Addiction Medicine Update
Part 2
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The Medical Management of HIV/AIDS and Hepatitis
San Francisco, California
December 8, 2018

Roadmap
• Drugs and stigma
  • Our words matter
• Methamphetamine madness
• Tobacco still deadly
• Cannabis intrigue
• Local notes
  • Surge in opioid overdose events
  • Safer consumption spaces
  • Pill control policies
  • What does stewardship look like?

Disclosures
• I have no financial interests to disclose.
• I will discuss the off-label use of some medications.

Drug use is common, some of it unhealthy
• 275 million people worldwide used illicit drugs in 2016
  • Annual prevalence, 5.6%
  • 192 million use cannabis
• Some 31 million of people who use drugs have substance use disorders
• Almost 11 million people inject drugs
  • Risk of acquiring HIV is 23 times higher among PWID
  • 1.3 million of PWID have HIV

Stigma = our biggest barrier

Negative attitudes by health care professionals about persons who use drugs lead to:
• Diminished feelings of empowerment (patients)
• Lower levels of empathy and engagement (providers)
• Suboptimal care

When patients are described as “substance abusers” instead of “persons with a substance use disorder” clinicians are more likely to recommend punitive approaches.

Sources: Van Boekel, et al. JAG 2013; Kelly, JF & Esterhoff, USP 2010

When drug use is unhealthy

Knowledge
• Make the diagnosis
• Determine severity*
• Evidence-based treatment

Skills
• Communication is our procedure
• Scientifically accurate terminology
• Non-stigmatizing language

Confidence
• Treat the person, save a life


SUBSTANCE USE WARMLINE:
PROVIDING CLINICIAN-TO-CLINICIAN CONSULTATION ON MANAGING SUBSTANCE USE DISORDERS
7 AM – 3 PM PST, MONDAY – FRIDAY
1.855.300.3595

The Clinician Consultation Center is pleased to offer free and confidential telephonic consultation focusing on substance use evaluation and management for primary care clinicians.

With special expertise in pharmacotherapy options for opioid use, our addiction medicine-certified physicians, clinical pharmacists, and nurses provide advice based on Federal treatment guidelines, up-to-date evidence, and clinical best practices.

Learn more at http://nccc.ucsf.edu/clinical-resources/substance-use-resources/
**Methamphetamine epidemiology**

- In 2015, 37 million people worldwide had used amphetamine-type stimulants (ATS).
- In 2016, 1.4 million people in the U.S. reported past year methamphetamine (MA) use; regional variability: West and Midwest >> East and South.
- Estimates of MA use among PLWH, 10-23%.
- Amphetamine-related hospitalizations quadrupled between 2008-15.
  - Annual hospital costs rose from $436M to $2.17B from 2003-15.
  - Deaths increased more than 250% from 2008-15.


**Project ECHO: Frequency of stimulant use and HIV-related sexual risk behavior**

[Graph showing adjusted log odds of stimulant use among MSM in San Francisco.]

**MSM, methamphetamine and HIV**

- MA use higher among HIV+ MSM (19–32%) compared to HIV- MSM (12–17%).
- 42% HIV prevalence in survey of MSM who used MA at least once per month for 6 months in LA.
- MA use independently associated with unsuppressed viral load in study of 2,896 HIV+ MSM in NY (AOR=1.8, CI=1.1-2.9).

Methamphetamine neurobiology

- Psychostimulant, sympathomimetic
- Direct presynaptic release of *dopamine*, *norepinephrine*, and *serotonin* into synaptic cleft
- Indirectly blocks reuptake at presynaptic transporters
- Fast uptake, wide distribution, slow clearance → prolonged effects


Acute life-threatening complications

- Dehydration
- Heat stroke, hyperthermia
- Acute coronary syndromes
- Arrhythmias, sudden death
- Stroke
- Seizure

Potential consequences of severe hyperthermia (T>104°F) in sympathomimetic toxidrome
- Brain damage
- Rhabdomyolysis
- Cardiovascular collapse
- Multiple organ failure

Effects of chronic MA use on brain loss, neuropsychiatric and neurologic function

- Most frequent deficits:
  - Episodic memory
  - Executive function
  - Motor function
- Largest impairments:
  - Episodic memory
  - Executive function
  - Information processing speed

**Cognitive, Behavioral & Emotional Effects**

<table>
<thead>
<tr>
<th>Rush 5-30 min</th>
<th>High 4-16 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euphoria, enhanced energy and alertness, feelings of increased physical and mental capacity, elevated self-esteem, increased libido</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Binge</th>
<th>Tweak 3-15 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in repetitive, focused activities; sleeplessness, heightened anxiety, paranoia, hallucinations, formication, delirium</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Crash 1-3 days</th>
<th>Withdrawal weeks</th>
<th>Craving months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue, hypersonia, dysphoria, depression, irritability, poor concentration, anxiety, paranoia, drug craving</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Image credit:** [http://magazine.ucla.edu/exclusives/substance‐abuse/](http://magazine.ucla.edu/exclusives/substance‐abuse/)

**Image credit:** [http://wwwrnceus com/meth/methpatterns html](http://wwwrnceus.com/meth/methpatterns.html)
MA effects on the HIV-positive brain

- Human studies and HIV-1 gp120 transgenic mouse models
- MA-induced immune activation + HIV-related immune activation in CNS → increase hazard of neural injury
- Electrochemical changes in neuronal circuits, injury to white matter microstructures, synaptodendritic damage → selective neuronal loss
- Mechanisms of combined HIV- and MA-induced CNS injury: increased macrophage trafficking into brain mediated by dopamine → neuroinflammation → viral reservoir in brain


Medications for MA Use Disorder

- No FDA-approved pharmacotherapies
- Small encouraging trials with mirtazapine, naltrexone, methylphenidate, bupropion
- Limitations
  - Small sample sizes
  - High dropout rates
  - Disagreements about outcomes
  - Short term follow-up
  - Specific subgroups, i.e., lower severity, MSM
  - Few studies in persons with HIV


Treatment for MA Use Disorders

BEHAVIORAL THERAPIES ARE THE ONLY CURRENT EVIDENCE-BASED TREATMENT

- Cognitive behavioral therapy
- Contingency management
- Mindfulness-based relapse prevention
- Mutual support groups
- CBT + CM


Psychostimulant medications for MA dependence (DSM-IV)

53 persons with intravenous MA dependence randomized to 54 mg/day of slow-release methylphenidate (MPH-SR) vs placebo x 20 wks in Finland, 2006

- Fewer AMP+ urines in methylphenidate arm; OR=0.46; 95% CI 0.26-0.81
- Could not be replicated in subsequent trial with high dropout rate

110 persons with MA dependence randomized to MPH-SR vs. placebo, plus CBT and motivational incentives x 10 weeks in LA and HNL, 2010-13

- No difference in primary outcome of self-reported MA use in last 30 days of active treatment
- Planned secondary analysis: lower craving scores, fewer MA use days during 10-week active treatment phase

Mirtazapine for MSM with MA dependence

- Double-blind, placebo-controlled RCT
  - Mirtazapine (30mg) vs matched placebo x 12 weeks
  - 30 min weekly SU counseling
  - 1:1 randomization
- N=60 MSM
  - Age 18-60
  - High risk: reporting anal sex with another man while using MA in prior 3 months
  - Methamphetamine dependent by DSM-IV
- Main outcome: MA metabolites in urine
- Secondary outcomes: Sexual risk behavior

Fewer MA-positive urines in mirtazapine group

43% risk reduction in methamphetamine urine-positivity in treatment arm

Parallel reductions in sexual risk behaviors

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Incident Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance Use</td>
<td></td>
</tr>
<tr>
<td>Methamphetamine urine positivity</td>
<td>0.57 (0.35, 0.93)</td>
</tr>
<tr>
<td>Sexual Risk</td>
<td></td>
</tr>
<tr>
<td>Number of male partners</td>
<td>0.39 (0.04, 4.63)</td>
</tr>
<tr>
<td>Number of male partners w/ whom meth was used</td>
<td>0.45 (0.24, 0.84)</td>
</tr>
<tr>
<td>Anal sex w/ serodiscordant partners</td>
<td>0.31 (0.14, 0.66)</td>
</tr>
<tr>
<td>Unprotected anal sex w/ serodiscordant partners</td>
<td>0.34 (0.17, 0.70)</td>
</tr>
<tr>
<td>Unprotected insertive anal sex w/ serodiscordant partners</td>
<td>0.29 (0.14, 0.66)</td>
</tr>
<tr>
<td>Unprotected receptive anal sex w/ serodiscordant partners</td>
<td>0.27 (0.05, 1.57)</td>
</tr>
</tbody>
</table>

Source: Colfax, G., Santos, G.M., et al., Arch Gen Psychiatry, 2011
Project IN: iNtermitent Naltrexone study

Double-blind, placebo-controlled RCT
- 50 mg oral naltrexone vs matched placebo
- PRN: during craving and in anticipation of MA use
- 1:1 randomization plus SU counseling for all
- N = 30 men reporting sex with men
  - Age 18-70
  - Dual methamphetamine and alcohol use
  - Non-dependent by DSM-IV criteria
  - HIV+ eligible if CD4>200

Outcomes
- Feasibility and acceptability
- Methamphetamine use and binge drinking
- Sexual risk behaviors

Efficacy of PRN naltrexone on MA use and sexual risk behaviors

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Treatment Effect IRR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methamphetamine use</td>
<td>0.82 (0.60-1.12)</td>
</tr>
<tr>
<td>Number of methamphetamine use days*</td>
<td>0.78 (0.62-0.99)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
<tr>
<td>Serodiscordant receptive anal intercourse events</td>
<td>0.15 (0.05-0.42)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
<tr>
<td>Serodiscordant condomless receptive anal intercourse events</td>
<td>0.11 (0.03-0.37)&lt;sup&gt;§&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

* Subgroup analysis § p-value <0.05

Source: Santos GM, JAIDS 2016

Managing methamphetamine withdrawal

- Brain concentrations of dopamine may stop decreasing only after several months of cessation
- Inform patient about the risk of depressive symptoms during acute and subacute withdrawal that can trigger return to use
- Develop a plan for addressing possible depression
  - Nutrition, exercise, psychiatric consultation, antidepressant therapy
  - Bupropion as a stimulating antidepressant may alleviate cravings & dysphoria
- Improvements in motor and verbal memory tests may take a year or more
- Mental health and other support services likely important for months after drug use stops

NIDA CTN Protocol 0068: Accelerated Development of Additive Pharmacotherapy Treatment (ADAPT-2) for Methamphetamine Use Disorder

- Recruiting 370 adults with moderate or severe MA use disorder from multiple U.S. sites: SF, LA, OR, MN, NY, SC, TX
- 12-week double-blind, placebo-controlled RCT
- Effectiveness and safety of 380 mg of extended-release naltrexone injected every 3 weeks combined with 450 mg once daily, extended-release oral bupropion
- Primary outcome: % urine drug screens negative for MA during the 12 weeks

Resource: https://www.clinicaltrials.gov/ct2/show/NCT03078075
Managing stimulant-induced psychoses

*Auditory and tactile hallucinations, ideas of reference, paranoid delusions*

- Worsened by sleep deprivation
- Profound distress, impairment, violence, and disability
- Antipsychotic medications, short-term anxiolytics, sleep medications, behavioral therapies (i.e. CBT)
- May require crisis team management and psychiatric hospitalization
- Typically transient, resolving within a week of cessation; but may recur or persist in some persons
- Consult and co-manage with experienced psychiatrist and behavioral therapist

Source: Glasner-Edwards and Mooney, CNS Drugs. 2014

Managing memory

Auditory memory more negatively impacted and returns more slowly than visual memory

- Write down instructions, HIV treatment plans, appointment dates
- Visually review treatment plans, schedules, medications
- Use medisets or blisterpacks as adherence reminders

Tobacco and HIV

- 50-70% prevalence of tobacco smoking in PLWH in U.S.
  - 2-3 times that of general population (20%)
  - No sex differences
- Nicotine metabolism rate enhanced in HIV and by EFV, associated with higher anxiety and more cigarettes per day
- Tobacco smoke induces mitochondrial dysfunction through oxidative stress
- Pre-HAART-era associations with HIV seroconversion, progression
- Disease risks in HIV+ smokers vs. HIV-positive non-smokers
  - 2x acute coronary events
  - 2x non-AIDS defining neoplasia
  - 9x pulmonary cancers

Lung cancer mortality associated with smoking and smoking cessation among people living with HIV in the U.S.

Microsimulation model of cumulative mortality (continues vs. quits smoking)
- Men, 2.3% vs. 6.1%
- Women, 20.9% vs. 5.2%

ART-adherent individuals continuing to smoke: 6-13x more likely to die from lung CA than from traditional AIDS-related causes

Source: Reddy et al. JAMA Intern Med. 2017

Smoking cessation in persons with HIV
- 60-70% PLWHA who smoke contemplate quitting
- 50-75% have tried at least once
- Efficacy of different strategies among PLWH, up to 42%
- Benefits of stopping
  - AIDS-defining illnesses
  - CVD events
  - non-AIDS-defining malignancies
  - bacterial pneumonia

Mortality attributable to smoking and HIV

**Number of Life-Years Lost and Population-Attributable Risk of Death Associated With Smoking and With HIV**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Lost Life Years (Age 25-89 yrs)</th>
<th>Years (% of C)</th>
<th>PAR, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV among never smokers</td>
<td>5.2 (4.4-6.8)</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>HIV among current smokers</td>
<td>6.1 (5.3-6.8)</td>
<td>34.4</td>
<td></td>
</tr>
<tr>
<td>Smoking among controls</td>
<td>3.6 (3.1-4.1)</td>
<td>61.5</td>
<td></td>
</tr>
<tr>
<td>Smoking among HIV patients</td>
<td>12.3 (11.5-13.0)</td>
<td>61.5</td>
<td></td>
</tr>
</tbody>
</table>

Survived by age, stratified by HIV and smoking

Source: Mahalingam S, et al. CID 2012

Provider Barriers to Smoking Cessation among Individuals Living with HIV

HIV care providers compared to non-HIV care providers
- Less likely to identify current smokers
- Less confident in smoking cessation skillfulness
- Overshadowed by managing complications of HIV infection
- Smoking cessation less of a priority if HIV considered a terminal illness

Even brief tobacco use disorder treatment is effective and should be offered to every patient who uses tobacco.

The "5 A'S" Approach

- **ASK** about tobacco USE
- **ADVISE** persons who use tobacco to QUIT
- **ASSESS** readiness to make a QUIT attempt
- **ASSIST** with the QUIT ATTEMPT
- **ARRANGE** FOLLOW UP care

Signs of severe physical dependence:
- Smoking more than 1 pack a day
- Smoking within 5 minutes of waking up
- Smoking even while sick
- Waking up at night to smoke
- Smoking to ease symptoms of withdrawal

Medication options:
- Nicotine patch, gum, or lozenge
- Nicotine inhaler, or nasal spray
- Varenicline
- Bupropion SR
- Combinations of above

AHRQ resource for clinicians

- [Source](http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/5steps.html)
- [ASK](http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/5steps.html)
- [ADVISE](http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/5steps.html)
- [ASSESS](http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/5steps.html)
- [ASSIST](http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/5steps.html)
- [ARRANGE](http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/5steps.html)

Clinical use of medications for the treatment of tobacco use disorder

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  - Bupropion SR
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Other tobacco resources for clinicians

- [Public Health Service Clinical Practice Guideline, Treating Tobacco Use and Dependence: 2008 Update](http://www.ahrq.gov/path/tobacco.htm)
- [Smoking and HIV: What Clinicians Need to Know, 2016](https://aidsetc.org/resource/smoking-and-hiv-what-clinicians-need-know)
- [UCSF Center for Tobacco Control Research and Education](https://tobacco.ucsf.edu/)
Cannabis overview

- Schedule I controlled substance: no currently accepted medical use and a high potential for misuse
- Legal recreational use in 10 states; medical use in at least 30 states
- Most commonly used "illicit" drug: prior month use reported by 19.8 million Americans >12 years [NSDUH 2002-14]
- High prevalence of cannabis use in persons with HIV, 20% to 38.5%*
- DSM-5 cannabis use disorder
  - 6.3% lifetime prevalence in US adults (14.8 million) [NESARC, 2012–2013]
  - In persons living with HIV?


State Marijuana Laws in 2018 current as of 11/7/2018

<table>
<thead>
<tr>
<th>Marijuana Legalization Status</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical marijuana broadly legalized</td>
<td>Medical marijuana broadly legalized for medical use</td>
</tr>
<tr>
<td>Marijuana legalized for non-medical use</td>
<td>No broad laws legalizing marijuana</td>
</tr>
</tbody>
</table>

The Health Effects of Cannabis and Cannabinoids

Conclusive or substantial evidence that cannabis or cannabinoids are effective:
1. For the treatment of chronic pain in adults (cannabis)
2. As anti-emetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids)
3. For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids)

Source: National Academies of Sciences, Engineering, and Medicine, 2017

HIV and cannabis

• Limited evidence that cannabis or cannabinoids are effective for increasing appetite and decreasing weight loss associated with HIV/AIDS (cannabis and oral cannabinoids)

• There is no or insufficient evidence to support or refute a statistical association between cannabis use and adverse effects on immune status in individuals with HIV (cannabis or dronabinol use)

Source: National Academies of Sciences, Engineering, and Medicine, 2017

Substance use and cannabis

• No or insufficient evidence to support or refute the conclusion that cannabis or cannabinoids are an effective treatment for achieving abstinence in the use of addictive substances

• There is moderate evidence of a statistical association between cannabis use and the development of substance dependence and/or a substance use disorder for substances, including alcohol, tobacco, and other illicit drugs

Source: National Academies of Sciences, Engineering, and Medicine, 2017
Mental health and cannabis

Limited evidence that cannabis or cannabinoids are effective for

- Improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders (cannabidiol)
- Improving symptoms of post-traumatic stress disorder (nabilone; a single, small fair-quality trial)

Source: National Academies of Sciences, Engineering, and Medicine, 2017

Cannabinoids and the immune system

- What are the immunomodulatory capabilities of cannabis?
- Can cannabinoids reduce immune activation and inflammation in HIV positive persons by
  - Decreasing cellular proliferation?
  - Reducing cytokine production?


Impacts of cannabis use on HIV clinical outcomes reported elsewhere

**POSITIVE**

- None on engagement in ART care
- None on ART adherence in casual users
- None on durable viral suppression in ART-treated persons
- High intensity use (> daily) associated with lower HIV VL in year following HIV seroconversion in untreated PWID

**NEGATIVE**

- Missed clinic appointments
- Risk factor for cardiovascular disease in middle aged men

Source: Manuzak, et al. CID June 2018

Heavy Cannabis Use Associated With Reduction in Activated and Inflammatory Immune Cell Frequencies in ART–Treated HIV-infected Individuals

Among 198 ART-treated PLWH, heavy cannabis users had:

- Decreased HLA-DR°CDSR°CDS4+ and CD8+ T-cell frequencies compared to non-users
- Decreased frequencies of intermediate and non-classical monocyte subsets, IL23- and TNF-α-producing antigen-presenting cells

Source: Manuzak, et al. CID 2018
### Risk factors for cannabis use disorder
- Male
- Native American
- Divorced or widowed
- Lower income
- Mood disorders
- Anxiety disorders
- Personality disorders
- Alcohol and other substance use disorders
- Conduct disorder in childhood
- Unstable home environment
- Family member with cannabis use disorder

Source: [https://www.hiv.uw.edu/go/basic-primary-care/substance-use-disorders/core-concept/all](https://www.hiv.uw.edu/go/basic-primary-care/substance-use-disorders/core-concept/all)

### Treating cannabis use disorder
- No medication consistently effective
- CBT, MI, or MET improve short-term outcomes
  - Frequency of cannabis use
  - Severity of dependence
  - Cannabis problems
- An intensive intervention of more than 4 sessions combining MET and CBT with abstinence-based incentives was most consistently supported in 2016 meta-analysis


### Treating other cannabinoid complications
- Symptoms of cannabis withdrawal: irritability, insomnia, decreased appetite, depressed mood, anxiety, restlessness
  - Cannabinoid receptor agonists: dronabinol, nabilone, nabiximols
  - Lefudadin + THC
  - Single 450 mg dose of nefazodone
- Cannabis hyperemesis syndrome in chronic, daily users (rare)
  - Short term: hot showers or baths
  - Reduce exposure to THC, increase CBD ratio
- Life-threatening coagulopathy associated with synthetic cannabinoids (e.g., K2, Spice, AK47)
  - Vitamin K to counteract antagonism by brodifacoum pesticide
  - Higher doses and duration of vitamin K for repeat exposures to synthetic cannabinoids

Sources: [Weinstein CV: Pharm Gen 2011, Shreck DAD 2016, CDC Alert](https://content.govdelivery.com/accounts/USCDC/bulletins/21e1a0f)

### Lower-risk cannabis use guidelines
#### A comprehensive update of evidence and recommendations
1. Most effective way to avoid cannabis use-related health risks is not using
2. Avoid early age initiation (<16)
3. Identify and choose low potency THC or balanced THC:CBD products
4. Don’t use synthetic cannabinoids
5. Avoid combusted inhalation
6. If you smoke, avoid deep or other risky inhalation practices
7. Avoid high-frequency use (e.g., daily or near-daily)
8. Refrain from cannabis-impaired driving
9. Populations at higher risk for cannabis-related health problems should avoid use altogether
10. Avoid combining risk behaviors (e.g., early initiation and high-frequency use)

California state cannabis resources

Compassionate Medical Use Act 1996
- [leginfo.legislature.ca.gov/faces/codes_displaySection.xhtml?sectionNum=11362.5.&lawCode=HSC](https://leginfo.legislature.ca.gov/faces/codes_displaySection.xhtml?sectionNum=11362.5.&lawCode=HSC)

Medical Board of California's Guidelines For The Recommendation Of Cannabis For Medical Purposes, April 2018
- [https://www.mbc.ca.gov/Publications/guidelines_cannabis_recommendation.pdf](https://www.mbc.ca.gov/Publications/guidelines_cannabis_recommendation.pdf)

The Adult Use of Marijuana Act 2016

CDPH website: “Let’s Talk Cannabis!”
- [https://www.cdph.ca.gov/Programs/DO/letstalkcannabis/Pages/LetsTalkCannabis.aspx](https://www.cdph.ca.gov/Programs/DO/letstalkcannabis/Pages/LetsTalkCannabis.aspx)

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### Opioid, MA and Cocaine Overdose Deaths in San Francisco

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>Opioids</th>
<th>MA</th>
<th>Cocaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>150</td>
<td>120</td>
<td>15</td>
<td>25</td>
</tr>
<tr>
<td>2007</td>
<td>165</td>
<td>135</td>
<td>15</td>
<td>25</td>
</tr>
<tr>
<td>2008</td>
<td>170</td>
<td>140</td>
<td>15</td>
<td>25</td>
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<td>2009</td>
<td>180</td>
<td>150</td>
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<td>2010</td>
<td>190</td>
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<tr>
<td>2016</td>
<td>250</td>
<td>220</td>
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<tr>
<td>2017</td>
<td>260</td>
<td>230</td>
<td>15</td>
<td>25</td>
</tr>
</tbody>
</table>

- Total
- Opioids
- Methamphetamine
- Cocaine

*Slide courtesy Phillip Coffin, SFDPH*
Recent Surge in Opioid Overdoses Events in San Francisco

**Health Advisory :: October 18, 2018**

- DOPE Project records 393 lay opioid overdose reversals in Civic Center area, Jun-Aug 2018
- SFFD administers naloxone to 113 persons in Sept 2018
  - Nearly twice given in Sept 2017
- 15 suspected opioid overdose deaths in first two weeks of Sept 2018
  - 3 times expected, most involving fentanyl
- SFGH Lab identifies potent fentanyl analogues in street drug samples, Sept 2018

San Francisco, fentanyl is here

- As a white powder in counterfeit pills, black tar heroin, cocaine, and methamphetamine
- Proportion of opioid overdose deaths due to fentanyl increased in SF from 6% in 2014 to 23% in 2017.
  - Cases frequently involved cocaine, methamphetamine, or another opioid
- Death from fentanyl toxicity can be more rapid than from other opioids

Prompt peer response essential

For anyone using any street-purchased drugs, at all times: **CARRY NALOXONE**

- Can be administered by witnesses as a first aid measure
- Covered by Medi-Cal, Healthy SF, and most health plans
- Can be furnished without a prescription by pharmacists registered to do so

For clinicians

1. **Prescribe naloxone** or direct patients using any street-purchased drugs to syringe services programs and pharmacies that furnish naloxone
2. **Treat** or refer patients with opioid use disorders to evidence-based treatment

3. Advise anyone using street-purchased drugs:

**Test your drugs for fentanyl**
- Fentanyl test strips available at syringe access sites

**Use “tester” doses**
- to ensure no unexpected effects

If using in a group, **stagger use**
- so that someone is alert to help others if needed

**ATTENTION METH USERS**

There is a new way to test your methamphetamine with fentanyl test strips that will produce the most accurate results.

**Additional Resources:**
- https://harmreduction.org/issues/fentanyl/

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**AB 186, Eggman. Controlled substances: overdose prevention program**

- Legally sanctioned facilities that allow people to consume pre-obtained drugs under the supervision of trained staff
- Designed to reduce health and public order issues often associated with public drug consumption
- Also called overdose prevention centers, safe or supervised injection facilities (SIFs), and drug consumption rooms (DCRs)

**Additional Resources:**
- www.leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill_id=201720180AB186
- www.drugpolicy.org/issues/supervised-consumption-services
AB 186, Eggman. Controlled substances: overdose prevention program

“I am returning AB 186 without my signature…. “Fundamentally, I do not believe that enabling illegal drug use in government sponsored injection centers—with no corresponding requirement that the user undergo treatment—will reduce addiction…. “I repeat, enabling illegal and destructive drug use will never work. The community must have the authority and the laws to require compassionate but effective and mandatory treatment. AB 186 is all carrot and no stick.”


Pill Control Policies

• 28 states have passed legal restrictions on prescribing
• Quality metrics on dose or duration (NCQA)
• Payer restrictions effectively mandate taper through payment (CMS, insurers)
• Pharmacies invoke legal liability or citizenship to reject the prescription, the prescriber or the patient
• Employer rules and pressures (VA)
• Prescription Drug Monitoring Programs (PDMP)– no warrant for search
• Legal investigation threats by medical boards
• Reinterpretation of CDC Guidelines for Prescribing Opioids for Chronic Pain

Slide adapted from Stefan Kertesz, MD MPH, UAB
CURES 2.0 – California’s PDMP

As of October 2, 2018, all DEA-registered physicians must:
1. Register and check the CURES database to review a patient’s controlled substance history before prescribing a Schedule II, III or IV drug for the first time.
2. Check CURES at least once every 4 months if a Schedule II-IV drug remains part of a patient’s treatment.
3. Check CURES no earlier than 24 hours, or previous business day, before prescribing the controlled substance.

Resource: https://oag.ca.gov/cures

CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016

- Exercise caution about starting opioids
- Evaluate and discuss risks and benefits with patient
- Prescribe lowest effective dose when needed
  - Reassess at MME >50 and >90
- For patients already on long-term opioid therapy, regularly reassess benefits vs. harms with patients [Recommendation #7]
  - No dose target or mandated tapers are recommended

Evidence quality: Low, for most recommendations

Resource: www.cdc.gov/drugoverdose/prescribing/guideline.html

Medical Board of California’s Death Certificate Project

“Proactive complaint” strategy for consumer protection
Invites families to file complaints against physicians who prescribed an opioid to family members that died in 2012-13 from possible opioid-related deaths

- 3700 death certificates obtained from CDPH for initial review
  - 450 cases opened
  - 100 closed, 145 referred for formal investigation; remainder pending (5/18)
  - Average time to resolution, 505 days

Cartoon courtesy S Kertesz
Unintended consequences of pill control policies?

- Medical providers have grown fearful, change prescribing practice
- Fewer providers willing to care for patients physically dependent on high-dose opioids for chronic pain
- Patients feel abandoned, leave medical care
  - Patients discontinued off opioids are more than twice as likely to use illicit drugs compared to those maintained, and these are increasingly contaminated with fentanyl [SFDPH 2018]
  - Rates of suicidal ideation and/or self-harm quadrupled among long-term opioid users after clinician-initiated prescription opioid discontinuation [Demidenko, et al. Gen Hosp Psychiatry 2017]
What does opioid safety look like?

- Opioids were vastly overprescribed through 2010-12
- Doing so caused harm
- A systems-level decline in opioid reliance is desirable
- Forced opioid reductions now quasi-mandated
  - Violate ethical and evidentiary norms of medical practice
- Opioid correction or opioid trauma?
- We must act now to protect a population we put at risk in the name of solving the U.S. overdose crisis
  - Clarify guidelines; oppose involuntary taper policies
  - Promote high-touch management of patients on high-dose opioids
  - Address structural and social determinants of health and suffering

Slide adapted from Stefan Kertesz, MD MPH, UAB

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