



COLUMBIA UNIVERSITY

*College of Physicians
and Surgeons*

Helping physicians diagnose and treat addiction to prescription drugs

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Clinical Pharmacology

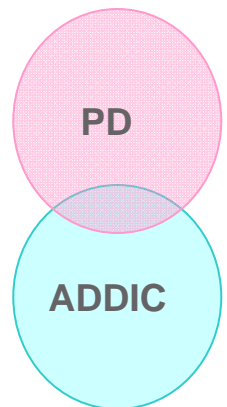
- ❖ Leading medication classes with addictive potential include:
 - ➔ Analgesics (opiates)
 - ➔ Sedative-hypnotics/anxiolytics (barbiturates, benzodiazepines)
 - ➔ Psychostimulants (ADHD, weight loss, sleepiness): amphetamines, MPH
- ❖ These medications are well-tolerated and highly effective and therefore have been widely prescribed BUT a small proportion of patients develop excessive/compulsive use (addiction)
- ❖ Adverse behavioral effect profile stimulated the development of new compounds
 - ➔ Better therapeutic index
 - ➔ More selective pharmacological effects
- ❖ It has been almost impossible to separate the primary pharmacological effect from adverse behavioral effects (abuse liability)

Behavioral Pathology Associated with Rx Drugs

- ❖ **Misuse:** use to achieve intoxication or for non-target effects
- ❖ **Abuse:** use leading to harmful effects/problems (accidents, arrests, family conflicts, missing work)
- ❖ **Addiction**
 - the escalation of drug use at the expense of other, personally and societally beneficial activities
 - use continues despite significant negative consequences
 - loss of control in limiting drug intake

Physiological Dependence

- ❖ Chronic exposure can produce neuroadaptations responsible for tolerance/physiological dependence/withdrawal, which happens with many medications
- ❖ Physiological dependence can create management problems BUT should not be confused with addiction
- ❖ Physiological dependence is probably not a significant factor determining development of compulsive drug use
- ❖ Strategies to prevent physiological dependence:
 - ➔ aggressive short-term treatment
 - ➔ using medications on “as needed” rather than on continuous basis
 - ➔ implementing drug “holidays”
- ❖ Unclear if prevention of physiological dependence would alter the risk of developing compulsive use



Prescribing medications with abuse potential

- ❖ Addiction is an adverse effect of medication, responsibility for preventing and managing it falls on the prescribing physician BUT this is not a part of medical training, additional expertise is required
- ❖ An assessment of abuse liability in the specific patient has to be determined before and while medication is prescribed
- ❖ All patients prescribed potentially addictive medications should be assessed at each visit for signs of misuse, abuse, or dependence
- ❖ Screening using non-threatening questioning and toxicology should be a part of regular medical checkups

Assessment: identifying high-risk individuals

- ❖ Many individuals at risk (e.g., psychiatric or addiction patients) are already in treatment which creates opportunity to prevent problematic use or intervene early
- ❖ Personal history of addiction should raise concerns but is not an absolute contraindication to therapeutic prescribing
- ❖ Positive family history of addiction/alcoholism and a history of neglect/sexual abuse are other risk factors
- ❖ All patients entering addiction treatment should be screened for the use of Rx drugs
- ❖ Positive screening should be followed with specialist evaluation with detailed addiction/psychiatric history, verified by collaterals and toxicology

SOAPP: *Screenener and Opioid Assessment for Pain Patients*

(IN THE PAST 30-DAYS, ...)

1. How often do you have **mood swings**?
2. How often have you felt a need for **higher doses** of medication to treat your pain?
3. How often have you felt **impatient with your doctors**?
4. How often have you felt that things are just too **overwhelming** that you can't handle them?
5. How often is there tension in the home?
6. How often have you **counted pain pills** to see how many are remaining?
7. How often have you been concerned that people will judge you for taking pain medication?
8. How often do you feel **bored**?
9. How often have you taken more pain medication than you were supposed to?
10. How often have you worried about being left alone?
11. How often have you felt a **craving for medication**?
12. How often have **others expressed concern** over your use of medication?
13. How often have any of your close friends had a problem with alcohol or drugs?
14. How often have others told you that you had a **bad temper**?
15. How often have you felt consumed by the need to get pain medication?
16. How often have you **run out** of pain medication early?
17. How often have others kept you from getting what you deserve?
18. How often, in your lifetime, have you had legal problems or been arrested?
19. How often have you attended an AA or NA meeting?
20. How often have you been in an argument that was so **out of control** that someone got hurt?
21. How often have you been sexually abused?
22. How often have others suggested that you have a drug or alcohol problem?
23. How often have you had to **borrow pain medications** from your family or friends?
24. How often have you been **treated for an alcohol or drug problem**?

Scored on a scale 0-4

0-never

4-very often

HIGH-RISK >18

Management plan for high-risk individuals

- ❖ Stratification based on the level of risk
- ❖ Close monitoring of medication taking
- ❖ Treatment of co-occurring psychiatric disorders

Prescribing in **low-risk** group

Distant history (>20yrs) of drug/alcohol dependence, no current use

❁ Brief office intervention

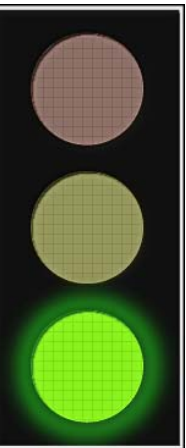
- Advise of the risk of combining Rx medication with other substances
- Warn about diversion and abuse liability

❁ Adjust prescribing practice

- Use safer medications (slower onset of action, longer-acting), or more selective agents
- Prescribe small quantities at a time, institute pill count

❁ Ongoing, close monitoring

- Monitor clinical response of primary target (pain, anxiety, attention problems)
- Monitor for adverse effects and for indications of inappropriate use
- Monitor use/misuse pattern
- Random urine toxicology/breath alcohol testing





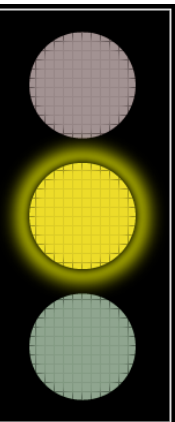
RED flags for misuse or diversion

- ❖ Symptoms of intoxication or withdrawal with the primary Rx medication or any other psychoactive substance
- ❖ Demands for a particular, usually fast acting, medication (alprazolam, amphetamine IR, morphine im)
- ❖ Repeated lost prescriptions
- ❖ Discordant pill count
- ❖ Excessive preoccupation with securing medication supply

Prescribing in moderate-risk group

Recent history (>2 yrs) of drug/alcohol dependence, some current use/misuse but no disorder

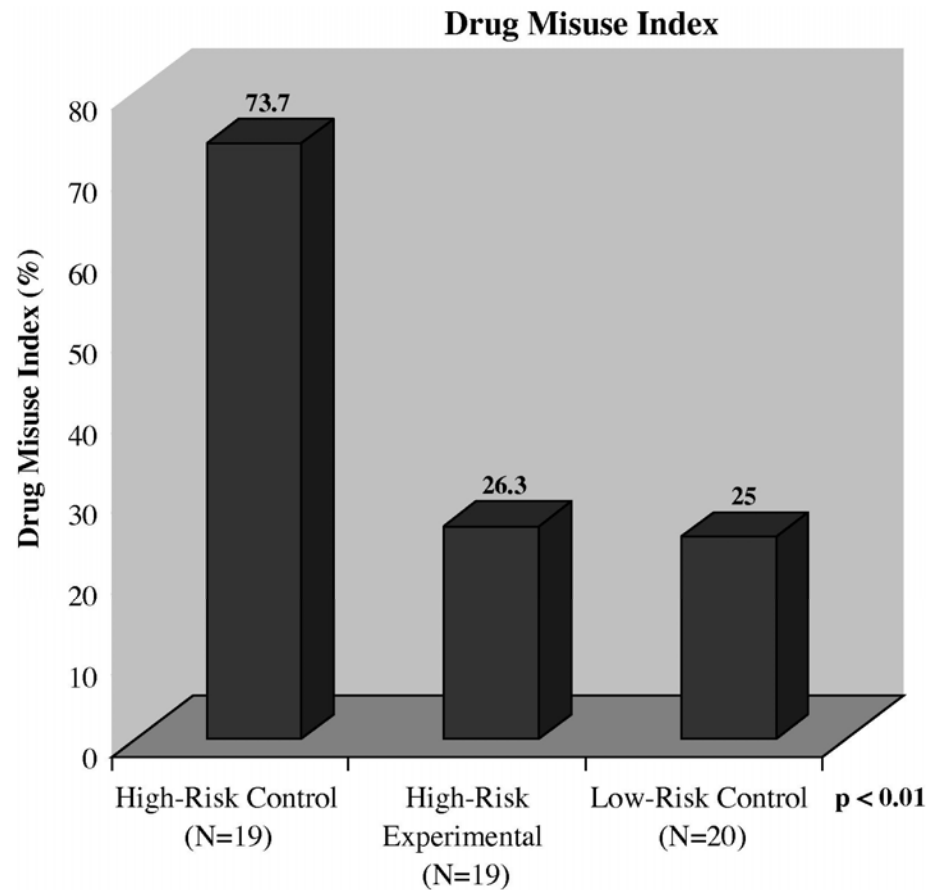
- ❁ Consider trial of agents with minimal/low abuse liability
 - ⊖ SSRI, anticonvulsants, atomoxetine, bupropion, butorphanol, tramadol
- ❁ If inadequate clinical response, consider a brief trial of agents with greater abuse liability
 - ⊖ Include strategies for low-risk group
 - ⊖ More frequent office visits (2-4/month) to have closer monitoring of problematic use, other drugs/alcohol use
- ❁ Involve family/spouse/friends if clinically indicated
- ❁ Implement behavioral strategies aimed at reducing risk of abuse
 - ⊖ Psychoeducation on Rx drugs abuse
 - ⊖ Enhancing motivation to abstain from drugs/alcohol
 - ⊖ Coping with urges to misuse Rx medications
 - ⊖ Problem solving/skills to manage “triggers” and high-risk situations
 - ⊖ Lifestyle changes/balance (increasing non-drug rewarding activities)



Experimental validation of management strategy

- Close monitoring and behavioral interventions in moderate-risk group led to similar outcomes as for low-risk group (6 mos)

- monthly urine screens
- compliance checklist
- group motivat. counselling

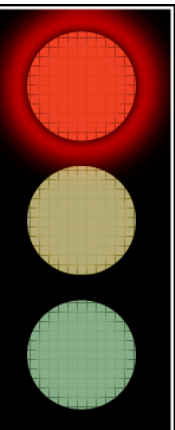


Jamison et al., 2010)

Prescribing in **high-risk** group

Current drug/alcohol use disorder

- ❖ Treatment of Rx drugs with abuse liability (opiates, benzos, stimulants) represent safety risk as it can further destabilize patient
- ❖ Emphasis should be on treating ongoing substance use disorders
 - ➔ Consider initiation of treatment in inpatient/residential setting (e.g., detox)
- ❖ Provide treatment of underlying psychiatric problems with agents without abuse liability
- ❖ If patient stabilizes and can be considered to be of moderate or low risk, can re-consider treatment with Rx drugs



Treatment of Sedative-Hypnotic Dependence

- ❖ S-H dependence is uncommon in the general population, but is concentrated among patients with other substance use disorders
- ❖ S-H dependence may, in part, represent self-medication of a co-occurring psychiatric disorder
- ❖ Slow, gradual taper and possibly adjunctive agents, is indicated when therapeutic goal is abstinence
 - ➔ Transition to equiv. dose of long-acting agent (clonazepam, chlordiazepoxide)
 - ➔ Gradual dose decreases interspersed with long periods of stabilization
 - ➔ Final taper with the use of adjunctive agents (valproate, imipramine, quetiapine) and behavioral/therapy techniques (relaxation)
 - ➔ Continuing adjunctive meds and relapse-prevention therapy during early abst.
 - ➔ If failed, consider inpatient rapid detox followed with residential treatment
- ❖ Consider stabilization on an alternative agent with low abuse liability (antidepressant, buspirone, carbamazepine, valproate, gabapentin, quetiapine)

Treatment of Rx Psychostimulant Dependence

- ❖ Rx stimulant misuse is very common, abuse or dependence are rare
- ❖ Switch to a safer stimulant (atomoxetine, bupropion, modafinil) if patient is otherwise motivated to remain in treatment
- ❖ Abrupt discontinuation is relatively safe, though need to monitor mood response (crash)
- ❖ Behavioral methods are mainstay of treatment for stimulant dependence (cocaine, MA) and should be used in these patients
- ❖ Medications that may be useful to prevent relapse include naltrexone or bupropion
- ❖ After period of stabilization off stimulant a tightly controlled trial may be attempted if psychiatric severity is significant

Treatment of RX Opioid Dependence

- ❖ Opioid dependence is a frequent complication of Rx opioid misuse, particularly in patients with co-existing anxiety or depressive disorders
- ❖ Traditional approach: detox followed by abstinence prevention in “drug-free” programs, however relapse rates can be high
- ❖ Alternative approach: detox followed by antagonist maintenance (oral or long-acting naltrexone)
- ❖ Agonist maintenance with methadone is unacceptable to many Rx opioid abusers but buprenorphine/naloxone becomes treatment of choice for many
 - ➔ Short term outpatient detox (7-28 days, equally (in)effective)
 - ➔ Long-term maintenance of buprenorphine becomes and main for of treatment in the US



Opioid Dependence: AGONISTS

- ❖ Very useful in detoxification
- ❖ Maintenance on agonist is a treatment of choice for individuals with a chronic and relapsing course of illness
 - ➔ not the best for newly diagnosed, youth, or Rx opioids abusers
- ❖ Problems:
 - ➔ many continue abusing heroin/cocaine/alcohol during agonist maintenance
 - ➔ relapse rates remain high following cessation of treatment, so it is most effective as a long-term maintenance
- ❖ Controversial perception has not changed, despite many years of clinical use
 - ➔ treatment approach often rejected on cultural and ideological grounds

Opioid Dependence: AGONISTS

❖ Methadone: full agonist

- ⊖ best suited for patients with relapsing course of illness, comorbid psychiatric problems, and limited social support

❖ Buprenorphine: partial agonist

- ⊖ safer in use than methadone but appropriate for less severe/higher functioning patients, painkiller abusers
- ⊖ flexible in use, may have added psychotropic effects
- ⊖ use of buprenorphine is rapidly expanding, so are associated problems (abuse, diversion)
- ⊖ easy to induct on but difficult to discontinue

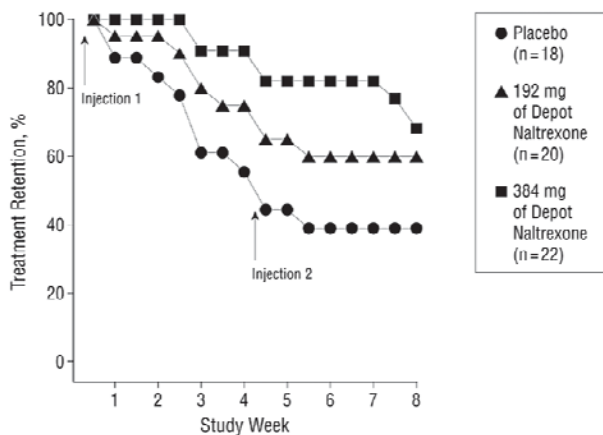
❖ Other agonists: morphine SR, diacetylmorphine IV

Opioid Dependence: ANTAGONISTS

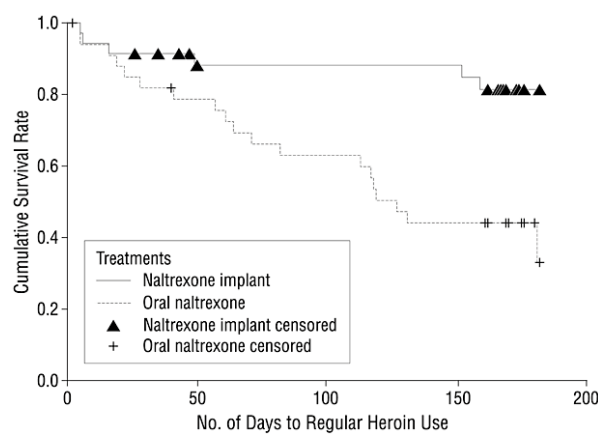
- ❖ Naltrexone is indicated for those who are:
 - not interested in agonists
 - wish to discontinue agonist (high risk of relapse)
 - abstinent but at risk for relapse
- ❖ Incompatible with ongoing use and may produce better long-term outcome (cure?)
- ❖ Appealing to clinicians and public (lawmakers, NA)
- ❖ **BUT:** difficult to use in clinical setting
 - active users require detoxification
 - discomfort persist during first weeks of induction
 - noncompliance with oral preparation is the main challenge
 - works best in combination with a sophisticated behavioral treatment

Opioid Dependence: ANTAGONISTS

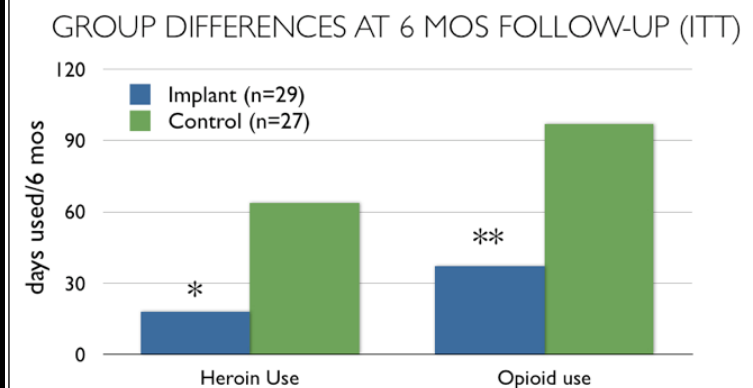
- ❁ Long-acting preparations limit the effect of ambivalence on compliance
 - ➔ VIVITROL™ is once-a month injectable form of NTX
 - ➔ IMPLANTS provide sufficient NTX levels for up to 6 month
 - ➔ most effective to retain in treatment those who use during the first month
- ❁ As compared to BUP, implant has more upfront effort but less treatment episodes, superior retention and minor morbidity



(Comer et al., 2006)



(Hulse et al., 2009)



Improvement on secondary outcomes:
* polysubstance use, ** craving, * life satisfaction

(Kunoe et al., 2009)

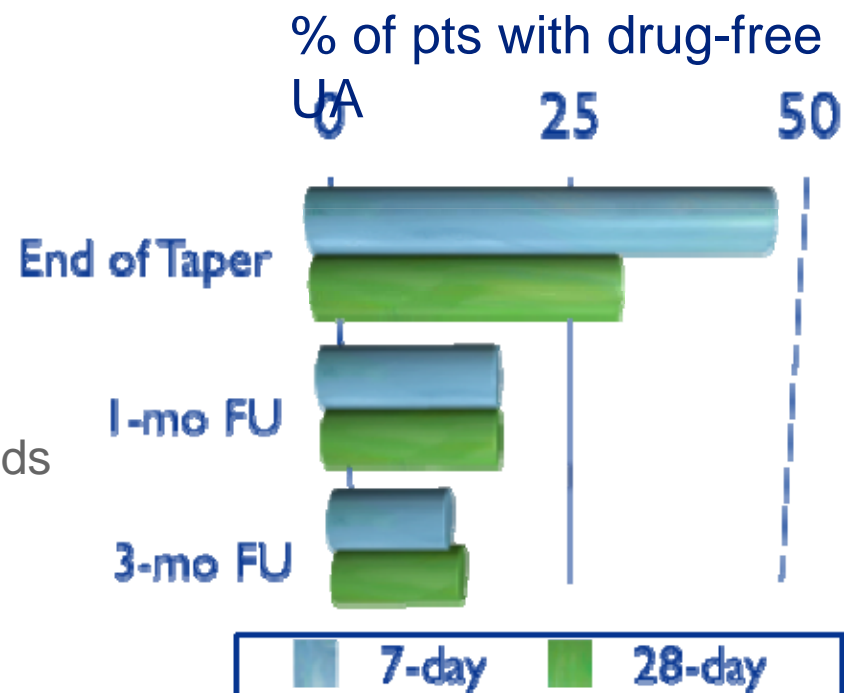
Opioid Dependence: detoxification

Outpatient

- slow (30-d) vs. fast (7-d) taper
- methadone or buprenorphine

Inpatient

- standard method: taper+supportive meds
- rapid method: clonidine/naltrexone
- anesthesia-assisted



(Ling et al., 2009)

Columbia Rapid Detox Protocol

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
Buprenorphine		4 mg bid				
Naltrexone				3 mg	6 mg	25 mg
Supportive medications	clonidine, clonazepam, toradol, ranitidine, zolpidem					