Models for Integrating Buprenorphine Therapy into the Primary HIV Care Setting

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Opiate dependence among human immunodeficiency virus (HIV)–infected patients has been associated with negative clinical outcomes, yet few affected patients receive appropriate and coordinated treatment for both conditions. The introduction of buprenorphine maintenance therapy into HIV care settings provides an opportunity for providers to integrate treatment for opiate dependence into their practices. Buprenorphine maintenance therapy has been associated with reductions in opiate use, increased social stability, improved adherence to antiretroviral therapy, and lowered rates of injection drug use. We describe the following 4 models for the integration of buprenorphine maintenance therapy into HIV care: (1) a primary care model, in which the highly active antiretroviral therapy–administering clinician also prescribes buprenorphine; (2) a model that relies on an on-site specialist in addiction medicine or psychiatry to prescribe the buprenorphine; (3) a hybrid model, in which an on-site specialist provides the induction (with or without stabilization phases) and the HIV care provider provides the maintenance phase; and (4) a drug treatment model that provides buprenorphine maintenance therapy services with HIV services in the substance abuse clinic setting. The key barriers against effective integration of buprenorphine maintenance therapy and primary HIV services are discussed, and we suggest several mechanisms to overcome such obstacles.

Nearly 1 million people in the United States are living with HIV infection; more than one-quarter of these persons acquired the virus through injection drug use (IDU), and many of those who have acquired it through sexual contact also use illicit drugs, particularly opiates [1]. Thus, there is a strong rationale for expanded treatment for opiate dependence among persons living with HIV infection.

HIV treatment services have been successfully integrated into some methadone maintenance treatment programs. Methadone maintenance treatment programs, despite their considerable success in treating opiate dependence, have been tightly regulated in the United States, such that as few as 15% of opiate-dependent people can access these services at present [2]. Methadone maintenance treatment programs are cost-effective to society [3] and improve patient health outcomes by reducing opiate use [4], prison recidivism [5], HIV transmission [6], and improving access to and retention within HIV care [7]. Untreated opiate dependence has been associated with later initiation of HAART [8] and reduced adherence to and retention within HIV care programs [9, 10].

The existing and most prevalent model for managing patients who are affected by both HIV and opiate dependence is to provide HIV and substance abuse services independently. This approach has evolved because methadone cannot be prescribed in general practice and because there are separate lines of funding for substance abuse and HIV care, patient confidentiality concerns, and a general lack of personnel with expertise on both conditions. The separated treatment approach can cause difficulties in communicating between the 2 sites of care, result in conflicting advice and prescriptions, and introduce treatment delays.

Buprenorphine maintenance therapy provides a new opportunity to integrate services for patients in need of treatment for both HIV infection and opiate depen-
Buprenorphine, a partial opioid agonist, was approved in 2002 for the treatment of opiate dependence. As a partial agonist, it is less likely than methadone to lead to abuse or respiratory depression; therefore, the Drug Enforcement Agency has classified it as a Schedule III medication (methadone is Schedule II). This makes it the first medication to fall under the new regulatory framework of the Drug Abuse Treatment Act of 2000, allowing certified primary care providers to prescribe it [11]. For the first time, HIV care providers can provide buprenorphine maintenance therapy within their own practices, rather than referring patients to methadone maintenance treatment programs. Buprenorphine maintenance therapy has shown impressive efficacy against opiate dependence when used in office-based settings; there are few examples of the provision of buprenorphine maintenance therapy by HIV care providers [2, 12, 13], but buprenorphine maintenance therapy has been shown to improve adherence to HAART [14, 15].

The Health Resources and Service Administration recently awarded 5-year grants to 10 US sites studying combined buprenorphine maintenance therapy with HIV care programs [16]; data from these sites will not be available in the near future. This article provides a framework to HIV providers intending to integrate buprenorphine maintenance therapy into their practices before the publication of these data.

The treating clinician should first note the basic structure of buprenorphine maintenance therapy. Buprenorphine maintenance therapy consists of 3 phases: induction, stabilization, and maintenance. The induction phase begins with an initial “test dose,” often given under observation, of 4 mg of buprenorphine after a patient has abstained from opiate use for 12–24 h and demonstrates objective signs and symptoms of early opiate withdrawal. After receipt of a successful test dose, rapid titration is possible, such that a therapeutic dose of typically 16 mg is achieved by day 2. The stabilization phase begins after the initial therapeutic dose of 16 mg is achieved. During this phase, the goal is for the patient to greatly reduce or cease opiate use without experiencing cravings or adverse effects. Stabilization may involve dosage adjustments or behavioral interventions, such as counseling, to achieve this goal. The maintenance phase begins when the patient is comfortably continuing to receive a steady dose of buprenorphine for a period to be determined by the patient and the practitioner.

CHALLENGES AND MODELS OF INTEGRATION

HIV care providers have a rich history of integrating varied services into the care of their patients [17]. Successful examples include the incorporation of mental health services, lipid level management, gynecological services, and hepatitis C virus infection treatment into HIV primary care [18–20], all of which have improved patient health outcomes [21]. To achieve a similar level of success with buprenorphine maintenance therapy integration, 4 key questions must be answered. (1) Who is to perform the induction and stabilization of patients receiving buprenorphine? (2) How are patients to be maintained on buprenorphine treatment appropriately? (3) What forms of counseling are necessary? And, (4) how can care be coordinated between providers? Four potential models of care exist that address these issues and begin incorporating buprenorphine therapy into a variety of HIV care programs.

These models include (1) a primary HIV clinical care program, in which induction, stabilization, and maintenance of buprenorphine treatment are provided by the HIV care clinician, who is also responsible for overall HIV care; (2) an on-site addiction specialist model, whereby another provider performs buprenorphine induction, stabilization, and possibly maintenance therapy within the HIV clinic; (3) a hybrid model, with a buprenorphine induction site that stabilizes patients and transfers the remainder of care to the primary HIV provider after the patient has markedly reduced illicit opiate use; and (4) a drug treatment setting that provides buprenorphine maintenance therapy (and possibly methadone maintenance), but that also has on-site HIV clinical services (table 1).

A common set of core services should be provided under any of the programs: at least 1 physician must be certified to prescribe buprenorphine, through online registration at SAMHSA [22]; both buprenorphine and antiretroviral medications must be stocked at a pharmacy accessible to the patient; and appropriate counseling services should be made available. Each physician is currently limited to 30 patients.

MODEL 1: THE PRIMARY CARE MODEL

Perhaps the most widely applicable model is one in which a HAART-prescribing physician also provides buprenorphine induction, stabilization, and maintenance services. This model may be most practical for practitioners in clinical settings in which addiction specialists are difficult to access or in which the low prevalence of opiate dependence among patients does not warrant the salary of an additional addiction specialist.

Rural settings and busy community health centers may be particularly keen on this model. This model may also be attractive to patients who distrust regimented substance abuse programs. It may be useful to patients who would prefer to treat their dependence just as they treat other health care needs, rather than moving to distinct, potentially stigmatizing substance abuse treatment sites. Having one provider control both HIV therapy and other prescribed medications may also reduce the likelihood of drug interactions between medications prescribed by multiple providers, and it may be more cost-effective than buprenorphine maintenance therapy models that require multiple staff members. This model avoids potential conflicts between providers.

There is a potential for loss of patient autonomy, however,
Table 1. Models for integrating buprenorphine maintenance therapy into HIV primary care settings.

<table>
<thead>
<tr>
<th>Model</th>
<th>Description</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV primary care model</td>
<td>HIV primary care physician provides all buprenorphine maintenance therapy services</td>
<td>Each provider provides totally integrated care</td>
<td>The workload for a single provider is high</td>
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<td>There is no need for on-site specialist, so applicability to resource-poor and staff-poor settings is wider</td>
<td>Lots of power is concentrated in 1 provider’s hands, leading to concerns about patient autonomy</td>
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<td>Possible increased levels of trust between patient and provider result in improved HAART adherence</td>
<td>Specialists/backup care providers are needed to answer questions and to cover leaves of absence</td>
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<td></td>
<td>Attitude towards substance abuse on the part of HIV provider is possibly improved</td>
<td>Many providers need buprenorphine certification for widespread use of this model</td>
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<td>Modified “hybrid” model allows specialist to induce treatment while the HIV care provider maintains treatment of the patient, reducing the HIV clinician’s burden</td>
<td>There is possible difficulty transitioning patients who are already in methadone maintenance programs</td>
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<td>On-site specialist model</td>
<td>Addiction specialist provides buprenorphine maintenance therapy services at an HIV primary care clinic</td>
<td>Specialist care is provided</td>
<td>Ryan White clinics face concerns about affordability</td>
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<td>More time is spent with patients on substance abuse issues</td>
<td>Communication is problematic unless medical records are integrated for both services</td>
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<td></td>
<td>Greater expertise is necessary for managing difficult cases</td>
<td>Care is only geographically integrated, and the providers for both HIV care and substance abuse treatment are not the same</td>
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<tr>
<td>Hybrid model</td>
<td>Induction by specialist and maintenance by HIV care provider</td>
<td>Specialist care is provided</td>
<td>Care is fragmented</td>
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<tr>
<td></td>
<td></td>
<td>Expertise is available for the most difficult phase of buprenorphine maintenance therapy</td>
<td>The potential for patient hassle exists if induction and maintenance are at different sites</td>
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<td></td>
<td>There is potential for miscommunication</td>
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<td>The second provider still needs to do full diagnostic evaluation</td>
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<td>Second provider does not participate in therapeutic alliance built during induction</td>
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<tr>
<td>Drug treatment model</td>
<td>Buprenorphine maintenance therapy is provided through a substance abuse clinic with HIV care services</td>
<td>Specialist care is provided</td>
<td>Clinical care sites are potentially more stigmatized</td>
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<td></td>
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<td>Methadone and naltrexone alternatives are more readily available</td>
<td>The model does not take advantage of buprenorphine’s regulatory advantage over methadone</td>
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<td>Subjects can possibly be transferred from methadone programs to more flexible buprenorphine maintenance therapy</td>
<td>The number of specialized substance abuse clinics is limited</td>
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<tr>
<td></td>
<td></td>
<td>Counseling services are available on site</td>
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when power over HAART and substance abuse treatment is in a single provider’s hands. It is important, therefore, that providers not withhold buprenorphine therapy as a threat against patients who are believed to be nonadherent to antiretroviral therapy. On the other hand, it is important that patients not use threats of nonadherence to HAART as a way of receiving supratherapeutic doses of buprenorphine or supplemental benzodiazepines. The effect of a patient “firing” the buprenorphine maintenance therapy provider is worse here than in the other models, because the patient would also be “firing” the HIV care provider.

Physicians may be less concerned by such power dynamics than by the amount of work involved in implementing this model of care. Specialists and “backup” physicians must be made available to take referrals and for leaves of absence.

There are little empirical data by which to evaluate this model of integration, although a pilot study undertaken by the authors is worth noting. Primary care buprenorphine maintenance therapy was instituted in New Haven, Connecticut, in a mobile health care van. Of the 22 HIV-infected patients treated through the van over the past 2 years, 1 has been transferred to a methadone program, 1 died of unrelated causes, and 3 were incarcerated. Seven continue receiving buprenorphine maintenance currently (duration of total therapy, 2–23 months). Of the other 10 patients, 1 elected to discontinue buprenorphine treatment, and 9 were slowly withdrawn from the program because of their failure to adhere to the program and to attend counseling sessions. The scheduled withdrawal of buprenorphine was protracted in all cases, because counselors and case managers continued outreach to these patients in an attempt to more fully engage them.

Components of this program include street-level case management staff able to engage with patients using motivation enhancement therapy and rapid assessment for treatment initiation of treatment with buprenorphine. Delaying treatment resulted in dramatic fallout. For example, when treatment with buprenorphine could begin rapidly (within 5 days of declaring a desire to begin treatment), it was generally possible to locate individuals to start therapy. Individuals whose treatment was delayed beyond the fifth day were more difficult to locate and less likely to return to the van for induction. It was also noted that street-level intervention brought into treatment persons who had severe mental illnesses or severe (often infectious) medical problems that would have otherwise gone untreated. Often, these individuals were receptive to treatment initially; some did, however, prove difficult to retain in the treatment program, especially the patients with comorbid psychiatric illnesses (at least 10 of the 22) and polysubstance abuse.

A major insight in designing interventions for the street level for individuals with multiple comorbidities was the recognition that these patients required flexible, convenient, co-located services. Buprenorphine, integrated with HIV primary care and on-site counseling and mental health services, provided this for several complicated clients.

**MODEL 2: THE ON-SITE ADDICTION SPECIALIST MODEL**

In the on-site addiction specialist model, an HIV practitioner would refer to the within-clinic substance abuse specialist, who would then triage the patient to determine the appropriateness of buprenorphine versus alternative courses of substance abuse treatment. If appropriate, the specialist would perform induction, stabilization, and maintenance of buprenorphine treatment for the patient. Buprenorphine therapy is only “integrated” into HIV care in the sense that it is provided in the same clinical setting.

This model offers the advantage of providing specialized care to the patient, and it may be particularly useful in clinics through which physicians rotate only a few hours of the week (e.g., HIV treatment centers at teaching hospitals). Patients would need, however, to schedule separate appointments with the clinic’s substance abuse specialist. Although this model provides HIV and drug treatment services in the same clinical setting, it may not provide true integration, because it perpetuates the notion of 2 different worlds of HIV care and substance abuse treatment. The lack of effective coordination between providers of the 2 services, along with poor scheduling of patient visits, may lead to the fragmentation of care, which has been noted to worsen outcomes. A French study observed higher dropout rates among patients receiving HIV care and buprenorphine maintenance therapy from 2 different providers, compared with those who received therapy from a single provider (40% vs. 20%), and the authors noted a greater numbers of patients with inadequate buprenorphine dosing and excessive benzodiazepine dosing when multiple providers were involved [23].

Regular case discussions or conference calls have reduced such errors in other clinical scenarios [24]. Nevertheless, this model for buprenorphine maintenance therapy and HIV care integration has not been evaluated in the United States and is currently being tested through a controlled trial (L. Sullivan, personal communication).

**MODEL 3: HYBRID MODEL**

HIV care providers who are concerned that they may not be able to handle the induction and stabilization phases of buprenorphine maintenance therapy may work through a “hybrid” model, in which inductions and stabilizations are performed by a physician skilled in buprenorphine maintenance therapy, after which patients are transferred to the HIV care provider for maintenance of therapy.

Although such a model offers the advantage of specialty care
for the induction and stabilization phases, the danger of this hybrid model is that care will be initially fragmented, and miscommunications could occur within a clinic if the HIV care provider is unaware of the nuances of a patient’s early experiences with buprenorphine therapy. If induction and stabilization are not performed within the HIV clinic itself, a patient may also need to travel to another location to see a counselor or may have to switch counselors, with possibly negative results and destabilization. One counselor could provide services at both locations to establish continuity of care. We would also recommend that induction and stabilization phases are kept “in house” and that HIV practitioners attend some of the induction appointments to participate in the therapeutic alliance that is constructed during the induction phase. The physician doing the induction and stabilization could transfer prescriptive responsibility to the primary HIV clinician, maximizing the number of patients that the specialist can treat under the 30-patient regulation.

A Boston, Massachusetts, clinic that uses this hybrid model noted that, of 37 opiate-dependent, HIV-negative subjects (84% were dependent on heroin, and 16% were dependent on sustained-release oxycodone), 30 (88%) remained in the buprenorphine maintenance therapy program after 4 months, whereas 3 switched to methadone, 1 tapered off buprenorphine, and 3 dropped out of treatment. Results of opioid urine tests were positive for all subjects at intake and for 18% of subjects at 4 months. Other drug use was not observed to change significantly. Many of the patients (54%) had existing psychiatric comorbidities, but only 13% had previously undergone psychiatric care, and 76% had no primary medical care provider.

**MODEL 4: DRUG TREATMENT MODEL**

Although we suggest that buprenorphine may be most helpful for HIV-infected patients and their clinicians when incorporated into the HIV clinical care setting, some practitioners may prefer that buprenorphine be provided by substance abuse specialty clinics. This model has been successful in New York City, where HIV clinicians do not merely refer patients to substance abuse clinics, but HIV care is provided at these clinics along with the substance abuse services. An additional advantage is that these licensed clinics can provide buprenorphine maintenance therapy to an unlimited number of patients. Typically, the clinics must comply with the same restrictions on methadone administration, which places limits on take-home dosing. Licensed clinics can, however, request a waiver to provide expedited take-home dosing to patients. Indeed, one of the authors (R.D.B.) was able to start administering take-home dosing for buprenorphine maintenance therapy from day one as the medical director of a licensed drug treatment clinic.

There are several advantages to this model. HIV treatment is integrated into a drug treatment setting, such that an alternative to buprenorphine (e.g., methadone) can be provided on site if buprenorphine maintenance therapy is not effective, and counseling practices that have been tailored to the drug treatment setting can be offered. This model may allow transition of patients who are receiving stable methadone maintenance to buprenorphine maintenance therapy if they are able to reduce their methadone dosages to relatively low levels, although this has not been tested. Drug treatment programs can also provide a greater level of structure through daily dosing (with either methadone or buprenorphine), which offices cannot support. Through this structure, diversion and abuse can be decreased, providing a safer harm-reduction alternative for the most challenging active drug users.

The disadvantage to this approach is that it may perpetuate a traditional drug treatment model and prevent new approaches to comanaging HIV infection and substance abuse. Integration of buprenorphine maintenance therapy into substance abuse clinics that provide HIV therapy should be considered by HIV care practitioners who are cautious about focusing solely on buprenorphine merely because of the looser regulatory structure that allows the medication’s incorporation into office-based practices. Providers may feel that the prescription of opiate maintenance therapy is beyond the role of the primary care HIV physician and that it would be safer to refer patients to specialized clinics.

Because substance abuse clinics are often overburdened and have long waiting lists, or because they are not available in the geographical region in which the subject lives, offering buprenorphine through a specialized clinic may not be feasible in many regions. In fact, the demand for buprenorphine appears to be driven by methadone specialty clinics’ inability to meet the need for treatment of opiate dependence. In addition, unless a substance abuse clinic offers comprehensive HIV treatment services, this model would still result in fragmented care.

**CHALLENGES AND RECOMMENDATIONS**

There are notable limitations to buprenorphine maintenance therapy that will present challenges to its integration into HIV care, regardless of the model used. As the first drug of its kind to be available for widespread use, buprenorphine will come under close scrutiny from regulators, although its formulation with naloxone will likely reduce diversion to street use. Nevertheless, insufficient public funding for substance abuse treatment may push opiate-dependent patients toward illegal activities to obtain funds to pay for buprenorphine. Placing buprenorphine on formularies for AIDS drug assistance programs should therefore be a top priority.

A large obstacle to the incorporation of buprenorphine into HIV care is the attitude of some practitioners who are wary of...
the concept of maintenance therapy—who expect that substance abuse treatment should lead to rapid cure without any recidivism. Many practitioners view substance dependence as different from other diseases, taking a harsher moral stance about nonadherence to treatment. These attitudes have been found to be barriers to entrance into and maintenance of antiretroviral therapy [8, 9, 28, 29].

In addition, an unfortunate effect of the 30-patient limitation is that it promotes short-term detoxification of patients. Because the demand for treatment often exceeds capacity, providers might feel obligated to remove some patients from buprenorphine maintenance therapy to allow new patients to access the therapy. Federal agencies should consider allowing providers who care for high-risk populations (e.g., HIV-infected patients) to exceed the 30-patient limit.

We have presented 4 models through which comprehensive care can be delivered incorporating buprenorphine maintenance therapy into HIV care. Although we have argued for a model in which HIV clinicians provide buprenorphine maintenance therapy, additional research and monitoring is required to determine the optimal parameters for these types of programs.

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