Provincial Guidelines for the Clinical Management of Opioid Use Disorder

BRITISH COLUMBIA CENTRE ON SUBSTANCE USE
Networking researchers, educators & care providers

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Faculty/Presenter Disclosure

- **Faculty:** Keith Ahamad

- **Relationships with commercial interests:**
  - **Grants/Research Support:** CIHR, NIH
  - **Speakers Bureau/Honoraria:** None
  - **Consulting Fees:** None
  - **Other:** BC Centre on Substance Use (MoH), Providence Health Care

Disclosure of Commercial Support

- I have NOT received financial support or in-kind support from any commercial interest.
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- **Potential for conflict(s) of interest:**
  - None

Mitigating Potential Bias

- No sources of bias


Leading the way in HIV prevention
and addiction services
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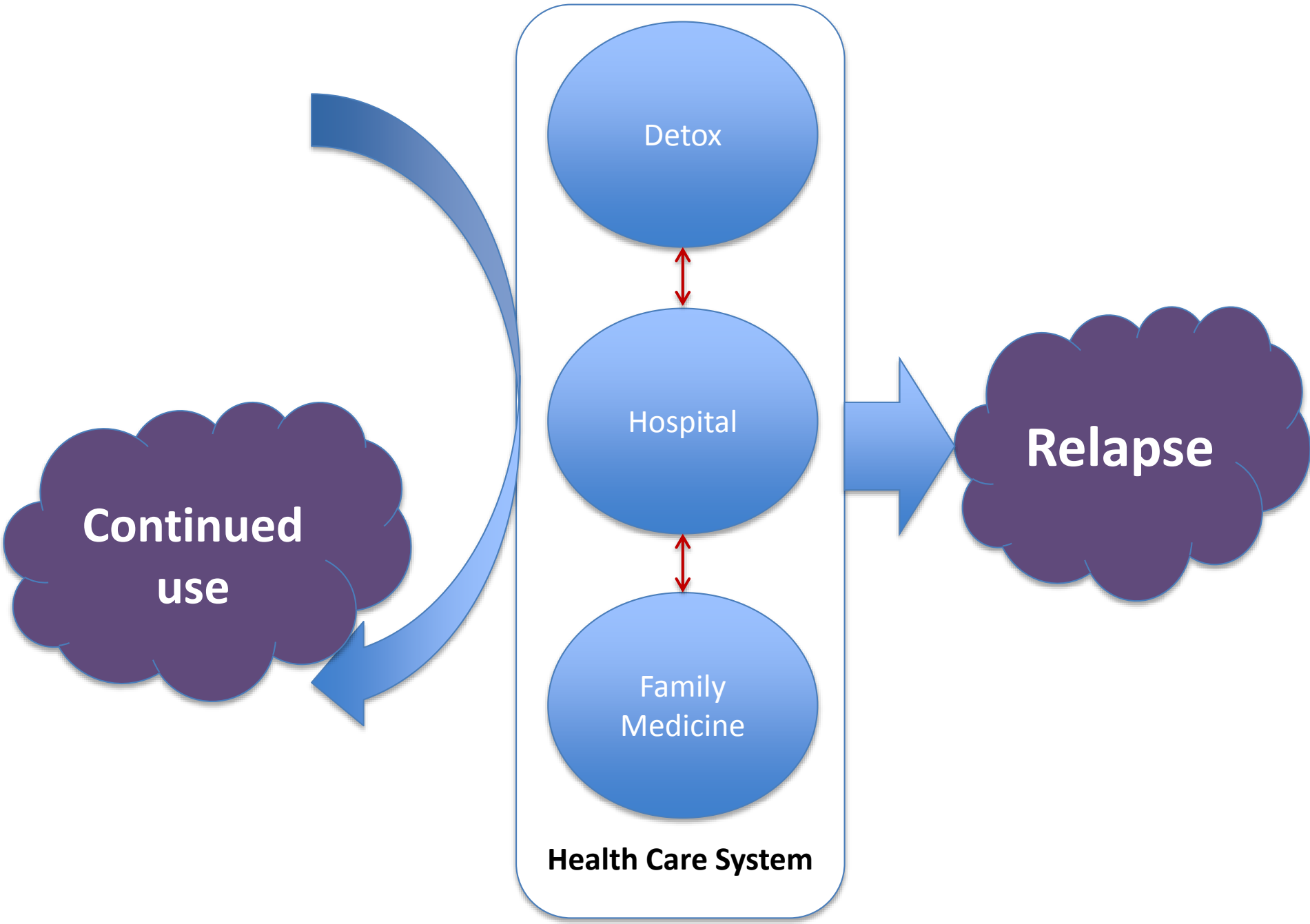
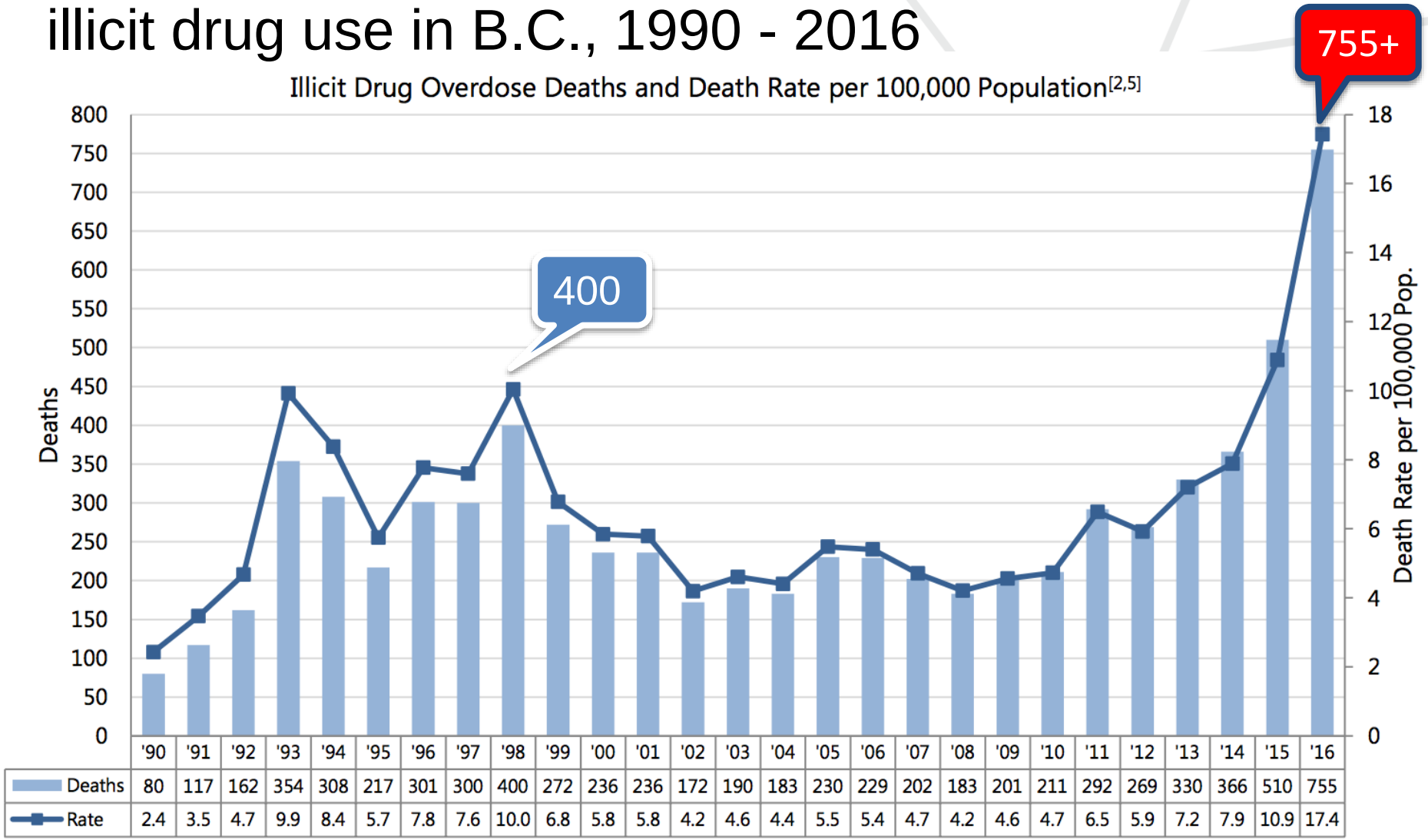
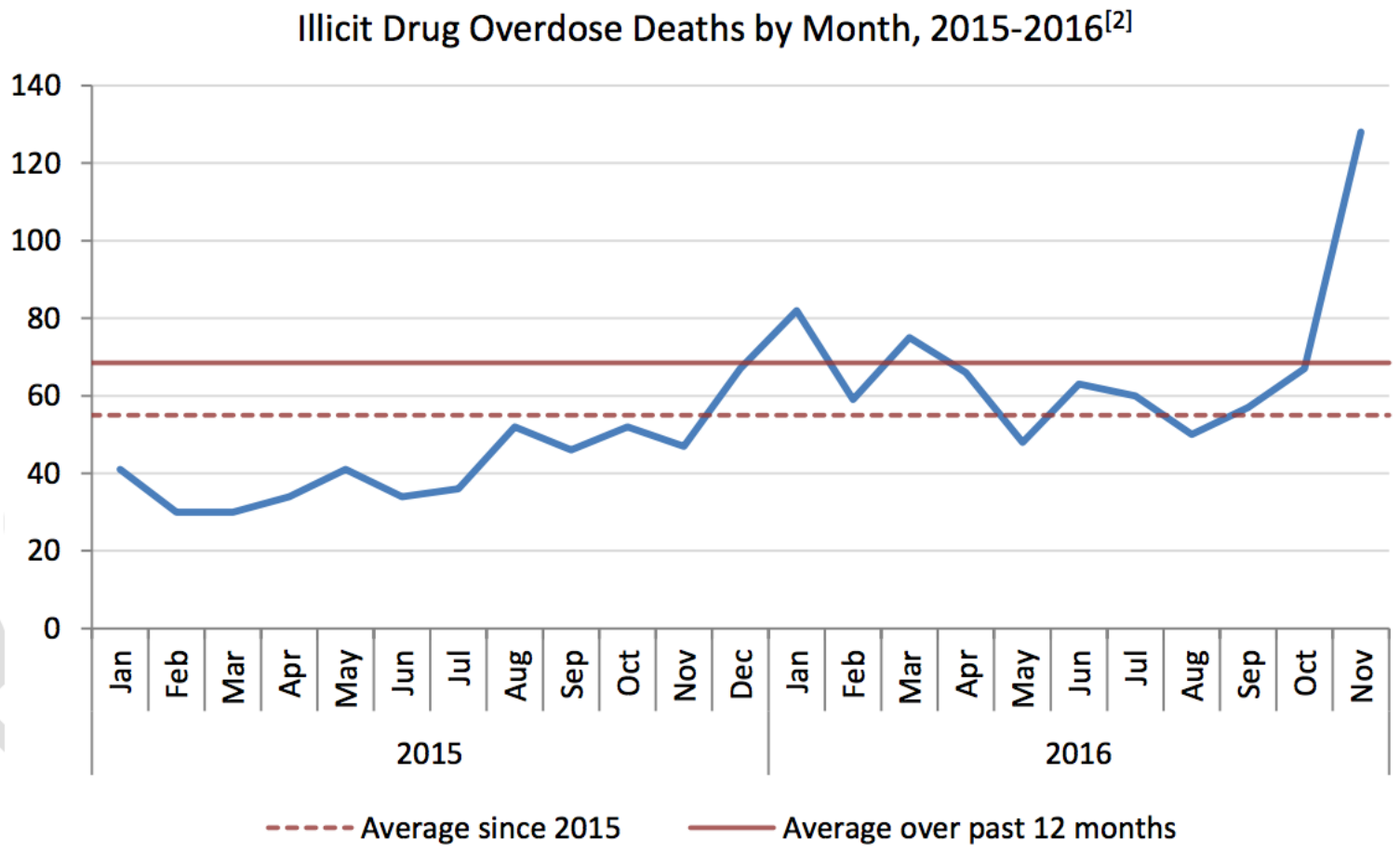

Detox
Hospital
Family Medicine
Health Care System
Continued use
Relapse

Number of deaths and mortality rate attributed to illicit drug use in B.C., 1990 - 2016



	'90	'91	'92	'93	'94	'95	'96	'97	'98	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14	'15	'16
Deaths	80	117	162	354	308	217	301	300	400	272	236	236	172	190	183	230	229	202	183	201	211	292	269	330	366	510	755
Rate	2.4	3.5	4.7	9.9	8.4	5.7	7.8	7.6	10.0	6.8	5.8	5.8	4.2	4.6	4.4	5.5	5.4	4.7	4.2	4.6	4.7	6.5	5.9	7.2	7.9	10.9	17.4

Source: Illicit Drug Overdose Deaths in BC, January 1, 2007 to November 30, 2016. Office of the Chief Coroner of BC. Released October 19, 2016.



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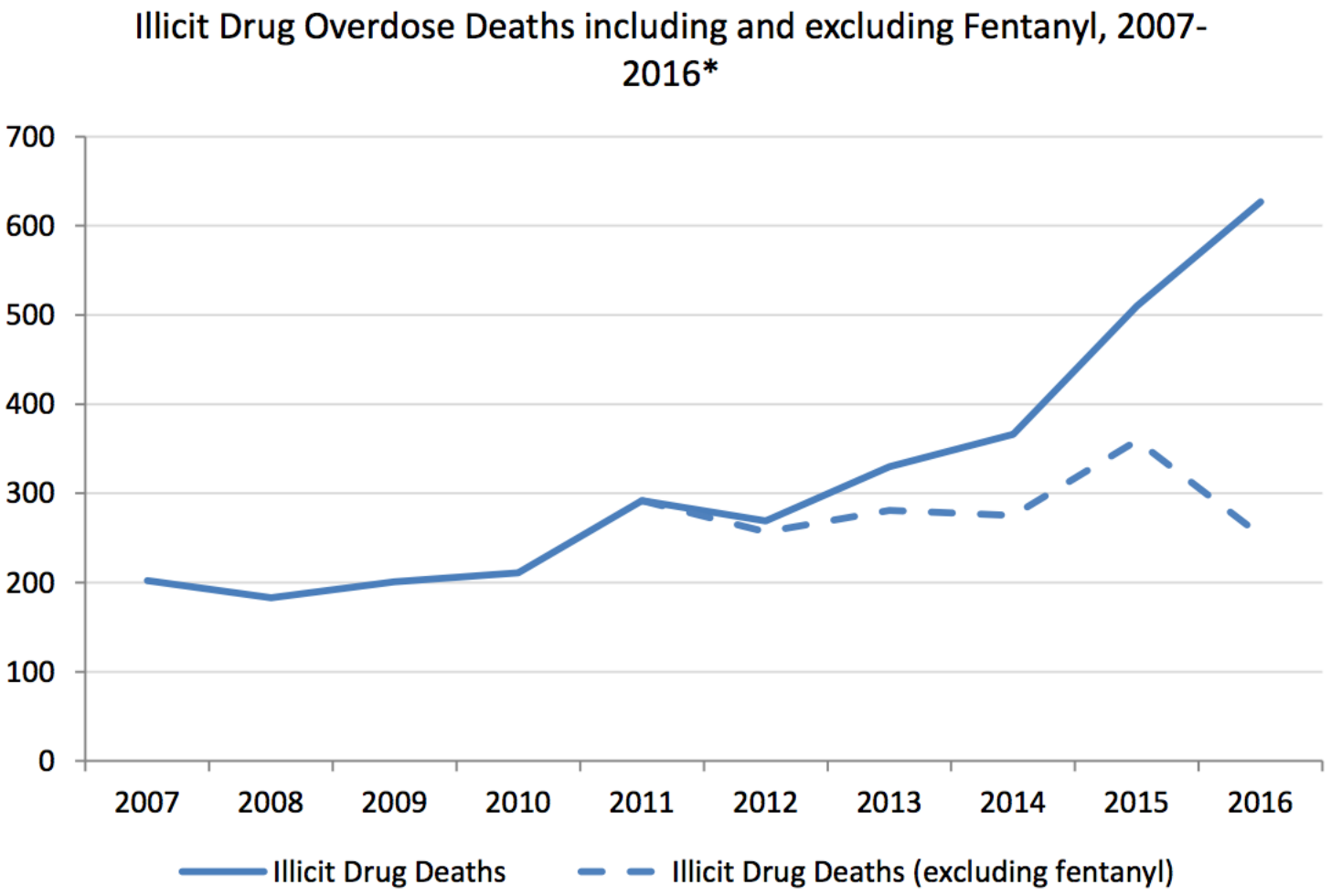

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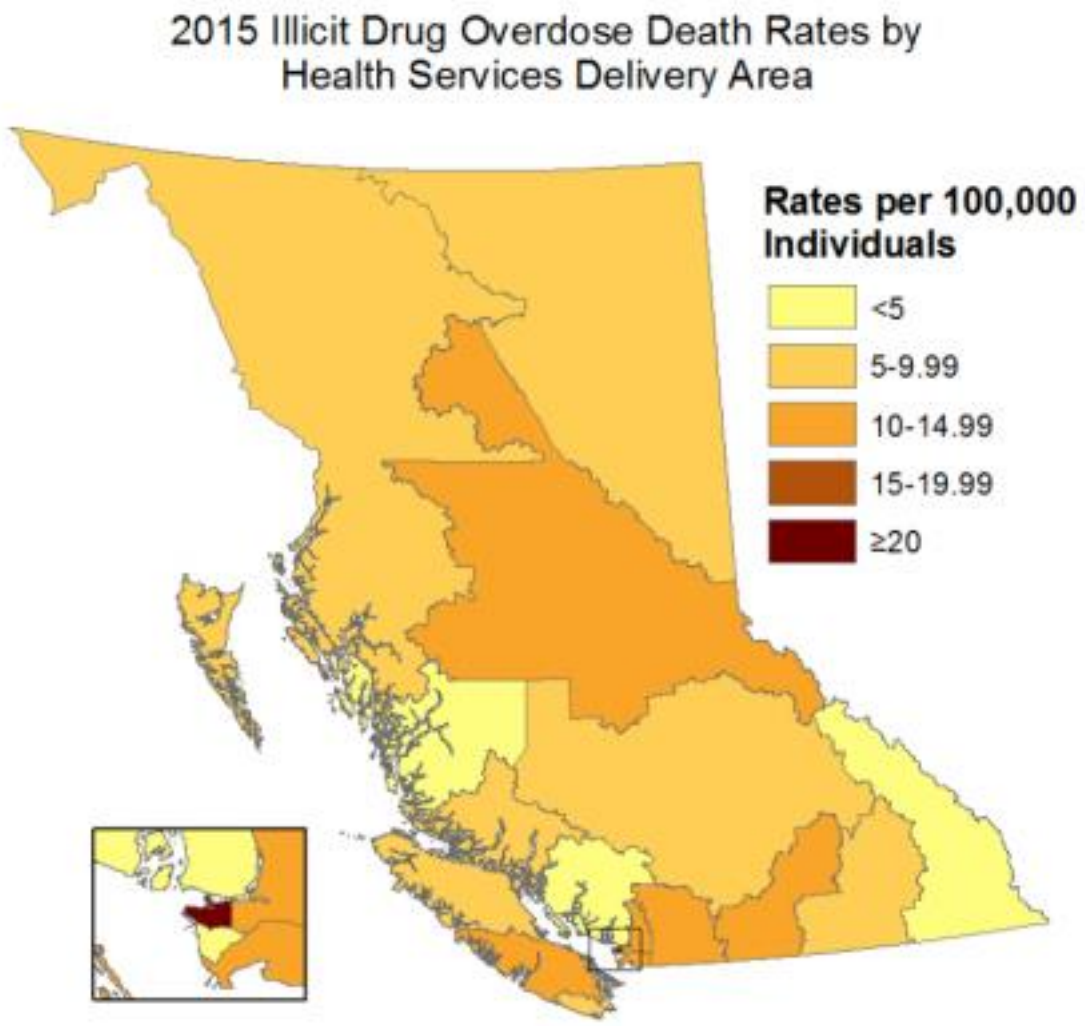

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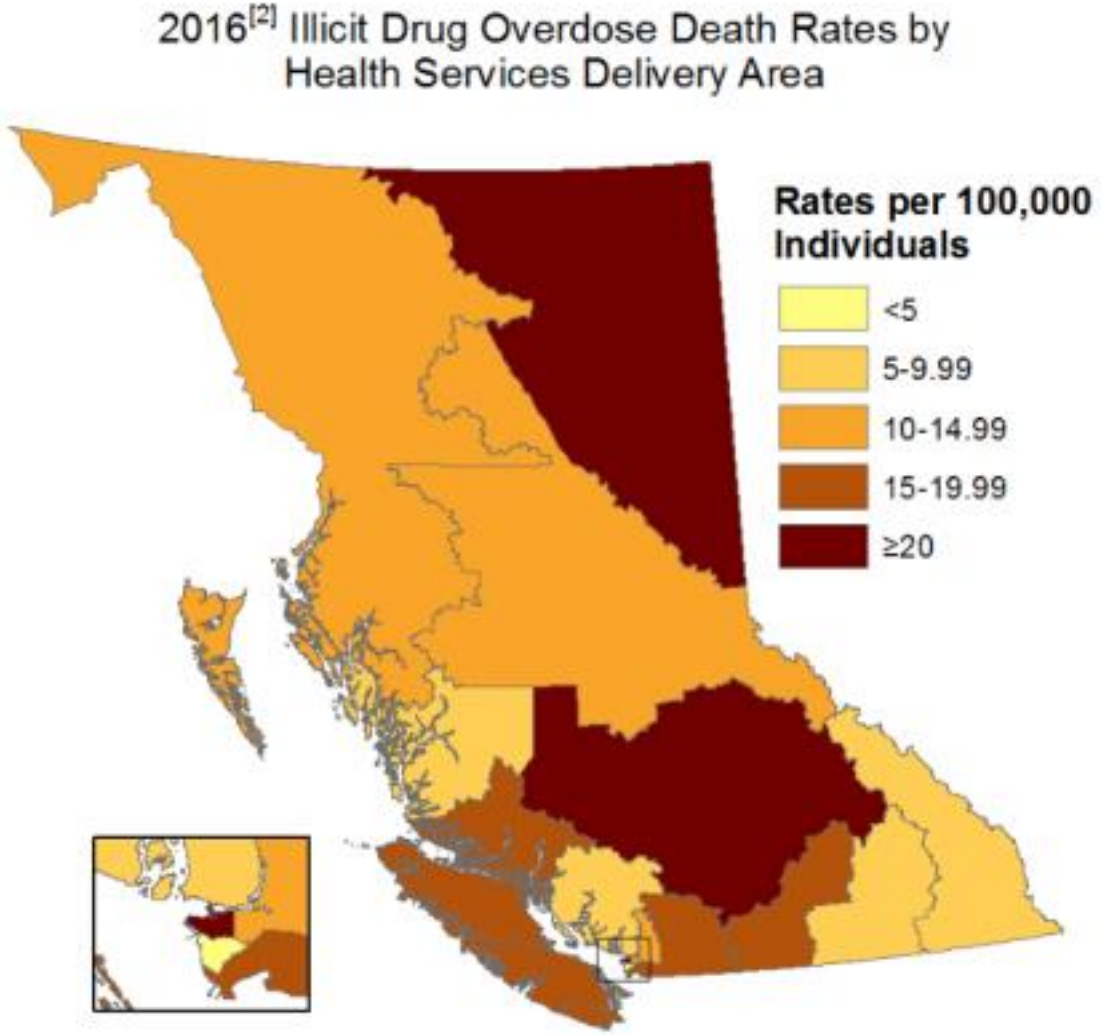
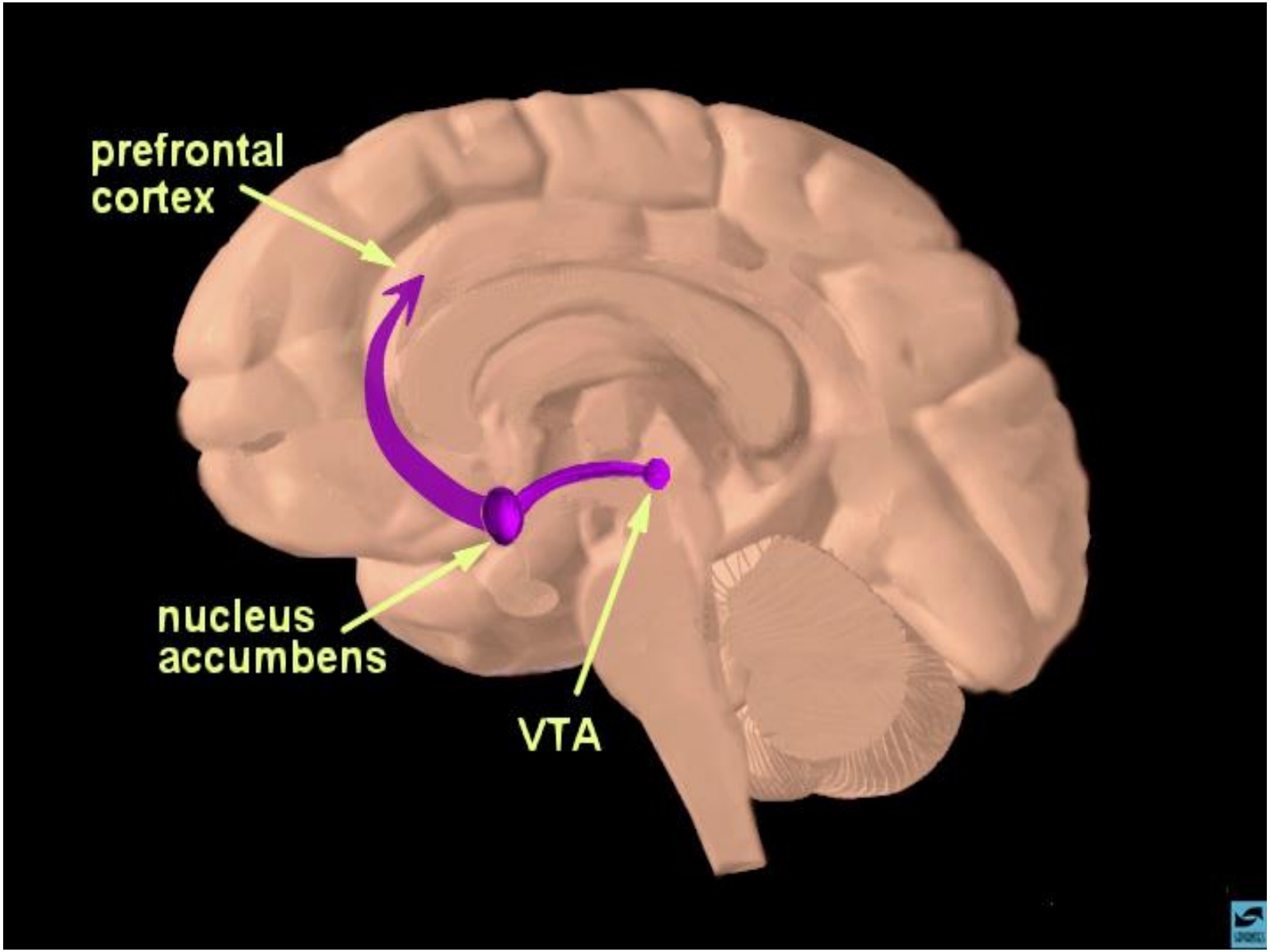
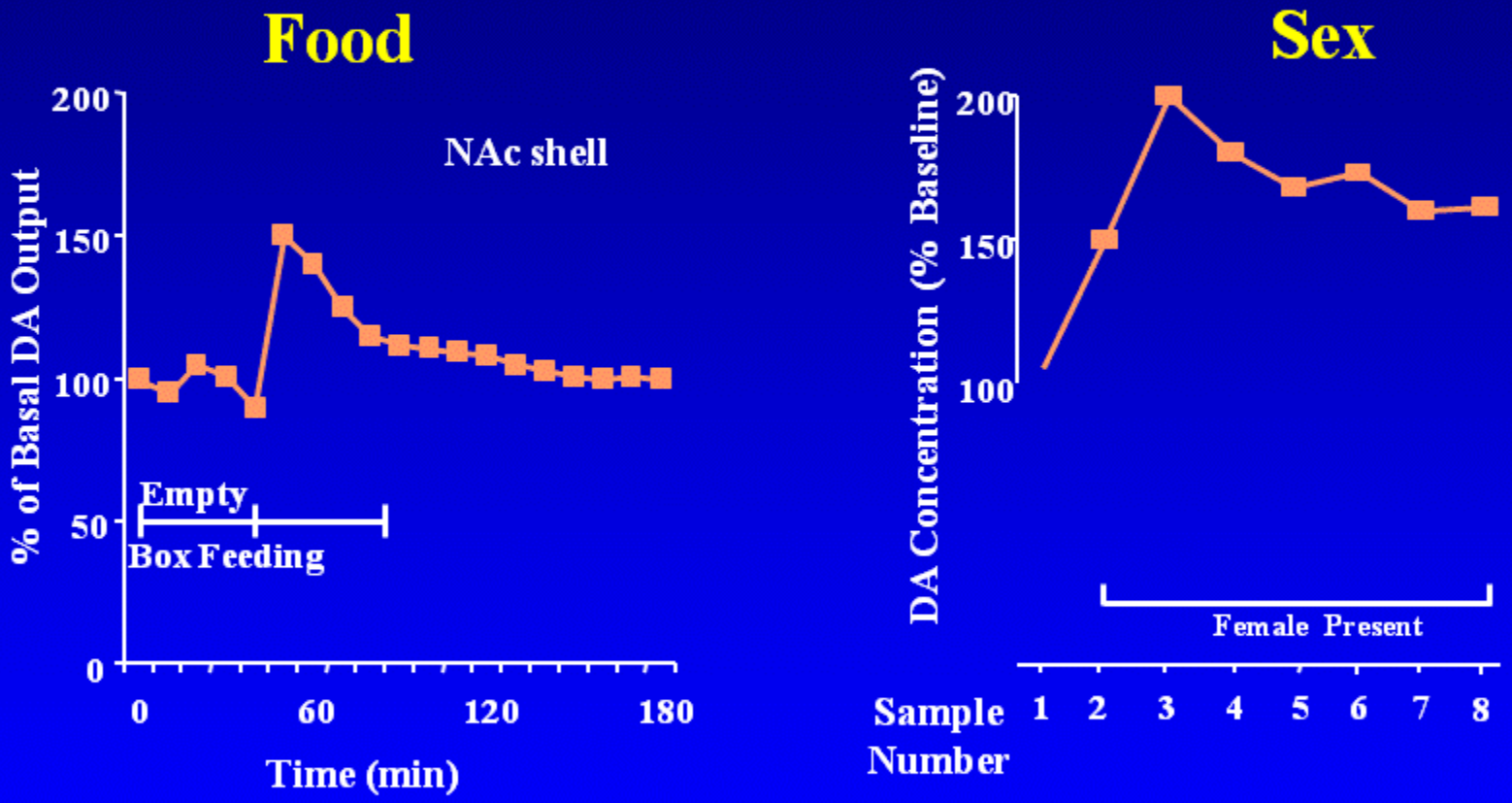


Source: Illicit Drug Overdose Deaths in BC, January 1, 2007 to September 30, 2016. Office of the Chief Coroner of BC. Released October 19, 2016.

Reward Pathway



Natural Rewards Elevate Dopamine Levels

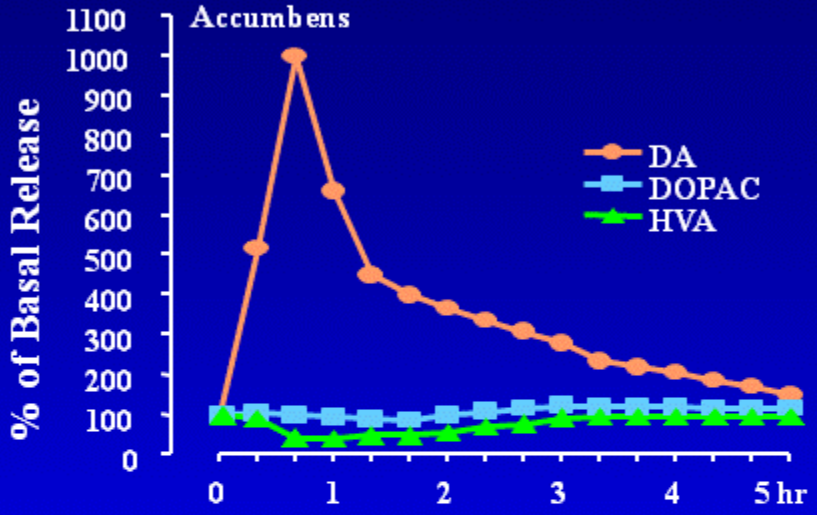


Di Chiara et al., Neuroscience, 1999., Fiorino and Phillips, J. Neuroscience, 1997.

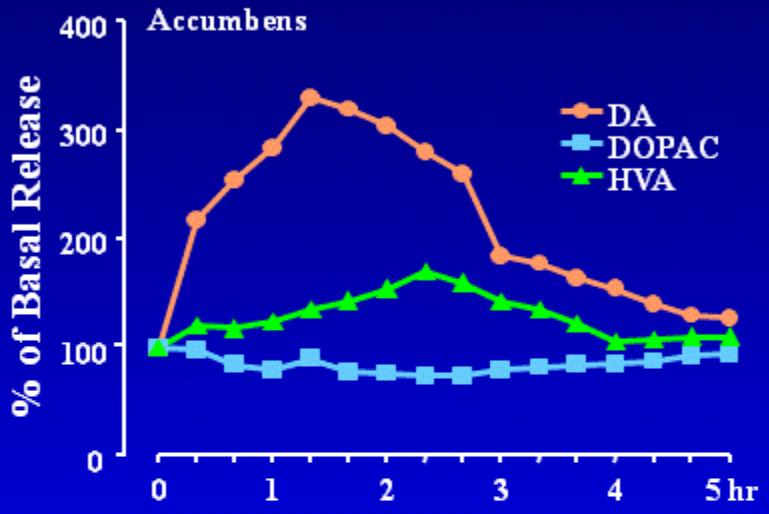
NIDA

Effects of Drugs on Dopamine Release

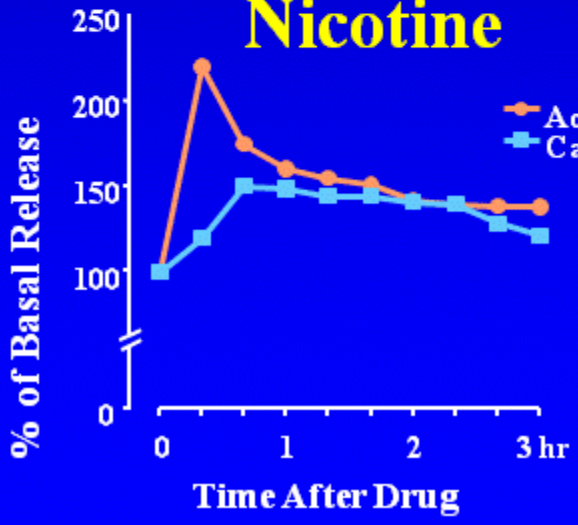
Amphetamine



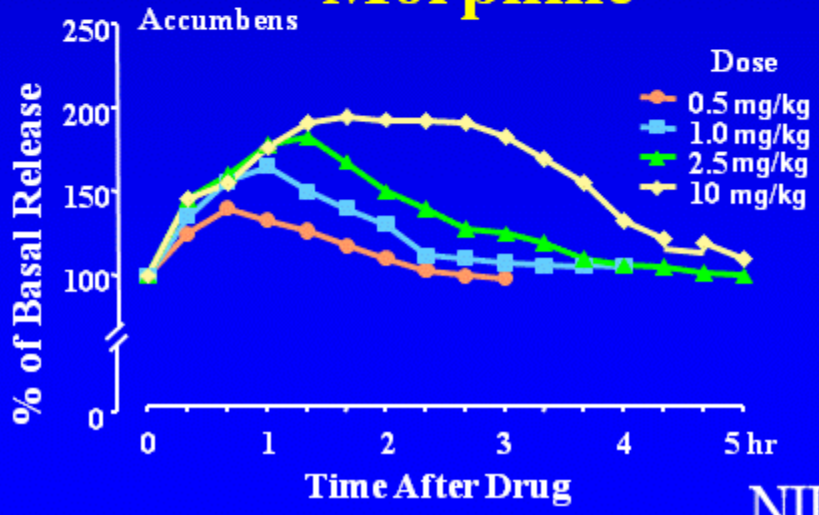
Cocaine



Nicotine

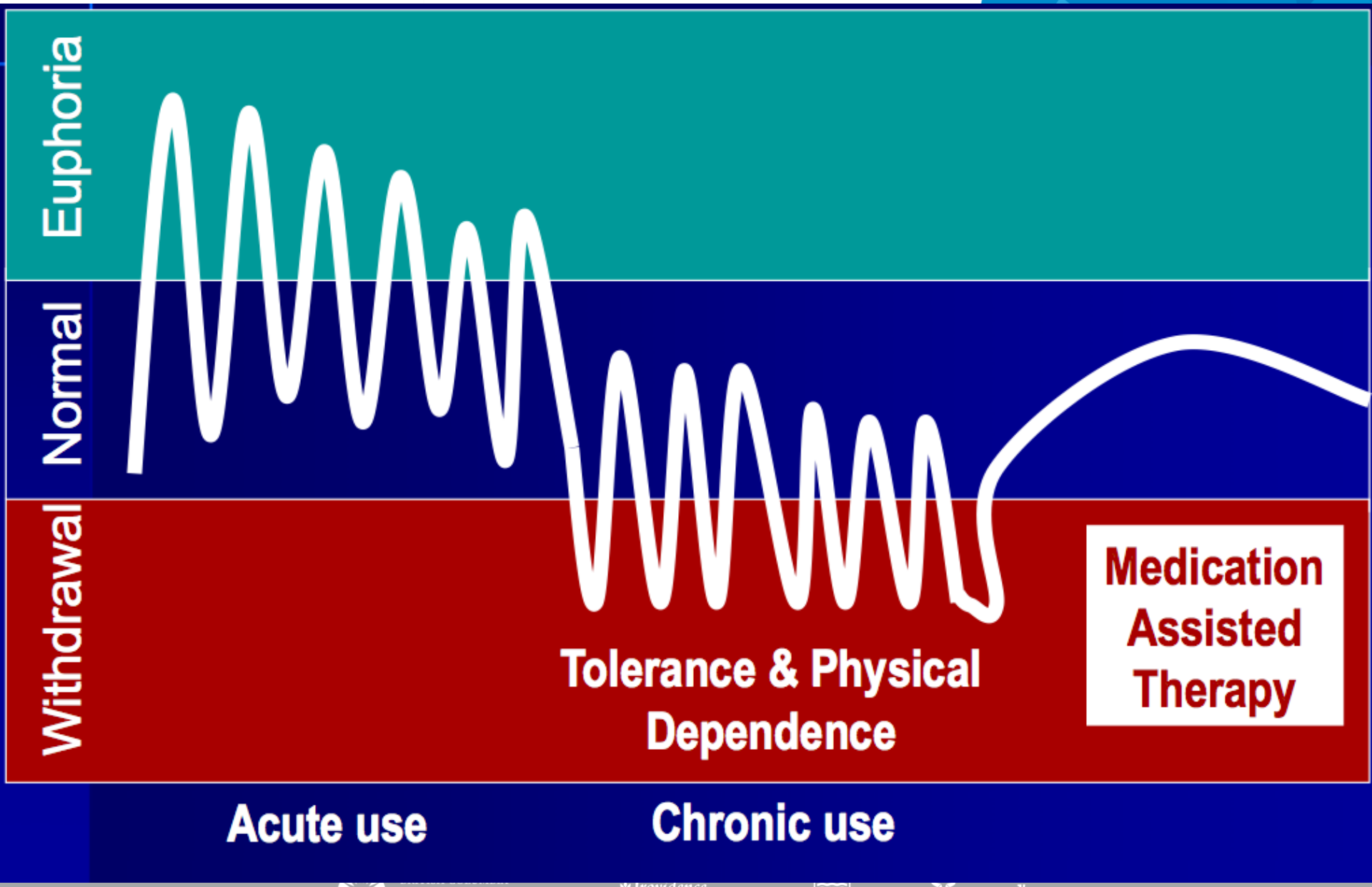


Morphine



Di Chiara and Imperato, PNAS, 1988

NIDA


Euphoria
Normal
Withdrawal
Tolerance & Physical Dependence
Medication Assisted Therapy
Acute use
Chronic use

Evidence for Use of Opioids Long-Term

REVIEW

Annals of Internal Medicine

The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop

Roger Chou, MD; Judith A. Turner, PhD; Emily B. Devine, PharmD, PhD, MBA; Ryan N. Hansen, PharmD, PhD; Sean D. Sullivan, PhD; Ian Blazina, MPH; Tracy Dana, MLS; Christina Bougatsos, MPH; and Richard A. Deyo, MD, MPH

Background: Increases in prescriptions of opioid medications for chronic pain have been accompanied by increases in opioid overdoses, abuse, and other harms and uncertainty about long-term effectiveness.

Purpose: To evaluate evidence on the effectiveness and harms of long-term (>3 months) opioid therapy for chronic pain in adults.

Data Sources: MEDLINE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, PsycINFO, and CINAHL (January 2008 through August 2014); relevant studies from a prior review; reference lists; and ClinicalTrials.gov.

Study Selection: Randomized trials and observational studies that involved adults with chronic pain who were prescribed long-term opioid therapy and that evaluated opioid therapy versus placebo, no opioid, or nonopioid therapy; different opioid dosing strategies; or risk mitigation strategies.

Data Extraction: Dual extraction and quality assessment.

Data Synthesis: No study of opioid therapy versus no opioid therapy evaluated long-term (>1 year) outcomes related to pain, function, quality of life, opioid abuse, or addiction. Good- and fair-quality observational studies suggest that opioid therapy for chronic pain is associated with increased risk for overdose, opioid abuse, fractures, myocardial infarction, and markers of sexual dysfunction, although there are few studies for each of these outcomes; for some harms, higher doses are associated with increased risk. Evidence on the effectiveness and harms of different opioid dosing and risk mitigation strategies is limited.

Limitations: Non–English-language articles were excluded, meta-analysis could not be done, and publication bias could not be assessed. No placebo-controlled trials met inclusion criteria, evidence was lacking for many comparisons and outcomes, and observational studies were limited in their ability to address potential confounding.

Conclusion: Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.

Primary Funding Source: Agency for Healthcare Research and Quality.

Ann Intern Med. 2015;162:276-286. doi:10.7326/M14-2559 **www.annals.org**

For author affiliations, see end of text.

This article was published online first at www.annals.org on 13 January 2015.

NEJM: Opioid Abuse in Chronic Pain –Volkow 2016

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Opioid Abuse in Chronic Pain — Misconceptions and Mitigation Strategies

Nora D. Volkow, M.D., and A. Thomas McLellan, Ph.D.

CHRONIC PAIN NOT CAUSED BY CANCER IS AMONG THE MOST PREVALENT and debilitating medical conditions but also among the most controversial and complex to manage. The urgency of patients' needs, the demonstrated effectiveness of opioid analgesics for the management of acute pain, and the limited therapeutic alternatives for chronic pain have combined to produce an overreliance on opioid medications in the United States, with associated alarming increases in diversion, overdose, and addiction. Given the lack of clinical consensus and research-supported guidance, physicians understandably have questions about whether, when, and how to prescribe opioid analgesics for chronic pain without increasing public health risks. Here, we draw on recent research to address common misconceptions regarding the abuse-related risks of opioid analgesics and highlight strategies to minimize those risks.

From the National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD (N.D.V.); and the Treatment Research Institute, Philadelphia (A.T.M.). Address reprint requests to Dr. Volkow at the National Institute on Drug Abuse, National Institutes of Health, 6001 Executive Blvd., Bethesda, MD 20892, or at nvolkow@nida.nih.gov.

N Engl J Med 2016;374:1253-63.
DOI: 10.1056/NEJMra1507771

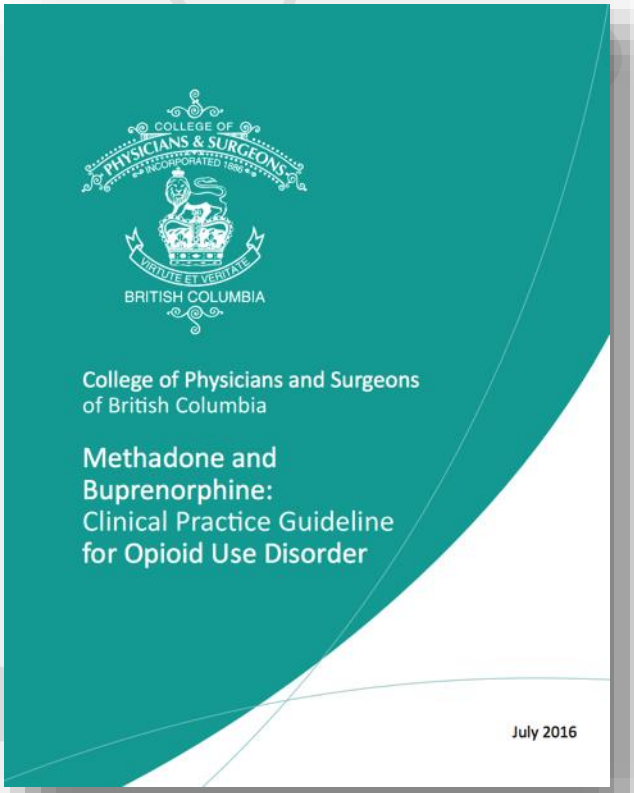
SOURCE OF THE OPIOID EPIDEMIC

More than 30% of Americans have some form of acute or chronic pain.[1,2] Among older adults, the prevalence of chronic pain is more than 40%.[2] Given the prevalence of chronic pain and its often disabling effects, it is not surprising that opioid

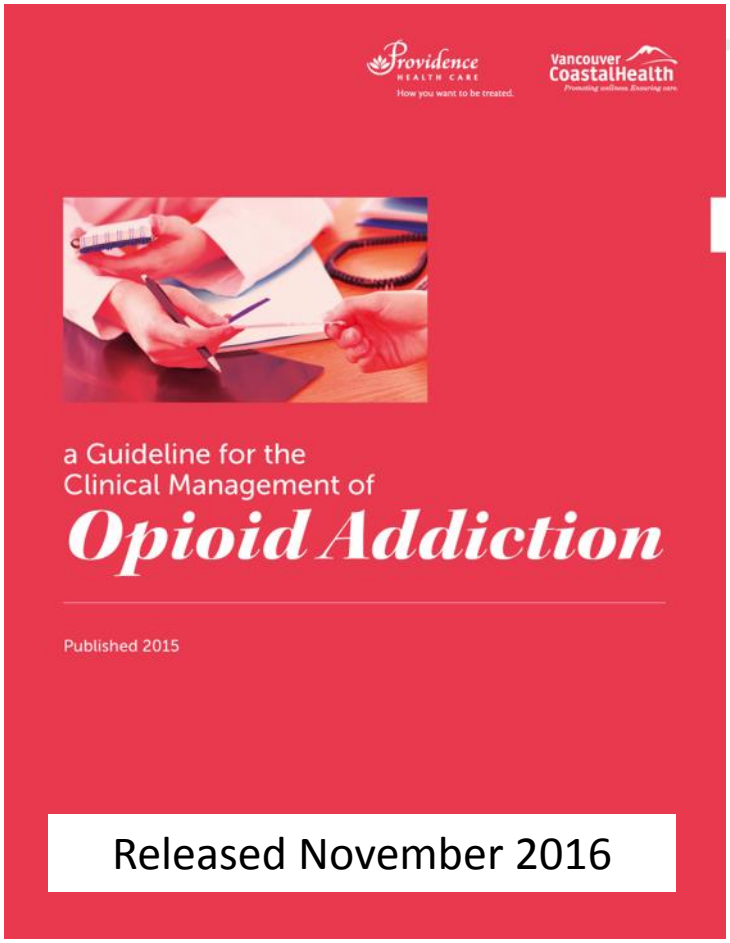

Overdose
Death
HIV
Infections
Crime
Family
Jobs
Legal
Hospital
Mental Illness
Science
Inpatient/Outpatient Detox
Withdrawal/Taper
Psychosocial Treatment
OAT
Methadone
Buprenorphine/Naloxone
Mandatory Counselling?
Tapers vs. Maintenance
Opiate Addiction

Background

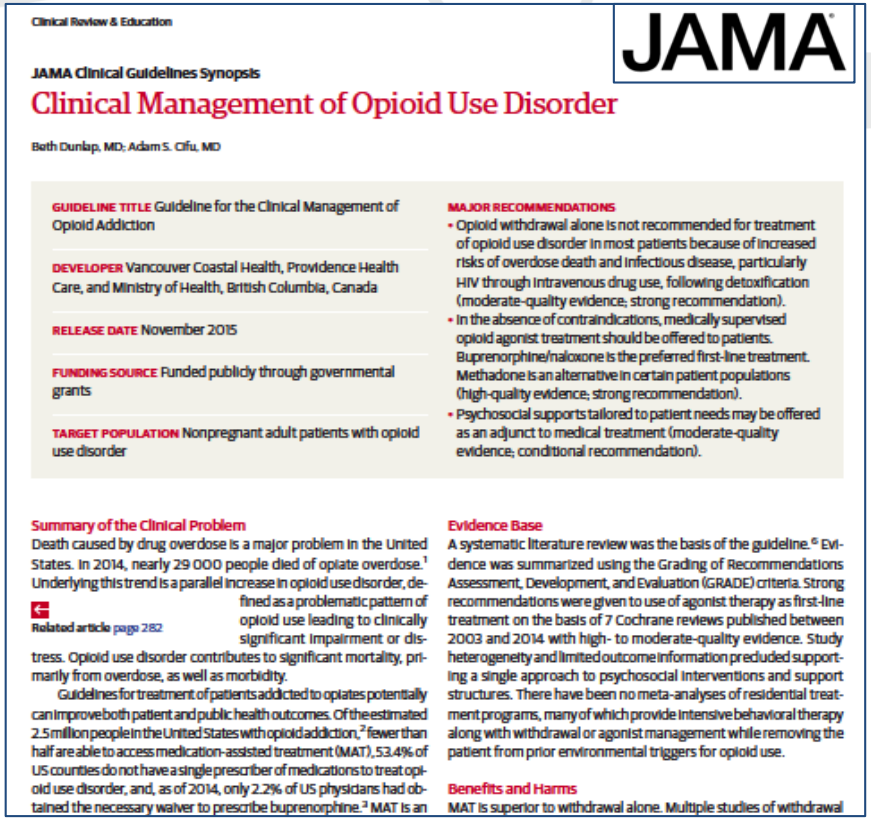
- The province has a guideline for the treatment of opioid use disorder with methadone
- Updated July 2016 to include buprenorphine
- Evidence-based guidance for when to use methadone versus other treatments lacking



Background



Released November 2016



Clinical Review & Education

JAMA

JAMA Clinical Guidelines Synopsis

Clinical Management of Opioid Use Disorder

Beth Dunlap, MD; Adam S. Cifu, MD

GUIDELINE TITLE Guideline for the Clinical Management of Opioid Addiction

DEVELOPER Vancouver Coastal Health, Providence Health Care, and Ministry of Health, British Columbia, Canada

RELEASE DATE November 2015

FUNDING SOURCE Funded publicly through governmental grants

TARGET POPULATION Nonpregnant adult patients with opioid use disorder

MAJOR RECOMMENDATIONS

- Opioid withdrawal alone is not recommended for treatment of opioid use disorder in most patients because of increased risks of overdose death and infectious disease, particularly HIV through intravenous drug use, following detoxification (moderate-quality evidence; strong recommendation).
- In the absence of contraindications, medically supervised opioid agonist treatment should be offered to patients. Buprenorphine/naloxone is the preferred first-line treatment. Methadone is an alternative in certain patient populations (high-quality evidence; strong recommendation).
- Psychosocial supports tailored to patient needs may be offered as an adjunct to medical treatment (moderate-quality evidence; conditional recommendation).

Summary of the Clinical Problem

Death caused by drug overdose is a major problem in the United States. In 2014, nearly 29 000 people died of opiate overdose.[1] Underlying this trend is a parallel increase in opioid use disorder, defined as a problematic pattern of opioid use leading to clinically significant impairment or distress. Opioid use disorder contributes to significant mortality, primarily from overdose, as well as morbidity.

Related article page 282

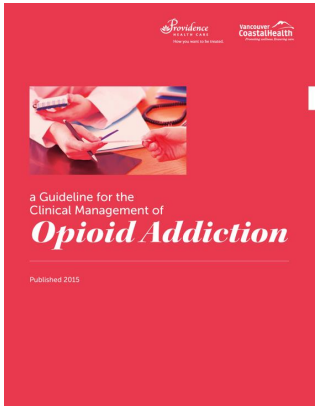
Guidelines for treatment of patients addicted to opiates potentially can improve both patient and public health outcomes. Of the estimated 2.5 million people in the United States with opioid addiction,[2] fewer than half are able to access medication-assisted treatment (MAT). 53.4% of US counties do not have a single prescriber of medications to treat opioid use disorder, and, as of 2014, only 2.2% of US physicians had obtained the necessary waiver to prescribe buprenorphine.[3] MAT is an

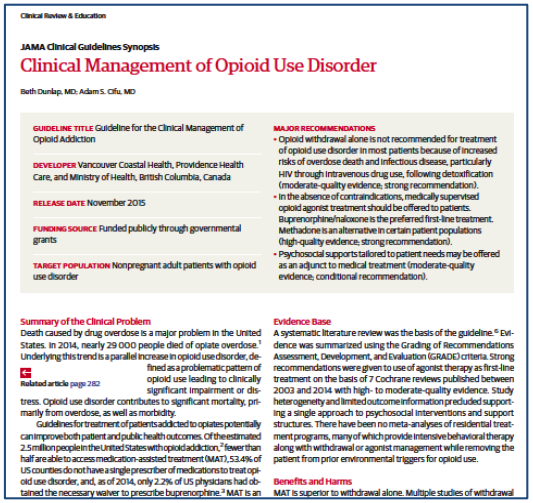
Evidence Base

A systematic literature review was the basis of the guideline.[6] Evidence was summarized using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria. Strong recommendations were given to use of agonist therapy as first-line treatment on the basis of 7 Cochrane reviews published between 2003 and 2014 with high- to moderate-quality evidence. Study heterogeneity and limited outcome information precluded supporting a single approach to psychosocial interventions and support structures. There have been no meta-analyses of residential treatment programs, many of which provide intensive behavioral therapy along with withdrawal or agonist management while removing the patient from prior environmental triggers for opioid use.

Benefits and Harms

MAT is superior to withdrawal alone. Multiple studies of withdrawal





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Release date:
Feb 7, 2017

A Guideline for the Clinical Management of Opioid Use Disorder

BRITISH COLUMBIA | Ministry of Health

BRITISH COLUMBIA CENTRE ON SUBSTANCE USE

Mac GRADE Centre | McMaster University

Rank		Type of Evidence
1		Systematic reviews of randomized controlled trials
2	a	Randomized clinical trials
	b	Nonrandomized clinical trials
3	a	Observational studies with controls
	b	Observational studies - no controls
4		Expert consensus

Disclosures

- No member of guideline committee reported direct financial or indirect conflicts of interest

Expert guideline – summary of recommendations

Summary of Recommendations

Recommendation	Quality of evidence*	Strength of recommendation*	Refer to Evidence Summary (pp.)
Approaches to avoid			
1. Withdrawal management alone (i.e., detoxification without immediate transition to long-term addiction treatment†) is not recommended, since this approach has been associated with elevated rates of relapse, HIV infection and overdose death. This includes rapid (< 1 week) inpatient tapers with methadone or buprenorphine/naloxone.	⊕⊕⊕ Moderate	Strong	17-20
Possible first-line treatment options			
2. Initiate opioid agonist treatment with buprenorphine/naloxone whenever feasible to reduce toxicities and facilitate recovery through safer take-home dosing.	⊕⊕⊕⊕ High	Strong	23-25, Table 2
3. Initiate opioid agonist treatment with methadone when treatment with buprenorphine/naloxone is not preferable (e.g., challenging induction).	⊕⊕⊕⊕ High	Strong	21-25, Table 2
4. If withdrawal management is pursued, for most patients, this can be provided more safely in an outpatient rather than inpatient setting. During withdrawal management, patients should be immediately transitioned to long-term addiction treatment† to assist in preventing relapse and associated harms. See also #9.	⊕⊕⊕ Moderate	Strong	17-20
Adjunct or alternative treatment options			
5. For individuals responding poorly to buprenorphine/naloxone, consider transition to methadone.	⊕⊕⊕⊕ High	Strong	23-25, Table 2
6. For individuals responding poorly to methadone, or with successful and sustained response to methadone desiring treatment simplification, consider transition to buprenorphine/naloxone.	⊕⊕⊕ Moderate	Strong	23-25, Table 2
7. For individuals with a successful and sustained response to agonist treatment desiring medication cessation, consider slow taper (e.g., 12 months). Transition to oral naltrexone could be considered upon cessation of opioids.	⊕⊕⊕ Moderate	Strong	29-31
8. Psychosocial treatment interventions and supports should be routinely offered in conjunction with pharmacological treatment.	⊕⊕⊕ Moderate	Strong	20-21

Withdrawal management only

- Detox: Inpatient vs. Outpatient
- Intensive Psychosocial Treatment?
- Residential Treatment
- OAT Tapers, Clonidine?
  Outcomes?

UNODC
United Nations Office on Drugs and Crime

World Health Organization

DISCUSSION PAPER
UNODC/WHO 2013

Opioid overdose: preventing and reducing opioid overdose mortality

UNODC
United Nations Office on Drugs and Crime

World Health Organization

D. Reduced tolerance due to a recent period of abstinence

Recent periods of abstinence (particularly when enforced, such as in a period of incarceration) are a major risk factor for fatal opioid overdose. Substantial evidence from a number of longitudinal studies indicates that the period immediately following release from prison[39] and the period immediately following discharge from a detoxification facility pose a significantly elevated risk of overdose.[40] The main causes of increased overdose mortality among released prisoners who were formerly opiate dependent were the individual's loss of tolerance and erroneous judgement with respect to dosage when returning to opiate use following a period of abstinence.[41]

Opioid overdose: preventing and reducing opioid overdose mortality

Safety considerations - Withdrawal management alone

- Detox can potentially be an important first point of contact and a bridge to other treatment options
- However, detox alone associated with:
  - HIV-transmission (MacArthur et al., 2012)
  - High rates of relapse (Strang et al., 2003)
  - Morbidity and Mortality (Luty 2003, Simpson and Friend, 1988)
- **THN Training**

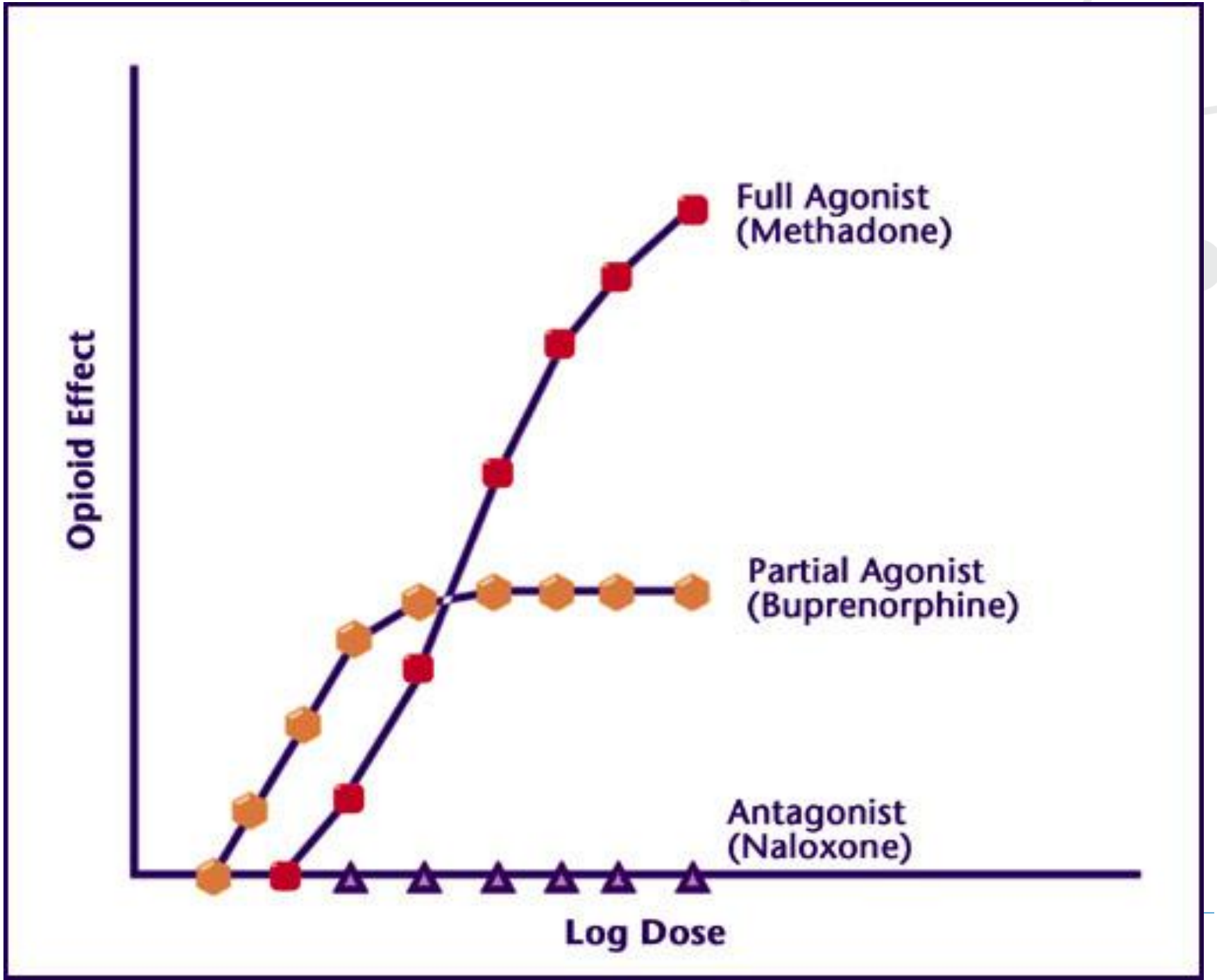
Residential Treatment

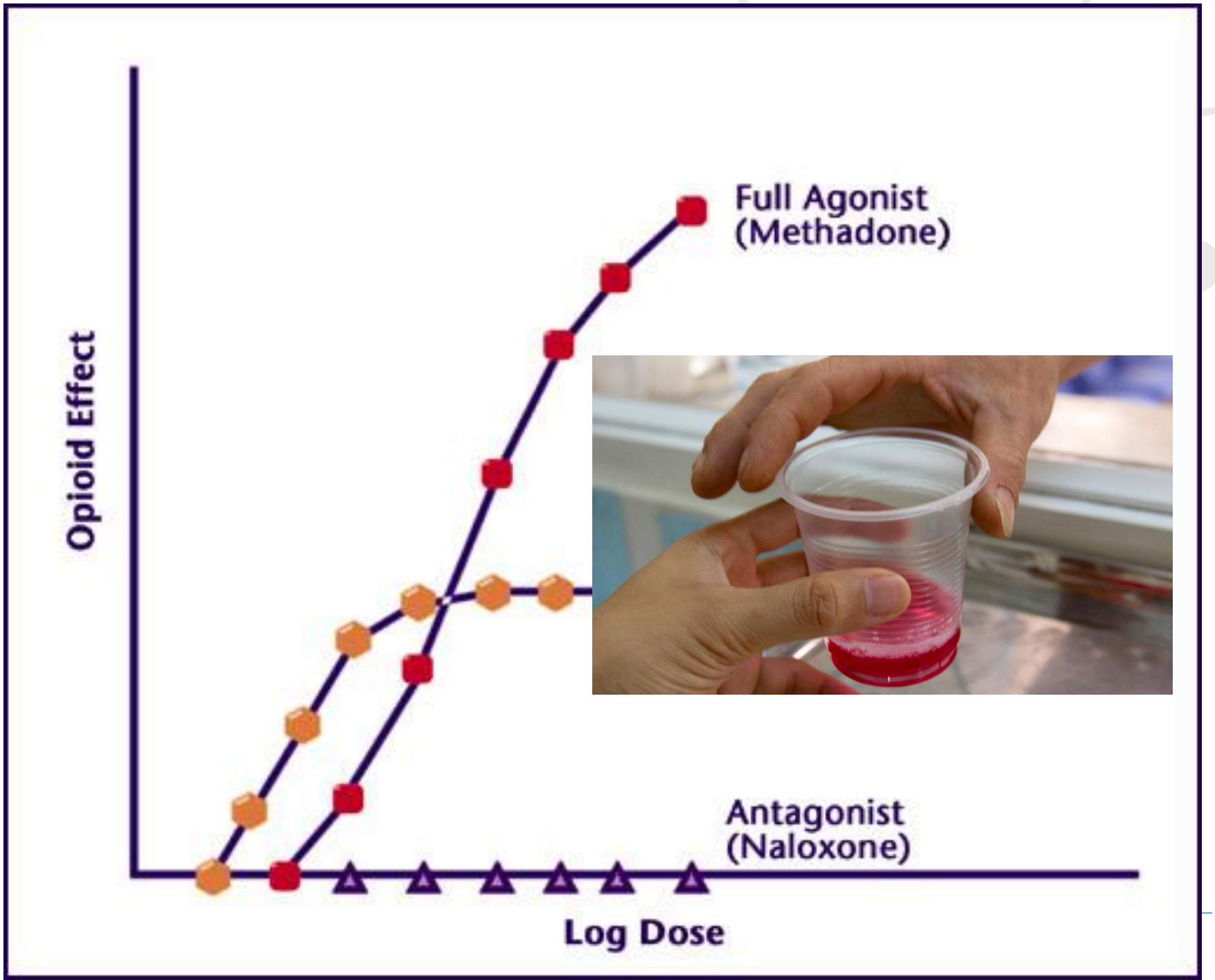
(without maintenance OAT)

- No systematic reviews or meta-analyses
- Signal to some clinical improvement, but much of the literature is outdated (Craddock 1997, Gossop 1999, Hubbard 1989, Simpson 1982)
- Relapse (Smyth et al., 2010)
- No OAT 2 times risk of death (Matthias Pierce 2016)

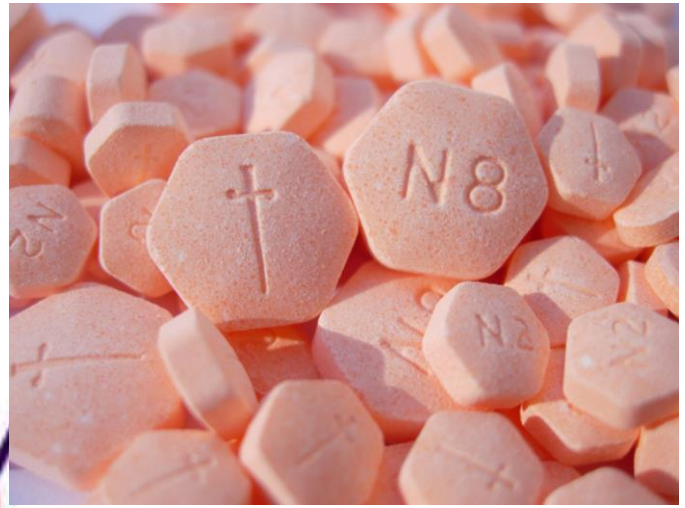
Maintenance Therapy

- Methadone vs. buprenorphine
- First line?
- Safety profile of medications
- Mandatory counselling
- Take home dosing vs. methadone?
- How long; when and how to taper
- Other evidence-based options


Opioid Effect
Full Agonist
(Methadone)
Partial Agonist
(Buprenorphine)
Antagonist
(Naloxone)
Log Dose


Full Agonist
(Methadone)
Opioid Effect
Antagonist
(Naloxone)
Log Dose


NDC 12496-1208-1
1 sublingual film
8 mg/2 mg
Suboxone
(buprenorphine and naloxone) sublingual film
8 mg/2 mg
Rx only
Children who accidentally take SUBOXONE will need emergency medical care. Keep SUBOXONE out of the reach of children.
suboxone.com

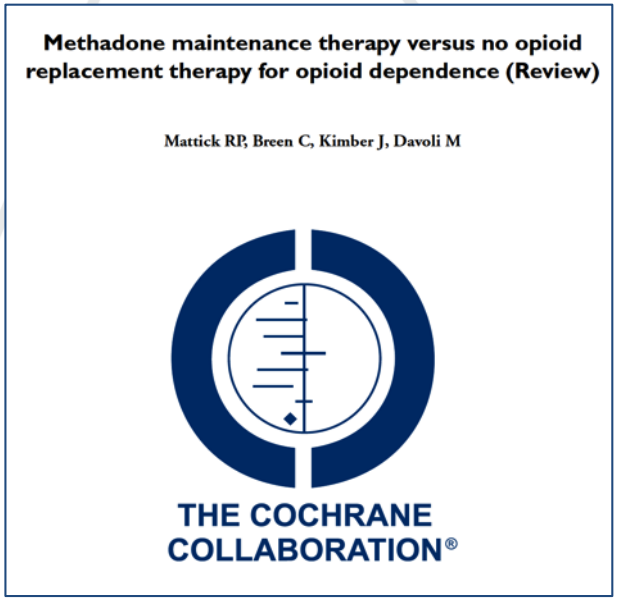

N8

Opioid Effect
Partial Agonist
(Buprenorphine)
Antagonist
(Naloxone)
Log Dose

Agonist Treatment | Methadone

MMT vs. no opioid replacement therapy (Mattick et al., Cochrane Review 2009)

- Methadone significantly more effective than non-pharmacological approaches in:
  - Treatment retention
  - Suppression of heroin use

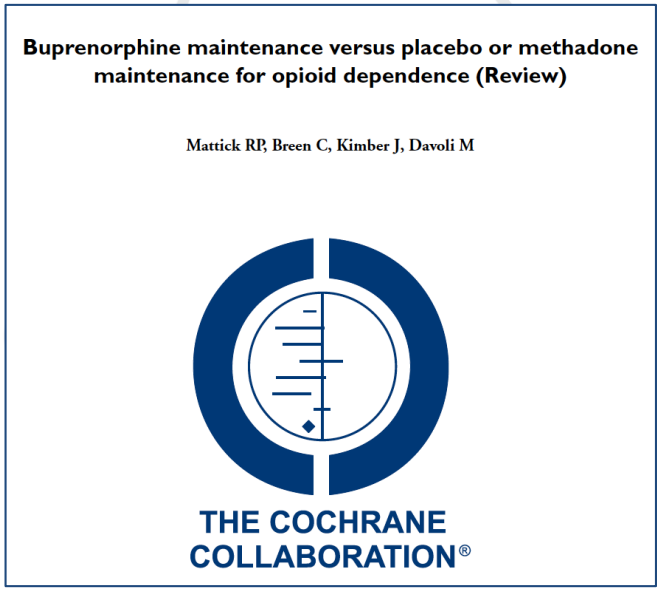


Agonist treatment | Buprenorphine/naloxone

Buprenorphine vs. Methadone Maintenance Therapy (Mattick et al., Cochrane Review 2014)

- At medium/high doses bup/nlx is not markedly different from methadone in terms of treatment retention

- No difference between bup/nlx and MMT in reducing illicit opioid use



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Buprenorphine vs. Methadone Maintenance Therapy (Mattick et al., Cochrane Review 2014)

- At medium/high doses bup/nlx is not markedly different f
  treatmer

Safety profile?

- No difference between bup/nlx and MMT in reducing illicit opioid use

Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence (Review)

Mattick RP, Breen C, Kimber J, Davoli M

THE COCHRANE COLLABORATION®

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Short communication

Buprenorphine infrequently found in fatal overdose in New York City

98 unintentional OD b/w June – Oct 2013

2/98 cases tested positive for the bup metabolite
Both tested + for 6-MAM, morphine (heroin OD)

Available online 15 August 2015

Keywords:
Buprenorphine
Overdose

post mortem blood specimens from decedents who had died of an unintentional drug overdoses in 2013.
Methods: We retrospectively tested consecutive drug overdose cases that occurred from June through October 2013. Cases with available blood specimens were tested for buprenorphine and norbuprenorphine using liquid chromatography-tandem mass spectrometry. Toxicology results were linked to death certificates and case files from New York City Vital Statistics and New York City Office of the Chief Medical Examiner.
Results: Of the 98 unintentional drug overdose fatalities tested, only 2 (2.0%) tested positive for buprenorphine metabolites. All 98 unintentional fatalities involved multiple substances.
Conclusions: Buprenorphine was infrequently found in drug overdose deaths in New York City. Since the safety and efficacy of buprenorphine are well documented, and overdoses resulting from buprenorphine treatment or diversion are very rare, facilitating access to buprenorphine treatment is strongly recommended.

The American Journal on Addictions, 19: 73–88, 2009

ISSN: 1055-0496 print / 1521-0391 online
DOI: 10.1111/j.1521-0391.2009.00008.x

Indicators of Buprenorphine and Methadone Use and Abuse: What Do We Know?

Jane Carlisle Maxwell, PhD,[1] Elinore F. McCance-Katz, MD, PhD[2]

[1]Addiction Research Institute, The University of Texas at Austin, Austin, Texas
[2]Department of Psychiatry, University of California San Francisco, San Francisco, California

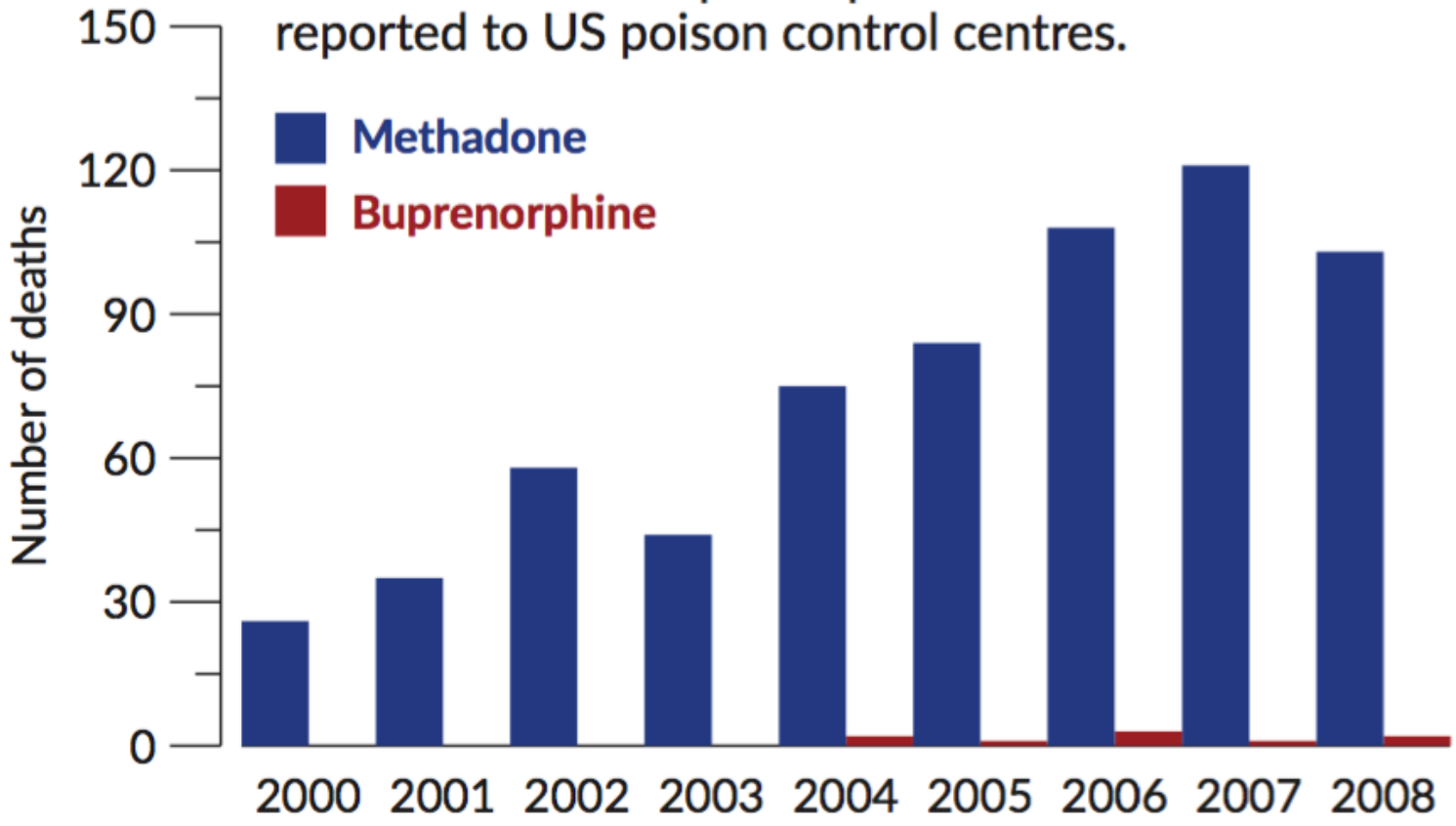
TABLE 1. Methadone and buprenorphine calls to the U.S. poison control centers: 2000–2008

	All methadone exposures	Methadone deaths	All buprenorphine exposures	Buprenorphine deaths
2000	1,387	26	13	0
2001	1,914	35	21	0
2002	2,696	58	29	0
2003	3,126	44	104	0
2004	3,885	75	318	2
2005	4,256	84	580	1
2006	4,555	108	909	3
2007	5,025	121	1,590	1
2008	4,765	103	2,607	2

Source: National Poison Data System, American Association of Poison Control Centers.

Figure 4

Methadone and buprenorphine deaths reported to US poison control centres.

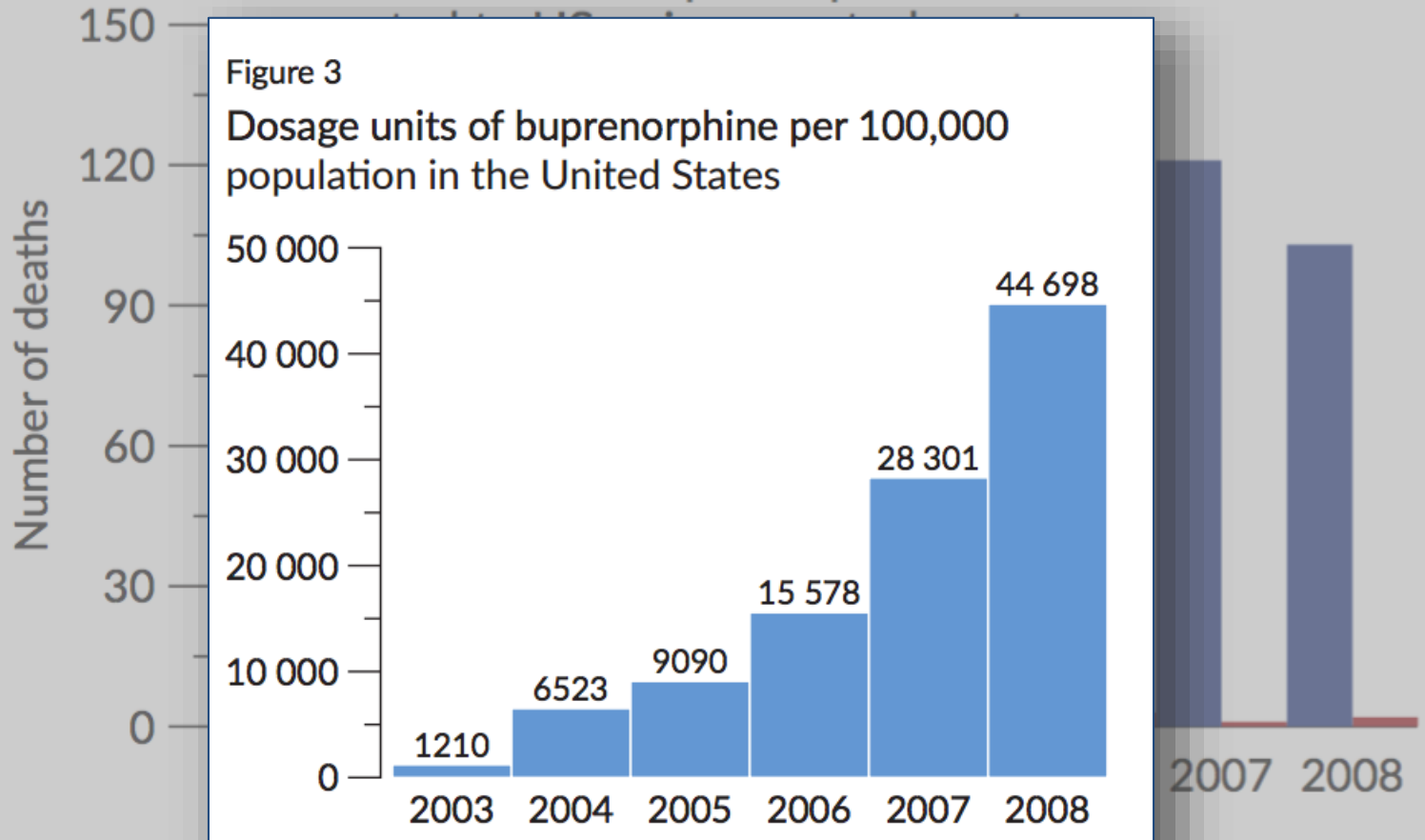


	2000	2001	2002	2003	2004	2005	2006	2007	2008
Methadone	26	35	58	44	75	84	108	121	103
Buprenorphine	0	0	0	0	2	1	3	1	2

Source: National Poison Data System, American Association of Poison Control Centers. Adapted from Maxwell J, McCance-Katz E. Indicators of buprenorphine and methadone use and abuse: What do we know? The American Journal on Addictions. 2009, 19:73–88

Figure 4

Methadone and buprenorphine deaths

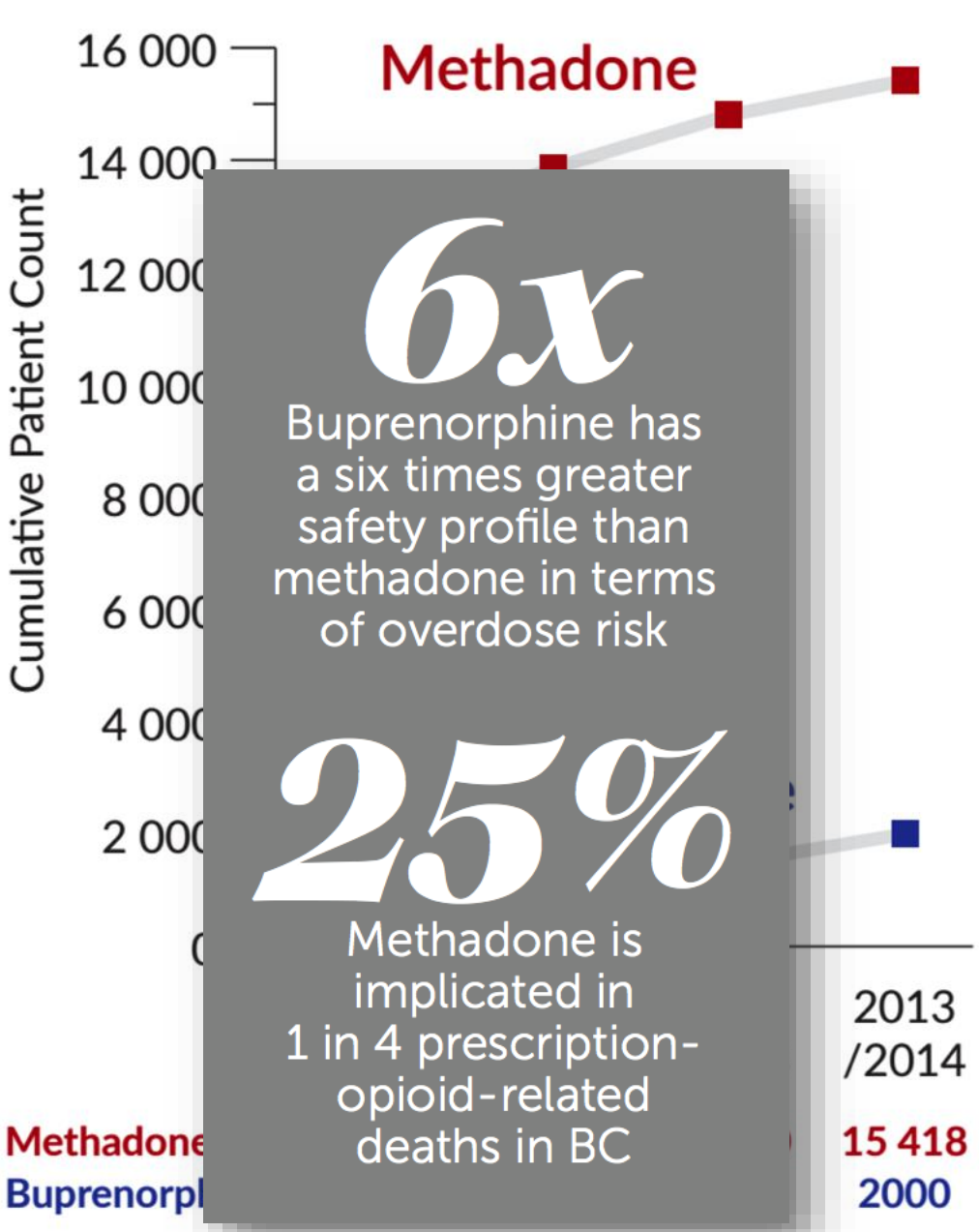


tion of Poison
z E. Indicators
of buprenorphine and methadone use and abuse: What do we know?
The American Journal on Addictions. 2009, 19:73–88

Figure 3

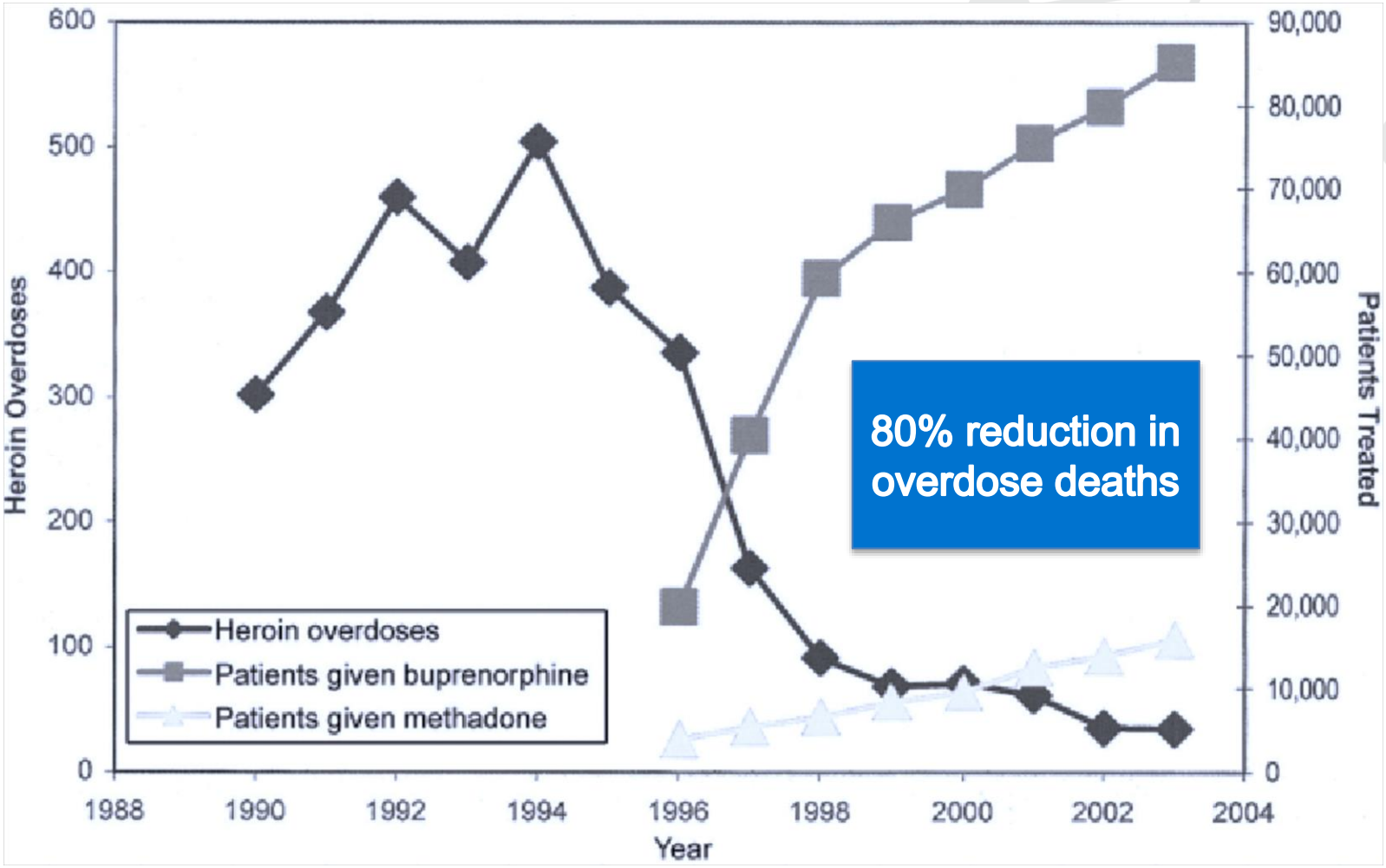
Dosage units of buprenorphine per 100,000 population in the United States

Source: DEA's Automation of Reports and Consolidated Orders System (ARCOS). Adapted from Maxwell J, McCance-Katz E. Indicators of buprenorphine and methadone use and abuse: What do we know? The American Journal on Addictions. 2009, 19:73–88



Source: BC Opioid Substitution Treatment System Performance Measures, 2013/2014. Office of the Provincial Health Minister, British Columbia Ministry of Health. Released July 2015.

Reduction in overdose mortality with expanded access to buprenorphine/naloxone (France)



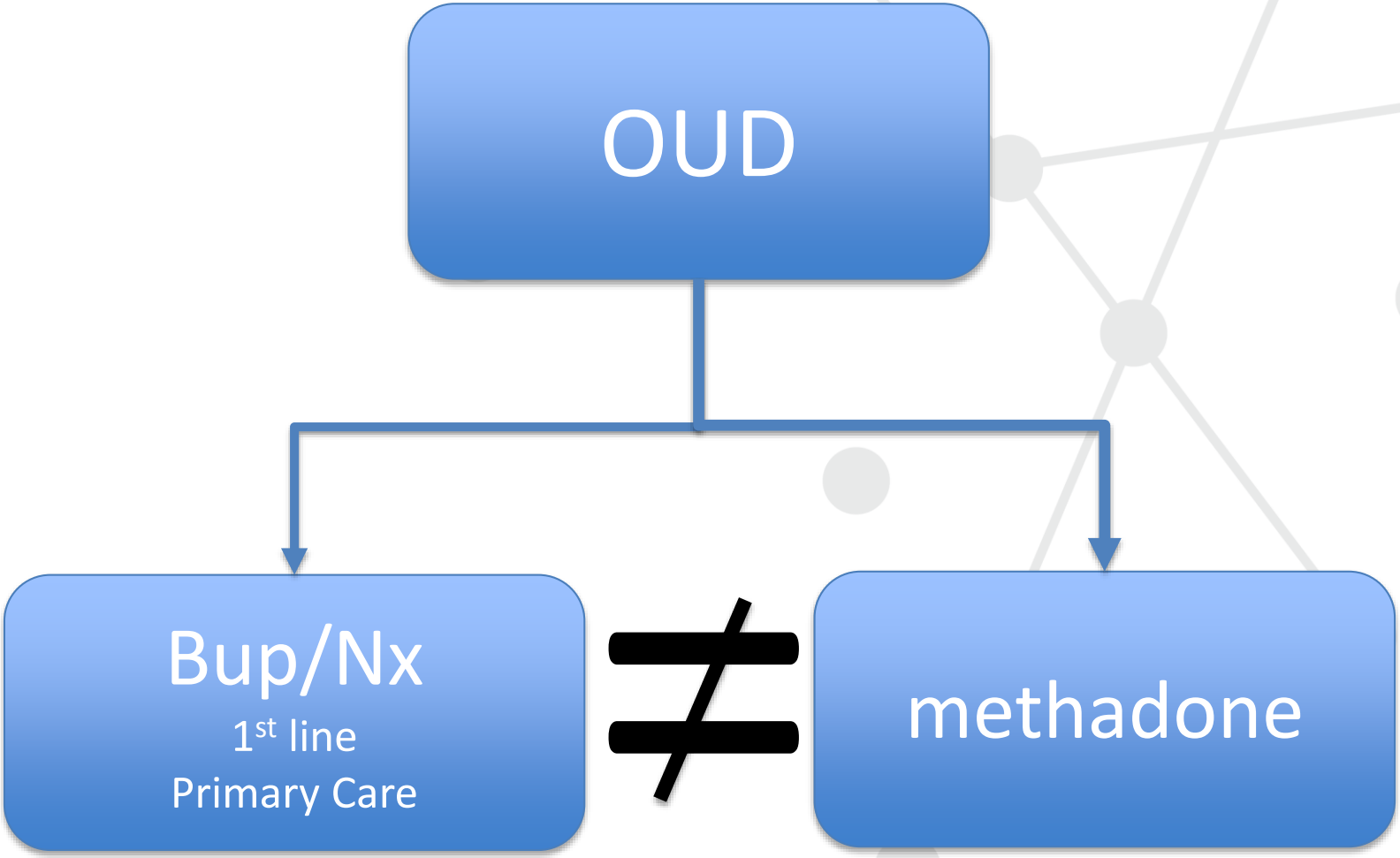
Carrieri et al., 2006

Methadone

Advantages	Disadvantages
Potent opioid agonist	Higher risk of overdose, particularly during treatment initiation
Potentially better treatment retention, particularly for unstable opioid-dependent individuals	Generally requires DWI
May be easier to initiate treatment	More severe side effect profile
Potentially better alternative if buprenorphine was unsuccessful at relieving withdrawal symptoms or associated with severe side effects	More expensive if DWI required
Approved in Canada for primary purpose of pain control (split dose BID or TID dosing); Health Canada exemption required for prescribing	Longer time to achieve therapeutic dose (>35 days)
	Higher potential for adverse drug-drug interactions (e.g. Abx, ARVs)
	Increased risk of cardiac arrhythmias as a result of QTc prolongation

Buprenorphine/Naloxone

Advantages	Disadvantages
↓ Risk of OD as partial agonist and ceiling effect for resp. depression	Potential ↑ risk of drop-out
Reduced risk of injection, diversion, and OD due to naloxone component	May cause precipitated withdrawal if induced inappropriately
Allows for safer take home schedules	May block opioid analgesics used for concurrent pain treatment
Milder side effect profile	Not approved in Canada for the purposes of pain control
Easier to rotate from bup/nlx to methadone	
Flexible take home schedules many contribute to ↑ cost savings and patient autonomy	
Shorter time to achieve therapeutic dose (1-3 days)	


OUD
Bup/Nx
1st line
Primary Care
≠
methadone

CBC INVESTIGATES | Fentanyl crisis: Easier access to Suboxone urgently needed, experts say

"We're losing the battle" mom says after ten-fold increase in B.C. fentanyl deaths

By Natalie Clancy, CBC News Posted: Jan 28, 2016 3:00 AM PT | Last Updated: Jan 28, 2016 1:36 PM PT

Elyse "Izzy" Bailey, died Dec 23, 2015 after buying heroin that turned out to be fentanyl. (Debra Bailey)

Equal efficacy
Bup = safer

- **1st Line**
- **Take home dosing schedule?**
- **Random pill counts**
- **Random UDS**

B.C. College of Physicians and Surgeons lifts 'outdated' restriction on Suboxone to help overdose crisis

Change is expected to expand access to drug that cut overdose deaths by 80% in France

CBC News Posted: Jul 05, 2016 1:29 PM PT | Last Updated: Jul 06, 2016 6:57 PM PT

Suboxone is considered 6 times safer than methadone and stops opiate withdrawal symptoms and heroin cravings. (Getty Images)

Diagnostic Accreditation Program

Drug Programs

Prescription Review Program

Methadone Maintenance Program

Methadone for Opioid Use Disorder

Preceptorship

Suboxone®

Methadone for Analgesia

Methadone for Hospitalists

Temporary Authorization

Patient Information

Suboxone®

Health Canada has released Suboxone® for the substitution treatment of opioid use disorder in adults. Suboxone® combines the partial agonist buprenorphine, a proven therapy for opioid use disorder, and the opiate antagonist naloxone, which limits intravenous misuse and the potential for diversion. The naloxone component of Suboxone® has limited sublingual and oral bioavailability, and is inactive when Suboxone® is taken as prescribed.

A federal authorization is not required to prescribe buprenorphine in British Columbia. Before prescribing more than short-term transitional treatment (no more than one week) physicians should do the following:

1. complete a recognized buprenorphine education program (www.suboxonecme.ca)
2. prescribe buprenorphine dispensed daily under the supervision of a healthcare professional (daily witnessed ingestion) until the patient has sufficient clinical stability and is able to safely store buprenorphine take-home doses
3. be familiar with and follow the *Methadone and Buprenorphine: Clinical Practice Guideline for Opioid Use Disorder* and the professional standard on *Safe Prescribing of Drugs with Potential for Misuse/Diversion*, including:
   a. reviewing a patient's current medication profile through PharmaNet (e.g. access in office, or via pharmacist communication)
   b. implementing urine drug testing protocol which involves supervised random testing
      (**Note**: buprenorphine may not be detected on standard UDT and may need to be ordered separately)
   c. documenting discussion of availability and benefits of biopsychosocial support

Physicians are advised to consult more experienced prescribers of buprenorphine when necessary to enhance their knowledge and ensure patient safety during induction or reinduction after missed doses. It is strongly recommended (but no longer mandatory) that buprenorphine prescribers obtain their federal authorization to prescribe methadone for opioid use disorder in order to be able to offer their patients a

College of Physicians and Surgeons
of British Columbia

Methadone and Buprenorphine: Clinical Practice Guideline for Opioid Use Disorder

July 2016

4. Carry Privileges

A "carry" refers to patients receiving doses of methadone/buprenorphine to be taken home for self-administration.

Patients starting MBMT must ingest methadone in the pharmacy under the supervision of a pharmacist (i.e. DWI). Patients who are biopsychosocially stable and who demonstrate appropriate UDT results may be considered for carries. The initial dose of a carry prescription is always witnessed. The decision to initiate carries can only be made by the treating physician. The reasons for granting carry privileges must be documented. Physicians must ensure that carries are safe for both patients and the public. The physician must be satisfied that safe storage of methadone will occur. Unsafe storage and diversion may result in lethal consequences.

The original 2007 manufacturer's product monograph "Serious Warnings and Precautions" section stated, "Suboxone® must be dispensed daily under the supervision of a healthcare professional, for a minimum of two months and until the patient is clinically stable and able to safely store Suboxone® take-home doses." In August 2015, the product monograph black box warning was changed to "Suboxone® must be dispensed daily under the supervision of a healthcare professional, until the patient has sufficient clinical stability and is able to safely store Suboxone® take-home doses." Although the two-month minimum has been removed, the concept of daily supervised dispensing remains, and is dependent upon the patient achieving clinical stability, which could develop sooner, or later than two months.

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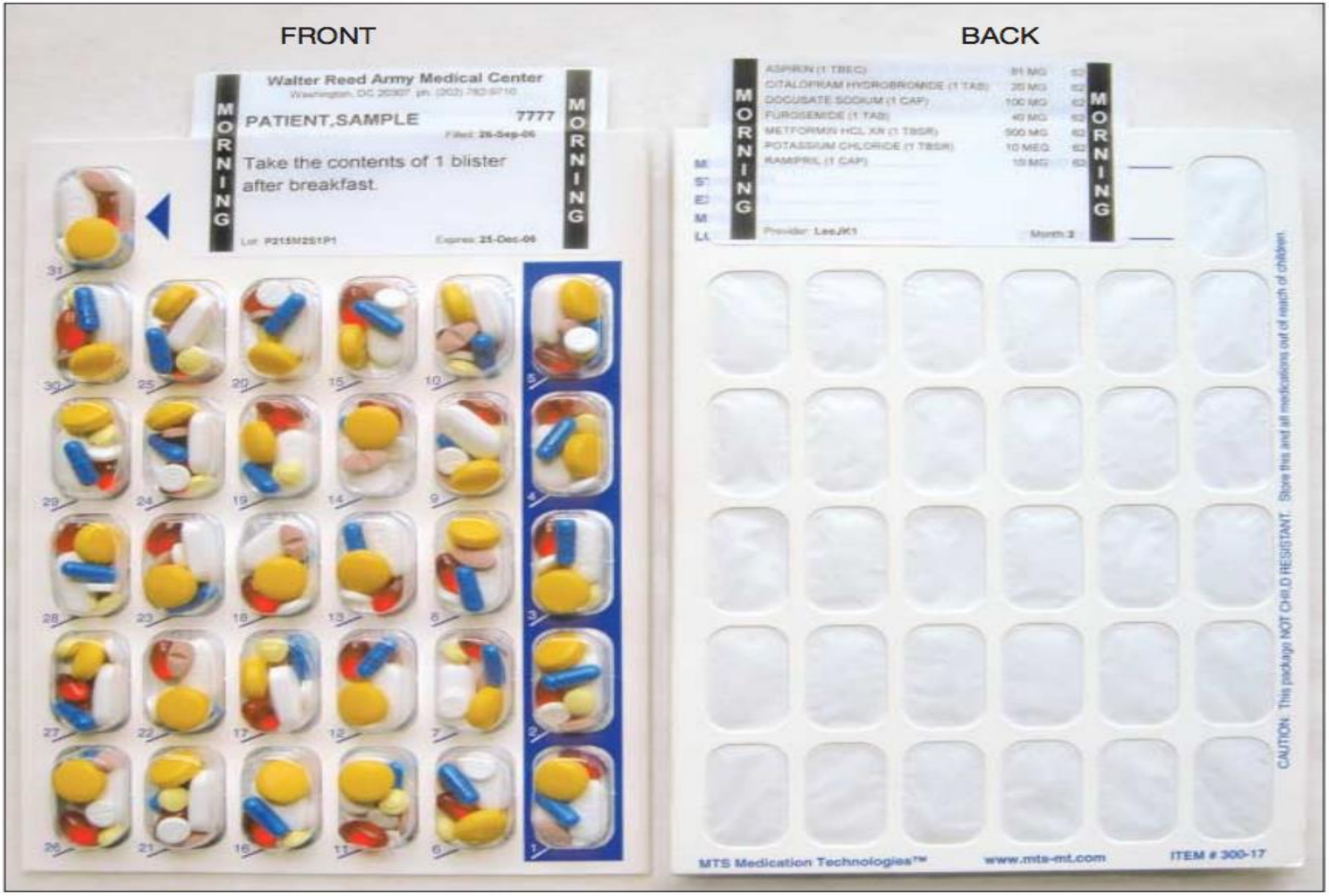
Figure 2. Sample Blister Pack of Medications for Morning



ANNALS OF FAMILY MEDICINE

Treating Opioid Addiction With Buprenorphine-Naloxone in Community-Based Primary Care Settings

Ira L. Mintzer, MD[1]
Mark Eisenberg, MD[2]
Maria Terra, BA[1]
Casey MacVane, MD, MPH[2]
David U. Himmelstein, MD[1]
Steffie Woolhandler, MD[1]

[1]Harvard Medical School/Cambridge Health Alliance, Cambridge, Mass

[2]MGH-Charlestown HealthCare Center/ Harvard Medical School, Boston, Mass

ABSTRACT

PURPOSE Office-based treatment of opioid addiction with a combination of buprenorphine and naloxone was approved in 2002. Efficacy of this treatment in nonresearch clinical settings has not been studied. We examined the efficacy and practicality of buprenorphine-naloxone treatment in primary care settings.

METHODS We studied a cohort of 99 consecutive patients enrolled in buprenorphine-naloxone treatment for opioid dependence at 2 urban primary care practices: a hospital-based primary care clinic, and a primary care practice in a free-standing neighborhood health center. The primary outcome measure was sobriety at 6 months as judged by the treating physician based on periodic urine drug tests, as well as frequent physical examinations and questioning of the patients about substance use.

RESULTS Fifty-four percent of patients were sober at 6 months. There was no significant correlation between sobriety and site of care, drug of choice, neighborhood poverty level, or dose of buprenorphine-naloxone. Sobriety was correlated with private insurance status, older age, length of treatment, and attending self-help meetings.

CONCLUSIONS Opioid-addicted patients can be safely and effectively treated in nonresearch primary care settings with limited on-site resources. Our findings suggest that greater numbers of patients should have access to buprenorphine-naloxone treatment in nonspecialized settings.

Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence (Review)

Amato L, Minozzi S, Davoli M, Vecchi S

THE COCHRANE COLLABORATION®

- 2011 review
- 35 studies, 4319 participants
- Psychosocial interventions + OAT vs. standard OAT
- No significant benefits – retention or treatment outcomes

Tapers?

Research Summary

Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-based retrospective cohort study.

NOSYK B, SUN HY, EVANS E, ET AL. ADDICTION 2012;107:1621–9.

Ten years: 1996–2006

Outcome:
Sustained successful taper
(no treatment re-entry, opioid-related hospitalization or death for 18 months following last dose)

Out of ***4917*** taper attempts,
646 sustained success (***13%***)

FACTORS

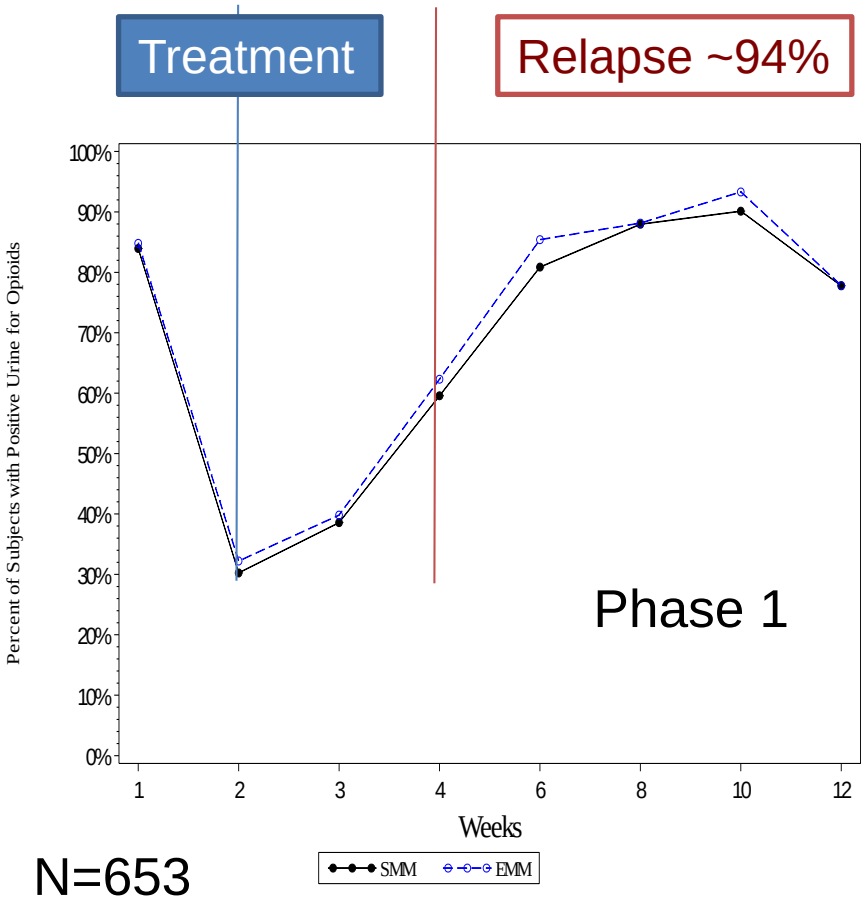
Taper over a *long period* (3 months–1 year)
Taper over 12–52 weeks vs < 12 weeks

+258% increased odds of success

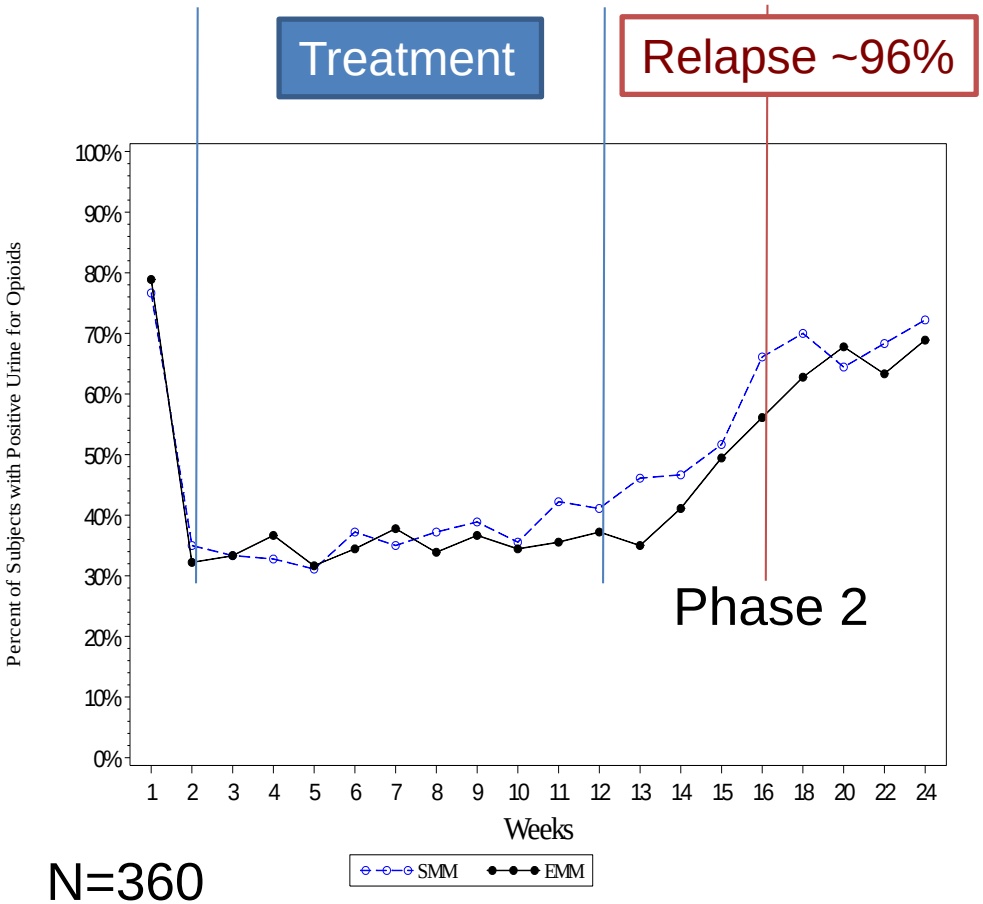
Plan dose reductions to occur bi-weekly or monthly
As opposed to more or less frequently

+61% increased odds of success

Prescription Opioid Addiction Treatment Study



N=653



N=360

Slow release oral morphine

Slow-release oral morphine for maintenance therapy (Ferri et al., Cochrane review 2013)

- Limited evidence in review (3 studies)
- Since this review further support Hammig 2014

Withdrawal Options

- Buprenorphine/naloxone taper
- Methadone taper
- Short-acting opioids
- Clonidine and ancillary meds

Encourage:

- Long, slow taper
- Intensive psychosocial follow-up
- outpatient taper

Ensure:

- take-home naloxone training

Warn:

- risk of OD and death with inpatient taper

Treatment

1st line:
Buprenorphine/naloxone

- Relatively safer
- Take home doses
- Easier to transition from partial to full agonist
- Primary care settings
- Rural and remote settings

Withdrawal Options

- Buprenorphine/naloxone taper
- Methadone taper
- Short-acting opioids
- Clonidine and ancillary meds

Treatment

- 1st line: Buprenorphine/naloxone
- If contraindications: Methadone

Withdrawal Options

- Buprenorphine/naloxone taper
- Methadone taper
- Short-acting opioids
- Clonidine and ancillary meds

Treatment

- 1st line: Buprenorphine/naloxone
- If contraindications: Methadone

2nd line: Transition

- bup/nlx to methadone
- methadone to bup/nlx

Withdrawal Options

- Buprenorphine/naloxone taper
- Methadone taper
- Short-acting opioids
- Clonidine and ancillary meds

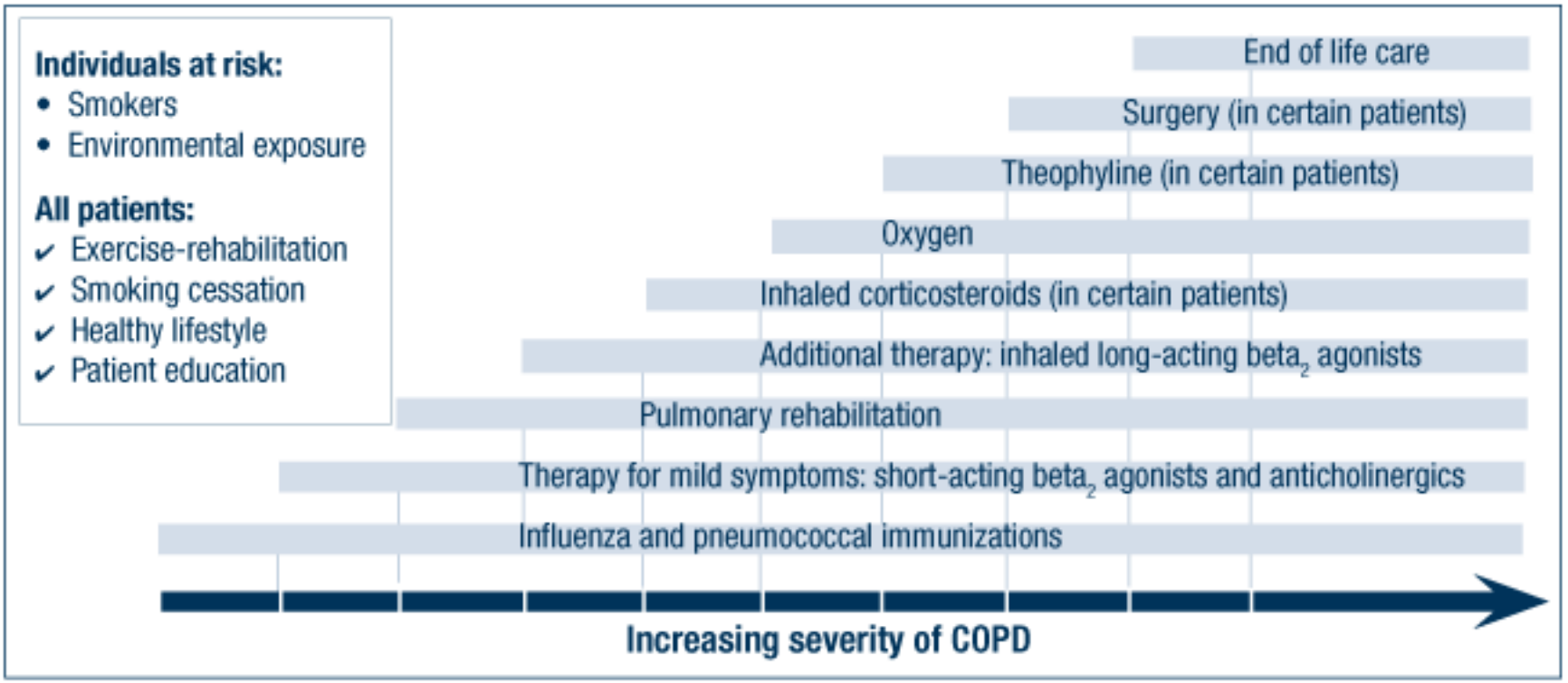
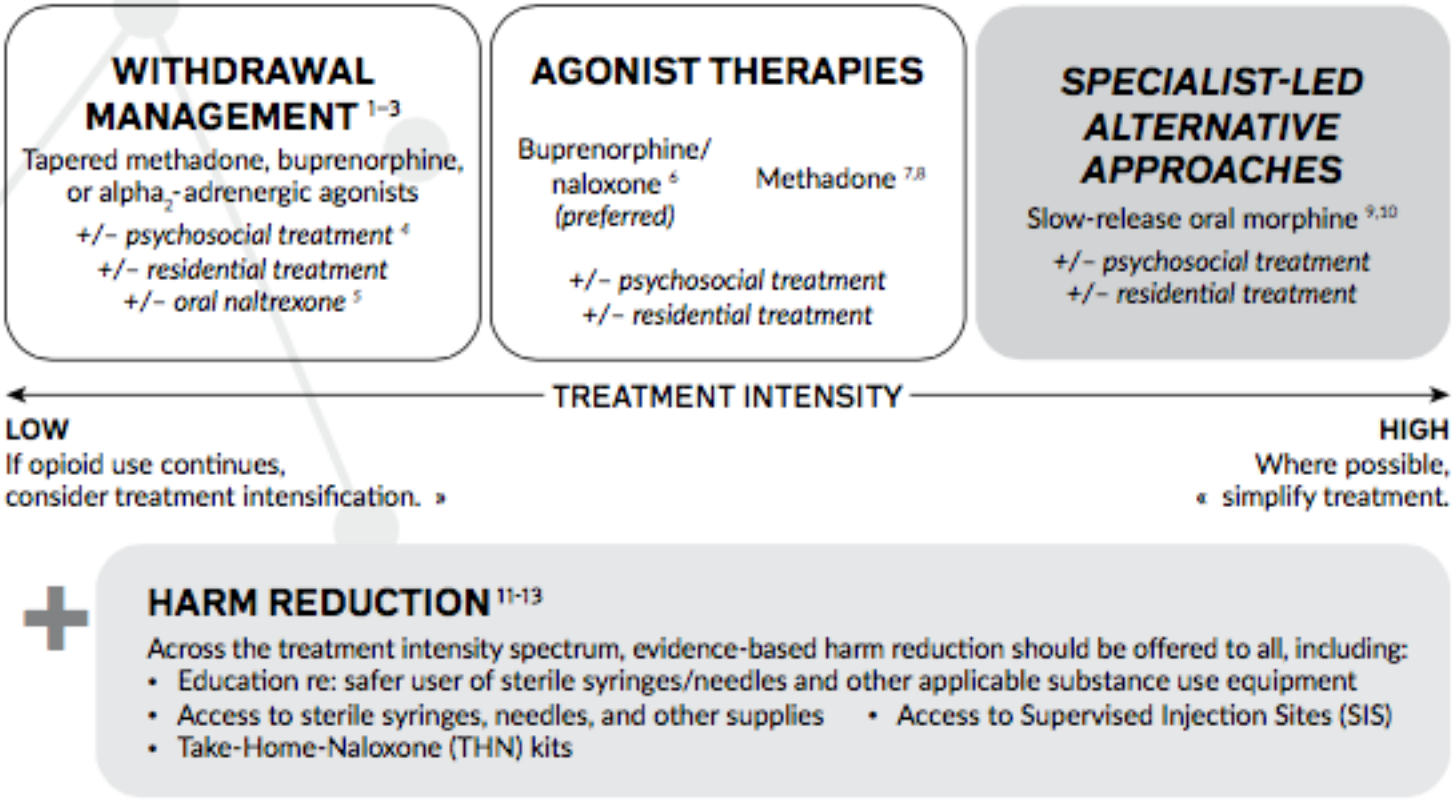
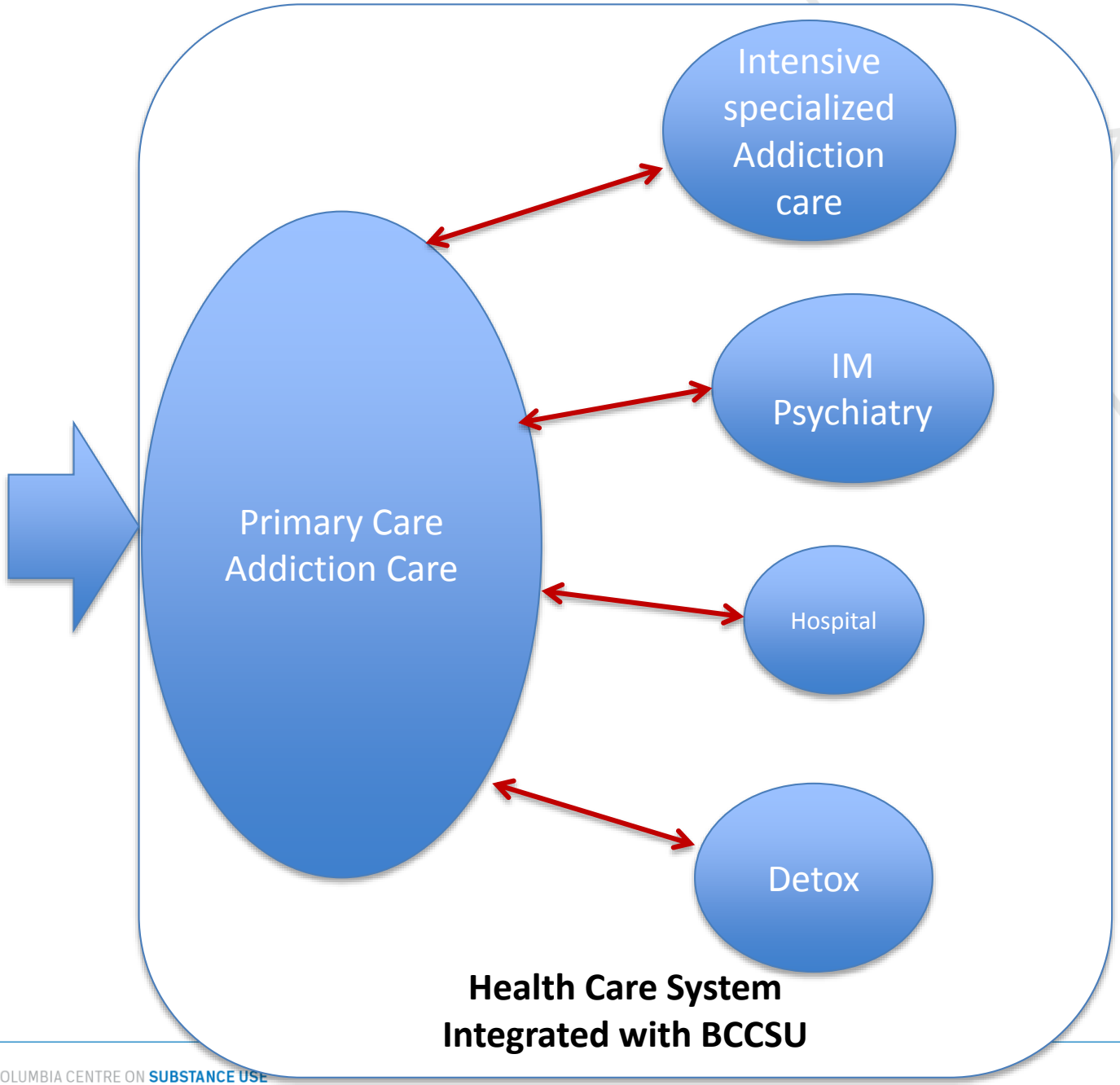

Individuals at risk:
• Smokers
• Environmental exposure
All patients:
✔ Exercise-rehabilitation
✔ Smoking cessation
✔ Healthy lifestyle
✔ Patient education
End of life care
Surgery (in certain patients)
Theophyline (in certain patients)
Oxygen
Inhaled corticosteroids (in certain patients)
Additional therapy: inhaled long-acting beta2 agonists
Pulmonary rehabilitation
Therapy for mild symptoms: short-acting beta2 agonists and anticholinergics
Influenza and pneumococcal immunizations
Increasing severity of COPD

Table 1. Clinical management of opioid use disorder



1. Amato et al. 2013
2. Gowing et al. 2009
3. Gowing et al. 2014
4. Amato et al. 2011
5. Minozzi et al. 2011
6. Mattick et al. 2014
7. Mattick et al. 2009
8. Faggiano et al. 2003
9. Ferri et al. 2013



Health Care System Integrated with BCCSU

Practical Tips: Continuing patients on Bup/Nx

- Collateral from initiating doctor
- Pharmnet!
- Improved retention: 12-16 mg/d
- Know how medication is taken (SL)
- Lower barriers: how long and who to DWI?
  - Benzos, AUD, youth, working, school, psych, homeless
- Random pill counts
- UDS
- RACE line!

RACE
RAPID ACCESS TO CONSULTATIVE EXPERTISE

REAP, Providence Health offer new addictions medicine training

Posted on September 29, 2016 by

The Rural Education Action Plan (REAP) and Providence Health are partnering to offer training in addictions medicine for BC practitioners interested in delivering clinical, inpatient and outpatient care.

This elective is based at St Paul's hospital within the addiction medicine consult team (AMCT) and consists of three (3) academic teams each staffed by one addiction physician. Consultations are requested from all areas of the hospital including the emergency department, medical, surgical and psychiatric wards. Most patients present to the hospital with medical consequences of substance use.

bweitzel@providencehealth.bc.ca

therapy such as methadone or buprenorphine/naloxone and managing complicated alcohol withdrawal).

St. Paul's Goldcorp

ADDICTION MEDICINE FELLOWSHIP

3 streams: Clinical, Nursing, and Social Work

Timeline for 2018-2019 **Clinical** Fellowship:

August 28, 2017	Application process opens
October 2, 2017	Application deadline
Nov 6, 2016 to Dec 4, 2017	Interview period
December 11, 2017	Acceptance notification
December 18, 2017	Deadline for acceptance
July 3, 2018	Fellowship begins

Questions? Please email Carmen Rock at ***crock@cfenet.ubc.ca***

St. Paul's Goldcorp

ADDICTION MEDICINE FELLOWSHIP

3 streams: Clinical, Nursing, and Social Work

Timeline for 2017-2018 **Nursing** Fellowship:

September 30, 2016	Application process opens
October 31, 2016	Application deadline
Nov 15, 2016 to Jan 16, 2017	Interview period
January 30, 2017	Acceptance notification
February 10, 2017	Deadline for acceptance
July 3, 2017	Fellowship begins

Questions? Please email Carmen Rock at ***crock@cfenet.ubc.ca***

St. Paul's Goldcorp

ADDICTION MEDICINE FELLOWSHIP

3 streams: Clinical, Nursing, and Social Work

Timeline for 2017-2018 **Social Work** Fellowship:

December 5, 2016	Application process opens
January 16, 2017	Application deadline
Feb 6 to Mar 3, 2017	Interview period
March 13, 2017	Acceptance notification
March 20, 2017	Deadline for acceptance
July 3, 2017	Fellowship begins

Questions? Please email Carmen Rock at ***crock@cfenet.ubc.ca***

The Canada
ADDICTION MEDICINE RESEARCH FELLOWSHIP
Training the next generation of addiction clinician scientists

Timeline for 2017-2018 **Research** Fellowship:

October 31, 2016	Application process opens
December 5, 2016	Application deadline
December 12, 2016	Interview period
January 23, 2017	Acceptance notification
January 30, 2017	Deadline for acceptance
July 3, 2017	Fellowship begins

Questions? Please email Carmen Rock at ***crock@cfenet.ubc.ca***

Training Opportunities

- 2- week sessional payment addiction team at St Paul's
- UBC Enhanced Skills 3-6 months

- *Questions? Please email Carmen Rock at* ***crock@cfenet.ubc.ca***

Job Opportunities

- Vancouver Coastal Health Connections Clinic

- *Questions? Please email Dr. Dan Pare at **Dan.Pare@vch.ca***

Treatment Guideline Committee

fraserhealth

First Nations Health Authority
Health through wellness

Vancouver Coastal Health

northern health
the northern way of caring

island health

Interior Health

BRITISH COLUMBIA
Ministry of Health

Acknowledgements

- Dr. Rolando Barrios
- Ms. Laura Case
- Ms. Anne McNabb
- Mr. Andrew McFarlane
- The BC Centre for Excellence in HIV AIDS
- Ms. Pauline Voon
- Ms. Deborah Graham
- Ms. Emily Wagner
- Mr. James Nakagawa
- Ms. Lianlian Ti
- Ms. Cheyenne Johnson
- Ms. Jessica Jun
- Ms. Maryam Babaei
- Ms. Josey Ross
- Mr. Peter Vann

BRITISH COLUMBIA CENTRE ON
SUBSTANCE USE

St. Paul's Hospital 608 - 1081 Burrard Street
Vancouver, BC Canada V5Z 1Y6
TEL: 604.806.8477 **FAX:** 604.806.8464

BRITISH COLUMBIA CENTRE for EXCELLENCE in HIV/AIDS

Providence HEALTH CARE
How you want to be treated.

UBC

stpaul's FOUNDATION

Indivior© Support for buprenorphine

- Buprenorphine CME course
- Additional in-services (upon request)
- RN sessions on induction education
- Patient support materials
- Buprenorphine pearls with an addiction expert

For more information, contact Kathleen MacDonald:

Kathleen.macdonald@indivior.com


Together, we can do this
Strategies to Address British Columbia's Prescription Opioid Crisis
Recommendations from the British Columbia Node of the Canadian Research Initiative on Substance Misuse
November 2015
BRITISH COLUMBIA CENTRE for EXCELLENCE in HIV/AIDS
CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

Recommendations

In light of the evidence and the unique characteristics of the system of care in BC, a number of steps should immediately be taken to reduce the harms of the pharmaceutical opioid epidemic in British Columbia. These steps include:

STRATEGIES FOR IMPROVED PRESCRIBING PRACTICES

1. Make registration for PharmaNet free, and legally require all clinicians with prescribing authority to be registered for PharmaNet and routinely check patients' PharmaNet profiles when writing prescriptions. Exemptions to this requirement could be provided for individuals who practice in areas without Internet access or with other barriers.
2. Revise duplicate prescription pads to include a checkbox indicating that the prescribing practitioner has fulfilled his or her legal responsibility to review a patient's PharmaNet record, thereby ruling out duplicate or high-risk co-prescriptions.

3. Put in place enforcement measures to ensure that pharmacies are checking PharmaNet to confirm that duplicate prescriptions or other evidence of inappropriate medical care is further brought to the attention of prescribing practitioners and regulatory authorities.
4. Change requirements for benzodiazepine prescribing such that benzodiazepines require a prescription on a duplicate prescription pad, in the same way that opioid prescriptions must be written in BC.[65,67]
5. Implement a maximum upper dispense limit for the amount of opioids that a patient may be dispensed at any one time.

STRATEGIES TO IMPROVE OPIOID ADDICTION CARE

6. Dedicate investments into addiction treatment. For instance, buprenorphine/naloxone—a proven treatment for opioid addiction—should be the first line pharmacotherapy option (along with methadone) for opioid addiction, given its superior safety profile with respect to overdose risk compared to methadone.[74-77]
7. Improve access to buprenorphine/naloxone by eliminating the requirement that prescribers must have methadone exemptions in order to prescribe buprenorphine/naloxone. This requirement is unnecessary given the low misuse potential of buprenorphine/naloxone and the low number of buprenorphine/naloxone prescribers the exemption requirement creates.[78] In lieu of the methadone exemption, prescribers would be required to complete an online training module on buprenorphine/naloxone prescribing.

8. Invest in recovery-oriented care for individuals with opioid addiction.
9. Consider comprehensive patient education with regards to risks of poly-substance use and overdose prevention, recognition and response including take home naloxone prescription.[79,80]
10. Increase prescribers' capacity for opioid agonist treatments (e.g., methadone and buprenorphine/naloxone) via novel collaborative strategies.

LONG-TERM STRATEGIES TO IMPROVE PRESCRIBER KNOWLEDGE

11. Invest in BC's medical curricula and continuing medical education for physicians, nurses and other clinicians in addiction diagnosis, treatment and recovery; pain management including the use of non-opioid analgesics; and safe opioid prescribing, including the potential for serious adverse effects when opioids are co-prescribed with benzodiazepines and other psychotropic medications.[38,81]

12. Coinciding with benzodiazepines transitioning to a duplicate prescription requirement, investment should be made in education for BC prescribers on the known serious harms and clinical limitations of benzodiazepines, as well as the availability of safer alternatives.[82]
13. Support research and educational interventions in emergency departments to enhance safer opioid prescribing practices in this setting.[83-86]

If these evidence-based recommendations are enacted quickly, BC has the potential to dramatically reduce fatal overdoses, abuse, addiction and other severe harms related to unsafe opioid prescribing.

Together, we can do this. The time for action is now.

Table 2. Advantages and disadvantages of methadone vs. buprenorphine/naloxone

ADVANTAGES

METHADONE	BUPRENORPHINE/NALOXONE
• Potentially better treatment retention • May be easier to initiate treatment • No maximum dose • Potentially better alternative if buprenorphine was unsuccessful in relieving withdrawal symptoms, or was associated with severe side effects • Approved in Canada for the primary purpose of pain control (as split dose BID or TID dosing; Health Canada exemption to prescribe methadone for analgesia also required)	• Less risk of overdose due to partial agonist effect and ceiling effect for respiratory depression (in the absence of benzodiazepines or alcohol) • Reduced risk of injection, diversion, and overdose due to naloxone component, allowing for safer take-home dosing schedules • Milder side effect profile • Easier to rotate from buprenorphine/naloxone to methadone • More flexible take-home dosing schedules may contribute to increased cost savings and patient autonomy • Shorter time to achieve therapeutic dose (1-3 days) • Potentially more effective analgesic for treatment of concurrent pain (however, see disadvantages) • Fewer drug interactions • Milder withdrawal symptoms and easier to discontinue, thus may be a better option for individuals with lower intensity opioid dependence (e.g., oral opioid dependence, infrequent opioid users, infrequent or non-injectors, short history of opioid dependence) and individuals anticipated to be successfully tapered off maintenance treatment in a relatively short period of time

DISADVANTAGES

METHADONE

- Higher risk of overdose, particularly during treatment initiation
- Generally requires daily witnessed ingestion
- More severe side effect profile (e.g., sedation, weight gain, erectile dysfunction)
- More expensive if daily witnessed ingestion required
- Longer time to achieve therapeutic dose (>35 days)
- More difficult to transition to buprenorphine once on methadone
- Higher potential for adverse drug-drug interactions (e.g., antibiotics, antidepressants, antiretrovirals)
- Higher risk of non-medical or other problematic use
- Increased risk of cardiac arrhythmias as a result of QTc prolongation

BUPRENORPHINE/NALOXONE

- Potentially higher risk of drop-out
- May cause precipitated withdrawal if induced inappropriately
- Doses may be suboptimal for individuals with high opioid tolerance
- May block opioid analgesics used for concurrent pain treatment
- Not approved in Canada for the primary purpose of pain control

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ADDICTION

SSA SOCIETY FOR THE STUDY OF ADDICTION

RESEARCH REPORT

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Impact of treatment for opioid dependence on fatal drug-related poisoning: a national cohort study in England

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ABSTRACT

Aims To compare the change in illicit opioid users' risk of fatal drug-related poisoning (DRP) associated with opioid agonist pharmacotherapy (OAP) and psychological support, and investigate the modifying effect of patient characteristics, criminal justice system (CJS) referral and treatment completion. **Design** National data linkage cohort study of the English National Drug Treatment Monitoring System and the Office for National Statistics national mortality database. Data were analysed using survival methods. **Setting** All services in England that provide publicly funded, structured treatment for illicit opioid users. **Participants** Adults treated for opioid dependence during April 2005 to March 2009: 151 983 individuals; 69% male; median age 32.6 with 442 950 person-years of observation. **Measurements** The outcome was fatal DRP occurring during periods in or out of treatment, with adjustment for age, gender, substances used, injecting status and CJS referral. **Findings** There were 1499 DRP deaths [3.4 per 1000 person-years, 95% confidence interval (CI) = 3.2–3.6]. DRP risk increased while patients were not enrolled in any treatment [adjusted hazard ratio (aHR) = 1.73, 95% CI = 1.55–1.92]. Risk when enrolled only in a psychological intervention was double that during OAP (aHR = 2.07, 95% CI = 1.75–2.46). The increased risk when out of treatment was greater for men (aHR = 1.88, 95% CI = 1.67–2.12), illicit drug injectors (aHR = 2.27, 95% CI = 1.97–2.62) and those reporting problematic alcohol use (aHR = 2.37, 95% CI = 1.90–2.98). **Conclusions** Patients who received only psychological support for opioid

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- There were **1499 DRP**
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  - men
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injecting status and CJS referral. **Findings** There were 1499 DRP deaths [3.4 per 1000 person-years, 95% confidence interval (CI) = 3.2–3.6]. DRP risk increased while patients were not enrolled in any treatment [adjusted hazard ratio (aHR) = 1.73, 95% CI = 1.55–1.92]. Risk when enrolled only in a psychological intervention was double that during OAP (aHR = 2.07, 95% CI = 1.75–2.46). The increased risk when out of treatment was greater for men (aHR = 1.88, 95% CI = 1.67–2.12), illicit drug injectors (aHR = 2.27, 95% CI = 1.97–2.62) and those reporting problematic alcohol use (aHR = 2.37, 95% CI = 1.90–2.98). **Conclusions** Patients who received only psychological support for opioid