Module III

Buprenorphine 101

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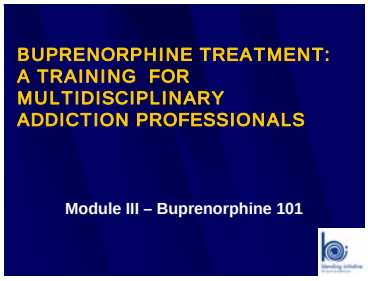
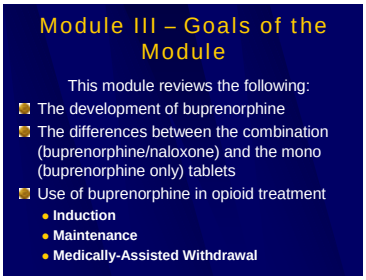
This module is designed to give the trainees an overview of the development and pharmacology of buprenorphine. It then provides, in summary form, information about treatment using the drug: induction, maintenance, and medically assisted withdrawal. The primary focus of the treatment section is to provide an overview of the medical aspects of treatment and the role of non-medical practitioners at each of these phases of treatment. Specific information on counseling patients who are taking buprenorphine will be provided in Module VI.

To avoid training participants perceiving the trainer(s) as "selling" buprenorphine, be sure to frame the availability of buprenorphine as an additional option (not just a replacement for/alternative to methadone). The availability of buprenorphine for the treatment of opioid addiction is allowing for an expansion of opioid treatment. The training is not, in any way, meant to advocate one treatment over another; instead, it is an addition to the repertoire of medications available for the treatment of opioid addiction.

	**Slide 1: Title Slide** Now it's time to talk specifically about buprenorphine. What is this medication and how does it work? That is the question that we will answer in this module.
	**Slide 2: Module III – Goals of the Module** Now that we have reviewed the basics of opioid addiction and treatment, we will now look specifically at buprenorphine and discuss how is was developed, compare the different formulations of the medication available for the treatment of opioid addiction and examine the ways it is used in the various phases of opioid treatment.

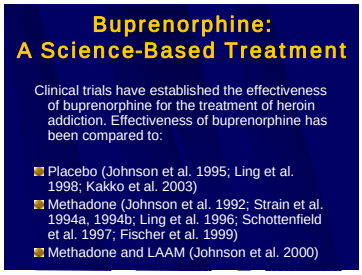
Slide 3: Development of Tablet Formulations for Buprenorphine

Subutex® = a sublingual tablet containing buprenorphine hydrochloride only

Suboxone® = a sublingual tablet containing both buprenorphine hydrochloride and naloxone hydrochloride in a 4:1 ratio

Suboxone® is the focus of U.S. marketing efforts, even though both formulations are available in the U.S.

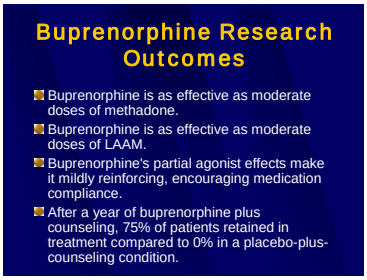
These medications have a tremendous amount of research behind them to show that they are both safe and effective in the treatment of opioid addiction.



Slide 4: Buprenorphine: A Science-Based Treatment

In the development of the medication, the effectiveness of buprenorphine has been compared to that of other medications that are currently available. These studies have shown that buprenorphine treatment:

- Is more effective than placebo; and
- Has similar effectiveness to moderate doses of methadone and LAAM.



Slide 5: Buprenorphine Research Outcomes

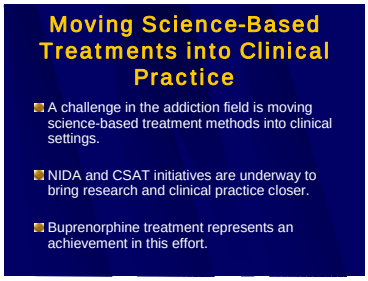
Clinical trials have established the effectiveness of buprenorphine for the treatment of opioid addiction. The clinical studies have shown the following about buprenorphine:

Bullet #1: Patients on buprenorphine did as well as patients on a moderate dose of methadone (60mg).

Bullet #2: Patients on buprenorphine did as well as patients on a moderate dose of LAAM (70mg/70mg/85mg on a Monday/Wednesday/Friday schedule).

Bullet #3: Patients found that taking buprenorphine was a pleasant experience, which encouraged them to be compliant.

Bullet #4: When compared to placebo-plus-counseling, 3/4 of the patients receiving buprenorphine and counseling were still in treatment after one year. None of the placebo patients were retained.



Slide 6: Moving Science-Based Treatments into Clinical Practice

Many treatments that are developed never make it into real-world practice.

This has been a problem for quite some time and both the National Institute on Drug Abuse (NIDA) and the Substance Abuse Mental Health Services Administration (SAMHSA) have recognized this. The Blending Team that developed these materials resulted from one initiative designed to help move scientific findings into practical application: The NIDA-SAMHSA Blending Initiative.

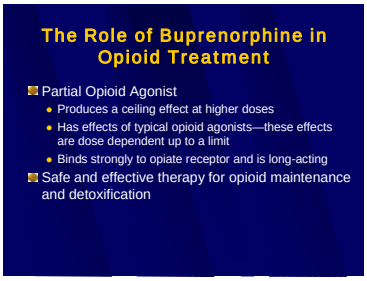
Buprenorphine is an important treatment advancement and represents an exciting opportunity for individuals to develop strategies to work with both providers and researchers to find ways to make this treatment a readily-available option.

Slide 7: Buprenorphine as a Treatment for Opioid Addiction

Several factors make buprenorphine a good option for some people.

Buprenorphine is a partial agonist, resulting in a good safety profile for the medication.

With the changes in the treatment legislation, this medication becomes the first available outside of the OTP system. This expands both the availability of and access to treatment.



Slide 8: The Role of Buprenorphine in Opioid Treatment

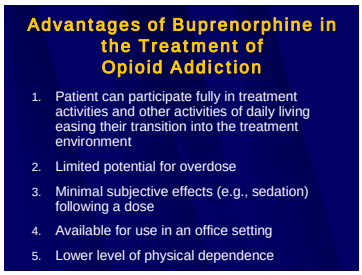
The partial agonist properties of the medication are important to understand.

The effects of the medication at lower doses are virtually the same as that of full agonists. However, as the dose is increased, the effects level out for buprenorphine (especially respiratory suppression), where they continue to increase with full agonist medications. This is called a "ceiling effect." This ceiling effect greatly decreases the risk of overdose when compared to full agonists.

Buprenorphine has a very HIGH affinity for opioid receptors. It displaces morphine, methadone, and other full agonist opioids from the receptor. Additionally, buprenorphine dissociates slowly from the receptor.

This high affinity for and slow dissociation from the receptor result in buprenorphine blocking the effects of other opioids, such as heroin. Additionally, the high affinity and slow dissociation give rise to buprenorphine's prolonged therapeutic effects.

Clinical trials have demonstrated that buprenorphine is a safe and effective medication for both opioid maintenance and medically assisted withdrawal (detoxification). Additionally, because buprenorphine is very long-acting, dosing can occur on a less-than-daily basis, as infrequently as three times per week.



Slide 9: Advantages of Buprenorphine in the Treatment of Opioid Addiction

When transitioned onto buprenorphine, patients can participate fully in treatment activities rather than being sick from withdrawal for several days. This means that treatment can begin as soon as they seek it (while motivation is high).

There are no known cases of overdose directly related to buprenorphine. To date, cases in which overdose has occurred involved use of alcohol or other respiratory depressants (e.g., benzodiazepines). *See Johnson, et al. 2003, for a more detailed discussion.*

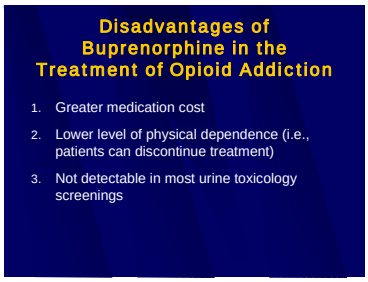
Patients report minimal sedation following a dose.

The treatment setting can be determined to fit the needs of the patient (OPT or office-based).

Slide 10: Advantages of Buprenorphine/Naloxone in the Treatment of Opioid Addiction

The marketing effort in the U.S. is focused on the combination formulation. This formulation has several advantages, including the following:

- It discourages injection use because, when injected, the naloxone in the product will lead to withdrawal, whereas when taken sublingually as prescribed, it will not have that effect.
- Because of the above point, the combination tablet lowers the likelihood that the medication will be diverted.



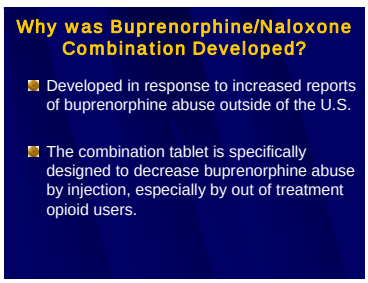
Slide 11: Disadvantages of Buprenorphine in the Treatment of Opioid Addiction

There are definitely disadvantages to the medication, as well.

Buprenorphine is more costly than methadone: According to the manufacturer, Suboxone® (16 mg/day) costs $287.50 for a month's supply, compared to less than $30 for a month's supply of methadone at usual doses.

Overall, the medication causes a lower level of physical dependence. While this is generally seen as an advantage of the medication, it does make it easier for patients to discontinue treatment and return to use.

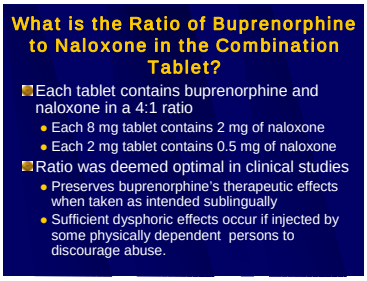
Buprenorphine is not detectable in most urine tests, making monitoring for compliance difficult. However, this could also be an advantage of buprenorphine (for people who are randomly drug tested in the workplace).



Slide 12: Why was Buprenorphine/Naloxone Combination Developed?

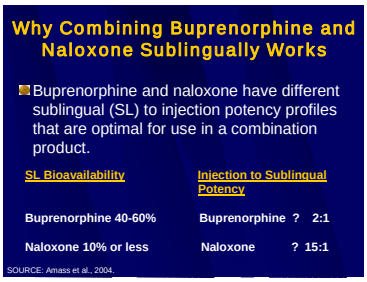
In other countries where buprenorphine has been available, there were reports of increasing abuse of the medication. Therefore, the US developers worked to find a way of preventing misuse of the medication as much as possible.

Since use of the buprenorphine/naloxone combination tablet by injection will cause withdrawal, the likelihood of misuse by out-of-treatment opioid users is greatly decreased.



Slide 13: What is the Ratio of Buprenorphine to Naloxone in the Combination Tablet?

The combination includes buprenorphine and naloxone in a ratio of 4:1. This ratio was found to maintain the clinical effects when taken sublingually as intended, BUT cause sufficient discomfort if injected by a physically dependent person (to discourage them from doing so).



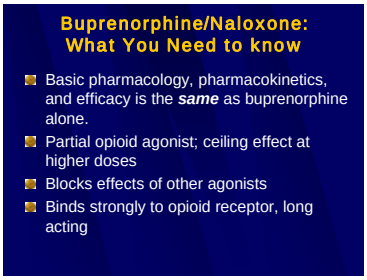
Slide 14: Why Combining Buprenorphine and Naloxone Sublingually Works

Digestive juices would kill buprenorphine's effects if you were to swallow it. By administering it sublingually, the medication dissolves under the tongue and is absorbed directly into the blood stream. Buprenorphine and naloxone have very different absorption rates when taken this way.

When taken under the tongue, the person receives approximately 40-60% of the buprenorphine available, but only 10% of the naloxone.

However, when you look at the relative potency comparing sublingual administration to injection, buprenorphine is approximately twice as strong when injected as when taken sublingually. Naloxone, on the other hand, is 15 times more effective by injection.

This means that when taken by injection, the naloxone is the stronger medication and the antagonist effects dominate.



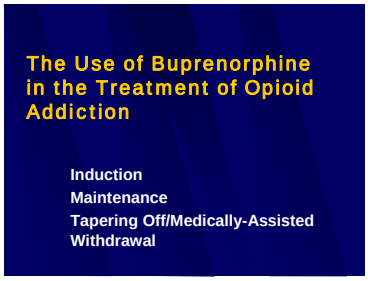
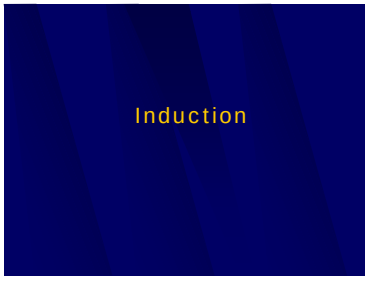
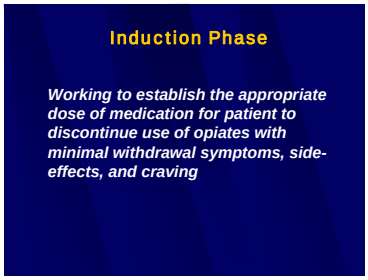
Slide 15: Buprenorphine/Naloxone: What You Need to Know

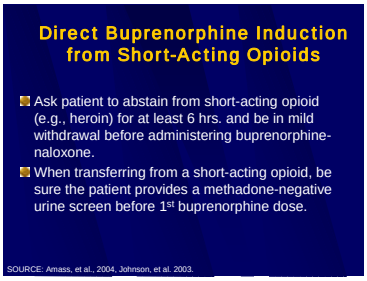
The effect of the combination tablet is virtually identical to the buprenorphine-only product when taken sublingually.

Both formulations demonstrate the ceiling effect at higher doses.

Both formulations prevent the intoxicating effects if someone decides to also use another opioid.

They are long-acting because of the high receptor affinity.

	**Transition** **Slide 16: The Use of Buprenorphine in the Treatment of Opioid Addiction (Induction, Maintenance, Tapering Off/Medically Assisted Withdrawal)** Now let's look at how people are transitioned onto buprenorphine and then examine the two primary treatment options: maintenance and medically assisted withdrawal.
	**Slide 17: Induction** The term induction refers to the procedures used to transition someone from other opioids onto buprenorphine.
	**Slide 18: Induction Phase** During induction, the physician works with the patient to figure out the most effective dose so that he/she can stop other opioid use with minimal withdrawal symptoms. While the physician primarily guides this process, the multidisciplinary team is critical in providing supportive care and counseling to help the patient through the process.



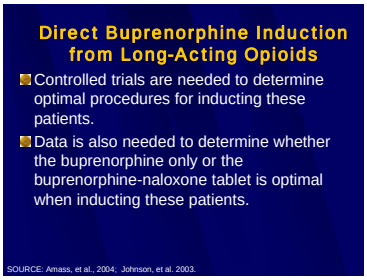
Slide 19: Direct Buprenorphine Induction from Short-Acting Opioids

People who are using either short- or long-acting opioids can be inducted onto buprenorphine/naloxone. The PHYSICIAN is responsible for this aspect of the patient's care.

The multidisciplinary addiction professional should be available, however, during the induction process to provide supportive counseling.

In order to be inducted onto buprenorphine, the person must be in mild withdrawal. This ensures that they have a smooth transition onto the medication and will not have unexpected withdrawal symptoms. Due to the high receptor affinity (removing other opioids from the receptor) and the ceiling effect at higher doses (causing a lowered experience of the drug), if patients transition immediately from heroin to buprenorphine, for example, buprenorphine will replace the heroin at the receptor and the patient will have the experience of suddenly having much less opioids in their system than they are used to – they will go into withdrawal. However, if they are already in mild withdrawal, the buprenorphine will have the expected agonist effects and the person will experience a comfortable transition.

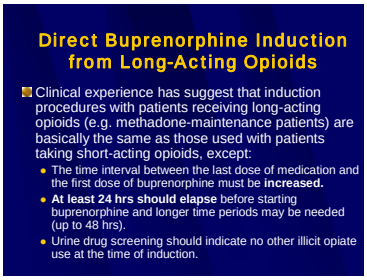
The patient should also be monitored for methadone use, as this can complicate the transition, as well.



Slide 20: Direct Buprenorphine Induction from Long-Acting Opioids

Less is known about how to transition people from long-acting opioids such as methadone.

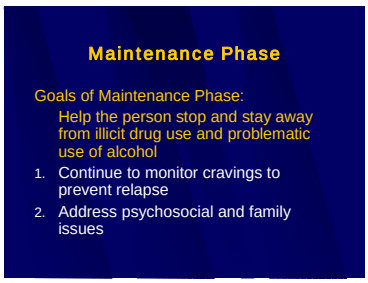
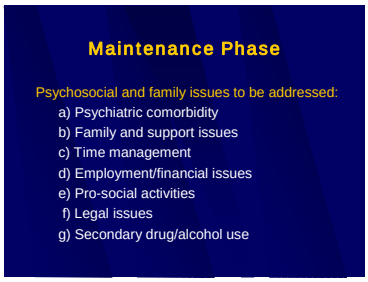
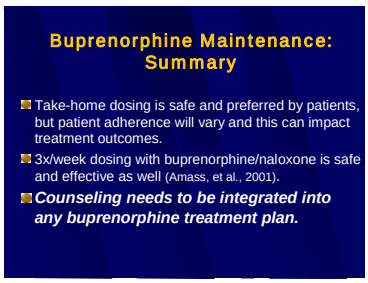
Clinical trials are needed to determine the most effective procedures and which formulation to use for these patients.



Slide 21: Direct Buprenorphine Induction from Long-Acting Opioids

Clinical experience has indicated that these patients can be successfully inducted using similar procedures as those used for short-acting opioids

The time interval between the last dose should be increased to allow for the longer active duration of the drug (24-48 hours).

	**Transition** **Slide 22: Stabilization and Maintenance** Once the person is on the medication, the next step is to make sure he/she is stabilized.
	**Slide 23: Stabilization Phase** By stabilization, we mean that they do not experience any negative symptoms or craving. At this point, the decision can be made to either move on to the maintenance phase or to withdraw with medically assisted withdrawal.
	**Slide 24: Maintenance Phase** Cessation of illicit drug use and problematic alcohol use. The treatment professional should address any underlying issues, such as psychiatric co-morbidity and psychosocial issues (employment, legal, family/social, etc.).
	**Slide 25: Maintenance Phase** During maintenance treatment, providers should assess the patient and provide treatment for other issues that the person is facing, to help get him/her stabilized and live a more fulfilled life. *Read/summarize the bullet points.*
	**Slide 26: Buprenorphine Maintenance: Summary** Use of take-home dosing is desired by many patients, but ongoing monitoring is critical to determine compliance. Dosing every day is not necessary. Researchers have demonstrated that a three-time-per-week dosing schedule was safe and effective. In order to be effective, it is imperative that counseling be incorporated into the treatment plan and supported by the entire multidisciplinary team.

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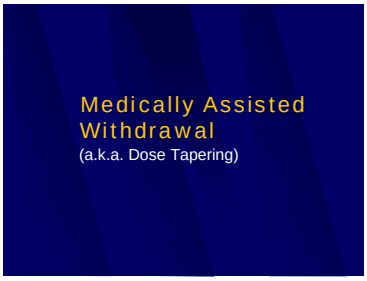
<td> 
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<td>Transition

Slide 27: Medically Assisted Withdrawal (a.k.a. Dose Tapering; a.k.a. Detoxification)
Not all patients are appropriate for withdrawal from the medications. Unstable living situations, multiple relapses, previous failed detoxification attempts, or lack of desire to withdraw from opioids, may indicate that maintenance is a better treatment option.</td>
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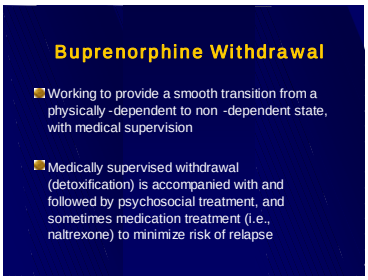
<td> 
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<td>Slide 28: Buprenorphine Withdrawal
However, if appropriate, the goal of medically assisted withdrawal is to help patients transition off of opioids so that they are no longer physically dependent.

Psychosocial treatment is a critical component of this (and all treatments) to help them avoid relapse.</td>
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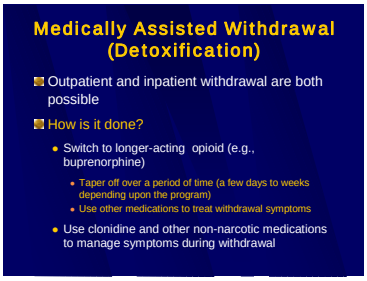
<td> 
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<td>Slide 29: Medically Assisted Withdrawal
Medically assisted withdrawal can be successful in either inpatient or outpatient settings. It is important for the multidisciplinary treatment professional to provide supportive wrap-around services to get the patient through this difficult stage.

This is done by transitioning the person onto a long-acting opioid like buprenorphine and then tapering him/her off over a period of time.

Other medications may be helpful if withdrawal symptoms are present to help the person to stay comfortable.</td>
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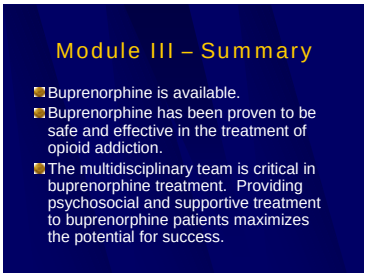
<td> 
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<td>Slide 30: Module III – Summary

Read/summarize the bullet points.</td>
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