VOLUME C
Pharmacological Treatment for Drug Use Disorders
Drug Treatment for Special Populations
VOLUME C

**MODULE 1**
Dependence Basics
- Drug use, addiction and dependence
- Management of Alcohol & benzodiazepine dependence
- Psychostimulants
- Volatile substances, cannabis and new psychoactive substances

**MODULE 2**
Basics of Opioid Dependence. Pharmacotherapy Options
- Opioids: Definition, effects and treatment implications
- Opioid dependence treatment with Methadone
- Opioid dependence treatment with Buprenorphine
- Opioids antagonist treatment

**MODULE 3**
Special Populations: Co-Occurring Disorders, Women and Young People
- Co-occurring psychiatric and substance use disorders
- Women: substance use disorders and treatment issues
- Young people: substance use disorders and treatment issues
MODULE 2

Basics of opioid dependence.
Pharmacotherapy options
Training goals

- Learn about key components of opioids dependence and its medical/psychiatric consequences
- Understand the benefits and limitations of methadone as a pharmacotherapy for opioid dependence
- Learn about benefits and limitations of buprenorphine as a pharmacotherapy for opioid dependence
- Increase knowledge about benefits and limitations of opioids antagonists for overdose (Naloxone) and relapse prevention (Naltrexone)
Module 2

Basics of opioid dependence
Pharmacotherapy options

1. Opioids: Definition, effects and treatment implications
2. Opioid dependence treatment with Methadone
3. Opioid dependence treatment with Buprenorphine
4. Opioid antagonist treatment
Pre-assessment
Icebreaker
Workshop 1

Opioids: Definition, effects and treatment implications
At the end of this workshop you will understand the:

► Epidemiology of opioids dependence worldwide and its relationship to infectious diseases
► Basic neurobiology of opioids dependence
► Medical and psychiatric co-morbidities and treatment strategies for these disorders
► Key issues in engaging opioids users into treatment with low threshold approaches
Opioids: an introduction
Opioids

Opiate (n)

“An unlocked door in the prison of identity. It leads to the jail yard.”

(Ambrose, 1906)

- Area under illicit opium poppy cultivation was at its highest in 2014 and in 2015, declined by 11%
- 17.4 million opioid users
- 33 million opioid users
- Cause the most burden of disease & drug-related deaths
Epidemiology

- Distribution of countries widespread, crossing various socioeconomic groups
- Rising group of chronic pain/prescription opioid dependent individuals
- Prevalence of opioid use has been increasing for past 5 yrs.
- Prevalence of opioid use stable globally & declining in some regions e.g. Europe
- Illicit drug use more common among men than women, but the non-medical use of pharmaceutical drugs is nearly equivalent, if not higher among women
- Users alternate between prescription opioids and heroin – which ever is easily available, accessible & cheaper
Epidemiology: regional variations and trends

- Asia: opium
- Europe: ↓ heroin use ↑ prescription opioids
- USA: opioid use still on increase but emerging phenomenon of synthetic opioids being replaced with heroin
- East & Southeast Europe: ↑ rate of IDU (5 x global rate)
- Estonia, Finland & USA injecting heroin users switching to Fentanyl
With an estimated 33 million users, opioids remain major drugs of potential harm and health consequences.

**FIG. 3** Trends in the use of heroin and prescription opioids in the United States, 2002-2014

**FIG. 4** Age-adjusted rates of death related to prescription opioids and heroin in the United States, 2000-2014
Opioid use prevalence in the United States

- 145% increase in heroin use between 2007 and 2014
- 914,000 people of aged 12 years or older had used heroin in the past year (2014)
- Mortality related to heroin use has increased fivefold since 2000
- Increase in heroin use, particularly among people who also reported the use of other substances in the past decade:
  - cocaine users (91.5 per 1,000 users)
  - non-medical use of prescription opioids
Global epidemiology: seizures of heroin and morphine 2003-2012

FIG. 32 | Quantities of heroin and morphine seized worldwide, by trafficking route, 1998-2014

- **Américas**
- **South-East Asia and Oceania**
- **Northern route**
- **Southern route**
- **Pakistan**
- **Balkan route**
- **Afghanistan**
- **Seizures involving Afghan opiates**
Disease burden attributable to drug dependence

Data from 2010, by age
Global epidemiology: use of opioids including heroin

Fig. 26. Ranking of past-year use of illicit opiates by subregion, based on prevalence and number of users, 2012

Number of past-year users of illicit opiates (right to left)

- 5,000,000
- 4,000,000
- 3,000,000
- 2,000,000
- 1,000,000

South America
Central America
Eastern Africa
Oceania
East/South-East Asia
North Africa
Caribbean
South Asia
Southern Africa
Western/Central Europe
West and Central Africa
North America
Central Asia
East/South-Eastern Europe
Near and Middle East/South West Asia

Annual prevalence of use of illicit opiates (percentage, left to right)

- Number of past-year users (midpoint)
- Opiate users as percentage of population aged 15-64, by subregion (midpoint)
- Opiate users as percentage of population aged 15-64 (global, midpoint)
Trends in prevalence of opioid use

Fig. 2. Trends in the prevalence of use of different drugs, 2009-2012
Opioids negative consequences
The consequences of drug use are vast and varied and affect people of all ages.

- Medical
- Social
- Economic
- Criminal Justice
Opioids related consequences:
Cost to individual and society

- Opioid dependence ➔ significant burden
- Unemployment
- Homelessness
- Family disruption
- Loss of economic productivity
- Social instability
- Criminal activities
- Major health consequences
Opioids related negative consequences: Criminal behaviour

- Strong links between opioid misuse & crime
- Often crimes are committed to fund drugs
- Crimes committed under influence of drugs
- Common factors in development of criminal behaviour & initiation of drug use
- Criminal offences are generally acquisitive crime, drug trafficking or sex trade
In some countries about 3/4 of people in prison have alcohol or other drug-related problems, and more than 1/3 may be opioid dependent.
1. Estimated 100,000+ people each year die of opioid overdose

2. Estimated 60% of opioid overdoses are witnessed, and 20% of fatal overdoses

3. Death resulting from opioid overdose usually occur within 1-3 hours after opioid administration (injection in most cases)

4. Signs of opioid overdose are sufficiently prominent for identification of suspected opioid overdose by non-professionals
Opioid overdose

- Overdose is a dangerous and deadly consequence of opioids use
- A large dose of opioids depresses heart rate and breathing to such an extent that a user cannot survive without medical help
- 43,000 deaths/year. Although data are limited, an estimated 70,000-100,000 people die from opioid overdose each year
- Life expectancy ↓ by 46 years
Death from opioids analgesic poisoning

FIG. 4 Age-adjusted rates of death related to prescription opioids and heroin in the United States, 2000-2014

Opioid-related problems

- Most prominent problems are associated with heroin dependence
- Not all users of heroin develop dependence. Between 1 in 4 to 1 in 3 regular users develop dependence
- Development of heroin dependence usually requires regular use over months (or longer, when use is more irregular)
Opioid dependence

- Opioid dependence is characterized by a cluster of cognitive, behavioral and physiological features.

- Opioid dependence does not develop without a period of regular use, although regular use alone is not sufficient to induce dependence.

- Long-term changes in neuronal circuitry, similar to those seen in learning and memory, can occur as a result of repeated opioid use. This effect creates a high risk of relapse to opioid use even after long periods of abstinence.
## Opioids effects on health

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Acute</strong></td>
<td>Euphoria, warm flushing of skin, dry mouth, heavy feeling in</td>
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<tr>
<td></td>
<td>extremities, clouded thinking. Alternate wakeful and drowsy</td>
</tr>
<tr>
<td></td>
<td>states, itching, nausea, depressed respiration</td>
</tr>
<tr>
<td><strong>Long-term</strong></td>
<td>Addiction, physical dependence, collapsed veins, abscesses,</td>
</tr>
<tr>
<td></td>
<td>infection of heart lining and valves, arthritis / other</td>
</tr>
<tr>
<td></td>
<td>rheumatologic problems, HIV, Hepatitis C</td>
</tr>
<tr>
<td><strong>In combination</strong></td>
<td>Dangerous slowdown of heart rate and respiration, coma or</td>
</tr>
<tr>
<td><strong>with alcohol</strong></td>
<td>death</td>
</tr>
<tr>
<td><strong>Withdrawal</strong></td>
<td>Restlessness, muscle and bone pain, insomnia, diarrhoea,</td>
</tr>
<tr>
<td><strong>symptoms</strong></td>
<td>vomiting, cold flashes with goose bumps (“cold turkey”) and</td>
</tr>
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<td></td>
<td>leg movements</td>
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</table>
The revolving door

- Heroin dependence is a chronic, relapsing disorder. It is a dependency that is very difficult to resolve.
- Relapse is extremely common. It is part of the process of resolving the dependence – much like giving up tobacco.
- A principle health care objective is to get the patient into treatment, help keep them in treatment, and return them to treatment when relapse occurs.
Polydrug use: patterns and risks

► Polydrug use is the norm among drug users
► Most people who use illicit drugs use a variety of different drugs
► Heroin users also are heavy users of alcohol and benzodiazepines
► As CNS depressants, these combinations are especially dangerous and known to be significant contributors to overdose
► Patients should be advised against the use of these combinations and told of the risks involved
Detecting opioid dependence

Look for a pattern, not an isolated event, in which:

► A patient frequently runs out of scripts for a prescribed opioid
► A patient is on a high and increases the dose of prescribed opioids
► In which a patient injects oral medications
► Of observed intoxication or being in withdrawal
► Which presents plausible conditions that warrant prescribed opioids, but with specific requests for medication type and amount
► A patient threatens or harasses staff for a fit-in appointment
► A patient alters, steals or sells scripts
► A patient is addicted to alcohol or other drugs
## Classification of opioids

<table>
<thead>
<tr>
<th>Classification</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure Opioid Agonists</td>
<td>Opium, Papaverine morphine, Codeine</td>
</tr>
<tr>
<td>Partial Agonists/Antagonists</td>
<td>Naltrexone, Buprenorphine</td>
</tr>
<tr>
<td>Semi-synthetic</td>
<td>Heroin, Hydromorphone, Oxycodone</td>
</tr>
<tr>
<td>Synthetic</td>
<td>Fentanyl, Meperidine, Hydrocodone, Methadone, Pentazocine, Pethidine</td>
</tr>
</tbody>
</table>
Heroin

► Morphine is produced through heroin hydrolysis

► Heroin → monoacetylmorphine (MAM) → morphine

► Heroin and MAM are lipophilic, hence more rapid action

► Heroin excreted in urine as free and conjugated morphine

► Heroin metabolites are present in urine for approximately 48 hours following use
PET scan of μ opioid receptors
3 main families of opioid receptors – $\mu$, $\kappa$, and $\sigma$

- **Agonists** e.g. morphine & methadone act on $\mu$

- **Partial agonist** e.g. buprenorphine, also act on $\mu$, but have less of a maximal effect as the dose increases.

- Opioid receptors located in CNS, PNS & GI tract

- Opioid receptors are **inhibitory**

- $\downarrow$ release of 5-HT, GABA, glutamate, acetylcholine

- $\uparrow$ the release of dopamine – may contribute to dependence
Where opioids operate in CNS

- **Limbic system (controls emotions)**
  - μ, Opioid binding produces feelings of pleasure, relaxation and contentment

- **Brainstem (controls breathing)**
  - Opioid binding slows respiration μ, κ, δ

- **Spinal cord (transmits pain)**
  - Opioid binding blocks pain messages μ, κ, δ
Where are we so far?

► What are opioids?
► Why understanding opioid dependence is important?
► How can opioid dependence be identified?
► How is opioid overdose dangerous?
► What are the effects of opioids on the brain?
Break
Opioids: Short term and long term effects
Opioids: immediate effects

- Perception altered, possible delirium
- Analgesia, to some degree
- Impaired cognition, though consciousness may be preserved
- Autonomic nervous system affected
- Suppression of cough reflex
- GI system affected
- Hypothermia
Opioids: immediate effects

- Miosis
- Urinary retention
- Reduced GI motility
- Endocrine
- Non-cardiogenic pulmonary oedema
- Coma or death (from respiratory depression)
- Other: pruritis, flushed skin, dry mouth, skin and eyes
Opioids: long term effects

► Little evidence of long-term direct toxic effects on the CNS from opioid use

► Long-term health-related complications may result from:
  – Dependence
  – Poor general self-care
  – Imprisonment
  – Infections (drug impurities or contaminants)

► Blood Borne infections (HBV, HCV, HIV)
Opioids: long term effects

Possible:

► Constipation/narcotic bowel syndrome
► Cognitive impairment from hypoxia as a result of repeated non-fatal overdose
► Reproduction and endocrine irregularity
► Medication-induced headaches
► Intense sadness (depression, dysthymia)
# Opioids: drug interactions

<table>
<thead>
<tr>
<th></th>
<th>Respiratory depression</th>
<th>Toxicity/risk of death</th>
<th>Hypotension</th>
<th>Coma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CNS depressants</strong></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>MAOIs</strong></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
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<tr>
<td><strong>TCAs</strong></td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td><strong>Betablockers</strong></td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
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<tr>
<td><strong>BZDs</strong></td>
<td>✓</td>
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</table>
Opioid dependence: neurobiology
In substance dependence, 2 signs of neuro adaptation that can be most easily measured biologically are:

- **Withdrawal** – the occurrence of unpleasant physical and psychological symptoms when use of the substance is reduced or discontinued

- **Tolerance** – the fact that increased amounts of the substance are required to achieve the same effect or that the same amount produces less effect
## Opioid withdrawal

### Signs
- Yawning
- Lacrimation, mydriasis
- Diaphoresis
- Rhinorrhea, sneezing
- Tremor
- Piloerection
- Diarrhoea and vomiting

### Symptoms
- Anorexia and nausea
- Abdominal pain or cramps
- Hot and cold flushes
- Joint and muscle pain or twitching
- Insomnia
- Drug cravings
- Restlessness/anxiety
Heroin withdrawal

- Non-life threatening
- Commences 6 – 24+ hours after last use
- Peaks at around 24 – 48 hours after use
- Resolves after 5 – 7 days

There is increasing recognition of the existence of a protracted phase of withdrawal lasting some weeks or months, characterised by reduced feelings of wellbeing, insomnia, dysthymia, and cravings.
Progress of the acute phase of opioid withdrawal since last dose

Withdrawal from heroin
Onset: 6–24 hrs.
Duration: 4–10 days

Withdrawal from methadone
Onset: 24–48 hrs., sometimes more
Duration: 10–20 days, sometimes more
Predictors of withdrawal severity

➢ Main predictors
   - Greater regular dose
   - Rapidity with which drug is withdrawn

➢ Also consider
   - Type of opioid used, dose, pattern, and duration of use
   - Prior withdrawal experience, expectancy, settings for withdrawal
   - Physical condition (poor self-care, poor nutritional status, track marks)
   - Intense sadness (dysthymia, depression)
   - Constipation or “Narcotic Bowel Syndrome”
   - Impotence (males) or menstrual irregularities (females)
Opioid dependence diagnosis
Opioid dependence: the ICD-10 criteria

Simultaneous presence of **three or more features** at any one time in the preceding year:

- A strong desire or sense of compulsion to take opioids
- Difficulties in controlling opioid use
- A physiological withdrawal state
- Tolerance
- Progressive neglect of alternative pleasures or interests because of opioid use
- Persisting with opioid use despite clear evidence of overtly harmful consequences
Diagnosis of opioid dependence DSM-V criteria

The recently released DSM-V, no longer separates Substance Abuse from Dependence, but instead provides criteria for Opioid Use Disorders that range from mild to severe depending on the number of symptoms, a patient has.
DSM-V criteria for substance use disorders

Presence of at least 2 of 11 criteria which are clustered into 4 groups

1. Impaired control
   (1) Substance taken more than or for longer than intended
   (2) Unsuccessful efforts to cut down or stop
   (3) Great deal of time spent to get/ use/recover from the drug
   (4) Craving

2. Social impairment
   (5) Failure to fulfill major obligations due to use
   (6) Continued use despite problems caused/exacerbated by use
   (7) Important activities given up/reduced because of use
3. Risky use

(8) Recurrent use in hazardous situations

(9) Persistent use despite physical/psychological problems due to use

4. Pharmacologic dependence

(10) Tolerance

(11) Withdrawal
Opioid dependence assessment
How to assess and diagnose opioid dependence?

A. History of substance use

Reason for presentation

► In crisis (health or economic or legal crisis)
► Brought in by a concerned parent/relative/spouse/employer/friend/outreach worker
► Want help for their drug use and motivated to change their behaviour
► Usual source of drugs not available
► Referred by another medical practitioner
► Pregnant
How to assess and diagnose opioid dependence?

A. History of substance use

Past and current drug use (last four weeks)

- The age of starting drug use (including alcohol and nicotine)
- Types and quantities of drugs taken (including concomitant alcohol misuse)
- Frequency of use, including routes of administration
- Experience of overdose
- Periods of abstinence
- What triggers a relapse?
How to assess and diagnose opioid dependence?

A. History of substance use

History of injecting and risk of HIV and hepatitis

- Past history
- Present usage and why changed to injecting
- Supply of needles and syringes
- Sharing habits (lending & borrowing injecting paraphernalia)
- Does the patient know how to inject safely?
- How does the patient clean equipment?
- How does the patient dispose of the used paraphernalia?
- Has he thought of / tried any other method of use?
- Knowledge of HIV, Hepatitis B& C and transmission
- Use of condoms
B. Medical history

- Complications of drug use – abscesses, thrombosis, viral illnesses, chest disease
- Hepatitis B, C status, if known
- HIV status, if known
- History and/or diagnostics for STIs
- Last menstrual period
- Operations, accidents and head injury
- Any current medication, on HIV drugs?
C. Psychiatric history

► Any psychiatric consultations?
► Any overdoses (accidental or deliberate)?
How to assess and diagnose opioid dependence?

D. Forensic history

- Any outstanding charges?
- Past imprisonment?
- Past custodial sentence?
How to assess and diagnose opioid dependence?

E. Social history

- Family situation
- Employment situation
- Housing situation
- Financial situations, including debts
F. Past contact with treatment services

- Previous efforts to reduce/stop taking drugs
- Contacts with doctors, addiction services, social services, community services
- Previous admissions, how long they lasted and the cause of relapses
G. Assessing motivation for change

Patients have different levels of motivation for changing their substance use – the five stages of change by Prochaska and Di Clemente (1983)

► Is the patient motivated to stop or change his/her pattern of drug use or to make other changes in life?
G. Assessing motivation for change

Stages Of Change

- Pre-contemplation: “I don't desire to stop”
- Contemplation: “I may want to think about stopping, some day”
- Preparation: “I am planning to stop soon”
- Action: “I have just stopped using drugs”
- Maintenance: “I have been away from drugs for months”
How to assess and diagnose opioid dependence?

H. Examination

Assessing general health

► General – Anaemia, nutritional status, dentition and overall hygiene
► Skin – Needle marks, tattoo, skin abscesses and open wounds
► Route specific – abscess, cellulitis
► Drug related
  – Side effects (e.g. constipation)
  – Overdose (e.g. respiratory depression)
  – Withdrawal (e.g. irritability, pain)
Physical examination

Signs of opioid dependence:

➢ **Needle marks** on wrists, antecubital fossa, legs (inner thighs), feet, hands, neck

➢ **Intoxication**: pinpoint pupils, “nodding off,” drowsiness, sweating

➢ **Withdrawal**: restlessness, “goosebumps,” sweating, increased bowel sounds, lacrimation, “sniffles,” dilated pupils, muscle tenderness, tachycardia, hypertension
How to assess and diagnose opioid dependence?

I. Investigations

- Haematological investigations
- Haemoglobin
- Liver function tests
- HIV
- Hepatitis B and C
- Urine drug screen: opioids persist in the urine for up to 24 hours
Opioids: special considerations for assessment

- Pregnancy
- Infectious diseases
- Polydrug dependence
- Opioid-related overdose
- Major medical conditions e.g., liver, cardiac
- Major psychiatric/mental health issues e.g., psychosis, depression, suicide
Complications from opioid use
Track marks form IV drug use
Track mark from heroin
Venous abscess – IV drug user
Dilated pupils – opioid withdrawal
Where are we so far?

► What are the short- and long-term effects of opioid use?
► What are the signs of opioid dependence?
► What are the components of assessment of opioid dependence?
► What are the components of diagnosis of opioid dependence?
► What are the complications of the opioid use?
Break
Management of opioid dependence
Drug dependence is a multifactorial health disorder

It often follows the course of a relapsing and remitting chronic condition

It is a treatable condition

Optimal results are achieved using a multidisciplinary approach combining pharmacological and psychosocial interventions
Dependent opioid use and treatment pathways

Abstinence ➚ Relapse Prevention
  • Residential (drug-free)
  • Outpatient (drug-free)
  • Psychological counselling
  • Support group
  • Antagonist (e.g., naltrexone)

Relapse ➙ Cessation
  • Setting
  • Medication
  • Speed

Withdrawal Management
  • Setting
  • Medication
  • Speed

Substitution Treatment
  Buprenorphine
  Methadone
  Buprenorphine+Naloxone

Reduce Health and Social Consequences
  • Education about overdose
  • HIV / HCV risk reduction info

Heroin use ➙ Dependence
  ➙ Abstinence

Dependence ➙ Cessation (drug-free)
  ➙ Withdrawal Management

• Education about overdose
• HIV / HCV risk reduction info
Components of comprehensive treatment of drug use disorders

The best treatment programs provide a combination of therapies and other services to meet the needs of the individual patient.
Opioid withdrawal management

Withdrawal management aims to:

► Reverse neuroadaptation by managing tolerance and withdrawal
► Promote the uptake of post-withdrawal treatment options

Withdrawal management may occur:

► As an outpatient
► In a residential / treatment setting
Opioid withdrawal treatment

Involves:

► Reassurance and supportive care
► Information
► Hydration and nutrition
► Medications to reduce severity of somatic complaints (analgesics, antiemetic, clonidine, antispasmodics)
► Opioid pharmacotherapies: methadone, buprenorphine, buprenorphine-naloxone combination (Suboxone)
Opioid withdrawal complications

- Anxiety and agitation
- Tolerance to discomfort & dysphoria
- Drug-seeking behaviour
- Muscle cramps
- Abdominal cramps
- Insomnia
Opioid withdrawal scales

► Guide treatment
► Monitor progress of withdrawal
► Do not diagnose withdrawal but describe severity
► Guide ongoing assessment

If the withdrawal pattern is unusual or the patient is not responding, suspect other conditions.
Main pharmacotherapies for opioid dependence

► **Maintenance treatment** (opioid agonist)
  – Methadone
  – Buprenorphine
  – Buprenorphine + Naloxone (Suboxone)
  – Others: Slow-release oral morphine, Dihydrocodeine, Injectable opioid treatment

► **Assisted Withdrawal** (opioid agonist)
  – Buprenorphine
  – Methadone
  – Buprenorphine + Naloxone (Suboxone)
  – Lofexidine / Clonidine

► **Relapse Management** (opioid antagonist)
  – Naltrexone: oral & implants

► **Treatment of overdose** (opioid antagonist)
  – Naloxone
General principles of pharmacotherapy

► **Agonists:** Opioid drugs that activate opioid receptors on neurons are opioid agonists. Morphine & Methadone are opioid agonists

► **Partial agonists:** Opioid drugs that activate opioid receptors, but not to the same degree as full agonists. E.g., Buprenorphine

► **Antagonists:** Opioids that bind to opioid receptors but block them, rather than activating them. Naltrexone and Naloxone are Opioid Antagonists
Rationale for opioid agonist treatment
Heroin vs. Methadone

Heroin

Plasmic levels (M)

Euphoria
Normal
Withdrawal

Source: DOLE, V.P. & NYSWANDER, M.E., Pharmacological Treatment of Narcotic Addiction (The Eight Nartan B. Memorial Award Lecture), NIDA, 1982.
Rationale for opioid agonist treatment
Heroin Vs. Methadone

Rationale for opioid agonist treatment

Advantages of opioid agonist/partial agonist medication over heroin

► Non-parenteral administration
► Known composition
► Gradual onset and offset
► Long-acting
► Far less reinforcing than heroin
► Medically supervised
Rationale for opioid agonist treatment

- Most effective treatment for opioid dependence
- Controlled studies have shown that with long-term maintenance treatment using appropriate doses, there are significant:
  - decreases in illicit opioid use
  - decreases in other drug use
Opioid agonist treatment

► Decrease in criminal activity
► Decrease in needle sharing and Blood Borne Viruses transmission (including HIV)
► Improvements in pro-social activities
► Improvements in mental health
The “Gold Standard” Treatment

- Synthetic opioid with a long half-life
- μ Agonist with morphine-like properties & actions
- Action – CNS depressant
- Effects usually last about 24 hours
- Daily dosing - same time, daily-maintains constant blood levels & facilitates normal everyday activity
- Adequate dosage prevents opioid withdrawal, without intoxication
Buprenorphine-partial agonist

- Derived from the morphine alkaloid thebaine
- Partial opioid agonist at $\mu$ opioid receptors
- Antagonist at $\kappa$ opioid receptor
- Blocks opioid receptors, diminishes cravings, prevents opioid withdrawal
# Buprenorphine vs Methadone

<table>
<thead>
<tr>
<th>Buprenorphine</th>
<th>Methadone</th>
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</thead>
<tbody>
<tr>
<td>• Partial Agonist</td>
<td>• Full agonist. Can produce significant intoxication</td>
</tr>
<tr>
<td>• Abstinence leads to mild withdrawal symptoms</td>
<td>• Abstinence leads to marked withdrawal symptoms</td>
</tr>
<tr>
<td>• Ceiling effect at high doses-risk of fatal respiratory depression by overdose minimal. But when combined with CNS Depressants e.g alcohol, benzodiazepines, respiratory depression has been reported.</td>
<td>• Risk of fatal overdose by respiratory depression</td>
</tr>
<tr>
<td>• Sublingual tablets are effectively absorbed. It is not orally active. Sublingual tablets can be crushed, easily dissolved and injected.</td>
<td>• Orally active</td>
</tr>
<tr>
<td>• Relatively expensive</td>
<td>• Cheaper</td>
</tr>
</tbody>
</table>
Naltrexone-antagonist

- Fully blocks μ receptors, preventing euphoria from opioid use ➔ "drug money spent = money wasted"
- Abstinence-based treatment option with primary role of relapse prevention
- Allows extinction of Pavlovian-conditioned response to opioid cues
- Non-dependence inducing
- Commenced at least 1 week after cessation of heroin
- Optimally effective with motivated individuals who have high levels of psychosocial functioning and family support
Key outcomes of maintenance pharmacotherapy programs

- ↑ Retention in treatment
- ↓ Opioid use
- ↓ Risky behaviours associated with opioid use
- ↑ Engagement in measures to reduce health and social consequences
- ↓ Mortality and morbidity
- ↑ Psychological, emotional, and physical wellbeing
- ↓ Social costs associated with illicit drug use
- ↓ Crime

“Substitution maintenance treatment is an effective, safe and cost-effective modality for the management of opioid dependence. Repeated rigorous evaluation has demonstrated that such treatment is a valuable and critical component of the effective management of opioid dependence and the prevention of HIV among IDUs.”
Injecting drug use & HIV
Drug dependence and HIV

1 out of 3 U.S. AIDS deaths are related to drug misuse
4 most important interventions for HIV, in order of priority, are:

1. Needle and syringe programmes
2. Agonist maintenance therapy (AMT)
3. HIV testing and counselling
4. Antiretroviral therapy
OST availability in regions with most PWID: the disparity

In 16 countries*, which account for 45% of PWID and 66% of PWID living with HIV, there is a low level of service provision, particularly with regard to needle and syringe programmes and AMT.

*Belarus, Canada, Georgia, Indonesia, Kazakhstan, Latvia, Malaysia, Myanmar, Pakistan, Republic of Moldova, Russian Federation, Spain, Tajikistan, Thailand, Ukraine and United States.
Injecting drug use (IDU) & HIV / AIDS

- IDU contributes significantly to spread of HIV
- 1.7 million are living with HIV (13% of IDU)
- Very High Prevalence (23-29%) in S.W Asia & Eastern Europe (Pakistan, Russia, Ukraine)
- 179 Deaths from AIDS attributed to IDU, in 2012 and 1358 deaths in 2006
- Sharp decline in death attributed to measures to reduce health and social consequences
Prevalence of HIV among people who inject drugs

FIG. 16 Estimated number of people who inject drugs living with HIV and prevalence of HIV among people who inject drugs, by region, 2014

- Number of people who inject drugs and are living with HIV
- HIV Prevalence among people who inject drugs (percentage)
AMT for prevention of HIV
Service coverage for people who inject drugs

Fig. 6. Levels of service provision for countries with the highest prevalence rates (among those reporting on service provision) of injecting drug use and HIV among people who inject drugs

- Coverage of HIV testing and counselling
- Coverage of needle and syringe programmes
- Needles & syringes distributed per person who injects drugs per year
- Coverage of opioid substitution therapy
- Coverage of antiretroviral therapy

Legend:
- No data
- No service coverage
- Low coverage
- Medium coverage
- High coverage
AMT availability across countries
In 1959, Paulus & Halliday from Vancouver set up what is believed to be the first MMT program in the world.

In the 60's, Methadone gained recognition as an effective treatment for heroin addiction.

Since then, opioid agonist treatment with MMT has become an effective treatment option for opioid-dependent individuals worldwide.

Many European countries such as UK, France, Holland, Germany, Spain, Finland, Greece and Australia currently operate large-scale methadone programs.
Global availability of OST

Global availability of opioid substitution therapy

Although heroin addiction is a global problem, much of the world remains without a form of substitution therapy.

Source: The Lancet

Infographic: Tom Howay
OST: Current global estimate

- OST provided in about 77 countries worldwide
- Globally 6–12% of PWID* are receiving OST
- Wide regional variations: 61% in western Europe vs 3% in Vietnam/Indonesia
- OST limited in sub-Saharan Africa, Latin America, Asia
- Provision ↑ in Asia, Eurasia, Middle East & N. Africa
- Newly introduced in Tajikistan, Kosovo, Kenya, Tanzania, Cambodia, Bangladesh since 2010
- OST still unavailable in 81 countries with IDU – 50 of them have reported HIV among PWID
Opioid dependence is:

- A neurobiological state, multi-factorial in its origins, with a final common pathway of neuro-adaptive changes resulting in:
  - Tolerance to opioids
  - A withdrawal syndrome when opioids are withheld
  - Drug seeking behaviours which take primacy in the lives of those afflicted (so called, salience)

- The costs to the individual and society are extremely high. Serious medical and psychosocial consequences can be avoided if this group is treated actively, with pharmacological agents and psychosocial support
Although themselves Opioids, Methadone & Buprenorphine are “Treatment,” not just Substitution

Treatment with them allows patients to hold jobs, avoid street crime and violence, and reduce their exposure to HIV by stopping or decreasing injection drug use and drug-related high-risk sexual behavior

Patients stabilized on these medications can also engage more readily in other behavioral interventions essential to recovery
Questions
What is the relationship between opioids dependence and infectious diseases?

Which 2 signs of neuro adaptation can be most easily measured biologically?

What kind of treatment options and strategies are there for people who are dependent on opioids?

Why engage opioid users into treatment?
Thank you for your time!
End of workshop 1