

Treatment of Patients with Drug Addiction and Tuberculosis: New Strategies for the Future Directions

Iván D. Montoya, M.D., M.P.H.

Deputy Director, Division of Pharmacotherapies and
Medical Consequences of Drug Abuse (DPMCDA)

Chair, Addictions IRB (NIDA & NIAAA)



Tuberculosis

- Substance abuse is the most commonly reported **modifiable behavior** impeding TB elimination efforts in the United States.
- Rates of TB remain high among foreign-born, homeless persons, **and those who use illicit drugs.**
- **About one in five US tuberculosis patients reports abusing alcohol or using illicit drugs,** and those appear more contagious and difficult to treat.

Drug Addiction

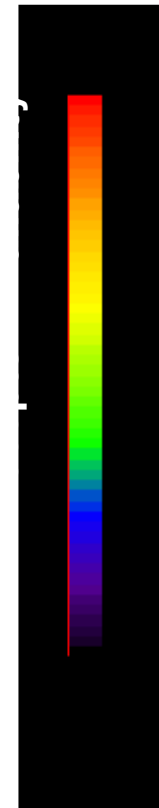
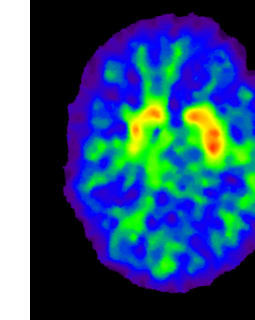
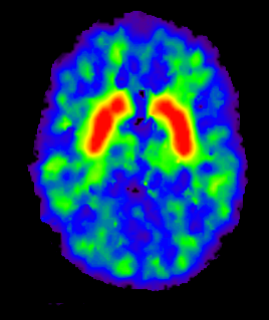
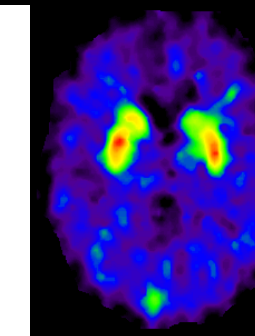
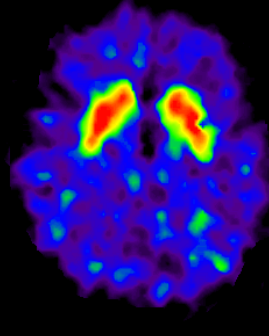
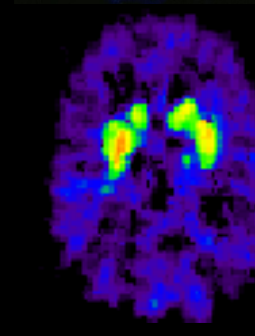
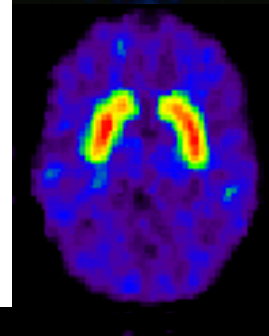
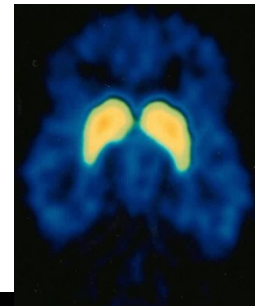
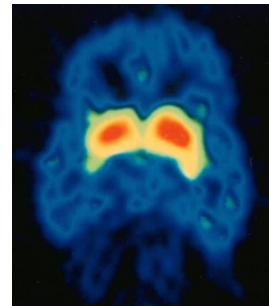
- Compulsive use of a drug
- Brain changes
- Developmental, chronic
- Medical, psychological, social consequences
- Genetic / environmental risk factors
- Preventable, Treatable , Relapsing

Drugs of Abuse

- Opioids
- Cocaine
- Cannabis
- Methamphetamine
- Nicotine
- Other

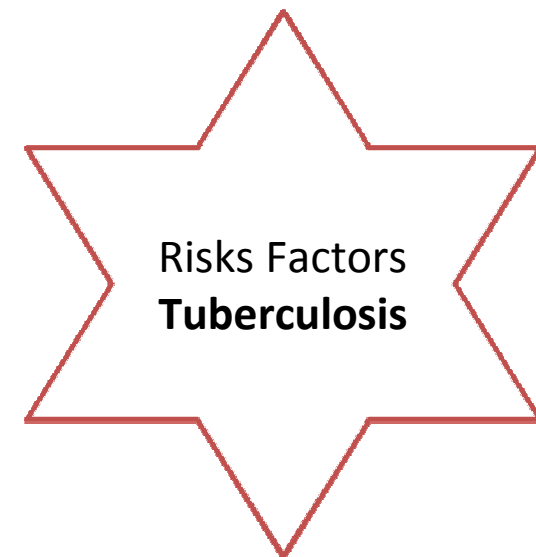
All drug addictions have common features but they are not the same

Dopamine D2 Receptors in Addiction



Illicit Drug Abuse

- High association with medical and psychiatric co-morbidities
- Poor treatment adherence
- Decrease economic and social status
- Unemployment
- Criminality - incarceration
- Cramped living conditions
- Sharing of utensils and paraphernalia
- High risk of infectious diseases
- Immunosuppression
- Respiratory complications



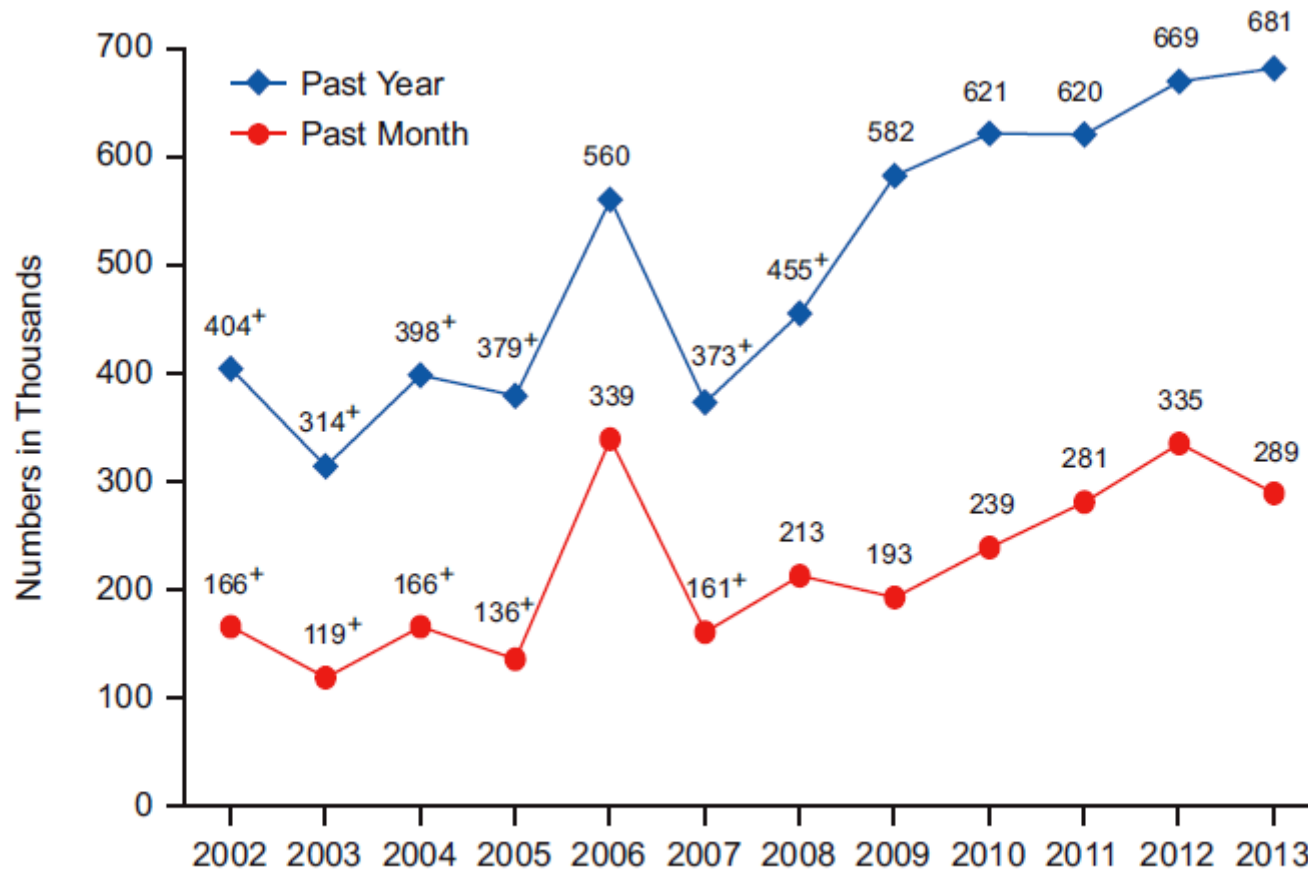
Illicit Drug Use and TB

- Delayed diagnosis
- Difficulties identifying at-risk contacts
- Less likely to be screened for TB
- Less access to routine medical care
- Difficulty treating patients with positive findings (poor tx adherence)
- Patients tend to become more contagious
- Less likely to complete treatment for latent infection or active disease
- Compromised immune systems
- Anti-TB meds are usually metabolized by the liver, which is often damaged by substance abuse.

Opioids

- Prescription (oral, injected)
- Illicit (injected, snorted)
- “Chasing the dragon” refers to inhaling smoke from heroin heated over a flame.

Trends in Heroin Use in the USA



⁺ Difference between this estimate and the 2013 estimate is statistically significant at the .05 level.

Cocaine

- Most frequent cause of drug-related death
- Available forms:
 - Hydrochloride salt (snorted, IV)
 - “freebase” (smoked)
 - Crack (smoked)
 - “bazuco” (smoked)
- Adulterants are found in all street samples of cocaine and result in additional toxicity

Cocaine and Lung



Acute chest syndrome
after IV cocaine binge



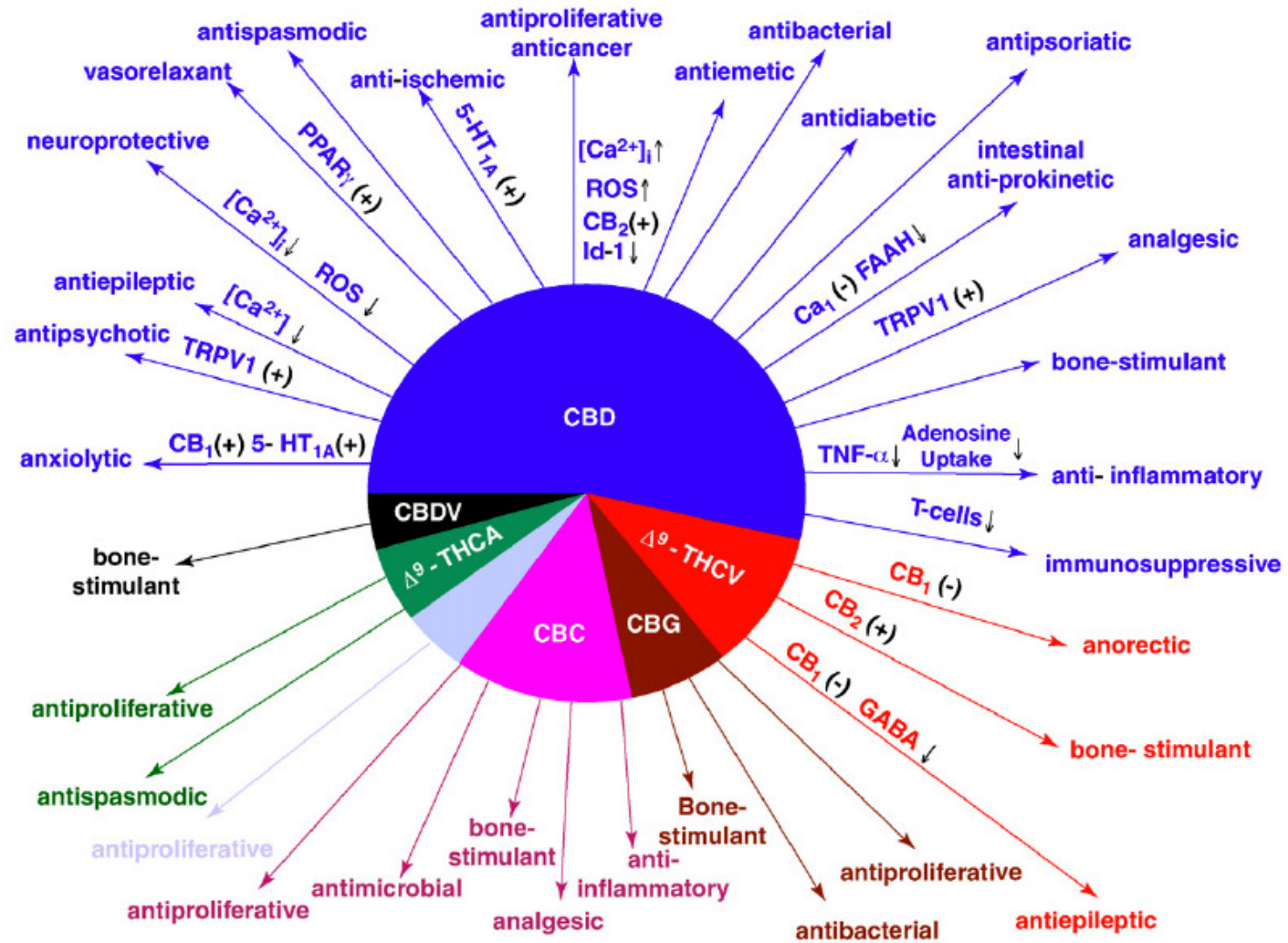
Talc granulomatosis in a
patient with history of IV
cocaine use

Restrepo et al, 2007 (Colombia)

Cannabis

- *Cannabis sativa*
- 421 chemical compounds
 - 80 phytocannabinoids
 - Δ^9 -tetrahydrocannabinol (Δ^9 -THC)
 - Cannabidiol (CBD)
 - Cannabigerol (CBG)
 - Cannabichromene (CBC)
 - Δ^9 -tetrahydrocannabivarin (Δ^9 -THCV)
 - Cannabidivarin (CBDV)
 - Δ^9 -tetrahydrocannabinolic acid (Δ^9 -THCA)
 - Cannabidiolic acid (CBDA)

Phytocannabinoids



TRENDS in Pharmacological Sciences

Marijuana

Route of Administration

- Smoked
- Inhaled (waterpipe)

TB Risk

- “Shotgunning”
 - Exhale smoke directly on other person’s mouth
- Hotboxing
 - Smoke with other people in room with windows closed
- “Bong”
 - Share waterpipe

Marijuana and TB

- Few studies
- Munckhof et al, 2003 (Australia)
 - Index case of the outbreak identified
 - 29 of 45 (64%) contacts who shared marijuana waterpipe had significant TST reaction
- Oeltmann, JE et al, 2004
 - N=11
 - High illicit drug-related activities, 10 of them hotboxing
- Thu, K. et al, 2013
 - 3 cases in Australia
 - Sharing marijuana waterpipe with active TB case increased risk of transmission (OR:6.5, CI:1.4.-30.4)

Drug Abuse and TB - Treatment

“An assumption among non-specialists is that substance use and TB are too complex to be managed concurrently”

(Gelmanova et al., 2007)

Challenges of TB treatment in Patients with SUDs

- SUD patients
 - Treatment is a low priority
 - Self-discrimination and Stigma
 - Poor treatment adherence
 - Risk taking behaviors
 - Lack social/family support
 - Antisocial behaviors
 - Paranoia suspicion
 - Drug use is priority (prevent withdrawal)
 - Incarceration
 - Psychiatric and medical comorbidities
 - Drug interactions

PRINCIPLES OF DRUG ADDICTION TREATMENT

A RESEARCH-BASED GUIDE

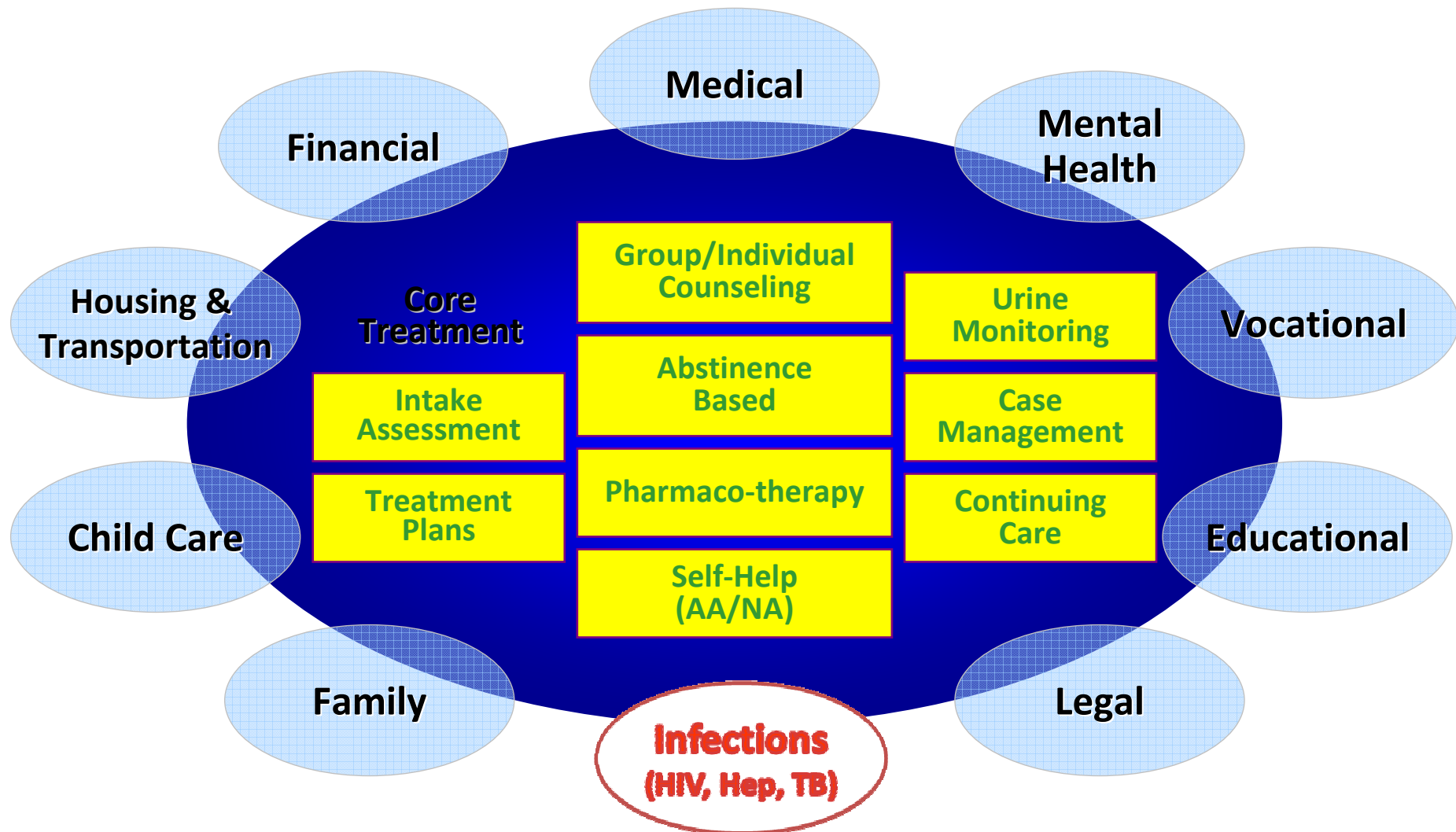
THIRD EDITION

National Institute on Drug Abuse
National Institutes of Health
U.S. Department of Health and Human Services

Principles of Drug Abuse Effective Treatment

1. Addiction is a complex but treatable disease that affects brain function and behavior
2. No single treatment is appropriate for everyone
3. Treatment needs to be readily available
4. Effective treatment attends to the multiple needs of the individual
5. Remaining in treatment for an adequate period of time is critical for treatment effectiveness
6. Counseling and other behavioral therapies are critical components of effective treatment
7. Medications are an important element of treatment for many patients
8. Treatment plans must be assessed and modified continually to meet changing needs
9. Co-existing disorders should be treated in an integrated way
10. Medical detox is a first stage of treatment
11. Treatment does not need to be voluntary to be effective
12. Possible drug use relapse during treatment must be monitored continuously
13. Treatment programs should assess for HIV/AIDS, Hepatitis B & C, Tuberculosis and other infectious diseases and help clients modify at-risk behaviors

Core Components of Comprehensive Drug Abuse Treatment Services



Drug Abuse Pharmacotherapies

- Opioid Dependence
 - Opioid agonists
 - Methadone
 - Buprenorphine
 - LAAM
 - Opioid antagonists
 - Naltrexone
 - Naloxone
 - Other: clonidine, lofexidine (investigational)
- Nicotine Dependence
 - Nicotine replacement therapies
 - Bupropion
 - Varenicline

TB - MEDICATIONS

- First - Line
 - Isoniazid
 - Rifampin
 - Pyrazinamide
 - Ethambutol
 - Rifabutin
 - Rifapentine
- Second – Line
 - Streptomycin (SM)
 - Cycloserine
 - p-Aminosalicylic Acid
 - Ethionamide
 - Amikacin
 - Capreomycin
 - Levofloxacin
 - Moxifloxacin
 - Gatifloxacin

Medications SUD + TB

- Rifampin, rifabutin, rifapentine
 - Induce CYP3A4
 - Can cause significant reduction in methadone and buprenorphine plasma concentrations
 - May precipitate opioid withdrawal
 - May require increase doses

Medications SUD + TB

- Methadone + Fluoroquinolones*
 - QT prolongation
 - Any patient found to have a QTc value greater than 480 ms should be managed carefully.
 - Repeat ECG and confirm the prolongation.
 - Check potassium, calcium, and magnesium. Electrolyte levels should be maintained in the normal range.
 - Avoid other drugs that increase the QT interval.
 - Monitor the patient's renal and hepatic function and adjust dose of fluoroquinolones if impairment is present.
 - Consider suspension of the fluoroquinolone if risk of torsades de pointes outweighs the benefits of the drug.

* ciprofloxacin (Cipro)
levofloxacin (Levaquin/Quixin)
gatifloxacin (Tequin)
moxifloxacin (Avelox)
ofloxacin (Ocuflox/Floxin/Floxacin)
norfloxacin (Noroxin)

POLICY GUIDELINES FOR COLLABORATIVE TB AND HIV SERVICES FOR
INJECTING AND OTHER DRUG USERS AN INTEGRATED APPROACH
Geneva, 2008

1. **Multisectoral coordination** at the local and national levels to plan, implement and monitor TB and HIV activities for drug users.
2. The **national strategic plans** for TB, HIV and substance misuse should clearly define the roles and responsibilities of all service providers delivering services
3. Adequate numbers of **personnel** and that education and training programs aim to build sustainable effective teams
4. Efficient and effective implementation of **collaborative** TB/HIV activities.
5. All congregate settings in the health, drug service and criminal justice sectors should have a **TB infection control plan**
6. All services dealing with drug users should have a **case-finding protocol for TB**
7. TB and HIV services and services for drug users should ensure **access** to appropriate treatment
8. All health services should ensure access to **isoniazid preventive** therapy for drug users living with HIV once active TB is reasonably excluded
9. All personnel working with TB suspects and patients, people living with HIV and drug users should be able to **assess risk factors for HIV infection** and transmission and should provide comprehensive HIV prevention information and services

In Summary...

- There is **high co-morbidity** between Substance Abuse and Tuberculosis
- They have **common risk factors** as well as disease moderators
- Both diseases carry a significant social **stigma**
- **WHO Guidelines**
- The **integrated** management of both disorders is critical
- **Screening and early intervention** is essential
- **Treatment is challenging**
- When prescribing anti-tuberculosis agents clinicians are aware of and monitor for psychiatric side-effects, including opioid withdrawal
- More research is greatly needed