



**Your Patient Suffered a
Non-fatal Overdose...**

Now What?

Learning objectives

- 1 Describe why it is important to understand how the opioid-related overdose happened.
- 2 Identify some questions to ask before determining the treatment plan for a patient who has recently overdosed.
- 3 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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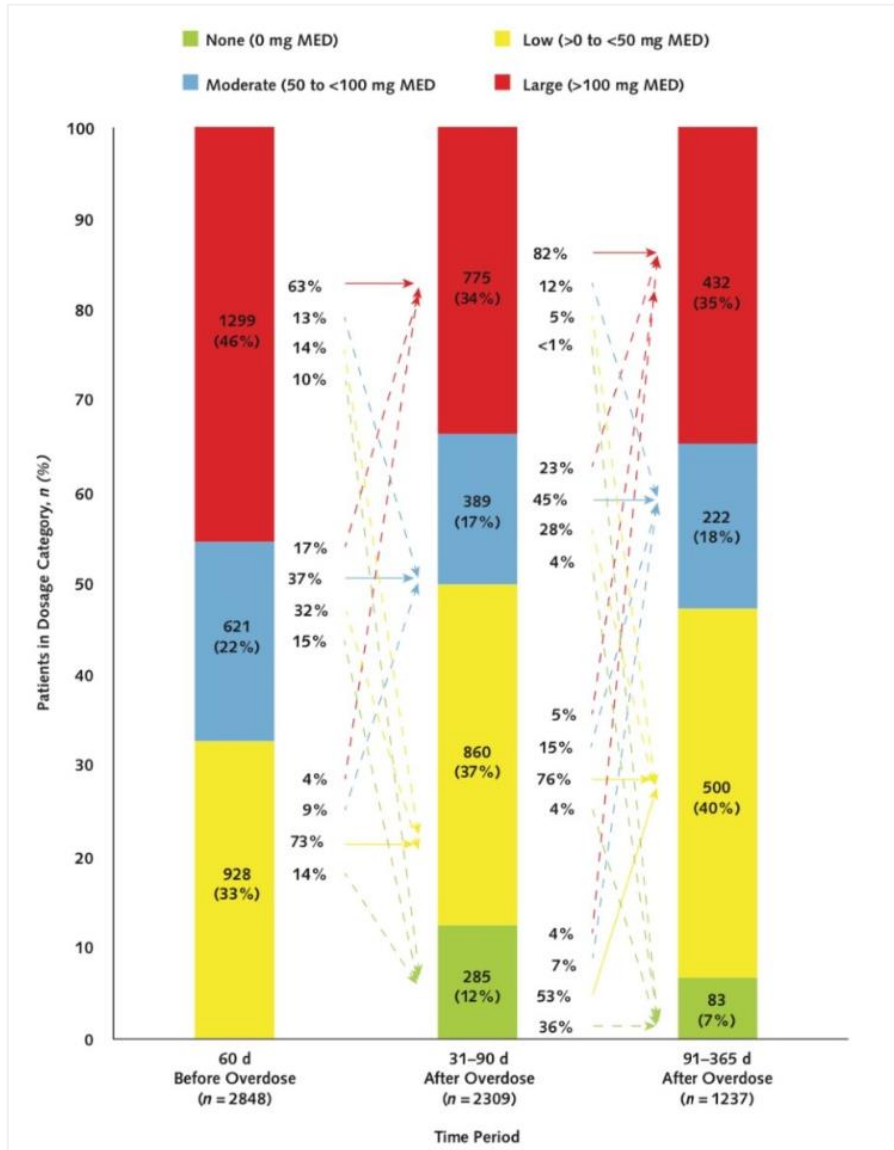
Opioid Prescribing After Nonfatal Overdose and Association With Repeated Overdose

A Cohort Study

Marc R. Larochelle, MD, MPH; Jane M. Liebschutz, MD, MPH; Fang Zhang, PhD; Dennis Ross-Degnan, ScD; and J. Frank Wharam, MB, BCh, BAO, MPH

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.

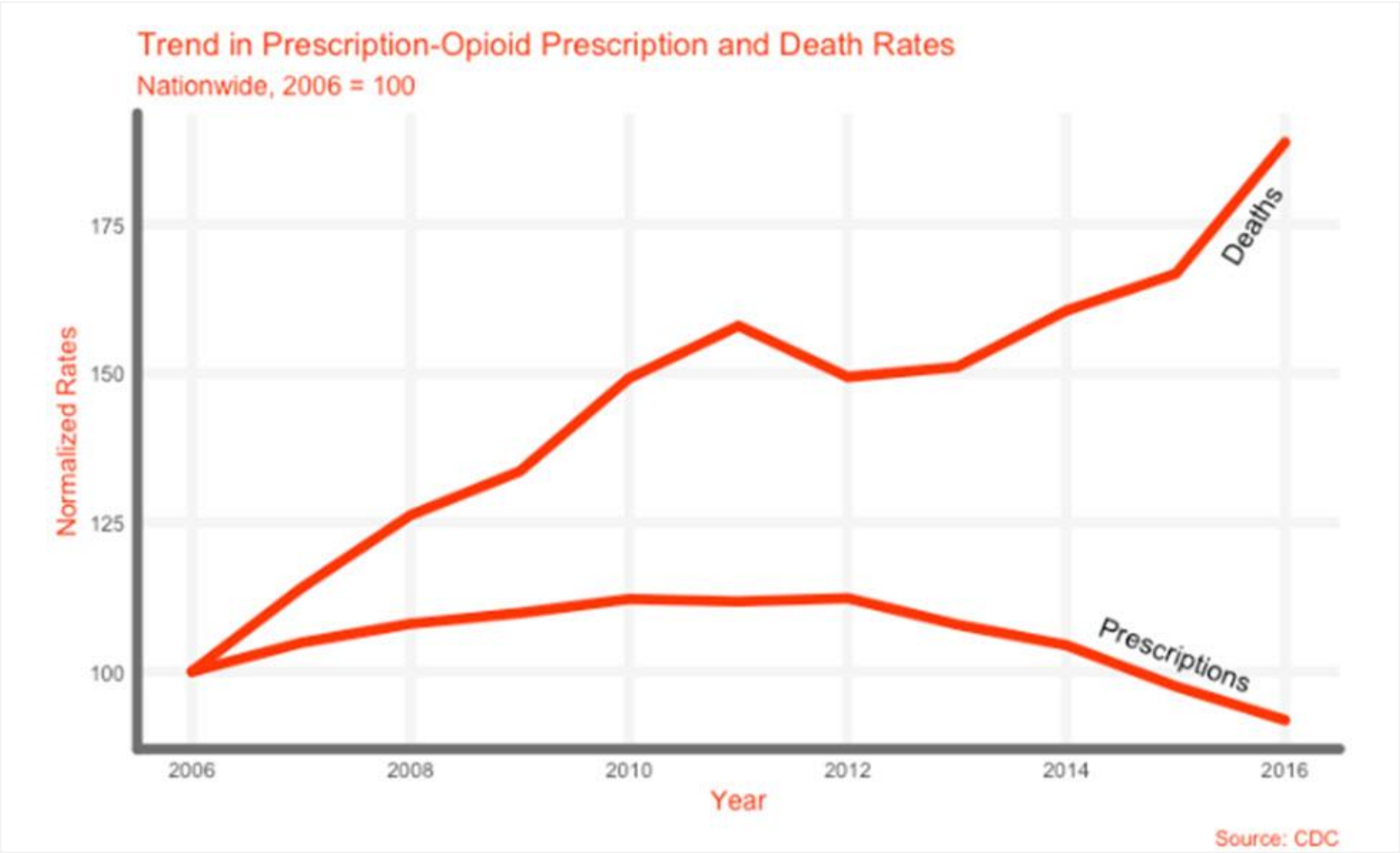
Annals of Internal Medicine

ORIGINAL RESEARCH

Opioid Prescribing After Nonfatal Overdose and Association With Repeated Overdose

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RESEARCH NEWS

Most fatal opioid overdoses are not caused by prescription drugs, US study finds

Elisabeth Mahase

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^{1,2} ; Dana Bernson, MPH²; Marc R. Larochelle, MD, MPH¹; Traci C. Green, PhD, MSc³; Leonard Young, MS, MA²; and Thomas Land, PhD⁴


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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^a

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

^aData source: Bharel (2017).³²

DOI: (10.1177/0033354919878429)

Blue Shield Data: Commercial

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

Numbers in parentheses are normalized per 10,000 members.

Blue Shield Data: Medicare

All Medicare Members	2017	2018	2019 (6 mo)
Opioid overdose non-fatal (all members)	11 (0.8)	7 (0.5)	6 (0.5)
Opioid overdose non-fatal (opioid rx)	8 (1.9)	7 (1.9)	3 (1.3)
Opioid Overdose FATAL (all members)	0	0	0
Opioid Overdose FATAL (opioid RX)	0	0	0

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?

- Intentional
- Accidental
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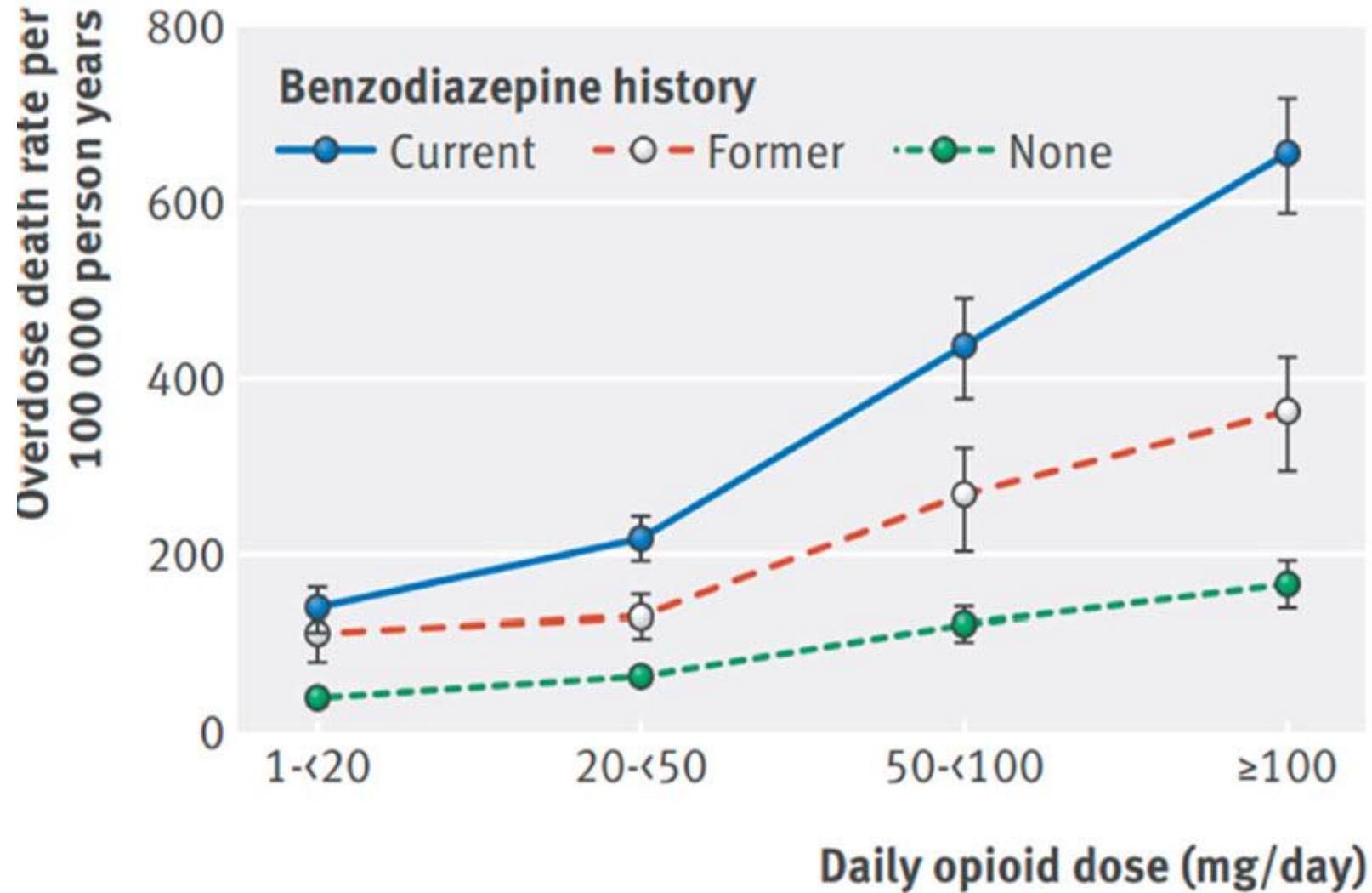
The “Pre-Mortem”

- 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:

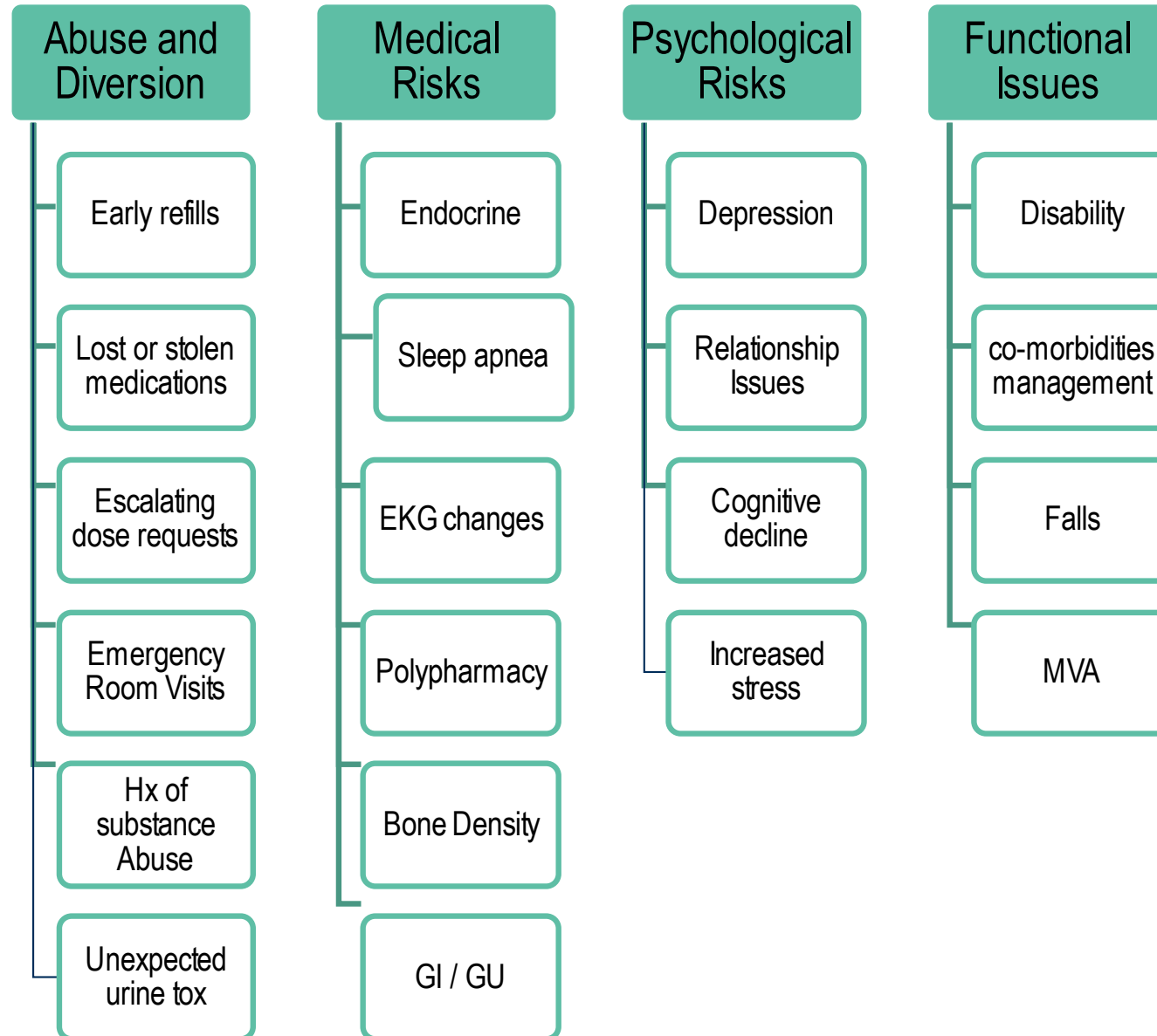
- This episode was felt to be due to “exhaustion” not overdose
- Neither felt that continuing this regimen represented significant risk

Case #1:

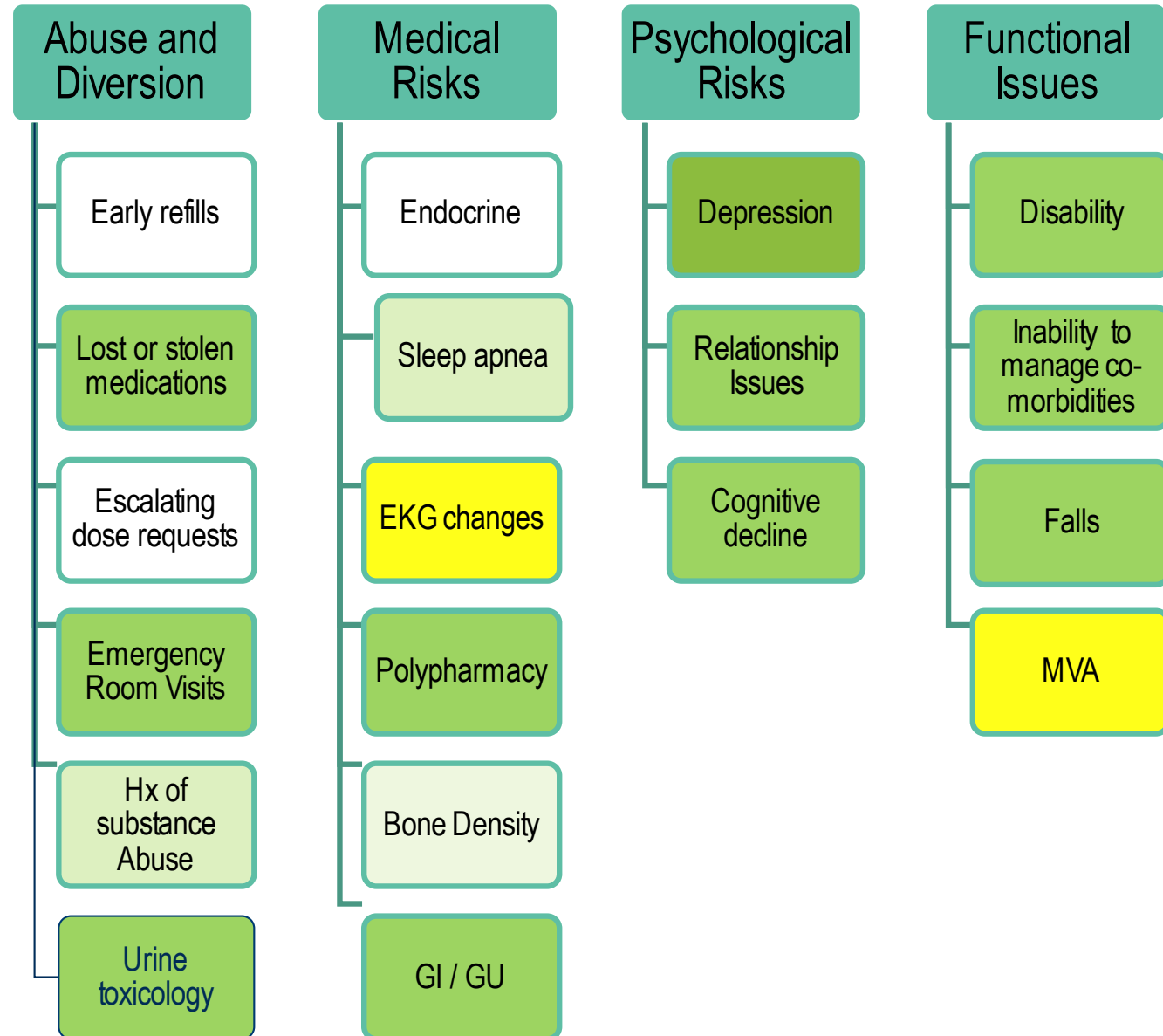
Beware minimization

Beware minimization
Beware rational disconnect

Case #1



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



HHS Public Access

Author manuscript

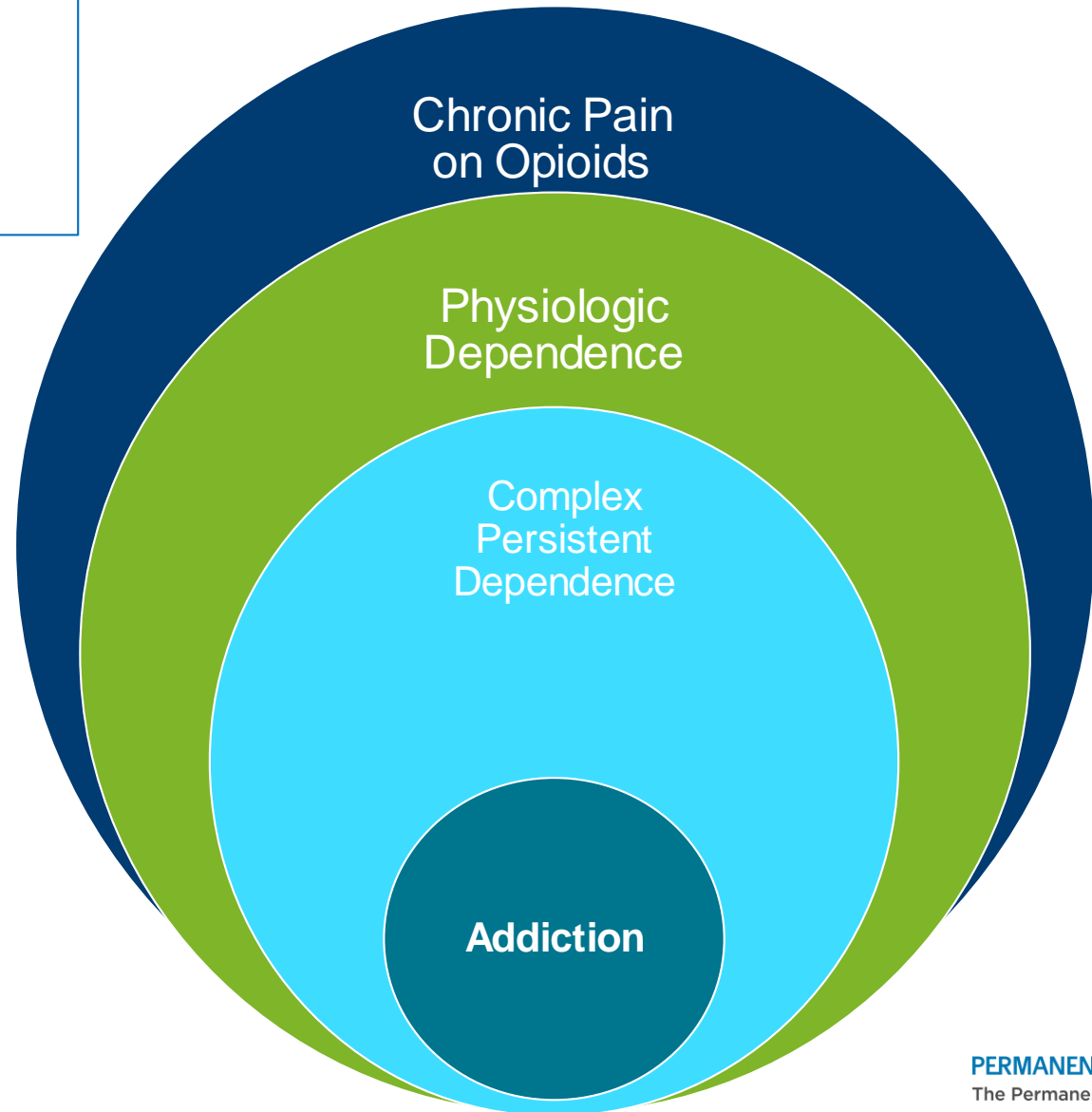
Subst Abus. Author manuscript; available in PMC 2019 March 20.

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Subst Abus. 2018 ; 39(2): 152–161. doi:10.1080/08897077.2017.1381663.

The conundrum of opioid tapering in long-term opioid therapy for chronic pain: A commentary

Ajay Manhara, MD^{a,b,c}, Albert A. Arias, MD^{a,c}, and Jane C. Ballantyne, MD^d



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



SUSAN FANELLI
Acting Director

State of California—Health and Human Services Agency California Department of Public Health



GAVIN NEWSOM
Governor

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

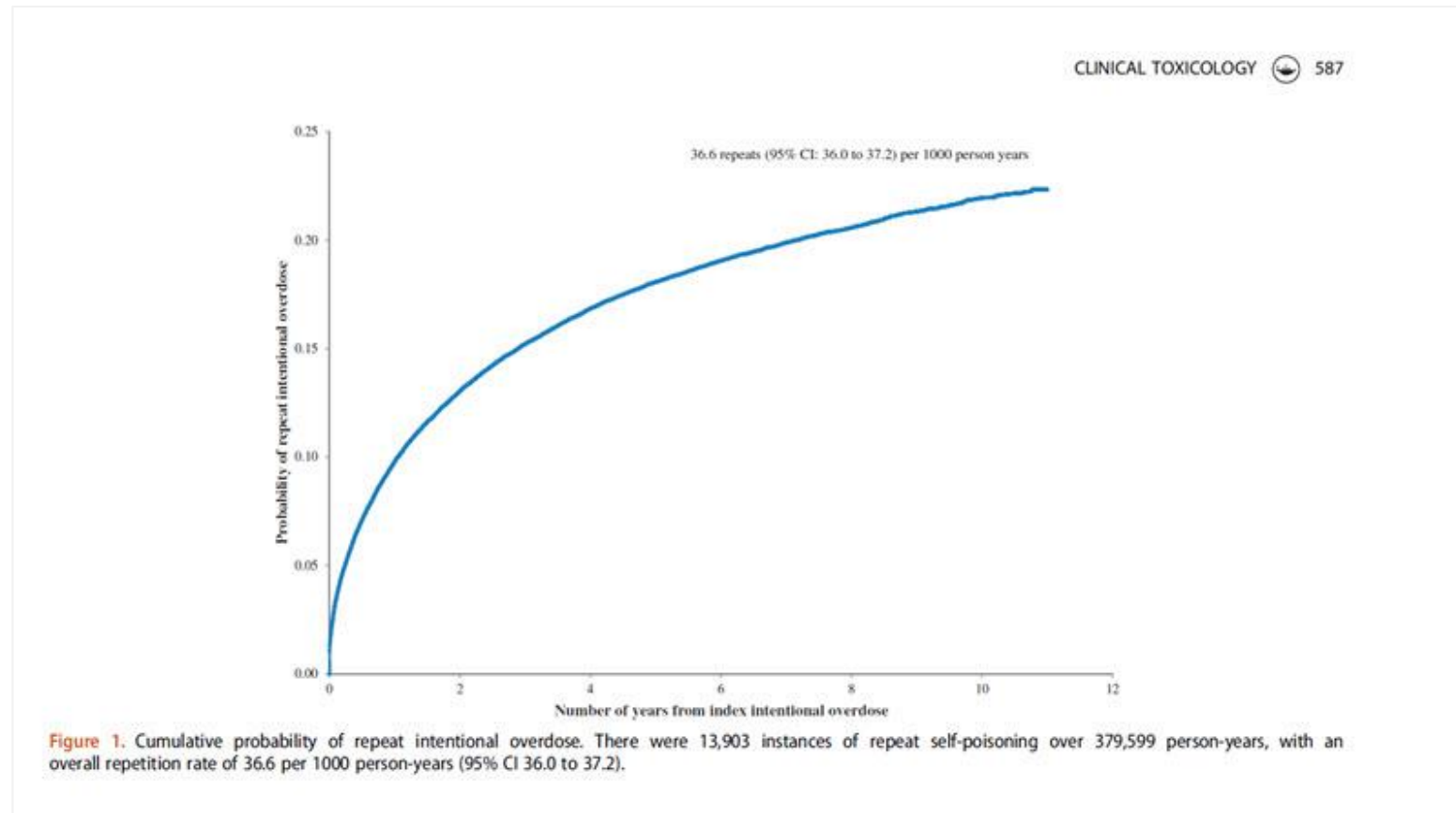
- Educate yourself on benzodiazepine pharmacology and equipotency
- Talk to all patients about co-use of benzodiazepines
- Talk to the prescribing doctor about your concerns
- Monitor for and reduce other risk factors (sleep apnea)
- Consider tapering one or the other
- Understand why they use benzodiazepines (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

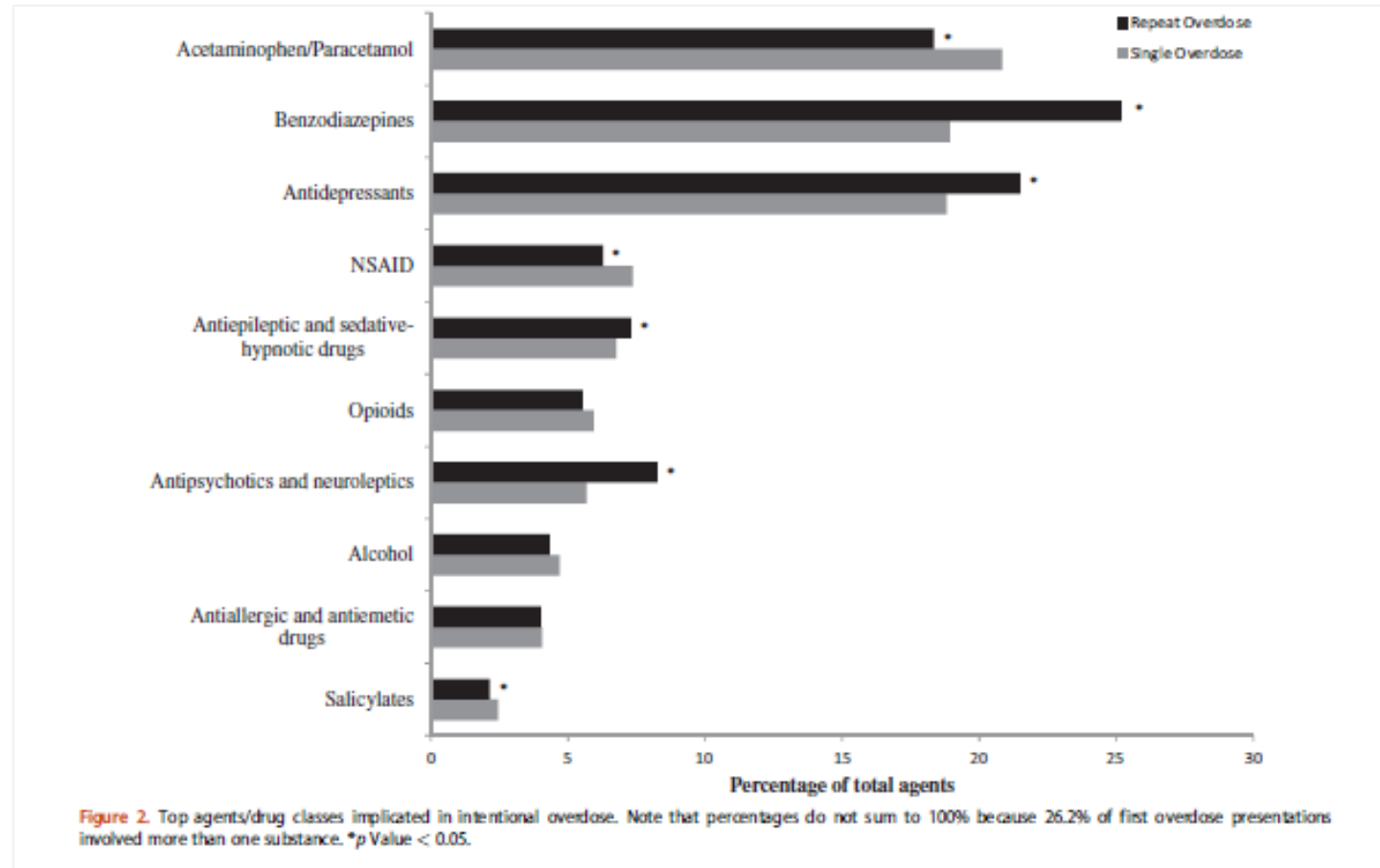
Yaron Finkelstein^{a,b,c}, Erin M. Macdonald^d, Simon Hollands^d, Marco L. A. Sivilotti^{e,f}, Janine R. Hutson^b, Muhammad M. Mamdani^{g,h}, Gideon Koren^{b,c} and David N. Juurlink^{d,i,j} for The Canadian Drug Safety and Effectiveness Research Network (CDSERN)



CLINICAL RESEARCH

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Yaron Finkelstein^{a,b,c}, Erin M. Macdonald^d, Simon Hollands^d, Marco L. A. Sivilotti^{e,f}, Janine R. Hutson^b, Muhammad M. Mamdani^{g,h}, Gideon Koren^{b,c} and David N. Juurlink^{d,i,j} for The Canadian Drug Safety and Effectiveness Research Network (CDSERN)



Case #2: Intentional overdose

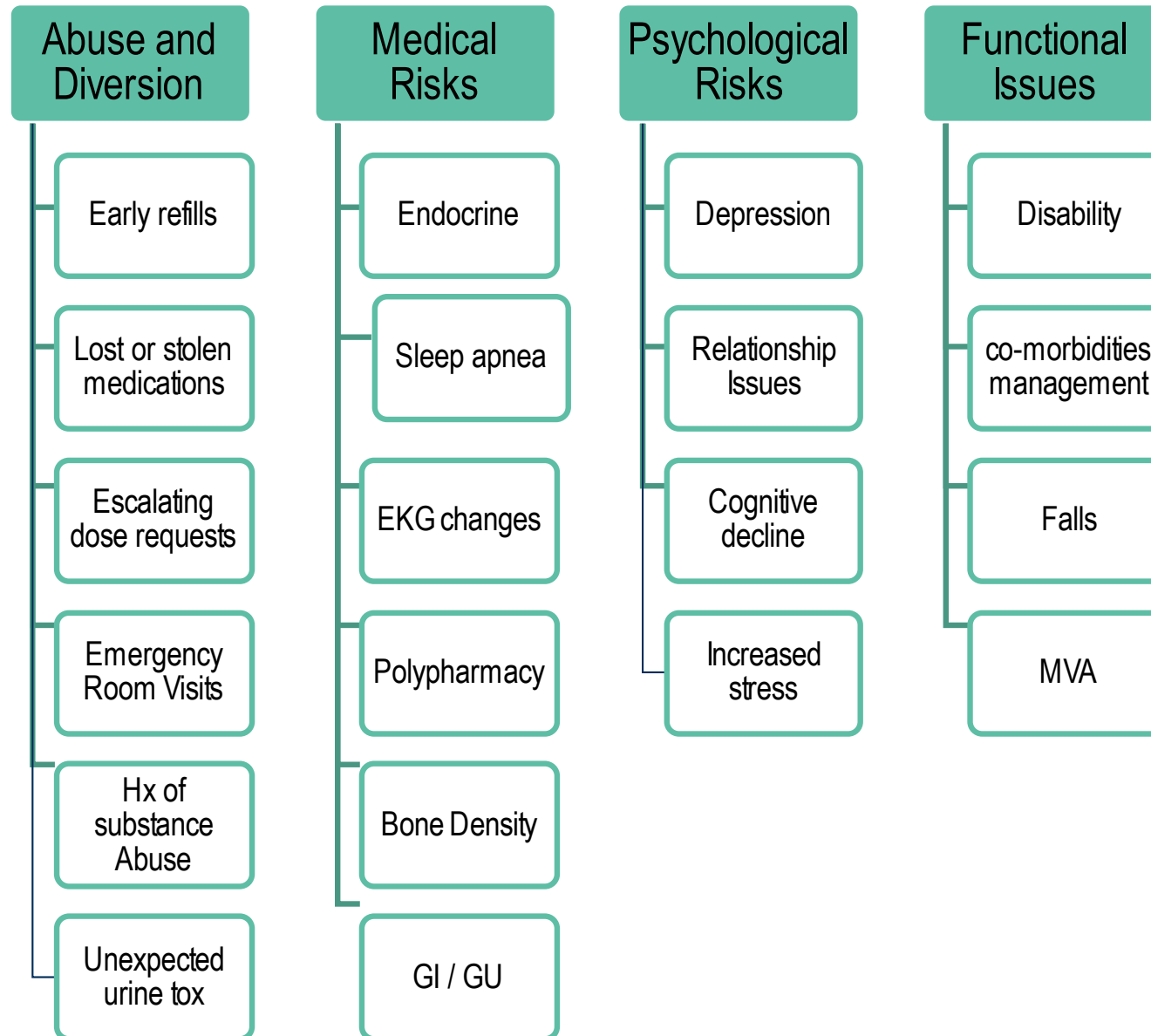
- 55 year-old C-5-6 quadriplegic man after surfing accident
- Depressed and difficulty adjusting to his disability
- On Oxycodone SR 20 mg TID (mme90)
- Valium 5mg TID for muscle spasm and Temazepam 15 mg for sleep
- Recent visit with psychologist, discussed suicidal ideation but no plan or intent
-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

Case #2: Intentional overdose

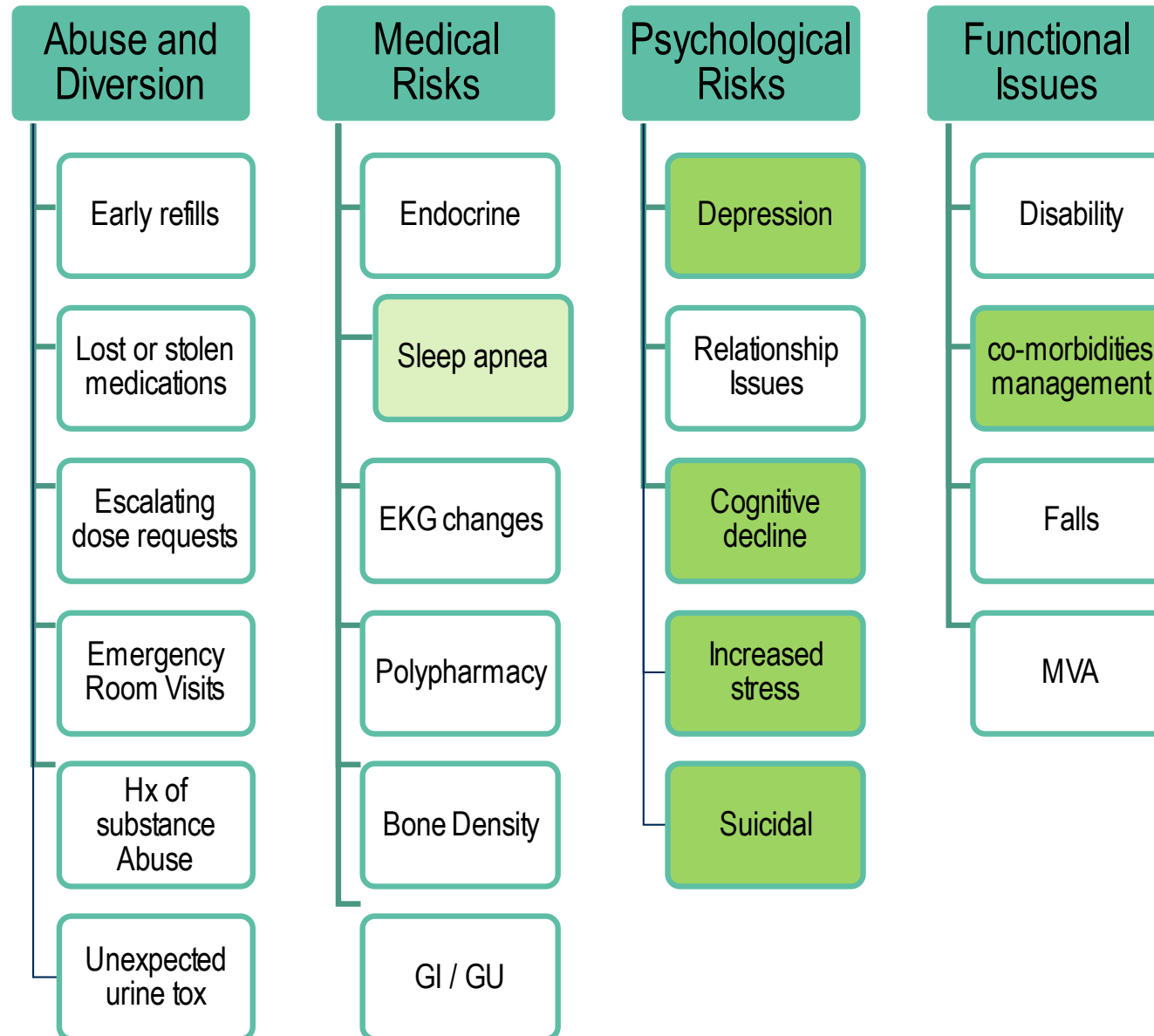
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 - *“I just didn’t care anymore. It seemed like it would be so easy to just go to sleep and not wake up.”*

Could we have anticipated?

Case #2



Case #2



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...

Usual Dosage: Read accompanying prescribing literature. Swallow tablets whole. Do not break, crush, dissolve, or chew. Dispense in a light, light resistant container.

Attention Dispenser: Accompanying Medication Guide must be provided to the patient upon dispensing.

NDC 42658-799-01

MS Contin®
(morphine sulfate extended-release tablets)

100 mg

Rhodes

Rx Only 100 Tablets

Do not break, crush, or chew. Dispense in a light, light resistant container.

Store at 25°C (77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Manufactured by:
Purdue Pharma L.P., Stamford, CT 06901

Marketed by:
Rhodes Pharmaceuticals L.P., Coventry, RI 02816



3043

Usual Dosage: Read accompanying prescribing literature. Swallow tablets whole. Do not cut, break, chew, crush, or dissolve.

Attention Dispenser: Accompanying Medication Guide must be provided to the patient upon dispensing.

NDC 59011-440-10
OxyContin®
(oxycodone hydrochloride) extended-release tablets

40 mg

100 Tablets Rx Only
Purdue Pharma L.P.

Dispense in a light, light-resistant container. Store at 25°C (77°F); excursions permitted between 15° to 30°C (59°-86°F).



Purdue Pharma L.P., Stamford, CT 06901-3431 302980-0F

Dosage: Read accompanying package insert. Dispense in a container with a child-resistant closure. Storage: Store at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F) [see USP-controlled room temperature].

Each capsule contains: Hydrocodone Bitartrate USP 50 mg
4802712-01
ZOH 10345-01 Rev. 12/14

Zohydro®ER
(hydrocodone bitartrate) EXTENDED-RELEASE CAPSULES

NDC 65224-350-60

50 mg

Dispense the accompanying Medication Guide to each patient.

Swallow capsules whole. Do not chew, crush, or dissolve.
60 Capsules Rx only



Manufactured for: Rhodes Pharmaceuticals Limited by PurduPharma (US), and distributed by Rhodes Pharmaceuticals, LLC, Marlborough, MA 01752



3 65224 3506 0

ALWAYS DISPENSE WITH MEDICATION GUIDE

NDC 60793-437-20

EMBEDA®
(morphine sulfate and naltrexone hydrochloride) Extended Release Capsules

100 mg/4 mg

THE PELLETS SHOULD NOT BE CHEWED, CRUSHED, OR DISSOLVED.

For use in opioid-tolerant patients only

30 Capsules

Rx only

Each capsule contains 100 mg morphine sulfate and 4 mg naltrexone hydrochloride as extended-release pellets. Usual Dosage: See accompanying prescribing information. Warning: As with all medication, keep out of the reach of children. Dispense in a child-resistant container. Store at 25°C (77°F); excursions permitted between 15° and 30°C (59° and 86°F).

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New York, NY 10017

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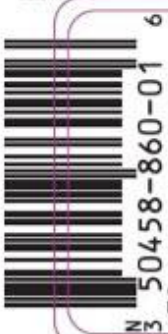
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NDC 50458-860-01

60 Tablets

Nucynta® ER
(tapentadol) Extended Release Tablets
50 mg

Each tablet contains 50 mg tapentadol.

Swallow tablets whole. Do not chew, crush or dissolve.

Dispense the accompanying Medication Guide to each patient.

Rx only

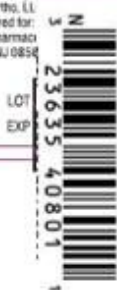
Usual Dosage: See package insert for full prescribing information. Store up to 25°C (77°F). Excursions permitted to 15°C-30°C (59°F-86°F) [see USP Controlled Room Temperature].

Protect from moisture. Keep out of reach of children.

Manufactured by:
Janssen Ortho, LLC
Manufactured for:
Janssen Pharmacia
Titusville, NJ 08560

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3 5045886001 6

NDC 23635-408-01

100 TABLETS

EXALGO® Once Daily
(hydromorphone HCl) Extended-Release Tablets

8 mg Rx only

Each tablet contains: Hydromorphone Hydrochloride USP 8 mg

For opioid tolerant patients only

PHARMACIST: Dispense a separate Medication Guide to each patient. Medication Guides available at: www.mallinckrodt.com/medguides/exalgo or call 1-800-778-7898

Mallinckrodt™

Swallow tablets whole. Do not break, crush or chew tablet.

See package insert for dosing information.

Store at room temperature 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F).

Distributed by:
SpecGx LLC
Webster Groves, MO 63119 USA

LOH136 Rev 09/2017

USUAL DOSAGE: ONCE DAILY. SEE PACKAGE INSERT. DO NOT CRUSH, CHEW OR DISSOLVE

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature]. PROTECT FROM LIGHT AND MOISTURE. OUT OF REACH OF CHILDREN. Pharmacist: Dispense in a light, light-resistant container as defined in the USP.



PC0417C
FPO 128 10 mil

ALWAYS DISPENSE WITH MEDICATION GUIDE

NDC 60793-606-01

60 mg

AVINZA®
(morphine sulfate extended-release capsules)



Rx Only
100 capsules

Manufactured for:
King Pharmaceuticals, Inc.
Bristol, TN 37620

Utilizing Technology Developed by:

Alkermes®

Alkermes Pharma Ireland Limited
Monksland, Athlone,
Co Wicklow, Ireland

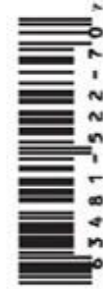
Active Ingredient: Each extended-release capsule contains 60 mg morphine sulfate, USP.
U.S. Patent No.: 6,066,339



FPO UPC
3 6079360600 1

LOT:

EXP:



3 6079360600 1

LOT NO:
EXP DATE:

Usual Dosage: Read accompanying prescribing literature. Swallow tablets whole. Do not break, crush, dissolve, or chew. Dispense in a light, light resistant container.

Attention Dispenser: Accompanying Medication Guide must be provided to the patient upon dispensing.

NDC 42858-799-01

MS Contin®
(morphine sulfate extended-release tablets)

100 mg

Rhodes

Rx Only 100 Tablets

100 mg
Rx Only
100 Tablets

Store at 25°C (77°F); excursions permitted between 15° to 30°C (59° to 86°F) (see USP Controlled Room Temperature).

Manufactured by:

Purdue Pharma L.P., Stamford, CT 06901

Marketed by:

Rhodes Pharmaceuticals L.P., Coventry, RI 02816



3043

Usual Dosage: Read accompanying prescribing literature. Swallow tablets whole. Do not cut, break, chew, crush, or dissolve.

Attention Dispenser: Accompanying Medication Guide must be provided to the patient upon dispensing.

NDC 59011-440-10

OxyContin®
(oxycodone hydrochloride) extended-release tablets

40 mg

100 Tablets Rx Only
Purdue Pharma L.P.

Dispense in a light, light-resistant container. Store at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F).



Purdue Pharma L.P., Stamford, CT 06901-3431 30298-0F

Zohydro®ER NDC 65224-350-60
(hydrocodone bitartrate) EXTENDED-RELEASE CAPSULES

50 mg

Dispense the accompanying Medication Guide to each patient.

Swallow capsules whole. Do not chew, crush, or dissolve.
60 Capsules Rx only

Design: Read accompanying package insert. Dispense in a container with a child resistant closure. Storage: Store at 25°C (77°F); excursions permitted between 15°C - 30°C (59°F - 86°F) (See USP controlled room temperature). Each capsule contains: Hydrocodone Bitartrate USP.....50mg
602773-01
ZOH 12045-01 Rev. 12/16

Manufactured by: Ames Inhibitors Limited
Parsippany, NJ 07054
Parsippany, NJ 07054
Parsippany, NJ 07054



1 65224 350 60

ALWAYS DISPENSE WITH MEDICATION GUIDE

NDC 60793-437-20

EMBEDA®
(morphine sulfate and naltrexone hydrochloride) Extended Release Capsules

100 mg/4 mg

THE PELLETS SHOULD NOT BE CHEWED, CRUSHED, OR DISSOLVED.

For use in opioid-tolerant patients only

30 Capsules

Rx only

Each capsule contains 100 mg morphine sulfate and 4 mg naltrexone hydrochloride as extended-release pellets. Usual Dosage: See accompanying prescribing information. Warning: As with all medications, keep out of the reach of children. Dispense in a child-resistant container. Store at 25°C (77°F); excursions permitted between 15° and 30°C (59° and 86°F).

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Pfizer Inc.

New York, NY 10017

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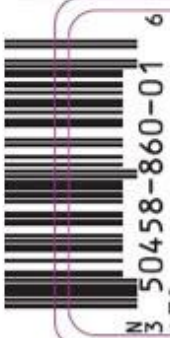
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3 6079343720 0



NDC 50458-860-01

60 Tablets

Nucynta® ER
(tapentadol) Extended Release Tablets

50 mg

Each tablet contains 50 mg tapentadol.

Swallow tablets whole, Do not chew, crush or dissolve.

Dispense the accompanying Medication Guide to each patient.

Rx only

Usual Dosage: See package insert for full prescribing information. Store up to 25°C (77°F); excursions permitted to 15°C-30°C (59°F-86°F) (see USP Controlled Room Temperature). Protect from moisture. Keep out of reach of children.

Manufactured by:
Janssen Ortho, LLC
Manufactured for:
Janssen Pharmaco
Titusville, NJ 08560

LOT
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NDC 23635-408-01

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EXALGO® Once Daily
(hydromorphone HCl) Extended-Release Tablets

8 mg Rx only

Each tablet contains: Hydromorphone Hydrochloride USP 8 mg

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PC0417C

FPO 128 10 mil

LOH136 Rev 09/2017

ALWAYS DISPENSE WITH MEDICATION GUIDE
NDC 60793-606-01 60 mg

AVINZA®
(morphine sulfate extended-release capsules)

King
Pharmaceuticals

Rx Only
100 capsules

Manufactured for:
King Pharmaceuticals, Inc.
Bristol, TN 37620

Utilizing Technology Developed by:

Alkermes®

Alkermes Pharma Ireland Limited
Meadlands, Athlone,
Co. Wicklow, Ireland

Active Ingredient: Each extended-release capsule contains 60 mg morphine sulfate, USP.
U.S. Patent No.: 6,066,339



LOT NO.:
EXP. DATE:

Usual Dosage: Read accompanying prescribing literature. Swallow tablets whole. Do not break, crush, dissolve, or chew. Dispense in a light, light resistant container.

Attention Dispenser: Accompanying Medication Guide must be provided to the patient upon dispensing.

NDC 42858-799-01

MS Contin®
(morphine sulfate)
extended-release tablets

100 mg

Rhodes

Rx Only 100 Tablets

Do not break, crush, dissolve, or chew.

Store at 25°C (77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Manufactured by:
Purdue Pharma L.P., Stamford, CT 06901

Marketed by:
Rhodes Pharmaceuticals L.P., Coventry, RI 02816



3043

Usual Dosage: Read accompanying prescribing literature.
Swallow tablets whole. Do not cut, break, chew, crush, or dissolve.

Attention Dispenser: Accompanying Medication Guide must be provided to the patient upon dispensing.

NDC 59011-440-10
OxyContin®
(oxycodone hydrochloride)
extended-release tablets

40 mg

100 Tablets Rx Only
Purdue Pharma L.P.

Dispense in a light, light-resistant container. Store at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F).

Purdue Pharma L.P.
Stamford, CT 06901-3431
302980-0F



3 59011-440-10 8

Dosage:
Read accompanying package insert.
Dispense in a container with a child resistant device.
Storage: Store at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F) [See USP controlled room temperature].

Each capsule contains:
Hydrocodone Bitartrate USP 30 mg

6802712-01
204 6245-81 Rev. 12/14

Zohydro®ER
(hydrocodone bitartrate)
EXTENDED-RELEASE CAPSULES

NDC 65224-350-60

50 mg

Dispense the accompanying Medication Guide to each patient.

Swallow capsules whole.
Do not chew, crush, or dissolve.
60 Capsules Rx only



Manufactured for: Amneal Pharmaceuticals, LLC
by Amneal Pharmaceuticals, LLC and distributed by
Purdue Pharmaceuticals, LLC, Miamisburg, OH 45342



1 65224 3506 8

ALWAYS DISPENSE WITH MEDICATION GUIDE

NDC 60793-437-20



EMBEDA®
(morphine sulfate and
naltrexone hydrochloride)
Extended Release Capsules



100 mg/4 mg

THE PELLETS SHOULD NOT BE CHEWED, CRUSHED, OR DISSOLVED.

For use in opioid-tolerant patients only

30 Capsules

Rx only

Each capsule contains: 100 mg morphine sulfate and 4 mg naltrexone hydrochloride in extended-release pellets. Usual Dosage: See accompanying prescribing information. Warning: As with all medication, keep out of the reach of children. Dispense in a child-resistant container. Store at 25°C (77°F); excursions permitted between 15° and 30°C (59° and 86°F).

Distributed by:
Pfizer Inc.
New York, NY 10017

40-006-00414
1302203

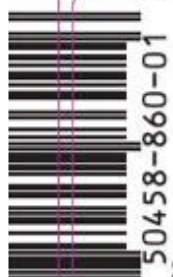
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50458-860-01 6

NDC 50458-860-01

60 Tablets

Nucynta® ER
(tapentadol)
Extended Release Tablets

50 mg

Each tablet contains 50 mg tapentadol.

Swallow tablets whole. Do not chew, crush or dissolve.

Dispense the accompanying Medication Guide to each patient.

Rx only

Usual Dosage: See package insert for full prescribing information. Store up to 25°C (77°F). Excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature].

Protect from moisture. Keep out of reach of children.

Manufactured by:
Janssen Ortho, LLC
Manufactured for:
Janssen Pharmaco
Titusville, NJ 08560

LOT
EXP



NDC 23635-408-01

100 TABLETS

EXALGO® Once Daily
(hydromorphone HCl)
Extended-Release Tablets

8 mg Rx only

Each tablet contains: Hydromorphone Hydrochloride USP 8 mg

For opioid tolerant patients only

PHARMACIST: Dispense a separate Medication Guide to each patient. Medication Guides available at:
www.mallinckrodt.com/medguide/exalgo or call 1-800-778-7898

Mallinckrodt™

Swallow tablets whole.
Do not break, crush or
chew tablet.

See package insert for dosing
information.

Store at room temperature
25°C (77°F); excursions permitted
to 15° to 30°C (59° to 86°F).

Distributed by:
SpecGx LLC
Webster Groves, MO 63119 USA

LOH136 Rev 09/2017

Usual Dosage: Read accompanying prescribing literature. Swallow tablets whole. Do not break, crush, dissolve, or chew. Dispense in a light, light resistant container.

Attention Dispenser: Accompanying Medication Guide must be provided to the patient upon dispensing.

NDC 42858-799-01

MS Contin®
(morphine sulfate)
extended-release tablets

100 mg

Rhodes

Rx Only 100 Tablets

Store at 25°C (77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Manufactured by:
Purdue Pharma L.P., Stamford, CT 06901

Marketed by:
Rhodes Pharmaceuticals L.P., Coventry, RI 02816



3043

Usual Dosage: Read accompanying prescribing literature. Swallow tablets whole. Do not cut, break, chew, crush, or dissolve.

Attention Dispenser: Accompanying Medication Guide must be provided to the patient upon dispensing.

MS Contin®
(hydrocodone bitartrate)
extended-release tablets

40 mg

100 Tablets
Purdue Pharma L.P., Stamford, CT 06901

Store at 25°C (77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Manufactured by:
Purdue Pharma L.P., Stamford, CT 06901



3 59011-440-108

Dosage: Read accompanying package insert. Dispense in a container with a child resistant closure.

Storage: Store at 25°C (77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP controlled room temperature].

Each capsule contains:
Hydrocodone Bitartrate USP 30 mg

480712-01
204 62945-01 Rev. 12/14

Zohydro®ER
(hydrocodone bitartrate)
EXTENDED-RELEASE CAPSULES

NDC 65224-350-60

50 mg

Dispense the accompanying Medication Guide to each patient.
Swallow capsules whole.
Do not chew, crush, or dissolve.
60 Capsules Rx only

Manufactured for: Amneal Pharmaceuticals, LLC, Morris Plains, NJ 07950



1 65224 35060 0

ALWAYS DISPENSE WITH MEDICATION GUIDE

NDC 60793-437-20

EMBEDA®
(morphine sulfate and
naltrexone hydrochloride)
Extended Release Capsules

100 mg/4 mg

THE PELLETS SHOULD NOT BE CHEWED, CRUSHED, OR DISSOLVED.

For use in opioid-tolerant patients only

30 Capsules

Rx only

Each capsule contains: 100 mg morphine sulfate and 4 mg naltrexone hydrochloride in extended-release pellets. Usual Dosage: See accompanying prescribing information. Warning: As with all medication, keep out of the reach of children. Dispense in a child-resistant container. Store at 25°C (77°F); excursions permitted between 15° and 30°C (59° and 86°F).

Distributed by:
Pfizer Inc.
New York, NY 10017

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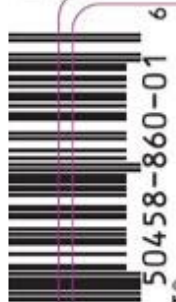
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50458-860-01 6

NDC 50458-860-01

60 Tablets

Nucynta® ER
(tapentadol)
Extended Release Tablets

50 mg

Each tablet contains 50 mg tapentadol.

Swallow tablets whole. Do not chew, crush or dissolve.

Dispense the accompanying Medication Guide to each patient.

Rx only

Usual Dosage: See package insert for full prescribing information. Store up to 25°C (77°F). Excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

Protect from moisture. Keep out of reach of children.

Manufactured by:
Janssen Ortho, LLC
Manufactured for:
Janssen Pharmaco
Titusville, NJ 08580

LOT
EXP



NDC 23635-408-01

100 TABLETS

EXALGO® Once Daily
(hydromorphone HCl)
Extended-Release Tablets

8 mg Rx only

Each tablet contains: Hydromorphone Hydrochloride USP 8 mg

For opioid tolerant patients only

PHARMACIST: Dispense a separate Medication Guide to each patient. Medication Guides available at:
www.mallinckrodt.com/medguide/exalgo or call 1-800-778-7898

Mallinckrodt™

Swallow tablets whole. Do not break, crush or chew tablet.

See package insert for dosing information.

Store at room temperature 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F).

Distributed by:
SpecGx LLC
Webster Groves, MO 63119 USA

LOH136 Rev 09/2017



OxyContin 80 pills (Liz Baylen / Los Angeles Times)

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A TIMES INVESTIGATION

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

by HARRIET RYAN, LISA GIRION AND SCOTT GLOVER

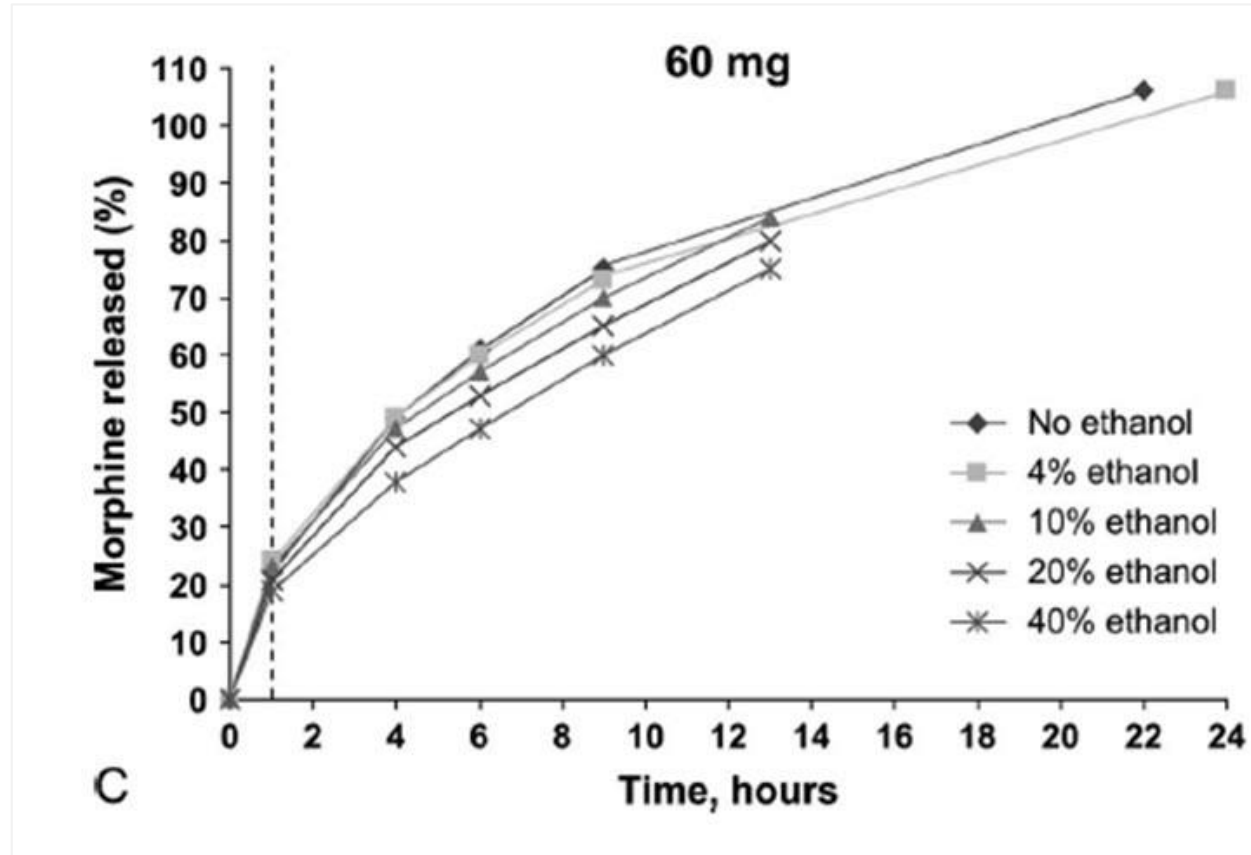
MAY 5, 2016

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

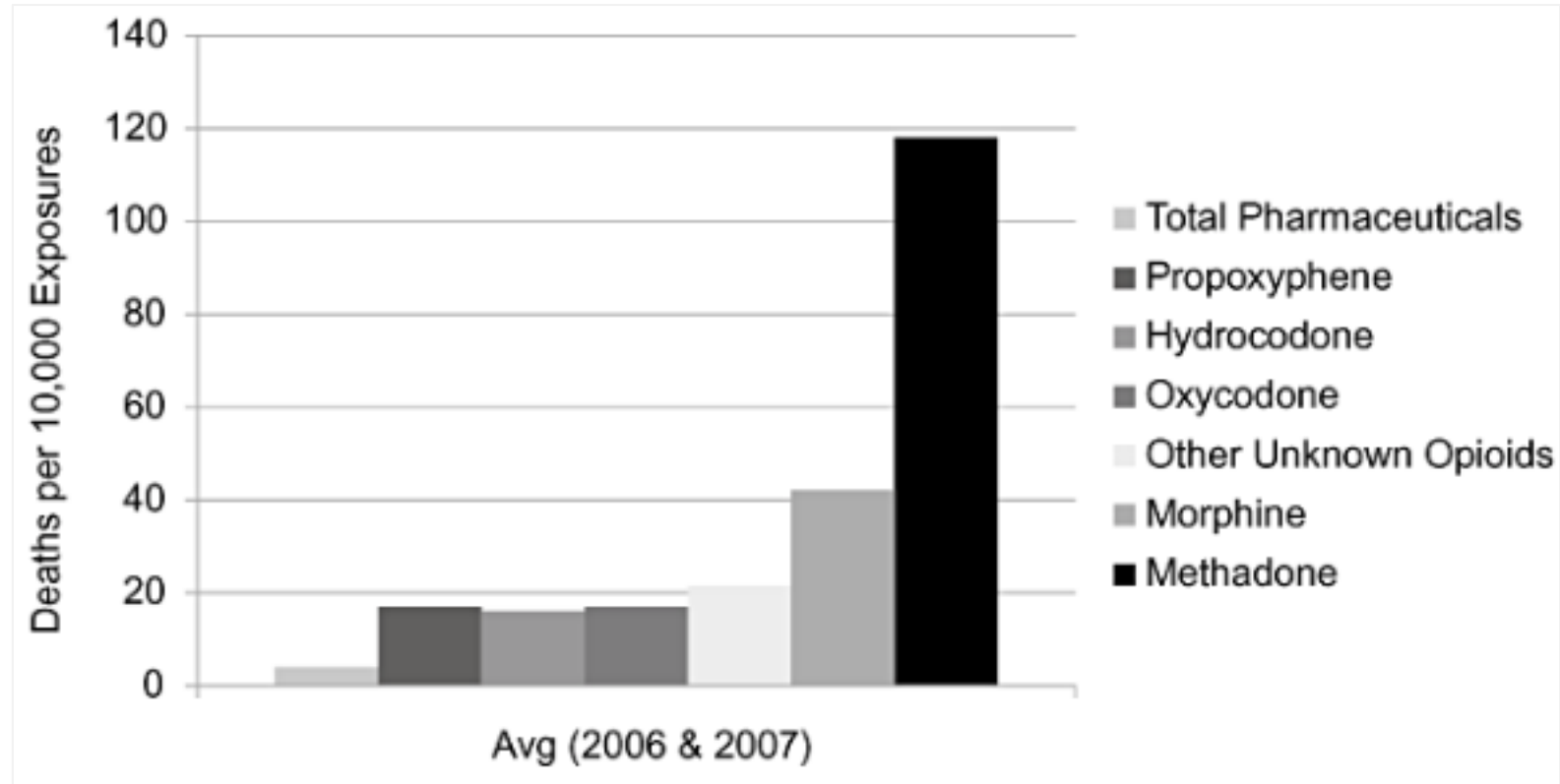


“MS CONTIN does not release morphine continuously over the course of a dosing interval. The administration of single doses of MS CONTIN on a q12h dosing schedule will result in **higher peak** and **lower trough** plasma levels than those that occur when an identical daily dose of morphine is administered 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
<http://onlinelibrary.wiley.com/doi/10.1111/j.1526-4637.2011.01134.x/full#10>

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



The NEW ENGLAND JOURNAL of MEDICINE

Perspective
JULY 5, 2018

**Primary Care and the Opioid-Overdose Crisis —
Buprenorphine Myths and Realities**

Sarah E. Wakeman, M.D., and Michael L. Barnett, M.D.

“To have any hope of stemming the overdose tide, we have to make it easier to obtain buprenorphine than to get heroin and fentanyl.”



PAIN MANAGEMENT BEST PRACTICES
INTER-AGENCY TASK FORCE REPORT

Updates, Gaps, Inconsistencies, and Recommendations

FINAL REPORT

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

Contact information

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Santa Rosa, CA 95403

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Twitter: @rubinsteinmd