

Prévention et Prise en charge de l'usage de drogues intraveineuses

Prevention and treatment of intravenous drug use

Une revue des évidences / A review of evidence

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Colloque VIH Océan Indien
Mardi 13 octobre 2015 / Tuesday October 13th 2015
Hôtel Savoy, Beau Vallon
Mahé, Seychelles



Conflits d'intérêts :

Absence

Conflict of interest :

None declared

Introduction

- L'usage illicite d'opiacés est le motif le plus fréquent de recours aux soins pour les usagers de drogues illicites.
- Illicit use of opiates is the main reason for seeking addiction treatment services for illicit drug use throughout the world.*

Degenhardt L, Bucello C, Mathers B, et al. Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. *Addiction* 2011;106:32–51.

- L'usage illicite de drogues injectables est associé à un haut niveau de morbi mortalité.
- Le risque de décès est 15 fois supérieur chez ces sujets comparé à la population générale.
- Ce niveau est lié au **VIH**, au **VHC**, **VHB** et aux **overdoses**, ou encore à la tuberculose.
- Intravenous drug use (IDU) is associated with significant morbidity and mortality related to HIV, hepatitis B, hepatitis C, and overdose.*
- The level of mortality among people who inject drugs is being nearly 15 times higher than would normally be expected among people of comparable age and gender in the general population.*

Degenhardt L, Bucello C, Mathers B, et al. Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. *Addiction* 2011;106:32–51.
UNODC. World Drug Report 2015.

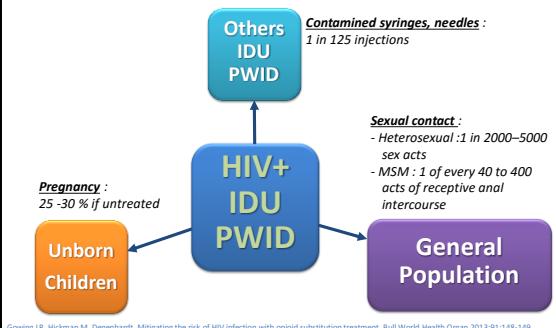
Injection de drogues et VIH

Drug injection and HIV

- 1 injection sur 125**, avec du matériel contaminé par le VIH, entraînera l'infection.
- L'injection avec du matériel contaminé est, avec la transfusion, l'un des risques les plus élevés de contamination.
- HIV infection results from one of every 125 injections with an HIV-contaminated syringe.*

Gowing LR, Hickman M, Degenhardt. Mitigating the risk of HIV infection with opioid substitution treatment. *Bull World Health Organ* 2013;91:148-149.

Risk of HIV infection



Prévalence du VIH chez les injecteurs

HIV prevalence among people who inject drugs

- L'injection de drogues intraveineuse est en moyenne à l'origine de **5 - 10 % des cas de VIH**.
- Ce risque peut atteindre les 40 % dans certains pays
- Injecting drug use accounts for approximatively 5 - 10 % of all cases of HIV.*
- It may be over 40% in many parts of the world.*

Gowing LR, Hickman M, Degenhardt. Mitigating the risk of HIV infection with opioid substitution treatment. Bull World Health Organ 2013;91:148-149.

Prevalence of HIV among people who inject drugs 2013 or latest year available (UNODC. World Drug Report 2015, XI).



Pays Zone Océan Indien	%IDU in HIV new cases	%IDU in cumulative HIV
Madagascar ¹	-	7.1 %
Maurice ²	38 % (92 % in 2005)	44.3 %
Réunion ³	0 %	6 %
Seychelles ⁴	31 %	14 %
Comores	-	-
Mayotte	-	-

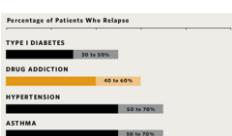
1. Rapport sur la réponse face au VIH et au sida à Madagascar (2014).
2. National AIDS Secretariat. Integrated Biological and Behavioural Studies among People Who Inject Drugs (2013)
3. ORS La Réunion. Infection à VIH et Sida à La Réunion, novembre 2013
4. Ministry of Health (Seychelles). 2014 Annual Epidemiological Report.

Généralités sur l'addiction aux opiacés

Facts about opiates addiction

- L'addiction aux opiacés est une **maladie chronique**
- Sa prise en charge se conçoit dans la durée
- En l'absence de traitement médicamenteux, la poursuite des produits illicites dépasse les 80 %,
- Opioid dependance is a chronic relapsing disorder*
- Treatment for opiate addiction requires long-term management.*
- Behavioral interventions alone have extremely poor outcomes, with more than 80% of patients returning to drug use.*

Bart G. Maintenance medication for opiate addiction: the foundation of recovery. J Addict Dis. 2012;31(3):207-25.



A. Thomas McLellan; David C. Lewis; Charles P. O'Brien; et al. Implications for Treatment, Insurance, and Outcomes Drug Dependence, a Chronic Medical Illness: **JAMA** 2000; 284(13):1689-1695

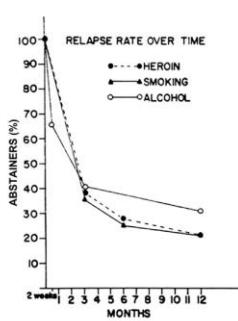


FIGURE 43.1 Relapse rate over time for heroin, smoking, and alcohol. Reproduced with permission from Hunt, W.A., Barnati, L.W., Branch, L.G. 1971. Relapse rates in addiction programs. *Journal of Clinical Psychology*, 27, 455-456.

FRONTIERS IN NEUROSCIENCE: THE SCIENCE OF SUBSTANCE ABUSE Addiction Is a Brain Disease, and It Matters

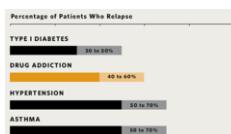
Alan I. Leshner

Scientific advances over the past 20 years have shown that drug addiction is a chronic, relapsing disease that results from the prolonged effects of drugs on the brain. As with many other brain diseases, addiction has affected behavioral and social context aspects that are important to the course of the disorder itself. Thus, effective treatment approaches will include biological, behavioral, and social-context components. Recognizing addiction as a chronic, relapsing brain disorder characterized by compulsive drug seeking and use can impact society's overall health and social policy strategies and help diminish the health and social costs associated with drug abuse and addiction.

Leshner AI. Addiction is a brain disease, it matters. *Science* 1997; Vol. 278 no. 5335 pp. 45-47



Alan I. Leshner was the NIDA's director (National Institute on Drug Abuse)

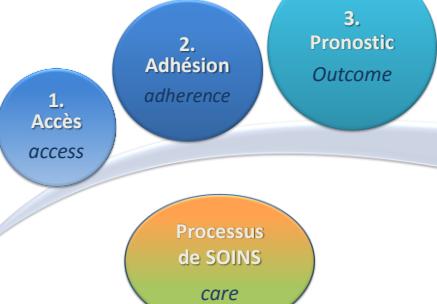


A. Thomas McLellan; David C. Lewis; Charles P. O'Brien; et al. Implications for Treatment, Insurance, and Outcomes Drug Dependence, a Chronic Medical Illness: **JAMA** 2000; 284(13):1689-1695

- Les addictions sont le résultats de l'interaction complexe entre plusieurs paramètres.
 - Une évidence : la problématique ne se limite pas au produit seul.**
 - Pour être efficace, il faut appréhender les addictions de façon globale sous un angle **bio psycho social**.
- Addictive disorders are the results of many parameters.
Evidence : The problem is not only the drug
To be efficient, interest of an approach based on the Biopsychosocial model.*
-

Prises en charge

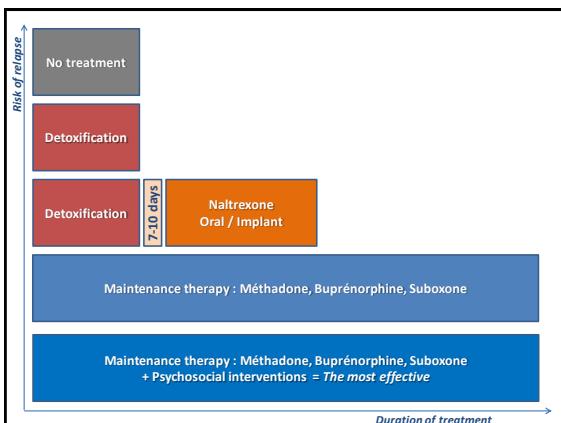
Management of Injection Drug Users



Accès aux soins / Access to Care

- Seul 1 usager de drogue à problème sur 6 a aujourd'hui accès aux soins.
- Only one out of six problem drug users globally has access to treatment.*
- Lorsqu'un usager est pris en charge pour son problème de drogue, il accède également aux autres soins : vaccinations, soins somatiques, psychiatriques. Sa réinsertion sociale, familiale, professionnelle est favorisée

UNODC. World Drug Report 2015.



- Le choix du traitement doit se faire après évaluation et information du l'usager.
- Selection of medication should be based on informed choice following a discussion of outcomes, risks, and benefits of each medication.*
- Le droit au respect du secret médical est fondamental.
- Patients should have the right to privacy. Confidentiality should always be respected*



Sevrage médicalisé

Medically assisted detoxification

- Les méthodes de sevrage sont codifiées.
- *Symptomatic relief (alpha-2 adrenergic agonists), or tapered doses of a substituted opioid (methadone, buprenorphine)*
- Le pronostic à long terme est **défavorable** avec un faible niveau d'abstinence.
- *Detoxification is ineffective in promoting abstinence*

WHO. Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. 2009.
http://www.who.int/substance_abuse/publications/Opioid_dependence_guidelines.pdf

- Les programmes basés sur l'abstinence ont des taux de mortalité supérieurs à ceux qui utilisent un traitement de maintenance.
- *Treatments based on opioid abstinence have a higher mortality rate than opioid agonist maintenance treatment.*
- Dans 4 études, il a été démontré que parmi les patients effectuant un sevrage l'incidence du VIH était augmentée.
- *HIV incidence was reported in four studies to be higher among those undergoing detoxification treatment*

MacArthur GJ, Minozzi S, Martin N, Vickerman P, Deren S, Bruneau J, Degenhardt L, Hickman M. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. BMJ. 2012 Oct 3;345:e5945.

Traitements de substitution

Opioid Substitution Treatment

- Traitements non injectés
- Longue durée d'action avec arrêt des cycles intoxication / sevrage
- Posologie adaptée à chaque individu
- High doses and extended treatment are associated with further reductions in drug use and HIV risk

- Aujourd'hui dans le monde, seuls **6 - 14 %** des injecteurs bénéficient d'un traitement de substitution.
- *The coverage of opiate substitution treatment is variable worldwide, with recent estimates indicating that only 6-12% of people who inject drugs receive it.*

AVAILABLE AGENTS FOR MAINTENANCE TREATMENT OF OPIOID DEPENDENCE

FULL AGONISTS

Methadone
Levo-acetyl-alpha-methadol (LAAM) *Removed*
Morphine sulfate
Heroin (Diamorphine)

PARTIAL AGONISTS

Buprenorphine (ex.SUBUTEX)
Buprenorphine/Naloxone (SUBOXONE, ZUBSOLV,..)
Buprenorphine film
Buprenorphine depot, implant

ANTAGONISTS

Naloxone *Intraveinous use only*
Naltrexone
Depot Naltrexone (VIVITREX,..)

Méthadone

Methadone Maintenance Treatment (MMT)

- Agoniste opiacé de longue durée d'action
- Existe sous forme orale : sirop, gelules voir formes dispersibles, forme injectable.
- *Long-acting, and orally effective, synthetic μ opioid receptor agonist*
- *Administered orally in liquid, tablet, or dispersible tablet formulation. Available also in injectable form.*
- Risques : Overdose, QTc

* Bart G. Maintenance Medication for Opiate Addiction: The Foundation of Recovery. J Addict Dis. 2012 Jul; 31(3): 207–225.

**Dole VP, Nyswander M. A medical treatment for diacetylmorphine (heroin) addiction. A clinical trial with methadone hydrochloride. JAMA 1965 Aug 23;193:646-50.

- La méthadone est le plus prescrit des MSO
 - 50 années de publications et de pratiques^{1,2}.
 - *Methadone is the most commonly prescribed replacement therapy for opioid dependence, the basis, the gold standard.*



1. Dole VP, Nyswander M. A medical treatment for diacetylmorphine (heroin) addiction. A clinical trial with methadone hydrochloride. *JAMA* 1965 Aug 23;193:646-50.
2. Kuehn BM. Methadone treatment marks 40 years. *JAMA* 2005 Aug 24;294(8):887-9.

- La substitution par méthadone s'accompagne de
 - Réduction de moitié de la mortalité
 - Réduction de 54 % du risque de cas de VIH
 - Réduction du craving, des prises d'opiacés illicites
 - Réduction des pratiques d'injection
 - Meilleure adhésion au traitement si VIH, VHC
 - Réduction de la criminalité
 - *Numerous studies have demonstrated that methadone maintenance substantially reduces mortality and morbidity, the risk of new HIV, criminal activity, and illicit opioid use*

Cornish R, Macleod J, Strang J, Vickerman P, Hickman M. Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK General Practice Research Database. BMJ 2010;341:c5475.

MacArthur GI, Minozzi S, Martin N, Vickerman P, Deren S, Bruneau J, Degenhardt L, Hickman M. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. *BMJ* 2012 Oct 3;345:e5945.

Degenhardt L, Mathers B, Vickerman P, Rhodes T, Latkin C, Hickman M. Prevention of HIV infection for people who inject drugs: why individual,

**WHO Model List
of
Essential Medicines**

La méthadone est reconnue comme médicament essentiel par l'OMS depuis 2005

19th List
(April 2015)
Amended August 2015)

Status of this document

This is a reprint of the text on the WHO Medicines website
<http://www.who.int/medicines/publications/essentialmedicines/en/>

BHD : Side effects / Misuse

- Problem of misuse : Intravenous, nasal
 - Deaths associated with buprenorphine have been reported following its more rapid delivery through injection or when combined with benzodiazepines
 - When patients have a history of injecting buprenorphine (either illicitly obtained or prescribed), methadone maintenance should be used in preference to buprenorphine.

Kintz P. Deaths involving buprenorphine: a compendium of French cases. *Forensic Sci Int* 2001 Sep 15; 121(1-2):65-9.
WHO (2009). Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence

Subutex® (Buprenorphine)



- La buprénorphine (BHD) est un **agoniste partiel** semi-synthétique qui possède une haute affinité pour le récepteur μ , un effet agoniste partiel modéré sur les récepteurs δ et κ .
 - *Buprenorphine (BHD) is a semi-synthetic mu opioid partial agonist (high receptor affinity) with weak partial agonist effects at both delta and kappa opioid receptors.*

Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev. 2014 Feb 6;CD002207.

Suboxone® (BHD + Naloxone)

- Buprenorphine presented in a fixed 4:1 ratio combination **with naloxone**.
 - Sublingually to avoid the hepatic first-pass effect.
 - The bioavailability of NLX after sublingual administration is too low to cause severe and protracted withdrawal symptoms.
 - Available :
 - Tablet
 - Film sublingual (US, Australia)

Soyka M. New developments in the management of opioid dependence: focus on sublingual buprenorphine–naloxone. *Subst Abuse Rehabil.* 2015; 6: 1–14.



Suboxone 2 mg/0.5 mg
comprimé sublingual
Buprenorphine/Naloxone

Chaque comprimé sublingual contient 2 mg de buprenorphine sous forme de chlorhydrate de buprenorphine et 0,5 mg de naloxone sous forme de chlorhydrate de naloxone.

7 comprimés sublinguals

Comprimés à 2 mg



Comprimés à 8 mg




- The BUP/NLX film take significantly less time to dissolve than the tablets.
- Patient preference appeared to be higher for the film (61%) than for the tablets (23%).

Sublingual delivery form

- Instruct your patients to place the SUBOXONE Film under the tongue and allow to completely dissolve¹
- Advise patients not to cut, chew, or swallow SUBOXONE Film¹
- Please see full Prescribing Information for additional information on how to use SUBOXONE Film¹

4 dosage strengths

- Available in a variety of 4 dosage strengths—2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, 12 mg/3 mg of buprenorphine and naloxone¹

<http://www.suboxone.com>

Traitements antagonistes

Opioid Antagonist Therapy

- La **Naltrexone** est un antagoniste du récepteur opioïde μ
- Naltrexone is a μ -opioid receptor antagonist that blocks the euphoric effects of heroin and prescription opioids.*
- Elle bloque efficacement les récepteurs morphiniques
- S'envisagent après un sevrage.
- After the completion of opioid withdrawal*

Accompagnement psychosocial

Psychosocial treatment

- Approches cognitivo-comportementales.
- They should be **systematically associated** with medication
- Developing coping skills, self-efficacy.
- Social support network.

- Fréquence des comorbidités psychiatriques : dépression, état de stress post-traumatique.
- high rates of psychiatric comorbidity – in particular, depression and post-traumatic stress disorder

Mesures de réduction des risques

Harm reduction

Programmes d'échanges de seringues

Needle Exchange Program

- A needle exchange program is a very cost-effective and cost-saving program
 - There is compelling evidence that increasing the availability and utilization of sterile injecting equipment by IDUs reduces HIV infection substantially
 - There is no convincing evidence of any major, unintended negative consequences
- WHO (2004). Effectiveness of sterile needle and syringe programming in reducing hiv/aids among injecting drug users
- Vlahov D, Robertson AM, Stratdee SA. Prevention of HIV Infection among drug users in Ressource-limited settings. Clin Infect Dis 2010;50(suppl 3):S114-S121.

• L'efficacité de ces programmes est proportionnelle au volume de seringues mises en circulation ainsi qu'au nombre d'usagers qui en bénéficient.

• *Their effect is likely to be proportional to the volume of needles and syringes distributed and entering circulation and the number of IDUs receiving*

• Un nombre estimé à au-moins 200 seringues par an et par injecteur.

• *Providing 200 sterile needles and syringes per drug injector per year is a figure that is achievable and likely to control HIV infection in this population.*

Autres programmes

- Salles d'injections sous supervisions ou salles d'injection à moindre risque.
- *Supervised injecting centres*

• Ces programmes facilitent l'accès aux soins de patients souvent exclus des systèmes de soins traditionnels

• *Such programmes also facilitates reaching out to people who inject drugs, who are a largely hidden population.*

Prévention des décès par overdoses

Management of opioid overdose



- Dans le monde, tous les ans, 69.000 personnes meurent d'overdose.
- 1 overdose sur 20-25 est fatale
- *Among people who inject drugs, opioid overdose is the second most common cause of mortality after HIV/AIDS*
- *Globally, an estimated 69 000 people die each year from opioid overdose.*

WHO (2014). Community management of opioid overdose
UNODC. World Drug Report 2015.

Coût – Efficacité Financement

*Cost effectiveness
Funding*

Methadone

- Réduction des admissions aux urgences, en milieu hospitalier
- 4 \$ d'économisés pour chaque dollar investi.
\$4 in benefit for each \$1 spent on the treatment
- 5915 \$ pour une année de vie sauvee
\$5915 per life-year gained In high-income countries
- Methadone is recommended over buprenorphine, because it is more effective and costs less.*

Barnett PG. The cost-effectiveness of methadone maintenance as a health care intervention. *Addiction*. 1999 Apr;94(4):479-88.
WHO. Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. 2009.

- Le coût d'un traitement de substitution au long court est de 1 \$ par jour dans les pays à niveau de revenu bas ou moyen.
- De l'ordre de 500 \$ / an
- The cost of providing long-term methadone and buprenorphine maintenance treatment in a low or middle-income country costs approximately US\$1/day (500 \$ / year)*



Buprenorphine

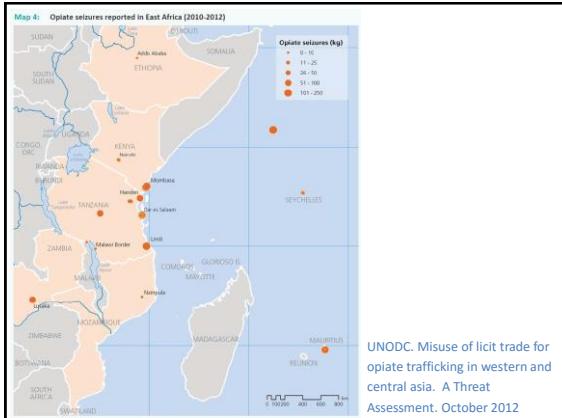
- buprenorphine is more expensive than methadone, substitution treatment with methadone can be provided cheaply in community settings and is therefore a feasible option for low- and middle-income countries.

- Lorsque les patients doivent payer leur traitement, le niveau de rétention et les résultats des programmes sont moins bons que lorsque la prise en charge est gratuite.
Where patients have to pay for treatment, retention rates and health outcomes are worse than where treatment is free.
- Même une participation modeste aux coûts du traitement aura une influence négative.
Even small financial costs for treatment can be a significant disincentive.

Trafic dans la zone Océan Indien

Opiate trafficking in Indian Ocean



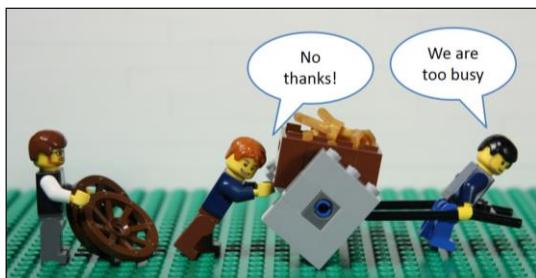


Les politiques de santé publiques

Public Policy and Health

- Il est important que les politiques de santé publique soient fondées sur les évidences scientifiques.
- There is a need to establish public health policies based on strong scientific evidence.*
- Ces évidences existent et sont bien codifiées dans le domaine de l'usage des opiacés illicites.
- Fortunately these evidence-based interventions are identified (Cochrane,etc.)*
- In facts, the final decisions are usually based on a non-scientific approach, focused more on what the public and policy-makers deem of value .

Strang J, Babor T, Caulkins J et al. Drug policy and the public good: evidence for effective interventions. Lancet 2012 Jan 7;379(9810):71-83.



- Les programmes à très haut niveau de preuve devraient être mis en place sans attendre

- Il n'y a pas de société sans drogue, il n'y en a jamais eu.
- L'usage de substances psychoactives est un invariant sociologique majeur (L.Laniel)
- The idea of a drug free society is an utopia*
- The psychoactive drugs use is part of every culture and epoch in human history*

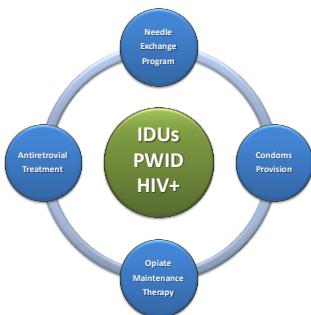
Prevention

- People initiate drugs use before 18 years old in 90 % of cases.
- Psychosocial developmental interventions can be effective, whereas knowledge and awareness are generally ineffective for prevention of use of illicit drugs, tobacco, and alcohol.
- Traumatic lifetime experience may increase the risk for opiate addiction.

CONCLUSION

- La **morbi-mortalité** est très élevée chez les injecteurs de drogues.
- Premature deaths is high among people who inject drugs*
- L'**association des traitements** de substitution aux programmes d'échanges de seringues, aux antirétroviraux donne les meilleurs résultats en matière de prévention de la transmission du VIH et du VHC chez les injecteurs de drogues.
- The combined use of antiretroviral therapy, needle and syringe programmes and opioid substitution treatment is likely to yield the greatest benefits in terms of the control of HIV and hepatitis C among people who inject drugs*

The need of a combination of approaches



Degernier L, Mathers B, Vickerman P, Rhodes T, Latkin C, Hickman M. Prevention of HIV infection for people who inject drugs: why individual, structural, and combination approaches are needed. *Lancet* 2010; 375:283–291.

- L'addiction aux opiacés est une **maladie chronique** qui nécessite des soins prolongés.
- *Opioid dependence is a complex condition that often requires long-term treatment and care.*
- Il n'y a pas de traitement unique qui convienne à tous les usagers.
- *No single treatment modality is effective for all people with opioid dependence.*



- Les traitements de **substitution** (ou de maintenance) sont efficaces, sûrs et économiques.
- *Substitution maintenance treatment is an effective, safe and cost-effective modality for the management of opioid dependence.*
- Les mesures de **réduction des risques et des dommages** sont très efficaces
- *Harmful reduction measures are very efficient*



- Chaque dollar investi dans les programmes intégrés basés sur des preuves permet économiser 6 \$
- *Every dollar invested in evidence based integrated treatment, up to six dollars are saved in terms of costs for health, security and welfare.*

MERCI / THANK YOU

Abréviations

- BHD : Buprénorphine haut dosage
- IDU : Injection drug user
- MSO : Médicament de substitution aux opiacés
- NSP : Needle Syringe Programmes
- OMS : Organisation Mondiale de la Santé
- PWID : People who inject drugs
- WHO : World Health Organisation

Bibliographie

- World Health Organization (2009). Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence.
http://www.who.int/substance_abuse/publications/Opioid_dependence_guidelines.pdf
- UNODC (2015). World Drug Report 2015.