Opioid Safety with Naloxone

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Philip Coffin, MD, MIA
Director of Substance Use Research, San Francisco Dept. of Public Health
Assistant Clinical Professor of HIV/AIDS, University of CA San Francisco
415-437-6282
philip.coffin@sfdph.org

Disclosures

- No financial disclosures
- Discussion of naloxone by intranasal administration, a route not yet FDA approved
- No support from the pharmaceutical industry was used for this educational activity.

- Slides prepared with Eliza Wheeler, MPH, director of the Drug Overdose Prevention and Education Project
Outline

- Background of opioid overdose
- Concept of lay naloxone
- Data for lay naloxone
- Legal framework
- Models of naloxone prescription
- Logistics of naloxone prescription

Poisoning: Leading cause of injury death

Opioid analgesic overdose mortality rates
Major opioid overdose risk factors

- Prior overdose
  - Overdose in any 1 year predicts a 6-fold increased likelihood of overdose in the subsequent year
  - Any history of overdose predicts a 4-fold increased risk of mortality (Australian Treatment Outcome Study)
- Concomitant use of other substances
  - Sedatives
  - Alcohol
  - Cocaine
  - Reduced tolerance

Concept of Lay Naloxone

- Overdose usually witnessed (McGregor, Addiction 1998)
- Death takes a while (Sporer, Ann Intern Med 1999)
- EMS not routinely accessed (Coffin, Ann Emerg Med, 2009)
- Naloxone very safe and effective (Terman, 2012 FDA Hearing on Naloxone)
- More rapid reversal with naloxone may reduce need for advanced respiratory support (Gonzva, Am J Emerg Med 2013)
- Possible behavior change (Lankenau, J Commhlth 2013, Kral J Urbhlth, 2005)

Naloxone Safety Profile

- Short-acting (30-60 minutes), highly specific, high affinity mu opioid receptor antagonist
- The only element of the coma cocktail that can be safely administered alone
- Only contraindication is a known allergy to naloxone
- Opioid withdrawal symptoms generally mild at lay-distributed doses
- Opioid effect will return, a significant concern mostly for long-acting opioids, so call 911
- Essentially no effects if opioids not present
US Programs:


- 60 programs distributing or prescribing naloxone, with approximately 240 individual sites, in 18 US states.*

*Unpublished results of 2013 US naloxone programs survey, completed by the Harm Reduction Coalition

Fatal Opioid Overdose Rates by Naloxone Implementation in MA

<table>
<thead>
<tr>
<th>Cumulative enrollments per 100,000 population</th>
<th>ARR*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No enrollment</td>
<td>Ref</td>
<td>-</td>
</tr>
<tr>
<td>1-100</td>
<td>0.73</td>
<td>0.57-0.91</td>
</tr>
<tr>
<td>&gt;100</td>
<td>0.54</td>
<td>0.39-0.76</td>
</tr>
</tbody>
</table>

*Adjusted Rate Ratios (ARR) adjusted for city/town population size at age<18, male, race/ethnicity (Hispanic, white, black, other), below poverty level, medically supervised inpatient withdrawal treatment, methadone treatment, BLS/R Funded/Licensed Treatment, prescriptions to doctor shoppers, year

Walley, BMJ 2013

Heroin-related Deaths, San Francisco, 1999-2012

[Graph showing trends in naloxone distribution, new enrollments, refills, reversals, and heroin deaths over the years 1999-2012.]
### Cost-effectiveness

<table>
<thead>
<tr>
<th>No Naloxone</th>
<th>Naloxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incremental cost per QALY gained, $</td>
<td>421</td>
</tr>
<tr>
<td>Kits needed to prevent 1 death, n</td>
<td>421</td>
</tr>
</tbody>
</table>

**Population outcomes (per 200 000 heroin users)**

**Baseline scenario**

<table>
<thead>
<tr>
<th></th>
<th>No Naloxone</th>
<th>Naloxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime overdoes, n</td>
<td>918 509</td>
<td>930 759</td>
</tr>
<tr>
<td>Lifetime overdose deaths, n</td>
<td>27 406</td>
<td>25 613</td>
</tr>
<tr>
<td>Naloxone kits delivered, n</td>
<td>—</td>
<td>294 484</td>
</tr>
</tbody>
</table>

Naloxone distribution reduces overdose risk

<table>
<thead>
<tr>
<th></th>
<th>No Naloxone</th>
<th>Naloxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime overdoes, n</td>
<td>918 509</td>
<td>698 868</td>
</tr>
<tr>
<td>Lifetime overdose deaths, n</td>
<td>27 406</td>
<td>18 895</td>
</tr>
<tr>
<td>Naloxone kits delivered, n</td>
<td>—</td>
<td>307 712</td>
</tr>
</tbody>
</table>

*Coffin & Sullivan, Ann Int Med 2013*

### Opioid stewardship and naloxone

**Opiate-Related Deaths from July 9th-December 31st by Year and Drug Type, Multnomah County**

![Opiate-Related Deaths chart]


### Naloxone and the Opioid Safety Agenda

![Naloxone and the Opioid Safety Agenda diagram]

**Modify prescribing practice**
- Staged treatment (FDA relabeling)
- Med reconciliation
- Risk factor screening
- Dose limits

**Reduce diversion**
- PDMP
- Pharmacy reviews
- Take-back programs
- Pain contracts
- Abuse detergents

**Manage substance use**
- Opioid agonist treatment
- Good Samaritan laws
- Comorbid SUD treatment
- Selected harm reduction services

**Expand non-medication pain management**
- PT/OT
- Behavioral therapy
- Acupuncture
- Massage

**Reduce morbidity/mortality**
- Naloxone
- Reduce adhesions
- Reduce drug interchanges
- Reduce false positives
- Reduce drug interactions
- Reduce fatalities
Naloxone and the Law

- Naloxone is not a controlled substance; prescribing naloxone to a patient is no different than prescribing other routine medications.
- States in orange have added legal protections, such as authorizing:
  - Prescribing/dispensing to potential bystanders
  - Administration of naloxone by lay bystanders
  - Prescribing/dispensing by standing order or directly from pharmacies
- Example of standing order

Models for prescribing naloxone

- Provider writes prescription, patient fills at pharmacy
  - Setting: clinics with insured patients, pharmacies alerted to prescribing plans, may need to have atomizers on-site for intranasal formulation, consider providing informational brochure
- Provider writes prescription and directly dispenses pre-assembled naloxone kit
  - Setting: medical care with resources to have and maintain kits on-site
- Prescriber writes non-patient specific standing order* for community-based program or treatment program, program staff provide the education and distribute pre-assembled kits
  - Setting: "Overdose prevention programs," commonly found at programs like syringe exchanges, drug treatment programs, drop-in centers, etc.

*By health departments or in states with legislative authorization (CA, IL, KY, NC, NJ, VT)

Target Groups for Naloxone

- Heroin users
- Correctional populations
- Substance use treatment patients
- Family / friends
- First responders
How to prescribe naloxone

- **Injectable**
  - Vial:
    - Naloxone 0.4mg/1mL IM if overdose. Call 911. Repeat if necessary. #2
    - IM syringes (3ml 25 g 1" syringes are recommended) #2
  - Autoinjector: Evio, 0.4mg naloxone ([available July 2014](#))
- **Intranasal (off-label)**
  - Naloxone 2mg/2mL needleless prefilled syringe, spray ½ into each nostril if overdose. Call 911. Repeat if necessary. #2
  - MAD (Mucosal Atomization Device) nasal adapter. #2 ([access for pharmacies rapidly improving](#))
- **SBIRT codes cover education in 15 minute intervals**
  - Medicare – G0396
  - MedicAid – H0050
  - Commercial – CPT 99408

Administering naloxone IM & IN

Patient education

- Minimum care involves ensuring patients know:
  - When to administer naloxone
  - How to administer naloxone
  - To alert others about the medication and how to use it
- Broader education, usually for dispensing under standing orders, generally includes:
  - Opioid overdose risk factors
  - Recognizing and responding to an “overdose”
    - stimulation (sternal rub)
    - calling 911
    - administering naloxone
    - performing rescue breathing or chest compressions
    - stay with person
Pharmacy access

- Consider contacting pharmacies your patients access prior to prescribing naloxone; this is new for most pharmacists.
- Ordering:
  - Injectable vial, NDC#00409-1215-01
  - Intranasal, NDC#76329-3369-01
  - MAD nasal (Teleflex, carried by McKesson, other distributors pending)
  - Evzio, expected to be available July 2014
- Counselling:
  - Instruct patients to administer if non-responsive from opioid use and how to assemble for administration.
  - Include family/caregivers in patient counseling or instruct patients to train others.
- Billing:
  - Varies by state (e.g. Medicaid Fee for Service rather than contracted)
- Additional information for pharmacists

Experience with Clinic-Based Naloxone

- Naloxone For Opioid Safety Evaluation (NOSE)
  - Primary care clinics in San Francisco safety net system
  - Naloxone prescribed to all patients receiving chronic opioids
  - Initiated spring of 2013, final clinic enrolled April 2014
  - Funded by the National Institute on Drug Abuse
  - 555 patients prescribed naloxone since initiation

Emerging Themes Among Patients Prescribed Naloxone

- Naloxone alerts patients to risks of opioids
  - “It made me think that I was playing with my life”
  - “I’ve probably been a little more cautious. Just being careful to take the right amount, count the hours, you know, think more cautiously about dosing”

- Naloxone increases patient comfort
  - “It just reassures me that if I do have a breathing problem, that drug is there to solve the problem”
  - “It’s a great idea... There have been at least 1 or 2 times where I’ve been the one to go ‘oh wait, I just took a pill 20 minutes ago and I just took another – oops!’ It does happen, even to young people who aren’t fuzzy...”

Preliminary data from “Naloxone for Opioid Safety Evaluation”, 2014
Talking about “opioid safety”

- Prescription opioid users, including former heroin users, may not perceive their own “overdose” risk.
- Consider focusing on “opioid safety” with language such as:
  - “Opioids can sometimes slow or even stop your breathing.”
  - “Naloxone is the antidote to opioids – to be [sprayed in the nose / injected] if there is a bad reaction where you can’t wake up.”
  - “Naloxone is for opioid medications like an Epi-Pen is for someone with an allergy.”

Funding for Programs

- County general fund (to purchase materials for pre-assembled kits and other costs)
- SAMHSA SAPT HIV set aside funds
  - The purpose of the HIV Set Aside is to provide HIV early intervention services to clients in substance abuse treatment programs (and out-of-treatment injection drug users).
- Billable to select insurances, including some Medicaid plans, many part D programs, and others
- Current costs for an injectable vial or intranasal kit of naloxone is ~$50; price for autoinjector not yet known

Resources for providers

- AHRQ description of Massachusetts naloxone program: http://www.innovations.ahrq.gov/content.aspx?id=3912
- Clinic-based prescribing information and guidelines: www.prescribethoprevent.org
- www.csam-asam.org/naloxone-resources
- Pharmacy resources: www.stopoverdose.org
- Advocacy film and materials: Reach for Me: Fighting to End the American Drug Overdose Epidemic www.reach4me.org
- Research updates and other overdose-related news: www.overdosepreventionalliance.org
Resources for recipients

- Videos about naloxone, opioid safety/overdose, and how to respond in emergencies:
  - www.prescribetoprevent.org/video

- How to find a community-based naloxone distribution program (for parents and drug users who do not have access through the health care system):

Resources for families:

- Learn to Cope: online discussion forum for parents of drug users: http://www.learn2cope.org/
- Grief Recovery from a Substance Passing (GRASP), for people who have lost a loved one to overdose: http://grasphelp.org/
- Broken No More, a support group and advocacy organization for parents interested in advocating for drug policy reform: http://broken-no-more.org/
- Al-anon and Nar-anon, 12 step recovery groups for families and friends affected by another person’s drinking or drug use.

Summary

- Naloxone access for laypersons is an evidence-based intervention that reduces mortality from overdose
- Any prescribers can provide naloxone to patients at risk of an opioid overdose; in states with additional legislation:
  - prescribers can:
    - provide naloxone to anyone at risk of witnessing an overdose
    - issue a standing order authorizing others to distribute naloxone
  - naloxone recipients may administer naloxone to others in the case of suspected opioid overdose
- Education can be brief or more detailed; SBIRT codes are available for billing
- Naloxone is covered by many MediAid programs; pharmacies may need guidance and atomizer access is limited
- Patients are receptive to naloxone prescription and there may be ancillary behavioral benefits
Questions

phillip.coffin@sfdph.org

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