Models of Buprenorphine Induction

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AMERSA
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Accreditation Statement

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- Date of Release December 16, 2014
- Date of Expiration December 16, 2017
System Requirements

• In order to complete this online module you will need Adobe Reader. To install for free click the link below:
  ▪ http://get.adobe.com/reader/
Target Audience

• The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.

• The target audience for the current module should have basic familiarity with the general process of BUP induction as covered by the standardized, designated 8-hour training programs.
Educational Objectives

- At the conclusion of this activity participants should be able to:
  - List barriers reported by physicians to initiating buprenorphine (BUP) in an office setting
  - Determine the goals of induction
  - Identify different clinical models of BUP induction and associated evidence
  - List the pros/cons of the various models of BUP induction
Induction Goals

• Initiate effective BUP dosing
  ▪ Reduce withdrawal
  ▪ Reduce cravings
  ▪ Stop non-rx opioid use

• Avoid adverse effects

• Establish care structure
  ▪ Sets the tone regarding structure, follow-up, and monitoring
  ▪ Helps establish patient rapport, develop therapeutic alliance
Induction Challenge

• Barrier for inexperienced MD adoption$^{1-4}$

• Concern related to:
  - Precipitated withdrawal transitioning from full -> partial mu agonist
  - Logistics of office induction: time/resources for assessment & monitoring response to initial doses
  - Economics
  - Guideline ambiguity: variable dosing/timing recs
  - Patient-specific factors: e.g., clinical stability

$^1$ Kissin 2006; $^2$ Gunderson 2006; $^3$ Egan 2010; $^4$ Netherland 2009
Patient Induction Concerns

- Withdrawal symptoms
- Travel for office induction
  - Rural: long distances potentially burdensome
  - Disenfranchised: limited transportation access
  - Driving discouraged after medication initiation. Unclear if driving ability is impaired by opioid withdrawal prior to visit.
  - Anonymity: potentially compromised if pt is in withdrawal in the office or if needs to access a ride
- Patient perspectives data are needed
This Lecture Covers

- 3 models of induction for office practice
  - General in-office approach: the standard approach recommended in CSAT, TIP 40 & 8-hr courses
  - Specialty approach (non-Opioid Treatment Program (OTP)): Could this facilitate induction for some patients/practices?
  - Unobserved “home” approach: patient self-initiated often with clinician phone support
General In-Office Induction

• National guidelines (CSAT, TIP 40, 2004)
  ▪ Withdrawal: should be mild – moderate, but no specific recommendations regarding measurement cut-offs
  ▪ Abstinence timing: varies based on opioid duration of action
    – 12 - 24 hr short-acting
    – 24+ hr methadone
  ▪ Dose: 2 – 4mg initial BUP dose, 8mg maximum on Day #1
  ▪ Monitor: 2+ hours, assessing treatment response
General In-Office Induction

- Updated PCSS guidance\(^1\)
  - Measure withdrawal, several scales available such as:
    - Clinical Opioid Withdrawal Scale (COWS 12–16 is mild/moderate and appears sufficient to avoid precipitated withdrawal\(^2\))
  - Hours of abstinence since last full mu opioid use
    - 12-16 short-acting, 17-24 intermediate-acting, 30-48 methadone
  - BUP dose: 2 – 4mg initial, 16mg max day #1
  - Monitor: 1+ hours
  - Follow-up: phone + visit in 3 – 4 days

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\(^1\) Cassadonte, 2013; \(^2\) Nielsen, 2014
Clinical Opioid Withdrawal Scale (COWS)

- 11 item scale, max 48 points
  - Includes both objective and subjective items
    - Pulse
    - Diaphoresis
    - Tremor
    - Pupils dilated
    - Yawning
    - Runny nose/tearing
  - GI upset
  - Restlessness
  - Bone/joint ache
  - Anxiety
  - Gooseflesh

- Objective withdrawal signs help establish physical dependence
- Serial scales for treatment response assessment

Wesson, 2003
Available at: http://www.naabt.org/documents/cows_induction_flow_sheet.pdf
In-Office Induction Effectiveness

- Few studies specifically assess induction outcome
  - 83% treatment retention after a 2 week induction phase in a primary care study\(^1\)
  - Variable precipitated withdrawal\(^2-4\)
    - 10% in a 1° care/specialist clinic\(^3\)
      * 6+ hr heroin abstinence minimum prior to induction
    - None in residential program\(^5\)
    - Mean COWS prior to induction: 8
      * 1/3 ancillary withdrawal medication use

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\(^1\) Fiellin 2006; \(^2\) Gibson 2003; \(^3\) Lintzeris 2002; \(^4\) Whitley 2010; \(^5\) Collins 2007
General In-Office Induction

- Summary
  - Variation in abstinence & dosing recommendations may pose a clinical challenge
  - Withdrawal scale cutoffs are useful to guide induction
  - Time requirement is potentially burdensome
  - Complication rate is generally low
This Lecture Covers

• 3 models of induction for office practice
  ▪ General in-office approach
  ▪ Specialty approach (non-OTP)
  ▪ Unobserved “home” approach
Specialty Induction Approaches

• Two specialized induction approaches will be reviewed:
  ▪ Outpatient Buprenorphine Treatment Program\(^1\)
    – Established 2003 with a goal as an induction center
    – Induction data were collected early after program inception
  ▪ General Medical Hospital Induction Study\(^2\)
    ▪ Examined induction vs. detoxification on a medical ward
    ▪ Coupled with outpatient primary care maintenance linkage

\(^1\) Gunderson, 2009; \(^2\) Liebschutz, 2014
Buprenorphine Program of Columbia University

- Outpatient psych practice established 2003
- Staffing
  - MD - 2 addiction specialists
  - Clinical psychologist
  - RN
  - Administrator
- Self-pay with insurance reimbursement
Clinical Procedures

• Pre-induction visit
  ▪ Clinical assessment by MD/psychologist
  ▪ Procedural review (changed 3 months after program start)

Abstinence: Initial
  – 12 hr short-acting
  – 24 hr long/methadone

~ 3 Months Later
  – 16 hr short-acting
  – 24 hr long-acting
  – 36 hr methadone

▪ Ancillary withdrawal medication available at the program
  – Clonidine
  – NSAIDs
  – Ondansetron
Induction Visit Procedures

- COWS on arrival and serially
  - General target score 5-12 prior to starting BUP
  - After the first 3 months of experience, began to require > 1 objective sign and raised the pre-dose COWS target to >7
  - Discharge after the COWS decreased to < 4
- Dosing
  - 2-4mg q1-2 hr (BUP/NX or BUP) started at program
  - Take home meds + instructions/phone #s
  - Max 16mg Day 1
  - Initial Rx/stored on site > dispensed (Requires locked storage and detailed documentation)
- Ancillary withdrawal meds taken prn before or after initiation
Induction Effectiveness Study

- Chart review\(^1\) for the first 41 patients examined:
  - Temporal process of induction
    - Time until first BUUP dose given
    - Time unit withdrawal was relieved
    - Total time at clinic
  - Procedures associated with efficiency
  - Withdrawal level and BUP dosing
  - Hypothesis: ↑efficiency over phases
    - Each phase included ~13-14 patients over a 2-3 month period after the program opened

\(^1\) Gunderson, 2011 (Supported by NIDA DA020000)
## Patient Characteristics (n=41)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>41 yr</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>59%</td>
</tr>
<tr>
<td>Race (White)</td>
<td>78%</td>
</tr>
<tr>
<td>Employed</td>
<td>56%</td>
</tr>
<tr>
<td>Insured</td>
<td>83%</td>
</tr>
<tr>
<td>Psychiatric d/o</td>
<td>68%</td>
</tr>
<tr>
<td>Primary opioid, past mo. daily</td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>41%</td>
</tr>
<tr>
<td>Rx opioid (non-methadone)</td>
<td>41%</td>
</tr>
<tr>
<td>Methadone</td>
<td>22%</td>
</tr>
<tr>
<td>Prior buprenorphine</td>
<td>5%</td>
</tr>
</tbody>
</table>
Total Time at the Clinic

- Efficiency improved across the phases
  - Time may pose less of a practical burden for office induction as experience is gained
  - Several factors may have influenced efficiency
Time Delay Until Initial Dose

- The delay until the initial dose was longer for Phase 1
  - May have related to change in recommended pre-BUP abstinence with patients from later phases arriving in more withdrawal
  - Means COWS on arrival: 6 for Phase 1, 10 for Phases 2 & 3
The time until withdrawal relief was longer for Phase 1
- Might have related to initial BUP dose size and pre-dose ancillary withdrawal medication use (depicted next slide)
- COWS immediately before the initial dose did not differ by Phase (mean score = 10)
# Medication Dosing

<table>
<thead>
<tr>
<th>Buprenorphine Dosing (mean mg)</th>
<th>Phase</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial dose</strong></td>
<td></td>
<td>2*</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total at program</strong></td>
<td></td>
<td>9</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total Day #1 (includes at program + take home)</strong></td>
<td></td>
<td>13</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td><strong>Ancillary withdrawal medication use (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pre-induction</strong></td>
<td></td>
<td>7*</td>
<td>31</td>
<td>57</td>
</tr>
<tr>
<td><strong>Post-induction</strong></td>
<td></td>
<td>20% overall (NS)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p<.05; NS = non-significant difference between groups*
Procedural Considerations

• Factors that may facilitate induction\(^1\)
  ▪ Longer abstinence before BUP initiation (16h, 24h, 36h for short-acting opioids, long-acting formulations, and methadone, respectively)
  ▪ COWS 8-10 with objective signs appears adequate, though 12 might be preferable based on a clinical trial\(^2\)
  ▪ Ancillary withdrawal meds could be considered
• Day 1 max 16mg was well tolerated
• Efficiency improves with experience, potentially could translate to other office settings

\(^1\) Gunderson, 2011; \(^2\) Liebschutz, 2014
Hospital-Based Induction

• General Medication Hospital Induction Study
  ▪ Objective: Examine effectiveness of buprenorphine treatment initiation during a 5-day medical hospitalization
  ▪ Design: Randomized clinical trial comparing 1) hospital-based buprenorphine induction with linkage to outpatient primary care after discharge for opioid agonist treatment (OAT) vs. 2) hospital detoxification
  ▪ Main outcome measures:
    – Entry and sustained buprenorphine maintenance at 1, 3, & 6 months
    – Prior 30-day use of illicit opioids (self-report)

1 Liebschutz, 2014
Hospital-Based Induction

• Invention
  ▪ Day 1: Induction with buprenorphine/naloxone 2/0.5, max QID, for both treatment groups
  ▪ Day 2 - 5:
    - Detoxification Group: BUP 8mg > 6mg > 4mg > 2mg (Days 2-5, respectively)
    - Linkage Group: BUP 12mg on Day 2, 16mg on Days 3-5 with research staff facilitated linkage to hospital-associated primary care buprenorphine OAT

1 Liebschutz, 2014
Patient Characteristics (n=139)

<p>| | |</p>
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>41 yr</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>71%</td>
</tr>
<tr>
<td>Race (White)</td>
<td>43%</td>
</tr>
<tr>
<td>Baseline illicit opioid use (past 30d), mean days</td>
<td>21</td>
</tr>
<tr>
<td>Baseline past month prescription opioid agonist treatment</td>
<td>41%</td>
</tr>
</tbody>
</table>

- The intervention groups did not differ significantly regarding demographics, baseline frequency of opioid use or opioid agonist treatment
Hospital-Based Induction

• Results

  ▪ Buprenorphine OAT entry was significantly more likely in the hospital-based induction and linkage group compared to the hospital detoxification group (72% vs. 12%, p < .001).
  
  ▪ At 6 months, 17% of linkage vs. 3% detox patients were receiving buprenorphine OAT (p=.007)
  
  ▪ Linkage patients reported less past 30d illicit opioid use at the 6 month interview

1 Liebschutz, 2014
Specialty Induction Approaches

• Potential Specialty Induction Approach Limitations
  ▪ Accessibility: dedicated outpatient and inpatient induction programs are of limited availability
  ▪ Cost: the cost of such approaches may be prohibitive for patients and may not be cost-effective relative to outpatient induction
  ▪ Resources: the staffing and other resources required for outpatient program induction and inpatient induction with linkage may be a barrier for approach adoption
This Lecture Covers

- 3 models of induction for office practice
  - General in-office approach
  - Specialty approach (non-OTP)
  - Unobserved “home” approach
Unobserved “Home” Induction

• PCSS Guidance (2013)¹
  ▪ Experienced clinicians (and patients) probably better suited for unobserved approach than inexperienced
  ▪ Provide written instructions about withdrawal assessment, dose timing and amount
  ▪ Maintain and document phone contact
  ▪ Follow-up visit within 2 days
  ▪ Overall supporting level of evidence: Low/Moderate, though many unobserved inductions likely performed without adverse effects

¹ Cassadonte, 2009 (Updated 2013 by M. Sullivan)
Implementation

• ~40% Massachusetts prescribers utilize unobserved induction at least some of the time\(^1\)
• >1100 patients in U.S. published reports\(^2-8\)
  - Procedures appear generally c/w PCSS guidance\(^9\)
  - Adoption appears more widespread in academic primary care clinics
  - Most data are prospective or retrospective cohort
  - Only 1 published RCT, a pilot study described as follow

\(^1\) Walley 2008; \(^2\) Alford 2007; \(^3\) Lee 2009; \(^4\) Gunderson 2010; \(^5\) Stohler 2010; \(^6\) Soeffing 2009, \(^7\) Mintzer 2007; \(^8\) Lee 2014, \(^9\) Cassadonte 2009; \(^10\) Gunderson & Fiellin 2010
Clinical Procedures

- Adapted from a NIDA-funded pilot study
  - Pre-visit phone
  - Initial visit
    - Patient assessment
    - Procedural review
    - Decision making discussed
    - Patient handouts reviewed

1Gunderson, 2010 (Supported by NIDA DA020000)
Clinical Procedures – Initial Visit

• Patient assessment
  ▪ Establish diagnosis
  ▪ Use pattern (type/amount/duration/route)
  ▪ Document physiological dependence
  ▪ Co-morbidity
  ▪ Goals and motivation
  ▪ UDS/Rx monitoring program
Clinical Procedures – Initial Visit

- Procedural review with patient
  - Abstinence timing: 16, 24 36+ hrs for transition form short/long-acting opioids, and methadone, respectively
    - Withdrawal toleration vs. precipitated withdrawal risk reduction
  - Subjective Opioid Withdrawal Scale (SOWS)¹
    - 16 items, 0-4 scale, ≥17 (mild) prior to initiation
  - Bup dosing: target the minimally effective dose*
  - Consider ancillary withdrawal medication but not standardized

¹ Handelsman 1987
Clinical Procedures – Initial Visit

- Procedural review, continued
  - Safety
    - Interaction risks, avoiding driving, safe storage
  - Precipitated withdrawal avoidance: review abstinence recommendations
  - Follow-up plan
    - Phone contact the day of induction and on subsequent days
    - Visit in 3-7 days
Clinical Procedures – Initial Visit

- Patient handouts: review when/how to start
  - SOWS ≥17 (higher if possible) as a goal before dosing
  - Bup dosing
    - 1-2 mg to start, then q2hr prn
    - Max 8 mg day #1 (16 mg maximum ok’d by phone)
  - Day #2
    - Total day #1 in the morning (can split BID)
    - 2 mg q2hr prn, mx 16 mg (24 maximum ok’s by phone)
Unobserved Induction Outcome Data Summary

- Effectiveness: 1 wk success ~70%\textsuperscript{1-2} defined as being in treatment, on Bup, and free of withdrawal
- Safe: AE’s appear generally mild/infrequent\textsuperscript{1-4}
  - 1-5\% precipitated withdrawal
  - 5-20\% prolonged withdrawal
- Increased risk of AE’s appears to occur with\textsuperscript{1-3}
  - Methadone transfers
  - Bup inexperience
  - Procedural non-adherence

\textsuperscript{1} Lee 2008; \textsuperscript{2} Gunderson 2010; \textsuperscript{3} Whitley 2010; \textsuperscript{4} Doolittle 2011
### Observed vs. Unobserved

<table>
<thead>
<tr>
<th>Potential factors to consider</th>
<th>Observed</th>
<th>Unobserved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective and tolerability</td>
<td>+++</td>
<td>+(+)</td>
</tr>
<tr>
<td>Establish treatment structure</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Development of therapeutic alliance</td>
<td>++</td>
<td>-/+</td>
</tr>
<tr>
<td>Confirm baseline withdrawal (and presence of physiologic dependence)</td>
<td>+++</td>
<td>-/+*</td>
</tr>
<tr>
<td>Convenience/preference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- MD</td>
<td>+/-</td>
<td>+++</td>
</tr>
<tr>
<td>- Patient</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Resources/cost</td>
<td>--</td>
<td>+</td>
</tr>
<tr>
<td>Co-morbidity</td>
<td>+/-</td>
<td>-/+</td>
</tr>
</tbody>
</table>

*Note: pt’s can present for evaluation in mild withdrawal but start Bup out of the office*
Summary

• Induction is challenging aspect of treatment
• Hopefully practice-based evidence from different induction approaches will help improve induction efficiency, implementation, and effectiveness
• Several models of induction are available for initiating buprenorphine treatment, including observed and unobserved “home” approaches
• Pros/cons of the various models of induction should be considered by clinicians, patients, and policy makers
References


References


PCSS-MAT Mentoring Program

- PCSS-MAT Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid addiction.
- PCSS-MAT Mentors comprise a national network of trained providers with expertise in medication-assisted treatment, addictions and clinical education.
- Our 3-tiered mentoring approach allows every mentor/mentee relationship to be unique and catered to the specific needs of both parties.
- The mentoring program is available, at no cost to providers.

For more information on requesting or becoming a mentor visit: pcssmat.org/mentoring
PCSSMAT is a collaborative effort led by American Academy of Addiction Psychiatry (AAAP) in partnership with: American Osteopathic Academy of Addiction Medicine (AOAAM), American Psychiatric Association (APA) and American Society of Addiction Medicine (ASAM).

For More Information: www.pcssmat.org

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