Rx OPIOIDS – Friend or Foe

DATA and MEDIA SPIN

SELF-MEDICATION and ABUSE

MEDICAL USES

PAIN MYTHS- UNDERTREATMENT of PAIN

BENEFITS of PROPER PAIN CONTROL

ADDITION-PSEUDOADDICTION–PHYSICAL DEPENDENCE-TOLERANCE

GOOD STUFF – BAD STUFF – SEXUAL ISSUES

WITHDRAWAL

DEATHS

DIFFERENT OPIOIDS

SS=Special Stuff…Fx=Effects…Px=Problem…Tx=Treatment…Sx=Symptoms
> = More – Greater – Increased…< = Less – Decreased – Not as much…~ = About

PHYSICAL DEPENDENCE DOES NOT MEAN ADDICTION

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When used correctly opioids are irreplaceable for pain relief and the reduction of suffering. They allow those who suffer from acute or chronic pain conditions to live productive lives, keep jobs, socialize and enjoy their partner.

According to most responsible and scientific studies 97-99% of people who are prescribed opioids for acute or chronic pain take them ‘correctly’. The same studies saw an “addiction rate” of ~ 1%. (“More recent” studies have placed the addiction rate at 20-30%. These studies used different criteria for their personal definition of addiction (Not DSM) that was heavily reliant on Physical Dependence and “Aberrant Behaviors”).

Sadly, this group of people who suffer painful conditions are not the group that gets the media attention and headlines.

On the other hand, when these drugs are abused, they can cause serious Px in all parts of a person’s life. If this does happen, anything that can go wrong usually does.

**DATA...Making it Say What You Want it To**
Recently there seems to be an effort to spin data in different directions
This has made the available info suspicious and at times unreliable
This makes it imperative that you do your homework and read the fine print
Incorrect-Bad or misleading info is much worse than no info

**Rx Med Abuse is Nothing New**
20’s-30’s = Rx Alcohol
60’s-70’s = Valium...Barbs...Quaaludes...Amphetamines...Percodan
80’-90’s = Cocaine and XTC seemed to < interest in Rx meds
Now = Xanax...Oxycodone...Hydrocodone

Use seems to be driven by demand for the most publicized fad of the day
Panic-Fear-Demonization will always follow the media frenzy
Media has become Gullible and Lazy = Good Headline > Important than Facts
Be Skeptical = Epidemic...Latest threat...Biggest Threat to America or Our Youth
Most Dangerous Drug in America...Increased Deaths
Just B/C something is repeated a lot does NOT make it true or relevant

We have now given this a Name = “Rx OPIOID/PAINKILLER EPIDEMIC”
Like most “Epidemics” it will inspire Fear and increase its Importance
As we all know: Once you give it a name and feed it, its not likely to go away

**ALWAYS ASK** = “Is this the whole story or is it just what you want me to know ?”
2013 CDC CONTRIBUTION
~16,000 deaths “Involved Opioids” or “Opioids contributed to their death”
If the death involved Illegal and Rx drugs the death WAS COUNTED FOR BOTH
~80% of these “Opioid drug deaths had more than one drug involved
SO…Using the same math, the actual # of deaths caused was closer to 5000

Linked to-Contributed to does NOT mean Caused by-Cause of death

CDC-NIH CAVEATS (Public Health Reports/July-August 2010/Vol.125)
“These results should be interpreted with caution for several reasons.”

“The accuracy of the findings depends on the accurate categorization of “overdose”
as a cause of death on death records.”

“Similarly it is possible that growing awareness of overdose as a public health Px
may increase the likelihood that deaths are categorized as overdoses.”

“Additionally the available data from CDC do not allow for determination of the
extent to which the overdose was due to a specific substance”

So a more accurate statement would be:
“~16,000 people in the US died with Rx opioids in their system in 2013. Blood levels
varied with each individual and most died with a combination of several drugs in
their system. Because of the variety of contributing factors, the actual cause of death
cannot be attributed to a specific drug. Any trends that are calculated from this
data should be considered as “Deaths caused by a COMBINATION of drugs”.
Having drugs in your system when you die does not automatically mean that the
drugs killed the person.”

“When multiple drugs are found in autopsy toxicology reports, the most likely cause
of death will be the accumulated damage of combination drug use-interactions.
NO SPECIFIC DRUG CAN BE BLAMED FOR THIS”.

CDC NUMBERS ARE:
22,700 Poisoning deaths from all Rx drugs…2.5 million people die yearly in US

“16,235” Deaths “Involved” Rx Opioids as one of several drugs found at autopsy
“9000”=Morphine-Hydrocodone-Oxycodone…4500=Methadone…2700=”Other”

14,000+ Deaths from All Illicit drugs=4500-Cocaine…8500-Heroin…~1000-“Other”
Deaths from illicit drugs has always been pretty low despite the media hype
This comparison implies that all other illicit drug use is safer than Rx opioids!
TOTAL DEATHS: 2008 = ~24,000  2013 = ~30,000
To Put this in perspective:

There were ~2.5 million deaths in the US in 2013
“16,235” Rx Opioid Deaths = 0.6% of all deaths
9,000 Morphine-Hydrocodone-Oxycodone Deaths = 0.4% of all Deaths
500,000 Tobacco and Alcohol Deaths = 20% of All Deaths

So which “Epidemic” is causing the most harm, costing the most money and creating the most Drama-Fear-Demons

OTHER DEATHS= Rx drug-any cause=100,000…NSAIDS=30,000+

TERMINOLOGY

NARCOTICS
Legal=”Opium /derivatives and their semi/fully synthetic derivatives as well as Cocaine – Marijuana – Methamphetamine and Barbiturates”
Medical Professionals should Never use this Term…Politicians/Gov. Only Shows a lack of understanding/Information…Sexy-Attack headline
If “Narcotic” is used, what comes next MUST be viewed with skepticism

OPIOIDS = Any substance that activates Opioid Receptors = Preferred Term
OPIATES= Drugs obtained from the Poppy plant = Morphine-Codeine-Thebaine
SEMI-SYNTHETIC= Lab-altered Opiates = Heroin…Oxycodone…Hydrocodone
FULLY SYNTHETIC = Lab only…Structurally dissimilar=Methadone-Fentanyl

Linked to—Contributed to—Associated with or Involved with does NOT mean Caused by—Died Because of—Killed by

WHY ABUSE-SELF MEDICATE with OPIOIDS

EUPHORIA…Feels very good…Far beyond normal pleasure…<Suffering or Buzz?

ADDITION…Euphoria becomes Emotionally Important…Acquired Drive State

AVOID W/D…W/D can be nasty…Afraid to quit…Dependence or Addiction?

EMOTIONAL Px…Dysphoric states…Mental illness…Depression…PTSD
These people can quickly “Fall in love” with Opioid “Relief”

DAMAGED ENDORPHIN…Born this way or Damaged by Opioids…Depression SYSTEM
Feel more “Normal” when using so it “Makes sense”

UNDERTREATED PAIN…Pt willing to do anything for relief…Opiophobia
Dr. misunderstands Physical Dependence vs. Addiction
HOW USED

ORTH=Swallow…Slowest…Lasts longer…Oxycodone-Hydrocodone
SUBLINGUAL=Dissolve under tongue…Break-thru pain…Swallow Px…Bupe.
BUCCAL=Between Cheek/Gum…Fast…Lipid Soluble…”Actiq Lollipop”…Fentanyl
NASAL=Fast…Snort Powder/Crushed pills…Spray Inhalation=Stadol
SMOKE=Fastest…Heat destroys so must be relatively pure…Heroin
SKIN PATCH=Absorbed directly thru skin…Bypasses liver…Duragesic-Fentanyl
RECTAL=Similar to Buccal…”Placement” is important…Oxymorphone
VAGINAL-GLANS=More of a sex thing than medical…Blood flow issues
SUBCUTANEOUS=“Skin Popping”…Like a TB test…Steady absorption…Heroin
INTRA-MUSCULAR=Steady absorption…Morphine
INTRA-VENOUS=Directly into a vein…Very fast…100% absorption…Morphine
INTRatheCAL=Directly into Spinal Cord…Labor and Delivery…Pump

MEDICAL USES:
PAIN
ASA-NSAIDS=< COX-Sub.P at site of pain…”Ceiling Effect”

Opioids work in the BRAIN and SPINAL CORD to < Perception of Pain
<Emotional Response-Fear-Threat-Intensity-Distress-Suffering of Pain
Pain Message is altered…It hurts less and you don’t care as much

Opioids relieve BOTH Emotional and Physical parts of pain
IMPORTANT: Severe pain can only be < by 30-40%…”No pain” is a myth

The Emotional Response to <Suffering and Relief of Symptoms is sometimes
incorrectly seen as getting high
Opioids also seem to < PTSD Sx if given in > doses soon after trauma – Esp. Burns

COUGH=Works in brain (Medulla) to < cough reflex

DIARRHEA
Opioids attach to Mu receptors in Lower GI=Colon
Slows/ Stops downward movement of digestion/elimination
Peristaltic propulsion stopped…Defecation reflex ignored
Water re-absorbed by body + Anticholinergic Fx = Stool hardens
DEPRESSION?
Ancient Greeks and Chinese used Opium to treat “Melancholy” = Depression
Opium used until Early 1900’s...Bad experiences w/Morphine/Heroin ended this
1950’s = Newer Antidepressants developed

Depression = >Cortisol…Opioids <Cortisol = Antidepressant Activity
<Endorphins…Dysfunction Endorphin System
Receptor Px = Not enough Mu and/or Too much Kappa

Explains some: “Self-Med” with Opioids…”Works” at first but soon “Turns on you”

SO = Endorphins play some role in depression…Current Opioids not too good
Some “Opioid Addicts” may be Self-Med for Depression then Depend. Occurs
Buprenorphine et.al may be more helpful than we thought…Naltrexone worst
Research into Antidepressants that involve Endorphin Sys. seems worthwhile

OPIOID MAINTENANCE THERAPY (OMT)
Few meds approved: Methadone and Buprenorphine - Bupe plus Naloxone
Helpful for some and not for others...Not a cure

OPIOID ANTAGONIST THERAPY...Only Naltrexone-Vivitrol Approved

UNDERTREATMENT of PAIN
Unrelieved pain can cause as many or more problems as Addiction or Med. Side Fx

>Use of NSAIDS-APAP-Triptans= GI-BP-Renal Liver-Cardiac Px
<Quality of Life= >Suffering-Weakness...<Mobility
<Work= Lost wages...<Quality of work
<Play=>Relationship Px...<Sex-Sex Play...<Energy-Independence...>Isolation
>Emotional Px= >: Depression-Hopelessness-Giving up-Anxiety-Anger-Resentment
<: Memory-Ability to Cope-Sleep

> AOD Use= >Self Medicating...>Relapse Rates
>Death Rate= Pain Kills= >Heart Attack-Stroke-BP-Stress-Energy Use-Suicides
<Health= Pain Interferes with Healing...>Obesity...Muscle Atrophy

You will be seeing more clients in this category:
”Baby Boomers”...Depressed kids...Surgery/Injury/War/Drug Survivors
Most are NOT “addicts” and will have a poor response to Tx-AA–NA

Drama Created by a gullible and lazy media tends to complicate things and makes it
nearly impossible to separate fact from fiction.
Dealing with “Pain Myths” can be difficult:
Everybody that uses opiates becomes addicted=Extremely rare in Pain Tx
Pain is harmless=>Emotional/Physical Px…Can be Suicidal
Suffering builds character-Makes you stronger=>Resentments-Anger-Depression
Pain meds are for “Weak People”=Religious / 12-Step / “Pain-Free” Bias
Pain sufferers are exaggerating or faking=”It can’t be that bad” unless it is you
High-Increasing doses mean addiction=Tolerance-Disease progression-New Disease
A “good client” does not “whine” about pain=Pain is severe enough to get fixed
Addicts can NEVER be prescribed opiates=Pain does not ignore this group
“Drug Hoarding” is a sign of addiction=Fear…<Pain=<Use…>Pain=>Use
Cts taking opioids chronically cannot Drive-Operate Machinery-Keep a job=False
Looking bad means you are an addict=Pain “Drains you”-<Sleep-Tired-Worry
Never use other CS while taking opiates= OK if Monitored…>Potential Px
Early refills mean taking too much=Fear of running out…Family steals…”No ride”
Only addicts use a drug for something other than what it prescribed for or “Share”
Relief of Suffering and “Getting High” are the same=Hard to separate…Perception
Getting sick if you miss a dose means addiction=Dependence is NOT Addiction
More people abuse Rx pain relievers than illegal street drugs=Read the Fine Print
There are limits on how long Opioids can safely be prescribed=Few long-term Fx

PSEUDOADDICTION…PSEUDO-ABUSE
LOOKS LIKE= “Aberrant Drug-Seeking Behavior” – Abuse – Addiction
Better suited to evaluate pain control – Determine if pain is treated properly

Drug Hoarding = Fear of running out…Saves meds for worst pain
Unauthorized dose > = Tolerance…Disease progression…Poor pain relief
Multiple Drs = Dr.Shopping?…Poor Tx…Insurance Px…Need to know each other
Internet-Street purchases = Inadequate pain control…This is a BAD Choice
Alcohol-MJ used medically for pain = <Relief from pain meds…Always a bad choice
Trades Meds= Not good but doesn’t tell you much…Common among most families
Demands= More meds-Different meds-Specific Brand-Name meds=Desperation
Past Hx of Abuse = Abusers can have legit pain…Poor Indicator…Monitor Closely
Clock-Watching = Effort to comply with Directions…Sign of under-treated pain
Manipulation-Adjustment-Lying? = Learn what will get them relief
Non-Pain related Opioid Use = Sleep issues…Futile attempt to treat depression
Enjoys Meds = Relief from pain makes you feel better…”High” vs “<Suffering”
Always tired= Takes >energy to deal with pain…<Sleep…<Rest…”Tired” Brain
Mood Swings = Pain makes you ill-pessimistic…”Why grumpy old men are grumpy”
Gets Sick if doses are missed= Physical Dependence is NOT Addiction

Simple lists of ‘Aberrant” behaviors are not predictive of addiction or anything else.
Will do almost anything to get some relief from their negative symptoms:
So Pseudoaddiction is due to Inadequate pain control or Tx of a Disease State
So this ends up being a relatively easy fix = Px disappear if pain controlled
So Increased dosage = <Px=>Life=>Quality of life=<Depression-Suffering = >Smiles
BENEFITS of PROPERLY TREATED PAIN

WORK-SOCIAL
Can go to work…>Quality of work…>Skills…>Cooperation
>Patience…<Isolation…>Active in community…>Friends

FAMILY
>Respect…<Damaging arguments…>Communication…>Laughing/fun
>Gratitude…>Intimacy…>Sex fun

EMOTIONS
<Chance of depression…>Sleep…>Hope…<Suicide…>Mood
>Emotional attachments

HEALTH
<Flight/Fight/Fear responses…<HR…<BP…<Cardiovascular Px
<Agitation…<Anger…>Energy…>Stable Blood Sugar/Cholesterol
Blood clotting normalizes…<Healing times…<Muscle atrophy
<Risk of acute pain becoming chronic pain…Proper repair of surgery

BRAIN
Function Improves…White matter “Re-wires”…Gray matter repairs
>Emotional control…Brain “Reboots”-Reorganizes…<Confusion

ABUSE
<Abuse/Addiction issues…<"Aberrant” behaviors…<Self-medicating

ADDITION
Is a Px MULTIPLIER= Loss of Control…Px’s Increase as the Dose Increases
Anything that can go wrong or get worse usually does
Use continues despite serious consequences=Jail-Relationships-Job-Health-Mental
Their <Ability to deal with it-Fix it or Adapt makes it worse

Behaviors are now under Subconscious control of the Limbic (Animal) Brain areas
These thoughts tell the addict that they will not survive, reproduce or be safe w/o the drug

Human Brain (Frontal and Pre-Frontal Cortices) no longer have control so Logical thinking becomes useless
TOLERANCE:
Need more of the drug to get desired Fx=>Liver enzymes…<Receptor response
Much variation between individuals

Eventually use just to stay “Normal”…Becomes harder to get high or pain relief
Cross-Tolerance is Incomplete so if you switch drugs the Fx will be “Different”

Normal and expected outcome of extended-chronic-high opiate use
THIS IS NOT ADDICTION…May also mean that Painful Disease state got worse

Tolerance varies= Low dose or sporadic use produces little tolerance
Quick Tolerance = Resp.Depression…Analgesia…Sedation…Euphoria…N/V
No Tolerance = Constipation…Miosis…Sexual Px…Sleep Px

Chronic users=Many show few signs of abuse…Can function if supply is dependable
Rarely Get High or OD…Few Driving Px…Px=Emotional Issues

PHYSICAL DEPENDENCE
Not the “Dependence” in DSM’s…DSM Dependence=Addiction=Confusion
DSM-5 seems to correct this

PLEASE use “Dependence” ONLY when referring to Physical Adaptations or
When dealing with Insurance Companies

When the body “Gets used to” a chemical then adapts to function normally

Normal and Expected Outcome of many types of drugs :
Ex=Opioids-Bz-Antidepressants-Beta Blockers-BP Meds-Laxatives-Nose Spray

Withdrawal will occur if drug is D/C too quickly…Sx will Return
Even though this “Looks Like Addiction” IT IS NOT
Addiction may or may not have a Physical Dependence Component

PHYSICAL DEPENDENCE IS NOT AND
NEVER HAS BEEN ADDICTION

Still have a CHOICE to quit…Few if any significant Brain Px at this point
GOOD STUFF:
Euphoria=Feeling far beyond what a human can normally feel="Hits Sweet Spot"
Sexual…Orgasmic…Contentment…Relaxation…Well-Being…Peaceful…”It’s OK”
Don’t Care…>Toleration…<Worthlessness/Despair…”Comfortably Numb”
<Physical and Emotional Pain…Sexual response altered(+/-)…Appreciate Pleasure
Decreases “Fear” part of pain/suffering…”Will it ever stop?”
Very Attractive drug for depressed-anxious-mentally ill people
The bigger the stress / depression, the bigger the relief of Sx

BAD STUFF - Usually Associated with Abuse:
HISTAMINE released by Mast cells-NOT an allergic response
VASODILATION=Blood vessels expand…<BP…Dizzy…Itch…Flushing…Sweat
NAUSEA=CTZ in Medulla activated=N/V…Inner ear Px=Motion Sickness
CONSTIPATION=Dry stool…Feces dehydrate…< Peristalsis…< Defecation reflex
URINARY PX= Urgency=Bladder Spasms-Incontinence
MIOSIS=“Pin-Point Pupils”…Blurred vision
RED EYES= >Histamine…Anticholinergic drying…Vasodilation + <BP
VISION =Nystagmus=Shaky Eyes…Miosis=Pin point Pupils…Hypoxia=>Pupils
BREATHING= <Respiration…<Tidal volume(Air in )…<CO2 response…<Brain O2
SLEEP APNEA=Made worse B/C you don’t wake yourself up to “Breathe Again”
SLEEPY=”On the Nod”=”Fade in and out”…<O2 to brain
CLUMSY=”Move message” delayed…Fall if you run…Parietal Lobe px
MOOD= Don’t care…<Energy…<Emotions…Start but don’t finish things
Aggression/Irritability possible with Oxycodone/Hydrocodone
IMPAIRED JUDGEMENT= Frontal Lobe Px…Confusion…”Don’t get it”
Slowed thought processing…< Cognitive Function
MEMORY=CRS…CRAFT…Hippocampus Px…Don’t understand message
Poor association of event with emotion
SLURRED SPEECH=Temporal Lobe = Tongue gets “Stupid”
RISKS=Amygdala…Aware of harmful situations but don’t care..<Situation Eval.
GERD= <Gastric motility-digestion-emptying
IMMUNOSUPPRESSION=Disrupts T-Cell balance that normally fights diseases
HORMONES
<Testosterone-Estrogen-Progesterone = Hypogonadism
SEXUAL ISSUES...MALE
LOW DOSE...>Libido...Horny...<Inhibitions...>Experimentation...>Interest

HIGH DOSE...CHRONIC USE:
<Libido=Lose interest...No fantasies...Sex=work & not fun...Penetration Nod-offs
Enlarged Prostate= <Volume of semen...Uncomfortable Ejaculation/Defecation/Sex
Delayed Ejaculation= Becomes common-Difficult to overcome=Frustration
Impotence=Becomes the rule...Poor sexual responses...SSRIs make this worse
Can’t keep it up=Poor Erection Maintenance...Slow “Brain-Penis” Communication

SEXUAL ISSUES...FEMALE
Women have some different sexual issues...Males/Females respond differently
While some things are obviously similar Emotional response to sex is very different
Women actually use their brain before-during-after sex=”Opioid Roller-Coaster”

At 1st=>Sexual response...Horny...>Interest in sex Talk-Clues-Innuendoes...Playful
>Risks and Experimentation...Less Inhibitions-Fears-Phobias
Later=Harder to get Aroused...Sexually functional BUT “Less Satisfied” W/O use
< Playful...No Experimentation...”Get it Over With”

Orgasms=Become elusive...“<Predictable”...Normally sensitive areas <Responsive

Oral lips= Less meaning...Less Emotional Response
Breasts/Nipples= Non-Sexual...Uncomfortable...< Enlargement or Lifting
Genitals= Take >Effort to respond... Response to Touch is Delayed
Less Lubrication...Uncomfortable Penetration

Pregnancy=Not teratogenic...Low birth wt / W/D Sx...Immature fetal liver
Px=Repeated W/D by mom=Fetal Hypoxia=Placental death=<Growth
Infant outcomes seem to be more influenced by what happens after birth

No infant has ever been more addicted to anything.
Withdrawal can occur, but can be managed by trained medical professionals

THESE Px CAN BE OVERCOME
Takes time for the delicate-sensitive sexual mechanisms to “Reboot”
Helps if partner(s) understand situation...Be patient and willing to “Practice”
It is very important that sexual issues be addressed during Tx and Recovery
DO NOT let your personal sexual phobias-fears-prejudices get in the way of helping
Sexual issues are important to everyone in some way...Can lead to > resentments
EMOTIONAL INDIFFERENCE
Potentially very destructive - hard to repair
You still love others BUT they are no longer Special – Important – Relevant
Makes it easy-Justifiable to disrespect Fam-Friends-Fellow Workers-Pets
When you lose your emotional link to the world, nothing really matters much
Not much=Sadness-Happiness-Expectations-Hope-Reward-Special Things
IN the END=All you have left is existing-Very few emotional highs or lows
Life begins to have less meaning-relevance-importance

This is why when a person quits or cuts down they are usually an emotional wreck
THIS TAKES TIME TO FIX

LONG-TERM USE Px = BRAIN CHANGES
Slow-shallow breathing=<Brain Oxygen
Leads to Poor=Decision making-Memory-Emotions-Sleep-Evaluations
All thought-processing is affected in some way
EMOTIONAL INSTABILITY=Very damaging-Long lasting Px…Mood Px
THIS INCLUDES=Further destabilization-worsening of mental illnesses

ORGAN DAMAGE
Contrary to popular belief there is virtually no other organ damage w/pure opioids
This is different from: Alcohol-Cocaine-Meth-XTC-DXM

CONTAMINANTS=Cause some very serious Px=Pain med combos…Street drugs
NSAIDS=Aspirin-Ibuprofen-Naproxen=GI Px-BP/Cardiac meds-Kidney/Renal Px
TYLENOL=Safe if <3000mg daily…Avg=300mg/pill*…Liver/Kidney Px if more
IV USE=Changes everything…>Contaminants-Infections-Disease transfer
    >Risk of OD death…Once its in your blood you can’t get it back
WITHDRAWAL (Primary):
Brain has evolved a truly vicious set of feedback systems whose functions are to monitor body systems for extreme highs and lows and then modulate them.

Some recreational drugs produce feelings beyond what these systems were designed to correct so they shift into “Overdrive” in an effort to make things work properly.

SO: The initial rush of drug use will always be followed by devastating W/D Sx:
- Crash…Depression…Mood swings…Emotional Instability

W/D Severity= Type of drug…Length of use…Dosage…How used…Use Frequency
Sx are Nasty…Like the Flu…Do anything to avoid it…Starts when next dose is due
Lasts 5-10 days…Worst= Days 2-3-4……Methadone lasts longer - > Intense
Rarely fatal…Just wish you were dead… Exceptions= Cardiovascular/Colon Px

Head Px= Runny nose…Sneezing…Tearing…Itchy eyes…Yawning
Temp. Px= Hot/Cold flashes= Shivering/Sweating…Piloerection=”Gooseflesh”
Muscle Px= Spasms…Horific aches…Heavy limbs…Weakness…Twitch/Kick
Bone Px= Overwhelming “Bone aches”…Joints “On Fire”…Any movement hurts
GI Px= N/V…Cramps…GERD…Gas…Appetite Px
  - Diarrhea= Water reabsorbed-> Pressure to go…> Anal Sphincter response
  - Anal sphincter is eager to respond to pressure= Don’t Poot until controlled
Mental Px= Confusion…”Hurts to think”…Irritable…Depression Sx…Mood swings
Sleep Px= Can’t get to sleep/Stay asleep…> Tired…REM Rebound= Crazy Dreams
Adrenalin Rebound=> HR…>BP…Dilated Pupils…Anxiety
Males= Horny… Ejaculation Px… Impotence… Priapism…< Performance
Females= Horny… > Genital Sensitivity= Uncomfortable… Poor Orgasmic Response

PROTRACTED (Secondary) WITHDRAWAL
What is left when you quit using…Initial W/D Sx are over…Dealing w/the damage
Sx can last for months-years…Takes effort to get better…Does not “Just happen”
Multiple Body Systems have been altered…Having trouble “Keeping up”
Damaged Endorphin System= Poor reward response…” Just feel bad”…Dysphoria
Mental= Depression… Anxiety… Confusion…” Don’t get it”… Abnormal responses
Memory Px… Sleep Px…< Energy…” Give up” easily… Can’t enjoy things
Anhedonia(No Pleasure)… Emotional Instability

GI Px= GERD…” Stomach does not feel right”… Ulcers… Liver/Kidney Px
Poor Bonding= Family… Friends… Co-Workers… Customers… Pets
Sex Px= < Intimacy… Insecurities… Poor Performance… Poor Response

All these issues “Repair” at different rates and degrees… Some may never repair
Relapses should be expected and prepared for to < their severity and damage
DEATHS:
OD=Can happen with Single dose or in combo with other CNS depressants
Sx=Act Stupid…Confusion…Sleepy…Stupor…Muscle flaccidity(No strength)
   Cold-Clammy Skin…Pin-point pupils will start dilating as brain gets < Oxygen

Respiratory Depression=Gets worse…”Forget to breathe”…Sleepy-Coma-Death

<<BP + <<HR + Vasodilation=Cardiovascular Collapse=<BP cannot support system
Weakened Heart Function=Lungs fill with fluid and make it hard to breath
Start choking but <Cough reflex prevents expulsion of fluid=Death by “Drowning”
Foam comes out of mouth at the end=Trying to breathe fluid=”Making Bubbles”

DETERMINING OD DEATHS
Harder than you might think…Many Complicating Factors
Current Technology cannot accurately determine whether/which/if drugs did it
Tolerance = High doses of chronic user easily kills naïve user…No “OD Standard”
Blood Levels = Vary wildly among individuals…Liver-Kidney-Meds-Sex
Post Mortem Distribution = Natural shift in drug levels after death-Organs to Blood
Heroin or Morphine ? = Morphine is major metabolite of Heroin…6-MAM=6-8 hrs
SO: Post-Mortem blood levels cannot be used by themselves to determine COD
   This makes “Number of Opioid OD Deaths” questionable at best

TYLENOL = ACETAMINOPHEN POISONING
Liver/Kidney damage starts= >3Gm/day x10d…Alcoholism=2Gm
10Gm=Min. Toxic Dose

Day 1=N/V…Confusion…<BP…Jaundice…Stomach pain
   Antidote=N-Acetylcysteine if given in <16hrs
Day 2-3=Feel better…All Sx improve…Antidote no longer helpful
Day 4-5=Everything gets much worse…Liver enzymes go bad
Day 7-8=Recover-Die-Transplant…Agonizing way to go

NSAIDS = Non-Steroidal-Anti-Inflammatory Drugs
Celebrex – Diclofenac – Vioxx Worst…Naproxen-Ibuprofen bad
High Dose Use= >BP…Kidney Px…GI Px…Cardiac Px…Clot Px…>Rick of MI
Death is NOT SUDDEN so <<Drama…Death estimates= 20-50,000/yr
Use only with extreme caution in those with existing or potential cardiac problems
DIFFERENT OPIOIDS

OPIUM= PAPAVER SOMNIFERUM…CII
"Turkish Poppy”…Afghanistan-Pakistan
Annual Plant…Growth cycle=120days
Pods= Opium latex…Ornamentals…”Poppy Tea”
Seeds= Morphine-Codeine-Thebaine =(+)UDS…This is a “True (+)”
   Also contain Papaverine (Vasodilator)…Noscapine(>N/V)
   Strengths vary up to 100mcg/Gm Morphine…Cook-Paint-Perfume
Raw Opium = Dark and Sticky…Stable
Entire plant contains Morphine…Roots have >Thebaine
PAREGORIC=Tincture of Opium…2mg Morphine/5ml…Used for Diarrhea
   “Modern-Day Laudanum”

MORPHINE…CII
Gold Standard for IV/IM pain relief…None more effective via Injection
Endogenous/Poppy seeds/Recently synthesized in Lab
VERY effective pain relief…Pain induced PTSD
MS Contin…Kadian…Avinza…ER/IR Tabs…Caps…Liquid…Injection
Embeda ER = Morphine + Naltrexone…Never use with alcohol
Alkaline blood=Antacids/Tums=Quicker absorption into brain
Not as efficient orally…Only 25% absorption
Metabolites: Morphine-6-Glucuronide=Active analgesia
   Morphine-3-Glucuronide=Hyperalgesia-Convulsions

HEROIN = Diacetylmorphine…CI
Invented 1874…Market 1898 via Bayer Drug Co…”Glyco-Heroin for TB cough
Illegal in US in 1924…Now CI Drug…Legal in Great Britain-Canada-Hong Kong
Acute pain…MI…Surgical…Terminal Illness…Opioid rotation…Cough
DAM is Probably Inactive…Rapid transport of Morphine/6-MAM into brain
Metab into 6-MAM(1st 3 hrs) – Morphine(Next 3-5 hrs) - 6-Morphine-6-Gluconate
Poor oral absorption…Metab into Morphine
Very fat soluble=IV use Hits brain quicker…3x more potent than morphine
IV OD deaths rare in long time users…Usually due to Contaminants-HIV-Hep.C
Can be Snorted or Smoked or Rectal Supp. if strong enough
Making a strong comeback…>Available/cheaper than Rx Opioids.…”Balloon Effect”
Black Tar Heroin= Impure form due to simpler/inefficient processing…>Vein Px
UDS Detection Px= Heroin=10 min…6-MAM=6-8 hrs…Morphine=3 days
CODEINE…Usually CIII
CIII=w/APAP for pain=Tylenol # 1-2-3-4 (1=7.5…2=15…3=30…4=60mg)
CIII= w/Guaifenesin or Cold meds for cough=Phenergan/Cod…Rob. AC
CII if used alone= Injection…Tabs…Capsules
Pro-Drug= Not effective until 2D6 enzyme metabolizes it into Morphine
Px= Very Weak analgesic…GI Px…Slow onset…Doesn’t last long
   More Histamine Increase=Itching-Swelling-Flushin
Likely to see more since Hydrocodone now a CII…POOR replacement

HYDROCODONE… CII in Oct. 2014
Vicodin..Lortab..Norco..Vicoprofen..Hycodan..Tussionex
Structurally similar to Codeine
Moderate pain=1980’s = Combo w/APAP= Vicodin…Lortab…Norco
1’d# =Opioid…2nd# =APAP/Ibuprofen (5/300…7.5/300..10/325)(All < 325mg in 2014)
Prior 15mg/combo limit no longer in effect…Look for > strengths
Cough=Orig.Use in 1950s=Hycodan(Homatropine)..Tussionex(Chlorpheniramine)
Lasts only 2-4 hours…Must re-dose often
ZOHYDRO ER=Single entity…10mg-50mg twice daily…”Not Tamper-Resistant”
HYSINGLA ER= Single entity…20-120mg once daily…”Tamper-Resistant”
2D6 metabolite=Hydromorphone=>Euphoria-Analgesia
SS = Good oral absorption…<GI upset…Initial stimulation…Aggression…Anger
   Associated with few deaths despite >Rx written->Availability

DIHYDROCODEINE…CIII
Synalgos DC…Panlor DC…Panlor SS…Anodynos DHC
Old drug…Developed in 1908
Twice as strong as Codeine (16mg DHC=32mg Codeine)…Fx are similiar
Combined with APAP-Aspirin-Caffeine-Antihistamines-Decongestants
Potential CIII opioid replacement since Hydrocodone changed to CII

HYDROMORPHONE…CII
Dilaudid=IR… Exalgo = Time-release Hydromorphone…Lasts 24 hours
Also Active metabolite of Morphine and Hydrocodone
10x more potent than Morphine…>Effective orally than Morphine
Best Rx available for cough…Excellent pain relief…Works quickly
DOC for Renal/Kidney Px – Kidney stones = No Active or Toxic Metabolites
More Effective in Opiate Maintenance than Methadone in Canada studies
**OXYCODONE...CII**
Most Prescribed CII Rx Opioid...Made from Thebaine
Excellent for Moderate-Severe pain...Chronic or Acute
Arthritis...Surgery...Trauma...Post-Herpatic Neuropathy=Shingles
IR Alone= Tabs...Capsules...Liquid
IR Combo= Percocet-Tylox(APAP)...Percodan(ASA)...Combunox(Ibuprofen)

**OXYCONTIN**=...Time-release mechanism changed...No initial dump...OC-OP
Pain relief and Buzz not the same...>Break thru meds

**TARGINIQ ER**= Oxy + Naloxone...5/2.5-10/5-20/10-20/40...Twice daily
Naloxone released if crushed=Antagonism of Opioid

**XARTEMIS ER**= Oxy + APAP...7.5/325...Twice daily
Transdermal Patch = In Phase 2 Trials
**SS**= More effectively orally than Morphine...>Aggression-Meanness
>>Emotional relief=<Suffering and fear...Females more affected
OxyContin is the most demonized drug in US despite helping many people
”Poster Child” for “Bad Drug”

**OXYMORPHONE...CII**
Opana oral tabs...Numorphan Rectal Suppositories
10x more potent than Morphine..Active metabolite of Morphine
SS = Few Drug Interactions...No Active Metabolites

**MEPERIDINE - PETHIDINE...CII**
Fully Synthetic...Developed in 1930’s Germany
Demerol...Mepergan Fortis (Plus Promethazine to <N/V)
1/10 as strong as morphine...Quick-effective analgesic/anesthetic...Oral-Inject
Use has decreased due to Bizarre Side Fx
Pain relief lasts only ~3 hrs...Must re-dose often
SS = Normeperidine=Toxic metabolite lasts 30 hrs and accumulates
  Anxiety-Delerium-Hallucinations-Twitching-Emotional Instability-Seizures
  DO NOT USE with Mental D/O’s or Kidney Px
  >Drying Fx...Pupil Dilation
  OD not reversed by Naloxone...No Antitussive Fx
Not a good drug to abuse...>Use = >Psychotic Fx
FENTANYL...CII
Duragesic=Patch...Actiq=Buccal...Sublimaze=IV...Fentora=SL
Anesthetic Analogs= Sufentanil...Alfentanil
“China White”=Easily made to cut Heroin...Easy to OD
Works Quickly BUT Does Not last very long
Alkaline pH=Tums= >Absorption= >All Fx
Absorbed best= Mucous membranes=Buccal-SL-Nasal-Anal
                  Skin= Apply patch to hairless-soft areas
                  Poor Absorption if Swallowed
80-100x more potent than Morphine
Uses= Anesthesia...Chronic pain...Break-Thru pain
       Swallowing difficulties...Scared Children
       Opioid-tolerant chronic pain sufferers
3A4 Inhibitors >Levels=Prozac-BCP-Grapefruit-etc
Patch= Opioid-Tolerant only...Tender/Irritated skin or Heat >Absorption
       Takes several hours for drug to clear after patch removed
       Takes 6-12 hours to start working to < pain
       Some drug is always left in patch...Flush...Keep away from child/pets
Actiq=Lollipop-Sucker-Lozenge...Dissolve next to cheek (Buccal)
Fentora= Dissolve under tongue (Sublingual)...Break-thru pain

TRAMADOL...Now CIV (August 2014)
Ultram...Ultram ER...Ultracet...Ryzolt
Activates: Mu-Serotonin-Norepi Receptors...6000x < affinity than Morphine
Uses= Mild pain...Nerve pain...Joint pain...
Off-Label= Depression-Anxiety-OCD-Premature Ejaculation...<WD Sx
SS= <Resp depression...No cardiac Fx...<Abuse risk...<Tolerance
       M1 Metabolite much more effective than Tramadol...>2D6=>Pain Relief
Recently found in Root bark of Nauclea Latifolia Plant in Africa

TAPENTADOL...CII
Nucynta...Newest Rx Opioid...CII Probably due to “Bad Timing”
50mg Nucynta = ~ 10mg Oxycodone...”No” Physical Dependence
Uses= Moderate-severe acute pain in people > 18
Structurally similar to Tramadol BUT >>>>>>Pain relief
BUPRENORPHINE...CIII
Invented in 1970 = CII...Buprenex in 1985 = CV...Suboxone in 2002 = CIII
Uses = Pain...Opioid Maintenance...Opioid Detox

BUPRENEX = IM / IV Injection for pain only
SUBUTEX = Sublingual Tab...Used for Opioid Maintenance and Pain...2 – 8mg
SUBOXONE = Subutex + Naloxone added at 4:1 Ratio...Film or Generic SL Tabs
ZUBSOLV = Similar to Suboxone...Claims better absorption so doses are less
BUNAVAIL= Similar to Suboxone...Muco-Adhesive Buccal “Patch”
BUTRANS = Once a week Transdermal Patch...Chronic Pain ONLY
PROBUPHINE =6 month Opioid Maintenance via “Drug Rod”...FDA rejected

Partial Mu Agonist= <Abuse...<Dependence...<W/D Fx...Safer...”Ceiling Effect”
Kappa Receptor Antagonist = >Antidepressant Fx...>Physical / Mental Activities

Ceiling Fx = NO FX on Pain-Maintenance-Euphoria-Breathing Above Max. dose
Attaches tightly to Mu but does not Fully Activate it...Released slowly

Poor GI Absorption = Not Very Effective if Swallowed or Infant is Breast-Fed
Good Mucous Membrane Absorption = Under Tongue-Nasal-Rectal-Vaginal-Alc.

PAIN DOSE = 4 – 32mg taken 3-4 times daily...Special DEA# NOT Needed
MAINTENANCE DOSE = 4-32mg taken ONCE daily...=~ 60-80mg Methadone

OD Doses produce Little Respiratory Depression unless combined with BZ-Alc

ABUSE = Has potential but not a very good buzz...Unless Liquefied or Injected
DIVERSION = Mostly Diverted to <W/D Sx...<Cravings...<Other Opioid Use

METHADONE...CII
Invented in 1939 Germany-Named AMIDON...Search for Synthetic Analgesics
Uses= Chronic Pain Only...Cough...Opioid Maintenance
Doses for pain/cough not the same as Maintenance doses

Biphasic Metabolism-Elimination: Takes place in 2 separate stages
1st=Rapid...Lasts 6-8hrs...Absorbed into tissue...>Pain relief...>Mu
2nd=Slower...Lasts 20-30hrs...Elim from tissue...<Mu

Absorption-Elimination is inconsistent and Varies greatly
Blood levels don’t correlate to pain relief or “Cause of death”

<Rush=<Emotional relief = <Abuse or >Dose...Easy to OD
QT Wave Prolongation=Arrythmias...Heart Px = Cause of death
Useful part of Opioid Rotation...<Pregnancy/Breastfeeding Px
DEATHS=Most are pain and NOT maintenance patients...35% of Opioid Deaths
ANTAGONISTS:

NALOXONE (Narcan)

Attach to Mu...Prevent other opioids from working...No Fx of their own
Injected...Lasts only ~30 minutes...Must be re-dosed...Immed. W/D Sx
Reverses Resp. Depression but No Fx on Pulmonary Edema (Lungs full of fluid)

NEW=Intra-Nasal Naloxone=Atomizer tip attached to pre-filled syringe-Squirt
Rx by Dr=New Rx for Long-term Opioid therapy...All Long-acting Opioids
Opioid Rotations...Any dose increase...Taking 2 or more Opioids

NALTREXONE (Trexan-Revia-Vivitrol)

Trexan=50mg-Opiates...Revia=Alcohol...Vivitrol=380mg IM Monthly Injection
Basically same Fx as Narcan BUT Effective orally if taken daily (50mg 1-3x daily)
<Opioid Use=Get < reward from Opioids...Must be motivated or Just switch drugs
Px=Hepatotoxic(Liver damage) in high doses=Dark Urine-Pale Poop-Yellow eyes
Don't use if Pregnant-Breast Feeding...Poor pain control if injured-surgery
N/V...Anxiety...Drowsy...HA...Depression...Suicide...Insomnia...Aches
Increases the Buzz associated with smoking Marijuana