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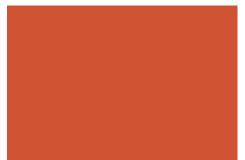




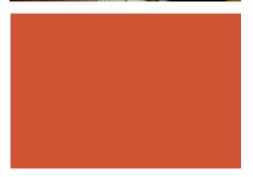












Integration of Buprenorphine into HIV Primary Care Settings

August 2012





U.S. Department of Health and Human Services Health Resources and Services Administration HIV/AIDS Bureau Special Projects of National Significance Program



Curriculum: Integration of Buprenorphine into HIV Primary Care Settings

U.S. Department of Health and Human Services Health Resources and Services Administration HIV/AIDS Bureau Special Projects of National Significance Program

August 2012

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The Health Resources and Services Administration (HRSA), HIV/AIDS Bureau (HAB) has developed the Integrating HIV Innovative Practices (IHIP) manuals, curricula, and trainings to assist health care providers and others delivering HIV care in communities heavily impacted by HIV/AIDS with the adoption of Special Projects of National Significance (SPNS) models of care. This IHIP curriculum is part of that effort. Additional IHIP materials can be found at www.careacttarget.org.













INTRODUCTION

PURPOSE AND BACKGROUND

The purpose of this curriculum is to provide physicians with the information they need to educate their clinic staff and other stakeholders about integrating medication-assisted treatment (MAT) with buprenorphine into HIV primary care. It provides a detailed overview of buprenorphine within clinical settings, from the legal requirements for implementation to step-by-step procedures for prescribing and administering buprenorphine.

The curriculum draws on the best practices developed under the Special Projects of National Significance (SPNS) initiative, *Innovative Methods for Integrating Buprenorphine Opioid Abuse Treatment in HIV Primary Care*, which took place from 2004–2009. This project marked the first time that the Health Resources and Services Administration (HRSA) HIV/AIDS Bureau (HAB) explored methods of integrating buprenorphine treatment into HIV care.

TARGET AUDIENCE

This curriculum is geared to clinical staff and other stakeholders with a vested interest in learning about the integration of buprenorphine into HIV primary care practice. This includes, but is not limited to, medical doctors, nurse practitioners, registered nurses, care coordinators, front desk staff, case managers, and medical assistance and other staff who will be involved in setting up and facilitating the clinic's buprenorphine program.

TRAINING DESIGN

Each of the trainings detailed in this curriculum has been set up to accommodate the busy schedules of HIV primary care clinics. Each training is designed as a standalone session and will take approximately 25-30 minutes to present. When longer periods of time are available, sessions may be combined.

Trainers should read through each module prior to presentation in order to familiarize themselves with its content and plan out the related learning activities.

INSTRUCTIONAL APPROACH

The medical doctor heading the buprenorphine program within the clinic should facilitate these trainings. No training experience, however, is required to deliver the information, and other appropriate staff may step in when the presiding medical doctor is not available.

Each module includes a PowerPoint presentation accompanied by a detailed description of its content and related enhanced learning activities. The success of the training depends on the willingness of the trainer to use the discussions and learning activities to ensure that participants grasp the objectives of each module. The material covered in the curriculum is reflected in the related training manual.

Each training module begins with an overview of sections in the module and the materials needed to complete the session. Activities follow a basic three-step approach: (1) explanation, (2) initiation, (3) debrief. The explanation step includes a brief overview of the module's learning objective.

The initiation step involves instructions and implementation of the activity. The debriefing step provides an opportunity for the trainer to review the activity, and clarify and reinforce key learning points.

The activities described in the curriculum easily accommodate up to 25 participants and can be modified as needed. They encourage learning through interaction rather than lecture alone in order to familiarize participants with buprenorphine treatment.

MATERIALS AND EQUIPMENT

Modules include a PowerPoint training slide presentation, as well as a script, learning activities, and additional explanation. The presentations may be accessed at [insert a link to the TARGET Center site once available].

Trainers will need the following items for each of the training sessions:

- · A computer and compatible LCD projector that can play each of the PowerPoint presentations
- · A screen or blank wall on which to project each training
- Microsoft Word to open and download handouts and factsheets
- A printer and/or copier to reproduce the materials to be reviewed in that day's training session.

To facilitate conversation during the learning activities, the trainer also may want to consider including:

- Paper and easel or whiteboard
- Colorful markers
- Tape to affix sheets to the walls.

MANUAL FORMAT

At the start of each module is a breakdown of the discussions and activities. A new discussion topic is designated by a section title, summary, and list of materials required. Throughout the manual are explanations of slides, talking points, and activities.

Below are the symbols used throughout the training:



The approximate length of time the session will take.



Trainer's note



PowerPoint slide



Group activity



Handout













MODULE 1: Do We Have a Problem? Examining Opioid Use and HIV

The goal of this module is to increase understanding of the intersection of opioid use and HIV and to assess the group's perceived risk among client populations. Successful integration of opioid treatment into HIV primary care depends on the provider community first agreeing that there is a problem to address.

SUMMARY

In small groups, participants measure their current knowledge and awareness of the local community and clinic use of opioids and its intersection with HIV.

MATERIALS NEEDED

- One piece of paper per small group
- One writing utensil per small group
- Whiteboard or paper and easel
- Clock or watch to time activity
- A computer and compatible LCD projector to play the PowerPoint presentation.



Two PowerPoint slides will be shown while participants work through the activity: Slide #1 during the explanation of the activity, and Slide #2 during the activity.



SLIDE # 1: WHAT IS SUBSTANCE DEPENDENCE?

What is Substance Dependence?

- The Diagnostic and Statistical Manual IV (DSM-IV) describes addiction as "a maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12month period:
 - (1) Tolerance, as defined by either of the following:
 - (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect
 - (b) markedly diminished effect with continued use of the same amount of the substance.
 - . 2) Withdrawal, as manifested by either of the following:
 - (a) the characteristic withdrawal syndrome for the substance
 - (b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms.
 - (3) The substance is often taken in larger amounts or over a longer period than was intended.



What is Substance Dependence? (cont.)

- 4) There is a persistent desire or unsuccessful effort to cut down or control the substance use.
- (5) A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
- (6) Important social, occupational, or recreational activities are given up or reduced because of the substance.
- (7) The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.

Source: American Psychiatric Association. Diagnostic and statistical manual of disorders. Fourth edition, text revision. Washington, DC, 2000: author.

SLIDE #2: WHAT IS SUBSTANCE DEPENDENCE? (cont.)

Activity

- Explain the activity.
 - You will work in small groups to identify and answer the following questions:
 - What indicators have you seen within the clinic or through chart and patient reviews to suggest opioid dependence?
 - Is our clinic writing a lot of prescriptions for opioid pain medications?
 - What trends have you seen within the community, read or heard through the media, or heard during patient consults to suggest local indicators of an opioid problem?
 - What has been your experience interacting with opioidaddicted patients with and without medication-assisted treatment (MAT)?
 - You will have 10 minutes to discuss and write down your group answers
- Initiate the activity.
 - Form small groups of approximately three people per group.
 - Distribute paper and writing utensils.
- Debrief the activity.
 - O Ask each group to identify a spokesperson for their group.
 - Go around the room and ask each group to share their findings.
 - Where further discussion may be possible, ask spokesperson to provide support for their response/finding.
 - Write down group responses for one comprehensive list.
 - o Address any misperceptions.



HIV and Substance Use

- Substance use is associated with:
 - · increased sexual risk behaviors,
 - · increased HIV risk and poorer health outcomes,
 - contributing to destabilizing conditions, (e.g. homelessness and mental illness).
 - HIV, injection drug use (IDU), and opioid addiction are intertwined
 - Since the beginning of the epidemic, one-third of all AIDS cases have been directly or indirectly related to IDU.
 - For people with HIV, untreated opioid addiction is associated with poor HIV treatment outcomes and a host of other medical, psychosocial, and legal consequences.

SLIDE #3: HIV AND SUBSTANCE USE

- Offer insight, and discuss with the full group the intersection of HIV and injection drug use.
 - The intersection of opioid addiction, particularly injection drug use (IDU), and HIV is well documented.
 - o IDU is the second most frequent route of HIV transmission.



Shocking Statistics

- IDU (either directly or via sexual contact with an IDU partner) accounts for 1/3 of cumulative est. AIDS cases, and 18 percent of new infections in the United States.
- •In the United States, there are an estimated 2.4 million opioid-addicted people.
- According to a 2010 Substance Abuse and Mental Health Services Administration (SAMHSA) national study, dependence/abuse of pain relievers ranked second (after marijuana) among illicit drug use in the past year. Heroin ranked fifth.
- National data, as well as clinical experience from a SPNS
 Buprenorphine Initiative grantee suggest prescription opioid abuse may be proportional to the number of opioid prescriptions written.

SLIDE #4: SHOCKING STATISTICS

- IDU, either directly or via sexual contact with an IDU partner, accounts for one-third of the estimated AIDS cases since the beginning of the epidemic, and 18 percent of new infections in the United States.
- With an estimated 2.4 million opioid-addicted people in the United States, opioids are among the most frequently abused drugs.
- According to a 2010 Substance Abuse and Mental Health Services Administration (SAMHSA) national study, dependence/abuse of pain relievers ranked second (after marijuana) among illicit drug use in the past year. Heroin ranked fifth.
- National data, as well as clinical experience from a SPNS Buprenorphine Initiative grantee suggest that prescription opioid abuse may be proportional to the number of opioid prescriptions written.
- Full group discussion.
 - o Is this information surprising?
 - O Does this confirm what you said in small group discussions?
 - How many of our HIV patients identified IDU as their transmission (or risk) category?
 - How often do we prescribe opioid pain medications to our HIV patients?
 - Oo we know whether our HIV patients are being prescribed opioids by another physician?













MODULE 2: Key Terms and Definitions

SUMMARY

The goal of this module is to increase understanding around the terminology of addiction, opioid use, and MAT. Review and discussion of this handout can serve as a helpful reference to staff as they work toward integration of opioid addiction treatment into your clinic. Understanding such terms and how they fit into the larger treatment picture will also improve overall health literacy.

Where applicable, this handout can be modified and provided to patients to include those terms used in patient–provider conversations. The primary audience, however, is clinic staff.

MATERIALS NEEDED

• Printer and/or copier machine (need one copy per person)



The handout starts on next page for easy printing/copying.

MEDICATION-ASSISTED TREATMENT (MAT) KEY TERMS AND DEFINITIONS

abstinence. Nonuse of alcohol or any illicit drugs, as well as nonabuse of medications normally obtained by prescription or over the counter. Abstinence does not refer to nonuse of or withdrawal from maintenance medications such as buprenorphine when used for treatment therapy.

acute stage. Initial and usually the most symptomatic intensive-treatment phase of MAT.

addiction. Combination of behavioral manifestations of use, and subjective sense of need and craving for a psychoactive substance, leading to compulsive use of the substance either for its positive effects or to avoid negative effects associated with abstinence from that substance. Compare *dependence*.

admission. Formal process of enrolling patients in a methadone or buprenorphine program, carried out by qualified personnel who determine that the patient meets acceptable medical criteria for treatment. Admission can include orientation to the program and an introduction to peer support, patient rights, services, rules, and treatment requirements related to MAT.

agonist. See opioid agonist.

analgesic. A compound that alleviates pain without causing loss of consciousness. *Opioid analgesics* comprise a class of compounds that bind to specific receptors in the central nervous system to block the perception of pain or affect the emotional response to pain. Such compounds include opium and its derivatives, as well as a number of synthetic compounds. Chronic administration or abuse of opioid analgesics may lead to addiction.

antagonist. See opioid antagonist.

assessment. Process of identifying the precise nature and extent of a patient's substance use disorder and other medical, mental health, and social problems as a basis for treatment planning. Assessment usually begins during program admission and continues throughout treatment. It includes a personal substance abuse history, present and past history of psychiatric and medical

disorders, family history of substance use, psychiatric and medical disorder, physical examination, laboratory evaluation (including urine toxicology), and determination of disease morbidity. Severity of disease is often assessed further in terms of physiologic dependence, organ system damage, and psychosocial morbidity. Assessment also involves determining patient motivation and readiness for change.

assessment tools. Instruments (e.g., questionnaires) used to capture the range of patient variables affecting treatment planning, methods, and outcomes. Valid assessment tools contain quantifiable indicators to measure patient progress and to track patients through treatment.

benzodiazepines. Group of medications having a common molecular structure and similar pharmacological activity, including antianxiety, sedative, hypnotic, amnestic, anticonvulsant, and muscle-relaxing effects. Benzodiazepines are among the most widely prescribed medications (e.g., diazepam, chlordiazepoxide, clonazepam, alprazolam, lorazepam).

buprenorphine. Partial opioid agonist approved by the U.S. Food and Drug Administration (FDA) for use in detoxification or maintenance treatment of opioid addiction and marketed under the trade name Suboxone® (containing naloxone). Subutex®, an all-buprenorphine tablet, has been discontinued by the manufacturer, although it remains available in generic form.

certification. Process by which SAMHSA determines that a physician is qualified to provide opioid addiction treatment under the Federal opioid treatment standards. There are separate certification processes for methadone and buprenorphine.

confidentiality regulations. Rules established by Federal and State agencies to limit disclosure of information about a patient's substance use disorder and treatment (described in 42 Code of Federal Regulations [CFR], Part 2 § 16). Programs must notify patients of their rights to confidentiality, provide a written summary of these rights, and establish written procedures regulating access to and use of patient records.

consent to treatment. Form completed with and signed by an applicant for MAT and by designated treatment program staff members which verifies that the applicant has been informed of and understands program procedures and his or her rights and treatment goals, risks, and performance expectations.

counseling. In MAT, a treatment service in which a trained counselor and a case manager evaluate both a patient's external circumstances and immediate treatment progress and offer appropriate advice and assistance or referral to other experts and services as needed. A major objective in MAT is to provide skills and support for a substance-free lifestyle and encourage abstinence from alcohol and other psychoactive substances.

cultural competence. Capacity of a service provider or organization to understand and work effectively in accord with the beliefs and practices of persons from a given ethnic/racial/religious/social group or sexual orientation. It includes the holding of knowledge, skills, and attitudes that allow the treatment provider and program to understand the full context of a patient's current and past socioenvironmental situation.

dependence. State of physical adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, and/or decreasing blood level of a substance and/or administration of an antagonist. Dependence includes increased *tolerance* (see below). Compare *addiction*.

detoxification. Treatment for addiction to an illicit substance in which the substance is eliminated gradually from a patient's body while various types and levels of reinforcing treatment (including pharmacological treatment) are provided to alleviate adverse physical or psychological reactions to the withdrawal process.

diversion. Sale or other unauthorized distribution of a controlled substance, usually for a purpose other than the prescribed and legitimate treatment of a medical or mental disorder.

diversion control plan. Documented procedures to reduce the possibility that controlled substances are used for other than their legitimate use. Federal opioid treatment standards [42 CFR, Part 8 § 12(c)(2)] require a

diversion control plan in an opioid treatment program as part of its quality assurance program.

dosage determination. Process of identifying the amount of medication that will minimize withdrawal symptoms and craving in patients in MAT in an effort to increase their chance to have a successful recovery. Much evidence supports a linear relationship among the amount of medication provided, the time frame over which it is allowed to act before another dose is administered (dose frequency), and treatment response.

drug-drug interaction. Action of one drug on the effectiveness or toxicity of another drug.

drug testing. Examination of an individual to determine the presence or absence of illicit or nonprescribed drugs or alcohol or to confirm maintenance levels of treatment medications.

elimination half-life. Time required after administration of a substance (e.g., buprenorphine) for one-half the dose to leave the body. Elimination half-life affects the duration of action of a substance or medication and can be influenced by patient factors, such as absorption rate, variable metabolism and protein binding, changes in urinary pH, concomitant medications, diet, physical condition, age, pregnancy, and even use of vitamins and herbal products.

opioid medication addiction. Addiction resulting from use of an opioid usually for pain management. (Prescription opioid medication may have been directly prescribed to a patient or they may have accessed it through other means.)

induction. Initial treatment process of adjusting maintenance medication dosage levels until a patient attains stabilization.

maintenance treatment. Dispensing of an opioid addiction medication at stable dosage levels for a set period of time.

medication-assisted treatment (MAT) for opioid addiction. Type of addiction treatment, usually provided in a certified, licensed Opioid Treatment Program (OTP) or a physician's office-based treatment setting, that provides

maintenance pharmacotherapy using an opioid agonist, a partial agonist, or an antagonist medication, which may be combined with other comprehensive treatment services, including medical and psychosocial services.

methadone. The most frequently used opioid agonist medication. Methadone is a long-acting synthetic opioid that binds to mu opiate receptors and produces a range of mu agonist effects similar to those of short-acting opioids, such as morphine and heroin. Long-acting opioids help keep blood levels steady and control pain for a longer period of time; short-acting opioids need to be taken more frequently but effects are felt more quickly.

naloxone. Short-acting opioid antagonist. Because of its higher affinity than that of opioids for mu opiate receptors, naloxone displaces opioids from these receptors and can precipitate withdrawal, but it does not activate the mu receptors, nor does it cause the euphoria and other effects associated with opioid drugs. Naloxone is not FDA approved for long-term therapy for opioid addiction, except in the combination buprenorphine-naloxone tablet. When taken orally, naloxone does not have an effect. Some programs use naloxone to evaluate an individual's level of opioid dependence. Naloxone is also used to help reverse opioid overdose. See *naloxone challenge test*.

opiate receptors. Areas on cell surfaces in the central nervous system that are activated by opioid molecules to produce the effects associated with opioid use, such as euphoria and analgesia. Opiate receptors are activated or blocked by opioid agonist or antagonist medications, respectively, to mediate the effects of opioids on the body. Mu and kappa opiate receptor groups principally are involved in this activity.

opioid. Natural derivative of opium or synthetic psychoactive substance that has effects similar to morphine or is capable of conversion into a drug having such effects. One effect of opioid drugs is their addiction-forming or addiction-sustaining liability.

opioid addiction. Cluster of cognitive, behavioral, and physiological symptoms resulting from continuation of opioid use despite significant related problems. Opioid addiction is characterized by repeated self-administration that usually results in opioid tolerance, withdrawal symptoms, and compulsive drug taking.

opioid addiction treatment. Dispensing of approved medication to prevent withdrawal and craving in patients with opioid dependence, with or without a comprehensive range of medical and rehabilitation services or medication prescribed when necessary to alleviate the adverse medical, psychological, or physical effects. This term encompasses medically supervised withdrawal, maintenance treatment, comprehensive maintenance treatment, and, under restricted timeframes, interim maintenance treatment (adapted from 42 CFR, Part 8 § 2).

opioid agonist. Drug that has an affinity for and stimulates physiologic activity at cell receptors in the central nervous system normally stimulated by opioids. Methadone is an opioid agonist.

opioid antagonist. Drug that binds to cell receptors in the central nervous system that normally are bound by opioid psychoactive substances and that blocks the activity of opioids at these receptors without producing the physiologic activity produced by opioid agonists. Naltrexone is an opioid antagonist.

opioid partial agonist. Drug that binds to, but incompletely activates, opiate receptors in the central nervous system, producing effects similar to those of a full opioid agonist but, at increasing doses, does not produce as great an agonist effect as do increased doses of a full agonist (ceiling effect). Buprenorphine is a partial opioid agonist.

opioid treatment program (OTP). SAMHSA-certified program, usually comprising a facility, staff, administration, patients, and services, that engages in supervised assessment and treatment, using methadone, buprenorphine or naltrexone, of individuals who are addicted to opioids. An OTP can exist in a number of settings, including, but not limited to, intensive outpatient, residential, and hospital settings. Services may include medically supervised withdrawal and/or maintenance treatment, along with various levels of medical, psychiatric, psychosocial, and other types of supportive care.

OxyContin®. Long-acting class II opioid drug usually obtained by prescription for treatment of pain. OxyContin is one of several prescription opioids increasingly obtained by illicit means and abused by people addicted to opioids.

pain management. Treatment of acute or chronic pain by various treatment methods, often including administration of opioid medications.

pharmacology. Science that addresses the origin, nature, chemistry, effects, and uses of medications and drugs.

pharmacotherapy. Treatment of disease with prescribed medications.

relapse. Breakdown or setback in a person's attempt to change or modify a particular behavior; an unfolding process in which the resumption of compulsive substance use is the last event in a series of maladaptive responses to internal or external stressors or stimuli.

remission. State in which a mental or physical disorder has been overcome or a disease process halted.

residential treatment. Therapy received within the context of a cooperative living arrangement.

screening. Process of determining whether a prospective patient has a substance use disorder before admission to treatment. Screening usually involves use of one or more standardized techniques, most of which include a questionnaire or a structured interview. Screening also may include observation of known presenting complaints and symptoms that are indicators of substance use disorders.

sedative. Medication with central nervous system sedating and tranquilizing properties.

side effect. Consequence (especially an adverse result) other than that for which a drug is used—especially the result produced on a tissue or organ system other than that being targeted.

stabilization (stability). Process of providing immediate assistance (as with an opioid agonist) to eliminate withdrawal symptoms and drug craving.

substance use disorder (frequently referred to as substance abuse or dependence). Maladaptive pattern of drug or alcohol use manifested by recurrent, significant adverse consequences related to the repeated use of these drugs or alcohol. The substance-related problem

must have persisted and occurred repeatedly during a 12-month period. It can occur sporadically and mainly be associated with social, legal, or interpersonal problems, or it can occur regularly and be associated with medical and mental problems, often including tolerance and withdrawal.

supportive-care phase. Phase of MAT in which patients maintain abstinence from substances.

take-home medication. Opioid addiction treatment medication dispensed to patients for unsupervised self-administration.

tapering phase. Phase of MAT in which patients maintained on medication attempt gradually to eliminate their treatment medication while remaining abstinent from illicit substances.

tolerance. Condition of needing increased amounts of an opioid to achieve intoxication or a desired effect; condition in which continued use of the same amount of a substance has a markedly diminished effect.

treatment barrier. Anything that hinders treatment. Examples include financial problems, language difficulties, ethnic and social attitudes, logistics (caring for children, transportation), and unhelpful patient behaviors (tardiness, missed appointments).

treatment efficacy. Ability of an intervention or medication in expert hands and under ideal circumstances to produce the desired therapeutic effect.

treatment eligibility. Relative qualification of a prospective patient for admission to an opioid treatment program.

treatment outcomes. Observable results of therapy, including decreased use of illicit psychoactive substances, improved physical and emotional health, decreased antisocial activities, and improved social functioning; considered the best indicator of treatment program effectiveness.

treatment plan. Documented therapeutic approach for each patient that outlines attainable short-term goals mutually acceptable to the patient and their physician.

12-Step program. Self-help program requiring mastery of a set of steps to achieve and maintain abstinence, based on the program of Alcoholics Anonymous. Many addiction treatment programs use a 12-Step structure or philosophy as a construct for treatment design.

urine drug testing. Most common laboratory assessment technique in addiction treatment which involves analysis of urine samples from patients for the presence or absence of specific drugs. Originally used as a measure of program effectiveness, urine testing now is used to make programmatic decisions, monitor psychoactive substance use, adjust medication dosage, and decide whether a patient is responsible enough to receive takehome medication. Methods of urine testing vary widely.

withdrawal. Reduction and elimination of substance use. See *medically supervised withdrawal, withdrawal syndrome*.

withdrawal syndrome (or withdrawal). Predictable constellation of signs and symptoms after abrupt discontinuation of or rapid decrease in use of a substance that has been used consistently for a period. Signs and symptoms of withdrawal are usually opposite to the direct pharmacological effects of a psychoactive substance.

Source: Adapted in part from Substance Abuse and Mental Health Administration (SAMHSA). *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs. Treatment Improvement Protocol (TIP) 43.* 2005. Available at: www.ncbi.nlm.nih.gov/books/NBK64166/.













MODULE 3: What are Opioids? What is MAT?

SUMMARY

The information in this module includes an overview of addiction and medication-assisted addiction treatment and, more specifically, of buprenorphine and methadone.

MATERIALS NEEDED

• A computer and compatible LCD projector to play the PowerPoint presentation.



What are Opioids?

- Opioids are natural, fully semisynthetic/entirely manmade drugs
- Opioids diminish the perception of and reaction to pain.
- They also produce feelings of euphoria.
- Heroin and some prescription medications (such as morphine, fentanyl, oxycodone, codeine, methadone and buprenorphine) are opioids.
- According to one SPNS study grantee, prescription opioid abuse may be proportional to the number of opioid prescriptions written to HIV-positive patients.

What Do Opioids Do?

Opioids bind to and activate receptors in the

brain, triggering the release of dopamine - a neurotransmitter linked with learning, pleasure,

Over time, opioid use changes both the amount and sensitivity of dopamine receptors in the brain,

leading some people to try to restore dopamine

levels by continuing their drug use.

and reward.

Opioids are natural, fully semisynthetic/entirely manmade drugs that bind to receptors in different parts of the body, including the brain. These drugs are analgesics. They lower both the perception of and reaction to pain. Heroin, morphine, fentanyl, codeine, oxycodone, buprenorphine, and methadone are opioids.



SLIDE # 6: WHAT DO OPIOIDS DO?

SLIDE # 5: WHAT ARE OPIOIDS?

- Our bodies produce substances that are very similar to opioids; these are known as endogenous opioids or endorphines. Exogenous opioids, such as heroin and methadone, bind to the same receptors as endogenous opioids, which explains their powerful effect on human beings.
- Opioids release an excess of dopamine into the body. Dopamine is a neurotransmitter (brain chemical) involved with learning, motivation, pleasure, and reward. Opioids change the amount and sensitivity of dopamine receptors and can make people feel euphoric; in addition, opioids can suppress pain and reduce anxiety. Eventually, users require an opioid to continuously occupy the opioid receptor in the brain, or they develop withdrawal symptoms.



SLIDE #7: WHAT IS MAT, AND WHY CONSIDER IT?

 Medication-Assisted Treatment (MAT) is "the use of medication such as methadone or buprenorphine in combination with counseling and behavioral therapies to provide a whole-patient approach to the treatment of opioid dependence."*

What is MAT, and Why Consider It?

 $\ensuremath{\scriptstyle\square}$ MAT is an integral part of comprehensive HIV services for opioid-addicted PLWHA.

■ MAT – combining pharmacotherapy and counseling – can improve HIV and addiction-related outcomes.

*Source: Cheever LW, Kresina TF, Cajina A, et al. A model Federal collaborative to increase patient access to buprenorphine treatment in HIV primary care. JAIDS. 2011;56 (Suppl 1):53.

A recent article by Dr. Laura Cheever and her colleagues defined MAT as "the use of medication such as methadone or buprenorphine in combination with counseling and behavioral therapies to provide a whole-patient approach to the treatment of opioid dependence."

 Methadone, buprenorphine, and naltrexone are the only medications approved by the U.S. Food and Drug Administration (FDA) for treating opioid addiction. Naltrexone is less commonly used to treat opioid addiction, in part because of poor adherence. An extended-release injectable form, however, was recently approved by the FDA which might overcome adherence barriers. Naltrexone prevents receptors from being activated by agonist compounds, such as heroin or prescribed opioids, and is reported to reduce opioid cravings and to prevent relapse. (See "advisory" in the online resources of Module 10 below to learn more.)

- Methadone can be dispensed at SAMHSA-certified OTPs.
- Buprenorphine can be dispensed at OTPs but is most readily dispensed by physicians with a waiver from the DEA.
- o Naltrexone can be given by health care providers licensed to give prescription medications.
- Regardless of the setting in which MAT is administered, opioidaddicted patients must be medically supervised at the inception of treatment and receive continuous followup.
- With few exceptions, methadone is provided through accredited, certified OTPs, whereas qualifying physicians can prescribe buprenorphine as part of a patient's medical care.
- Substance abuse has been associated with increased risk behaviors, including increased risk for acquiring and transmitting HIV. In contrast, MAT is associated with improved health outcomes and social functioning.
- Integrating MAT into Ryan White HIV/AIDS Program grantee sites adds a crucial component to the ever-growing, comprehensive scope of Program services. Integrating substance abuse treatment into HIV primary care sites provides the opportunity to address opioid addiction as part of medical care, thereby improving HIV medication adherence and treatment outcomes.



 "With buprenorphine you just feel like you're just normal. It's kind of like it takes me back to before I had ever done

Patient Testimonials

- "Seemed like when I got on the program, everything just came - the sun came out. This is so cliché, but I started smelling the flowers. You know, I just, I started loving
- Buprenorphine "makes me take care of [my HIV] more. If I have to take my buprenorphine every morning, then I have to take my medications every morning. I remember and I can take it all together. I eat, take my vitamins, take my meds, take my buprenorphine, and then I go."

Reference: Egan JE, Netherland J, Gass J. Patient perspectives on buprenorphine/naloxe treatment in the context of HIV care. [AIDS. 2011;56(Suppl 4):548.

On the whole, patients who have participated in the Health Resources and Services Administration HIV/AIDS Bureau's Special Projects of National Significance Buprenorphine Initiative had very positive feedback about their experiences with opioid addiction treatment.

SLIDE #8: PATIENT TESTIMONIALS

- Patients have noted that they were more lucid, had improved social and cognitive functioning, and experienced a reduction in
- Positive patient responses to opioid addiction treatment have correlated with improved retention in care and antiretroviral therapy adherence.













MODULE 4: Which Medications are Used and How do They Work? About Methadone and Buprenorphine

SUMMARY

The purpose of this module is to more readily examine opioid addiction treatment, specifically buprenorphine—how it works, its formulation, safety profile, and variance from methadone and naltrexone (other opioid addiction treatment options).

MATERIALS NEEDED

- A computer and compatible LCD projector to play the PowerPoint presentation.
- Printer or copier machine (need one copy for each person)



Suggest providing copies of "What is Precipitated Withdrawal. What it is. How to Avoid it." sheet found on page 2 at the following Web address: www.careacttarget.org/library/bup/COWS_ClinicalOpiateWithdrawlScale.pdf. SPNS grantees found the visual representation of opioid withdrawal to assist with understanding and health literacy levels. It is recommended that the handout be passed around at the end of the trainer's PowerPoint presentation; this will enable participants to give the trainer their full attention. A few minutes, however, should be allotted at the end of the training session to discuss the handout. Participants are encouraged to take the handouts with them for future reference.



SLIDE #9: WHAT IS METHADONE, AND HOW DOES IT WORK?

What is Methadone, and How Does It Work?

- Methadone is a full opioid agonist. It prevents withdrawal symptoms by binding to and fully activating opioid receptors; higher doses reduce cravings for, and effects of, other opioids.
- Methadone is administered only by accredited, certified opioid treatment programs (OTPs) or methadone clinics; some OTPs also provide buprenorphine.
- OTPs are highly structured programs.

- Methadone is a synthetic full opioid agonist. It works to block withdrawal symptoms by binding to and triggering opioid receptors. Higher doses of methadone reduce the craving for and effects of other opioids.
- Methadone is administered by accredited, certified opioid treatment programs (OTPs), or methadone clinics; some OTPs also provide buprenorphine.
- Methadone-based MAT may be a good option for some patients.



SLIDE # 10: WHAT IS BUPRENORPHINE, AND HOW DOES IT WORK?

What is Buprenorphine, and How Does It Work?

- Buprenorphine is a partial opioid agonist, so it does not fully activate opioid receptors; therefore, its effects are milder.
- Buprenorphine works by displacing other opioids from their receptors and binding to the same receptors, thereby preventing withdrawal symptoms and drug cravings while blocking the effects of other opioids.
- Buprenorphine can be offered within primary care settings by qualified physicians.
- Buprenorphine is a semisynthetic partial opioid agonist, so it does not stimulate the brain's opioid receptors as much as full agonists (such as heroin, morphine, OxyContin, fentanyl, and methadone), thus the typical opioid effects—such as euphoria and respiratory depression—are milder with buprenorphine.
- Buprenorphine works by knocking other opioids in the brain off their receptors and binding tightly to the same receptors, so that other opioids cannot occupy them. Buprenorphine prevents withdrawal symptoms and reduces drug cravings.
- Buprenorphine stabilizes brain neurochemistry.

SLIDE #11: SUBOXONE

 Buprenorphine may be offered within primary care settings by qualified physicians.



Bunrenorphin

Suboxone is a co-formulation of buprenorphine and naloxone, available as a tablet or film; both are administered sublingually.

Suboxone

- Naloxone reverses overdose by binding to—and blocking—opioid receptors.
- Sublingual naloxone is poorly absorbed, but when injected, naloxone causes immediate onset of withdrawal symptoms.
- Naloxone was added to buprenorphine to reduce the risk of diversion; Suboxone is the preferred form of treatment (over buprenorphine monotherapy).
- Suboxone tablets are orange, hexagonal pills. Suboxone tablets and film contain buprenorphine and naloxone in a 4:1 ratio.

- Buprenorphine monotherapy is available only in generic form. (Subutex, the brand version, was discontinued in September 2011.)
- Buprenorphine monotherapy is used less commonly, generally during pregnancy or under directly observed therapy though its use is increasing with the arrival of the generic on the market because of lower cost to patients.
- Suboxone is a coformulation of buprenorphine and naloxone that comes as an orange, hexagonal tablet or film containing buprenorphine and naloxone in a 4:1 ratio; both are administered sublingually (meaning under the tongue).
- Naloxone is used to reverse overdose because it binds to—and blocks—opioid receptors. When naloxone is taken sublingually, it is poorly absorbed, but when injected, naloxone causes the immediate onset of withdrawal symptoms (also known as "precipitated withdrawal").
- Naloxone was combined with buprenorphine to reduce the risk of diversion.
- For this reason, Suboxone is the preferred method of treatment.



Buprenorphine/Suboxone Safety Profile

Partial agonists have a more favorable safety profile than full agonists.

 Risk of overdose is lower due to a "ceiling effect," meaning increasing buprenorphine dose will not increase effects.

Overdose risk increases when buprenorphine is used with alcohol, benzodiazepines, and other opioids.

Drug-drug interactions:

- Can be safely used with most HIV medications, although monitoring and dose adjustment may be needed with certain drugs.
- · Buprenorphine withdrawal symptoms are less severe.

SLIDE #12: BUPRENORPHINE/SUBOXONE SAFETY

- Suboxone has a favorable safety profile.
- Buprenorphine is associated with the risk of psychological and physical dependence, though the risk involved with buprenorphine is generally considered to be lower than that associated with full opioid agonists.
- Since buprenorphine is a partial agonist, its effects plateau within a 16- to 32-mg dose range. Increasing the dose of buprenorphine beyond this range does not increase the effect, unlike full agonists, such as morphine, methadone, oxycodone, hydrocodone, heroin, codeine, and fentanyl. This is called the "ceiling effect." Buprenorphine's "ceiling effect" lowers the risk of overdose.
 - O However, the risk of overdose increases when buprenorphine is used with alcohol, benzodiazepines, and other opioids. Monitoring is recommended when buprenorphine is coadministered with CYP 3A4 inhibitors (overdosing) and inducers (underdosing).
- Buprenorphine has fewer drug-drug interactions with HIV medications and other commonly used drugs than methadone.
- All patients should be screened for use of other medications.
- Potential drug—drug interactions should be discussed with patients before initiation of buprenorphine.
- Buprenorphine withdrawal symptoms are less severe than methadone withdrawal symptoms.
- Patients who choose to discontinue buprenorphine should have their dosing gradually reduced, and undergo monitoring to reduce the risk of relapse and avert onset of withdrawal symptoms.



SLIDE #13: CAN BUPRENORPHINE BE USED FOR DETOX?

Can Buprenorphine be Used for Detox?

- Can be used on an inpatient basis with medical supervision.
- Transitions people from physical dependence to non-dependence.
- Detox inpatient use was NOT studied in HRSA/HAB SPNS initiative on buprenorphine in HIV primary care settings.
- Buprenorphine can be used for detoxification on an inpatient basis with medical supervision.
- Buprenorphine detoxification can help people ease physical dependence on opioids by transitioning them to a non-physically dependent state.
- Detoxificiation with buprenorhpine was NOT studied in HRSA's HIV/AIDS SPNS initiative on the integration of buprenorphine into HIV primary care settings.
- Nor has buprenorphine detox been extensively studied among people living with HIV/AIDS (PLWHA).



Naltrexone

- Naltrexone is an opioid antagonist and another MAT option.
- Older forms of naltrexone used less commonly because of poor adherence.
- New extended-release injectable form, however, recently released from FDA.
- Offers new promise for adherence and can be offered in primary care settings.
- SAMHSA released new advisory: http://store.samhsa.gov/shin/content// SMA12-4682/SMA12-4682.pdf

Buprenorphine, Methadone, and

Naltrexone

 These medications have shown effectiveness and have demonstrated benefits to individuals

buprenorphine, or injectable naltrexone. There is no one size fits all."

■ Some patients prefer methadone to

and society.

SLIDE #14: NALTREXONE

- Naltrexone is an opioid antagonist.
- It's another option of MAT that can be prescribed in primary care settings.
- Oral tablets of naltrexone were not readily used due to adherence issues. The FDA-approved injectable form of naltrexone (taken monthly), however, helps address this issue.
- Medical personnel with prescribing powers may prescribe naltrexone.
- SAMHSA has released an advisory outlining more specifics on the drug: http://store.samhsa.gov/shin/content//SMA12-4682/SMA12-4682. pdf.
- Naltrexone was *not* investigated in the SPNS study.



SLIDE #15: BUPRENORPHINE, METHADONE, AND NALTREXONE

- Methadone has been used to treat opioid addiction for decades, whereas buprenorphine was approved in 2002.
- Thus, more information is available on long-term safety and treatment outcomes with methadone versus buprenorphine.
- Methadone can be administered only through a certified and accredited OTP (a methadone clinic), where certain restrictions apply.
- In contrast, buprenorphine and naltrexone can be administered within primary care settings.
- Methadone is a full opioid agonist, whereas buprenorphine is a partial opioid agonist and naltrexone is an opioid antagonist.
- When buprenorphine is coformulated with naloxone (Suboxone) it has a low abuse profile, since naloxone can precipitate withdrawal when it is injected.
- Methadone is taken once daily, whereas buprenorphine may be taken once daily or three times weekly, on alternate days. Naltrexone oral tablets are taken daily whereas the injectable form is taken monthly.
- Naltrexone has higher pharmacy costs associated with it than does buprenorphine and methadone, which may be a deterrent for some patients.
- Buprenorphine has fewer drug-drug interactions with antiretrovirals than methadone.
- Methadone may be more effective than buprenorphine when patients require a more structured setting or would respond better to a full opioid agonist.
- It is important for patients to have options for MAT.













MODULE 5: Key Findings From the SPNS Buprenorphine Initiative

SUMMARY

This module investigates the SPNS Buprenorphine Initiative, the reasons behind its funding, and its overall findings across grantee sites.

MATERIALS NEEDED

 A computer and compatible LCD projector to play the PowerPoint presentation.



Background on the SPNS Initiative

- SPNS Initiative overview
 - · 5 years
 - · Ryan White HIV/AIDS Program sites
 - · 10 grantees
 - Best practices compiled into monograph, training manual, and online wiki.

(Monograph can be accessed at: www.hab.hrsa.gov/abouthab/files/hab_spns_buprenorphine_monograph.pdf.)

SLIDE #16: BACKGROUND ON THE SPNS INITIATIVE

- To study opioid treatment among the HIV-infected population, HRSA's HIV/AIDS Bureau funded a SPNS project.
- The project was called "An Evaluation of Innovative Methods for Integrating Buprenorphine Opioid Abuse Treatment in HIV Primary Care."
- It was a 5-year, national, multisite study involving 10 HIV primary care sites and more than 300 HIV-positive opioid-addicted patients.
- This represented the largest study of buprenorphine implementation and outcomes among opioid-addicted people living with HIV/AIDS in the United States.



SLIDE #17: WHY INTEGRATE BUPRENORPHINE INTO HIV PRIMARY CARE SITES?

Why Integrate Buprenorphine into HIV Primary Care Sites?

- Increased collaboration
- Improved communication
- Increased comprehensive care offerings
- Intersection of opioid use and HIV incidence and transmission
- Improved retention among disenfranchised populations.
- Integrated medical care and treatment for opioid dependence dismantles a significant barrier for disenfranchised patient populations.
- Integrated treatment models foster better communication and collaboration among HIV care providers, psychiatrists, and specialists in addiction medicine and treatment.
- Data from randomized, controlled trials suggest that integrating services at a single site improves both medical and substance abuse treatment outcomes.



SLIDE #18: KEY FINDINGS FROM INITIATIVE

Patients and providers were overwhelmingly satisfied with the treatment and its results. The Buprenorphine Initiative:

- Allowed for integration—rather than fragmentation—of services, resulting in improved retention in care.
- Facilitated initiation of antiretroviral therapy (ART) among patients not previously on treatment.
- Improved drug and HIV treatment outcomes, particularly among those not previously on ART.
- Increased CD4 counts among patients who initiated ART during this project.
- Resulted in decreased use of heroin and other opioids.
- Increased social stability.
- Decreased HIV transmission risk behaviors.
- Decreased stigma associated with substance abuse treatment.
- Was associated with improved mental and physical healthrelated quality of life.

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Key Findings from Initiative

- Providers and patients were overwhelmingly satisfied with results.
- Improved HIV medication adherence and viral load
- Reduced risk behaviors.
- Improved overall health outcomes.
- Patients felt incredibly lucid and stated improved quality of life and social functioning.



SLIDE #19: DEBUNKING MYTHS: PROVIDER AND PATIENT FEARS WERE UNFOUNDED

Debunking Myths: Patients' and Providers' Fears Were Unfounded

- Patients were increasingly receptive to buprenorphine offerings, especially once they were better educated about withdrawal state, level of cravings, and other information about buprenorphine administration and continuation.
- Providers found administration of buprenorphine easier than expected.
- Medical and support staff found integration of substance abuse treatment into their clinics beneficial rather than burdensome.

Case Example

clinic-based buprenorphine and individual counseling

or to case management with referral to drug treatment,

Significantly more likely to participate in treatment for opioid dependence (74 percent versus 41 percent),

More likely to attend their HIV primary care visits

than were people in the group referred to drug

 In one grantee site study among 93 HIV-positive, opioid-dependent patients who were assigned either to

people in the buprenorphine group were:

Less likely to use opioids and cocaine,

treatment.

- HIV clinicians at the majority of SPNS Buprenorphine Initiative sites had limited or no prior experience administering Suboxone to opioid-dependent patients before project initiation.
- Physicians across sites overwhelmingly found Suboxone treatment to be a good service to provide to their patients. They reported that administering buprenorphine was easier than they expected it would be, and, in fact, no harder than anything else they were overseeing within their clinics.
- When patients started buprenorphine, some were initially worried about being in a withdrawal state but after education and administration found the results to be achievable and effective.



SLIDE #20: CASE EXAMPLE

- SPNS research supports MAT and integration of buprenorphine into HIV primary care settings.
- Results from the SPNS initiative encourage replication at other sites.
- One grantee site study compared outcomes among 93 HIVpositive, opioid-addicted patients assigned to clinic-based buprenorphine and individual counseling or to case management with referral to drug treatment.
 - o People in the buprenorphine group were significantly more likely to participate in treatment for opioid addiction (74 percent versus 41 percent), less likely to use opioids and cocaine, and more likely to attend their HIV primary care visits than people in the group receiving referral to drug treatment.



Testimonials

- The University of California, San Francisco, Positive Health Program at San Francisco General Hospital SPNS grantee "found that the buprenorphine induction process was feasible and went well. They induced patients with many years of heroin use, high-dose heroin use, methadone use, and cocaine use."
- One patient participant stated, "It couldn't be better, and here's the reason why: if it's something with either one of them [drug use or HIV], right, by your medical people and your program [being] in the same building, I can always go to my doctor and find out what combination, how this is working with this and that."

References: HIV/AIDS Bureau, Special Projects of National Significance Program, Integrating Ingremorphine Iburapy into HIV prinsing care settings, Rockville, MID: U.S. Oppartment of Health and Human Services; 2011. Available at sww.hab.has.go.y/abuthabs/files/hab.spm. Jupercomphine.monograph.pdf. Egan JE, Netherland J, Gass J, Patient perspectives on buprenorphine/naloxone treatment in the context of HIV care, IAIDS. 2011;56(9):pdf) 45(2):

SLIDE #21: TESTIMONIALS

 Providers and patients alike have reported positive outcomes with and experiences initiating opioid-addiction treatment.













MODULE 6: Prescribing Buprenorphine: How to Get Started

SUMMARY

Module 6 focuses on the major steps required to get going in buprenorphine certification and administration.

MATERIALS NEEDED

• A computer and compatible LCD projector to play the PowerPoint presentation.



Prescribing Buprenorphine: How to Get Started

図 DATA 2000

- · Landmark legislation
- Enabled qualified physicians to prescribe FDAapproved Schedule III, IV, and V opioid medications.
- Buprenorphine is a Schedule III narcotic.

(To read the full law, visit www.buprenorphine.samhsa.gov/fulllaw.html)

Prescribing Buprenorphine

 If approved, receive notice and DEA registration number
 First year=maximum treatment of 30 patients per

authorized physician. After first year, may apply

Who can prescribe buprenorphine?

Notify SAMHSA for waiver to treat

· Qualifying physicians

What training is necessary?

Required board specialty, or8 hours of approved training

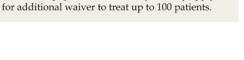
SLIDE #22: DATA 2000

- The Drug Addiction Treatment Act of 2000 (DATA 2000)
 - This enabled *qualifying physicians* outside of opioid treatment programs (i.e., methadone clinics) to prescribe and/or dispense Schedule III, IV, and V opioid medications approved by the FDA.
 - Buprenorphine, as a Schedule III narcotic, could now be prescribed in office-based settings by qualifying physicians.
 - Currently, buprenorphine/naloxone is available as a tablet (Suboxone) or film. Both are made to be dissolved under the tongue.
 Buprenorphine is also available as a tablet in generic form.



SLIDE #23: PRESCRIBING BUPRENORPHINE

- Who can prescribe buprenorphine? Physicians with:
 - Subspecialty board certification from the American Board of Medical Specialties
 - Addiction certification from the American Society of Addiction Medicine
 - Subspeciality board certification from the American Osteopathic Association
 - Completion of 8 hours of approved training from a certifying board.
- Physicians must submit a waiver and notify SAMHSA of intent to dispense or prescribe opioid treatment.
- Typically, 45 days after submitting waiver request, physicians receive an identification (ID) number and the Drug Enforcement Administration (DEA) registration number (to be included on all prescriptions). For the first year, authorized physicians can treat up to 30 patients. After 1 year, they can submit another request, this time to treat up to 100 patients.

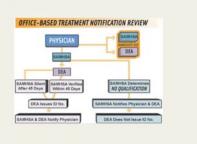




SLIDE #24: DIAGRAM OF THE WAIVER PROCESS

 Here you see a diagram from SAMHSA of the waiver process and its various steps.

Diagram of the Waiver Process





Setting the Stage for MAT

- Communication is key.
- Secure buy-in up front from clinic and local partners as well as organizations with vested interest in patient population.
- Identifying and addressing structural barriers.
- □ Counseling: mental health and support groups
- Patient and provider education
- Evaluation component

SLIDE #25: SETTING THE STAGE FOR MAT

- Prepare program- and clinic-wide communication to best facilitate administration of buprenorphine-based MAT.
- Establish and maintain a system to allow clear communication across program staff and volunteers, patients, residential and outpatient addiction treatment and mental health-care providers, and other stakeholders, such as city and State health departments and correctional facilities, so they are aware of policies and procedures.
- Address structural issues: Create appointment slots, assign exam rooms, and add more clinic space if needed.
- Work with pharmacies to ensure and monitor the supply of buprenorphine, and identify resources to help with reimbursement.
- Offer clear, patient-centered buprenorphine education, and describe program expectations.
- Prepare patients for induction. (One program developed "kick packs" with medications to alleviate withdrawal symptoms.)
- Establish and maintain linkages with mental health-care providers in the community to ensure that individual and group counseling is available to patients, both onsite and offsite.
- Facilitate support groups.
- Provide additional resources to all staff for support, mentoring, and training, as well as regular program updates.
- Develop a process for program monitoring and evaluation.



SLIDE #26: STAFFING

- Although a team approach is key to successful implementation and administration of MAT, SPNS initiative grantees have identified a key staffing configuration: a dyad, involving both a prescribing physician and an accessible service provider, who is often called the "glue person" or buprenorphine coordinator.
- The glue person may be a nurse, pharmacist, or nonclinician who
 is closely supervised by medical and mental health care providers. The glue person has experience with, and training in, providing services to people with substance use disorders, and receives
 additional training in addiction medicine, pain management, and
 other related areas.
- The glue person facilitates implementation of MAT in HIV primary care settings by serving as the point of contact for patients, providers, and issues related to buprenorphine.
- The glue person arranges or provides counseling, case management, outreach, and all other ancillary services.

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Staffing

- Team approach and buy-in vital.
- SPNS grantee sites relied primarily on dyad model:
 - Prescribing physician and
 - Clinical coordinator (i.e.,"glue person")
- See figure for possible glue person responsibilities.





SLIDE #27: THREE PHASES OF BUPRENORPHINE TREATMENT

Three Phases of Buprenorphine Treatment

- 1. Induction
- Stabilization
- Maintenance

- The three phases of buprenorphine treatment are induction, maintenance, and stabilization.
- Phases are completed in that order, so no one phase can begin until the previous phase is complete.



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■ Induction is done under medical supervision.

Induction

- Patient must be in early withdrawal to undergo induction.
 - This is because buprenorphine causes acute withdrawal in patients with opioids in their bloodstream.

SLIDE # 28: INDUCTION

- Induction is the term for buprenorphine initiation, which is done
 under medical supervision in a doctor's office. Usually, the first
 induction visit lasts 2 to 4 hours; the induction phase usually lasts
 7 days.
- The goal of induction is to identify the lowest possible buprenorphine dose that will allow patients to reduce or stop their opioid use without experiencing withdrawal symptoms or uncontrollable drug cravings.
- Patients must be in the early stages of withdrawal to undergo induction, because buprenorphine causes acute withdrawal in people who have opioids in their bloodstream. Therefore, use of opioids must be avoided for 12 to 24 hours before induction.
- The Clinical Opioid Withdrawal Scale (COWS) can be used to assess withdrawal symptoms before initiating buprenorphine.



The COWS Scale* is included in the training manual that complements this curriculum. It can also be accessed here: www.careacttarget.org/topics/buprenorphine.asp.

• If patients are experiencing withdrawal symptoms on day 2 or day 3, buprenorphine dose adjustments may be necessary.

^{*}Note: This publication is a non-Federal resource and is included in order to provide additional information. The views and content in these resources have not been formally approved by the U.S. Department of Health and Human Services (HHS) or the Health Resources and Services Administration (HRSA). Listing these resources is not an endorsement by HHS or HRSA.



SLIDE #29: STABILIZATION

- Stabilization
- During stabilization:
 - · Reduce patient opioid use.
 - · Adjust buprenorphine dosage as necessary.
 - · Reduce withdrawal symptoms.
 - · Monitor patients.

- During the stabilization phase, which lasts 1 to 2 months, patients should be seen on a weekly basis in case further dose adjustments are necessary. When people receive the proper dose of buprenorphine, they will not experience withdrawal symptoms or strong drug cravings.
- Usually, people will reduce or stop their drug use during stabilization; if opioid use continues, consider dose adjustment.



SLIDE #30: MAINTENANCE

- Once patients are medically stable, they may remain on buprenorphine indefinitely; there is no set length of time that patients remain in this phase. The SPNS initiative lasted 5 years.
- Counseling is an important part of maintenance, since people are able to address psychosocial issues.
- If patients wish to discontinue buprenorphine, dosing should be gradually tapered unless there is a reason for patients to stop buprenorphine more rapidly, such as relocation or travel to a country where it is not available, upcoming incarceration, or conditions of employment.

Maintenance

- There is no "one size fits all" length of time for the maintenance phase.
- Counseling is very important during this phase.
- Patients discontinuing buprenorphine must be tapered off gradually.













MODULE 7: Buprenorphine: Know the Facts

SUMMARY

Module 7 is a factsheet that serves as a quick reference guide to providers and staff. It outlines some of the most frequently asked questions and their corresponding answers.

MATERIALS NEEDED

• A printer or copier to reproduce the handout.



The factsheet begins on the following page for ease of printing and copying.

BUPRENORPHINE: KNOW THE FACTS

HIV and Injection Drug Use

The overlap of HIV and injection drug use, often of opioids, is well known. Since the beginning of the epidemic, the U.S. Centers for Disease Control and Prevention (CDC) estimates that more than one-third of all AIDS cases have been directly or indirectly linked to IDU. More recently, addiction to prescription opioids has become widespread. For people with HIV, untreated opioid addiction is associated with poor HIV treatment outcomes and a host of other medical, psychosocial, and legal consequences. The good news is that HIV primary care providers can successfully treat opioid-addicted patients.

1. What is addiction?

According to the American Society of Addiction Medicine (ASAM), "Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. . . . Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death."*

2. What are opioids?

Opioids are illicit or prescribed drugs, such as heroin, morphine, OxyContin, and methadone that bind to opioid receptors located in the nervous system (especially the brain and digestive tract). Opioids are often used to manage pain, since they reduce both perception of and reaction to pain; they also induce euphoria (as well as nausea, vomiting, constipation, sedation, respiratory depression, and overdose).

3. What do opioids do?

When opioids attach to receptors in the brain, they activate nerve cells and trigger the release of abnormal amounts of dopamine, a neurotransmitter—or messenger—associated with learning, pleasure, and reward. Over time, opioid use changes brain chemistry, leading people to try to restore dopamine levels by continuing drug use.

4. How do you treat opioid addiction?

The preferred mode of treatment is MAT, which combines pharmacotherapy with methadone, buprenorphine, or naltrexone, individualized counseling, and behavioral therapy.

5. What is Suboxone?

Suboxone is a coformulation of two medications, buprenorphine and naloxone. It comes as tablets or film and is administered sublingually (under the tongue).

Buprenorphine works in two ways. First, it displaces other opioids from the receptors they occupy in the brain. Then, it binds tightly to these same receptors, so that other opioids cannot occupy them. People who take buprenorphine do not experience withdrawal symptoms or strong cravings for other opioids.

Naloxone reverses opioid overdose by binding to and blocking opioid receptors. Sublingual naloxone is poorly absorbed, whereas injecting naloxone causes the immediate onset of withdrawal symptoms (also known as "precipitated withdrawal"). Naloxone was added to buprenorphine to discourage injection and diversion.

6. What are the differences between buprenorphine, methadone, and naltrexone?

Buprenorphine is a partial opioid agonist. Effects from a partial opioid agonist are weaker than those produced by a full opioid agonist, because they do not fully activate the brain's opioid receptors. Buprenorphine also blocks the effects of other opioids. Buprenorphine is available in either mono or combination (with naloxone) form. Buprenorphine monotherapy, however, is available only in

^{*}American Society of Addiction Medicine. *Public policy state-ment: definition of addiction.* August 15, 2011. Available at: www.asam.org/docs/publicy-policy-statements/1definition_of_addiction_long_4-11.pdf?sfvrsn=2#search=%22addiction%20 is%20a%20primary%20%20chronic%20disease%20of%20 brain%20r%22.

generic form. (Subutex, the brand version, was discontinued in September 2011.)

Naloxone is an opioid blocker but is not very effective unless it is injected. It is added to buprenorphine to discourage injection. In contrast, methadone is a full opioid agonist. Methadone blocks other opioids while producing the full effects of opioids.

Naltrexone is an opioid antagonist. It is not a controlled substance like methadone and buprenorphine and thus does not have abuse potential. It does not activate the opioid receptors in any way; rather, it blocks opioids from activating them. Injectable naltrexone is available for monthly injection rather than daily doses (like buprenorphine and methadone), however, this form of naltrexone is more costly. Patients need to have refrained from opioid use for 7–10 days, longer than is required for buprenorphine or methadone initiation; as such, naltrexone may be best for those patients with shorter or less severe abuse histories.

Buprenorphine can be administered as part of HIV primary care by qualified physicians, whereas methadone is available through certified, accredited OTPs, which are highly regulated and structured entities. Naltrexone can be prescribed by any medical personnel with prescribing privileges.

7. How do I qualify to become a buprenorphine prescriber?

The Drug Addiction Treatment Act of 2000 (DATA 2000) made it possible for qualified physicians to obtain a waiver allowing them to prescribe and dispense medications that the FDA has approved for treatment of opioid addiction; buprenorphine is approved for this indication.

Nurse practitioners and physician assistants cannot prescribe buprenorphine. To qualify, doctors who do not already have credentials in addiction medicine need to complete 8 hours of training, demonstrate the capacity to refer their patients for counseling and other non-pharmacologic therapies, and apply for a special DEA number. Initially, qualified prescribers can treat 30 patients; after a year they can submit notification of need and intent to treat 100 patients.

8. How safe is Buprenorphine?

Buprenorphine has a "ceiling effect"; after a certain threshold, increasing the dose does not increase the effects, resulting in a lower risk of overdose. However, the risk of overdose is greatly increased when buprenorphine is combined with alcohol, benzodiazepines, or other opioids.

Common side effects include depression, constipation, dizziness, drowsiness, headache, muscle aches, nausea, sweating, and vomiting.

9. Can buprenorphine be used with HIV drugs?

Buprenorphine may share metabolic pathways with some HIV drugs and thus, monitoring and dose reduction are not always necessary. (Also see drug chart in training manual for buprenorphine with specific HIV medications.)

10. How quickly does buprenorphine work?

Three stages are involved. Patients must be in mild withdrawal before they start buprenorphine, a process called *induction*, which can be done in a doctor's office over a 2- to 4-hour interval. The goal of induction is to identify a dose of buprenorphine that will stop withdrawal symptoms and block drug cravings.

After approximately a week, *stabilization* begins; over 1 to 2 months, patients are seen on a weekly basis to assess the need for buprenorphine dose adjustments.

Once patients are medically and psychosocially stable, the *maintenance* phase begins. Maintenance can last indefinitely, depending on the goals of individual patients, or buprenorphine can be very gradually tapered in patients who wish to stop.













MODULE 8: Role Playing

SUMMARY

Module 8 is a group activity that allows clinic staff to practice patient—provider role playing with one another. This offers an opportunity for the instructor to identify any communication or cultural competency issues that may need addressing. It also allows clinic staff to familiarize themselves with talking about the issues of addiction and treatment prior to opioid-addiction treatment rollout on a larger scale.

MATERIALS NEEDED

- Small strips of paper
- Writing utensil
- Clock or watch to time activity.

ACTIVITY

Have participants count off as "1" or "2." Pair a 1 and a 2. Assign the 1's as patients and the 2's as providers.



If participants wish to switch roles with their partner, allow them to do so. The important part is that there are equal numbers of patients and providers and that each group consists of one of each. In the event that there is an odd number of participants, a provider can perform the activity with two patients; otherwise, it should be a 1-to-1 ratio.

SCENARIOS



Write down one of the following scenarios on each strip of paper and fold up so participants can't read them.

- 1. Patient has been using opioids and is afraid that he/she will be cut off; instead, provider offers additional support, counseling, buprenorphine dose increase, and so on.
- 2. Although the patient wants to start buprenorphine, he/she is afraid of undergoing withdrawal during induction; provider walks him/her through the process and recommends (if available at clinic site) working with a peer who has been through induction.
- 3. The regular clinic physician is on vacation; the substitute is not familiar with buprenorphine and the patient needs to explain why it is working for him/her when they go to pick up a refill. *Note: Refill must be written by a waivered physician.*
- 4. Patient is sick of addiction and wants to stop opioid use. Provider explains options.
- Patient comes in for induction but appears to be high, rather than in withdrawal. Provider must address the situation and appropriate steps to be taken.
- 6. Patient is a medical provider from a local hospital.
- 7. Patient wants to quit using opioids but is afraid of the stigma of methadone, unaware that he/she has an additional option.

Each group role-plays one of these activities. If working with a large group, each activity will take place concurrently for approximately 10 minutes. Then, the facilitator ends the activity and goes around the room group by group asking how the dyad worked and what it felt like to be the patient or the provider. (If the group is small then the role play can be done in front of the group if participants are comfortable with this format. Similar discussion would follow.)











MODULE 9: Patient Education

SUMMARY

Miriam Hospital Immunology Center, a SPNS grantee and Brown University teaching affiliate, created a set of PowerPoint slides for the purpose of educating patients about opioid addiction and opioid addiction treatment. These slides are included as slides #31-54.*

MATERIALS NEEDED

- A computer and compatible LCD monitor to play PowerPoint slides
- Printer.

ACTIVITY

1. Give a brief introduction. Explain what motivated the clinic to consider integrating opioid-addiction treatment into your setting.



It is recommended that the dyad team of prescribing physician and care coordinator ("glue person") participate in the patient education portion. This will help interested patients have both their clinical and social service-related questions answered, put a face to a name, and establish or strengthen their relationship with staff prior to any actual buprenorphine induction.

^{*}Note: In some instances, edits have been made to original slides for consistency in style and language.

- 2. If possible or available, ask a peer who has undergone buprenorphine treatment to briefly discuss his/her experience and identify any initial worries that were ultimately unfounded. If no peers are available, feel free to pull some testimonial quotes from earlier sections of this curriculum and earlier PowerPoint presentations.
- Let patients know there will be a question and answer session at the end of the presentation. Walk through each slide one by one. (The slides are designed to be straightforward and intuitive.)
- 4. Give specific directions or a flyer outlining how patients can follow up to enroll/who to talk to.
- 5. Provide printouts of useful information targeting consumers and their health literacy levels. You can create a printout customized to your own clinic or consider printing out some or all of the following helpful brochures and factsheets:**
 - "Bupe": A Drug Used to Treat Addiction to Heroin and Prescription Pain Pills: www.health.ny.gov/diseases/aids/harm_reduction/buprenorphine/ docs/consumer_fact_sheet.pdf
 - The Facts about Buprenorphine for Treatment of Opioid Addiction: www. kap.samhsa.gov/products/brochures/pdfs/buprenorphine_facts.pdf
 - Buprenorphine: A New Drug for Treatment Heroin Addiction: www. health.ny.gov/publications/9555/

These documents allow patients to have resources at their disposal that they can review at their leisure.

^{*}Note: These publications are non-Federal resources and are included in order to provide additional information to consumers. The views and content in these resources have not been formally approved by the U.S. Department of Health and Human Services (HHS) or the Health Resources and Services Administration (HRSA). Listing these resources is not an endorsement by HHS or HRSA.

SLIDES 31-36



Slide 31

What do Opioids do? (cont.)

Any person who uses opioids regularly may become physically dependent on them.

This means that you need more drug over time to get the same effect (tolerance) and that you have withdrawal symptoms if you stop using the drug.

Slide 33

From Physical Dependence to Addiction

When you endure the negative consequences of ongoing drug use but don't seek change...

When you try to stop using drugs but cannot... it is likely that you are living with addiction.

What do Opioids do?

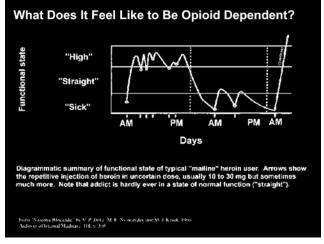
- Opioids may be taken by mouth, through the skin (patch), or by a needle into the fat, muscle, or vein.
- They attach to special opioid receptors in the brain where they help to relieve pain.
- Some opioids cause euphoria ("high") and sleepiness or, if taken in large amounts, unconsciousness that may progress to death (overdose).
- Other side effects may include itching, headache, nausea, constipation, confusion, slow pulse, and slow breathing.
- Some opioids last a few hours and some more than a day.

Slide 32

From Physical Dependence to Addiction

- When you use more drug than prescribed/needed to control your pain...
- When you begin to spend more and more of your time seeking your drug of choice...
- When you consistently choose drug use over social activities and responsibilities...

Slide 34

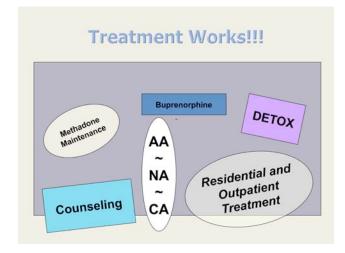


Slide 35 Slide 36

SLIDES 37–42

Addiction is a Brain Disease Over time, nerve cells in the brain learn to crave opioids. When opioids are not present, the opioid receptors send pain signals to the rest of the brain (withdrawal). This is a physical condition, not caused by a lack of willpower or morals and not cured by good advice. Addiction is a chronic and treatable disease, like diabetes and heart disease.

Slide 37 Slide 38



Slide 39 Slide 40



Methadone Maintenance

Methadone satisfies the brain's opioid receptors without causing a "high." It acts for up to 48 hours. It has saved countless lives and may be taken indefinitely. Each person has a unique methadone requirement and their dose is calculated to their needs. Federal laws require that only certified clinics dispense methadone and only according to strict standards.

Detox

"You are not alone."

Over 800,000 people in the USA

are dependent on heroin

or other opioids.

Medical detoxification from opioids is usually a 3 to 7 day process that helps you manage withdrawal by either giving you small doses of opioids (methadone, buprenorphine) or by treating your symptoms with non-opioid medications.

Detox is important but is only the first step toward successful treatment and recovery.

Already on Methadone?

- Although not encouraged, some people on methadone maintenance may look for alternative treatment.
- For someone on low doses of methadone (less than 40 mg), buprenorphine may be an optional treatment.
- Abstinence-based therapy is also an option.
- Many who stay on methadone manage their opioid addiction and lead healthy and productive lives.

Slide 41 Slide 42

SLIDES 43-48

Buprenorphine

Buprenorphine blocks other opioids and prevents physical craving for those opioids. Many people describe feeling "normal" or "energized" when they take it

Buprenorphine tablets and film are absorbed only by completely dissolving them under the tongue. If swallowed, they will not help craving or withdrawal.

Slide 43

More About Buprenorphine

- Buprenorphine may be prescribed only by a specially trained physician.
- It may be taken daily in the privacy of your home or wherever you choose.
- Although buprenorphine has some pain-relieving qualities, people with addiction and pain may or may not be able to get good pain management while on buprenorphine. It is not currently approved by the FDA for treatment of pain.

Slide 45

For How Long Can I Take It?

How long will my addiction last?

- •Buprenorphine may be lifelong therapy or used for a shorter period. (SPNS initiatives were for 5 years.)
- Like other opioids, it creates dependence and, if stopped suddenly, will cause withdrawal symptoms.
- •Individualized tapering to lower doses will limit or eliminate withdrawal symptoms.
- Linkage to recovery-based programs decreases the likelihood of relapse.

Suboxone is a Two-Drug Combo

<u>Buprenorphine</u>: an opioid that acts to fill up the brain's opioid receptors without causing sleepiness or "high" feelings. It has a low risk of overdose.

and...

Naloxone, a drug that is not absorbed orally but helps persuade people not to inject Suboxone in the vein, as it causes instant withdrawal.

This dual therapy is most common. Buprenorphine monotherapy is available, however, only in generic form. (*Subutex*, the brand version, was discontinued in September 2011.)

Slide 44

More About Buprenorphine (cont.)

- Buprenorphine is an opioid that blocks craving as well as the action of other opioids in the brain's mu receptors.
- Someone taking an adequate dosage of buprenorphine would not likely "get high" from heroin, for example.
- People tend to function at a higher level when they are not craving and chasing opioids.
- WARNING: Concurrent use of buprenorphine with alcohol, benzodiazepines (Valium-like drugs), or large amounts of other opioids could cause overdose and death.

Slide 46

ABSTINENCE AND RECOVERY

Viva la différence!

Slide 47 Slide 48

SLIDES 49-54

With Any Opioid Replacement...

Stopping the physical craving is just the beginning.

Changing the thinking and behaviors associated with substance use is the process of recovery.

Slide 49

Counseling works well with other recovery activities.

Sometimes it is the only way to learn to cope with the pain, blame, and shame linked to addiction. It is a safe and tested way to treat depression or to face abuse that may have occurred in your past.

Counseling and Talk Therapy

Most importantly, you will have a supportive ally in your recovery from drug addiction.

Slide 51

The Best Teachers on the Road to Recovery...

...may be people who have been through similar experiences and challenges, like the people who gather at NA meetings.

Treatment Paths

 Intensive Outpatient Treatment Residential Treatment

Common elements may include:

- Focus on self esteem, coping skills, 12-Step model
- •Group and individual work
- Relapse prevention education
- · Family support and education
- · Development of strong aftercare program

Self-help Groups: Proven Effective

Groups like NA and AA are welcoming places for people on the journey to recovery. There are also Internet-based groups, faith-based groups, and non-faith-based groups.



 Recovery is hard work and, like addiction, lifelong. Please give yourself a chance to get extra support.

Slide 52

Slide 50

Referrals

www.naabt.org

Consumer and professional education about buprenorphine, step-by-step linkage to treating physicians, chat rooms and advocacy.

www.samhsa.gov

Government site that lists certified doctors in your area and information about buprenorphine treatment.

www.Suboxone.com

The drug manufacturer's site will also help you link to a treating doctor.

Slide 53 Slide 54













MODULE 10: Online Resources

This module identifies online resources that are particularly helpful and may offer further assistance into particular areas of opioid treatment administration.

Integrated Buprenorphine Therapy into HIV Primary Care Settings and Appendices

www.hab.hrsa.gov/abouthab/files/hab_spns_ buprenorphine_monograph.pdf www.careacttarget.org/topics/buprenorphine.asp

Medication-Assisted Addiction Treatment Newsletter www.hab.hrsa.gov/newspublications/careactionnewsletter/ may2011.pdf

Substance Abuse Suboxone Treatment Program www.careacttarget.org/2010_rw_grantee_meeting/papers/F-15.pdf

Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction: A Treatment Improvement Protocol, TIP 40

http://buprenorphine.samhsa.gov/Bup_Guidelines.pdf

Buprenorphine: A Guide for Nurses, TAP 30, Technical Assistance Publication Series

http://buprenorphine.samhsa.gov/TAP_30_Certified.pdf

Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs: Inservice Training, Based on A Treatment Improvement Protocol, TIP 43 http://buprenorphine.samhsa.gov/tip43_curriculum.pdf www.kap.samhsa.gov/products/tools/keys/pdfs/KK_40.pdf

Patient Assistance Program www.patientassistance.com/profile/reckittbenckiser-314/

Buprenorphine Physician & Treatment Program Locator http://buprenorphine.samhsa.gov/bwns_locator/

State Substance Abuse Treatment Facility Locator http://findtreatment.samhsa.gov/

Treatment Improvement Protocols www.ncbi.nlm.nih.gov/bookshelf/ br.fcgi?book=hssamhsatip;

Knowledge Application Program www.kap.samhsa.gov

Physician Clinical Support System www.pcssmentor.org/ (primary care) www.pcssb.org (buprenorphine)

Obtaining a Buprenorphine Waiver http://buprenorphine.samhsa.gov/waiver_qualifications. html

National Alliance of Advocates for Buprenorphine Treatment www.naabt.org/

Medication-Assisted Treatment for Substance Use Disorders http://dpt2.samhsa.gov/treatment/directory.aspx http://dpt.samhsa.gov/index.aspx

Screening Tools
www.hivguidelines.org/resource-materials/screening-tools/
substance-use-screening-tools/
www.drugabuse.gov/nidamed/screening/

Opioids Glossary http://opioids.com/glossary/index.html

Buprenorphine Treatment of Opioid Addiction: A Counselor's Guide www.danya.com/dlc/courseprofile.asp?cid=7

Frequently Asked Questions
http://buprenorphine.samhsa.gov/faq.html
www.fda.gov/downloads/Drugs/DrugSafety/Post
marketDrugSafetyInformationforPatientsand
Providers/UCM191532.pdf

American Society of Addiction Medicine www.asam.org

Association for Addiction Professionals www.naadac.org

National Institute on Drug Abuse www.nida.nih.gov

Reckitt Benckiser (manufacturer) www.suboxone.com

Buprenorphine: A Guide for Nurses, TAP 30, Technical Assistance Publication Series http://buprenorphine.samhsa.gov/TAP_30_Certified.pdf

California Society of Addiction Medicine www.csam-asam.org

American Psychiatric Association www.psych.org

Common Substance Use Screening Tools www.hivguidelines.org/resource-materials/screening-tools/ substance-use-screening-tools/ www.drugabuse.gov/nidamed/screening

Buprenorphine Treatment: A Training for Multidisciplinary Addiction Professionals (Blending Team Product) www.ctndisseminationlibrary.org/display/85.htm

Buprenorphine Treatment for Young Adults
(Blending Team Product)
http://drugabuse.gov/blending/buprenorphineYoung
Adults.html

New York State Office of Alcoholism and Substance Abuse Services: Buprenorphine Information and Resources www.oasas.ny.gov/AdMed/meds/bupindex.cfm

SAMHSA: Buprenorphine, Additional Resources http://buprenorphine.samhsa.gov/otherlinks.html

Consumer Fact Sheet and Brochures
www.health.ny.gov/diseases/aids/harm_reduction/
buprenorphine/docs/consumer_fact_sheet.pdf
www.kap.samhsa.gov/products/brochures/pdfs/
buprenorphine_facts.pdf
www.health.ny.gov/publications/9555/

American Academy of Addiction Psychiatry www.aaap.org

American Osteopathic Association www.aoa-net.org

International Center for Advancement of Addiction Treatment http://opiateaddictionrx.info/

The Chronic Care Model
www.improvingchroniccare.org/index.php?p=The_
Chronic_Care_Model&s=2

Information for Pharmacists
www.fda.gov/downloads/Drugs/DrugSafety/Post
marketDrugSafetyInformationforPatientsand
Providers/UCM191533.pdf

International Antiviral Society-USA, Presentation #54 www.iasusa.org/cow/cow-instructions.php?cowid=156

Buprenorphine and Primary HIV Care: Report of a Forum for Collaborative HIV Research Workshop www.pcssbuprenorphine.org/pcss/documents2/Training/HIV%20Forum%20Report.pdf

Advisory: An Introduction on Extended-Release Injectable Naltrexone for the Treatment of People With Opioid Dependence http://store.samhsa.gov/product/SMA12-4682