (1995, June). *Buprenorphine dependence among injecting drug users in Madras City, India*. Paper presented at the annual meeting of College on the Problems of Drug Dependence, Scottsdale, AZ.

Lebedevs, T. (1985). Buprenorphine abuse. *Pharmaceutical Journal*, *235*, 641.

Lefort, C. (1998). *Le crack: Le connaitre pour mieux prévenir* [Crack: Understanding it to improve prevention]. Réseau des hautes Etudes des pratiques socialisés: Groupement des Colleges Cooperatifs.

Leinwand, D. (2000, May 30). Heroin's new fix and why it matters to you. *USA Today*, p. 1.

Lert, F., Bégaud, B., Fuhrer, R., Henrion, R., Lalande, M., Ledit, D., Lovell, A., Obadia, Y., Parquet, P., Puech, A., Tassin, J. P., & Vittecoq, D. (1998). *Evaluer la mise à disposition du Subutex pour la prise en charge des usagers de drogue* [An evaluation of the prescription of Subutex for the treatment of drug users]. Paris: INSERM.

Lovell, A. (in press). Ordonner les risques [Prescribing risk]. In D. Fassin & J. P. Dozon (Eds.), *Anthropologies et Santé Publique*.

Mello, N. K., Mendelson, J. H., & Kuehnle, J. C. (1982). Buprenorphine effects on human heroin self administration: Operant analysis. *Journal of Pharmacology and Experimental Therapeutics*, *223*, 30-39.

Mendelson, J., Jones, R. T., Welm, S., Brown, J., & Batki, S. L. (1997). Buprenorphine and naloxone interactions in methadone maintenance patients. *Biological Psychiatry*, *41*, 1095-1101.

Michman, R. D. (1994). *Marketing to changing consumer markets: Environmental scanning*. New York: Praeger.

Nath, R. P. (1999). Buprenorphine and naloxone combinations: The effects of three dose rations in morphine stabilized opiate-dependent volunteers. *Psychopharmacology*, *141*, 37-46.

Navaratnam, V. (1995). The Asian multicity epidemiology work group: 1994 update. *Proceedings of the Community Epidemiology Work Group Chicago Meeting* (pp. 313-319). Rockville, MD: National Institute on Drug Abuse.

O'Connor, P. G., Oliveto, A. H., Shi, J. M., Triffleman, E., Carroll, K. M., Kosten, T. R., & Rounsaville, B. J. (1996). A pilot study of primary-care-based buprenorphine maintenance for heroin dependence. *American Journal of Drug and Alcohol Abuse*, *22*, 523-531.

O'Connor, P. G., Oliveto, A. H., Shi, J. M., Triffleman, E. G., Carroll, K. M., Kosten, T. R., Rounsaville, B. J., Pakes, J. A., & Schottenfeld, R. S. (1998). A randomized trial of buprenorphine maintenance for heroin dependence in a primary care clinic for substance users versus a methadone clinic. *American Journal of Medicine*, *105*, 100-105.

Petry, N. M., Bickel, W. K., & Badger, G. J. (1999). A comparison of four buprenorphine dosing regimes in the treatment of opiod dependence. *Clinical Pharmacology and Therapeutics*, *66*, 306-314.

Pickworth, W. B., Johnson, R. E., Holicky, B. A., & Cone, E. J. (1993). Subjective and physiologic effects of intravenous buprenorphine in humans. *Clinical Pharmacology and Therapeutics*, *53*, 570-576.

Preble, E., & Miller, T. (1977). Methadone, wine, and welfare. In R. Weppner (Ed.), *Street ethnography* (pp. 229-248). Beverly Hills, CA: Sage.

Quigley, A. J., Bredemeyer, D. E., & Seow, S. S. (1984). Case of buprenorphine abuse. *Medical Journal of Australia*, *140*, 425-426.

Resnick, R., & Falk, F. (1987). Buprenorphine: Pilot trials in borderline patients and opiate dependence—treatment of a common disorder? In L. S. Harris (Ed.), *Problems of drug dependence* (pp. 155-168). Washington, DC: National Institute on Drug Abuse Research.

Resnick, R., Galanter, M., Psycha, C., Cohen, A., Grandison, P., & Flood, N. (1992). Buprenorphine: An alternative to methadone for heroin dependence treatment. *Psychopharmacology Bulletin*, *28*, 109-113.

Resnick, R., Resnick, E., & Galanter, M. (1991). Buprenorphine responders: A diagnostic subgroup of heroin addicts. *Psychiatry*, *14*(4), 531-538.

Rosen, M. I., Pearsall, H. R., McDougle, C. J., Price, L. H., & Kosten, T. R. (1993). Effects of acute buprenorphine on responses to intranasal cocaine: Pilot study. *American Journal of Drug and Alcohol Abuse*, *19*(4), 451-464.

San, L., Torrens, M., Castillo, C., Porta, M., & De La Torre, R. (1993). Consumption of buprenorphine and other drugs among heroin addicts under ambulatory treatment: Results from cross-sectional studies in 1988 and 1990. *Addiction*, *88*(10), 1341-1349.

Schottenfeld, R. S., Pakes, J. R., & Kosten, T. R. (1998). Prognostic factors in buprenorphine versus methadone-maintained patients. *Journal of Nervous and Mental Disorders*, *186*, 35-43.

Schottenfeld, R. S., Pakes, J. R., Oliveto, A., Ziedonis, D., & Kosten, T. R. (1997). Buprenorphine vs. methadone maintenance treatment for concurrent opioid dependence and cocaine abuse. *Archives of General Psychiatry*, *54*, 713-720.

Seyer, D., Dif, C., Balthazard, G., & Sciortino, V. (1998). Maintenance treatment with high-dose buprenorphine: Are the recommendations being followed? *Thérapie*, *53*, 349-354.
Sherden, W. A. (1998). *The fortune sellers: The big business of buying and selling predictions*. New York: John Wiley.
Stewart, M. J. (1991). Effect of scheduling of buprenorphine (temgesic) on drug abuse patterns in Glasgow. *British Medical Journal*, *302*, 969.
Strang, J. (1991). Abuse of buprenorphine (temgesic) by snorting. *British Medical Journal*, *302*, 969.
Tracqui, A., Kintz, P., & Ludes, B. (1998). Buprenorphine-related deaths among drug addicts in France: A report on 20 fatalities. *Journal of Analytic Toxicology*, *22*, 430-434.
Waldorf, M. M. (1992). *Complexity: The emerging science at the edge of order and chaos*. New York: Simon & Schuster.
Wodak, A. D. (1984). Buprenorphine: New wonder drug or new hazard? *Medical Journal of Australia*, *140*, 389-390.

Michael Agar has worked in the drug field since 1968, most recently on the contextual explanation of drug use trends. He also consults and teaches ethnographic/qualitative methods, as reflected in his book The Professional Stranger, *and works on issues of language-based ethnography, introduced in his book* Language Shock.

Philippe Bourgois, Ph.D., is with the Department of Anthropology, History and Social Medicine in the University of San Francisco's School of Medicine. He is a cultural anthropologist who studies the interface of violence, poverty, and substance abuse with a special emphasis on the experience of ethnic discrimination among inner-city residents and among Latin American immigrants. He is currently conducting fieldwork in the homeless encampments of a network of heroin injectors in San Francisco. His most recent book, In Search of Respect: Selling Crack in El Barrio *(1995, Cambridge), won the Margaret Mead and the C. Wright Mills Prizes. He has published numerous articles on substance abuse in venues ranging from* New York Times Magazine *to* Social Problems *and* Culture, Medicine and Psychiatry.

John French is now semiretired after 30 years with the New Jersey Department of Health, where his longest and latest tenure was as the director of research for addiction services. His areas of expertise include both quantitative and qualitative methodology, as well as program administration.

Owen Murdoch received a master's degree in anthropology from the University of Maryland. In addition to conducting ethnographic research on trends in drug abuse, he has worked on designing and implementing HIV-prevention projects in Baltimore, Maryland, and Denver, Colorado. He is currently pursuing a career in medicine.