



Opioid Use Disorder

Welcome
We will begin shortly.




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Today's Speaker(s)

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Pharmacist Consultant, Infinity Medical Specialists Clinic
Clinical Instructor, University of British Columbia



Disclosure(s)

None related to the development of this presentation

I respectfully acknowledge that I am a humble guest on the unceded traditional territories of the Musqueam, Squamish, and Tsleil-Waututh Nations.

Outline of our time

- **Background**
- **National Guideline Development**
- **Medications:**
 - Methadone
 - Suboxone (Buprenorphine/Naloxone)
 - Microdosing (not in guideline)
 - Slow Release Oral Morphine
 - iOAT (not in guideline)
- **Stigma**

What is happening in the news?





BC Coroners Service, Illicit Drug Overdose Deaths in BC, January 1, 2008 – July 31, 2018
<https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/statistical/illicit-drug.pdf>

Images from StopOverdoseBC.ca campaign

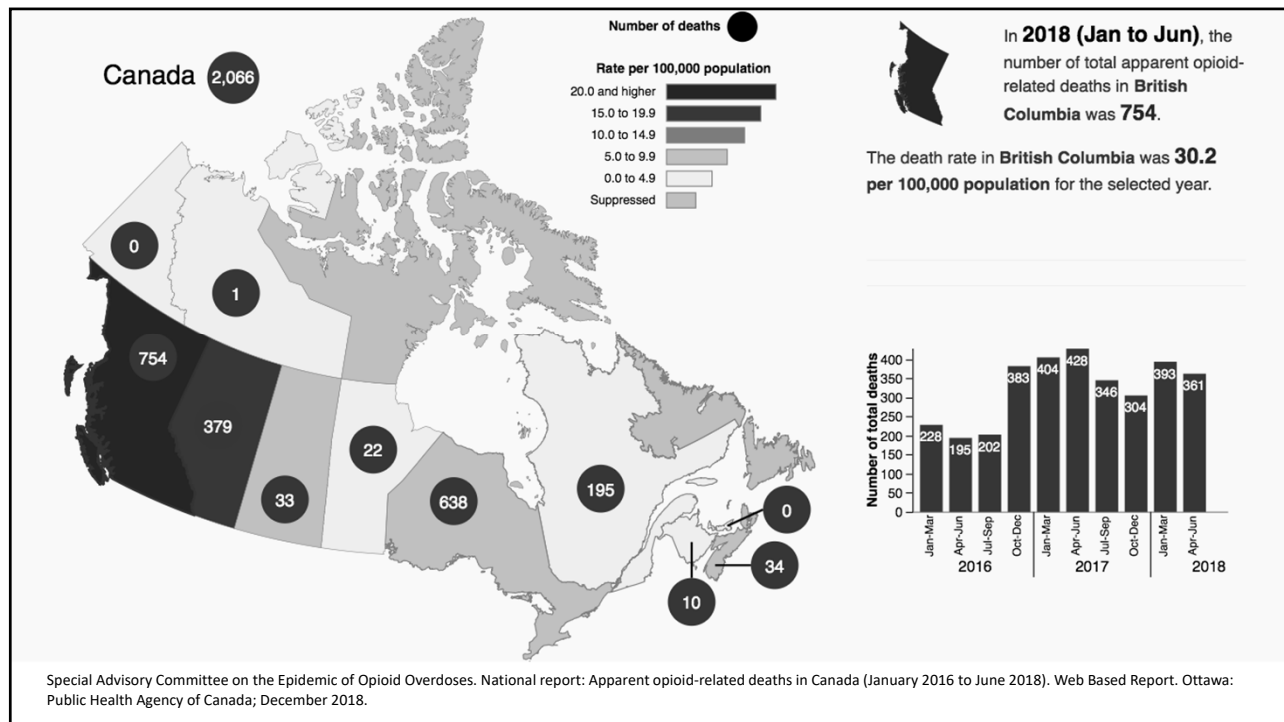
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Key Findings from the National report

Apparent opioid-related deaths in Canada (released November 2018)

- The opioid crisis has affected every part of the country, but some provinces and territories have been impacted more than others. According to data reported as of November 16, 2018: there were **9,078** apparent opioid-related deaths between January 2016 and June 2018
- in 2016, there were **3,014** apparent opioid-related deaths (corresponding to a death rate of **8.3 per 100,000** population) and
- In 2017, there were **3,998** apparent opioid-related deaths (corresponding to a death rate of **10.9 per 100,000** population)
- from January to June 2018, there were **2,066** apparent opioid-related deaths, corresponding to a death rate of **11.2 per 100,000** population
- Special Advisory Committee on the Epidemic of Opioid Overdoses. National report: Apparent opioid-related deaths in Canada (January 2016 to June 2018). Web Based Report. Ottawa: Public Health Agency of Canada; December 2018.



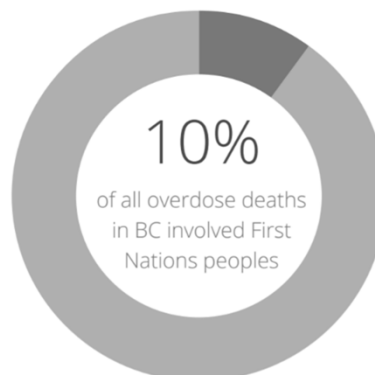
- Most accidental apparent opioid-related deaths were among young and middle aged adults
 - 20% were individuals between the ages of 20 and 29
 - 27% were between the ages of 30 and 39, and
 - 21% were between the ages of 40-49.
- The Canadian Institute for Health Information found that between 2016 and 2017, rates of emergency department visits due to opioid poisoning rose in Ontario and Alberta by 73% and 23%, respectively.
- Based on available emergency medical services data between January and June 2018, 71% of suspected opioid-related overdoses occurred among men.

<https://www.canada.ca/en/health-canada/services/substance-use/problematic-prescription-drug-use/opioids/data-surveillance-research/harms-deaths.html>

Opioid overdose crisis has a disproportionate impact on First Nations in BC



First Nations people are **5X** more likely than non-First Nations to experience an overdose event



First Nations people are **3X** more likely than non-First Nations to die due to an overdose

First Nations Health Authority, Overdose Data and First Nations in BC Preliminary Findings
http://www.fnha.ca/newsContent/Documents/FNHA_OverdoseDataAndFirstNationsInBC_PreliminaryFindings_FinalWeb_July2017.pdf

Why First Nations are at a greater risk for opioid overdoses

- Racism toward First Nations and intergenerational trauma are barriers to health care
- Intergenerational trauma is associated with risk of substance use
- First Nations peoples report reduced access to mental health and addiction treatment prevention sites

First Nations Health Authority, Overdose Data and First Nations in BC Preliminary Findings
http://www.fnha.ca/newsContent/Documents/FNHA_OverdoseDataAndFirstNationsInBC_PreliminaryFindings_FinalWeb_July2017.pdf

Cultural Safety

- Cultural safety is an outcome based on respectful engagement that recognizes and strives to address power imbalances inherent in the healthcare system.
- It results in an environment free of racism and discrimination, where people feel safe when receiving health care.

Cultural Humility

- Cultural humility is a process of self-reflection to understand personal and systemic conditioned biases, and to develop and maintain respectful processes and relationships based on mutual trust.
- Cultural humility involves humbly acknowledging oneself as a life-long learner when it comes to understanding another's experience.

Prescription Opioids and Heroin/Fentanyl

- Efforts to reduce opioid prescribing created **inadvertent vacuum in illicit opioid supply**
- Heroin became a **cheaper, more accessible alternative**
- **Increasing contamination** of heroin and other high-potency synthetic opioids (eg. carfentanil)

Systemic Racism

- Systemic racism is enacted through societal systems, structures and institutions in the form of “requirements, conditions, practices, policies or processes that maintain and reproduce avoidable and unfair inequalities across ethnic/racial groups”.
- It is commonly manifested in social exclusion and isolation that limits access to and participation in social systems.



POLL – Do you know about the Good Samaritan Overdose Act?

Tell people about the Good Samaritan Overdose Act

Government of Canada, Good Samaritan Drug Overdose Act,
<https://www.canada.ca/en/health-canada/services/publications/healthy-living/good-samaritan-drug-overdose-act-poster.html>, <https://www.canada.ca/en/health-canada/services/substance-abuse/prescription-drug-abuse/opioids/about-good-samaritan-drug-overdose-act.html>

Suspect an
Overdose?
Stay and
CALL 911

Canada's new
Good Samaritan law
can protect you.

Learn more at Canada.ca/Opioids
 Together we can **#StopOverdoses**

 Government of Canada / Gouvernement du Canada 



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Know how to use and talk about Naloxone



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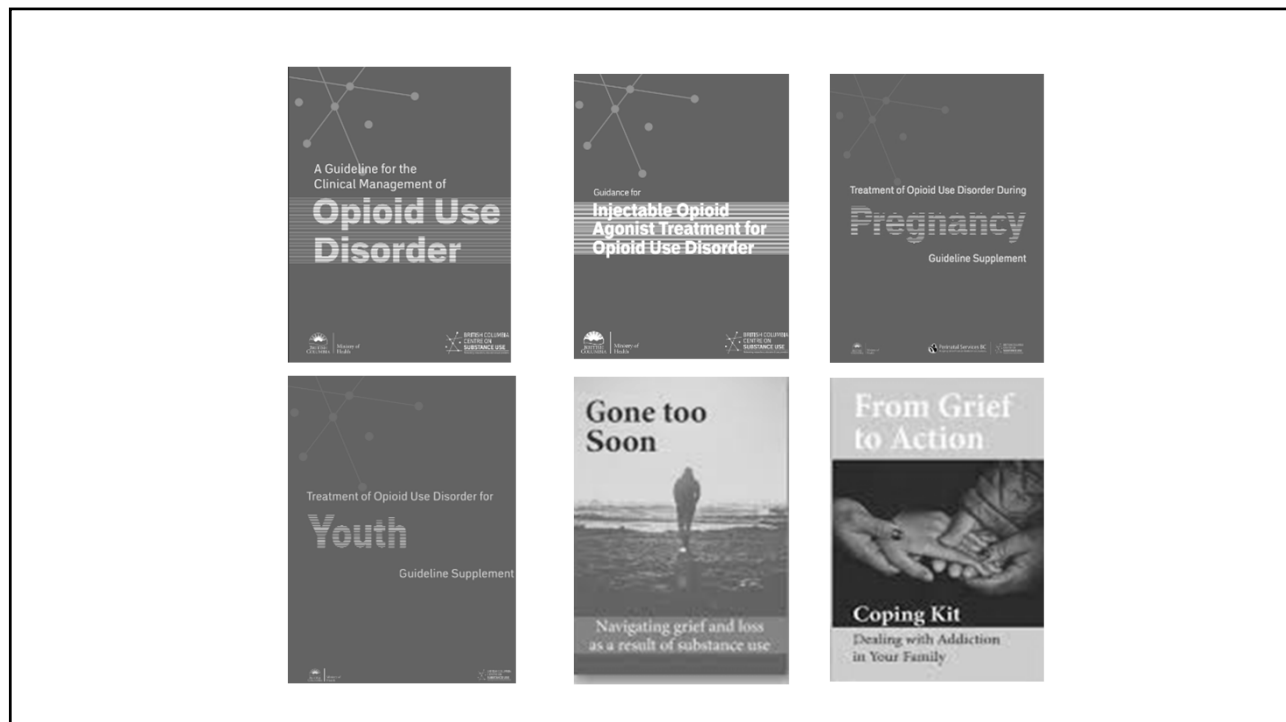
What's included in What's included

- 2 to 3 Safety Syringes
- 2 to 3 (0.4mg) Ampoules of Naloxone
- Alcohol Swabs
- Mouthpiece for mouth-to-mouth resuscitation
- Gloves
- Overdose Response Information form
- Instructions such as the “SAVE ME Instructions” in some provinces



BC Centre on Substance Use & Guidelines

- BC Centre on Substance Use (BCCSU), is the provincial organization with a mandate to develop, implement and evaluate evidence-based approaches to substance use and addiction.
- In June 2017, the BCCSU released, “*A Guideline for the Clinical Management of Opioid Use Disorder*”.
- In October 2017, the BCCSU released, “*Guidance for Injectable Opioid Agonist Treatment for Opioid Use Disorder*”.
- New guidelines are for all clinicians who prescribe OAT and iOAT drugs (i.e., methadone, slow release oral morphine and buprenorphine/naloxone, and primarily hydromorphone) for treatment of patients with opioid use disorder.



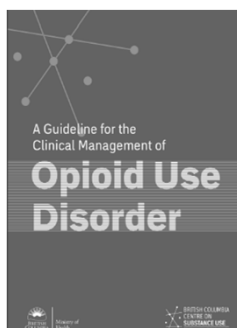
Canadian Research Initiative in Substance Misuse (CRISM)

- Funded by the Canadian Institutes of Health Research (CIHR)
- National research consortium focused on substance use disorder, comprising four large interdisciplinary regional teams (nodes)
 - British Columbia
 - the Prairie Provinces
 - Ontario
 - Quebec/Atlantic
- Each CRISM node is an expert network of research scientists, service providers, policy-makers, community leaders, and people with lived experience of substance use disorder.
- CRISM's mission is to translate the best scientific evidence into clinical practice and policy change.

Development of CRISM National Guidelines for the Clinical Management of Opioid Use Disorder



VCH Opioid Guidelines, 2015



BC Opioid Guidelines, 2017



National Opioid Guidelines, 2018



Other Provincial Opioid Guidelines



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GUIDELINE ■ VULNERABLE POPULATIONS **CPD**

Management of opioid use disorders: a national clinical practice guideline

Julie Bruneau MD MSc, Keith Ahamad MD, Marie-Ève Goyer MD MSc, Ginette Poulin MD, Peter Selby MBBS MHSc, Benedikt Fischer PhD, T. Cameron Wild PhD, Evan Wood MD PhD; on behalf of the CIHR Canadian Research Initiative in Substance Misuse

■ Cite as: *CMAJ* 2018 March 5;190:E247-57. doi: 10.1503/cmaj.170958

DSM-5 Clinical Diagnostic Criteria for Opioid Use Disorder

1	Opioids are often taken in larger amounts or over a longer period than was intended	The presence of at least 2 of these symptoms indicates an Opioid Use Disorder (OUD)
2	There is a persistent desire or unsuccessful efforts to cut down or control opioid use	
3	A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects	
4	Craving or a strong desire to use opioids	
5	Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home	The severity of the OUD is defined as:
6	Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids	
7	Important social, occupational, or recreational activities are given up or reduced because of opioid use	
8	Recurrent opioid use in situations in which it is physically hazardous	MILD: The presence of 2 to 3 symptoms
9	Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.	MODERATE: The presence of 4 to 5 symptoms
10	Tolerance*, as defined by either of the following: a) Need for markedly increased amounts of opioids to achieve intoxication or desired effect b) Markedly diminished effect with continued use of the same amount of opioid	SEVERE: The presence of 6 or more symptoms
11	Withdrawal*, as manifested by either of the following: a) Characteristic opioid withdrawal syndrome b) Same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms	

* Patients who are prescribed opioid medications for analgesia may exhibit these two criteria (withdrawal and tolerance), but would not necessarily be considered to have a substance use disorder.

Reference:

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5™ 5th ed. Arlington, VA: American Psychiatric Publishing, Inc.

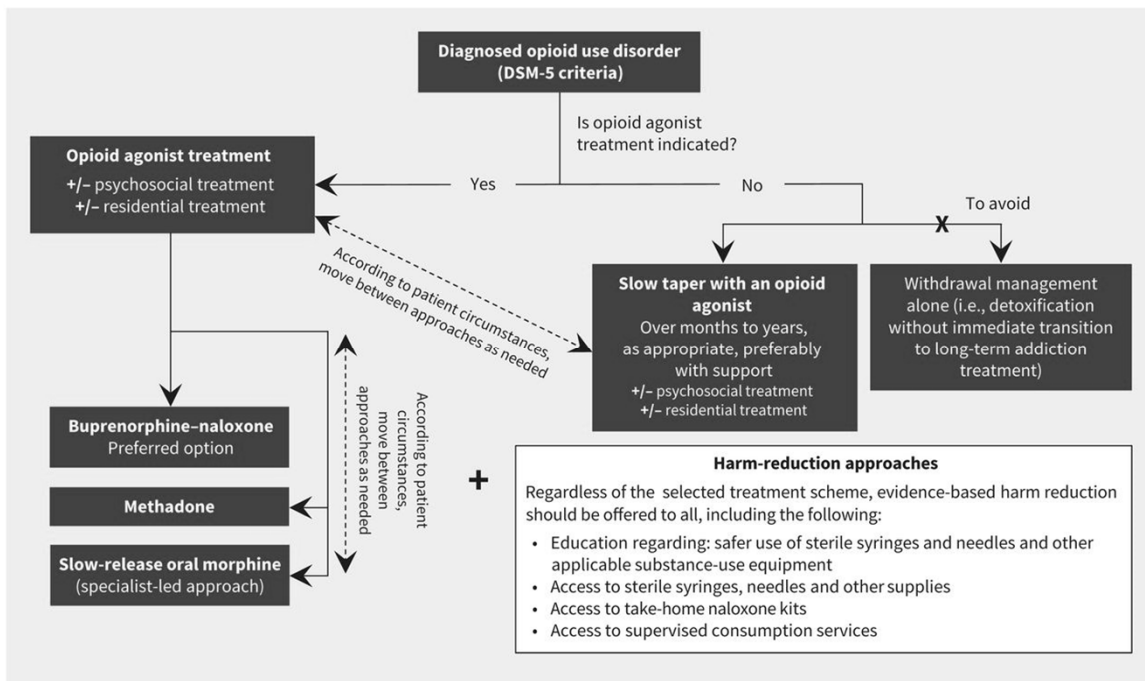
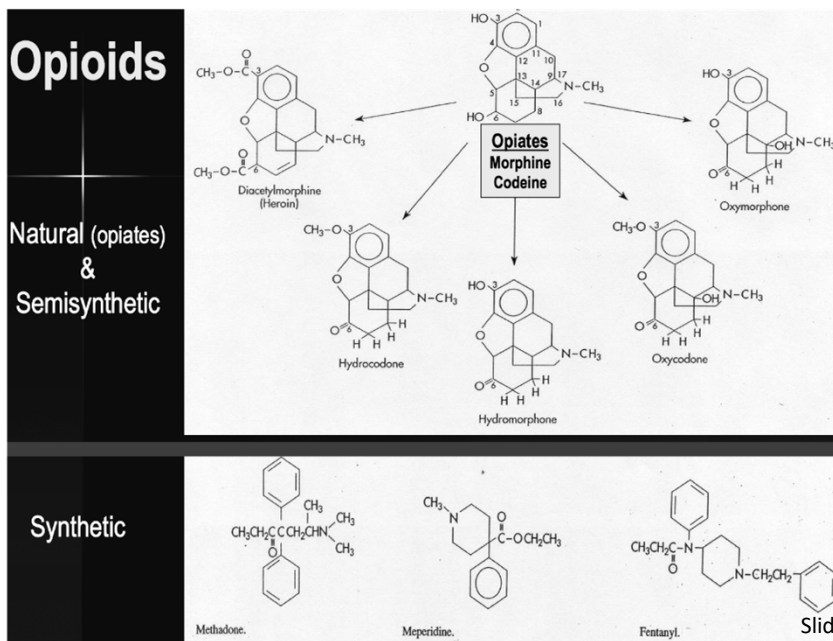
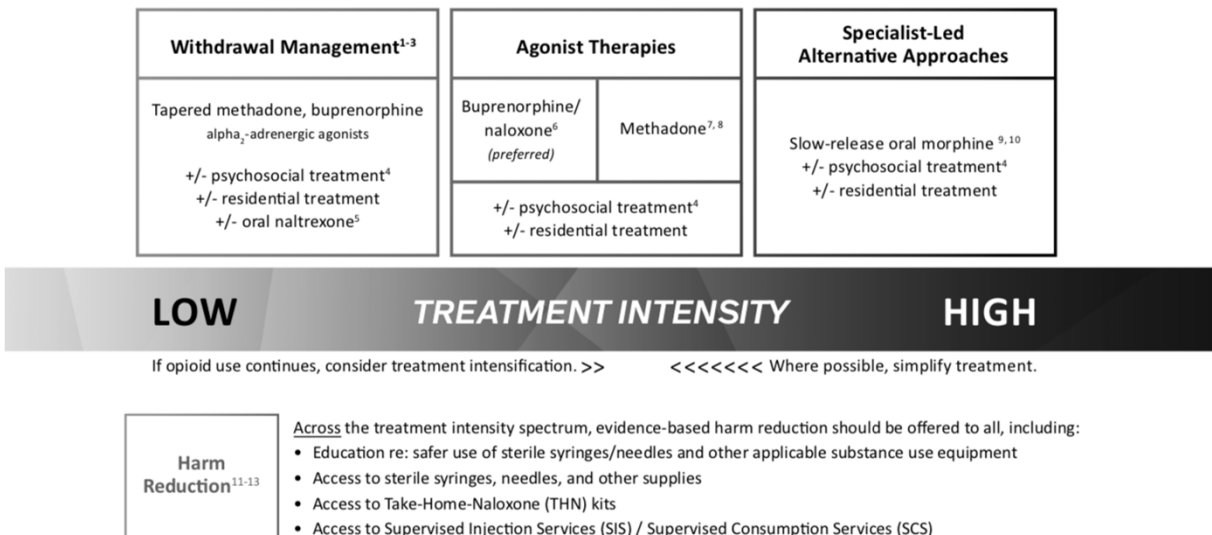


Figure 2. Clinical management of opioid use disorder



Slide courtesy of Dr. Mark McLean

Opioid Receptors and Function

RECEPTOR TYPE	MU	DELTA	KAPPA
SUPRASPINAL ANALGESIA	+++	-	-
SPINAL ANALGESIA	++	++	+
PERIPHERAL ANALGESIA	++	-	++
RESPIRATORY DEPRESSION	+++	++	-
CONSTIPATION	++	++	+
EUPHORIA	+++	-	-
DYSPHORIA	-	-	+++
SEDATION	++	-	++
PHYSICAL DEPENDENCE	+++	-	+

Slide courtesy of Dr. Mark McLean



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Methadone

- Has been used since 1950s for treatment of OUD
 - Thorough body of literature with established benefits in treatment of OUD in dose-dependent manner
 - Use is also associated with reduced risk of HIV and HCV transmission, and improved ARV adherence
 - Unfortunately, most patients tapering off methadone within the first year will return to opioid use
- Last few years – Commercially available methadose 10mg/mL available for coverage
- 2018 period – Canadian guidelines (buprenorphine/naloxone first line for OUD)
- Dec 2018 – Mandatory OAT training by regulatory College in BC



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Detailed treatment procedures and dosing protocols are province-specific and therefore outside the scope of the provincial guidelines document.

Healthcare professionals should refer to provincial guidelines for this information, for example:

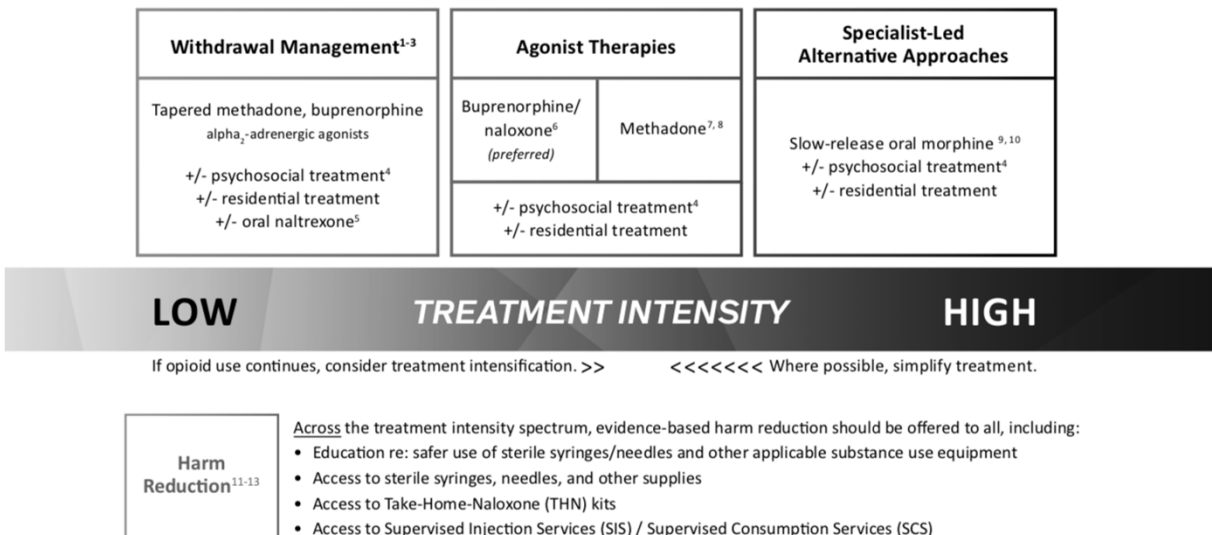
- British Columbia: A Guideline for the Clinical Management of Opioid Use Disorder
- Manitoba: Manitoba Methadone & Buprenorphine Maintenance – Recommended Practice
- CAMH: Buprenorphine/Naloxone for Opioid Dependence: Clinical Practice Guideline
- Quebec: La buprénorphine dans le traitement de la dépendance aux opioïdes

Sample Missed Dose Protocol Chart from BC Provincial Guideline

Suggested Protocol for Managing Missed Doses

Missed Days (consecutive)	Dose	Suggested Dose Adjustment
1-2	Any dose	Same dose (no change)
	30 mg	Same dose (no change)
3-4	31-60 mg	Restart at 30 mg (lower dose if safety concerns)
	> 60 mg	Restart at 50% of previous dose
5 or more	Any dose	Restart at 5-30 mg (depending on tolerance)

Figure 2. Clinical management of opioid use disorder

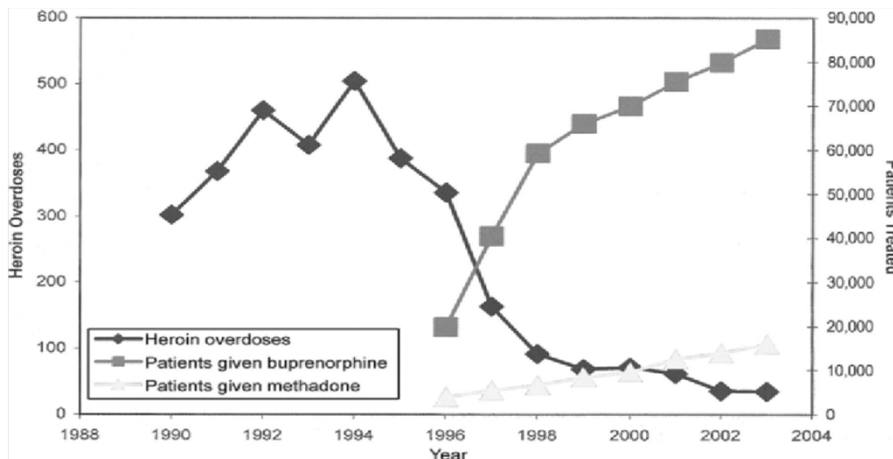


Buprenorphine/Naloxone

- Buprenorphine/Naloxone is the preferred first-line OAT for treating patients with an opioid use disorder.
- Buprenorphine/Naloxone is a 4:1 combined formulation of buprenorphine and naloxone administered as a sublingual tablet(s).



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

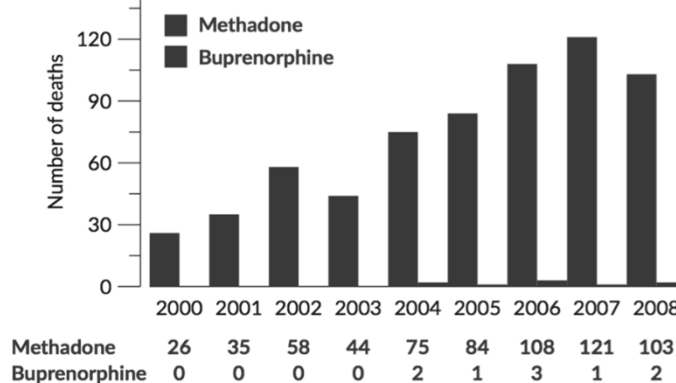


**80%
reduction in
overdose
deaths**

Carrieri et al., 2006

Figure 4

Methadone and buprenorphine deaths reported to US poison control centres.



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

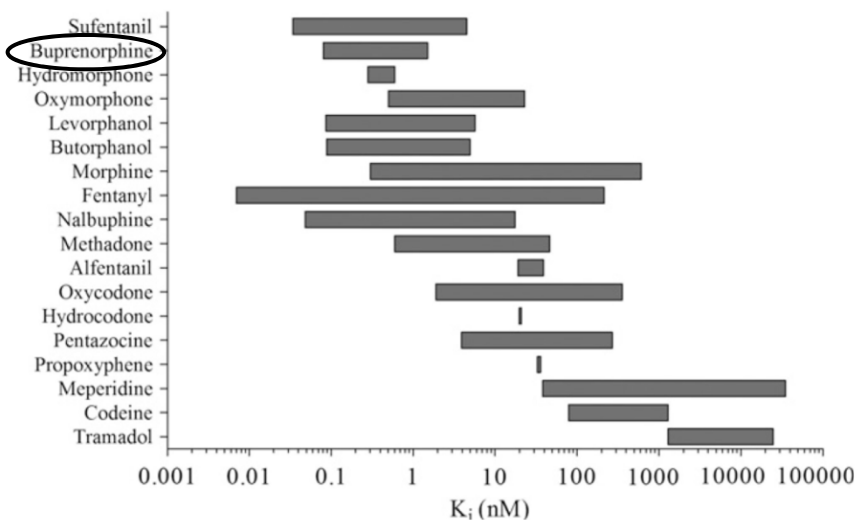
Bioavailability

	Buprenorphine	Naloxone
Oral	3%	~0%
Sublingual	55%	<5%
Parenteral	<5%	70%

Partial Mu Agonist and Kappa Antagonist

RECEPTOR TYPE	MU	DELTA	KAPPA
SUPRASPINAL ANALGESIA	+++	-	- ★
SPINAL ANALGESIA	++	++	+
PERIPHERAL ANALGESIA	++	-	++
RESPIRATORY DEPRESSION	+++	++	-
CONSTIPATION	++	++	+
EUPHORIA	+++	-	-
DYSPHORIA	-	-	+++
SEDATION	++	-	++
PHYSICAL DEPENDENCE	+++	-	+

High Binding Affinity



Volpe, 2011

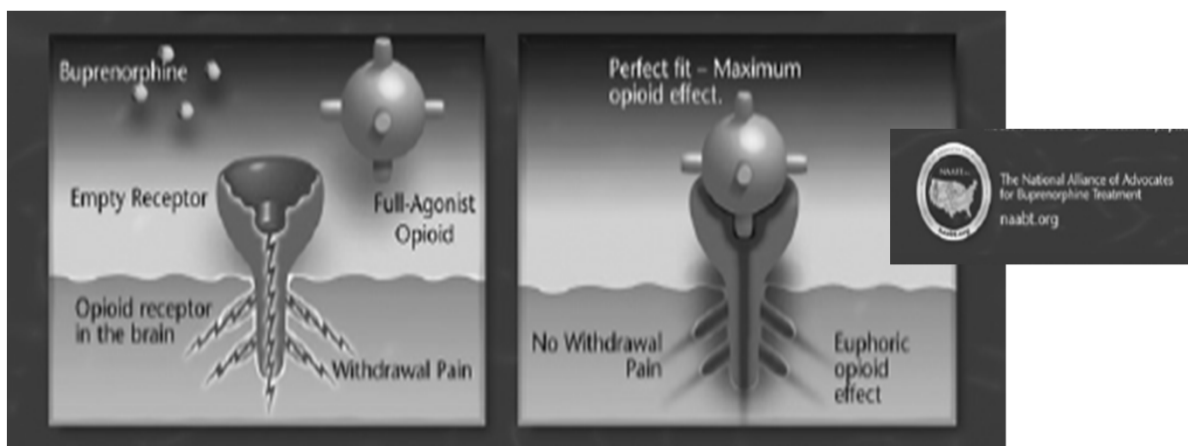


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Lower Intrinsic Activity

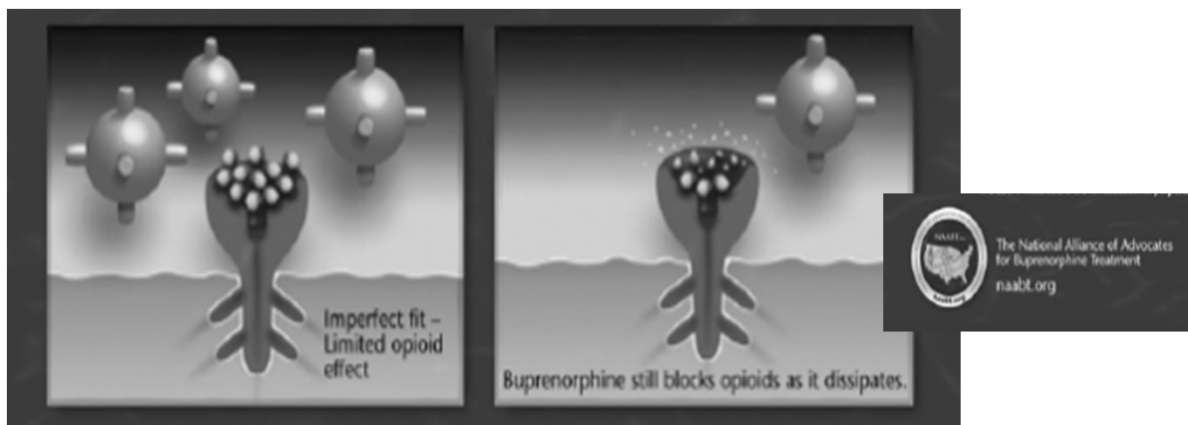


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Lower Intrinsic Activity



How Does Buprenorphine-Naloxone Compare to Methadone?

Methadone	Buprenorphine-Naloxone
Higher risk for overdose, particularly during treatment initiation	Decreased risk of overdose and parenteral abuse
Full mu agonist	Partial mu agonist
Generally requires daily witnessed ingestion in pharmacy	Allows for safer take home schedules
More severe side effect profile including CNS/Respiratory depression	Milder side effect profile
Long time to achieve therapeutic dose (weeks-months)	Rapid titration to achieve therapeutic dose (hours-days)
Higher potential for drug-drug interactions (i.e. ABx, ARVs)	Lower potential for drug interactions, monitor for meds metabolized by CYP 3A4
Increased cardiac arrhythmias as a result of QTc prolongation	Decreased risk of QTc prolongation

Sample Missed Dose Protocol Chart from BC Provincial Guideline for Buprenorphine/Naloxone

- a. For missed doses ≤ 5 days, resume previous dose.
- b. For missed doses ≥ 6 days, a conservative dosing guideline is:

Dose	Number of Missed Days	Suggested Dose Adjustment
2 mg/0.5 mg–4 mg/1 mg	≥ 6 days	No change
6 mg/1.5 mg–8 mg/2 mg	≥ 6 days	Restart at 4 mg/1 mg
> 8 mg/2 mg	6–7 days	Restart at 8 mg/2 mg
> 8 mg/2 mg	> 7 days	Restart at 4 mg/1 mg

- c. For missed doses with relapse or return to full agonist opioid use, advise patient to suspend use of buprenorphine/naloxone until they are ready to resume opioid agonist treatment. Schedule a new induction date and proceed as described in steps 1 and 2 above.
- d. For missed doses with an alternating day schedule, it is recommended that if a patient misses two consecutive alternating day doses, buprenorphine/naloxone should be suspended pending reassessment by a clinician. Patients should be returned to a daily dose schedule, possibly at a lowered dose, to re-stabilize prior to resuming an alternating day schedule.



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Alternative: What about Microdosing Protocol? (not in any guidelines but pharmacists have been seeing this)

- Recent case report in 2016 using “Bernese” method of gradually introducing small doses of buprenorphine-naloxone without stopping the full-agonist opioid
- Increasingly used by Addictions Teams in various parts of the country, not evidence-based or within recommended guidelines



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Alternative: Microdosing Protocol

Substance Abuse and Rehabilitation

Dovepress

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Open Access Full Text Article

CASE SERIES

Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method

This article was published in the following Dove Press journal:
Substance Abuse and Rehabilitation
20 July 2016
Number of times this article has been viewed

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University of Basel Psychiatric
Hospital, Basel, Switzerland

Background: Buprenorphine is a partial μ -opioid receptor agonist used for maintenance treatment of opioid dependence. Because of the partial agonism and high receptor affinity, it may precipitate withdrawal symptoms during induction in persons on full μ -opioid receptor agonists. Therefore, current guidelines and drug labels recommend leaving a sufficient time period since the last full agonist use, waiting for clear and objective withdrawal symptoms, and reducing pre-existing full agonist therapies before administering buprenorphine. However, even with these precautions, for many patients the induction of buprenorphine is a difficult experience, due to withdrawal symptoms. Furthermore, tapering of the full agonist bears the risk of relapse to illicit opioid use.

Cases: We present two cases of successful initiation of buprenorphine treatment with the Bernese method, ie, gradual induction overlapping with full agonist use. The first patient began buprenorphine with overlapping street heroin use after repeatedly experiencing relapse, withdrawal, and trauma reactivation symptoms during conventional induction. The second patient was maintained on high doses of diacetylmorphine (ie, pharmaceutical heroin) and methadone during induction. Both patients tolerated the induction procedure well and reported only mild withdrawal symptoms.

Discussion: Overlapping induction of buprenorphine maintenance treatment with full μ -opioid receptor agonist use is feasible and may be associated with better tolerability and acceptability in some patients compared to the conventional method of induction.



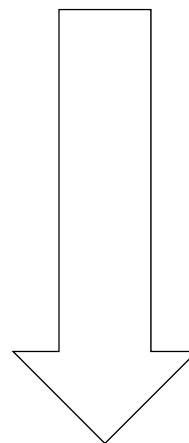
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Alternative: Microdosing Protocol

- Local protocol is typically:
 - Day 1: 0.5 mg SL od, continue full-agonist opioid
 - Day 2: 0.5 mg SL bid
 - Day 3: 1 mg SL bid
 - Day 4: 2 mg SL bid
 - Day 5: 3 mg SL bid
 - Day 6: 4 mg SL bid
 - Day 7: 12 mg SL od, stop full-agonist opioid



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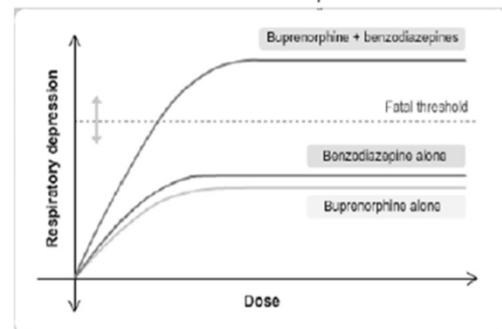
Ongoing Management

- Follow-up assessments:
 - adequacy of dosage, side effects, substance use
 - Start with weekly visits, can decrease frequency of visits with increased stability
- Take-home dosing may be provided at any time at the discretion of the provider, however it is recommended to begin with daily dosing
- Review safe storage, assess risk of diversion, caution about combined alcohol/BZD use

Buprenorphine-Naloxone and Adverse Drug Reactions

- Most common: headache, nausea, dry mouth
- Respiratory/CNS depression is very rare, but increased risk when used in combination with alcohol or other sedative-hypnotics

Additive Effects of Buprenorphine and Benzodiazepines



Suboxone Education Program

Buprenorphine-Naloxone Contraindications

- Caution in patients with severe hepatic or respiratory disease
- History of hypersensitivity reactions to either buprenorphine or naloxone
- Pregnancy: typically Rx buprenorphine-only formulation (Subutex), with superior outcomes in pregnancy

Figure 2. Clinical management of opioid use disorder

Withdrawal Management ¹⁻³	Agonist Therapies		Specialist-Led Alternative Approaches
Tapered methadone, buprenorphine alpha ₂ -adrenergic agonists +/- psychosocial treatment ⁴ +/- residential treatment +/- oral naltrexone ⁵	Buprenorphine/ naloxone ⁶ (preferred)	Methadone ^{7,8}	Slow-release oral morphine ^{9,10} +/- psychosocial treatment ⁴ +/- residential treatment
	+/- psychosocial treatment ⁴ +/- residential treatment		

LOW

TREATMENT INTENSITY

HIGH

If opioid use continues, consider treatment intensification. >>

<<<<<< Where possible, simplify treatment.

**Harm
Reduction**¹¹⁻¹³

Across the treatment intensity spectrum, evidence-based harm reduction should be offered to all, including:

- Education re: safer use of sterile syringes/needles and other applicable substance use equipment
- Access to sterile syringes, needles, and other supplies
- Access to Take-Home-Naloxone (THN) kits
- Access to Supervised Injection Services (SIS) / Supervised Consumption Services (SCS)

Slow Release Oral Morphine (SROM)

- OAT with SROM (24 hour formulation) prescribed as once-daily witnessed doses.
- May be considered for patients who have not benefited from treatment with first and second-line treatment options (i.e., buprenorphine/naloxone and methadone).

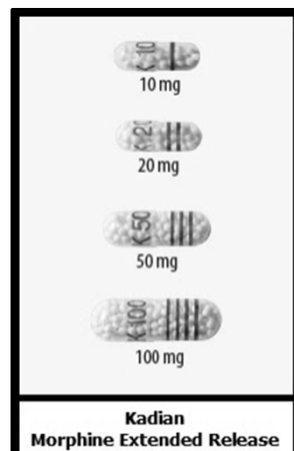


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	+/- psychosocial treatment ⁴ +/- residential treatment		

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- Access to sterile syringes, needles, and other supplies
- Access to Take-Home-Naloxone (THN) kits
- Access to Supervised Injection Services (SIS) / Supervised Consumption Services (SCS)

Injectable Opioid Agonist Therapy (iOAT) (not in Canadian guidelines but in the iOAT supplemental guideline in BC)

- OAT therapy, whether oral or injectable, is designed to prevent withdrawal symptoms and manage cravings.
- OAT therapy replaces ongoing injection use of non-medical drugs that may be adulterated, with safe, pharmaceutical-grade opioid agonists in safe and hygienic environments.
- OAT therapy aims to reduce the potential harms of IV drug use.
- iOAT is indicated for individuals who have not benefited from oral OAT (i.e., methadone, buprenorphine/naloxone, and/or slow-release oral morphine).

iOAT

BCCSU Guideline:

- Injectable OAT is highest intensity treatment option available for people with severe opioid use disorders who have been unsuccessful with lower-intensity treatment options.
 - Diacetylmorphine (prescription heroin) available to small # of patients in BC
 - Injectable hydromorphone
- Patients must be prepared to attend for supervised injection at least daily.
- Patients should be supported and encouraged to move from iOAT to oral OAT (i.e., methadone, buprenorphine/naloxone, or slow-release oral morphine).
- (Some pharmacists have seen use of oral opioid agonist therapies for use during the night in conjunction to injections during the day)



iOAT BCCSU Guideline

Three potential models of care:

1. Comprehensive and dedicated supervised iOAT program (clients can access a full complement of care in one setting);
2. An integrated or embedded supervised iOAT program (for clients in a less intensive setting within pre-established services); and,
3. An emerging model, a pharmacy-based supervised iOAT program allowing for access to care in communities where other, more intensive models may not be appropriate or feasible.

How Stigma Contributes to the Opioid Overdose Crisis


- Makes it difficult for people with substance use disorders to ask for help – creating barriers to accessing mental health and addiction treatment
- Creates an environment where people who are addicted to drugs are not seen as victims of a disease
- Those who need help are judged for their addiction and accused of being responsible for their own illness
- Stigmatizing language, shame and judgement prevents constructive dialogue about seeking help



**CO-WORKER
TEAMMATE
DRUG USER
HOCKEY FAN**

People who use drugs are real people.
Get involved. Get informed. Get help.



StopOverdoseBC.ca



**COUSIN
STUDENT
DRUG USER
FRIEND**


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Problematic substance use can affect anybody and it can be difficult to ask for help. Let's work together to #EndStigma around drug use. ow.ly/zV7Q30iZBSm



@GovCanHealth, March 19, 2018.
<https://twitter.com/GovCanHealth/status/975764200898179072>

9:01 AM - 19 Mar 2018

Help Eliminate Stigma

- Learn how to be a safe person to talk with
- Use extra care and respect – come from a place of compassion and empathy
- Recognize that people who use drugs are real people
- Recognize that addiction is a health issue, not a moral issue
- Use respectful language
- Help share the campaign to eliminate stigma

Respectful Language and Stigma

- People-first language – *“Person with a cocaine-use disorder” instead of “cocaine user” or “addict.”*
- Use language that reflects the medical nature of substance use disorders – *“Addictive disease” and “substance use disorder” instead of “abuser” or “junkie.”*
- Use language that promotes recovery – *“Opted not to” and “not in agreement with the treatment plan” instead of “unmotivated” or “non-compliant.”*
- Avoid slang and idioms – *“Positive” or “negative” when referring to drug tests, instead of “dirty” or “clean”*

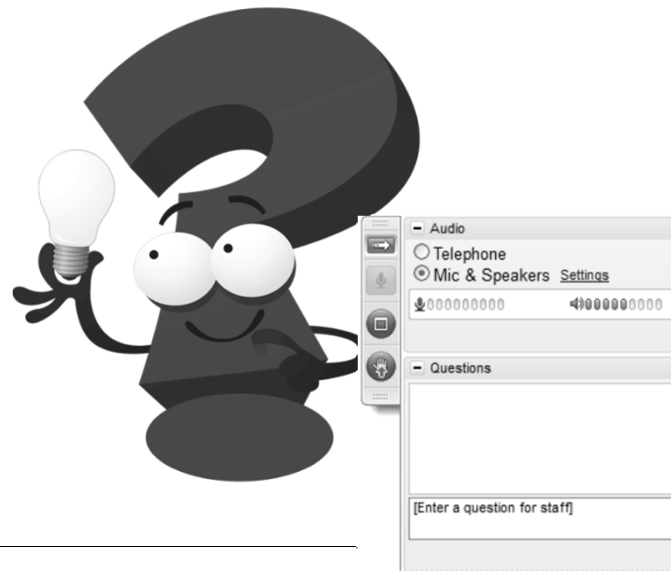
Language matters: reduce stigma, combat overdose, BCCDC, <http://www.bccdc.ca/about/news-stories/news-releases/2017/language-matters>



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Thank you!

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