Your Patient Suffered a Non-fatal Overdose…

Now What?
Learning objectives

- Describe why it is important to understand how the opioid-related overdose happened.
- Identify some questions to ask before determining the treatment plan for a patient who has recently overdosed.
- List some strategies for treating patients based on the causes of their opioid overdose.
Welcome from Blue Shield of California

Salina Wong, Pharm.D.
Director, Clinical Pharmacy Programs
Pharmacy Services
Blue Shield of California
Blue Shield’s Narcotic Safety Initiative (NSI)

Reduce opioid use by 50% among Blue Shield members with non-cancer pain by the end of 2018

Reduce # of members on chronic high doses

Prevent progression from acute to chronic use

Reduce # of prescriptions and refills for those newly starting opioids

Through evidence-based interventions including:

✓ Provider awareness
✓ NSI case management
✓ SafeMed LA collaboration
✓ Chronic pain management program
✓ Limit high doses and over-prescribing for acute pain and cough/cold
✓ Restrict ER opioids
✓ Inhibit stockpiling
✓ Prevent extended use for acute pain
✓ NSI provider education webinar series
✓ Increase access to medication assisted therapy (MAT)

Achieved a 56% reduction by year-end 2018
Introducing Dr. Rubinstein

Andrea Rubinstein, MD
Chief, Department of Pain Medicine
Department of Anesthesiology
The Permanente Medical Group / Kaiser Permanente
Santa Rosa, California
Your Patient Suffered a Non-fatal Overdose…

Now what?

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Most patients who have a fatal overdose have had a previous non-fatal overdose.
After non-fatal overdose, most patients remain on opioids.
• 1/3 of initial overdose were in people “prescribed” less than 50 mme.
• Post non-fatal overdose doses change very little.
• Even when opioids were stopped initially they seem to be resumed after 90 days.
Most fatal overdoses are not from prescription opioids.
The Contribution of Prescribed and Illicit Opioids to Fatal Overdoses in Massachusetts, 2013-2015

Alexander Y. Walley, MD, MSc; Dana Bernson, MPH; Marc R. Larochelle, MD, MPH; Traci C. Green, PhD, MSc; Leonard Young, MS, MA; and Thomas Land, PhD

Table 3. Decedents whose postmortem toxicology reports indicated presence of opioids individually or in combination among 2916 residents aged ≥11 years who died of an opioid-related overdose and had a complete postmortem toxicology report in Massachusetts, June 1, 2013, through December 31, 2015

<table>
<thead>
<tr>
<th>Opioid</th>
<th>No. (%) of Decedents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual</td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>1789 (61.4)</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>1322 (45.3)</td>
</tr>
<tr>
<td>Prescription opioid</td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>402 (13.8)</td>
</tr>
<tr>
<td>Morphine</td>
<td>283 (9.7)</td>
</tr>
<tr>
<td>Methadone</td>
<td>281 (9.6)</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>213 (7.3)</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>122 (4.2)</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>109 (3.7)</td>
</tr>
<tr>
<td>Tramadol</td>
<td>91 (3.1)</td>
</tr>
<tr>
<td>Codeine</td>
<td>21 (0.7)</td>
</tr>
<tr>
<td>Combination</td>
<td></td>
</tr>
<tr>
<td>Heroin only, no fentanyl or prescription opioids</td>
<td>846 (29.0)</td>
</tr>
<tr>
<td>Heroin and fentanyl, no prescription opioids</td>
<td>510 (17.5)</td>
</tr>
<tr>
<td>Fentanyl only, no heroin or prescription opioids</td>
<td>389 (13.3)</td>
</tr>
<tr>
<td>Prescription opioids only, no heroin or fentanyl</td>
<td>481 (16.5)</td>
</tr>
<tr>
<td>Heroin and prescription opioids, no fentanyl</td>
<td>267 (9.2)</td>
</tr>
<tr>
<td>Fentanyl and prescription opioids, no heroin</td>
<td>257 (8.8)</td>
</tr>
<tr>
<td>Heroin, fentanyl, and prescription opioids</td>
<td>166 (5.7)</td>
</tr>
</tbody>
</table>

aData source: Bharel (2017).
DOI: (10.1177/0033354919878429)
## Blue Shield Data: Commercial

<table>
<thead>
<tr>
<th>All Commercial Members</th>
<th>2017</th>
<th>2018</th>
<th>2019 (6 mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid overdose non-fatal (all members)</td>
<td>73 (0.3)</td>
<td>89 (0.4)</td>
<td>31 (0.1)</td>
</tr>
<tr>
<td>Opioid overdose non-fatal (opioid rx)</td>
<td>36 (1.0)</td>
<td>39 (1.1)</td>
<td>13 (0.7)</td>
</tr>
<tr>
<td>Opioid Overdose FATAL (all members)</td>
<td>0</td>
<td>5 (0.0)</td>
<td>0</td>
</tr>
<tr>
<td>Opioid Overdose FATAL (opioid RX)</td>
<td>0</td>
<td>3 (0.1)</td>
<td>0</td>
</tr>
</tbody>
</table>

Numbers in parentheses are normalized per 10,000 members.
## Blue Shield Data: Medicare

<table>
<thead>
<tr>
<th>All Medicare Members</th>
<th>2017</th>
<th>2018</th>
<th>2019 (6 mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid overdose non-fatal (all members)</td>
<td>11 (0.8)</td>
<td>7 (0.5)</td>
<td>6 (0.5)</td>
</tr>
<tr>
<td>Opioid overdose non-fatal (opioid rx)</td>
<td>8 (1.9)</td>
<td>7 (1.9)</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Opioid Overdose FATAL (all members)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Opioid Overdose FATAL (opioid RX)</td>
<td>0</td>
<td>0</td>
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Numbers in parentheses are normalized per 10,000 members.
What the %$^@ happened?

• Intentional
• Accidental
• Due to overuse/misuse
• Due to polypharmacy or mixing substances
• Due to pharmacokinetic/dynamic changes
• Comorbid contributions
• Poor supervision by caregivers
• Other
What the %$^@ happened?

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The “Pre-Mortem”

- Discussion with patient and family – their view of what happened
- Warning signs: Minimization by patient or family
- How to reduce risk (ANY RISK)
- Make a new plan and document it, including steps to:
  - Reduce risk
  - Increase monitoring or therapy
  - Provide education
Polypharmacy risk and overdose…
What do we know?
Role of polypharmacy: Focus benzodiazepines
Case #1: How could we have missed this?

- 55 year old woman; wife of physician
- Found down, unresponsive at home
- Taken to ER, resuscitated with naloxone
- Last thing she remembers…going downstairs for a drink
- Denies misusing her medication or intentionally trying to harm herself
Case #1: Complicated co-morbidities

- ADHD on dextroamphetamine 20mg BID
- Depression on Sertraline 100 mg QD
- Anxiety and insomnia on Alprazolam 2 mg QHS plus clonazepam 1-2 mg QD
- Chronic pain on oxycodone 315 mg daily (472 MME) being tapered
- Fatter liver and frequent alcohol use
- History of traumatic brain injury
- Abdominal pain
- Obstipation / abdominal pain / chronic nausea
Case #1: Opioid related issues and risk

- Documented falls before, during and after non-fatal overdose
- Refused sleep apnea evaluation
- Polypharmacy with co-use of two benzodiazepines
- Cognitive issues including using amphetamine to stay awake for three days prior to her being found down
- Hypertension not well managed
Case #1: Monitoring “risk”

- Naloxone prescription written and picked up
  - Both Patient and husband verified they knew how to use it
- CURES appropriate
- SOAPP-5 =1
- No dose changes in seven years
- One lost prescription in seven years
- Two urine toxicology screens positive for unprescribed opioids in the last year
Case #1: Risk mitigation theatre?

Well SOAPP-5 = 1, CURES is appropriate, Patient has naloxone prescribed. Dose is stable, urine is appropriate. They are therefore “low risk.”
Case #1: Pre-mortem meeting

Follow up office visit with pain physician and husband:

• This episode was felt to be due to “exhaustion” not overdose

• Neither felt that continuing this regimen represented significant risk
Case #1:
Case #1:

Beware minimization
Case #1:

Beware minimization
Beware rational disconnect
Case #1

Abuse and Diversion
- Early refills
- Lost or stolen medications
- Escalating dose requests
- Emergency Room Visits
- Hx of substance Abuse
- Unexpected urine tox

Medical Risks
- Endocrine
- Sleep apnea
- EKG changes
- Polypharmacy
- Bone Density
- GI / GU

Psychological Risks
- Depression
- Relationship issues
- Cognitive decline
- Increased stress

Functional Issues
- Disability
- co-morbidities management
- Falls
- MVA
Abuse and Diversion
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Psychological Risks
- Depression
- Relationship issues
- Cognitive decline

Functional Issues
- Disability
- Inability to manage co-morbidities
- Falls
- MVA

Case #1
Case #1: New plan

- Discussed risk mitigation strategies including follow up for sleep apnea, alcohol cessation assistance, physical reconditioning, referral to psychiatry.
- Outpatient taper not likely to be successful in a timely manner and risk > benefit.
- Psychiatry felt that tapering benzodiazepines was not appropriate.
- Offered extended inpatient treatment to taper – declined.
- Offered buprenorphine treatment – declined.
- Offered to continue care but without opioid prescribing – declined.
The conundrum of opioid tapering in long-term opioid therapy for chronic pain: A commentary

Ajay Manhapra, MD, Albert A. Arias, MD, and Jane C. Ballantyne, MD

Chronic Pain on Opioids

Physiologic Dependence

Complex Persistent Dependence

Addiction
Case #1:

- Patient’s neurologist resumes next opioid prescription for chronic daily headache
- Care is then transferred to another pain provider
- Taper is slowed to 5 mg per month
Recognize When and Understand How to Taper Patients on Opioids
Health care professionals should not abruptly discontinue opioids in a patient who is physically dependent on opioids, nor should they implement rapid tapers in patients with long-term dependence. Safe tapers may take months to years to accomplish. Ensure patients understand the risks and benefits of dose maintenance versus dose tapering and develop an individualized plan in collaboration with patients.

The CDC recently clarified that its 2016 guidelines only recommended dose limits for new patients. The CDC does not recommend applying arbitrary dose limits to patients dependent on long-term opioids, as there is insufficient data supporting this practice. In a recent study in the Journal of Substance Abuse Treatment, after an abrupt taper almost half (49%) of people had an opioid-related hospitalization or emergency department visit. ¹

Offer Medication Assisted Treatment (MAT)
For patients experiencing opioid use disorder, the use of some MAT, such as buprenorphine, has been shown to be highly safe and effective in lowering overdose risk, decreasing HIV and hepatitis C occurrences, and increasing retention in treatment. If you are not yet certified to prescribe buprenorphine, consider obtaining X-waiver certification. There are several short online MAT training programs available as well as additional MAT treatment resources for X-waivered health care professionals on our resource list.
Six months later patient found in her home, dead.
What you can do before there is a poly-pharmacy problem

• Educate yourself on benzodiazepine pharmacology and equipotency
• Talk to all patients about co-use of benzodiazepines
• Talk to the prescribing doctor about your concerns
• Monitor for and reduce other risk factors (sleep apnea)
• Consider tapering one or the other
• Understand why they use benzodiazepines (anxiety is often a manifestation of inter-dose withdrawal)
• Document all steps taken to mitigate risk
Intentional overdoses
CLINICAL RESEARCH

Repetition of intentional drug overdose: a population-based study


Figure 1. Cumulative probability of repeat intentional overdose. There were 13,903 instances of repeat self-poisoning over 379,599 person-years, with an overall repetition rate of 36.6 per 1000 person-years (95% CI 36.0 to 37.2).
Repetition of intentional drug overdose: a population-based study

Yaron Finkelstein<sup>abc</sup>, Erin M. Macdonald<sup>d</sup>, Simon Hollands<sup>d</sup>, Marco L. A. Sivillotti<sup>de</sup>, Janine R. Hutson<sup>ab</sup>, Muhammad M. Mamdani<sup>ab</sup>, Gideon Koren<sup>abc</sup> and David N. Juurlink<sup>ab</sup> for The Canadian Drug Safety and Effectiveness Research Network (CDSERN)

Figure 2. Top agents/drug classes implicated in intentional overdose. Note that percentages do not sum to 100% because 26.2% of first overdose presentations involved more than one substance. *p Value < 0.05.
Case #2: Intentional overdose

- 55 year-old C-5-6 quadriplegic man after surfing accident
- Depressed and difficulty adjusting to his disability
- On Oxycodone SR 20 mg TID (mme90)
- Valium 5mg TID for muscle spasm and Temazepam 15 mg for sleep
- Recent visit with psychologist, discussed suicidal ideation but no plan or intent
- Found down in his back yard with empty bottle of pills 11 days after a 30-day refill (#90)
Case #2: Intentional overdose

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- Recent visit with psychologist, discussed suicidal ideation but no plan or intent
- Found down in his back yard with empty bottle of pills 11 days after a 30-day refill (#90)
  - “I just didn’t care anymore. It seemed like it would be so easy to just go to sleep and not wake up.”
Could we have anticipated?
Case #2

Abuse and Diversion
- Early refills
- Lost or stolen medications
- Escalating dose requests
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Medical Risks
- Endocrine
- Sleep apnea
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Functional Issues
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Psychological Risks
- Depression
- Relationship Issues
- Cognitive decline
- Increased stress
- Suicidal

Functional Issues
- Disability
- co-morbidities management
- Falls
- MVA
Case #2: The new plan

- Change to sublingual buprenorphine
- Mood improved within first 24 hours
- Pain well controlled
- Patient returns to volunteer work with Habitat for Humanity and helping other disabled people
- No suicidal ideation or attempts in 10 years
- Tapered off valium and temazepam
A brief digression about long-acting opioids…
A TIMES INVESTIGATION

‘YOU WANT A DESCRIPTION OF HELLC?’ OXYCONTIN’S 12-HOUR PROBLEM

by HARRIET RYAN, LISA GRION AND SCOTT GLOVER
MAY 5, 2016

The drugmaker Purdue Pharma launched OxyContin two decades ago with a bold marketing claim: One dose relieves pain for 12 hours, more than twice as long as generic medications.

Patients would no longer have to wake up in the middle of the night to take their pills, Purdue told doctors. One OxyContin tablet in the morning and one before bed would provide “smooth and sustained pain control all day and all night.”
Effect of Ethanol on the Release of Morphine Sulfate From Oramorph SR Tablets

Robert L. Barkin, MBA, PharmD,1* Dean Shirazi, PhD,2 and Eric Kinzler, PhD3
“MS CONTIN does not release morphine continuously over the course of a dosing interval. The administration of single doses of MS CONTIN on a q12h dosing schedule will result in higher peak and lower trough plasma levels than those that occur when an identical daily dose of morphine is administered using conventional oral formulations on a q4h regimen.“

*FDA document from Purdue Pharmaceuticals 2009*

https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/019516s034lbl.pdf
A word about methadone

Pain Medicine, pages S26-S35, 13 JUN 2011 DOI: 10.1111/j.1526-4637.2011.01134.x
An ounce of prevention

• Pill counts mid-cycle can indicate appropriate use
• Depression screening and treatment as condition
• Thorough risk assessment and mitigation
• Substance use disorder discussions without judgement
• Avoid benzodiazepines
• Avoid EtOH
• SLOW TAPER if tapering, unless overdose risk feels imminent
• Know now to use buprenorphine as part of harm-reduction
• Involve the entire family
“To have any hope of stemming the overdose tide, we have to make it easier to obtain buprenorphine than to get heroin and fentanyl.”
GAP 4: Barriers include lack of coverage and reimbursement for buprenorphine as well as the lack of education and training on the proper usage of buprenorphine. There has been a lack of access to buprenorphine treatment for chronic pain.143

- **RECOMMENDATION 4A**: Make buprenorphine treatment for chronic pain available for specific groups of patients, and include buprenorphine in third-party payer and hospital formularies.

- **RECOMMENDATION 4B**: Encourage CMS and private payers to provide coverage and reimbursement for buprenorphine treatment, both for OUD and for chronic pain. Encourage primary use of buprenorphine rather than use only after failure of standard mu agonist opioids such as hydrocodone or fentanyl, if clinically indicated.

- **RECOMMENDATION 4C**: Encourage clinical trials using buprenorphine for chronic pain to better understand indication, usage, and dosage.
Bottom line: When a patient has an overdose

• The patient took more than their body could tolerate
• Find out why
• Reduce their risk by any means necessary
• See them often
• Engage a team approach
• Involve the family
• Understand long-acting opioids and their risks
• Understand the role of buprenorphine for pain
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