# Medication Assisted Treatment:
## 20 years of lessons … some learned and some not

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# MAT Lessons learned: OUTLINE

- Model of TX: implications for MAT
- Principles guiding duration of MAT decisions
- MAT for Different SUDs:
  - Opioid Dependence
  - Nicotine Dependence
  - Alcohol Dependence
  - Benzodiazepine Dependence
  - Stimulant Dependence
  - Cannabis Dependence

# MAT: "what is your TX model?"

- Current common TX Models:
  - Harm Reduction …
  - Adjunct to Sobriety …
  - Adjunct to Abstinence …
  - I don't know … (not a good sign)
- Which ever model you use … be sure you know what it is in each patient circumstance (WHY?)
- The TX Model DICTATES TREATMENT PLANNING!!

# Treating Addiction as a chronic brain disease - the BASIC skill set challenge

- Study the natural history
- Implement screening strategies (CAGE)
- Practice presenting the diagnosis (SOAPE)
- Assess patient's readiness for change
- Negotiate treatment plans
- **Comfort with pharmacotherapy (MAT)**
- Strategies for long-term monitoring

# The Pharmacotherapy of Addiction

- "To Prescribe or Not to Prescribe My Dear Watson … That is the Question!"
- Three Models:
  - The "***HARM REDUCTION***" MODEL
  - The "***TREATMENT IMPROVEMENT***" or "***ADJUNT TO TREATMENT***" MODEL
  - The ***"ADJUNCT TO ABSTINENCE"*** MODEL

# The ***Harm Reduction*** Approach

- Pharmacotherapy first – Addiction TX second
- Criteria the must be met:

  If there is an increase in morbidity in the population ***without*** the pharmacotherapy than there is ***with*** the pharmacotherapy … then provide the pharmacotherapy!

  (and gradually introduce additional suggested adjuncts to the pharmacotherapy that might further decrease the morbidity using MI techniques)

# The ***Adjunct to Treatment*** Approach

- Addiction TX first – Pharma second if these criteria are met:
  1. MAT SAFE?
     1. SOBRIETY / PHYSICALLY
  2. EFFICACIOUS?
  3. WELL TOLERATED?
  4. INTEGRATED INTO TX PROGRAM?
  5. PREFERRED NON-EUPHORIA PRODUCING (CRX only if ***large body of RCT*** evidence of ***efficacy & safety***

# The ***Adjunct to Abstinence*** Approach

- Addiction TX first – Pharma second if these criteria are met:
  1. MAT SAFE?
     1. SOBRIETY / PHYSICALLY
  2. EFFICACIOUS?
  3. WELL TOLERATED?
  4. INTEGRATED INTO TX PROGRAM?
  5. **NO** EUPHORIA PRODUCING MAT (even if large body of RCT data for efficacy and safety)

# Know your model!

- Identifies MAT candidates (and those who are not)
- Helps to ID which MAT approach
- Guides TX planning
- PROVIDES FOR BOUNDARY MAINTENANCE (CRX)

# MAT Update: DURATION

- Methadone Data:
  - If doing well on methadone (i.e. full adherence & THD)
  - Taper in less than two years = poorer outcomes
- AA Data: lead on year 1 anniversary, consider sponsoring on year 2 anniversary
- 60% relapses in first 3 mos, 80% in first 6 mos
- PET scan data with low GABA and high glutamate for 3-6 months – brain healing

# MAT Update: DURATION

- Tegretol for 6 months post benzo = 50% increased benzo free state at 12 months
- So … MAT for *at least* 3-6 months (Nicotine & Alcohol) and probably 2 or more years (Opioids)
- IF patient wants to continue with MAT … absent contraindications … probably open-ended duration

# Opioid MAT Update: naltrexone

- Efficacy (sobriety & decreased cravings) of IM =/> SL-bup ***ONCE*** on active drug … but 30% of randomized never start IM naltrexone
- ? PO naltrexone augment at end of month (last week) due to decreasing serum levels (50mg/d)
- Duration and cost v PO formulation:
  - If adjunct to sobriety IM for 3-6 mos then PO for 2 yrs
  - If harm reduction … ? Don't stop?

# Opioid MAT Update: Bup #1

- IM-bup has emerged as a well tolerated approach
- IM-bup more expensive $$$
- IM-bup 300 mg or 100 mg
- Probably best in sub-populations: (harm reduction)
  - Pre-contemplative / contemplative re: counseling etc
  - H/O or suspicion of diversion
  - ? Continued *benzo / alcohol use* (sed hypnotic) 100mg

# Opioid MAT Update: Bup #2

- Bup is 20-30X potency of MS for pain but a CIII (or CV) euphoriant, high affinity long T1/2 agent: MANY IMPLICATIONS
- Sl-bup for analgesia should be q12 or q8h divided
- 2mg SL TID=120-180 MME, 4mg TID = 240-360
- Residual pain once on divided SL-bup is "opioid nonresponsive pain" and needs pain mgmt. not more bup!

# Opioid MAT Update: Bup #3

- Potency means "WSA" tapers of 0.5-2mg depending on dose (e.g. 16 mg dose to 14 mg, but 2mg dose to 1.5mg)
- Timing of WSA dose decreases: T ½ 3d = 15 day steady state. 3 X "steady state" to down regulate tolerance … *thus decreases Q6-12 weeks!*
- Bigger or more frequent decreases = trigger W/D and cravings … and markedly increased relapse risk

# Opioid MAT Update: Bup #4

- Sl-bup serum levels *dependent* on technique. Pt ED
- Given potency, lower doses now than in 2003-2006
- Green/Yellow/STOP: 0-16 / above 16 / above 24
- Boundaries are KEY
- Individualized TX plans (**i.e. dosing**)
- READ (and follow) the SMBO RULES
- FDA Guidance re: benzo use (?IM preparation?)

# Opioid MAT Update: Methadone

- Dose of methadone per Mary Jean Kreek MD:
  - Optimal doses are 80-150mg … and typically 80-120mg
  - No evidence for efficacy of doses above 150mg
  - Clear evidence of increased patient risk above 150mg
  - Much lower if also on sedative hypnotics (alc/benz)
- Admin taper / "detox" ~ 10mg or 10% / week
- WSA taper 5-10% Q3weeks D/T T ½ of 24+hours

# Nicotine MAT Update: #1

- Use it, just please use it!!!!!!!!! PLEASE
- SUD and MH clients require heavy lifting to help stop smoking … we ***MUST*** be skilled in counseling AND MAT.
- TX programs must integrate smoking cessation curriculum into their very nature!

# Nicotine MAT Update: #2

- Relatively similar efficacy of HIGH DOSE NRT v buproprion v varenicline

1. Buproprion – slower titration than thought (AEs)
2. Varenicline – mental health concern ?exaggerated
3. High dose NRT = 21mg patch / pack smoked PLUS a rapid delivery system PRN

# Nicotine MAT Update: #3

- 1+2 OK. 2+3 OK. 1+3 varied advice – IF adding NRT to varenicline start NRT low and go slow
- Smoking on the patch … perfectly safe!
- 3-6 month duration and then slow taper
- If increased sx – resume higher dose
- For NRT, taper fast delivery method first, then patches

# Alcohol MAT Update:#1

- Genetic influences on efficacy of naltrexone:

*"Our overall results support the evidence that naltrexone-treated patients carrying the G allele of the A118G SNP of OPRM1 have lower relapse rates when compared with those carrying the AA genotype, but similar abstinence rates."*

- Naltrexone efficacy on slips v. relapses

# Alcohol MAT Update:#2

- Acamprosate: … what can be said about acamprosate?
  - Largest RCT = VA trial: similar to placebo
- Gabapentin: … what can be said about the gabapentinoids?
  - Small RCTs suggest benefit re: adherence in TX
  - Low dose (100-300mg BID or TID)
  - Probably going to become a CV drug … so avoid?

# Alcohol MAT Update:#3

- Alcohol PAWS or anxiety in early sobriety:
  - Small studies suggest Baclofen or Topirimate or Lamictal or Trileptal may be helpful.
  - These medications do not appear to carry risk
- Disulfiram (Antabuse) little used, little evidence for efficacy, substantial risk.
- NO ROLE FOR BENZODIAZEPINES (post detox) IN THE MANAGEMENT OF ALCOHOLISM

# Benzodiazepine MAT Update:#1

- Tegretol 200mg BID for 6 months post detox improves benzodiazepine free state at 1 year.
- Valproic acid 250 mg BID (up to 500mg BID) same
- Small studies of topirimate, lamictal, gabapentin and trileptal show similar results.
- All patients removed from benzodiazepines should receive an anti-seizure (mood stabilizer) medication for 6 months

# Psycho-stimulant MAT Update:#1

- No strong data for any MAT intervention
- Small open trials of low dose gabapentin iproved treatment retention at 6-8 weeks.
- Many are trying topirimate instead (25BID – 50 TID) for irritability / mood swings
- Amantadine 100 BID PRN can decrease cravings but not relapse

# Psycho-stimulant MAT Update:#2

- Vegetative sx / anhedonia are TX with SNRI (typically buproprion) but worsened insomnia and anxiety
- Two small studies of mirtazapine showed improved TX retention v placebo
- Very active areas of research
- THERE IS NO ROLE FOR THE USE OF STIMULANT MEDICATIONS IN PSYCHOSTIMULANT ADDICTION

# Cannabis MAT Update:#1

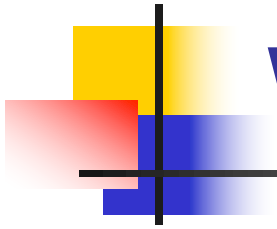
- Some are recommending "medical MJ" or "medicinal cannabis" in the treatment of MJ addiction … but then again some are recommending this for the treatment of almost everything. Zero evidence needless to say.
- Typically no evidence for any MAT, but MOST MAT tried for psycho-stimulant and benzodiazepine dependence is tried for symptomatic relief

# Cannabis MAT Update:#2

- One likely quite efficacious MAT for MJ dependence never was released on the market: Rimonabant
- CB1 receptor antagonist blocks many effects of THC
- Not released due to increased depressive symptoms in phase three obesity treatment trials.

# MAT Lessons learned: SUMMARY

- KNOW YOUR MODEL
- Critique ALL future MAT recommendations via the following patient safety principles:
  - Harm Reduction: If there is an increase in morbidity in the population ***without*** the pharmacotherapy than there is ***with*** the pharmacotherapy … then provide the pharmacotherapy!
  - Adjunct to Sobriety: MAT SAFE re: SOBRIETY/PHYSICALLY? EFFICACIOUS? WELL TOLERATED? INTEGRATED INTO TX PROGRAM? PREFERRED NON-EUPHORIA PRODUCING (CRX only if ***large body of RCT evidence of efficacy & safety***)



# Whew … Questions Concerns ???