The role of behavioral interventions in buprenorphine treatment of opioid use disorders

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Today's talk

- Review of studies of behavioral interventions in addition to buprenorphine to treat opioid use disorders
- Pose key questions to help understand the results of these studies
- Suggest research strategies to further understand this issue
- Suggest clinical approaches in treating this population

Drug Abuse Treatment Act of 2000 in U.S.A.

"Physicians must attest that they have the capacity to refer addiction treatment patients for appropriate counseling"

What is “appropriate counseling?”

Counseling in the context of buprenorphine treatment

- 4 major studies have shown that adding counseling to buprenorphine + medical management (MM) is not superior to buprenorphine + MM alone
- What is the role of behavioral interventions in office-based buprenorphine treatment?

Review of the 4 major studies

Study #1: Standard MM vs. Enhanced MM (Fiellin et al., 2006)

- N=141 (64% heroin users) randomized to
  - Standard (20') MM w/ bup dispensed 1x/week
  - Standard MM w/ bup dispensed 3x/week
  - Enhanced (45') MM w/ bup dispensed 3x/week
- No added effect of enhanced MM
  - Self-reported days of opioid use per week dropped from 5.3 to 0.4, no group diffs
  - 40-44% opioid-negative urines, no group diffs
  - 45% completed 24-week trial

Fiellin DA et al. *N Engl J Med.* 2006

Study #2: Adding Cognitive Behavioral Therapy (CBT) to MM (Fiellin et al., 2013)

- N=166 (86% primary heroin users)
  - Standard MM
  - Standard MM + CBT (weekly x 12 weeks)
- No added effect of CBT
  - Self-reported days of opioid use dropped from 5.3 to 0.4 per week, no group diffs
  - 41% completed 24-week trial

Fiellin DA et al. *Am J Med.* 2013

Study #3: CBT, Contingency Management (CM), and MM (Ling et al., 2013)

- N=166 (59% primary heroin users)
  - Standard MM (1-2x/week)
  - Standard MM + CBT (16x, weekly in 1-16)
  - Standard MM + CM (2x/week in weeks 1-16; drug-free urines given chance for $1-$4 reward)
  - Standard MM + CBT + CM
- No added effect of behavioral treatment
  - Days of past-month heroin use dropped from >20 days to 3.3 – 5.4 days, no diffs among groups
  - 50% completed 32-week trial

Ling W et al. *Addiction*. 2013

Study #4: Prescription Opioid Addiction Treatment Study (POATS; Weiss et al., 2011)

- N=653 (77% exclusively PO-dependent, 23% had hx of minimal, non-injection heroin use)
  - Standard MM
  - Standard MM + Individual Drug Counseling (1-2x/week)
  - Different lengths of buprenorphine tx: 4-week taper and 12-week stabilization for those who relapsed during taper
- Conducted at 10 U.S. sites as part of National Institute on Drug Abuse Clinical Trials Network
- Largest study ever conducted for prescription opioid dependence

Weiss RD et al. *Arch Gen Psychiatry*. 2011

POATS Results

- Phase 1: 7% successful (i.e., abstinent or nearly abstinent from opioids) after 4-week bup taper
- Phase 2: 49% successful during bup stabilization
  - No added benefit from adding individual drug counseling either during taper or stabilization
  - 90% of phase 2 Ss completed 12-week bup stabilization

Weiss RD et al. *Arch Gen Psychiatry.* 2011;68(12):1238-1246

Key questions

1. Is buprenorphine that good?
2. Is MM that good?
3. Is counseling that ineffective for this population?
4. How might research designs have affected outcome?
5. Are there subgroups of patients who benefit from additional counseling?
6. What outcomes should clinicians aim for?

Question #1:
Is buprenorphine that effective?

Is buprenorphine that effective?

- Yes-- but room for improvement
- Higher **retention** for methadone
  - 74% vs. 46% at 6 months in one multi-site RCT (Hser et al., 2014)
  - Methadone retention higher even if treatment self-selected (70% vs. 43% at 6 months) (Pinto et al., 2010)
- However, those retained in bup tx had fewer opioid-positive urine tests than those retained in methadone tx

Question #2:
Is medical management that effective?

‘Active ingredients’ of MM

- Overall health check
- Urine monitoring
- Check on medication:
  efficacy, adherence, tolerability
- Monitor craving
- Advice to abstain
- Advice to attend mutual-help groups
- But, MM in these studies more intensive than community standard

Question #3:
Are behavioral treatments that ineffective with this population?

Are all behavioral interventions ineffective with this population?

No

Are behavioral interventions that ineffective?

- 3 studies show benefit of behavioral tx
- Bickel et al., 2008 (N=135)
  1. Standard methadone-style counseling
  2. Clinician-delivered community reinforcement + CM: vouchers for negative urines
  3. Computer-delivered community reinforcement + vouchers for negative urines
- Outcome
  - Community reinforcement + CM → longer period of abstinence from opioids and cocaine

Are behavioral interventions that ineffective?

- Christensen et al., 2014 (N=170)
  1. Bup + contingency management (CM): $2.50 for initial opioid/cocaine (-) urine, then $.75 extra for additional (-) screens and $10 bonus for 3 consecutive negative urines
  2. Bup + CM + computerized Therapeutic Education System (TES): three 30-minute web-based topics per week
- Outcome
  - Better retention in CM + TES group
  - Longer continuous abstinence for CM + TES

Are behavioral interventions that ineffective?

- Schottenfeld et al., 2005 (N=162)
  - 2x2 factorial design
  - Bup or methadone + contingency management (CM) or performance feedback (telling them if their urine tests were positive or negative, no reward for negatives)
- Outcome
  - Benefit of CM when voucher values escalating
  - Lower retention in bup group vs. methadone

Question #4:
How might research designs have affected outcomes?

Effect of research design on outcomes?

- Four studies that found no additional benefit of behavioral interventions all had many solid features:
  - Rigorous RCTs
  - Large sample sizes
  - Manualized interventions
  - Regular urine toxicology tests

Effect of research design on outcomes?

- Studies with no benefit of behavioral tx:
  - More intensive MM
  - Higher bup doses (max. of 24-32 vs.16-18 mg/day)
- All studies with benefit of behavioral tx on opioid use outcomes used **contingency management and/or computer-based treatment**

Question #5: Are there subgroups that benefit from behavioral treatments?

Are there subgroups of patients who benefit from behavioral interventions?

POATS analysis compared patients with

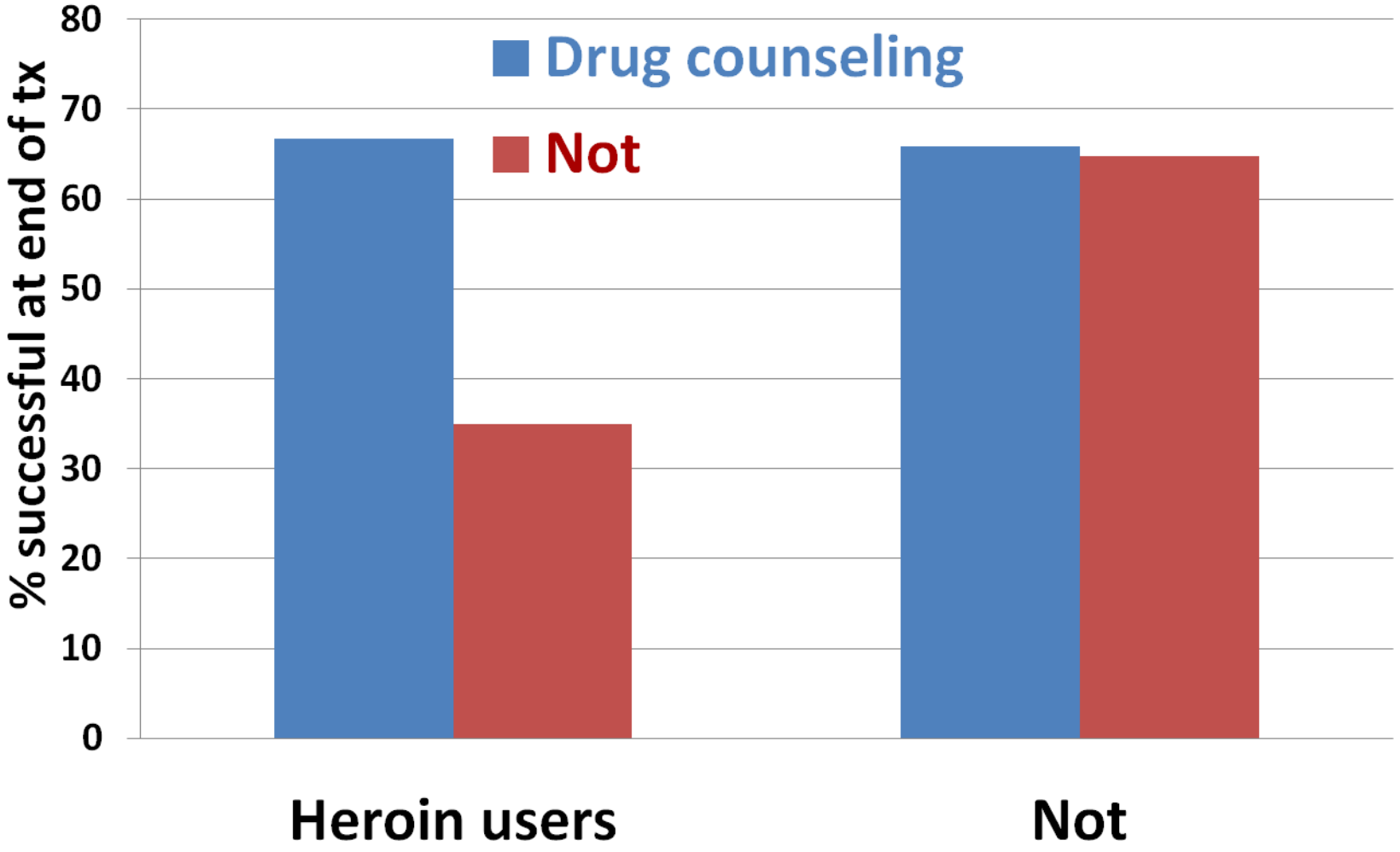
- More **severe** problems (e.g., those who had also used heroin)
- Greater **attendance** at treatment sessions, i.e. **adherence**
- The **interaction** of the two
- Dual disorders: chronic pain, psychiatric illness

Did drug counseling improve outcomes in patients with co-occurring psychiatric disorders?

50% of POATS pts had another psychiatric disorder

- Those with psychiatric illness had more successful outcomes if they received drug counseling (61% successful with counseling vs. 43% successful with MM alone)
- Ss without psych illness had same outcomes with and w/o counseling (45% v.49% success)
- Interaction significant ($p<0.05$)

Did drug counseling improve outcomes in patients with **more severe** problems? (n=266 with **adequate adherence**)



Interaction between heroin & treatment p=.03

Are there subgroups of patients who benefit from behavioral interventions?

Moore et al. (2016): secondary analysis of Fiellin et al. (2013) study of adding CBT to bup + MM

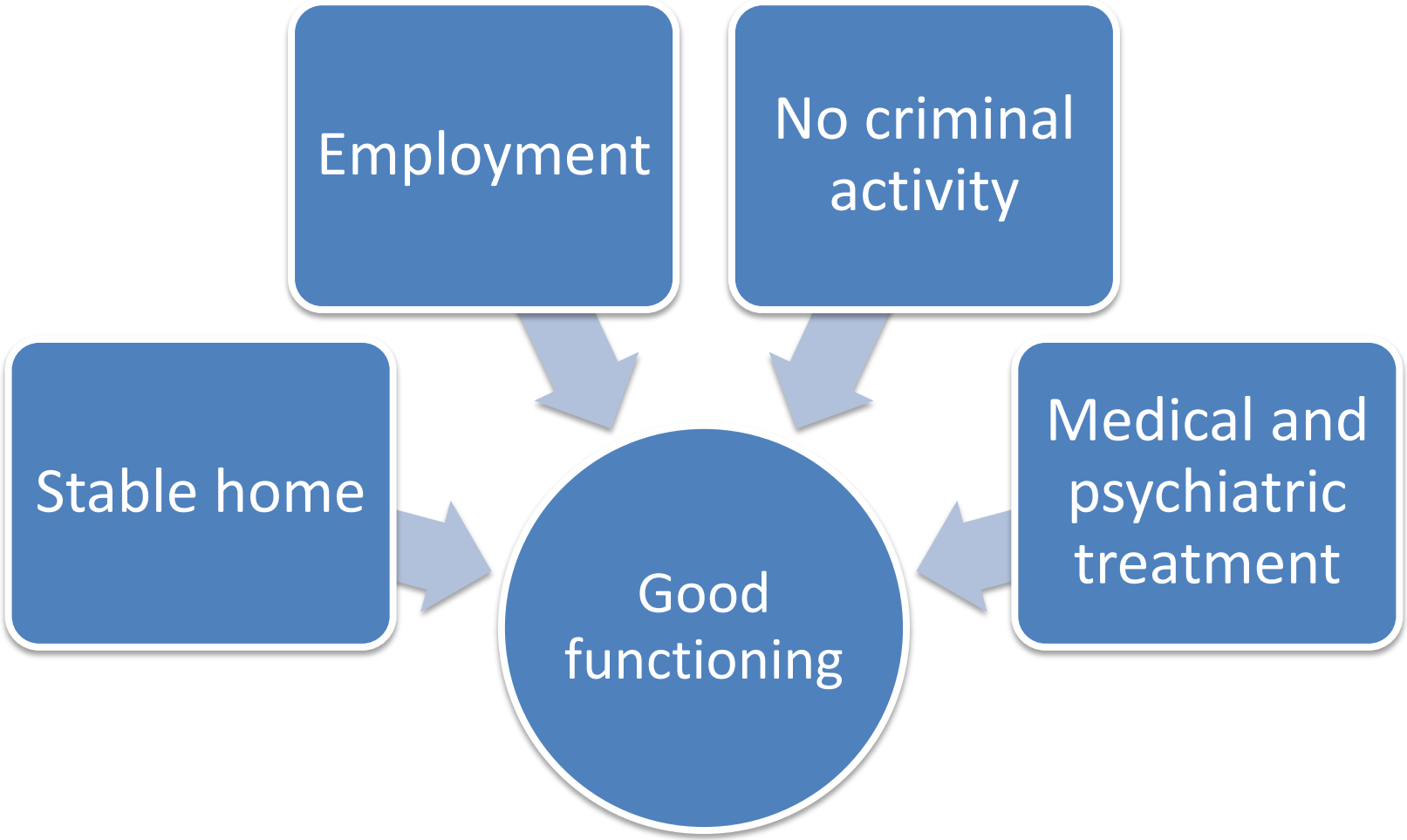
- Pts dependent upon prescription opioids had better outcomes when CBT was added (abstinence from all drugs)
- Primary heroin users did not benefit from adding CBT

Question #6:
What outcomes should clinicians aim for?

What outcomes should clinicians aim for?

- Literature focuses on
  - Treatment retention
  - Negative urine drug screens
- **Less emphasis on other important areas of functioning or well-being**
- **Perhaps behavioral treatments improve these areas**

What outcomes should clinicians aim for?



What have we learned?

What have we learned?

- Buprenorphine is an excellent medication, but much room for improvement
- MM is a robust intervention, but exceeds community standard
- CM is likely useful in this population
- Research designs (intensity of MM, bup dose) influence outcomes
- Some subgroups respond better to counseling (prescription users, CODs)
- We should focus on functional outcomes

How to proceed? Consider a stepped care model

Factors to weigh in considering behavioral treatment with buprenorphine

- Many patients do well with bup and MM alone, but we're not good at predicting who will and who won't do well
- Limited resources for MM, behavioral tx
- Some patients don't want counseling
- Understanding the importance of early treatment response may help our decision-making

Does early response to buprenorphine-naloxone predict treatment outcome in prescription opioid dependence?

Background and Rationale

1) Some medications, e.g., antidepressants, may take a number of weeks to work optimally. Therefore, waiting several weeks to examine treatment response may be helpful.
2) We do not know the typical time course of treatment response to buprenorphine-naloxone in the treatment of prescription opioid dependence.
3) Knowing this could help guide clinical practice early in the treatment of this population.

Research questions

1) Is it possible to tell early in treatment whether a prescription opioid dependent patient is likely to have a successful bup-nx outcome?

2) How early can bup-nx treatment response be evaluated accurately?

Methods

Positive predictive value = the degree to which initial opioid abstinence predicted final successful outcome at the end of 12 weeks of bup-nx stabilization.

Negative predictive value = the degree to which initial opioid use predicted final unsuccessful outcome at the end of 12 weeks of bup-nx stabilization.

Predicting abstinence at end of tx (weeks 9-12)

	Initial abstinence and final abstinence, n	Initial abstinence and final lack of abstinence, n	**Positive Predictive Value, %**
Week 1	101	107	**49%**
Weeks 1-2	88	70	**56**
Weeks 1-3	73	54	**57**
Weeks 1-4	68	45	**60**

Predicting use in weeks 9-12

	Initial use and final lack of abstinence, n	Initial use and final abstinence, n	**Negative Predictive Value, %**
Week 1	122	30	**80%**
Wks 1-2	89	6	**94**
Wks 1-3	72	3	**96**
Wks 1-4	58	2	**97**

Conclusions: the importance of early tx response

1) The first 2 weeks of treatment with bup-nx yield important information
2) Patients who abstain from opioids in the first two weeks have a pretty good chance of good 12-week outcome
3) However, those who use opioids in each of the first 2 weeks (even in week 1 alone) have very little chance of abstaining by week 12
4) Although not possible in POATS, increasing intensity of psychosocial treatment should be considered if patients don't do well initially (stepped care model)

What can we conclude?

Conclusions

- Is buprenorphine *that* effective?
  - **Yes**, but there is room for improvement
  - We need to **improve retention** in office-based treatment
- Is medical management *that* effective?
  - **Probably**, but **intensive MM may not be feasible** in community-based settings

Conclusions

- Are behavioral treatments *that* ineffective?
  - Evidence for **contingency management, perhaps computer-based tx**
  - Behavioral treatments may play larger role when MM is less intensive
- Effect of research design?
  - No studies of bup + counseling without high-quality MM

Conclusions

- Do **subgroups** benefit?
  - Data needed on which patients benefit from MM alone vs. those who need more intensive behavioral intervention
- What **outcomes** should be considered?
  - Improvements in **overall functioning**
  - Approaches that appeal to patients → **increase retention**
  - Consider stepped-care models

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Thank you.

Questions?