Pain Management for Chronic Non-Cancer Related Pain Conference

L.A. Care HEALTH PLAN®

Almansor Court in Alhambra, CA

Lakeview Room

Saturday, August 20, 2016

Opening Remarks & Conference Overview

Clayton Chau, MD, PhD

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Disclosure

All planners and speakers of this CME/CE activity do not have relevant financial relationships with commercial interests.

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Understanding Chronic Pain, New Guidelines for Management of Chronic Pain and Role of Naloxone

Melissa Durham, PharmD

L.A. Care HEALTH PLAN®

Management of Chronic Non-Oncologic Pain

Melissa Durham, Pharm.D., MACM, BCACP, DAAPM

Disclosure

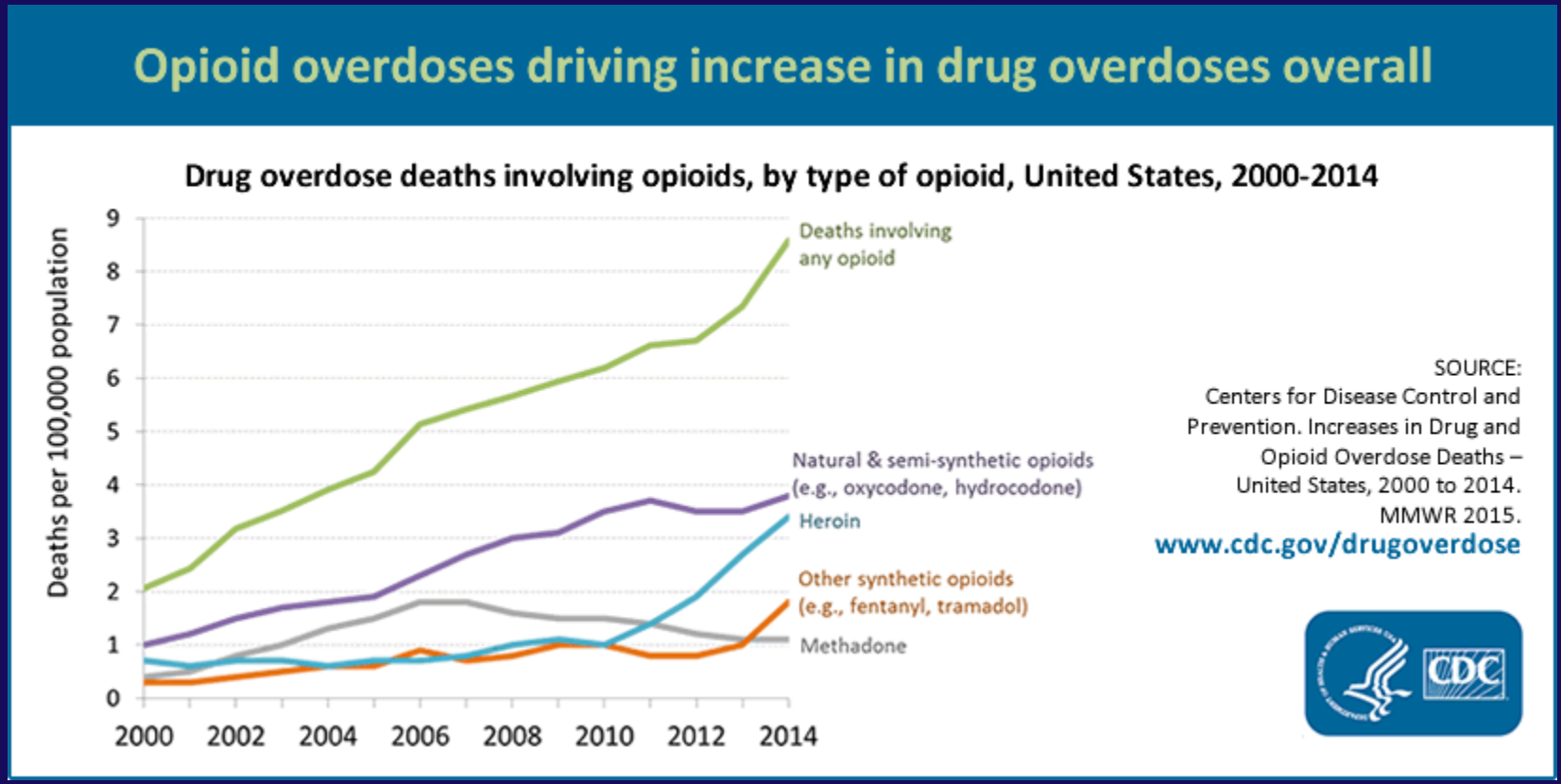
I do not have relevant financial relationships with commercial interests.

Session Objectives

By the end of the session, participants will be able to:

1) Summarize the CDC Guidelines for Prescribing Opioids for Chronic Pain
2) Explain the assessment and treatment approach to a patient with chronic pain
3) List ways in which clinicians may minimize risk when prescribing opioids

The Opioid Epidemic



- 78 people die each day in the U.S. from an opioid overdose

https://www.cdc.gov/drugoverdose/epidemic/

Pain Can Affect All Aspects of Life

Functional Status

- Physical functioning
- Activities of daily living
- Work
- Recreation

Psychological Morbidity

- Depression
- Anxiety, anger
- Sleep disturbances
- Loss of self-esteem

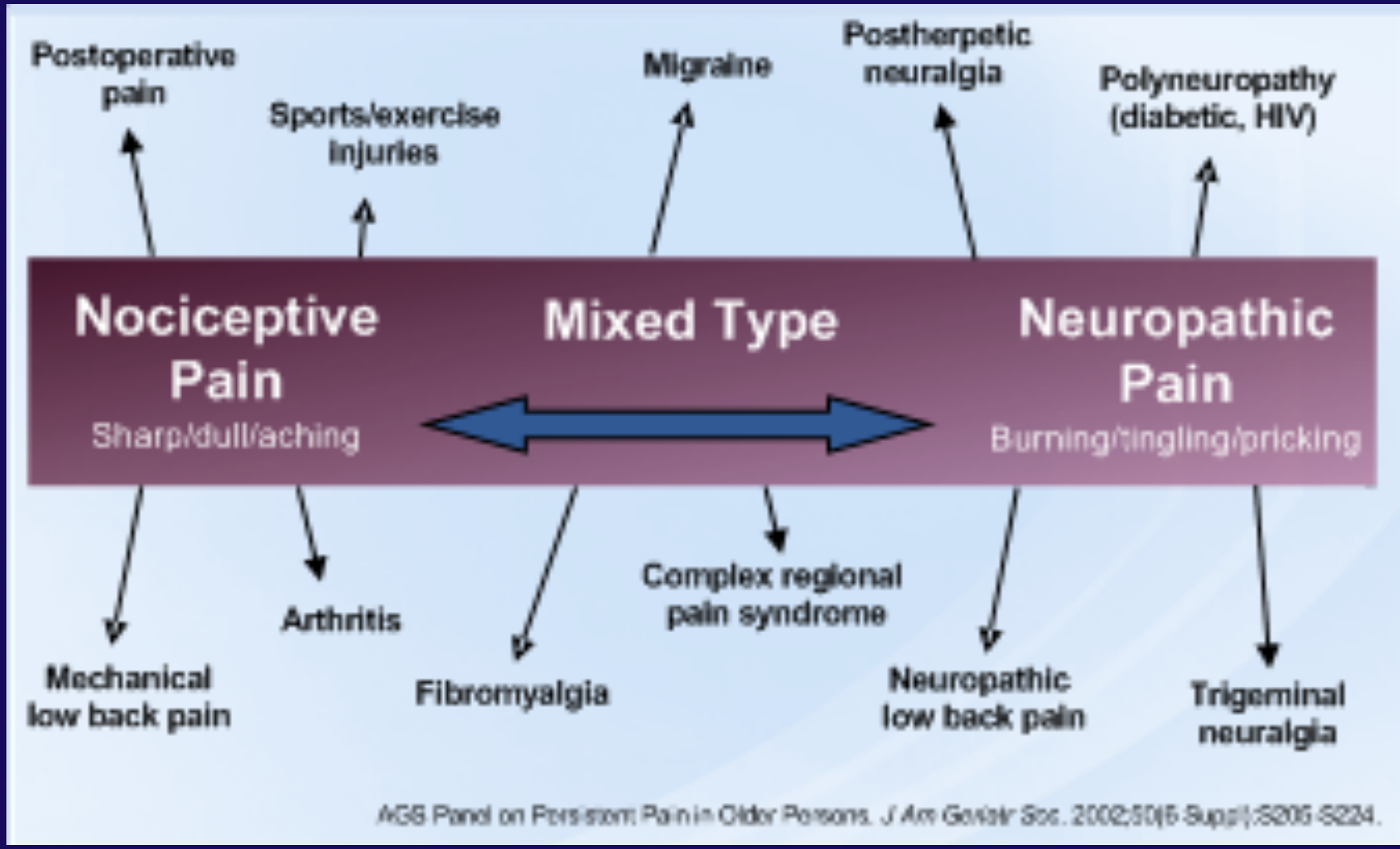
Social Consequences

- Marital/family relations
- Intimacy/sexual activity
- Social isolation

Socioeconomic Consequences

- Healthcare costs
- Disability
- Lost work days

The Spectrum of Pain



Acute vs. Chronic Pain

Characteristic	Acute Pain	Chronic Pain
Relief of Pain	Highly Desirable	Highly Desirable
Dependence & Tolerance to Medication	Unusual	Common
Psychological Component	Usually Not Present	Often a Major Problem
Organic Cause	Common	Often Not Present
Environmental Contributions & Family Involvement	Small	Significant
Insomnia	Unusual	Common Component
Treatment Goal	Cure	Functionality

CDC Guidelines for Prescribing Opioids for Chronic Pain

Determining when to initiate or continue opioids for chronic pain outside end-of-life care

- Preference for non-pharm and non-opioid pharm therapy
- Providers need to establish treatment goals for pain and function
- Providers need to discuss patients' risks and realistic benefits

https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

CDC Guidelines for Prescribing Opioids for Chronic Pain

Opioid selection, dosage, duration, follow-up, and discontinuation

- At start of opioid therapy providers should:
  - Prescribe short-acting opioids instead of ER/LA opioids
  - Prescribe the lowest possible effective dosage and be cautious of increasing dose to ≥50 MME/day
- Long-term opioid use often begins with treatment of acute pain

https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

CDC Guidelines for Prescribing Opioids for Chronic Pain

Opioid selection, dosage, duration, follow-up, and discontinuation

- Re-evaluation of patients within 1 to 4 weeks of starting long-term opioid therapy or dose escalation
- Re-evaluation of long-term opioid therapy every 3 months

https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

CDC Guidelines for Prescribing Opioids for Chronic Pain

Assessing risk and addressing harms of opioid use

- Before starting and periodically during continuation of opioid therapy, evaluate risk factors for opioid-related harms
- Offer naloxone when factors increase risk of opioid-related harms
- Review of patient's hx of controlled substance prescriptions using state PDMP data

https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

CDC Guidelines for Prescribing Opioids for Chronic Pain

Assessing risk and addressing harms of opioid use

- Urine drug testing before starting and at least annually in long-term opioid therapy
- Avoid prescribing opioid pain meds and benzodiazepines concurrently
- Offer or arrange evidence-based treatment (opioid agonist in combination with behavioral therapies) for patients with opioid use d/o

https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

The Four A's of Pain

- Analgesia
- Activities of daily living
- Adverse effects
- Aberrant drug behaviors

- 2 other important A's
  - Assessment
  - Action (treatment plan)

Passik SD, Weinreb HJ. Adv Ther. 2000;17:70-83.

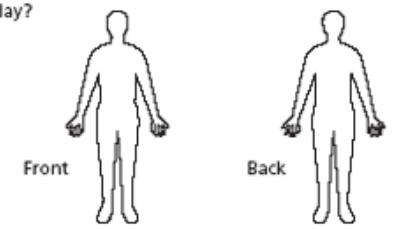
Brief Pain Inventory

- Need detailed hx of pain, medical/ surgical hx, liver/ renal function, previous opiate use

Brief Pain Inventory

Name Date Time

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, toothaches). Have you had pain other than these everyday types of pain today?
   1. Yes 2. No
2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its worst in the past 24 hours.

   0 1 2 3 4 5 6 7 8 9 10
   No pain — *Pain as bad as you can imagine*

4. Please rate your pain by circling the one number that best describes your pain at its least in the last 24 hours.

   0 1 2 3 4 5 6 7 8 9 10
   No pain — *Pain as bad as you can imagine*

5. Please rate your pain by circling the one number that best describes your pain on average.

   0 1 2 3 4 5 6 7 8 9 10
   No pain — *Pain as bad as you can imagine*

6. Please rate your pain by circling the one number that tells how much pain you have right now.

   0 1 2 3 4 5 6 7 8 9 10
   No pain — *Pain as bad as you can imagine*

7. What treatment or medication are you receiving for the pain?

   _____
   _____
   _____
   _____
   _____

8. In the past 24 hours, how much relief have pain treatments or medication provided? Please circle the one percentage that most shows how much relief you have received.

   0% 10 20 30 40 50 60 70 80 90 100%
   No relief — *Complete relief*

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

   A. General activity
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere — *Completely interferes*

   B. Mood
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere — *Completely interferes*

   C. Walking ability
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere — *Completely interferes*

   D. Normal work (includes both work outside the home and housework)
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere — *Completely interferes*

   E. Relations with other people
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere — *Completely interferes*

   F. Sleep
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere — *Completely interferes*

   G. Enjoyment of life
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere — *Completely interferes*

   H. Ability to concentrate
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere — *Completely interferes*

   I. Appetite
   0 1 2 3 4 5 6 7 8 9 10
   Does not interfere — *Completely interferes*

Assessment of Pain - PQRSTU

- P – Provocative/Palliative
  - What makes if worse/better?
- Q – Quality
  - Describe the pain.
- R – Radiation
  - Where is the pain?
- S – Severity
  - How does it compare with other pain you have experienced?
- T – Temporal factors
  - Does the pain change with time?
- U – YOU
  - How has the pain affected your daily life?

Pain Assessment Scales

Verbal Pain Intensity Scale[1]

Visual Analog Scale[1]

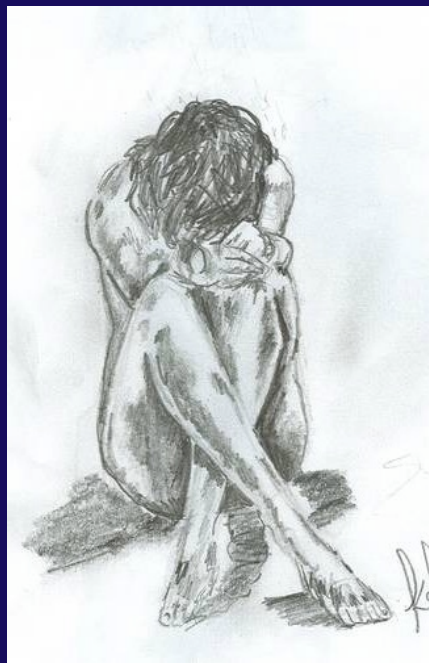
0–10 Numeric Pain Intensity Scale[2]

"Faces" Scale[3]

1. Portenoy RK, Kanner RM, eds. *Pain Management: Theory and Practice*. 1996:8-10.
2. McCaffery M, Pasero C. *Pain: Clinical Manual*. Mosby, Inc. 1999:16.
3. Wong DL. *Waley and Wong's Essentials of Pediatric Nursing 5th ed.* 1997:1215-1216.

Importance of Identifying Psychopathology

- Interferes with successful rehabilitation
- Increases pain intensity and disability
- Anxiety decreases pain thresholds and tolerances
- Depression is linked to poor treatment outcomes with traditional medical approaches
  - Significantly higher rates in patients with chronic pain
- 3X more likely to be non-adherent



Clin J Pain 1996;12:118-125
Pain 1998;35:105-113
J Clin Consult Psychiatry 1998;05:434-439

Barriers to Effective Pain Management

Patients

- Fear of not being believed
- Cultural barriers
- “Pain is something I just have to try to live with”
- Fear of addiction
- Intolerance to side effects
- Economic barriers

Healthcare Providers

- Fail to routinely assess and document pain
- Inappropriate or unknown diagnosis
- Misunderstanding of pharmacology or PK
- Fear of patient addiction
- Fear of regulatory scrutiny

Multidisciplinary Approach to Pain Management

- Physicians
  - Anesthesiologists, pain management specialists, often with background in psych
  - Orthopedists, rheumatologists, endocrinologists
- Pain psychologists, psychiatrists
- Physical therapists
- Occupational therapists
- Acupuncturists
- AND Pharmacists!!

Opioids for Breakthrough Pain

- Morphine Sulfate IR (MSIR, Roxanol)
- Oxycodone IR (Oxy IR, Roxicodone)
- Hydromorphone (Dilaudid)
- Fentanyl (Actiq, Fentora, Sublimaze, Onsolis, Lazanda, Subsys)
- Tramadol (Ultram, Ryzolt),Tramadol/APAP (Ultracet)
- Tapentadol (Nucynta)
- Buprenorphine (Subutex, Buprenex)
- Codeine/APAP (Tylenol #2, 3, 4)
- Hydrocodone/APAP (Vicodin, Vicodin ES, Vicodin HP, Lortab, Lorcet, Norco), Hydrocodone/Ibuprofen (Vicoprofen, Reprexain)
- Oxycodone/APAP (Percocet), Oxycodone/ASA (Percodan), Oxycodone/Ibuprofen (Combunox)

Long-Acting Opioids

- Hydrocodone (Zohydro ER, Hysingla ER)
- Oxycodone/Naloxone (Targiniq)
- Oxycodone/Acetaminophen (Xartemis XR)
- Morpine Sulfate ER (Avinza, Kadian, MS Contin, Oramorph SR)
- Hydromorphone ER (Exalgo)
- Oxycodone ER (Oxycontin)
- Oxymorphone ER (Opana ER)
- Fentanyl Transdermal (Duragesic)
- Methadone (Dolophine)
- Tapentadol ER (Nucynta ER)
- Tramadol ER (Ultram ER)
- Buprenorphine patch (Butrans)

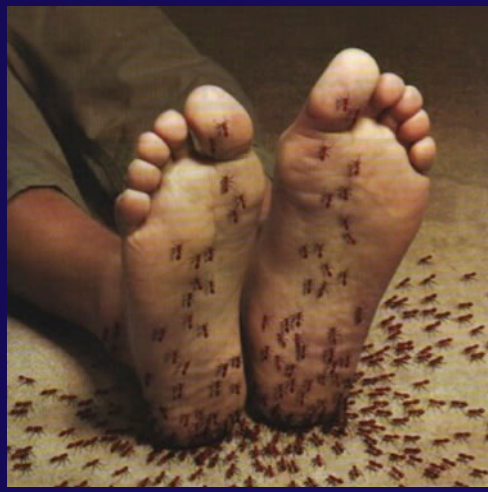
Tamper-Deterrent Formulations

- Hydrocodone (Hysingla ER, Zohydro ER)
- Oxycodone/Naloxone (Targiniq ER)*
- Oxycodone (Oxycontin)*
- Oxycodone (Oxecta)*
  - Off Market
- Tapentadol (Nucynta ER)
- Morphine/Naltrexone (Embeda)*
  - Withdrawn 2011, will be back early 2015
- Oxymorphone (Opana ER)

* = “Abuse Deterrent” per FDA

Pharmacotherapy for Neuropathic Pain

- SNRIs
  - Venlafaxine, Duloxetine, Milnacipran
- TCAs
  - Amitriptyline, Desipramine, Nortriptyline
- Opiates
- AEDs
  - Gabapentin, Pregabalin Topiramate, Carbamazepine, Oxcarbazepine
- Anesthetics
  - Lidocaine
- Corticosteroids



Topical Therapy

- Menthol
- Capsaicin
- Lidocaine
- NSAIDs
  - Salicylates
  - Diclofenac
  - Ketoprofen
- Clonidine
- Gabapentin
- Muscle relaxants

Codeine Allergy

- If a patient has a true allergy to codeine, morphine, hydrocodone, etc. he/she may safely take
  - Methadone
  - Meperidine
  - Fentanyl
- Probably ok, but avoid if allergic reaction is severe
  - Tapentadol
  - Tramadol
  - Buprenorphine

Opioid Receptor Antagonists

- Competitively bind to opiate receptor sites in the body to reverse the effects of the opiates
- Naloxone (Narcan®)
  - For overdose of opiates, patients with respiratory or cardiovascular depression from therapeutic doses of opiates, coma of unknown etiology
    - 0.4-0.8 mg IV, with repetitive doses required
- Naltrexone (Revia® (PO) and Vivitrol® (IM))
  - For adjuvant treatment of alcoholism, opioid detox and relapse prevention following detox
- May precipitate withdrawal in patients addicted to opiates

Paradox of Opioids

- Some patients taking chronic opioids for pain may be unable to discern negative impact on quality of life
- Similar to alcoholics, these patients have poor insight into loss of function secondary to opioids
- Many of these patients have pain reduction following opioid cessation

Hyperalgesia

- Increasing pain despite increasing opioid doses
- Possibly related to
  - Morphine 3-glucuronide
  - Loss of spinal GABA neurons to apoptosis
  - NMDA receptor agonism
  - Enhanced release of excitatory neurotransmitters
- Some studies show amlodipine and ketamine may help prevent hyperalgesia

Tolerance and Physical Dependence

- Repeated administration of therapeutic doses results in gradual loss of effectiveness
  - Analgesia
  - Sedation
  - Respiratory depression
  - Not constipation!!
  - Not miosis!! – OD
- Larger dose must be administered to produce original response
- Physical dependence develops along with tolerance
- Dependence vs. Addiction vs. Pseudo-Addiction

Predictors of Abuse

- Past substance abuse[1, 3] or family Hx[3]
- Psychopathology[2, 3, 4]
- Age (16-45 years)[3]
- Hx of preadolescent sexual abuse[3]
- Predictors for continued use after treatment[4]
  - High level of use pre-treatment
  - Depression, high stress
  - Employment problems
  - Substance abusing peers

1) Ives, et al. BMC Health Services Research 2006, 6:46
2) Manchikanti L, et al. J Opioid Manag. 2007 Mar-Apr;3(2):89-100.
3) Webster LR, Webster RM. Pain Med. 2005 Nov-Dec;6(6):432-42
4) Brewer D, et al. Addiction, Volume 93, Number 1, 1 January 1998, pp. 73-92(20)

Aberrant Drug-Taking Behaviors

- Major
  - Selling Rx drugs
  - Prescription forgery
  - Stealing or borrowing drugs
  - Injecting oral formulations
  - Obtaining prescription drugs from nonmedical sources
  - Concurrent abuse of related illicit drugs
  - Multiple unsanctioned dose escalations
  - Recurrent prescription losses
- Minor
  - Aggressive complaining about need for higher doses
  - Drug hoarding during periods of reduced symptoms
  - Requesting specific drugs
  - Acquisition of similar drugs from other medical sources
  - Unsanctioned dose escalation 1-2 times
  - Unapproved use of the drug to treat another symptom

Adapted from:

Portenoy RK. Journal of Pain and Symptom Management, 1996; 11;203-217.
Manchikanti L. Pain Physician 2008; Opioids Special Issue: 11:S155-180

Dichotomous Roles

- Caring clinician
  - Moral/ethical responsibility to relieve pain and suffering
- Policing investigator
  - Legal/regulatory obligation to control abuse-prone medications
- Both prescribers and dispensers share responsibility

Good Clinical Processes to Minimize Abuse Risk

- Thorough history
  - Personal or family drug issues, past or present
- Patient informed consent
- Controlled substance agreement
- Risk Assessment Tools
  - Opioid Risk Tool (ORT)
  - Current Opioid Misuse Measure (COMM)™
  - Screener and Opioid Assessment for Patients with Pain (SOAPP)®

Date _____

Patient Name _____

OPIOID RISK TOOL

		Mark each box that applies	Item Score If Female	Item Score If Male
1. Family History of Substance Abuse	Alcohol	[ ]	1	3
	Illegal Drugs	[ ]	2	3
	Prescription Drugs	[ ]	4	4
2. Personal History of Substance Abuse	Alcohol	[ ]	3	3
	Illegal Drugs	[ ]	4	4
	Prescription Drugs	[ ]	5	5
3. Age (Mark box if 16 – 45)		[ ]	1	1
4. History of Preadolescent Sexual Abuse		[ ]	3	0
5. Psychological Disease	Attention Deficit Disorder, Obsessive Compulsive Disorder, Bipolar, Schizophrenia	[ ]	2	2
	Depression	[ ]	1	1
		TOTAL	_____	_____

Total Score Risk Category
Low Risk 0 – 3
Moderate Risk 4 – 7
High Risk ≥ 8

Reference: Webster LR. Predicting aberrant behaviors in opioid-treated patients: Preliminary validation of the opioid risk tool. *Pain Medicine.* 2005;6(6):432-442. Used with permission.

http://www.opioidrisk.com

Good Clinical Processes to Minimize Abuse Risk

- Rational Controls
  - Small quantities
  - Frequent visits
  - One prescriber/group
  - One pharmacy
  - Tamper-deterrent formulations
- Monitoring
  - Pain diary
  - Urine testing
  - Prescription Drug Monitoring Programs
  - The 4 A's of Pain

Urine Drug Testing (UDT)

- Incomplete evidence for urine testing preventing opioid misuse
  - Weak evidence, but theoretical value
- Consider UDT in all patients
  - Especially those starting opioid therapy
  - When making changes in therapy
  - When pain persists despite reasonable opioid therapy
  - In response to aberrant behavior
- Cheap, effective, and well-tolerated
- Note: Parent compound and metabolites should be present

1) Chou R, Fanciullo GJ, Fine PG, et al. *J Pain* 2009;10(2):113-30

2) Christo PJ, et al. *Pain Physician* 2011; 14:123-143.

3) Federation of State Medical Boards of the United States, Inc. Model policy for the use of controlled substances for the treatment of pain. *J Pain Palliat Care Pharmacother* 2005;19(2):73-8

Prescription Drug Monitoring Programs Example: California

- Controlled Substance Utilization and Evaluation System (CURES)
- Pharmacies transmit data electronically on a weekly basis
- Schedules II-IV
- Supposed to be “real-time” but there is some lag
- All providers that prescribe or dispense controlled substances may (should) register for online access.

Thank You

Overview of State and Federal Regulations, Take Back Program and CURES

Holly Strom, PharmD

L.A. Care HEALTH PLAN®

Safe Med LA

Los Angeles County
Prescription Drug Abuse Coalition

Holly A. Strom, RPh.
Pharmacy Practice Action Team
SafeMedLA
Los Angeles County Prescription Drug Abuse Coalition

Disclosure

The financial relationships listed below are not relevant to the activity.

COMMERCIAL INTEREST FOR HOLLY STROM		
Commercial Interest	Nature of relevant Financial relationship	
	What was received?	For What Role?
Becton Dickinson & Co.	Dividends	Investor
Bristol Myers Squibb	Dividends	Investor
Johnson & Johnson Co.	Dividends	Investor
Mead Johnson Nutrition Co	Dividends	Investor
Target Corp	Dividends	Investor
Wal-Mart Stores Inc	Dividends	Investor
Abbvie Inc	Dividends, capital gains	Investor
Abbott Labs	Dividends, capital gains	Investor
Biogen	Dividends, capital gains	Investor
Fund STMSX: Ligand Pharmaceuticals	Dividends	Investor
Fund SEITX: Teva Pharmaceutical Industries, Novartis AG, Sanofi SA, Akzo Nobel NV	Dividends	Investor
Joel L Strom DDS-spouse's dental office	Salary, distributions	Married, filing joint tax returns

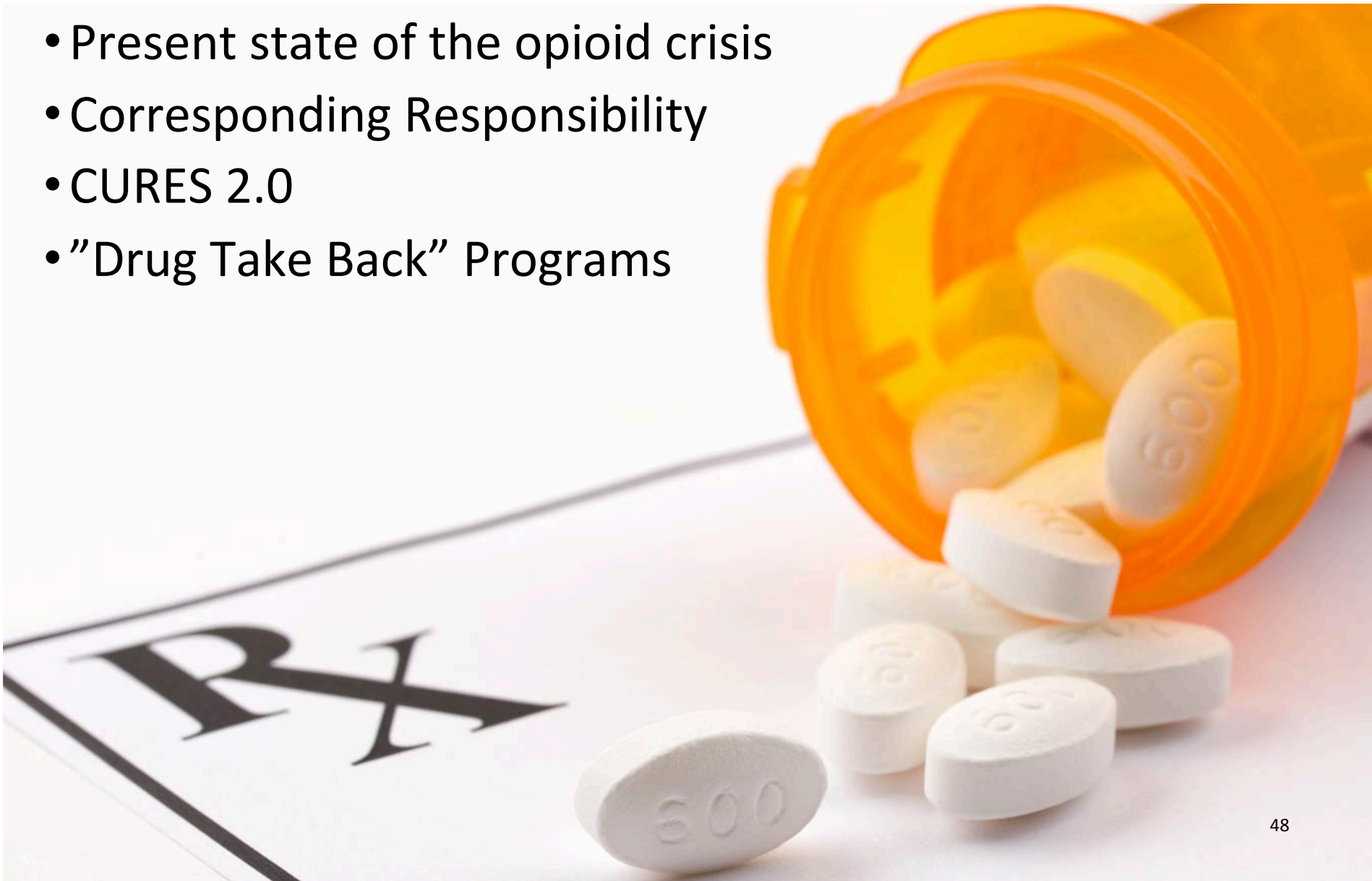
Safe Prescribing Pharmacy Practice Action Team

- Focuses:
  - Provide **education for pharmacists about their critical responsibility and role in the dispensing of opioid pain relievers**, particularly when prescribing practices are inconsistent with recommended safe prescribing practices.
    - **Education and training for the furnishing of naloxone**, which can be provided by pharmacists in CA without a prescription (per regulations adopted by the CA State Board of Pharmacy effective January 2016).

Getting To Know You

Goals for this section

- Present state of the opioid crisis
- Corresponding Responsibility
- CURES 2.0
- ”Drug Take Back” Programs



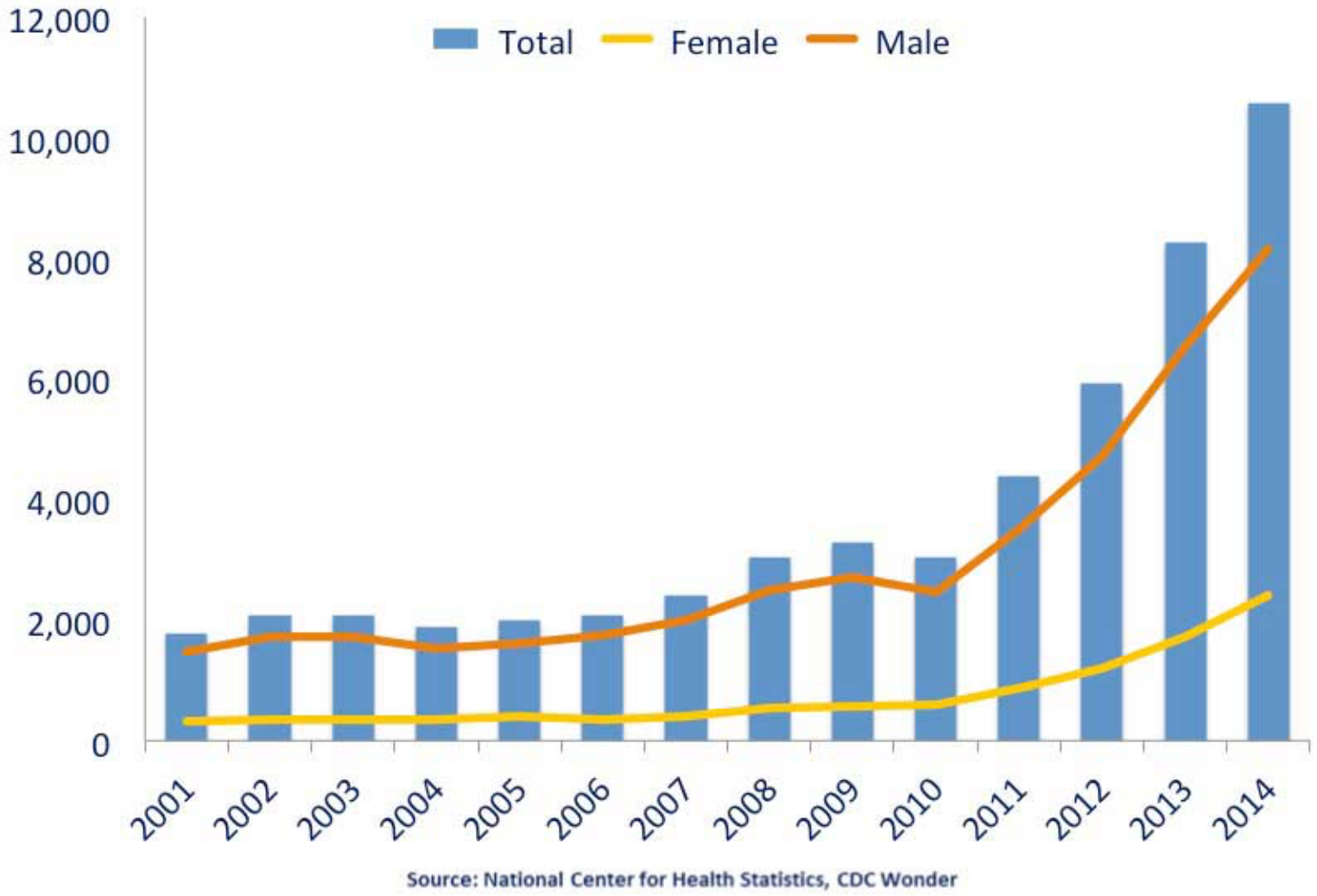
Present state of the opioid crisis

- Opiate related deaths are gaining a lot of attention nationwide
- http://www.nhmagazine.com/September-2015/Drug-Abuse-Is-a-Primary-Issue-in-NH/
- A Call to Candidates on opiate abuse, San Francisco Chronicle, Feb 8, 2016 http://sfchron.cl/1S5ZL3j
- Pharmacists sued for wrongful death; elder abuse

National Institute on Drug Abuse

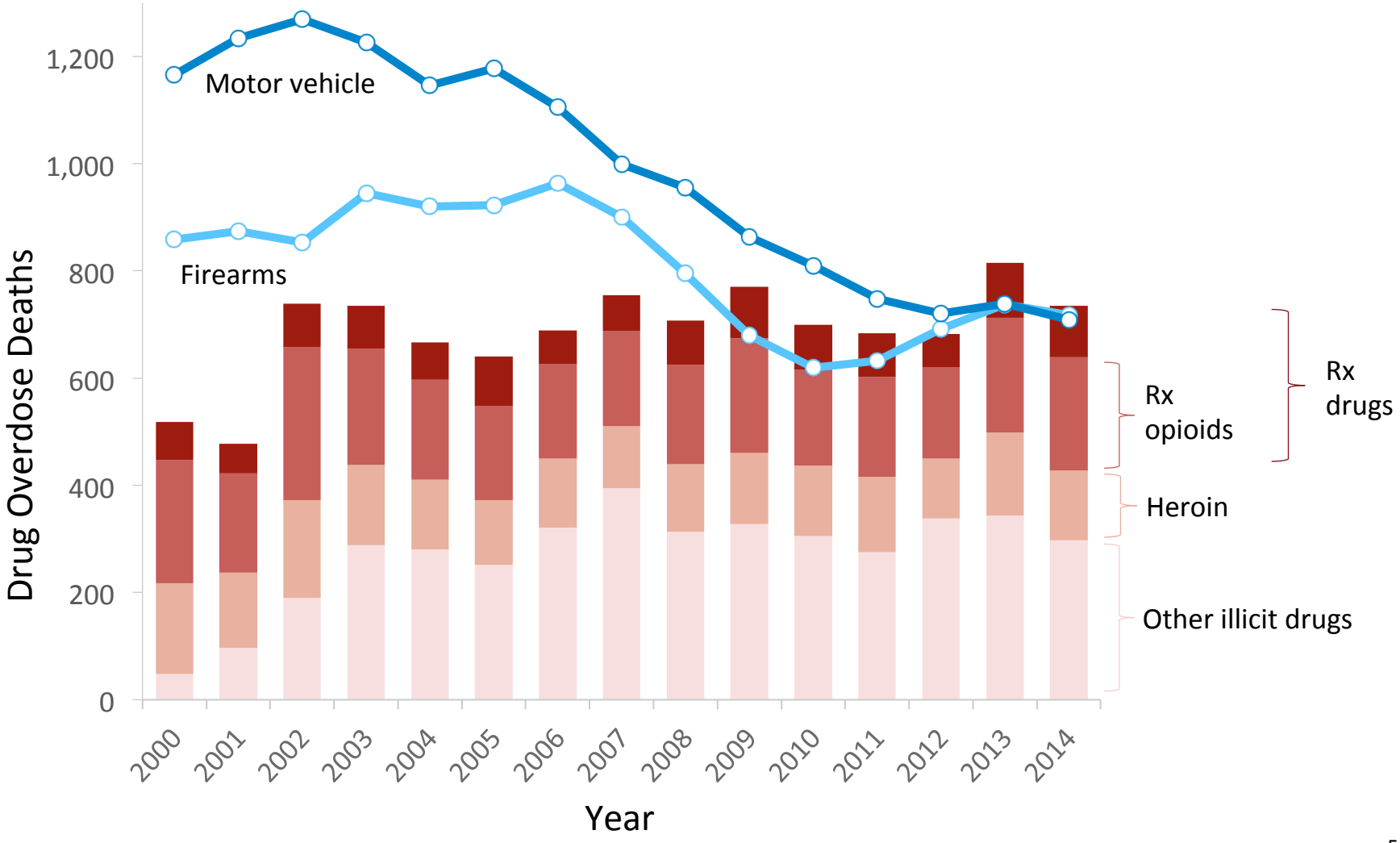
National Overdose Deaths

Number of Deaths from Heroin

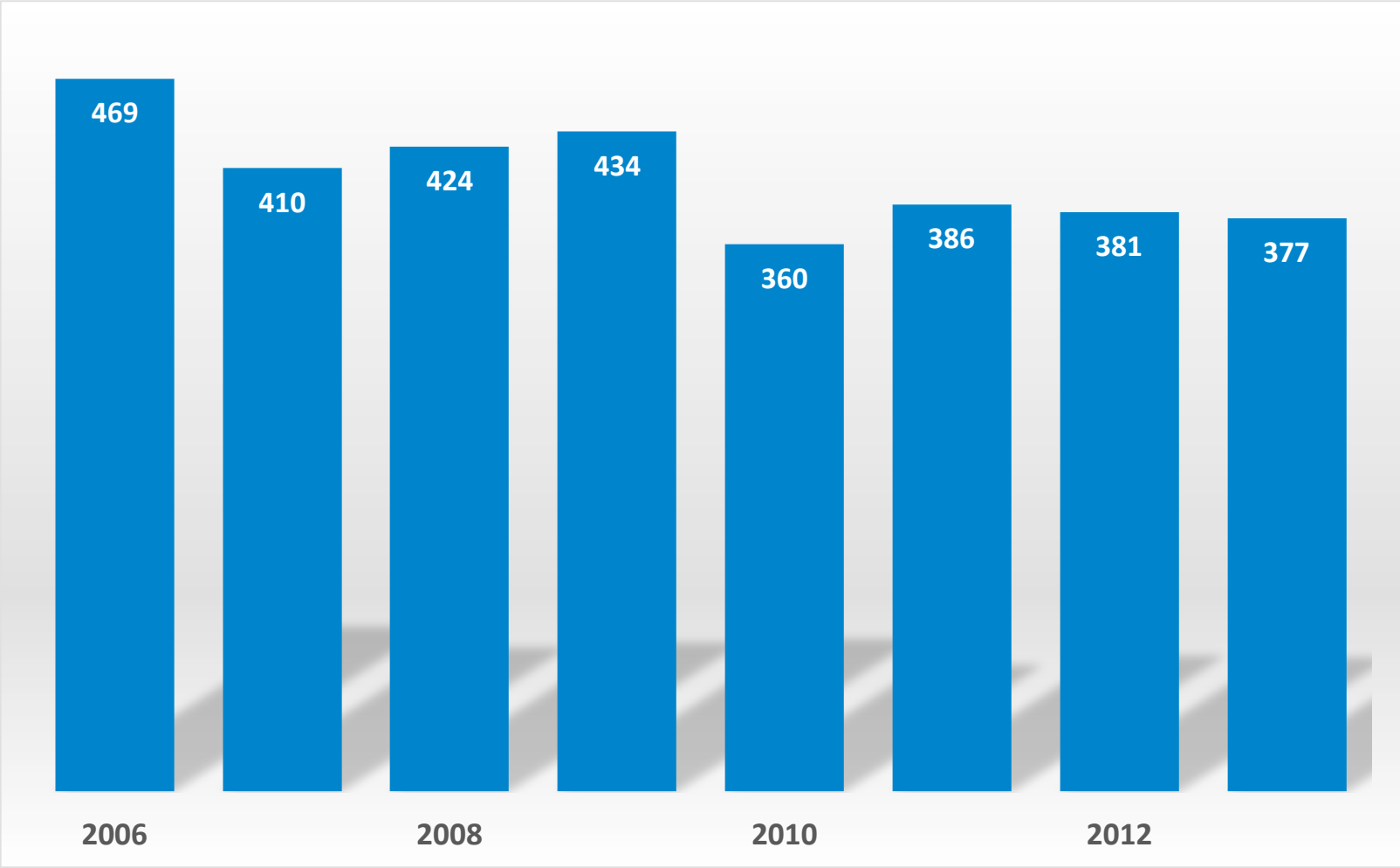


Source: National Center for Health Statistics, CDC Wonder

Drug overdose, motor vehicle, and firearm injury deaths in Los Angeles County (LAC), 2000-2014

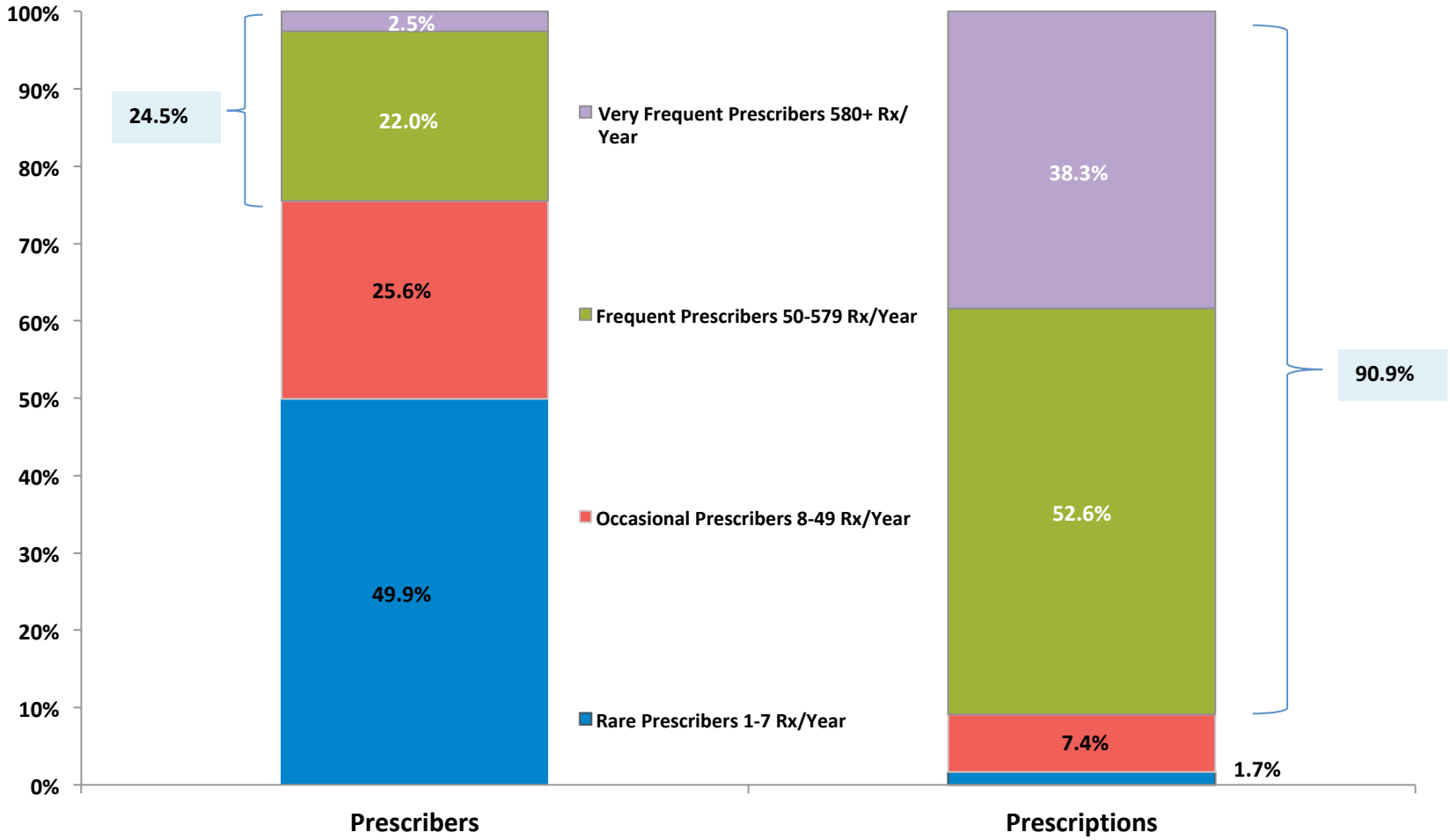


Opioid-Related Deaths in LAC, 2006-2013



Emergency Department and Inpatient Discharge Data Set. Office of Statewide Health Planning and Development. California Department of Public Health.

25% of LAC prescribers wrote 91% of opioid prescriptions, 2012 (N = 4,142,662)



Department of Justice, California Prescription Drug Monitoring Program (PDMP)/ Controlled Substance Utilization Review and Evaluation System (CURES) data.

Corresponding Responsibility

- “corresponding responsibility” a pharmacy/pharmacist owes under California law to determine the legitimate medical purpose of controlled substance prescriptions before dispensing, under Health and Safety Code section 11153, subdivision (a).

Corresponding Responsibility

- Red Flags: The precedential decision included a list of some of the “red flags” that warn pharmacists there could be a problem with the prescription. A pharmacist must also rely on his or her professional judgment to discern when a prescription seems suspicious.
- Precendential Decision Against Pacifica Pharmacy and Thang Tran: http://www.pharmacy.ca.gov/enforcement/fy1011/ac103802.pdf

Corresponding Responsibility Red Flags

- ▸Irregularities on the face of the prescription itself
- ▸Cash payments
- ▸Requests for early refills of prescriptions
- ▸Prescriptions written for an unusually large quantity of drugs

Corresponding Responsibility

- Nervous patient demeanor
- ▸Age or presentation of patient (e.g., youthful patients seeking chronic pain medications) ▸Multiple patients all with the same address ▸Multiple prescribers for the same patient for duplicate therapy

Corresponding Responsibility

- Prescriptions written for duplicative drug therapy
- ▸Initial prescriptions written for strong opiates ▸Long distances traveled from the patient's home to the prescriber's office or to the pharmacy
- ▸Irregularities in the prescriber's qualifications in relation to the type of medication(s) prescribed

Corresponding Responsibility

- ▸Prescriptions that are written outside of the prescriber’s medical specialty
- ▸Prescriptions for medications with no logical connection to an illness or condition

CURES 2.0

- Established by CA Health & Safety Code section 11165
- CURES registration is REQUIRED, but utilization is voluntary.
- It's impossible to exercise corresponding responsibility without checking CURES
- http://www.chcf.org/events/2016/webinar-cures-20

1.https://cures.doj.ca.gov/registration/confirmEmailPnDRegistration.xhtml
2.htthttps://oag.ca.gov/cures/faqs#
3.ps://oag.ca.gov/sites/all/files/agweb/pdfs/pdmp/cures-2.0-user-guide.pdf?

CURES 2.0 ALERTS

- Alerts are presented at the following therapy thresholds:

1. Patient is currently prescribed more than 100 morphine milligram equivalents per day
2. Patient has obtained prescriptions from 6 or more prescribers or 6 or more pharmacies during last 6 months
3. Patient is currently prescribed more than 40 morphine milligram equivalents of methadone daily
4. Patient is currently prescribed opioids more than 90 consecutive days
5. Patient is currently prescribed both benzodiazepines and opioids

CURES 2.0

- California Health Care Foundation (CHCF) webinar on what the busy clinician needs to know about CURES 2.0: http://www.chcf.org/events/2016/webinar-cures-20
- CHCF webinar: Use of Buprenorphine for pain: http://www.chcf.org/events/2016/webinar-opioid-safety-coalitions-buprenorphine

Drug Take Back Programs

- DEA currently allows registrants who become authorized collectors to NOW operate drug disposal kiosks and mail back programs
- http://www.deadiversion.usdoj.gov/fed_regs/rules/2014/2014-20926.pdf
- http://www.deadiversion.usdoj.gov/drug_disposal/dear_practitioner_pharm_waste_101714.pdf

Drug Take Back Programs

- Counties which have Extended Producer Responsibility(EPR) Programs
- http://calpsc.org/products/pharmaceuticals/
  - Marin
  - San Mateo
  - Alameda
  - Santa Clara
  - San Francisco (and the city of SF)

Drug Take Back Program: CA Board of Pharmacy

- Proposal to add new Article 9.1 of Division 17 of Title 16 of the California Code of Regulations and a new Article title as follows: Article 9.1. Prescription Drug Take-Back Programs as discussed at BOP mtg on July 27, 2016
- http://www.pharmacy.ca.gov/meetings/agendas/2016/16_jul_rx_take_back.pdf

Drug Take Back Program: Los Angeles County Proposed Ordinance

- L.A. County supervisors roll back plans for a drug take-back program (at June 14 L.A. County Board of Supervisor's meeting)
- LA County Sheriff's drop off sites available 24/7: http://ladpw.org/epd/hhw/pdf/SheriffsSites.pdf

Safe Medication Disposal Bin

http://www.businesswire.com/news/home/20160725005180/en/Walgreens-Safe-Medication-Disposal-Kiosks-300-Pharmacies

Thank you!

Questions or interested in joining Safe Med LA?

www.SafeMedLA.org

Holly Strom, RPh
Co-chair
Pharmacy Practice Action Team
stromholly1@gmail.com

Important Links

- Sternberg case decision: http://www.pharmacy.ca.gov/enforcement/fy1516/sternberg_lexis.pdf
- Precendential Decision Against Pacifica Pharmacy and Thang Tran: http://www.pharmacy.ca.gov/enforcement/fy1011/ac103802.pdf
- SafeMedLA: http://www.safemedla.org/
- Board of Pharmacy CURES 2.0 page: www.pharmacy.ca.gov/licensees/cures.shtml
- Pharmacy Law Book California: http://www.pharmacy.ca.gov/laws_regs/lawbook.pdf
- Corresponding Responsibility video on CA BOP website: https://www.youtube.com/watch?v=jdeQ0GeJjAM&feature=youtu.be
- California Health Care Foundation website: http://www.chcf.org/topics/opioid-safety

Important Links

- Current CDC opiate prescribing guidelines: http://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm
- LA County Substance Abuse Prevention and Control: http://publichealth.lacounty.gov/sapc/
- Los Angeles County Addiction Treatment Centers: http://sapccis.ph.lacounty.gov/registration/providerlocator/providerdirectory2.aspx
- Los Angeles Substance Use Disorder system of care, this link provides a quick survey of the current philosophy of addiction treatment: http://publichealth.lacounty.gov/sapc/PolicyBrief/TransformationLACSUDSystemCare012616.pdf

Break

L.A. Care HEALTH PLAN®

Medication Assisted Therapy

Larissa Mooney, MD

L.A. Care HEALTH PLAN®

UCLA ISAP Research Training Series

Medication Assisted Treatment for Substance Use Disorders

Larissa Mooney, M.D.

Associate Professor of Psychiatry
UCLA Integrated Substance Abuse Programs

August 20, 2016

UCLA

DISCLOSURE

I have no relevant financial relationships with commercial interests.

Overview

- Epidemiology of SUD
- Neurobiology of Addiction
- Alcohol use disorder medications
  - Disulfiram
  - Acamprosate
  - Naltrexone
- Opioid use disorder medications
  - Buprenorphine
  - Naltrexone
  - Methadone
- Selection of candidates for agonist vs. antagonist treatment

Introduction

- Addiction is a chronic, relapsing brain disease characterized by compulsive use despite harmful consequences
- Medications may be used as part of *comprehensive* treatment plan
- Treatment approaches incorporate Bio-Psychosocial Model:
  - Medications (Bio)
  - Therapy, lifestyle changes (Psycho-Social)

Substance Use Disorders: DSM-5

- Use in larger amounts/longer periods than intended
- Persistent desire or unsuccessful attempts to cut down
- Excess time spent obtaining or recovering from use
- Craving or strong desire to use
- Failure to fulfill major role obligations
- Important social or recreational activities given up
- Recurrent use in physically hazardous situations
- Continued use despite knowledge of medical or psychological consequence(s)
- Continued use despite recurrent social or interpersonal problems
- Tolerance
- Withdrawal

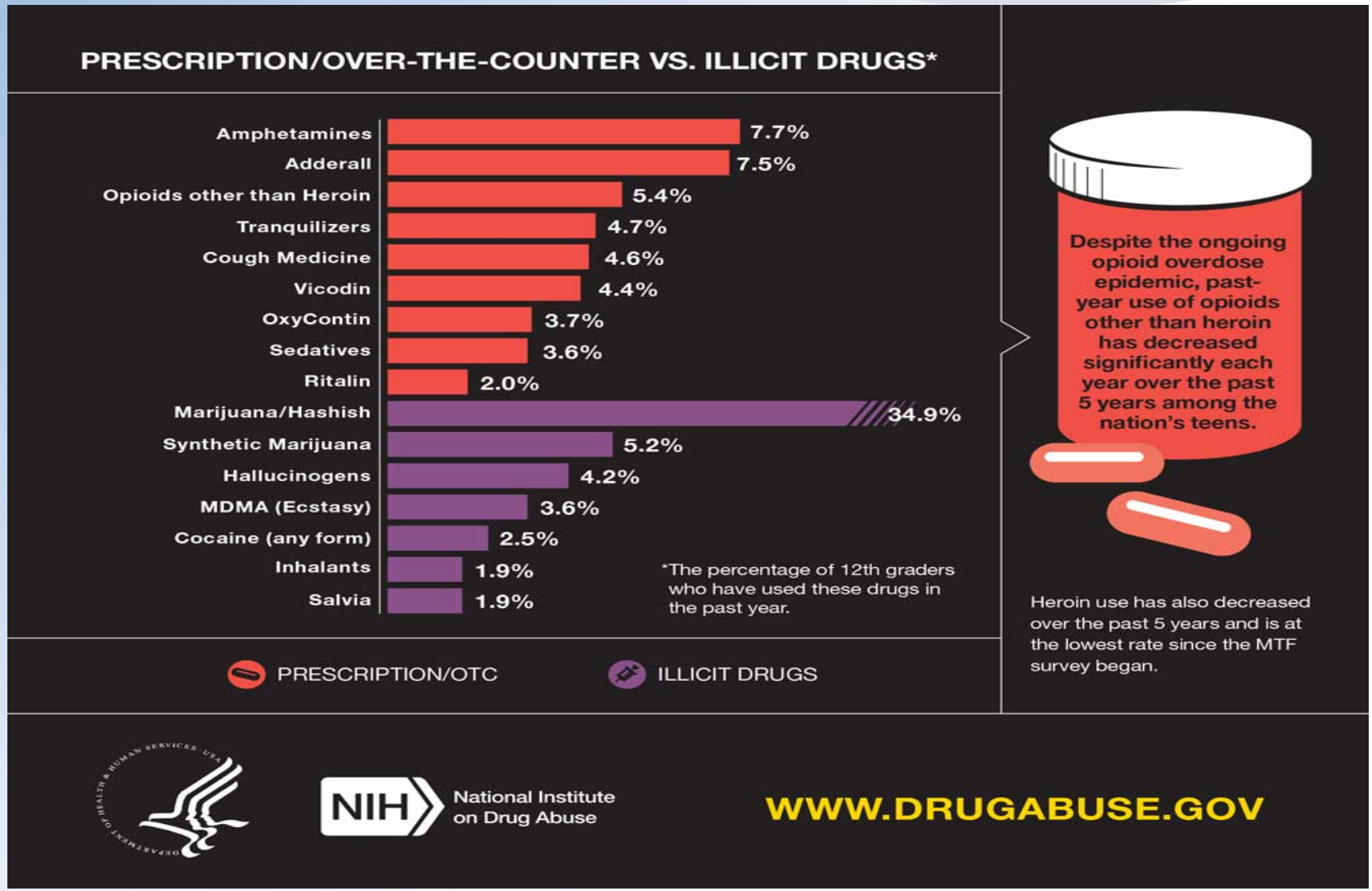
Epidemiology: NSDUH Survey 2013

- 9.4% US adults with past-month illicit drug use
  - 8.8% adolescents age 12-17
- 56.4% adults with past-month alcohol use
  - 24.6% binge use
  - 6.8% heavy use
- 8.5% adults with past-month substance use disorder (SUD)
  - Of those who needed treatment, only 11% received treatment

Nonmedical Opioid Use: Epidemiology

- Of 21.5 million with SUD in US in 2014, 1.9 million with SUD involving Rx opioids and 586,000 with SUD involving heroin.
- 4 in 5 new heroin users started out misusing prescription painkillers. As a consequence, the rate of heroin overdose deaths nearly quadrupled from 2000 to 2013. The rate of heroin overdose increased 6% per year from 2000-2010, followed by an increase of 37% per year from 2010 to 2013.
- Overdose deaths from opioid prescription medications now outnumber deaths from all illicit drugs including heroin and cocaine combined

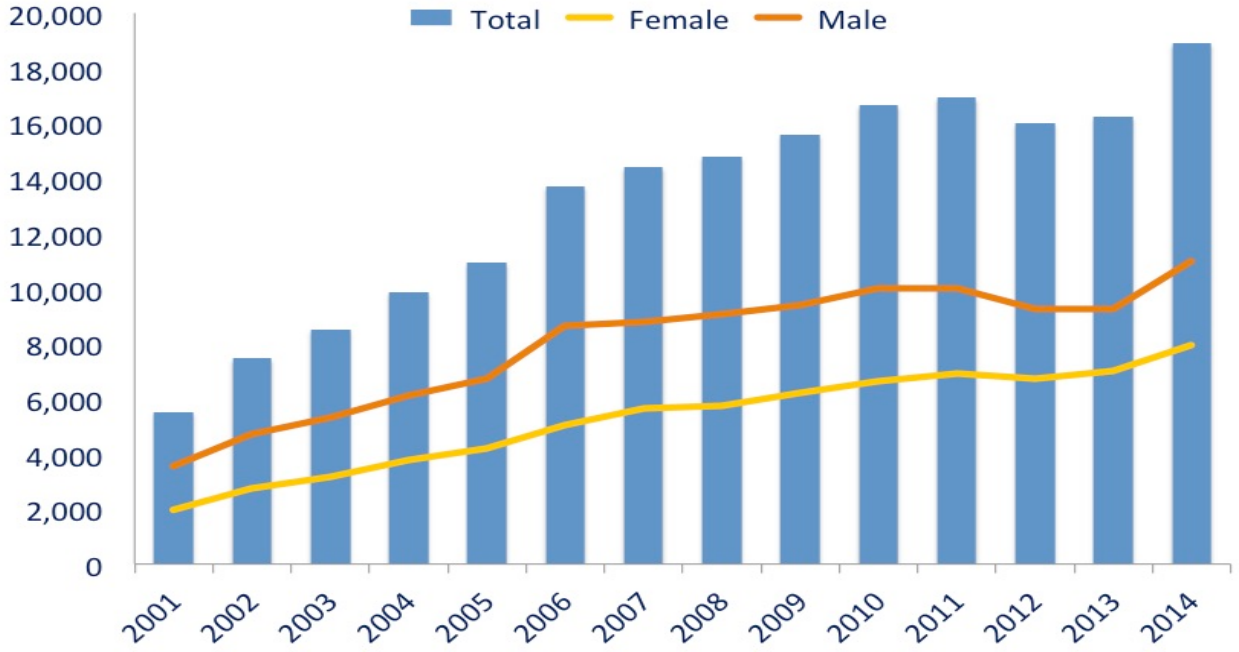
2014 NSDUH, Hedegaard MD et al, 2015


PRESCRIPTION/OVER-THE-COUNTER VS. ILLICIT DRUGS*
Amphetamines 7.7%
Adderall 7.5%
Opioids other than Heroin 5.4%
Tranquilizers 4.7%
Cough Medicine 4.6%
Vicodin 4.4%
OxyContin 3.7%
Sedatives 3.6%
Ritalin 2.0%
Marijuana/Hashish 34.9%
Synthetic Marijuana 5.2%
Hallucinogens 4.2%
MDMA (Ecstasy) 3.6%
Cocaine (any form) 2.5%
Inhalants 1.9%
Salvia 1.9%
*The percentage of 12th graders who have used these drugs in the past year.
PRESCRIPTION/OTC
ILLICIT DRUGS
Despite the ongoing opioid overdose epidemic, past-year use of opioids other than heroin has decreased significantly each year over the past 5 years among the nation's teens.
Heroin use has also decreased over the past 5 years and is at the lowest rate since the MTF survey began.
NIH National Institute on Drug Abuse
WWW.DRUGABUSE.GOV

NIH National Institute on Drug Abuse

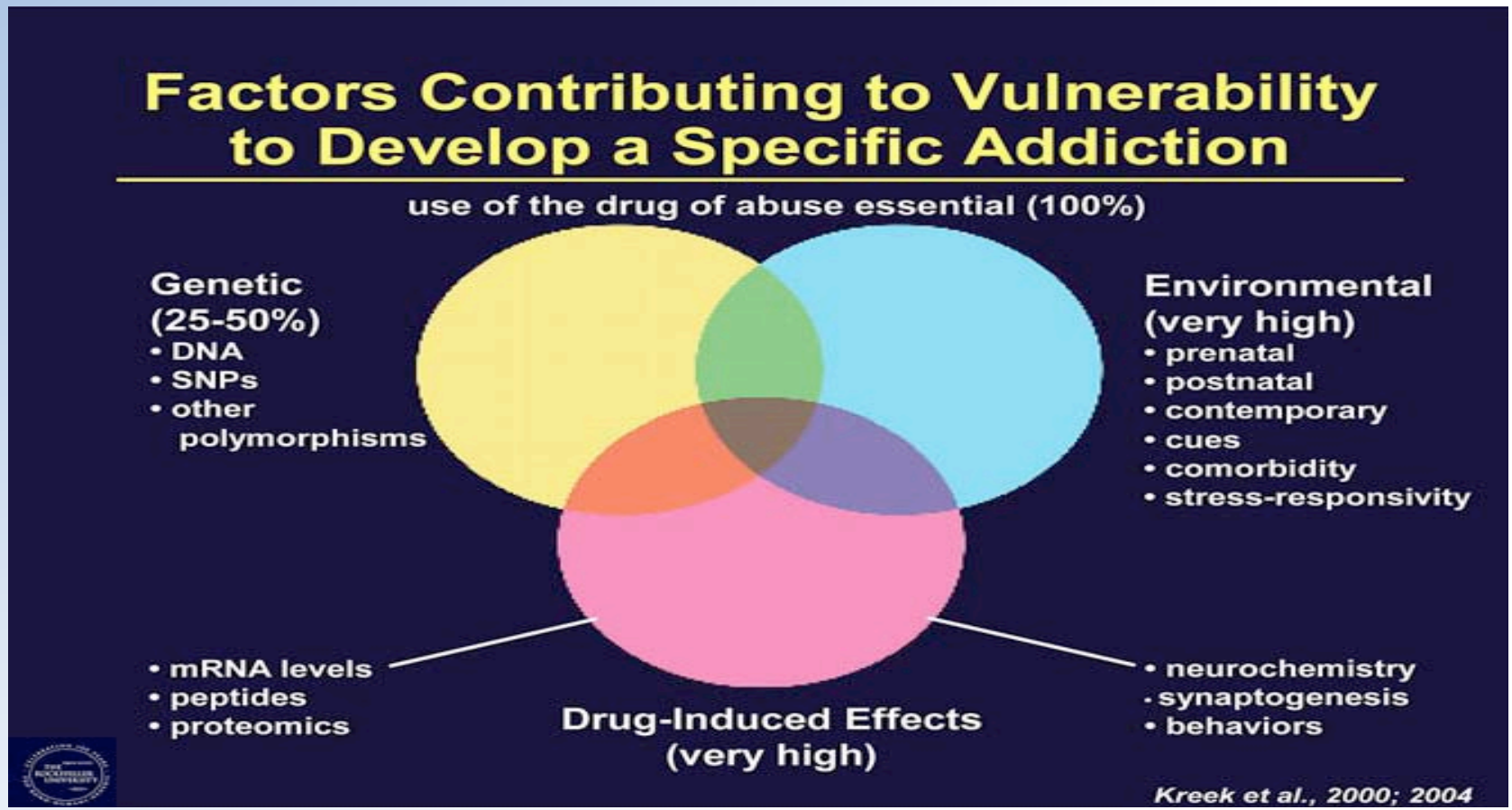
National Overdose Deaths

Number of Deaths from Prescription Opioid Pain Relievers

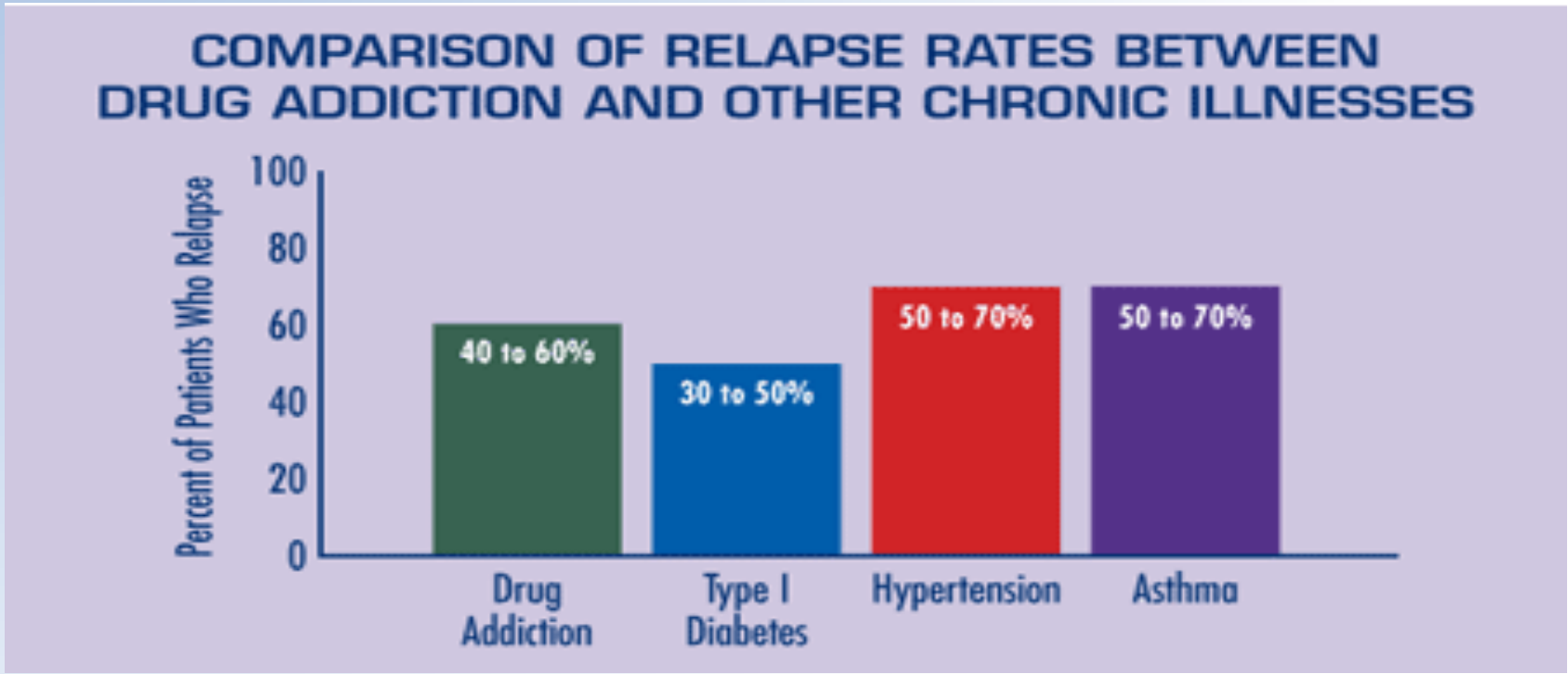


Source: National Center for Health Statistics, CDC Wonder

Addiction Risk Factors



Chronic Disease Model of Addiction

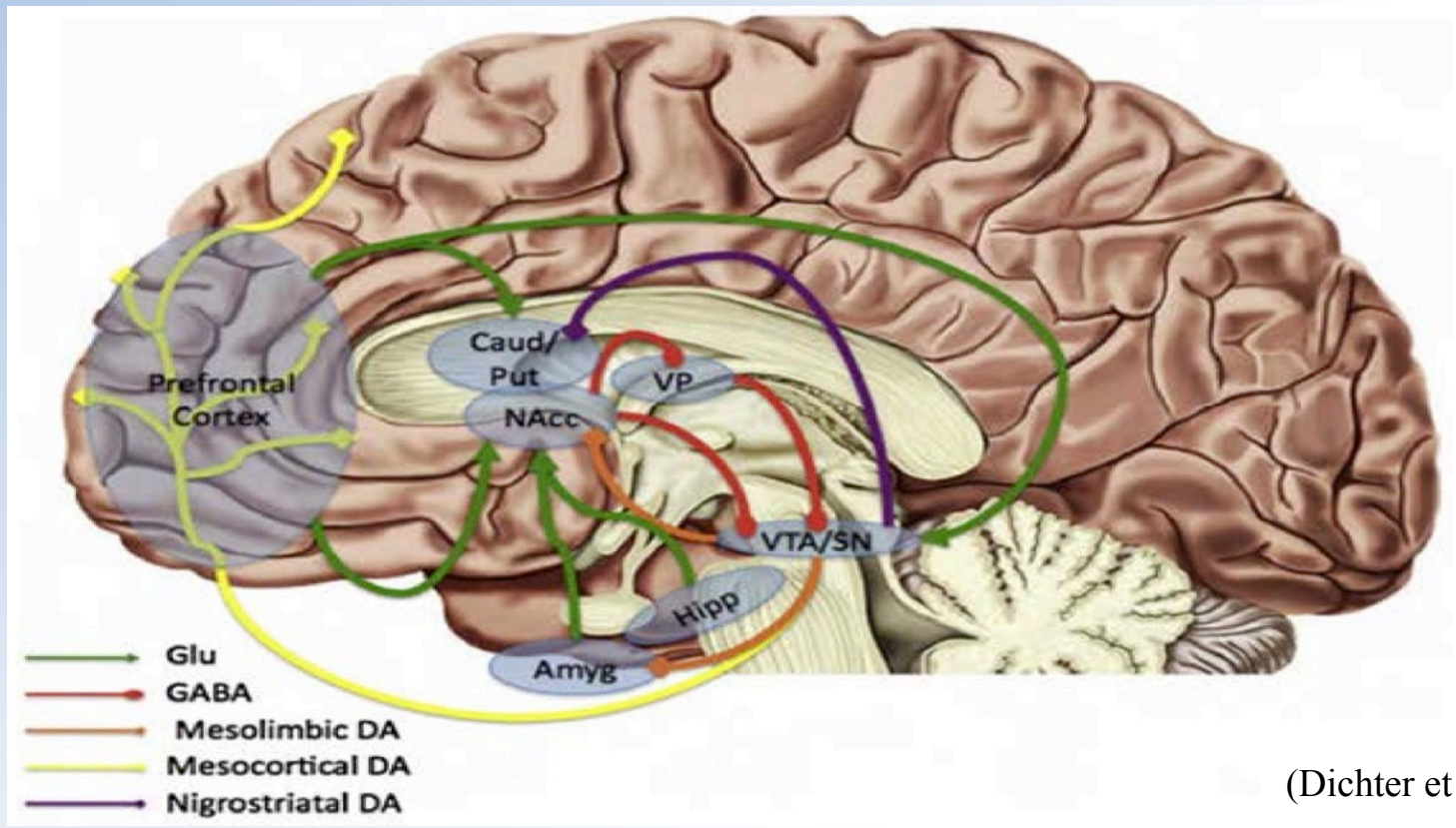


McLellan et al., JAMA, 2000

Neurobiology of Addiction

- Reward system: dopamine pathway
  - Natural vs. drug rewards
  - Dopamine release in nucleus accumbens: pleasure and reinforcement
- Process of addiction causes dysfunctional learning and maladaptive behavioral patterns
  - Over-learning of drug seeking via excess dopamine release
- Impaired decision-making, loss of control (PFC)

Reward/Reinforcement Circuitry



(Dichter et al., 2012)

Later stage addiction

- Repeated drug use: gradual recruitment of PFC and glutamatergic efferents to accumbens
- Once addicted, glutamate release in accumbens (from PFC projection) by stress or cue is more important than dopamine release
- End stage addiction*: Excessive motivational importance* of drug seeking.
  - Addiction associated with enhanced *motivation* (craving) to procure drug, not with augmented pleasure response or dopamine release in striatum
- Altered neurobiology: relapse risk even after extended periods of abstinence

Volkow & Kalivas, 2005, Am J Psychiat


SANDWICHS
LET'S HAVE ONE MORE
AND THEN WE'LL GO !!

Four main neurotransmitters relevant to alcohol effects:

endogenous opioids
Deadens pain and causes euphoria

glutamate
excitatory neurotransmitter…
speeds you up

dopamine
makes you happy

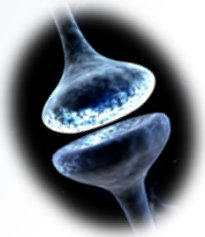
GABA
inhibitory neurotransmitter…
slows you down

Alcohol Neuronal Activity

1. Alcohol is consumed.

2. The endogenous opioids are released into the pleasure centers of the brain.

3. In response to this increased endogenous opioid activity, dopamine is released.



4. Dopamine make the drinker feel good. This reinforces the behavior and increased the likelihood that it will recur.

At the same time…

GABA is increased, slowing the brain down

Over time, the brain reacts to the over-abundance of GABA, by creating more receptors for Glutamate—increasing the effect of Glutamate, energizing the system and restoring balance

Neuronal Activity during Withdrawal

What do you think will happen once alcohol is taken away?

WITHDRAWAL

How can we treat Alcohol Addiction?

Medications for alcoholism can:

- **Reduce** post-acute withdrawal
- **Block or ease** euphoria from alcohol
- **Discourage** drinking by creating an unpleasant association with alcohol

Treatment of alcohol withdrawal symptoms

Medications for Symptomatic Treatment

- Benzodiazepines
  - Symptom-triggered vs. standing taper
- Thiamine & multivitamins
- Antiemetic, supportive meds

Disulfiram

Antabuse ®

Disulfiram

- Marketed as Antabuse®
- FDA Approved in 1951
- **Indication:** An aid in the management of selected chronic alcohol patients who want to remain in a state of enforced sobriety so that supportive and psychotherapeutic treatment may be applied to best advantage.
- Disfulfiram discourages drinking by making the patient physically sick when alcohol is consumed.

Additional Disulfiram Information

Third-Party Payer Acceptance:

Covered by most major insurance carriers, Medicare, Medicaid, and the VA.

Dosing:

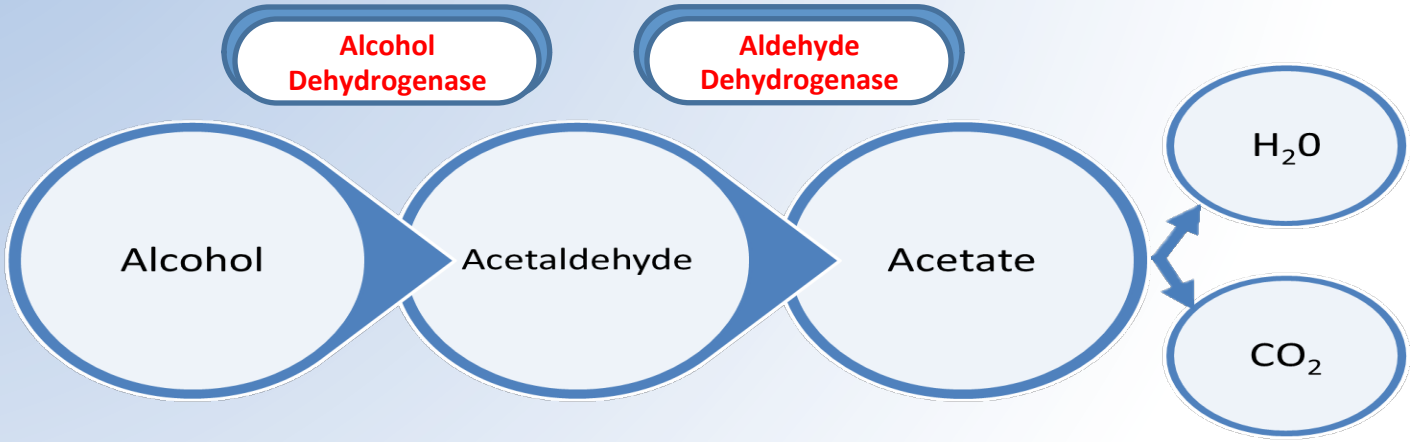
One 250mg tablet, once a day

Can be crushed, diluted or mixed with food.

Abstinence Requirements:

must be taken at least 12 hours after last alcohol use

Disulfiram Mechanism of Action



Disulfiram works by blocking the enzyme aldehyde dehydrogenase. This causes acetaldehyde to accumulate in the blood at 5 to 10 times higher amounts than what would normally occur with alcohol alone.

Disulfiram-alcohol reaction

Since acetaldehyde is toxic, a buildup of it produces a highly unpleasant series of symptoms

- throbbing in head/neck
- brief loss of consciousness
- throbbing headache
- lowered blood pressure
- difficulty breathing
- marked uneasiness
- copious vomiting
- nausea
- flushing
- sweating
- thirst
- weakness
- chest pain
- dizziness
- palpitation
- hyperventilation
- rapid heartbeat
- blurred vision
- confusion
- respiratory depression
- cardiovascular collapse
- myocardial infarction
- congestive heart failure
- unconsciousness
- convulsions
- death

Disulfiram-alcohol reaction

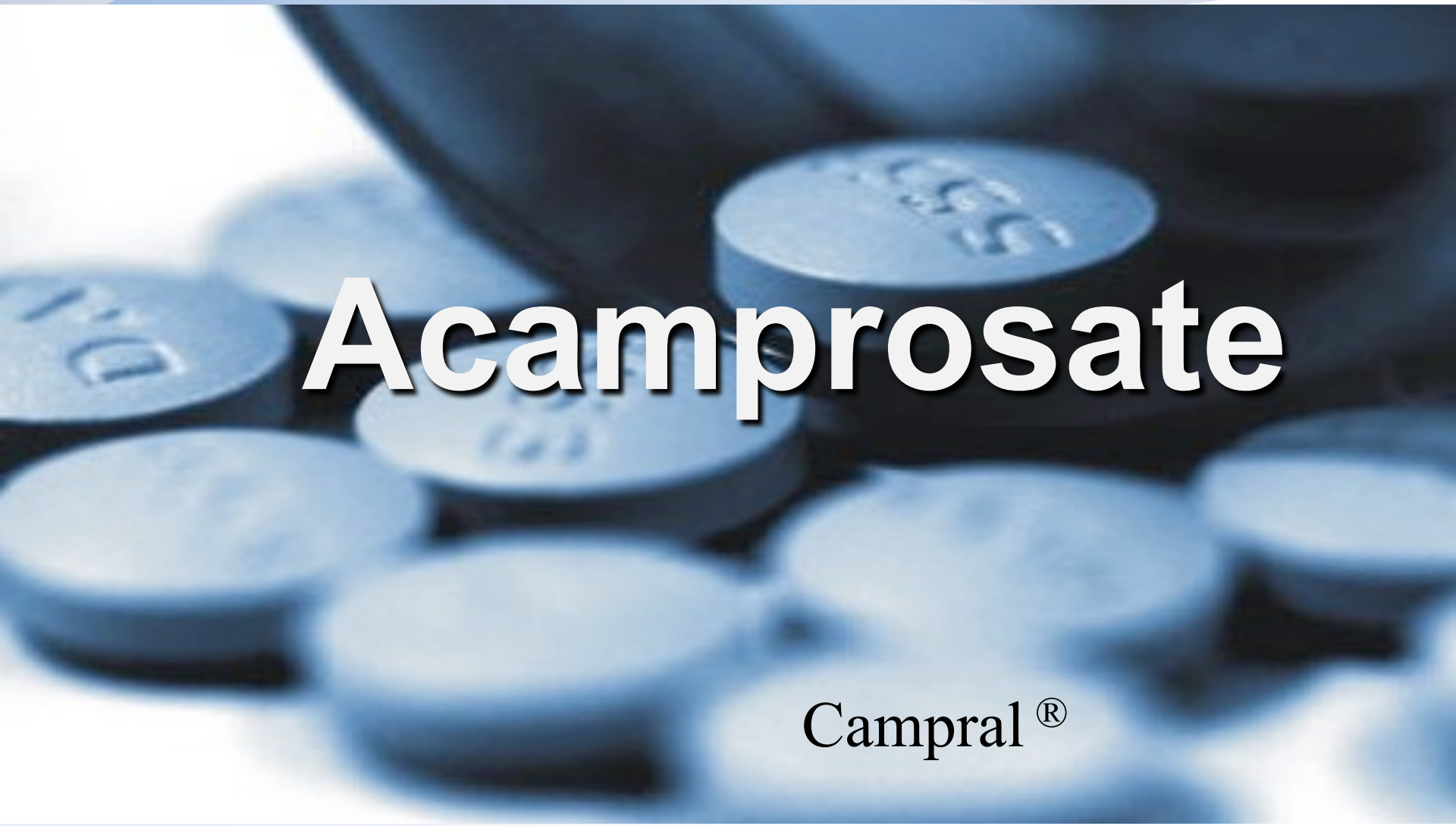
- As long as there is alcohol in the blood, the disulfiram-alcohol reaction will continue.
- Symptoms are usually fully developed when the patient's blood alcohol concentration is 50 mg per 100 mL, but mild reactions can occur in sensitive patients with levels as low as five to ten mg per 100 mL.
- Further, the disulfiram-alcohol reaction can be triggered when alcohol is consumed one or even two weeks after the last dose of disulfiram was taken.

Disulfiram Contraindications

- The disulfiram-alcohol reaction usually lasts for 30 to 60 minutes, but can continue for several hours depending on the amount of alcohol consumed.
- Should never be administered to a patient when he or she has consumed alcohol recently or is currently intoxicated from alcohol.
- Should never be administered to a patient that has consumed alcohol-containing preparations such as cough syrup, tonics, etc.

Research about Disulfiram

- Participants treated with disulfiram **did not maintain complete abstinence** more frequently than those treated with placebo.
- Participants treated with disulfiram had a **greater reduction in the number of drinking days** during the entire study than those treated with placebo.



Acamprosate

Campral ®

Acamprosate Calcium

- Marketed as Campral®
- FDA Approved in 2004

- **Indication:** For the maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at treatment initiation by reducing post-acute withdrawal symptoms.
- **Side effects**: diarrhea, GI upset

Additional Information

Third-Party Payer Acceptance:

Patient Assistance Program (Forest Laboratories, Inc.)

Covered by most major insurance carriers,

Covered by Medicare, Medicaid, and the VA (if naltrexone is contraindicated).

Dosing:

Two 333mg tablets, three times a day

Cannot be crushed, halved or diluted, but can be mixed with food.

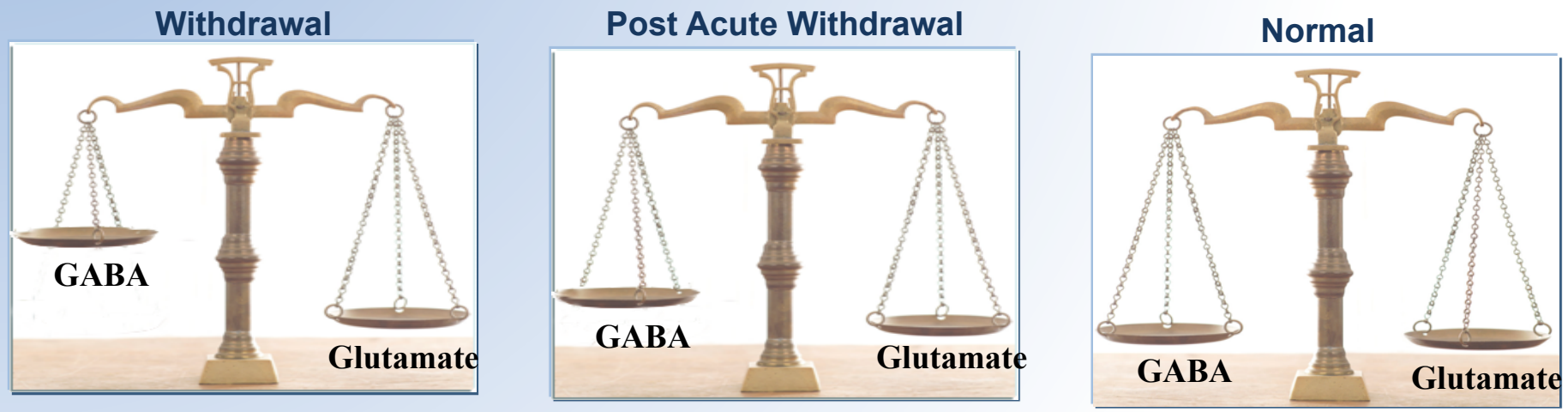
Acamprosate mechanism of action

While the exact mechanism of action is not known, acamprosate is thought to be:

a glutamate receptor modulator

The brain responds to repetitive consumption of alcohol causes by increasing glutamate receptors, thereby counteracting alcohol's depressive effects.

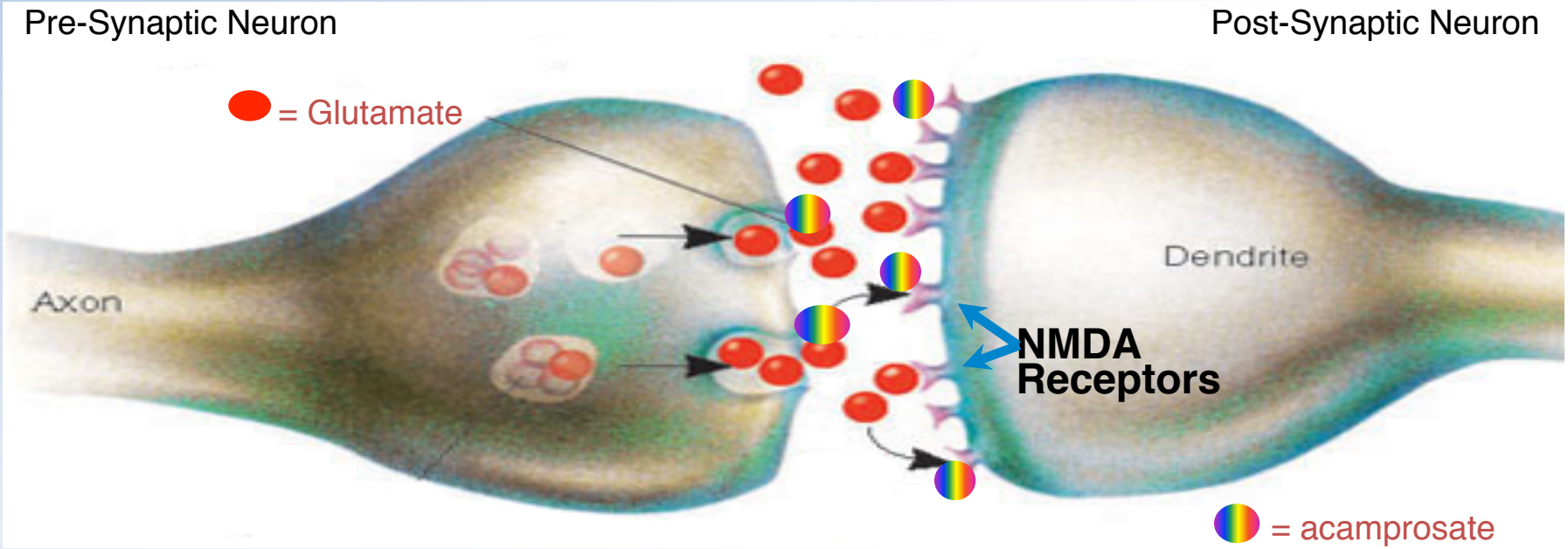
How Does Acamprosate Work?



- Even after acute withdrawal, the glutamate system continues to be overactive as it readjusts by down regulating the glutamate receptors.
- During this time, the patient continues to feel anxiety and agitation that can lead to relapse.

Acamprosate and glutamate

- Acamprosate is thought to reduce amount of glutamate released, and
- Reduce the activity of the glutamate receptors



Research about Acamprosate

- Participants treated with acamprosate were able to **maintain complete abstinence** more frequently than those treated with placebo
- Participants treated with acamprosate had a greater reduction in the number of drinking days during the entire study than those treated with placebo.
- In all three studies, participants treated with acamprosate were able to **regain complete abstinence** after one relapse more frequently than those treated with placebo.

Naltrexone

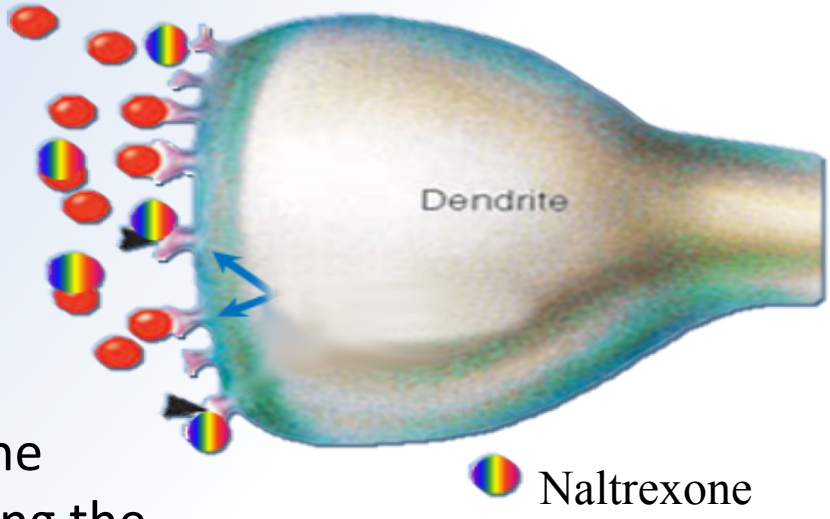
Revia ® or Depade ®

Naltrexone Mechanism of Action

- Naltrexone is an opioid receptor antagonist and blocks opioid receptors.

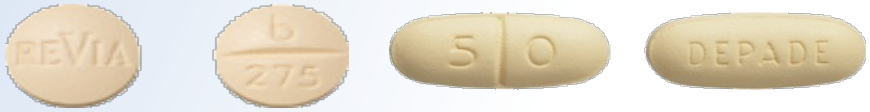
  This prevents the effects of self-administered opioids.

  It also diminishes release dopamine when alcohol is consumed, reducing the pleasurable effects



Naltrexone Hydrocholoride

Marketed As: ReVia® and Depade®



Indication

-Used in the treatment of alcohol or opioid dependence and for the blockade of the effects of exogenous administered opioids and/or decreasing the pleasurable effects experienced by consuming alcohol.

-Administering naltrexone will cause opioid withdrawal symptoms in patients who are physically dependent on opioids.

Side Effects: nausea, vomiting, elevated liver function enzymes

Additional Information

Third-Party Payer Acceptance:

Covered by most major insurance carriers, Medicare, Medicaid, and the VA.

Dosing:

One 50mg tablet, once a day

Can be crushed, diluted or mixed with food.

Abstinence requirements: must be taken at least 7-10 days after last consumption of opioids; abstinence from alcohol is not required.

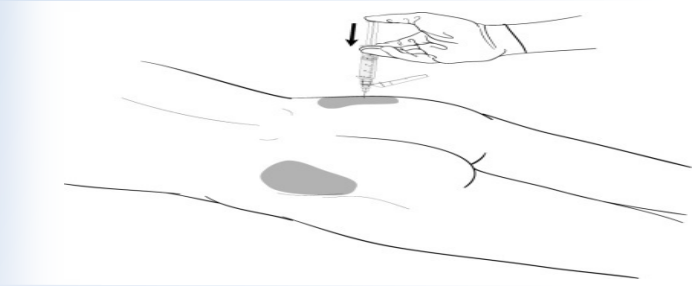
Research on Naltrexone for Alcoholism

- In some studies, participants treated with naltrexone were not able to maintain complete abstinence more frequently than those treated with placebo.
- Participants treated with naltrexone had a **greater reduction in relapse** during the study than those treated with placebo and had **reduced cravings**.
- Patients treated with naltrexone had **fewer heavy drinking days** than those treated with placebo

Extended-Release Injectable Naltrexone

Extended-Release Naltrexone

Dosing:



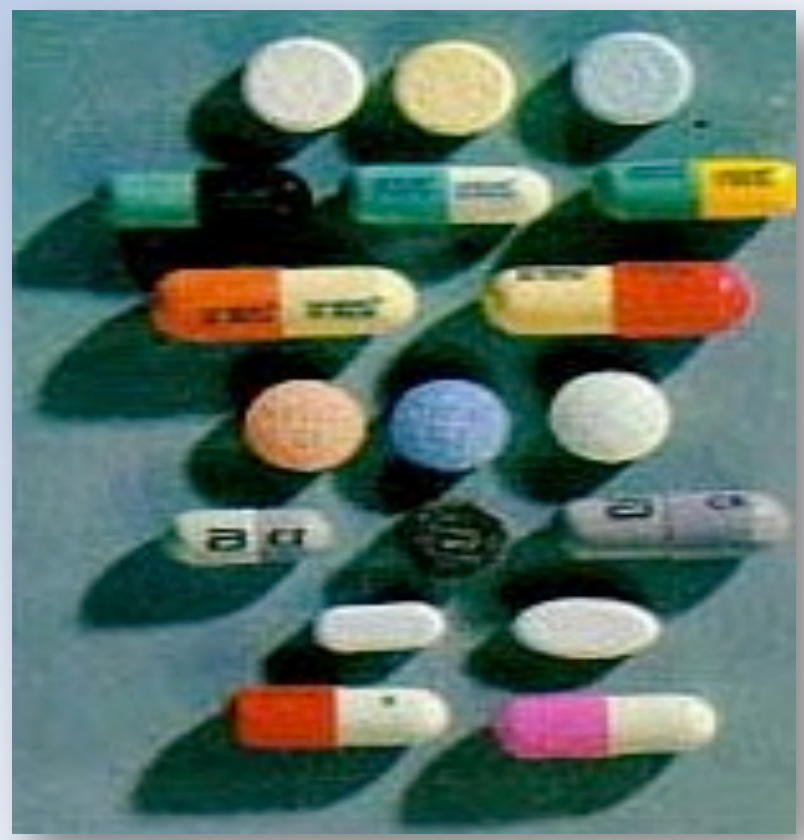
- 380mg injection in deep gluteal muscle every 4 weeks
- Must be administered by a healthcare professional and should alternate sides each month.
- Blocks opioid receptors for **one entire month** compared to approximately 28 doses of oral naltrexone.

It is **not possible to remove** it from the body once extended-release naltrexone has been injected. Large doses of opioids may be required to override the blockade in a medically monitored setting

Research about Extended-Release Naltrexone for Alcohol Use Disorder

- Participants treated with extended-release naltrexone did not maintain complete abstinence more frequently than those receiving placebo.
- Participants treated with extended-release naltrexone had a greater reduction in the number of heavy drinking days during the study than those receiving placebo.
- Participants treated with extended-release naltrexone who had **at least four days of abstinence from alcohol** prior to treatment initiation had a greater reduction in the number of heavy drinking days during the study than those receiving placebo.


Class A
Opiates/Opioids
Scag - Smack - Dragon - Tiger - Horse - Powder
Methadone liquid
Pethidine
Morphine
Diamorphine
Physeptone (tablets & ampoule) containing methadone
Typical packaging
Heroin powder



Treating Opioid Dependence: Aims

- Detoxification:
  - Opioid-based (methadone, buprenorphine)
  - Non-opioid based (clonidine, supportive meds)
- Relapse prevention:
  - Agonist maintenance (methadone)
  - Partial agonist maintenance (buprenorphine)
  - Antagonist maintenance (naltrexone)
- Psychosocial treatment
  - To promote lifestyle and behavior change

Opioid Detoxification

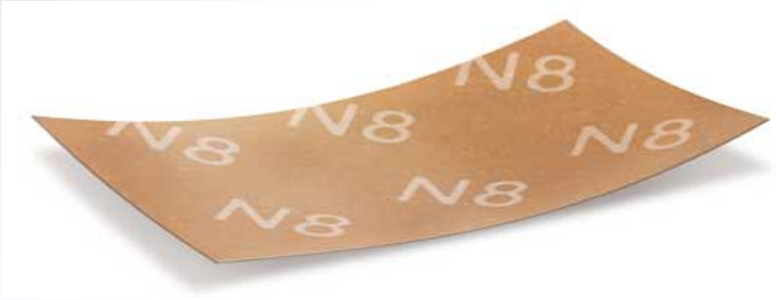
Medications used to alleviate withdrawal symptoms:

- Opioid agonists (methadone, buprenorphine)
- Clonidine (alpha-2 agonist)
  - Dose: 0.1 mg PO tid (increase as tolerated)
  - Caution: hypotension
- Other supportive meds
  - anti-diarrheals, anti-emetics, ibuprofen, muscle relaxants, BDZs

Why Not Detoxification?

POST-DETOXIFICATION RELAPSE RATES APPROACH 100% WITHIN THE FIRST 90 DAYS FOLLOWING COMPLETION OF DETOXIFICATION.

Buprenorphine



Buprenorphine Formulations

- Sublingual dose: 2mg-24mg/day
- Subutex (buprenorphine)

  -2mg, 8mg
- Suboxone (4:1 bup:naloxone)

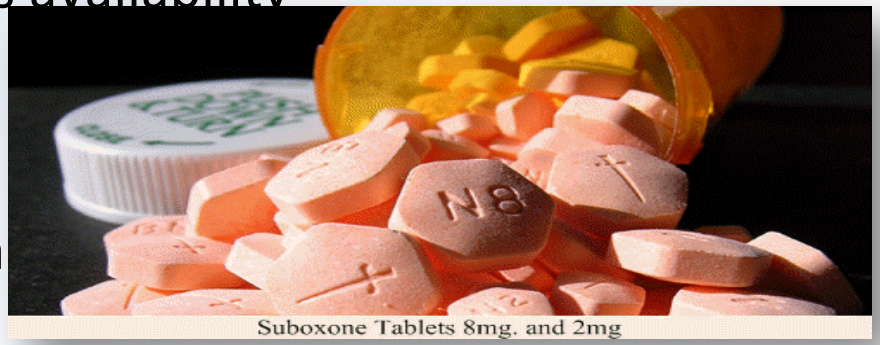
  -2mg/0.5 mg , 8mg/2mg
- Zubsolv (4:1 bup:naloxone)

  -(1.4/0.36mg- 11.4/2.9mg)
- Bunavail (6:1 buccal film bup:naloxone)

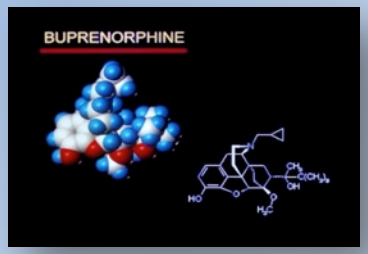
  -(2.1/0.3mg, 4.2/0.7mg, 6.3/1mg)

Buprenorphine for Opioid Dependence

- FDA approved 2002, age 16+
- Mandatory certification from DEA (100 pt. limit)
- Mechanism: partial mu agonist
- Office-based, expands availability
- Analgesic properties
- Ceiling effect
- Lower abuse potential
- Safer in overdose



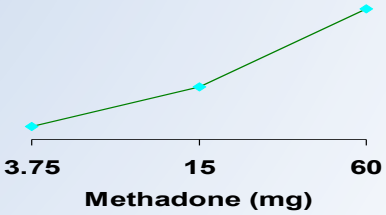
Suboxone Tablets 8mg. and 2mg

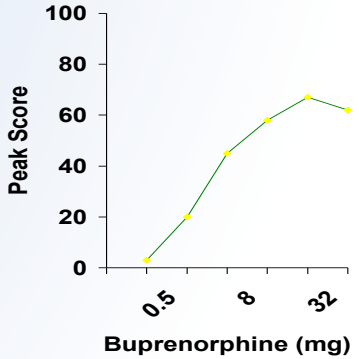


Buprenorphine: Pharmacological Characteristics

Partial Agonist (ceiling effect)

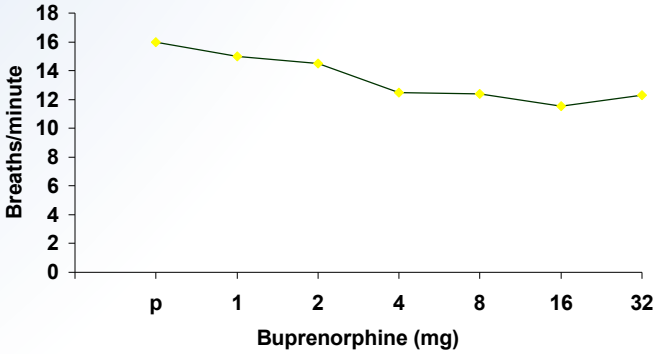
- -less euphoria
- -safer in overdose





Strong Receptor Binding

- -long duration of action
- -1st dose given during withdrawal



Extended-Release Injectable Naltrexone

Research About Extended-Release Naltrexone for Opioid Use Disorder

When compared to placebo, those receiving extended release naltrexone for 6 months:

- Had fewer opioid positive urines
- Stayed in treatment longer (improved retention)
- Had fewer cravings
- Showed greater improvement in the mental component of quality of life and overall health status
- Generally tolerated the medication without significant adverse effects

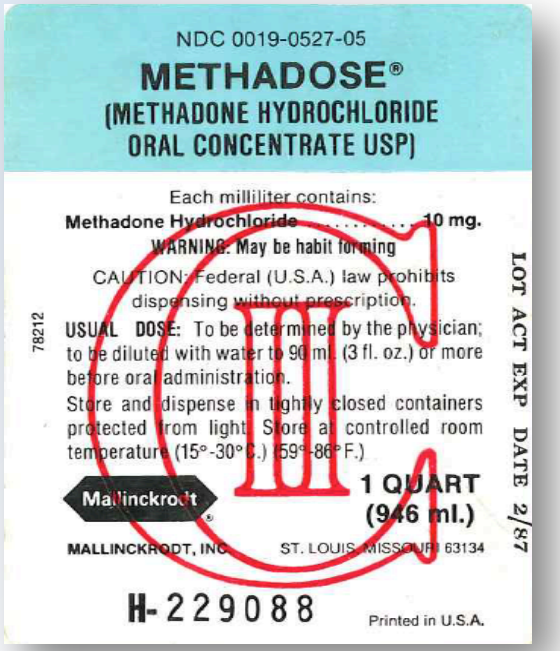
Krupitsky, et al., 2010

Research About Extended-Release Naltrexone Cont'd

- Importantly, there were no attempts to override the blockade with large doses of opioids
- No accidental or intentional overdoses during or post-treatment
- No increase in rates of non-opioid drug use
  - Consistent with other studies demonstrating reduced use of other drugs when heroin use declines
- No clinically significant elevations in liver function enzymes
- Adverse effects: fatigue, nausea, injection site reactions

Comer et al., 2006

Methadone

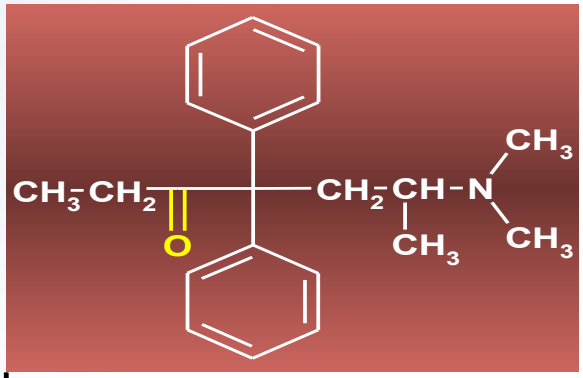

NDC 0019-0527-05
METHADOSE®
(METHADONE HYDROCHLORIDE
ORAL CONCENTRATE USP)
Each milliliter contains:
Methadone Hydrochloride ..... 10 mg.
WARNING: May be habit forming
CAUTION: Federal (U.S.A.) law prohibits dispensing without prescription.
78212
USUAL DOSE: To be determined by the physician; to be diluted with water to 90 ml. (3 fl. oz.) or more before oral administration.
Store and dispense in tightly closed containers protected from light. Store at controlled room temperature (15°-30° C.) (59°-86° F.)
III
Mallinckrodt
1 QUART
(946 ml.)
MALLINCKRODT, INC. ST. LOUIS, MISSOURI 63134
LOT ACT EXP DATE 2/87
H-229088
Printed in U.S.A.

Methadone

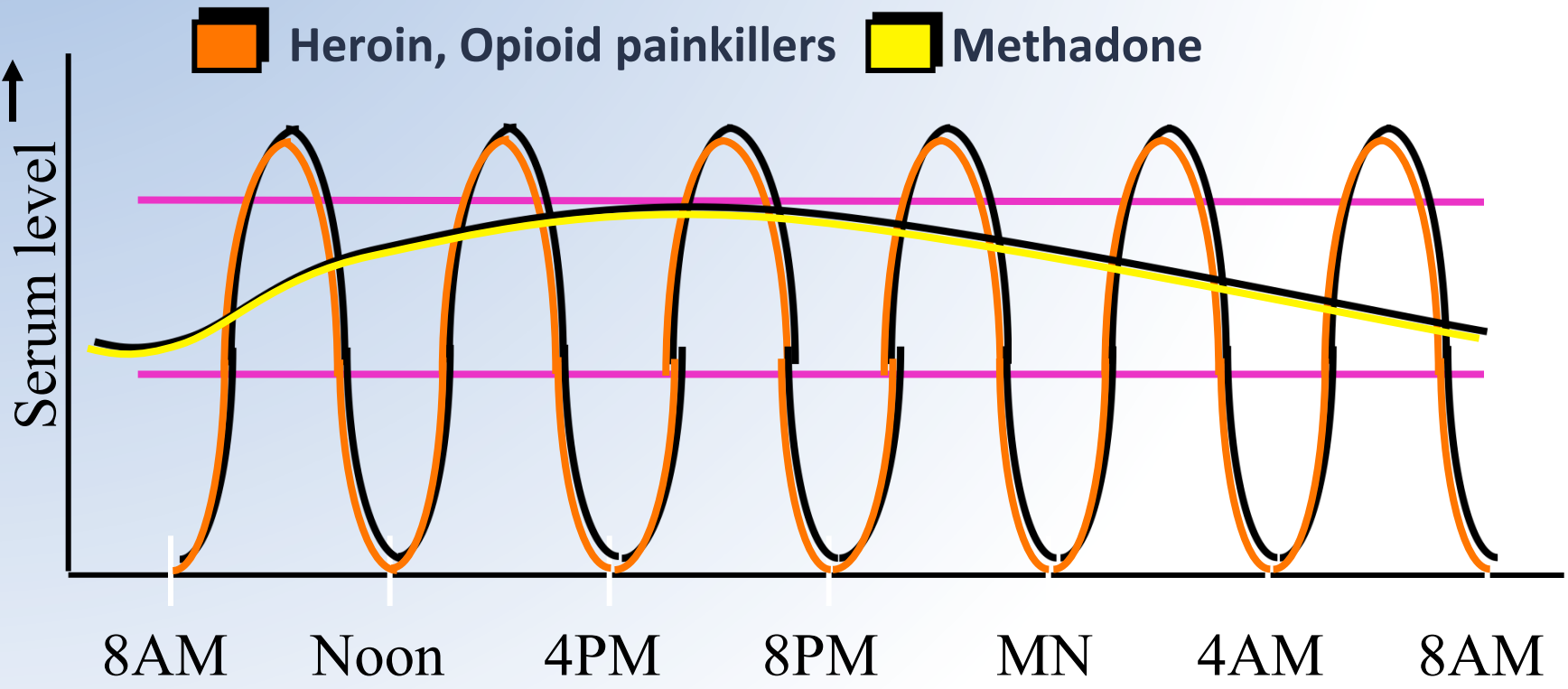
- Alleviates opioid withdrawal and craving (without intoxication)
- Used for opioid detoxification or maintenance therapy; also used as analgesic.
- Also known under brand names:
  - Methadose®
  - Dolophine®
- FDA approved in 1964

Methadone: Clinical Properties

- Orally active synthetic μ agonist
- Action: CNS depressant/ analgesic
- Long half-life, slow elimination
- Effects last 24 hours
- Once daily dosing maintains constant blood level
- Prevents withdrawal, reduces craving and use
- Facilitates rehabilitation
- Clinic dispensing limits availability



Blood levels: methadone vs. short-acting opioids



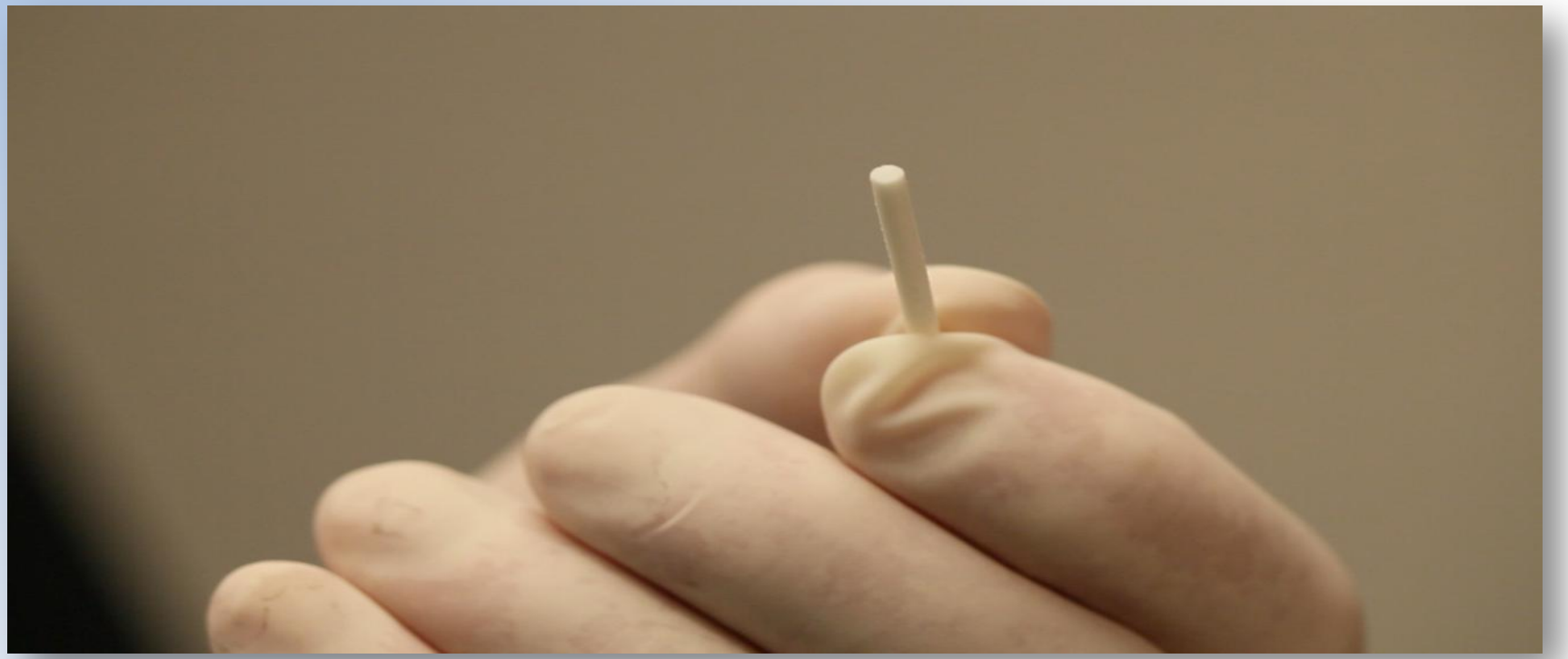
Treatment Outcome Data: Methadone

- 8-10 fold reduction in death rate
- Reduction in drug use
- Reduction in criminal activity
- Increased treatment retention
- Engagement in socially productive roles; improved family and social function
- Increased employment
- Improved physical and mental health
- Reduced spread of infectious disease/HIV

Methadone Maintenance: Disadvantages

- Withdrawal from methadone can be difficult
- Clinic dispensing: daily travel and time commitment
- Variable duration of action
- Diversion

Probuphine Implant



Probuphine

- **Recently FDA Approved**
- Implantable formulation of buprenorphine HCL (80 mg) for the treatment of opioid dependence following clinical stability on low to moderate doses of sublingual buprenorphine (8mg/day or less)
- Probuphine is inserted subdermally into the inner side of the upper arm in a brief in-office procedure under local anesthetic, and provides sustained release of bu **ths**
  - At the end of each 6-month period, Probuphine is removed in a brief, in-office procedure


OVERDOSE PREVEN
PREVENCION
EQUIPO DE
LOT

Naloxone Rescue Kits

- Community programs initiated worldwide to prevent overdose
- Example: Project Lazarus in North Carolina
- 85% of unintentional overdoses occur in the presence of others; window of 1-3 hours during which naloxone may be used to reverse OD
- Naloxone may be used by family members, friends or bystanders in cases of suspected overdose
- PrescribeToPrevent.org

Naloxone with opioid agonist therapy

- Consider naloxone prescription for patients on opioid agonist medication for opioid use disorder
  - Buprenorphine
  - Methadone
- Formulations: intramuscular, intranasal, IM/SC auto-injector

What Patients are Better Candidates for Opioid Agonist Treatment?

- Worsening of psychiatric symptoms when opioid free (e.g depression, anxiety)
- Patients requiring chronic opioid treatment (e.g. chronic pain)
- Patients with advanced liver disease (Brewer and Wong, 2004)
- Resources/insurance/availability

Selection of Candidates for Opioid Antagonist

- Not interested or able to be on agonist maintenance (ex: healthcare professionals, pilots; treatment in certain residential treatment programs)
- Patients with less severe form of disorder (i.e. short hx of use, lower use levels)
- Failed prior treatment with agonist
- Continued use of opioids, failure to improve, and/or dropped out
- Youth/naïve to agonist replacement therapy
- Longer periods of abstinence between relapses
- Criminal justice populations
  - Eliminates diversion risk
  - Potential to reduce crime and overdose associated with relapse post-release

Thank you!

Larissa Mooney, M.D.

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Lunch

L.A. Care HEALTH PLAN®

Naloxone Training and Certification Program

Kathleen Besinque, PharmD
Chloe Blalock, MA

L.A. Care HEALTH PLAN®

Overdose Prevention and Naloxone Furnishing

CHLOE BLALOCK, HOMELESS HEALTH CARE LOS ANGELES

KATHLEEN BESINQUE, PHARM.D.,MSED.

LOMA LINDA UNIVERSITY SCHOOL OF PHARMACY

Disclosure

We do not have relevant financial relationships with commercial interests.

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Meeting people where they're at.

Objectives

After attending the presentation participants will be able to:

1. Identify appropriate candidates to receive naloxone rescue products
2. Describe opioid overdose risk factors, overdose prevention strategies, symptoms of an opioid overdose, and overdose treatment with naloxone
3. Compare the different administration methods of naloxone
4. Counsel a person receiving naloxone regarding how and when to use the product.
5. Apply the California Board of Pharmacy protocol for furnishing naloxone

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Pharmacists and Naloxone

- 2013: Pharmacy practice act amended to authorize pharmacists to furnish naloxone under Board of Pharmacy protocol

- Protocol requires pharmacists to do the following:
  - Receive training (1 hour CE is required)
  - Screen potential recipients
  - Provide education to the recipient
  - Provide referrals and drug treatment information

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Source: http://www.pharmacy.ca.gov/licensees/naloxone_info.shtml

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Pharmacists and Naloxone

Naloxone is not a controlled substance. Naloxone is a life-saving medication and it should not be confiscated by law enforcement

A.B. 1535: authorizes pharmacists to furnish naloxone

A.B. 472, 635: Good Samaritan Laws

-provide protection from civil and criminal liability for lay persons who respond to an overdose

-provide limited protection from drug charges for people who call 911 re: an overdose

-provide protection from civil and criminal liability for medical providers who establish standings orders to distribute naloxone

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Objective 1: Identify potential recipients

Persons who take opioids or associates of persons who take opioids are all potential recipients for naloxone

Pharmacists screening for patients and/or recipients

- Self-identification by patients

Patient vs recipient

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Screening Questions

1. Does the potential recipient currently use or have a history of using illicit or prescription opioids?

If yes, skip question 2

2. Is the potential recipient in contact with anyone who uses or has a history of using illicit or prescription opioids?

If yes, continue

3. Does the person to whom the naloxone hydrochloride would be administered have a known hypersensitivity to naloxone?

If yes, the pharmacist should not provide naloxone.

If no, the pharmacist may continue

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Objective 2: Overdose prevention & response

Opioid overdose risk factors

Overdose prevention strategies

Symptoms of an opioid overdose

Overdose treatment with naloxone

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Overdose risk factors

- Previous overdoses
- History of substance use, dependence or addiction
- High dose opioids
  - MED >20mg/day
- CNS depressants
  - alcohol
  - gabapentin
  - benzodiazepines
  - barbituates
- Being alone while using opioids
- Changes in use:
  - intermittent abstinence or reduced use
  - Changes in substance, dose, or formulation
  - Illicit substances- unpredictable
- Sleep apnea
- Chronic renal or hepatic insufficiency
- Potential for accidental exposure
  - Children, others in household

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Pharmacological Effects of Opioids

- Depressed central nervous system
  - -Sedation, drowsiness (“nodding”)
  - -Slow/slurred speech
  - -Euphoria, pain relief
- Respiratory depression
  - -Shallow and/or infrequent breathing
  - -Constricted breathing; choking sounds, gasping
- Dilated pupils
- Nausea/Vomiting
- Flushed skin; itching

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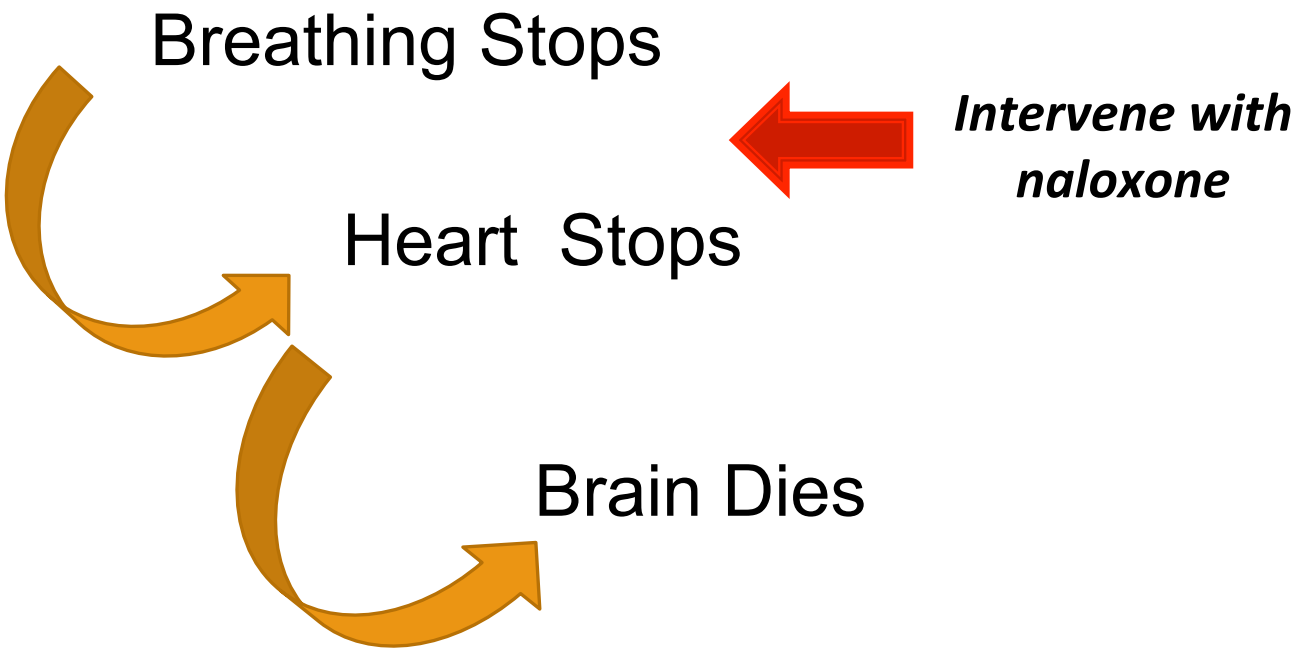
Mechanics of an Opioid Overdose



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Assessing for Overdose: ABC

1) Awake *Can you wake the person up?*

Sternum Rub: rub knuckles on sternum/breastbone- HARD

Trapezius Pinch: Pinch muscle that connects shoulder to neck

2) Breathing *Is breathing normal?*

Are breaths more than 8-10 seconds apart?

Do you hear choking or gurgling sounds?

3) Color *Is color changing?*

Are face, lips, fingernails turning blue or purple?

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Naloxone

Temporary opioid blocker that causes complete or partial reversal of respiratory and/or CNS depression

Only impacts opioid receptors (mu, kappa, delta)

Onset 2-5 minutes, peaks in 15-20 minutes, duration of action 20-90 minutes

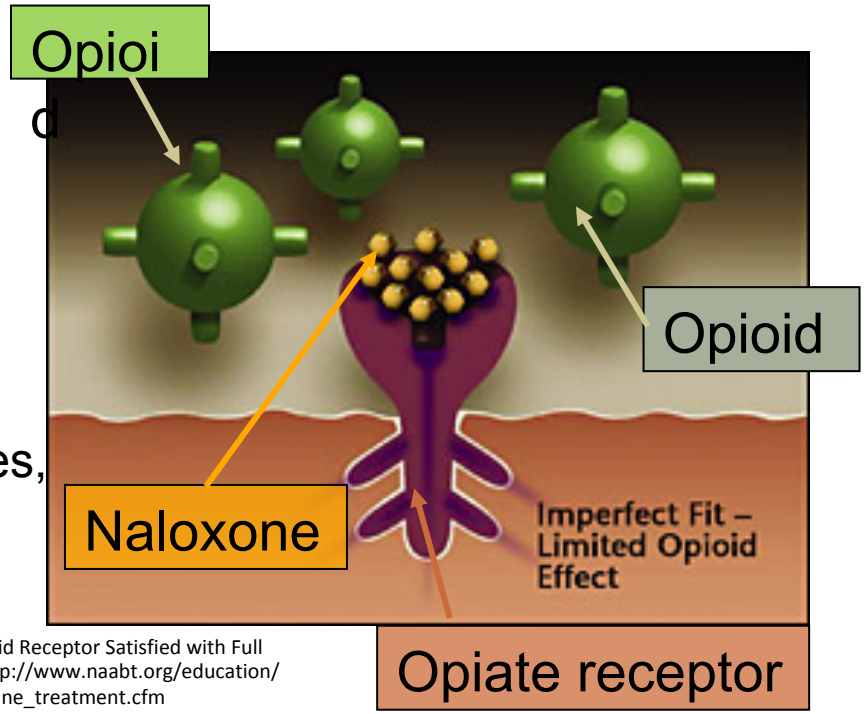

Image: Opioid Receptor Satisfied with Full Agonist http://www.naabt.org/education/buprenorphine_treatment.cfm

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Effects of Naloxone

- Temporary opioid blocker
  - cannot be abused
  - no dosage limit; more naloxone = more receptors blocked
  - no drug interactions beyond opioids
  - does not eliminate opioids from brain/body
- Precipitated withdrawal (temporary)
  - Pain
  - nausea/vomiting
  - Anxiety, irritability
  - Sweating
  - Goosebumps
  - Rapid heart rate, hypertension

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Recipient Training: Overdose Prevention

Encourage buddy system

-Tell friends/family/caregivers where naloxone is kept and how to use it

Educate on polysubstance use

-Mixing sedatives makes overdose more likely

-Mixing stimulants with sedatives does not reduce overdose risk

Educate on tolerance changes

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Meeting people where they're at.

	Recipient Training: Responding to an Overdose
S	Stimulation: assess for responsiveness with sternum rub or trapezius pinch
C	Call 911: follow dispatcher's instructions
A	Airway: Lay person flat and check mouth for food/objects
R	Rescue Breathing: tilt head back, pinch nose and breathe into mouth; give 2 breaths every 5 seconds
E	Evaluate for change
M	Medicine: administer naloxone; wait 2-3 minutes; continue rescue breathing
E	Evaluate for change; administer more naloxone if needed

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Recipient Education: After an Overdose

Overdose symptoms can return;

- encourage person who overdosed to go to hospital

Withdrawal symptoms cannot be treated with opioids after an overdose

Recovery position

Return for more naloxone if it gets used or lost

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Meeting people where they're at.

Furnishing Naloxone

1. Conduct Screening (3 questions)
2. Provide training & consultation **(required)**
    a. Risk factors and prevention
    b. Assessing for overdose
    c. Responding to overdose emergency
    d. Naloxone consultation
    e. Legal protection

- Naloxone is a bystander administered drug; instruct patients to tell a potential caregiver where naloxone is kept and how to use it

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Documentation

Medication label:

http://pharmacy.ca.gov/licensees/naloxone_labels.shtml

Notifications

- If recipient is also the person at risk of overdose, they are considered the patient
- Primary care provider will be notified if patient gives consent
- If primary care provider cannot be notified, refer patient to a primary care provider and complete a written record of items furnished

Document each product in medication record/profile

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Labeling

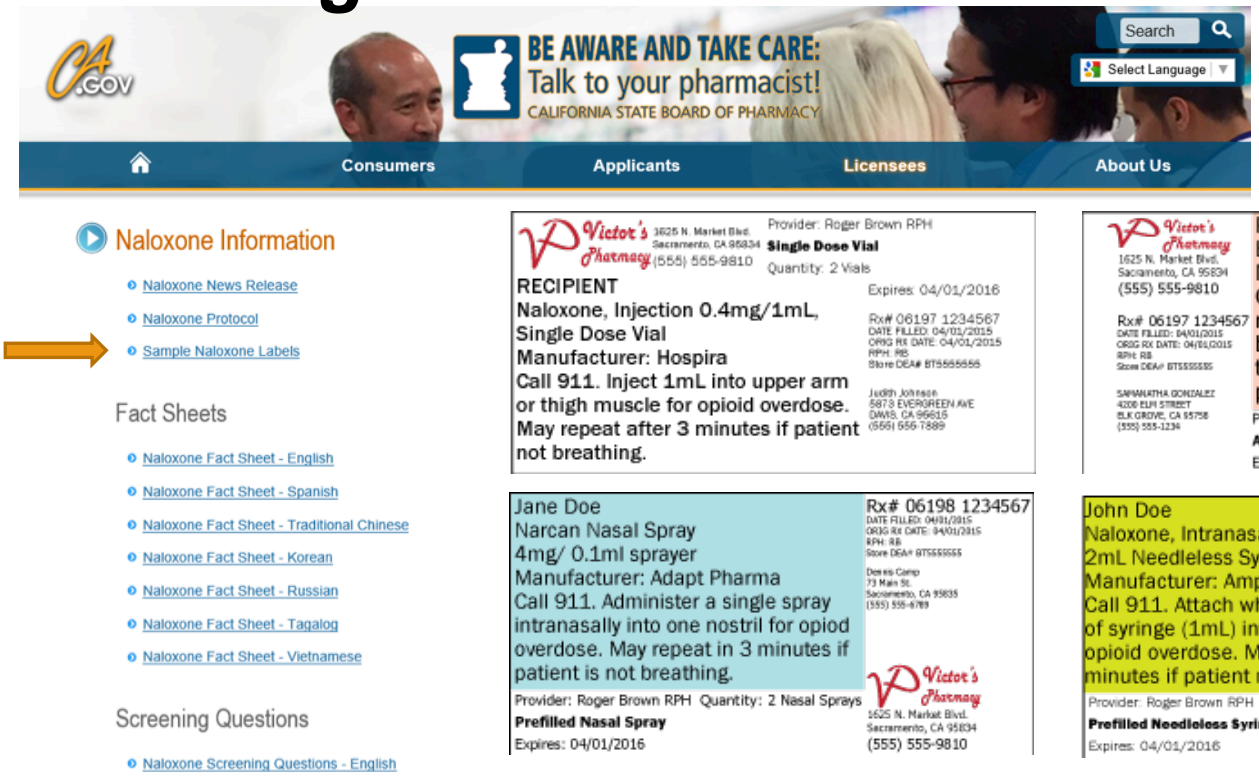

Image: Sample Naloxone Labels http://www.pharmacy.ca.gov/licensees/naloxone_labels.shtml

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Furnishing Naloxone

1. Conduct Screening
2. Provide training & consultation **(required)**
3. Provide resources

- Naloxone Fact Sheet: http://www.pharmacy.ca.gov/publications/naloxone_fact_sheet.pdf

- Referrals for drug treatment:

SAMHSA's National Helpline: 1-800-662-HELP (4357)1-800-487-4889 (TDD)

Community Assessment Service Centers: (888) 742-7900

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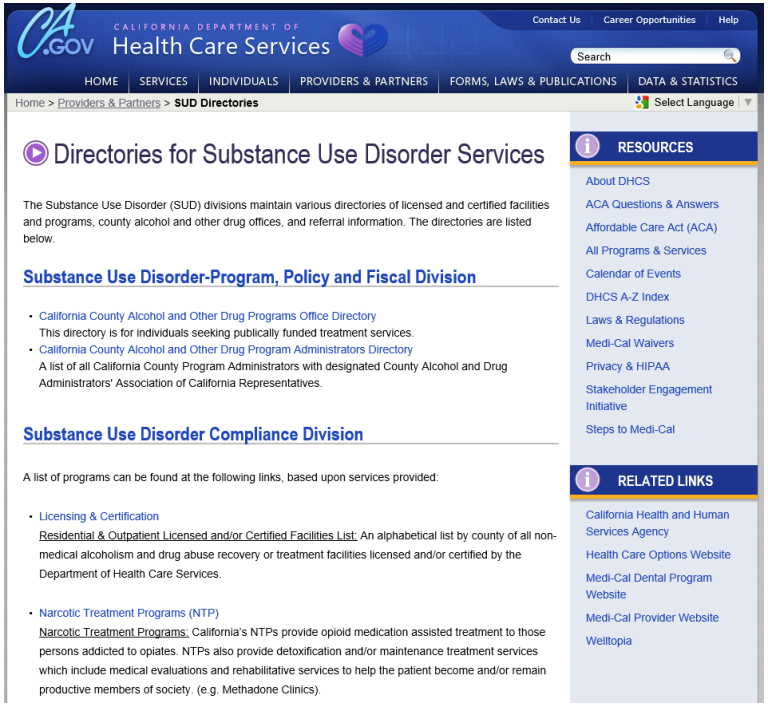
Treatment Referrals

SAMHSA's National Helpline:
1-800-662-HELP (4357)
1-800-487-4889 (TDD)

Community Assessment Service Centers:
(888) 742-7900



http://www.dhcs.ca.gov/provgovpart/Pages/SUD-Directories.aspx

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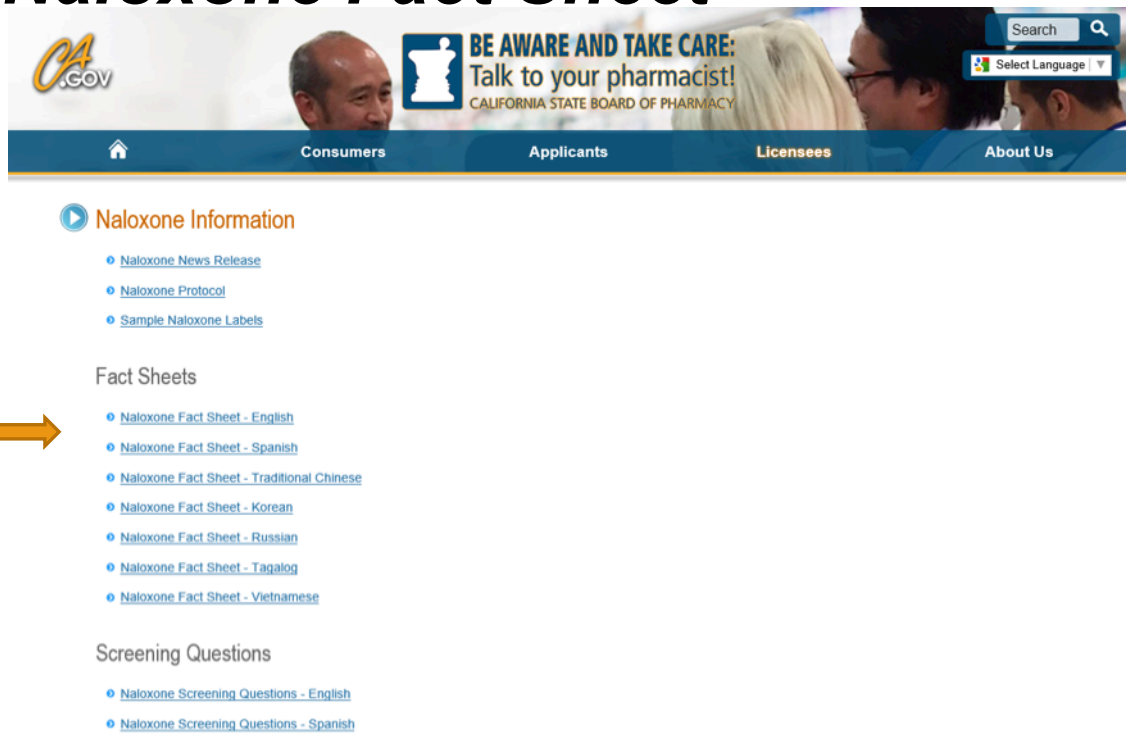
Naloxone Fact Sheet



Source: http://www.pharmacy.ca.gov/licensees/naloxone_info.shtml

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Naloxone Fact Sheet

What is an opioid overdose?

Opioids can cause bad reactions that make your breathing slow or even stop. This can happen if your body can't handle the opioids that you take that day.

TO AVOID AN ACCIDENTAL OPIOID OVERDOSE:

- Try not to mix your opioids with alcohol, benzodiazepines (Xanax, Ativan, Klonopin, Valium), or medicines that make you sleepy.
- Be extra careful if you miss or change doses, feel ill, or start new medications.

Now that you have naloxone...

Tell someone where it is and how to use it.

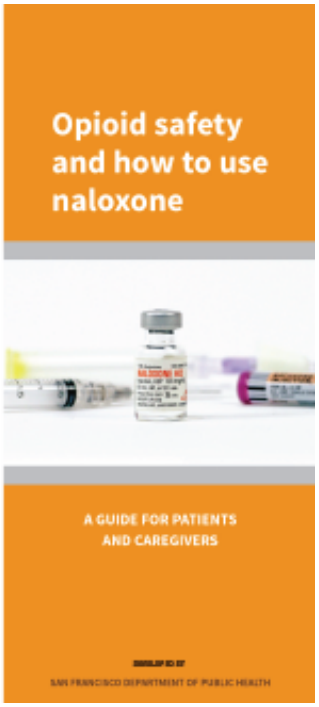
Common opioids include:

GENERIC	BRAND NAME
Hydrocodone	Vicodin, Lorcet, Lortab, Norco, Zohydro
Oxycodone	Percocet, OxyContin, Roxicodone, Percodan
Morphine	MSContin, Kadian, Embeda, Avinza
Codeine	Tylenol with Codeine, TyCo, Tylenol #3
Fentanyl	Duragesic
Hydromorphone	Dilaudid
Oxymorphone	Opana
Meperidine	Demerol
Methadone	Dolophine, Methadose
Buprenorphine	Suboxone, Subutex, Zubsolv, Bunavail, Butrans

* Heroin is also an opioid.

For patient education, videos and additional materials, please visit **www.prescribetoprevent.org**

SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH



Source: http://www.pharmacy.ca.gov/publications/naloxone_fact_sheet.pdf

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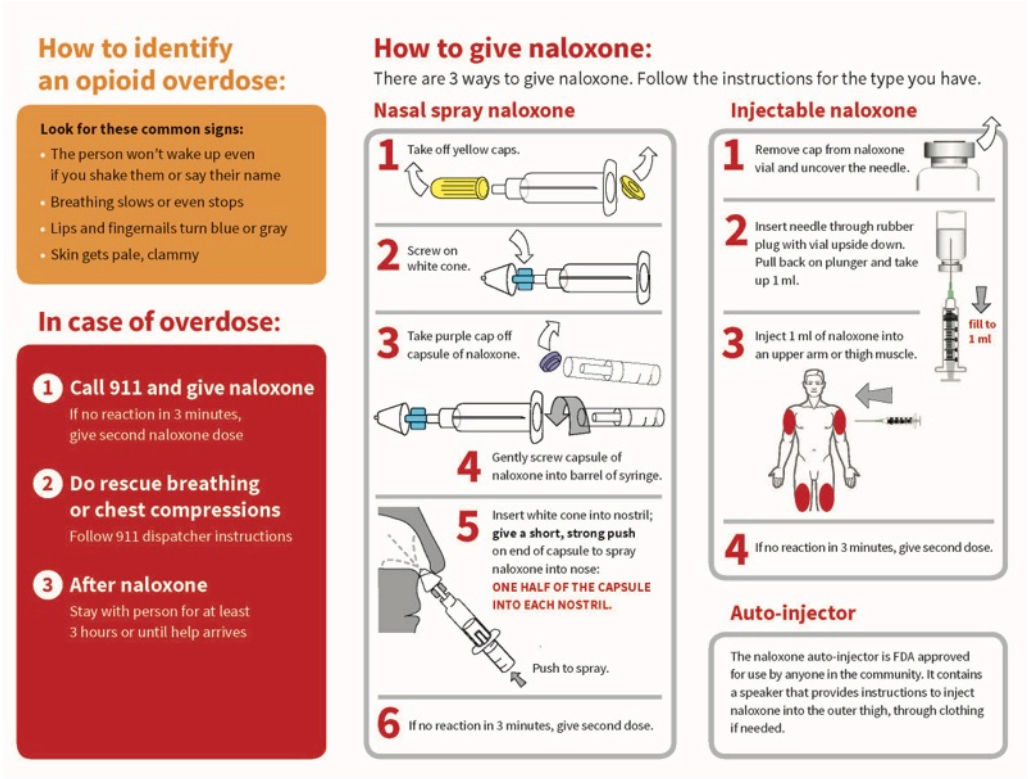
Naloxone Fact Sheet



Source: http://www.pharmacy.ca.gov/publications/naloxone_fact_sheet.pdf

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Naloxone Consultation

Advise on product choice

Dosing

Expiration dates

Storage

- protect from sunlight, extreme temperatures

Adverse effects

- Recipient cannot waive consultation

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Naloxone Formulations

Naloxone formulations allowed:

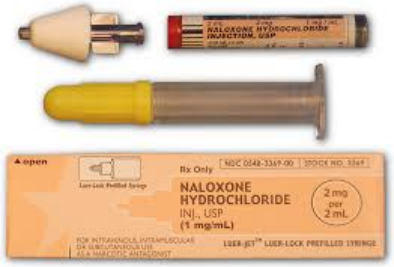
- Any FDA-approved formulation
- May advise recipient on product selection
- May recommend other items
  - Alcohol pads
  - Gloves
  - Rescue breathing masks

May provide in advance

May refill orders

Source: https://yourblogondrugs.wordpress.com/page/2/

Source: http://www.narcan.com/



Source: http://www.mass.gov/eohhs/docs/dph/substance-abuse/core-competencies-for-naloxone-pilot-participants.pdf

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Naloxone Formulations

Route of administration	Advantages	Disadvantages	Other notes
Intramuscular (IM)	Fastest onset May be least expensive	Potential exposure to blood Requires user to have injection training	Lowest cost
Intranasal	Onset fast (similar to IM) Easy to administer No blood exposure	May require assembly May not work as well as IM (especially if nasal passages are clogged) May need repeat doses	Intermediate cost
Auto-injector device	Easy to use (voice directed instructions) Trainers devices are available to train users	Expensive	Highest cost

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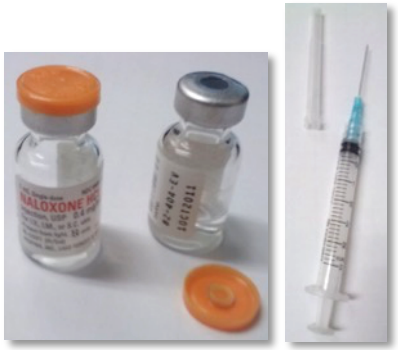
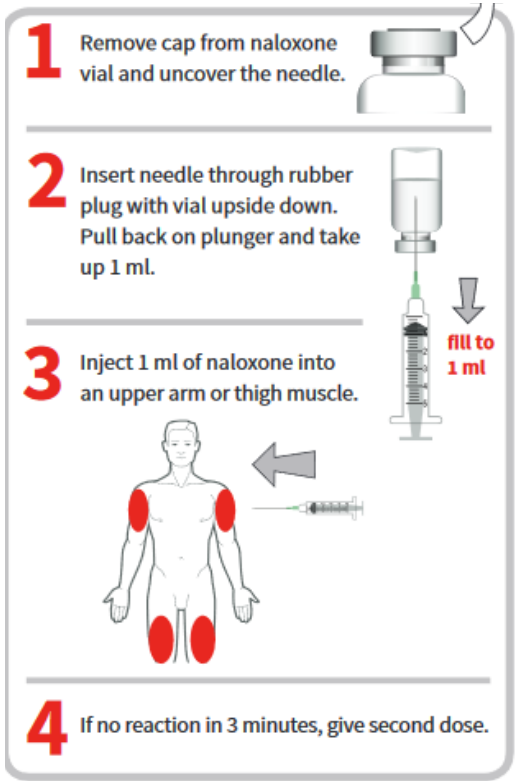
Injectable Naloxone

1. Remove orange cap from vial
2. Draw up all liquid (single dose vial)
3. Insert needle into skin at a 90ºangle
4. Inject in muscle: upper arm or thigh
5. Push down on plunger slowly





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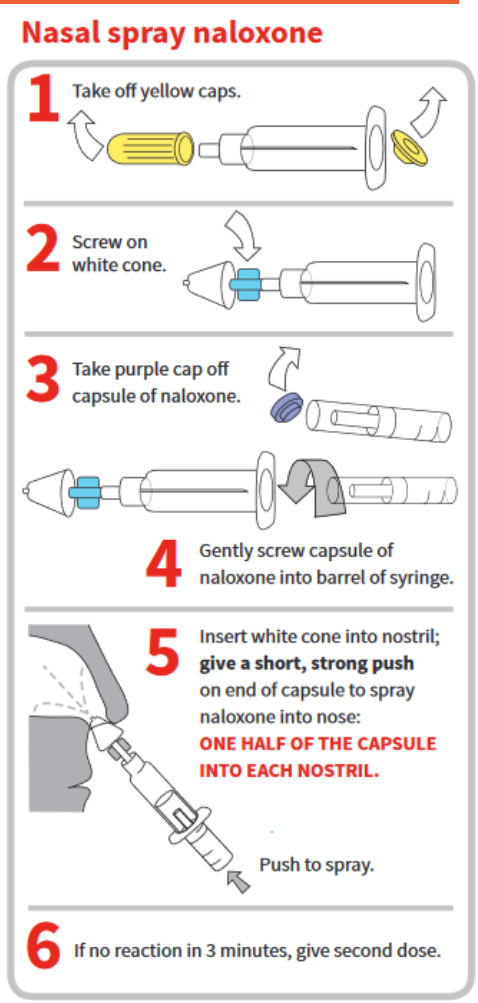
Intranasal Naloxone

Amphastar® Luer Lock Prefilled Syringe: 2 mg per 2 mL single dose syringe or vial

1. Remove protective caps from vial and syringe
2. Insert vial into syringe
3. Affix nasal device
4. Spray ½ of solution into each nostril

Source: http://www.mass.gov/eohhs/docs/dph/substance-abuse/core-competencies-for-naloxone-pilot-participants.pdf



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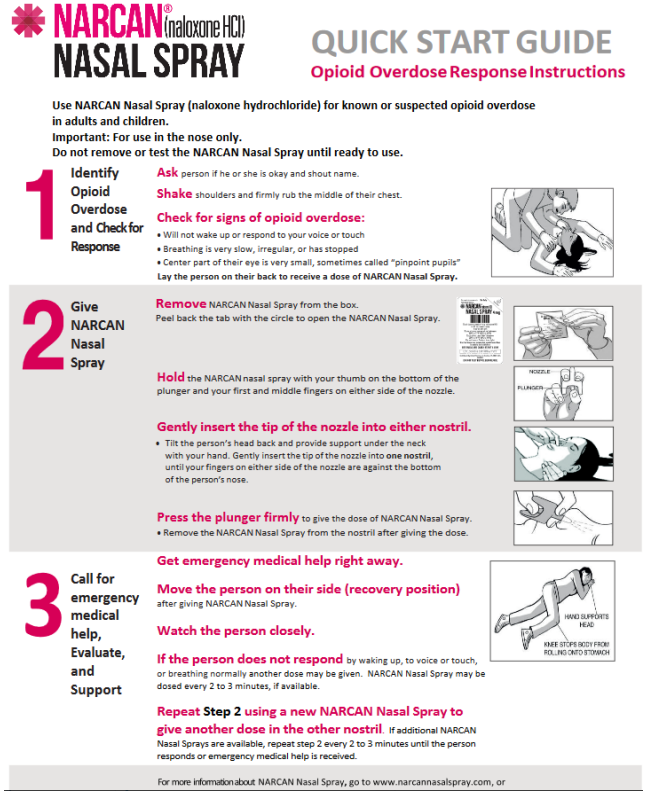
Intranasal Naloxone

Adapt Pharma Narcan® Device:
4 mg per 1 mL single dose device

1. Place tip of device in either nostril until your fingers touch the bottom of the patient's nose
2. Press plunger to release medication into nose



NARCAN® (naloxone HCl) NASAL SPRAY

QUICK START GUIDE

Opioid Overdose Response Instructions

Use NARCAN Nasal Spray (naloxone hydrochloride) for known or suspected opioid overdose in adults and children.
Important: For use in the nose only.
Do not remove or test the NARCAN Nasal Spray until ready to use.

1 Identify Opioid Overdose and Check for Response

Ask person if he or she is okay and shout name.

Shake shoulders and firmly rub the middle of their chest.

Check for signs of opioid overdose:
- Will not wake up or respond to your voice or touch
- Breathing is very slow, irregular, or has stopped
- Center part of their eye is very small, sometimes called "pinpoint pupils"

Lay the person on their back to receive a dose of NARCAN Nasal Spray.

2 Give NARCAN Nasal Spray

Remove NARCAN Nasal Spray from the box.
Peel back the tab with the circle to open the NARCAN Nasal Spray.

Hold the NARCAN nasal spray with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle.

Gently insert the tip of the nozzle into either nostril.
- Tilt the person's head back and provide support under the neck with your hand. Gently insert the tip of the nozzle into **one nostril**, until your fingers on either side of the nozzle are against the bottom of the person's nose.

Press the plunger firmly to give the dose of NARCAN Nasal Spray.
- Remove the NARCAN Nasal Spray from the nostril after giving the dose.

3 Call for emergency medical help, Evaluate, and Support

Get emergency medical help right away.

Move the person on their side (recovery position) after giving NARCAN Nasal Spray.

Watch the person closely.

If the person does not respond by waking up, to voice or touch, or breathing normally another dose may be given. NARCAN Nasal Spray may be dosed every 2 to 3 minutes, if available.

Repeat Step 2 using a new NARCAN Nasal Spray to give another dose in the other nostril. If additional NARCAN Nasal Sprays are available, repeat step 2 every 2 to 3 minutes until the person responds or emergency medical help is received.

For more information about NARCAN Nasal Spray, go to www.narcannasalspray.com, or

Source:
http://www.narcan.com/

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Meeting people where they're at.

Naloxone Auto-injector

EVIZIO® Naloxone Auto-injector:

1. Remove from outer case
2. Pull out red safety tab
3. Press black end firmly into thigh muscle & hold down for 5 seconds
4. OK to inject through clothing

Source:
http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205787Orig1s000lbl.pdf

HOMELESS HEALTH CARE LOS ANGELES

Meeting people where they're at.

Naloxone Auto-injector

A Trainer is Included for Practice

Each EVZIO prescription comes with a black-and-white Trainer that can be used for practice. Unlike EVZIO, the Trainer:

- Does not have a needle
- Does not have an expiration date
- Does not contain medicine or any liquid
- Can be reused (more than 1000 times)

To be prepared in an opioid overdose emergency, patients, family members, caregivers, and other individuals who may have to administer EVZIO should practice using the Trainer to become familiar with the injection process. After practicing with the Trainer, the electronic voice system should be reset by:

- Replacing the red safety guard
- Sliding the Trainer all the way back into the outer case

The Trainer should be left in its outer case for at least 5 seconds between each practice interval to allow the electronic voice system to reset properly. For more information on the Trainer, view the **Trainer Information**.

How to Use EVZIO

Visual and voice instructions help guide the way

EVZIO is designed to be easy to use for patients, their family members, and other caregivers who do not have medical training.[1] It contains the Intelliject® Prompt System (IPS™) with visual and voice instructions that help guide the user through the injection process.

Administration steps

1. **Pull EVZIO from the outer case.**

Do not go to Step 2 (do not remove the **red** safety guard) until you are ready to use EVZIO.
If you are not ready to use EVZIO, put it back in the outer case for later use.

2. **Pull off the red safety guard.**

To reduce the chance of an accidental injection, do not touch the **black** base of the auto-injector, which is where the needle comes out. If an accidental injection happens, get medical help right away.

Note: The **red** safety guard is made to fit tightly. **Pull firmly to remove.**

Do not replace the red safety guard after it is removed.

3. **Place the black end against the middle of the patient's outer thigh, through clothing (pants, jeans, etc) if necessary, then press firmly and hold in place for 5 seconds.**

If you give EVZIO to an infant less than 1 year old, pinch the middle of the outer thigh before you give EVZIO and continue to pinch while you give EVZIO.

Note: EVZIO makes a distinct sound (click and hiss) when it is pressed against the thigh. This is normal and means that EVZIO is working correctly. Keep EVZIO firmly pressed on the thigh for 5 seconds after you hear the click and hiss sound. The needle will inject and then retract back up into the EVZIO auto-injector and is not visible after use.

4. **After using EVZIO, the user should immediately seek emergency medical help.**

Source:
http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205787Orig1s000lbl.pdf

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Meeting people where they're at.

Sources & Additional Resources

California Board of Pharmacy

College of Psychiatric and Neurologic Pharmacists

Managing Pain Safely (MPS): Pharmacy Toolkit

Homeless Health Care Los Angeles Overdose Prevention and Response Training

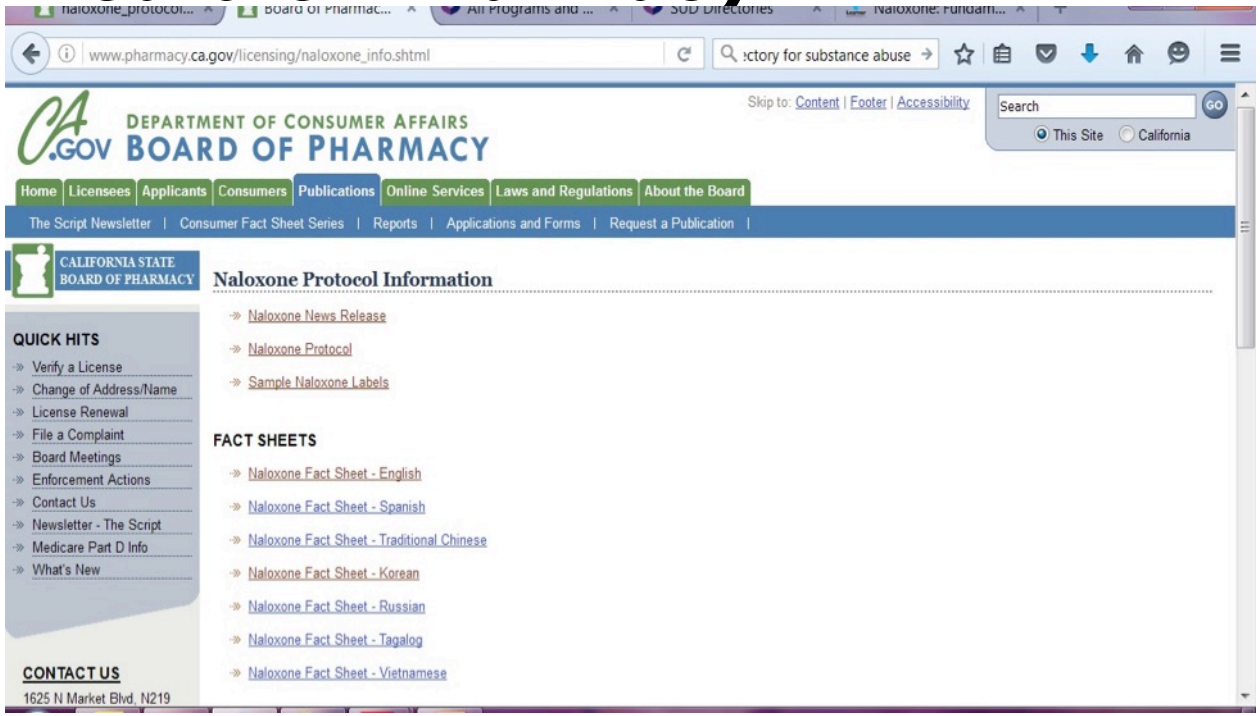
PrescribeToPrevent.org

GetNaloxoneNow.org

HOMELESS HEALTH CARE LOS ANGELES

Meeting people where they're at.

Board of Pharmacy



Panel Discussion

L.A. Care HEALTH PLAN®

Closing Remarks & Evaluations

Clayton Chau, MD, PhD

Gayle Butler, PharmD