Medication Assisted Treatment (MAT)

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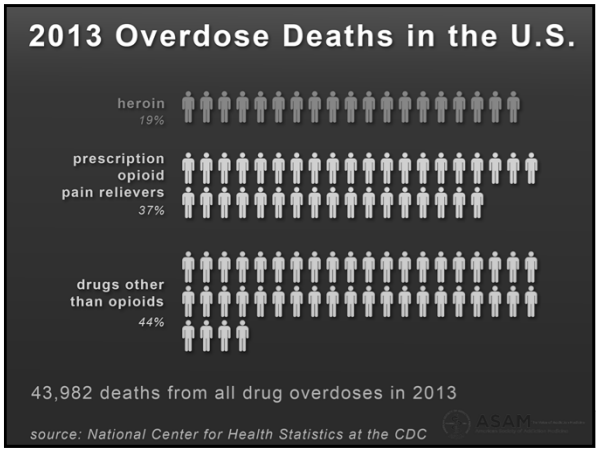
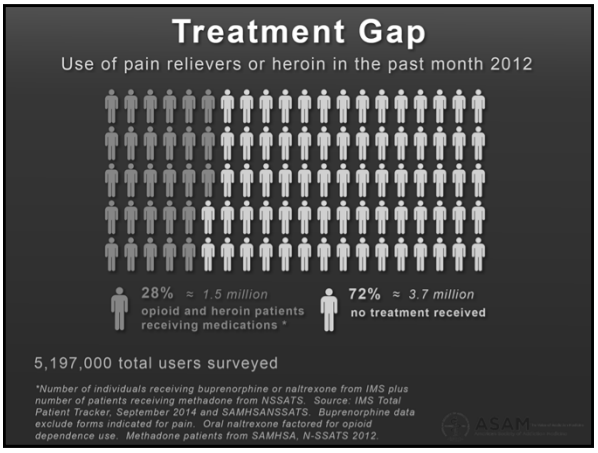
OR

If Addiction is a Disease, Why am I not at the Doctor?!

INTRODUCTION

- Today's subject: opioid use disorder
- Opioid drugs used for thousands of years
- Medicine has used them for hundreds of years
- Prescription of opioids regulated since Harrison Narcotic Act
- People have "misused" opioids for as long as they've been around
- But in the last 15 years: epidemic of opioid addiction





Contributors to the epidemic

Human "nature"/genetics

Availability of Rx opioids, at least partially due to the "enlightening" of physicians in the 1990s about our inadequate treatment of pain, accompanied by unprecedented pharmaceutical company marketing of opioids

Availability of purer heroin, making intranasal use an effective route of use, which vastly increased the number of willing users

Nomenclature

- DSM-I through IV: opioid use, misuse, abuse, dependence
- Addiction
- DSM 5
- Opioid use disorder
- The "disease" debate
- Lawyers and doctors agreed publically in the 1950s that alcoholism is a disease

Addiction the Disease

- A disease OF the brain
- Chronic
- Treatable
- Not curable
- Sometimes fatal

Alan Leshner, Ph. D. 1998, then Director of NIDA

- The brain of someone addicted to drugs is a changed brain; it is qualitatively different from that of a normal person in fundamental ways, including gene expression and responsiveness to environmental clues

Leshner (cont)

- Just as depression is more than a lot of sadness, drug addiction is more than a lot of drug use. The addict cannot voluntarily move back and forth between abuse and addiction because the addicted brain is, in fact, different in its neurobiology from the nonaddicted brain.

How do you "come down with" a chronic disease?

- Host
- Agent
- Environment
- Analogy to infectious disease paradigm

Chronic Disease

- Once you have it, you've got it
- "Disease" implies there is a "medical" component
- Causes are usually multifactorial
- Treatments must usually be multi-modal
- Response rates are variable and depend on the patient, the treatment itself, and outside factors

Chronic Disease Comparison

Diabetes	Addiction
• Genetic predisposition	• Genetic predisposition
• Lifestyle choices are a factor in development of the disease	• Lifestyle choices are a factor in development of the disease
• Severity is variable	• Severity is variable
• There are diagnostic criteria	• There are diagnostic criteria
• Once diagnosed, you've got it	• Once diagnosed, you've got it

Disease Comparison (cont.)

Diabetes	Addiction
• Primary treatment is lifestyle modification	• Primary treatment is lifestyle modification
• Small percentage of patients comply with same	• Small percentage of patients comply with same
• Medications can help	• Medications can help
• Patients often don't comply with medical regimen	• Patients often don't comply with medical regimen

Drug Dependence, a Chronic Medical Illness

- Title of an article in JAMA, Oct 4, 2000, Vol. 284, no. 13, pp 1689-1695
- Compares drug dependence to type 2 diabetes, hypertension, and asthma
- Genetic heritability, personal choice, and environmental factors are comparably involved
- Medication adherence and relapse rates similar across these illnesses

Disease Comparison (cont.)

Diabetes	Addiction
• Patients who are partially compliant are the rule, and outcomes are better than those who do not get treatment	• Patients who are partially compliant are the rule, and outcomes are better than those who do not get treatment
• Support systems improve outcomes	• Support systems improve outcomes

Disease Comparison (cont.)

Diabetes	Addiction
• Since suboptimal patient compliance is expected, medication use is titrated to maximize outcome	• Since suboptimal patient compliance is expected…….blame them for lack of motivation? withhold medication till they try harder?

Disease Comparison (cont.)

Diabetes	Addiction
• Even in highly motivated patients, only a small percentage will succeed without medication. "Abstinence" from medication is lowest priority	• Abstinence is still often the underlying goal, without which treatment (and the patient) is judged a failure???

Disease Comparison: Conclusion

- Chronic disease may be controllable, but not usually curable
- Medications, if available, are useful to promote this "disease control"
- Results will be suboptimal
- There is a "disconnect" between treatment of addiction vs. other chronic diseases
- In fact, there is a special term: Medication Assisted Treatment
- In other chronic diseases in medicine, we just call it:

TREATMENT!

Choices in Dealing with Opioid Addiction

- Withdrawal management, formerly referred to as "detoxification"
- Short-term medication use
- Long-term medication use
- But always accompanied by "counseling"

Withdrawal Management

- Assume "good" counseling
- Relapse rate for opioid addiction in 1 year: 95%
- There is no such thing as an "addictionectomy"
- Analogy: "Let's get your diabetes controlled, and then send you home with diet and exercise only"

Short Term Medication

- Assume "good" counseling
- Relapse rate uncertain, not enough study, likely poor
- But appears to be better than just withdrawal management
- Analogy: "You can have your diabetes medication for awhile, but after that you shouldn't need it anymore"

Long Term Medication

- Assume "good" counseling
- Lots of research (50years) to show good results
- Good results = improved functioning as a person, as a family member, as an employee and as a member of society
- Many studies consistently show societal expenses are reduced as well, ranging from $4 to 7 for each dollar spent on maintenance treatment

Medications for Opioid Addiction

- Methadone
- LAAM – no longer marketed
- Buprenorphine=subutex and suboxone: partial opiate agonist +/- antagonist
- Naltrexone
- We're decades behind in research compared with diabetes

Opioids - methadone

- Synthesized in Germany in the 1940s
- Claim to fame is its long duration of action, unlike other opioids, due to protein binding in tissues
- Researched in 1960s by pharmacologist Vincent Dole and psychiatrist Marie Nyswander
- Concept of methadone maintenance

Opioids - methadone

- Mu receptor agonist
- Large numbers of studies consistently show efficacy
- It allows normalization of the hypothalamic-pituitary-adrenal axis
- Heavily federally regulated when used for opiate dependence (vs. use for pain)

Why Opioid Maintenance?

Theory	Reality
Stable brain levels eliminate alternating euphoria and withdrawal that encourage continued use	Opiate-dependent patients rarely report euphoria after use, or craving at 24 hr.

Why Opioid Maintenance?

Theory	Reality
Hence, long-acting opioids are not reinforcing, reducing abuse potential	Patients' "illicit" use of methadone is primarily to "hold" them until they can get more short-acting opiates. Use of methadone rarely meets DSM 5 substance use disorder criteria

Why Opioid Maintenance?

Theory	Reality
These stable levels appear to allow a "repair" or "return toward normal" of opioid receptor systems in the brain	Research confirms "improved" opioid systems, including, e.g., the hypothalamic-pituitary-adrenal axis, which affects stress response, immunity, and other systems

Why Opioid Maintenance?

Theory

- Given the foregoing, the phrase "just substituting one drug for another" completely fails to capture the idea

Reality

- In fact, patients stabilized on methadone, "look" more like normal non-addicted individuals, both psychometrically and in their behaviors

Why All the Negative Press?

- Continued social stigma attached to addiction, especially if you can't "fix it yourself"
- Continued stigma on the part of the treatment community---outcomes-based science has not yet replaced ideology
- Opiate-addicted individuals stigmatize themselves, believing they are "guilty"

Negative Press (cont.)

- Federal regulations previously did not promote adequate quality or quantity of programs; better under CSAT
- Federal regulations operationalized as more of a barrier to, than a catalyst for, effective use of methadone
- Consequently, consistency of treatment was poor in programs, which varied between **"low-dose"** and **"methadone mills"**

Program Type: Comparison

Low-Dose

- Doses < 50 mg, thinking abstinence is easier to achieve if dose is lower
- Counseling pushes short-term meth to abstinence. Subtle value judgment against methadone

Meth Mill

- Doses = 100mg+, not individualized
- Counseling virtually non-existent, thought of as just an expense without much benefit

Comparison (cont.)

Low-Dose

- "Dirty" urines are confronted, even if not opioid, creating a punitive atmosphere; you could even be "kicked off" the program

Meth Mill

- Often do minimal urine screens as required by regs, don't address same, but still call them "dirty"

Comparison (cont.)

Low-Dose

- Look at take-home doses suspiciously, watching for diversion, furthering an adversarial relationship between the patient and the "treatment" program

Meth Mill

- Aim for maximal take-home ASAP, mostly as an expense-reduction measure; may be prone to overlook diversion

Comparison (cont.)

Low-Dose	Meth Mill
Have poor retention in treatment, and those in treatment continue opiate use to supplement inadequate dosing	Have longer retention, but patients may attend sporadically and continue opiate use for euphoria, using the program to "hold" them in between use episodes

Comparison (cont.)

Low-Dose	Meth Mill
Consequently, recovery is difficult to achieve, creating a negative opinion in the patient, staff, and the public	Consequently, recovery is difficult to achieve, creating a negative opinion in the patient, staff, and the public

Things have changed

- Marked improvement in overall quality of methadone clinics
- Doses more individualized
- More care with take-home medication
- More counseling provided
- The general public is relatively unaware of the improvement in treatment programs

Opioids - methadone

- Can only be used in the treatment of opiate addiction by Opioid Treatment Programs – OTPs
- OTPS require Federal licensing and are HIGHLY regulated in operation
- An individual physician (who is not a licensed OTP) MAY NOT USE METHADONE for the purpose of treating addiction, be it withdrawal management or maintenance (exception: hospitalized pt)
- But it CAN be used by individual physicians to treat pain

Opioids - methadone

- Does it work
- Yes, but –
- Must be adequate dosing; metabolism is markedly individualized; blood levels are available
- Must be sufficient length of treatment, often years
- Must have counseling
- Charleston Center's results

Opioids – methadone

Best used for patients who:

- Have high tolerance
- Have more severe disease
- May be using multiple other substances
- Have higher psychiatric co-morbidity
- Have failed other treatments
- Have more "dysfunctional" lifestyle

Opioids -- LAAM

- LAAM = levo-alpha-acetylmethadol
- Long-acting up to 3 days, allowing fewer administration days per week
- Removed from the market due to potential adverse cardiac effects

Opioids - buprenorphine

- Partial opiate agonist
- Buprenorphine = Subutex
- Buprenorphine + naloxone = Suboxone
- Buprenorphine sublingually absorbed, naloxone not
- But if broken down to use IV, the naloxone's opioid blocking effect predominates, preventing intoxication and possibly precipitating acute withdrawal

Opioids - buprenorphine

- DATA 2000 (Drug Addiction Treatment Act)
- Allows licensed physicians who undertake the required education to be "waivered"
- Receive special "X" DEA number to allow use of buprenorphine for treating opiate addiction in office practice -- OBOT=office-based opiate treatment

Opioids - buprenorphine

- Suboxone use is opioid maintenance analogous to methadone maintenance
- Schedule V medication
- The idea is to bring drug treatment into the privacy of the primary care doctor's office, de-stigmatizing opioid dependence, and getting people into treatment earlier in the course of their disease

Opioids - buprehorphine

- Does it work
- Yes, but –
- Not all doctors (or their office staff) are skilled at dealing with the addicted population
- Counseling still necessary, but availability is not always optimum
- It IS abusable
- An individual doc can only treat 30 patients at a time for the first year, and no more than 100 at a time thereafter; up to 275 now, under certain circumstances

Opioids - buprenorphine

Best used for patients who:

- Have less developed tolerance
- Have less severe disease or are earlier in disease course
- Are using no other substances, or using only minimally
- Have less psychiatric co-morbidity
- Have a more functional lifestyle, who have "lost less"
- Are able to be more compliant with recommendations

Opioids - naltrexone

- Naltrexone is a complete opiate antagonist
- If taking naltrexone, the idea is to block all effects of any opioid administered, thereby preventing intoxication, hopefully ultimately extinguishing opioid drug-taking behavior
- May reduce craving as well
- May be given orally or by IM injection
- Not a controlled substance, can be Rx'ed by any licensed physician

Opioids – naltrexone: oral

- Does it work
- Yes, but –
- Compliance is an issue; one can just stop taking it
- Probably works best with supervised/closely followed administration
- Has been useful especially in professionals

Opioids – naltrexone: IM

- Brand name Vivitrol, lasts 28 days through slow release
- Does it work
- Yes, but –
- Very expensive (~$1,000/dose)
- You can't get any pain relief from opioids if you need it
- Can be over-ridden under close medical supervision in an emergency

Opioids - naltrexone

Best used for patients who:

- Have less severe disease
- Do not need opioids for chronic pain
- Refuse, for whatever reason, the use of agonist therapy
- Have professional standing, and/or may be under close monitoring

Pregnancy Considerations

- Misuse of short-acting opiate drugs is associated with complications: miscarriage, infections, premature delivery, low birth weight and others
- Other factors influence outcomes: access to prenatal care, socioeconomic status, use of nicotine/alcohol/non-opiate drugs, and other factors

(Cont)

- Relapse to opiate drugs after a detoxification (medically supervised withdrawal) is >90%
- After decades of research, the standard of care is: methadone maintenance through pregnancy
- Measurable/treatable neonatal abstinence syndrome is preferable to fetal abstinence syndrome
- Buprenorphine appears to be equal in efficacy

Pregnancy: Proper Dose

- Individualized
- Methadone dosing may need to be higher later in pregnancy due to increased volume of blood and tissue distribution
- It's not how many milligrams go down the throat, but rather what gets to the brain (and fetus) that matters
- Patient report of effectiveness is generally reliable in adjusting dose

Medically Supervised Withdrawal During Pregnancy?

- Not "officially" advised at this time due to risk of relapse
- But patients may (1) refuse meds, (2) not tolerate meds, (3) have financial or geographic barriers to getting meds
- Slow taper in second trimester is advised, avoiding increased chance of miscarriage in the first trimester and premature labor in the third; recent literature says first or third may be ok, but second trimester is still officially advised
- Can use methadone or buprenorphine
- Should have fetal monitoring, but this is not always practical

Outcomes

- Applies to methadone-maintained mothers, but probably applies to buprenorphine
- May have slightly lower birthweight/head circumference than non-drug using, but still better than illicit opiate users
- Ultimate development, when other variables are taken into account, no different than normal
- Neonates may be opioid-dependent, but they are NOT ADDICTED

NAS

- Neonatal abstinence syndrome may occur, but frequently does not
- Occurrence/severity not consistently correlated with maternal dose of med
- Occurrence/severity may be improved when neonate stays in room with mother vs NICU placement
- Treatment can prevent complications (medications used for tapering include morphine, methadone phenobarbital, clonidine)

Breastfeeding

- Benefits outweigh any potential problems
- Methadone shows minimally in breast milk, may ameliorate withdrawal symptoms somewhat, not shown to cause any developmental issues; same probably true of buprenorphine

Conclusion

- Opiate dependent pregnant patients should be encouraged to use MAT, i.e., opioid maintenance treatment for the duration of pregnancy
- However, tapering remains an option

Soooooooooo…….

Why am I NOT at the doctor?

Because you have not been apprised of everything we just talked about, as summarized in the next slide!

SUMMARY

- Opioid addiction is a chronic, relapsing "disease" similar to diabetes mellitus type 2
- While primary treatment for both is "counseling," medications are often/usually necessary, including during pregnancy
- Relatively few medications exist for opioid addiction, but efficacy is good when used properly
- The choice of medication should be individualized, as always in medicine -- there is no "one size fits all"
- Ideology, stigma and lack of knowledge still remain significant barriers to effective MAT

QUESTIONS

Resources

- American Society of Addiction medicine: www.asam.org
- Substance Abuse and Mental Health Services Administration: www.samhsa.gov
- Treatment Improvement Protocol 43 (TIP): Medication-Assisted Treatment in Opioid Addiction

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