
eudynia
maledynia
allodynia
Central sensitization
hyperalgesia
Temporal summation
Wind up

Integrated Treatment of Pain and Rx Opioid Abuse

"PROJECT PAIN"
NIDA DA13169

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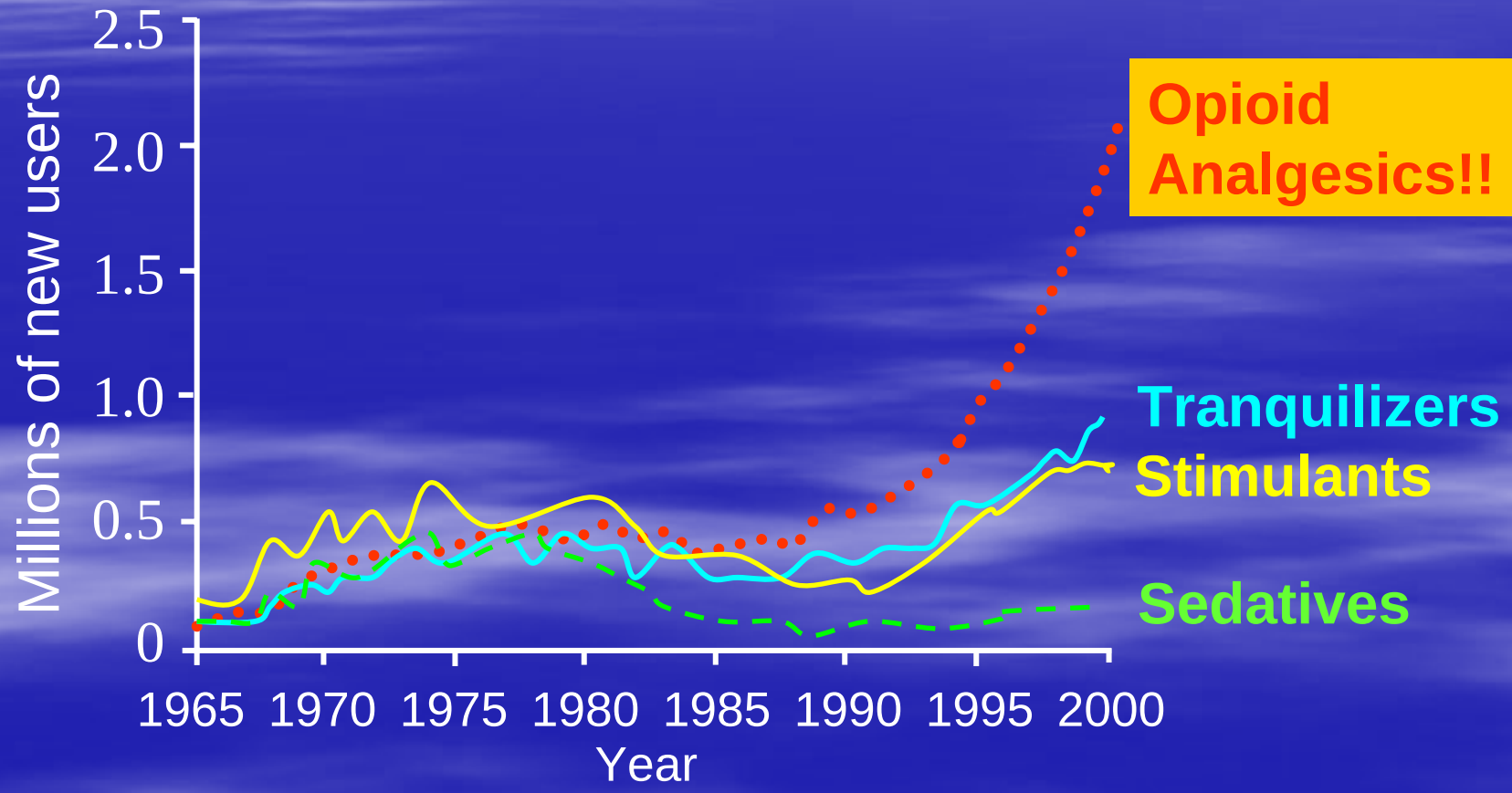
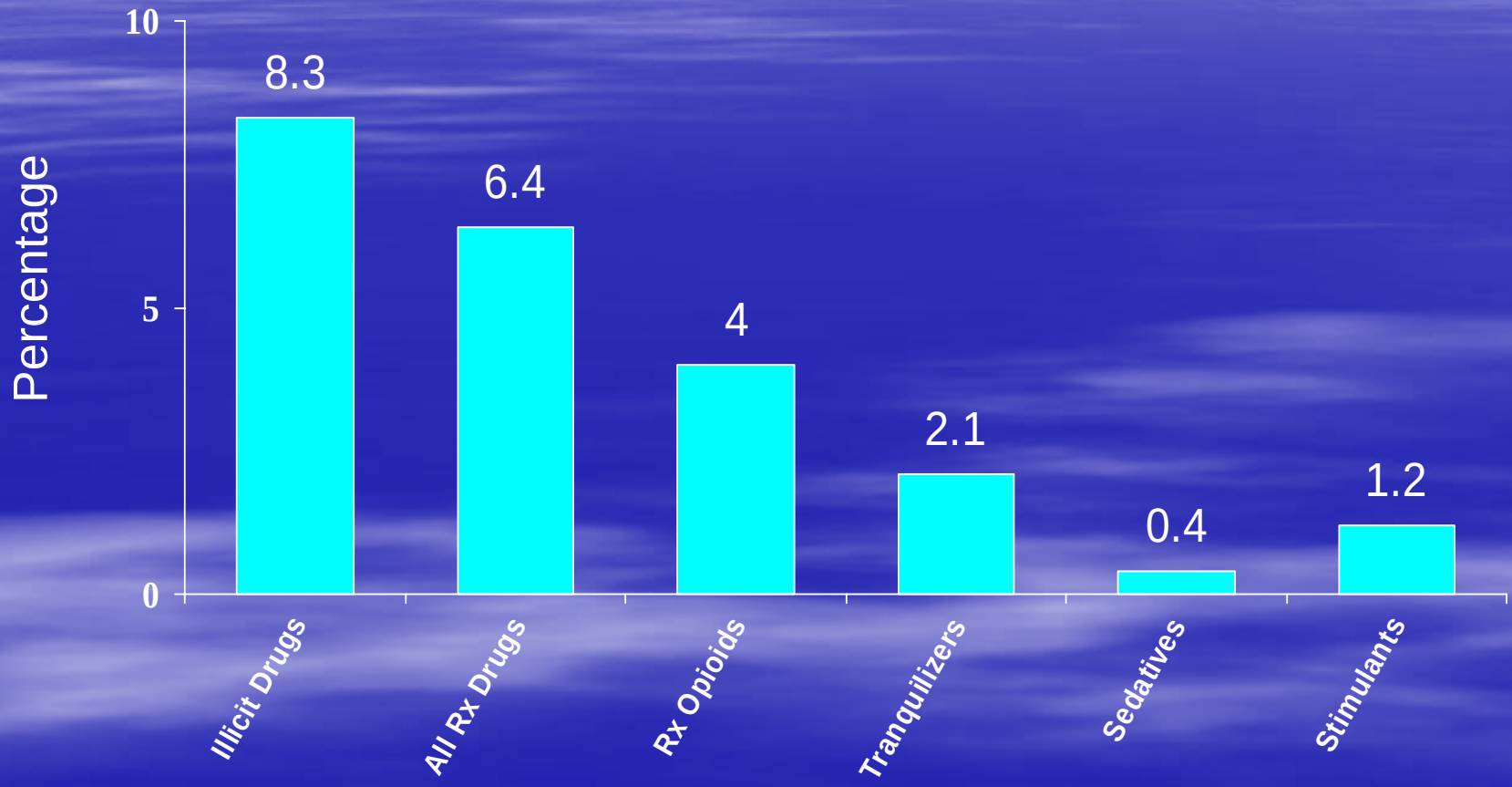
New "Nonmedical Users" of Psychotherapeutics



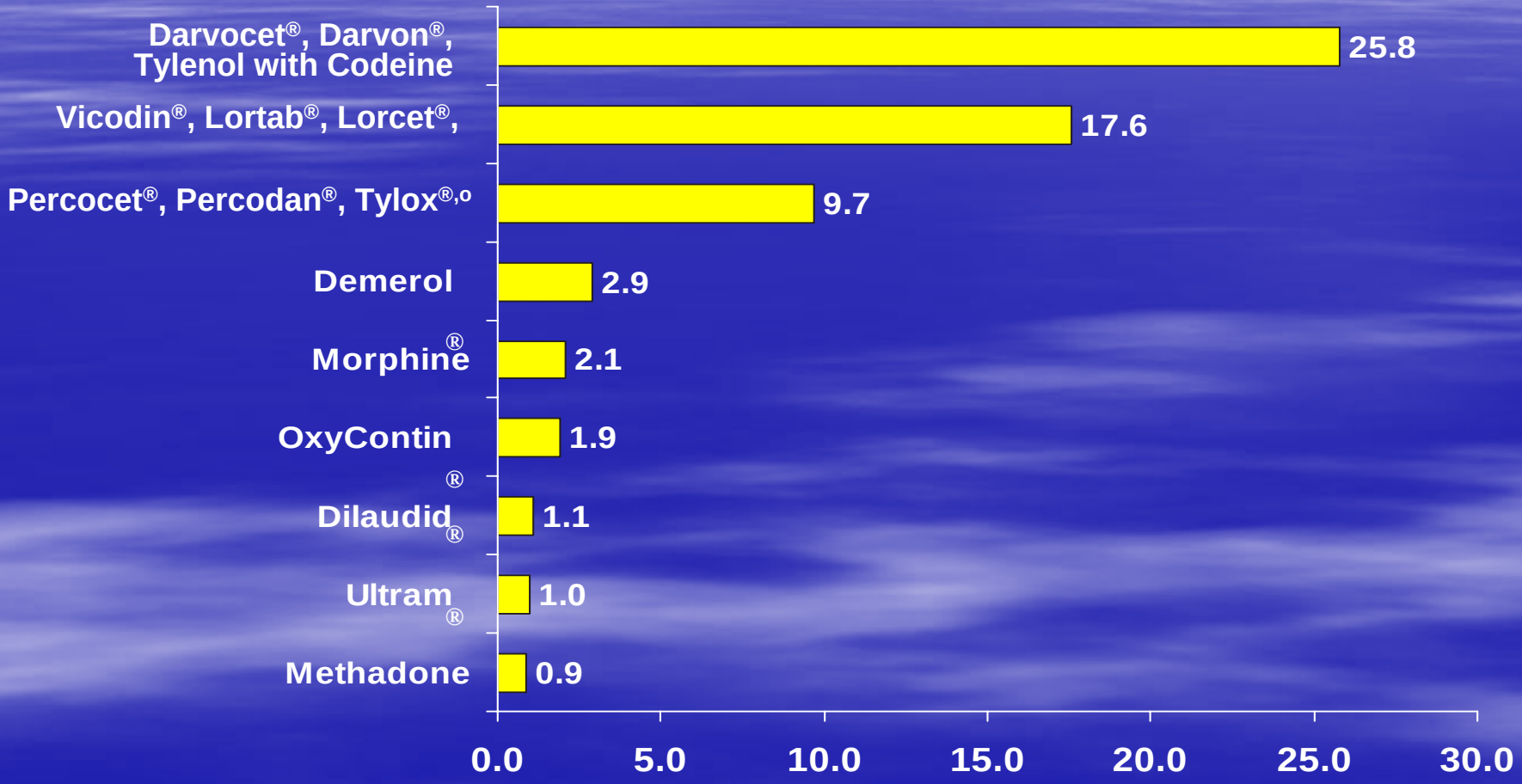
Household Survey www.samhsa.gov

% of U.S. Population Reporting ***Current*** non-medical Use of Prescribed Drugs



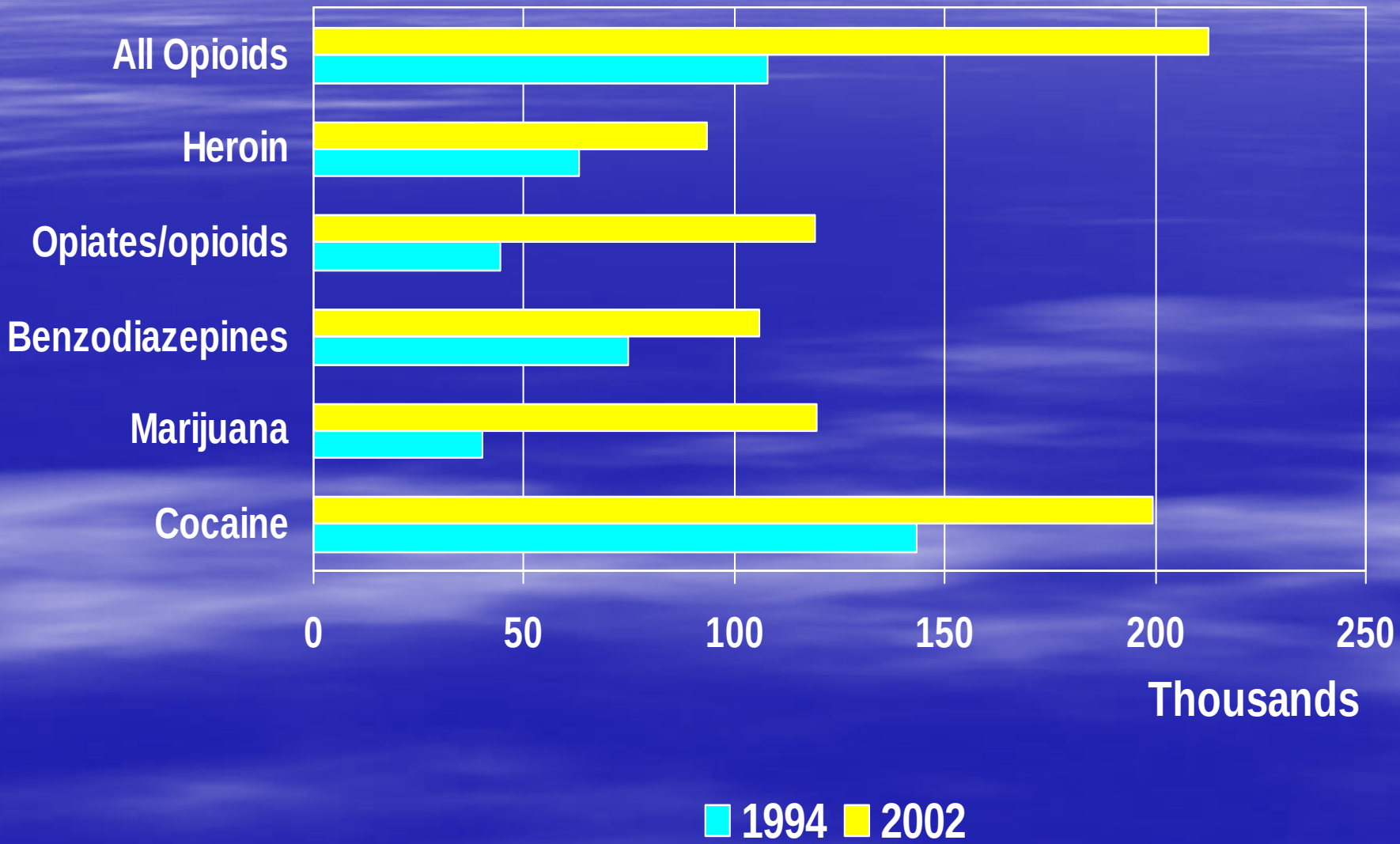
Source: SAMHSA (2003). Results from the 2002 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NHSDA Series H-22, DHSS Publication No. SMA 03-3836). Rockville, MD.

Lifetime Nonmedical Use of Rx Opioids (Age 12 or Older)



Source: SAMHSA (2003). Results from the 2002 National Survey on Drug Use and Health: National Findings

DAWN Mentions of Selected Drugs



… but what about patients with legitimate pain complaints who take opioids by Rx?

How Common a Problem?

- Higher prevalence in pain patients compared to general public (Zacny et al., 2003)
- 18-60% misuse Rx opioids depending on population and setting (Reid et al., 2002; Manchikanti et al., 2005)
- Highest rate in Medicaid recipients who also use illicit drugs (Manchikanti et al., 2005)
- Diagnosis challenging in pain patients:
  - Many meet DSM tolerance/withdrawal criteria
  - Standard drug screens don't detect synthetics
  - Many pain medications only detectable by GCMS

Providers' Contribution to Problem

- Inadequate training in pain management and addictions
  - Legitimate pain complaints misattributed to addiction
  - Addiction symptoms unrecognized/untreated
- Negative attitudes towards pain patients and drug abusers that develop during training
- Strained doctor-patient relations due to prior bad experiences
- Fear ("OPIOPHOBIA")
  - Creating addicts
  - Re-activating addiction
  - Being manipulated by drug seeking patients
  - Being "monitored" by Board
- Poor understanding of opioid pharmacology
- Under-treatment leading to increased drug-seeking behavior ("PSEUDO-ADDICTION")

Opioid Controversy

- **Antiopioid perspective:**
  - Causes tolerance, dependence, and addiction
  - Impedes rehabilitation process
  - Sustains “illness behaviors”
  - Should be avoided other than for brief “flare ups”
- **Pro-opioid perspective:**
  - Many patients benefit, including those with substance abuse history
  - Failure to adequately treat pain in substance abusers increases drug-seeking behavior, unsanctioned opioid use, and relapse
  - Unethical not to use when other approaches fail or when quality of life may be improved

Proposed Models of Care

Sequential: Drug treatment prior to pain treatment

1. Failure of drug treatment programs to appreciate/treat pain
2. Misattribution of pain complaints to addiction (drug-seeking behavior)
3. Incompatible treatment goals (abstinence)
4. High attrition rates

Segregated: Pain patients to pain programs and opioid abusers in MMTPs (IOM; Rettig & Yarmolinsky; 1995)

1. Failure to recognize co-morbidity
2. MMTPs not equipped to treat patients with pain

Modified office-based treatment: (Sees and Clark, 1993; Miotto et al., 1997; Weaver & Schnoll, 2002; Wesson, Ling, & Smith,1993)

1. No protocols (who's appropriate?)
2. No empirically validated interventions

"One Stop Shopping": Concurrent treatment in drug treatment setting such as MMTP (e.g., DOT for TB, HepC, HIV etc.)

1. Not tried for pain
2. Methadone clinics lack personnel with appropriate training
3. Medication regimens inappropriate

"PROJECT PAIN":R01DA13169

- Objectives:
  - Develop and pilot test novel interventions to address Rx opioid abuse and pain concurrently
- Questions to be answered:
  - Feasibility (Can this be done in office setting?)
  - Acceptability (Do patients/providers like it?)
  - "Promise" (How well does it work?)
- Outcomes of interest:
  - Decreased pain (P)
  - Decreased functional interference (F)
  - Increased Rx opioid adherence (OA)
  - Decreased ETOH/other drug use (AOD)
  - Good enough "Working Alliance" (WA)

Pre-Screening Protocol

- Provider Referral Packet:
  - Medical information (inclusion/exclusion criteria)
  - “PROBLEMS WITH PAIN MEDS” (AMTBs)
- Provider Agreement:
  - Will not prescribe opioids during trial
  - Will accept patient back, regardless of outcome
  - Will continue patient on therapy during follow-up period
- Telephone pre-screen:
  - DSM opioid use disorder (abuse/dependence)
  - Items suggestive of pseudo-addiction
- Baseline assessment:
  - Pain
  - Other medical
  - Substance abuse
  - Psychiatric/psychological

Inclusion/Exclusion Criteria

- Pain:
  - ≥ 6 months duration
  - Constant vs. intermittent pain
  - Moderate-severe intensity (VAS ≥7-10)
  - Diagnosis that responds to opioid therapy
  - No headache/facial or cancer pain
- Addiction:
  - ≥ 2 AMTBs (“PROBLEMS WITH PAIN MEDS”)
  - SCID diagnosed opioid use disorder (abuse or dependence)
  - No other current substance dependence (lifetime dependence/ current abuse permissible)
- Psychiatric Disorders:
  - No unstable major psychiatric disorder
  - No current suicidal/homicidal ideation
- Medical Disorders:
  - No unstable medical condition
  - Not taking medications that interact with methadone
  - No planned surgery within 6 months

2 Behavioral Interventions

- "Adherence Therapy" (AT):
  - Education (pain, methadone as analgesic)
  - Pill counts
  - UA (Rapid Tests and GCMS)
  - Supportive counseling style
  - 15-20 minutes
- "Motivational Adherence Therapy" (MAT):
  - AT package
  - Optional family session
  - CBT strategies (decisional balance, behavioral analysis of slips, goal setting)
  - Self-monitoring (pain/medication diary)
  - MI counseling style (OARS)
  - 45-50 minute sessions

Methadone Therapy (MT)

- Pharmacotherapy:
  - Convert all opioids to methadone
  - Q6h “regular” dosing
  - 3-5mg “rescue” doses
  - Dose titration “to effect” (decreased pain in absence of signs of abuse/intoxication)
  - Monitoring of therapeutic and adverse effects (checklist)
  - Dose “stabilization” (dose levels off with breakthrough meds used sparingly)
  - Taper (as indicated)
- Adherence interventions:
  - Supportive counseling
  - Methadone education
  - Opioid contract (execution and enforcement)
  - Review of pill counts
  - Review of UA results
  - Communication with behavioral therapist (“MD Feedback Form”)
  - Communication with other providers
  - Joint session with therapist

Design

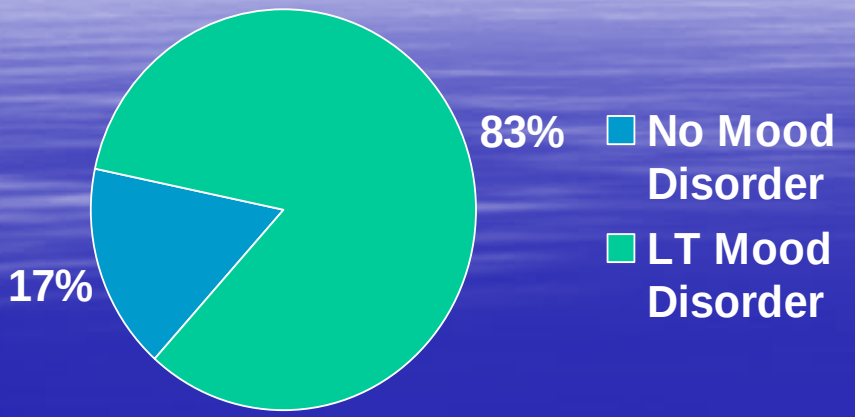
- Treatment schedule:
  - 8 back-to-back medical/counseling visits (Wks 1-5, 7, 9, & 12)
  - “Stabilization” visits during wks 1-3 (vitals, UA, pill counts)
- Assessment schedule:
  - BL, Visits 1-8, 3-month FU
  - Structured clinical interviews, computer administered questionnaires, VAS pain/functioning scales
  - UA (Rapid & GCMS)
- Outcomes algorithm (maintain vs. taper)
  - Pain (P)
  - Functional Interference (F)
  - Opioid adherence (OA)
  - Alcohol and other drug (AOD)
- Transferred back to referring MD
- Support to provider to continue prescribing regiment during the 3-month follow-up period

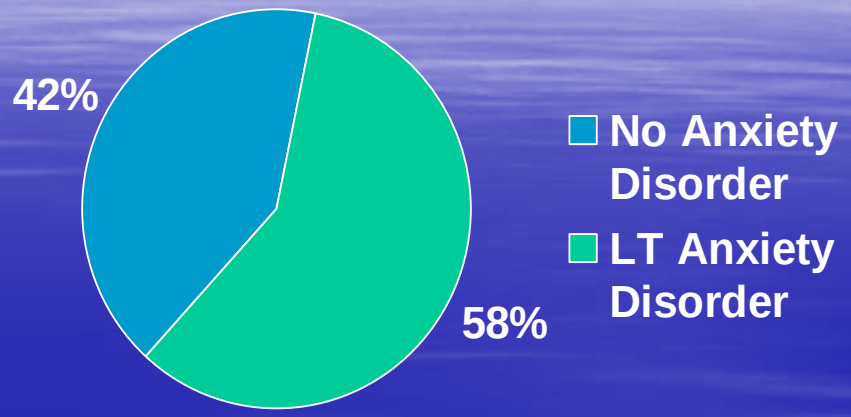
Participants

- 36 randomized participants (25 “completers”)
- Demographics:
  - M = 42.8 yrs (SD=10.0); range: 23-64
  - 57% male
  - 83% White, 11% Black, 6% Hispanic
  - 83% HS or equivalent; 17% > HS
  - 78% disabled/unemployed
  - 36% married/partnered
- Pain characteristics:
  - Duration: M=8.9 years (SD=8.2)
  - Intensity (10-point VAS):
    - Worst pain M=9.0 (SD=1.1)
    - Typical pain M=7.1 (SD=1.7)
    - Least pain M = 4.8 (SD = 2.75)
  - Functional interference:
    - General activity M=7.6 (SD=2.4), Mood M=7.2 (SD=2.4), Work M=8.5 (SD=2.1), Sleep M=7.9 (SD=2.1), Life enjoyment M=8.4 (SD=2.0)

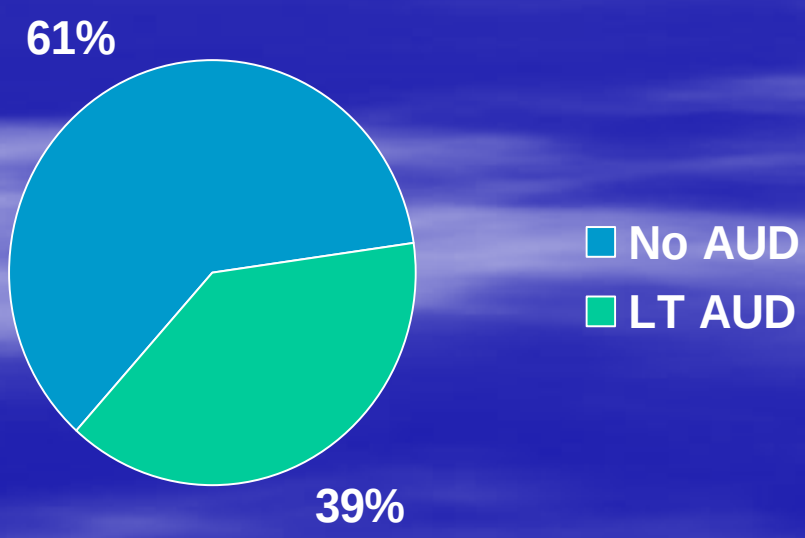
Co-Morbidity (SCID)

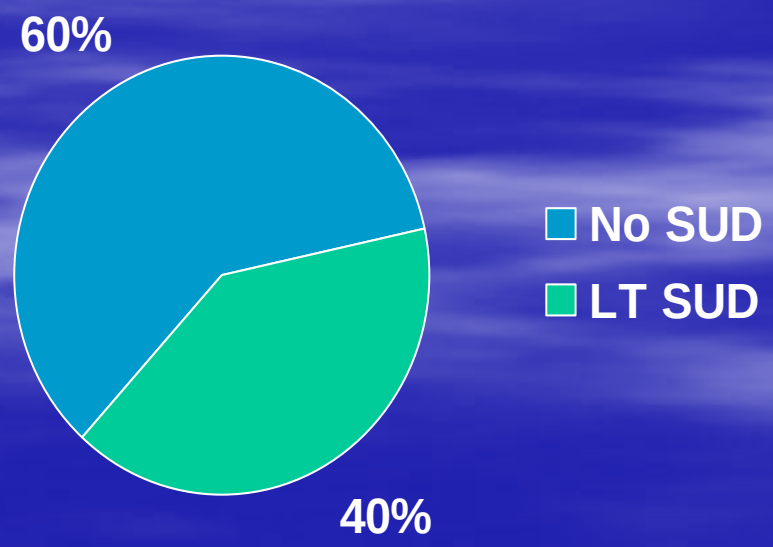
- High prevalence of mood and anxiety disorders





- High prevalence of AOD disorders





Feasibility: Can we Detect Pain Patients with Rx OUDs?

- "PROBLEMS WITH PAIN MEDS" (PPM)
- 6 Experts generated items characterizing patients with this co-morbidity
- Items with multiple mentions included on scale (N = 48)
- Items assigned to 1 of 5 content scales:
  - Mental preoccupation with drug
  - Misuse of drug
  - Behavior problems associated with drug use
  - Illegal behavior; and
  - Concerns of others' (family, doctors etc.)
- Scale to be factor analyzed once sufficient data have been collected

"PPM" Sensitive Detection Tool

- Of 62 patients with PPM scores ≥2, 92% had a current Rx OUD (28% abuse & 72% dependence)
- Item endorsement rates similar for patients and doctors (N = 25 pairs):
  - 0-64% for patients (M = 10.6; SD = 8.4)
  - 4-48% for providers (M = 9.5; SD = 8.4)
- However, patients and doctors see the problem differently:
  - Only fair-poor agreement about AMTBs (KAPPA values = - .29 to 0.69)
  - Patients more concerned about efficacy and access
  - Doctors more concerned about bad behavior

Endorsement of AMBTs on PPM Checklist.

Item	Patient % Endorsement	Provider % Endorsement
Misuse of Drug Subscale		
Has increased dose without permission from doctor	64%	48%
Frequently requests more or stronger meds	40%	36%
Uses more medication than is warranted given problem	20%	32%
Takes opioid pain medication, even though relief is minimal	64%	20%
Uses pain meds to treat problems other than pain	36%	24%
Uses despite side effects	44%	4%
Mental Preoccupation Subscale		
Has expressed concern about own use of pain medication	52%	32%
Is overly concerned about access to pain medication	32%	44%
Admits use of pain medication is “out of control”	28%	36%
Others’ Concerns Subscale		
Feels treated like “addict” by providers	52%	32%
Family members/friends complain about use of pain meds	32%	8%
Behavioral Difficulties Subscale		
Argues w/providers about use of pain meds	36%	40%
Uses pain medication that is not authorized by treating doctor	32%	28%
Manipulates provider to get pain medication	12%	40%
Has more than one prescriber of pain medication	16%	40%
Goes to ER to obtain pain medication	20%	40%
Illegal Behavior Subscale		
Uses recreational drugs	28%	32%
Borrows pain medication from someone else	44%	8%

*** Pink items in top 25% endorsed by both patients and providers; Green items most endorsed**

Feasibility: Will Pain Patients Participate in an Opioid Adherence Trial?

- Many patients tried to get into trial without a pain clinic referral
- Numerous calls based on CRISP listing
- Of 40 appropriately referred patients who met inclusion/exclusion criteria, 90% enrolled
- Likely reasons for high interest:
  - Alternative to detoxification/discharge from pain clinic
  - Unable to access adequate pain medication

Feasibility: Can the interventions be delivered as envisioned?

- MAT-TACS fidelity tool
  - Adherence (to what extent did they follow the manual?)
  - Competence (how well did they execute?)
  - Multiple domains (e.g., adherence interventions, MI, CBT, med management, proscribed behaviors)
- Sessions taped/rated by independent raters
- Cronbach's standardized alpha values > .70, demonstrating acceptable internal consistency reliability (Nunnally, 1978)
  - .71 for the Adherence Subscale
  - .74 for the Competence Subscale
- Clinical supervision of both MD and therapist interventions to improve competence/adherence

Acceptability: How well Do Patients Like the Treatment

- 58% in “PREPARATION” Stage of Change at BL
- M = 6.5/8 sessions attended
- 70% of randomized patients attended all 8 sessions
- 11 non-completers
  - 4 dropouts (11%)
  - 2 deaths (1 study related polydrug OD)
  - 5 discontinued by researchers
- No differences in completion rates for MAT vs. AT

Acceptability: Satisfaction

- "Satisfaction with Services Questionnaire" (N = 24)
- Items with highest endorsement rates (5-point Likert):
  - "The program motivated me to change how I use pain medicine" (4.20/.82)
  - "I plan to continue practicing what I learned in this program" (3.92/.86)
  - "My ability to manage pain medicine has improved as a result of being in this program" (3.85/1.33)
  - "The medication I was given relieved my pain" (3.77/1.09)
- Items with the lowest endorsement rates were:
  - "Signing a contract helped me stick with the program" (2.77/ 1.17)
  - "Having my urine tested on a regular basis was helpful" (2.92/ 1.55)
- Even the least popular elements of the interventions (i.e., drug screens and contracts) were well-tolerated.

Acceptability: Satisfaction (2)

- No differences on SSQ for patients in AT/MT vs. MAT/MT [$F(3,20)=0.2$, $p=1.0$]
- However, significant differences in SSQ scores for successful vs. non-successful patients [$F(3,20)=16.0$, $p<.05$].
- Successful patients rated the following domains higher:
  - Program structure (duration, intensity etc.)
  - Treatment content
  - Efficacy of methadone as an analgesic
  - Attitude of medical and counseling staff
  - Helpfulness of monitoring strategies
- Successful patients also reported:
  - Better understanding of their problem
  - Better outlook on life
  - Greater improvements in functioning
  - Greater confidence in their ability to manage pain medication

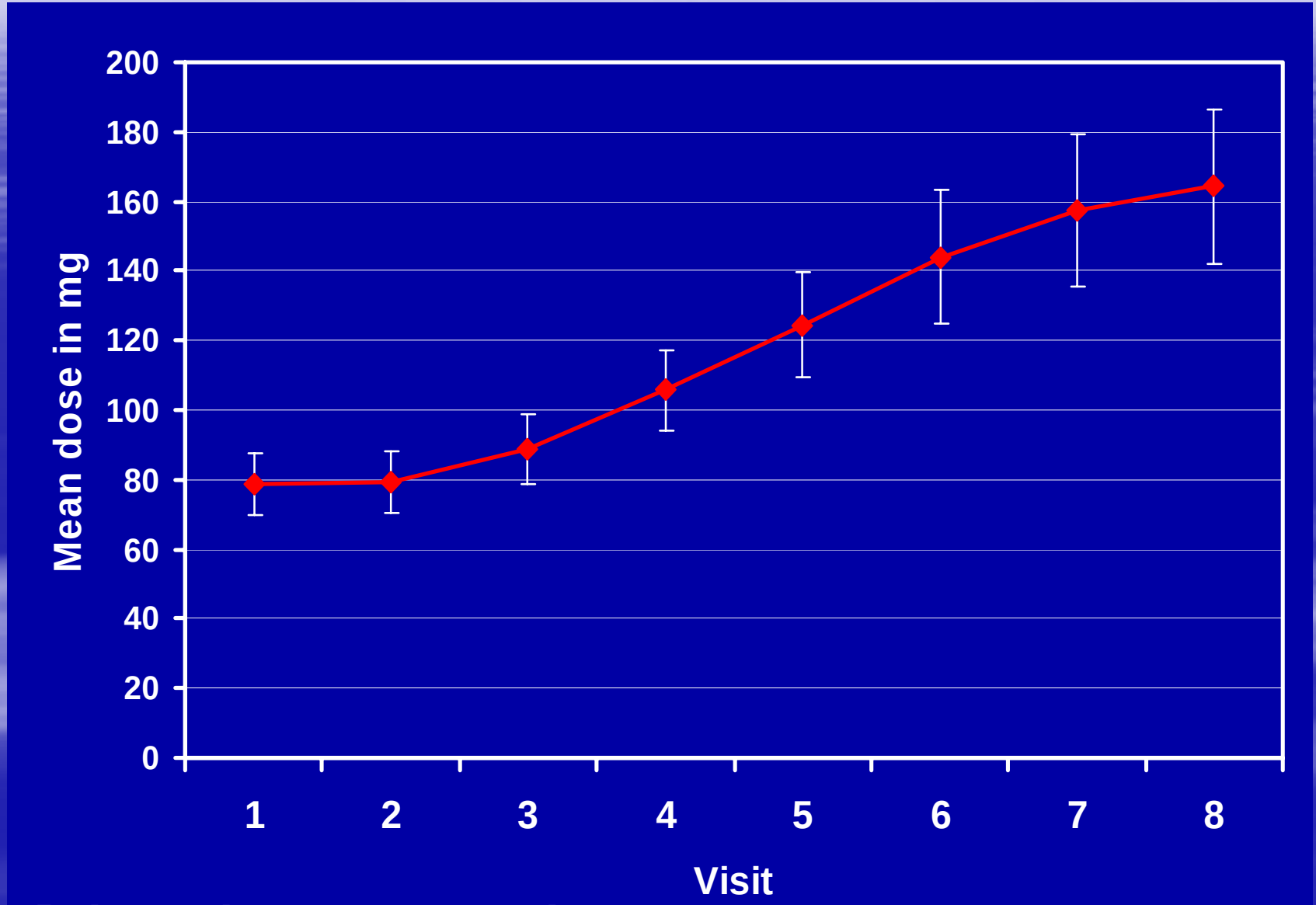
Acceptability: Alliance

- Therapeutic alliance predicts retention and outcome
- Haq-II given to patients and therapists at each visit
- High scores across treatment groups and sessions
- For patients, alliance grew significantly over time [Session 1 M = 96.9, SD = 8.3; Session 8 M = 101.3, SD = 11.5; $F(7,119) = 3.0$, $p < .01$]
  - Alliance was not impacted by treatment group or outcome.
- For therapists, an interaction was observed between time and treatment outcome [$F(7,119) = 6.5$, $p < .01$];
  - For treatment failures, alliance ratings did not change over time
  - For treatment successes, alliance ratings increased over time, with significant increases from baseline seen in sessions 4-8
- Surprisingly, neither patient nor therapist alliance scores were correlated with VAS ratings of pain or functioning

Promise: Primary Outcomes

- Opioid dose increased significantly
- Pain (P) VAS scores decreased significantly
  - "worst" (8.9 to 6.4; $p < .001$)
  - "typical" (7.2 to 4.0; $p < .001$)
  - "least" pain (5.6 to 2.7; $p < .001$)
- Functional interference (F) VAS scores decreased significantly (all p's < .01)
  - activity, mood, work, relationships, sleep, life enjoyment, concentration, and appetite
- Opioid adherence (OA) increased substantially
  - 78% of patients met criteria for opioid maintenance; 22% required taper
- Non-methadone opioid use decreased significantly
- Trends toward decrease AOD use

Total Daily Methadone Dose



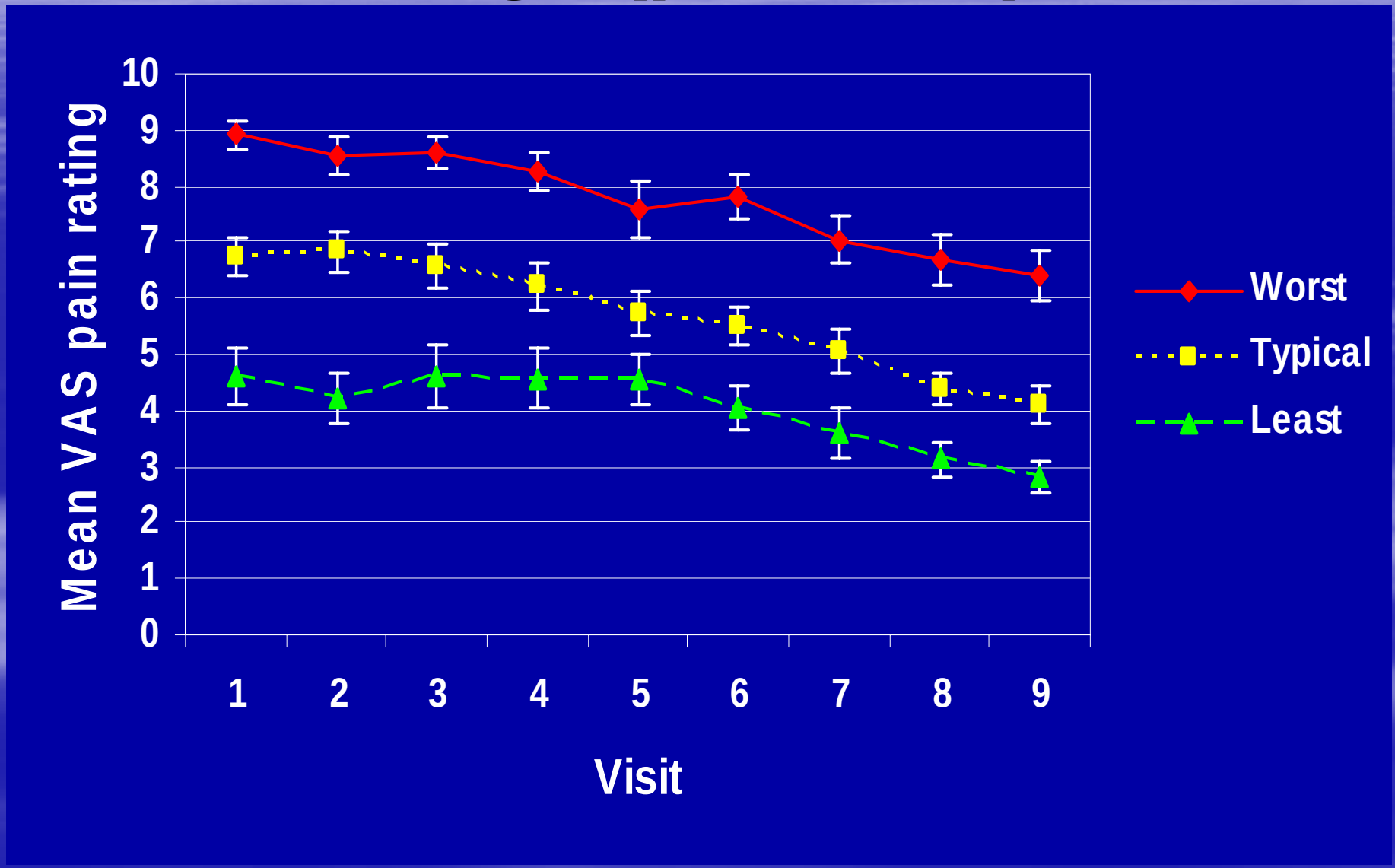
[F(7,126)=15.7, p < .01)

Pre-Post Treatment Effect Sizes

Pain	η2 – MAT/MT	Rank	η2 – AT/MT	Rank
Worst Pain	0.40		0.33	
Least Pain	0.30		0.24	
Typical Pain	0.48	#4	0.38	#3
Functioning				
Activity Level	0.47	#5	0.31	#4
Mood	0.60	#2	0.30	#5
Walking	0.45		0.21	
Relationships	0.16		0.24	
Sleep	0.49	#3	0.44	#2
Concentration	0.37		0.18	
Appetite	0.23		0.12	
Life Enjoyment	0.68 #	#1	0.45	#1

Eta squared values range from 0-1 and represent the % variance accounted for
For Eta squared effect sizes, small = .01; medium = .06; and large = .14

Decreases in VAS Pain Ratings (p's < .01)

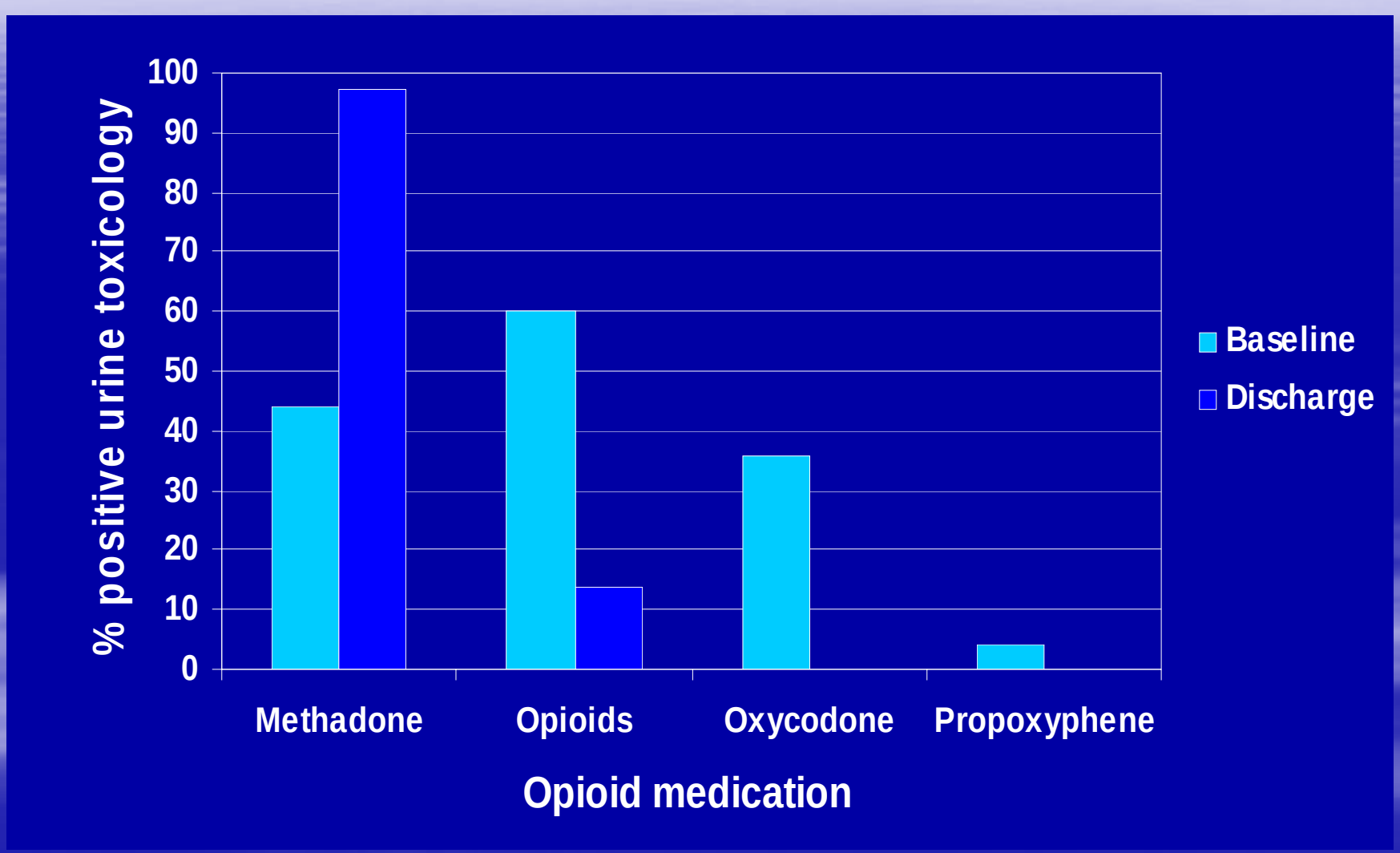


Decreases in 10-Point VAS Functional Interference Ratings

Domain	Change Scores (SD)
General Activity	-3.0(3.2)
Mood	-3.3(3.2)
Walking	-2.4(2.5)
Work Routine	-3.6(2.8)
Relationships	-2.2(3.3)
Sleep	-4.1(2.6)
Concentration	-2.8(3.0)
Appetite	-2.6(3.9)
Life Enjoyment	-4.3(3.0)

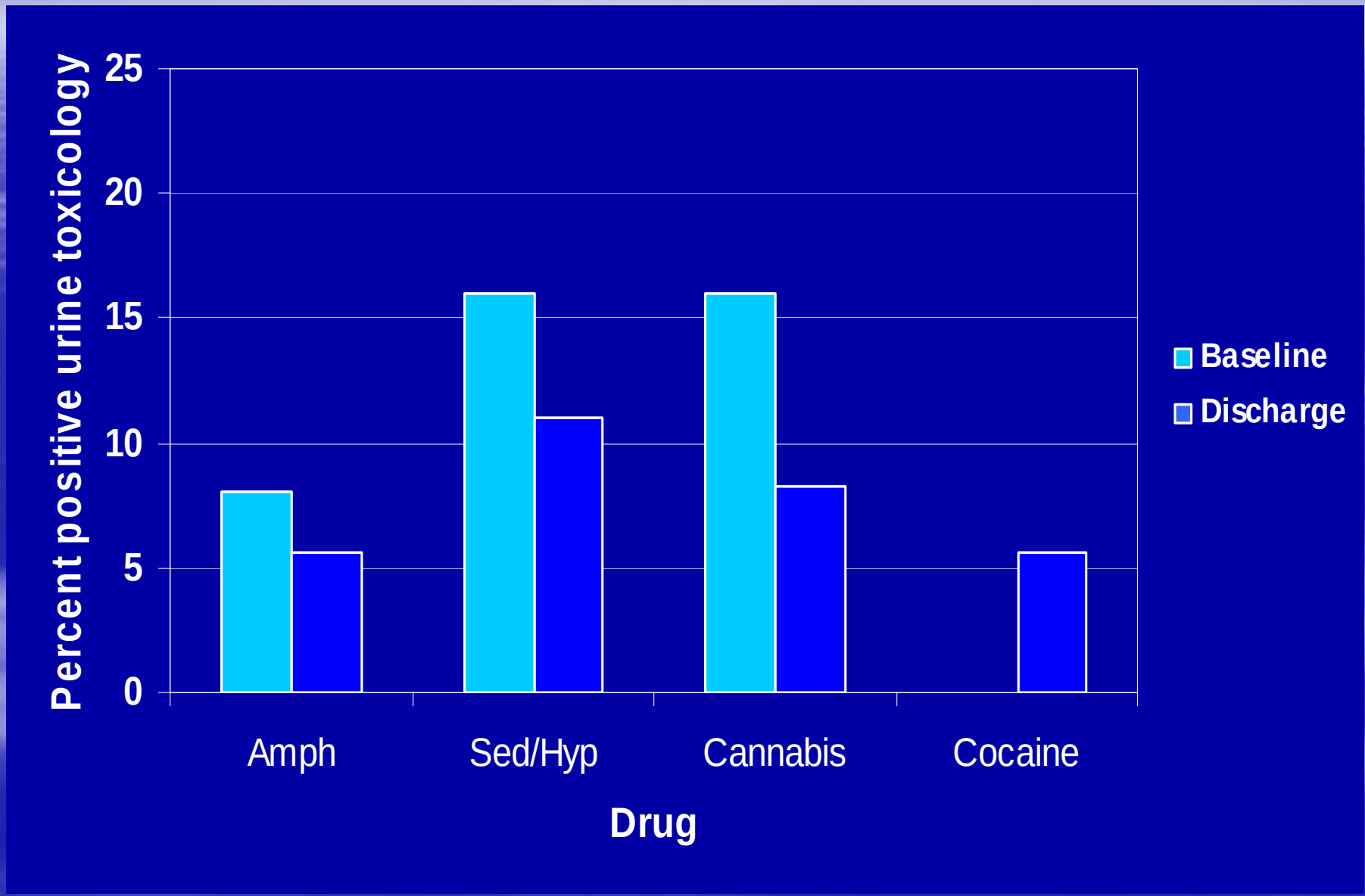
All p's < .01

Changes in Opioid Use**



For methadone, opioids, and oxycodone p's < .01

Trends in AOD Use

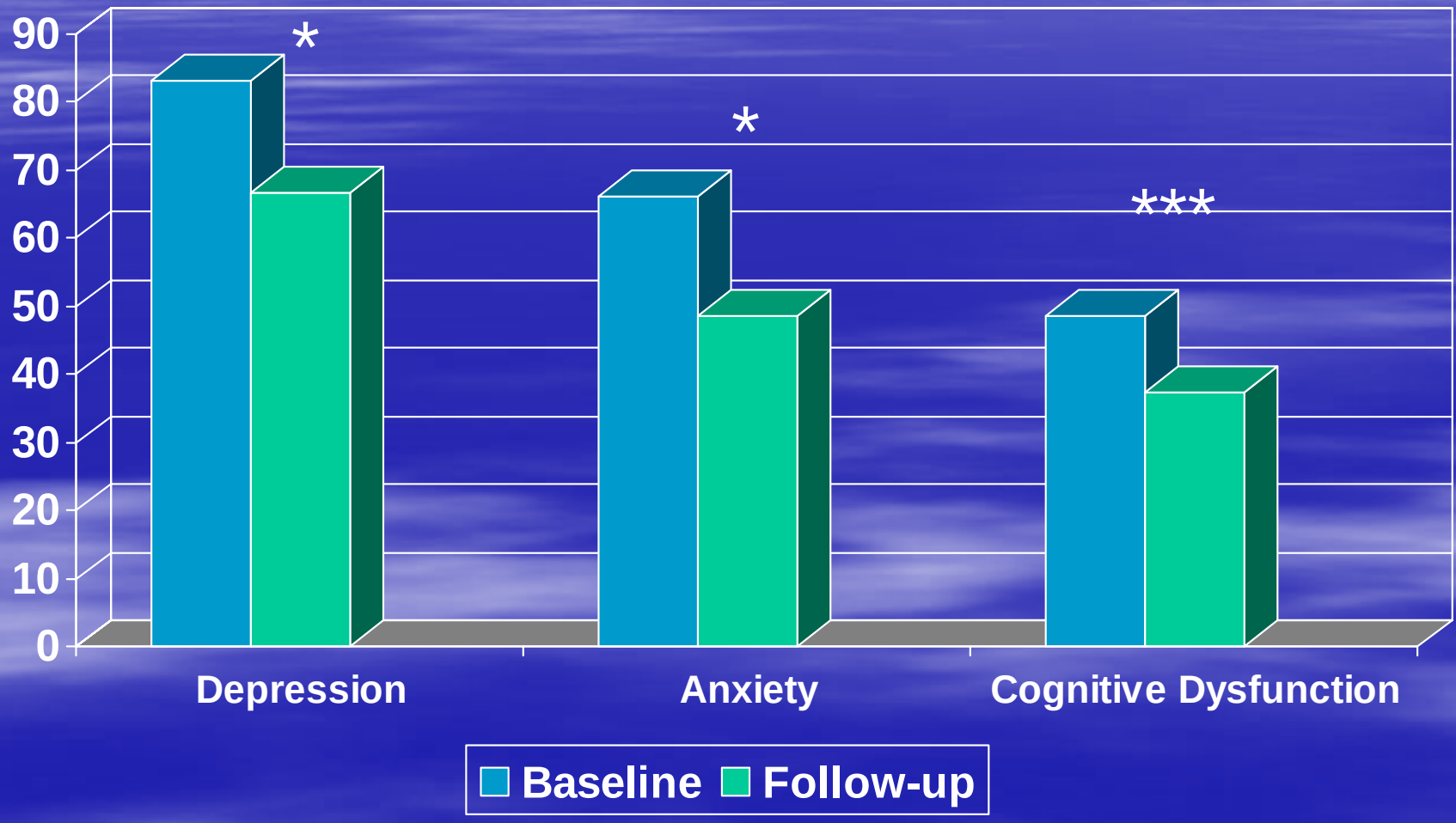


3-Month Follow-Up Outcomes

Outcome Domain	Measure	Variable	BL Scores (M; SD)	FU Scores (M; SD)
Pain	MPI	Pain Severity	52.1 (9.14)	42.7 (15.0)***
Functioning	MBMD	Functional Deficits	84.3 (13.2)	78.7 (23.8)
	MPI	Interference	50.1 (7.3)	39.2 (12.5)***
		Life Control	46.6 (6.5)	53.7 (9.1)***
		Affective Distress	50.4 (8.2)	41.1 (10.8)**
Adherence	MBMD	Utilization Excess	65.4 (25.5)	64.5 (18.1)*
		Problematic Compliance	44.1 (23.8)	57.4 (23.0)
		Intervention Fragility	59.8 (24.8)	46.4 (17.7)**
		Medication Abuse	68.1 (18.1)	54.2 (22.9)*

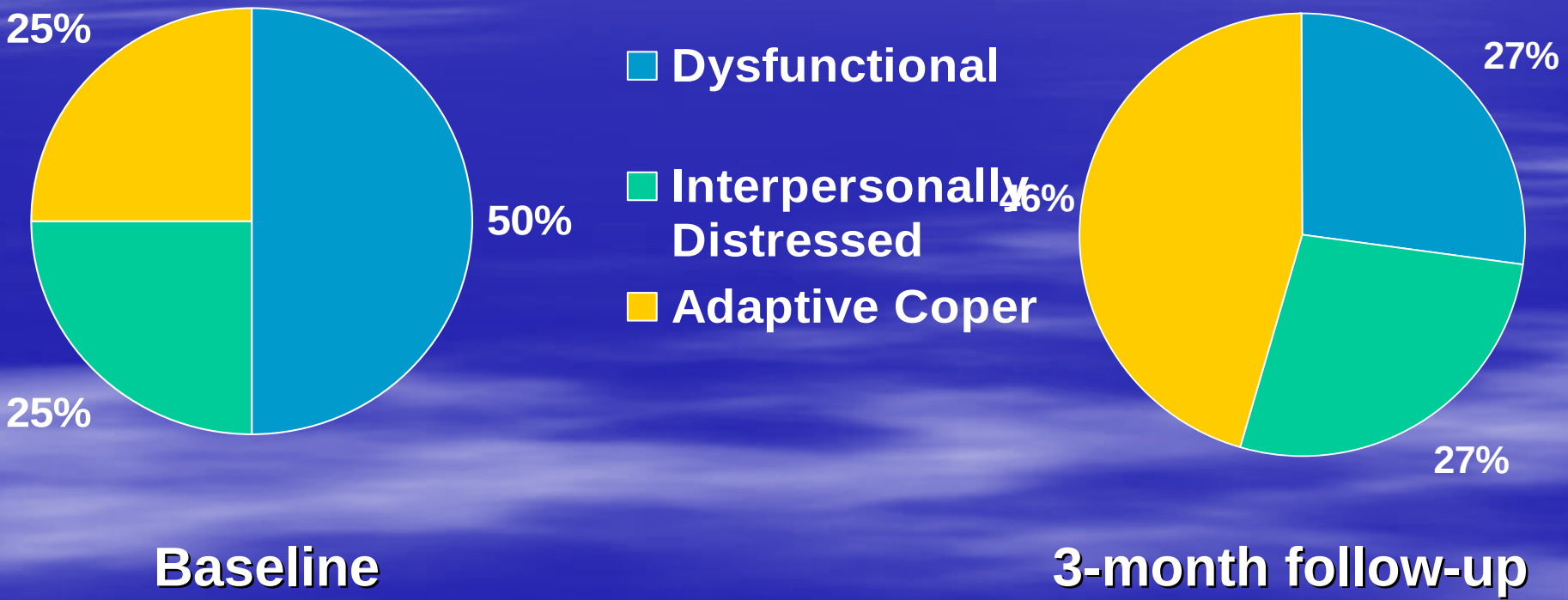
* p < .10; ** p < .05; *** p < .01

Improved Psychological Functioning (MBMD)



* P < .05; ** p < .01; *** p < .001

MPI Pain "Types" ($\chi^2=11.1$, $p<.05$)



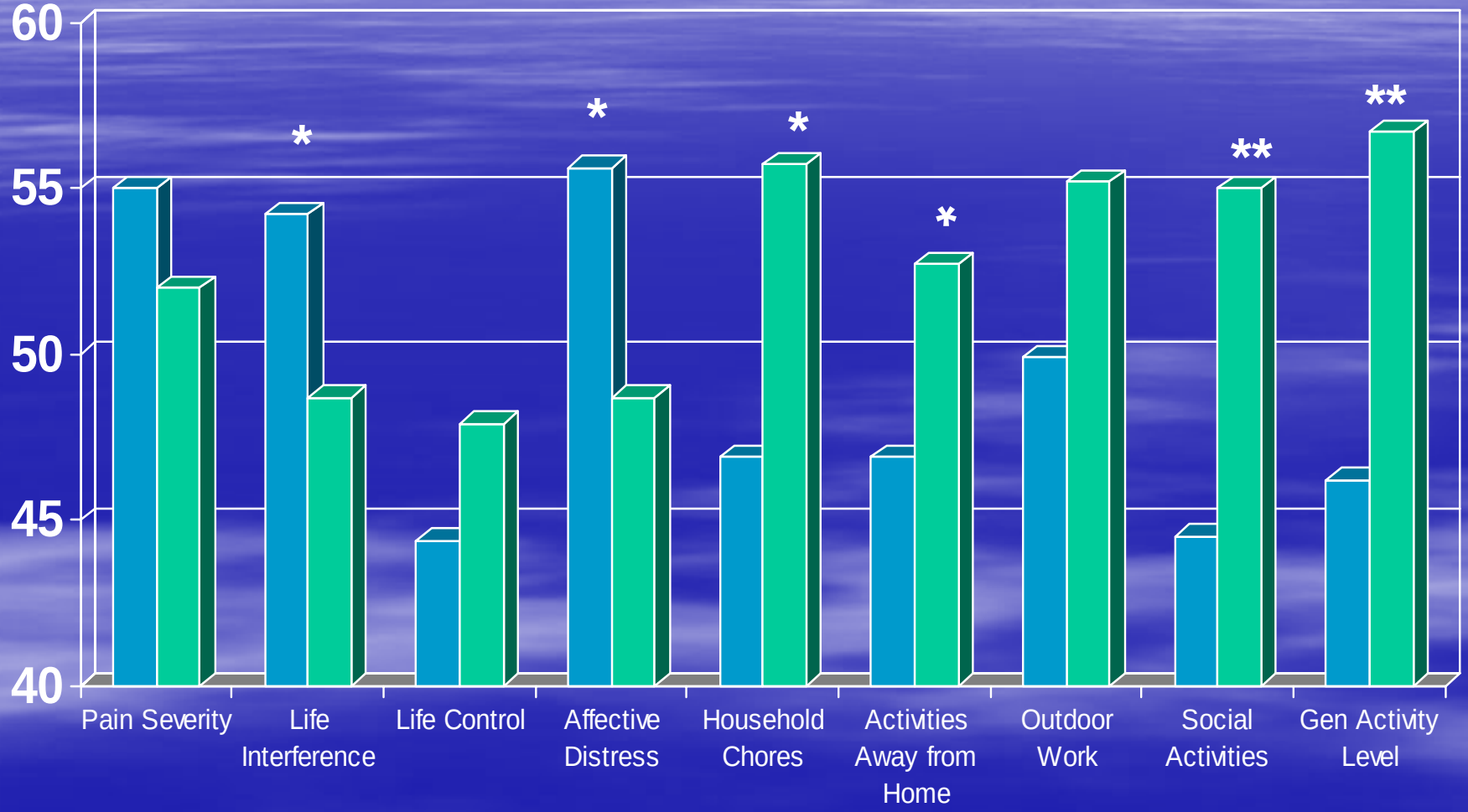
Impact of Personality and Psychopathology on Outcome

… do individual factors
make a difference?

Personality

- NEO-FFI assesses “Big 5” personality factors: neuroticism (N), agreeableness (A), openness (O), extroversion (E), and conscientiousness (C)
- M = 50; SD = 10
- More deviant scores “align” with personality disorders
- Consistent with pain and addiction literature, patients scored high on N (M= 60/10.26) and relatively low on C (M= 42/10.11)
- Cluster analysis produced 2 subgroups
- Cluster 1 (41%); Neurotic/Introverted/Non-Conscientious)
- Cluster 2 (59%); Normal personality traits

MPI Functioning by Personality Type



* < .05; ** < .01

Personality and Treatment Outcomes

- Trend towards higher completion rate for patients with normal personality characteristics (p = .11)
  - 47% of Cluster 1 vs. 71% of Cluster 2
- No differences in success rate for patients who complete treatment (p = .35)
  - 88% of Cluster 1 vs. 71% of Cluster 2
- Greater effort should be expended to "engage" these difficult, poorly related patients

Impact of AOD Co-Morbidity

- Treatment completion was not associated with AOD (lifetime/current)
- However, AOD patients had lower success rates compared to those without other substance abuse problems
- ETOH (chi-square = 6.2, p<.01)
  - 93% without ETOH diagnosis were successful
  - 50% with an AUD successful
- Drug chi-square =7.2, p<.01
  - 93% without a lifetime/current DUD successful
  - 44% with a DUD disorder
- While the majority of patients with AOD co-morbidity had successful outcomes in this pilot study, about ½ of those with co-morbid AOD still did well
- Interventions may need to be “enhanced” to better address AOD involvement

Impact of Co-Morbidity

- Pts with current mood disorders had lower treatment completion rates (47%) compared to those with either lifetime (100%) or no (80%) mood disorder ($p < .05$)
- Pts with current anxiety disorders had lower completion rates (43%) compared to those with either lifetime (86%) or no (86%) anxiety disorder ($p < .05$)
- However, neither mood nor anxiety disorder was associated with “success” at Wk 12

Summary of Pilot Findings

- **Feasibility:**
  - PPM score ≥ 2 successfully ID'd patients with Rx OUDs
  - Identified patients enrolled
  - Interventions delivered with fidelity
- **Acceptability:**
  - Low "drop out" rate
  - Patients expressed satisfaction with services
  - Patients and clinicians developed a strong working alliance
- **Promise:**
  - Pain decreased and functioning increased
  - Opioid adherence increased
  - Trend toward decreased other drug use (not targeted)

Summary (cont.)

- Methadone very effective in treating pain while also curbing unauthorized opioid use
- Stabilization dose similar to that used to treat addiction, while treating 2 problems concurrently
- Despite slow onset of action, methadone was effective as breakthrough medication
- Patients required double the starting dose to experience pain relief, indicating substantial under-treatment even in highly respected pain management programs
- Once stabilized, use of breakthrough meds minimal
- Patients with co-occurring substance use disorders had poorer outcomes
- Patients with troublesome personality traits and co-occurring psychiatric disorders were harder to retain, but did well if retained

Proposed Future Directions

- Continue to refine and test the PROJECT PAIN interventions in “real world” settings:
  - Columbia Pain Management Center
    - Interventions delivered by anesthesiology staff, not addictions experts
    - Compare combined intervention with pharmacotherapy as “stand alone” intervention
  - Beth Israel/St. Luke’s-Roosevelt MMTPs
    - Interventions delivered by MMTP staff
    - Compare combined intervention with pharmacotherapy as “stand alone” intervention
    - Determine feasibility of divided dose methadone to treat pain and addiction concurrently

Thanks to my Collaborators

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  - Michael Weinberger, MD
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