The Use of Buprenorphine To Treat Co-occurring Pain and Opioid Dependence in a Primary Care Setting

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Disclosures

- No Conflict of Interest to disclose
- The reported data is a clinical quality improvement project performed at the New Mexico VA Health Care System.

Objectives

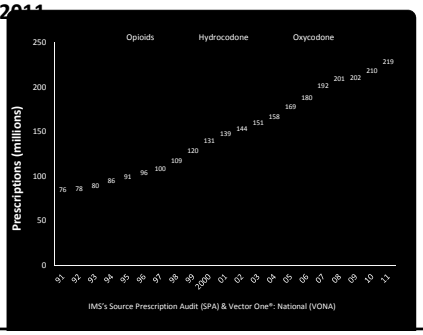
- To provide a brief overview of the epidemiology and prevalence of chronic pain and opioid dependence and increasing overdose rates and fatalities along with pharmacology of buprenorphine.
- To review and analyze data from a clinic integrating primary care pain management and opioid dependence to evaluate effectiveness of buprenorphine therapy.
- To describe the induction process and utilization of buprenorphine in the treatment of pain and opioid dependence in an outpatient setting along with the monitoring process to assess efficacy.

Epidemiology

Chronic Pain

- 116 million people in the US suffer with chronic pain – which is more than diabetes, cancer and heart disease combined[1]
- 35% American adults experience chronic pain
- Annual health care costs – expenses, lost wages, productivity loss estimated to be $635 billion[1]

Steady Increases in Opioid Prescriptions Dispensed by U.S. Retail Pharmacies, 1991-2011



Opioid Use

- Use of opioids has increased substantially over the past 20 years despite limited evidence for efficacy in chronic noncancer pain [3,4]
- Rise in opioids utilization corresponds to rise in opioid abuse and dependence – rates of opioid misuse (includes abuse and dependence as well as recreational use) estimated between 18 to 41% [5] and aberrant medication behavior as high as 50% [6]

Abuse of Prescription Opioids

- 7 million Americans (2.5% of the population) over the age of 12 admit to misuse of prescription psychotherapeutic medications
- 1.9 million prescription narcotic users meet diagnostic criteria for opioid abuse or dependence (second only to marijuana, 4.3 million)
- New users of prescription opioids are about the same as that of marijuana (National Survey on Drug Use and Health, 2010)

Fatal Drug Poisoning

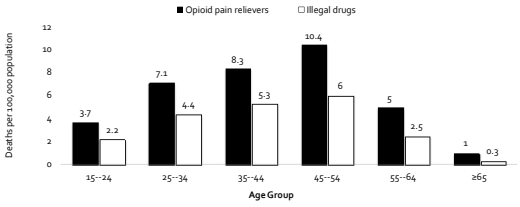
- Between 1999 and 2002, the number of opioid analgesic poisonings on death certificates rose 91.2%
- During this time period, poisoning from methadone surpassed both cocaine and heroin poisoning as the most frequent type of drug poisoning found on death certificates in the U.S.
- New Mexico led the country in overdose deaths and one of the higher rates of nonmedical use of prescription opioids.

CDC MMWR Nov 4, 2011 60(43) 1487-1492

Paulozzi, L.J., Budnitz, D.S., Xi, Y, 2006. Increasing deaths from opioid analgesics in the United States. Pharmacoedidemiology and Drug Safety 15, 613-7.

Consequences of Rx Drug Use and Abuse are Increasing

Deaths from Opioid Pain Relievers Exceed Those from Illegal Drugs in all Age Groups

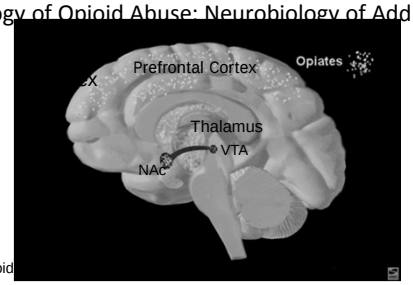


More Drug Overdose Deaths are Associated with Opioid Pain Relievers than with Illegal Drugs. Data are for 2008. Illegal drug deaths include deaths from overdose of heroin, cocaine, hallucinogens, or stimulants. Source: CDC, Morbidity and Mortality Weekly Report, 60(43): 1489, 2011.

Unintentional Overdose Deaths have quadrupled since 1998

Opioid Pharmacology: How do these Medicines Work?

Etiology of Opioid Abuse: Neurobiology of Addiction



- Mu opioid
- While binding in the thalamus produces analgesia, binding in the cortex produces impaired thinking/balance;
- Ventral tegmental area (VTA)/nucleus accumbens (NAc) is associated with euphoria that some experience (i.e. the "high"). This area is the reward pathway
- Binding in this reward pathway is believed responsible for reinforcing effect leading to potentially to addiction.

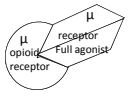
Repeated Dosing: Opioid Tolerance and Withdrawal

- Tolerance:
  - Need more for same effect
  - Less effect with same amount
  - Occurs for euphoria, sedation, respiratory depression, vomiting, analgesia
  - Minimal tolerance to constipation, miosis, sweating
  - Can attain high levels of tolerance with gradual increases to doses that would otherwise be lethal
- Withdrawal:
  - Upon reduction or cessation of opioid use/administration

DSM-IV Criteria for Opioid Dependence

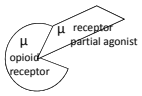
- **The substance is often taken in larger amounts or over a longer period than was intended**
- **There is a persistent desire or unsuccessful efforts to cut down or control substance use**
- **A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects**
- **Important social, occupational, or recreational activities are given up or reduced because of substance use**
- **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**

Brief pharmacology overview: full opioid agonists



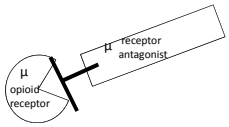
- Full agonist binding activates the μ opioid receptor
- Is highly reinforcing
- Is the most abused opioid type
- Full agonists are: heroin, oxycodone, methadone, and others

Brief pharmacology overview: partial opioid agonists



- Partial agonist binding activates the μ opioid receptor at lower levels
- Is less reinforcing
- Is a less abused opioid type
- Blocks opioid agonist (and antagonist) binding
- Partial agonists include: Buprenorphine

Brief pharmacology overview: opioid receptor antagonists



- Antagonist binding to the μ opioid receptor occupies without activating
- Is not reinforcing
- Blocks abused opioid agonist binding
- Antagonists include: Naloxone and Naltrexone

Buprenorphine's Unique Properties

- Partial Agonist/Antagonist: has better safety profile – less respiratory depression
- Highest affinity for the opioid receptor: will replace a pure agonist and even antagonist off the receptor
- Long half-life – will bind the receptor for long period – elimination ½ life is ~ 37 hrs.
- Has no oral bioavailability - its use in opioid dependence is the

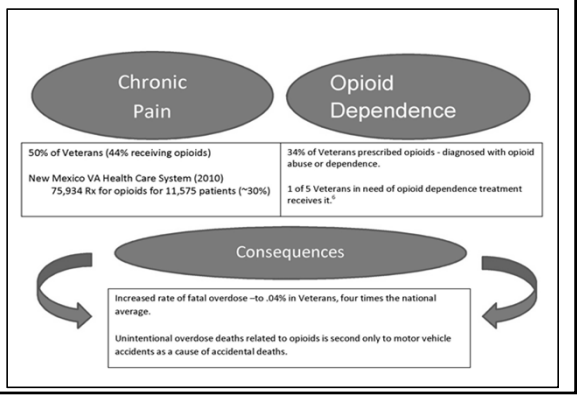
The Use of Buprenorphine/Naloxone to treat opioid dependence

- Buprenorphine/Naloxone:
  - In 2002, Drug Abuse Treatment Act approved sublingual formulations of buprenorphine for treating opioid addiction
  - Effectively treats opioid addiction by reducing illicit opioid use, improving treatment retention (55-60%)[9], and increasing negative urine toxicology screens[10]
  - Physicians fulfilling certification requirements can apply to Center for Substance Abuse Treatment for a special waiver to prescribe.

Buprenorphine/Naloxone for the treatment of pain and opioid dependence

- Must meet DSM-IV opioid dependence criteria
- No contraindications to treatment
- Follow established guidelines for induction and maintenance
- Buprenorphine efficacy vs opioid agonist such as morphine is unclear and probably varies with type of pain. In the Buprenorphine trainings, we teach that buprenorphine has analgesia 30 X that of morphine.[11] However, to compare efficacy is difficult.
- Buprenorphine dosed three to four times daily for control of pain (versus daily in opioid dependence alone).

The Problem for Veterans



Delivery Problems in the Old System

- Providers:
  - Addiction providers uncomfortable treating pain
  - Pain Management providers uncomfortable treating addiction
  - PCPs uncomfortable treating both and PCPs prescribe the opioids
  - Lack of training of providers in addiction
  - Regulations surrounding opioids
  - Perceive patients as difficult and time-consuming.
- Patients
  - Stigmatization to addiction
  - Believe pain is primary problem not addiction
  - Fear their pain will not be addressed
  - Denial
  - SUD programmatic treatment is overwhelming
  - Not ready for treatment
  - Many will agree to treatment in Primary Care but are reluctant to go to "Bldg. 1."

Improvement Change: Creation of Co-occurring Disorders Clinic (CODC)

- Establishment of unique clinic within Ambulatory Care Service to evaluate, treat, manage and monitor co-morbid pain and addiction:
  - High risk opioid patients
    - history of substance use disorder
    - family history of substance use disorder
    - younger age
    - psychiatric illness
  - Noncompliant patients
  - Complex pain regimens
  - Prescribed high dose opioids

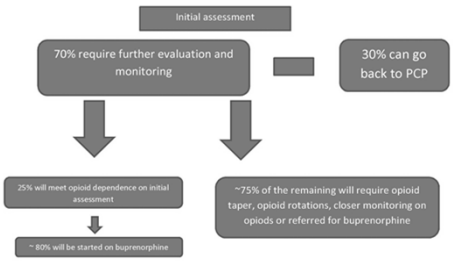
Plan of CODC

- Integrate treatment of co-occurring pain and addiction
  - Can provide treatment for pain and addiction simultaneously
  - Can provide pharmacologic and nonpharmacologic treatments for pain to minimize opioid use
- Embed the clinic within primary care
  - CODC providers available for immediate consultation
  - Greater acceptance of pain and addiction as a disease such as medical conditions
  - Decreased stigmatization
- Utilize the chronic care model to treat co-occurring pain and addiction
  - Versus episodic care that is traditionally offered
- Utilize pharmacotherapy such as Buprenorphine/Naloxone to treat opioid dependence and pain.

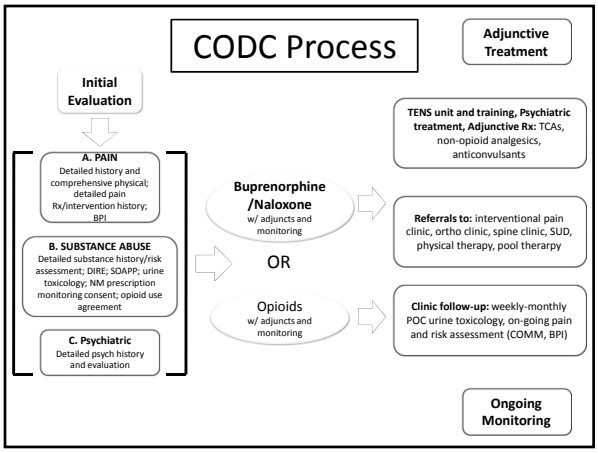
Patient population

- Referrals from primary care providers, interventional pain management specialists, internal medicine and surgical specialties.

Referral statistics



CODC Process



Pre-induction opioid management

- Recommendations are to stop short acting opioids 12-24 hrs before starting buprenorphine.
- TIP-40 recommends that patients taper on methadone to 30mg per day and abstain 36 hours.
- If we are prescribing long acting opioids for pain, then we will taper to 90 morphine mg equivalents per day, and first convert to short acting opioids for 2-4 weeks. We have found the induction goes far smoother.

Buprenorphine induction process

- If prescribed short acting opioids:
  stop 12-24 hrs before induction.
- If prescribed long acting opioids:
  will taper to a dose of 90mg of morphine equivalents then switch to short acting opioids

Data from the Co-occurring Disorders Clinic June 2009 to Nov. 2011

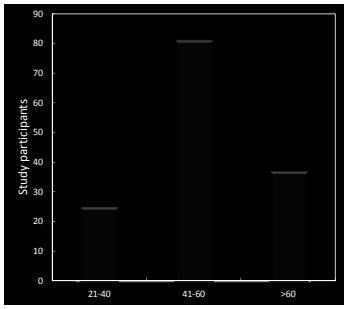
Hypothesis: Major barrier to utilizing buprenorphine in chronic pain patients would be inadequate pain relief.

Few studies utilizing buprenorphine SL in pain and addiction.

Pade P, Geppert C, Cardon K, Hoffman R, "Co-occurring Disorders Clinic" SAMHSA Science and Service Award for Office Based Opioid Therapy, Feb 2012.

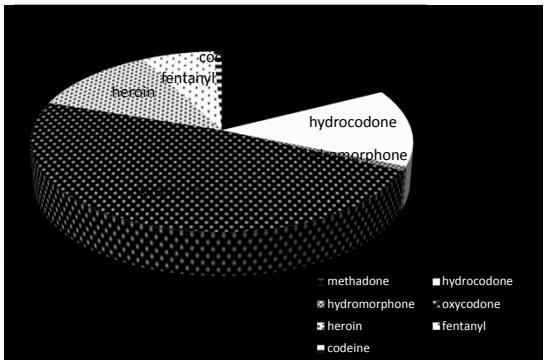
Pade P, Cardon K, Hoffman R, Geppert C, "Prescription Opioid Abuse, Chronic Pain, and Primary Care: A Co-Occurring Disorders Clinic in the Chronic Disease Model" JSAT, 43(2012) 446-450.

Participant Data
n = 143

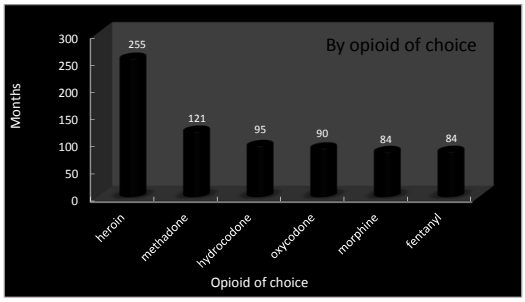


- Average age: 52
- Age range: 25-74
- Gender:
  - M = 133
  - F = 10

Participant Opioid of Choice (OOC)

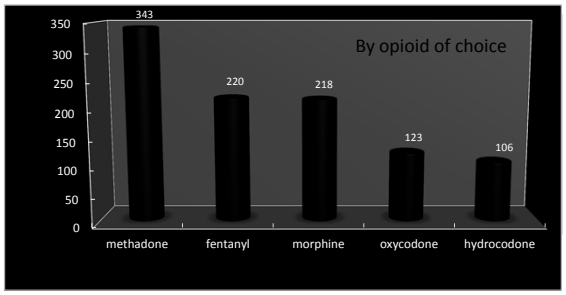


Average duration of opioid use



Average: 115 Months Range: 7-360 Months

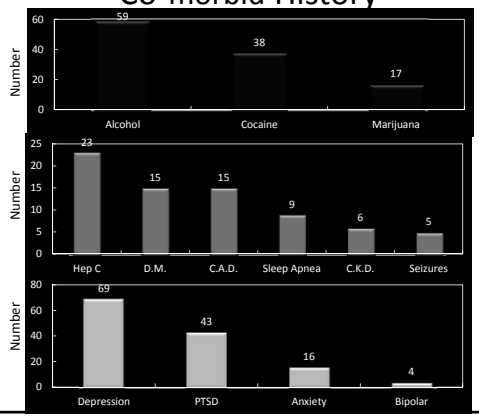
Dosage in morphine mg equivalents/day



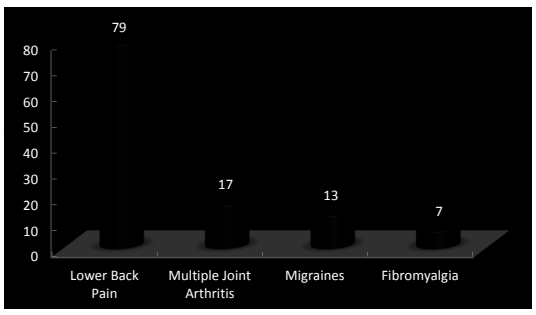
Average: 184 morphine mg equivalents/day

Range: 30-1290 morphine mg equivalents/day

Co-morbid History



Pain Location



Adjuvant Medications and Interventions

Na
N = 143

Antidepressants	#	NSAIDS	#	Anticonvulsants	#	M. Relaxers	#	Other	#
Amitriptyline	3	Celebrex	1	Gabapentin	31	Baclofen	11	Capsaicin	7
Duloxetine	5	Ibuprofen	25	Pregabalin	9	Cyclobenzaprine	7	ESI	3
Nortriptyline	1	Ketoprofen	1			Methocarb.	7	Lidocaine patch	5
Paroxetine	6	Meloxicam	4			Tizanidine	2	Intra-art. injection	13
Venlafaxine	18	Naproxen	8					TENS	10
		Salsalate	1					Pain group	5
TOTALS	33		40		40		27		43

Buprenorphine dosage for pain

- Mean daily dose: 16 mg of BUP/NLX

Most common regimens:

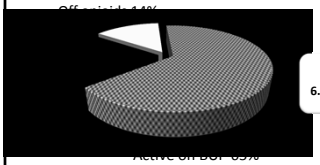
- 38 patients (26%) – BUP/NLX 8mg/2mg bid
- 28 patients (19%) – BUP/NLX 8mg/2mg tid
- 26 patients(18%) – BUP/NLX 4mg/1mg tid.

Ongoing monitoring for compliance

- Patient compliance with appointments
- Clinical assessment
- Pharmacy records/Clinical record
- Prescription monitoring program
- Urine toxicology screening
  - POCT in clinic: opiates, THC, Cocaine, benzos, barbiturates, oxycodone, Bup, amp
- Collateral from significant others

Outcomes

Outcomes: 65% of participants are still active in the program

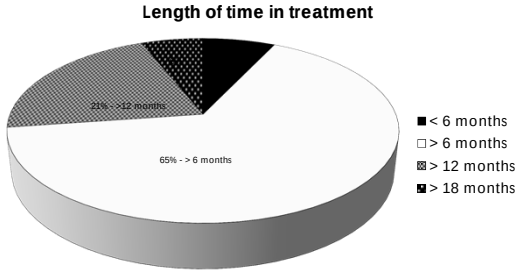


Outcomes: pain scores before and during buprenorphine treatment

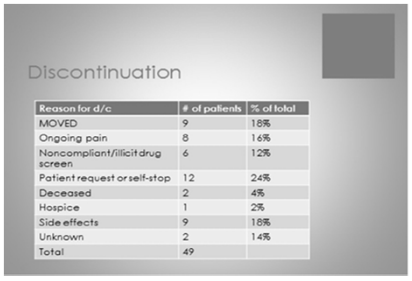
BEFORE	DURING
Mean score: **6.39 (95% CL 6.2, 6.6)**	Mean score: **5.6 (95% CL 5.4, 5.8)**

Pain scores **DECREASED** after buprenorphine treatment. This difference is statistically significant.

93/143 patients remained in treatment – 65%



Reasons for discontinuing



Discontinuation

Reason for d/c	# of patients	% of total
MOVED	9	18%
Ongoing pain	8	16%
Noncompliant/illicit drug screen	6	12%
Patient request or self-stop	12	24%
Deceased	2	4%
Hospice	1	2%
Side effects	9	18%
Unknown	2	14%
Total	49	

Conclusions

11. Patients with co-occurring chronic pain and opioid dependence can be successfully treated in a primary care setting.

2. Buprenorphine/Naloxone can successfully be utilized in conjunction with adjunctive treatments available to primary care providers to treat co-occurring chronic pain and opioid dependence.

3. Patients with co-occurring chronic pain and opioid dependence showed improved pain scores utilizing Buprenorphine/Naloxone treatment.

Solution: The Force Multiplier

VA VISN 18 SCAN ECHO
Specialty Care Access Network

- Began in August 2011
- Utilizes tele-medicine to train primary care providers to deliver specialty care
- Utilizes case-based training and didactic sessions to increase proficiency and confidence of primary care providers in their management of complex cases

Office Based Opioid Treatment: Buprenorphine Training

- March 7, 2012: conducted the first SCAN OBOT training held at the VA
- 52 attended; 8 hour session enabled physicians to apply for a DATA 2000 waiver to prescribe Buprenorphine for the treatment of opioid dependence
- 23 submitted applications
- Physician waivers:
  - Year 1: prescribe for 30 patients at one time
  - After year 1: up to 100 patients at one time

The authors wish to thank the following individuals for their dedication to the patients in CODC and the clinic

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