Module 1

Drug Dependence basics

1. Drug use, addiction and dependence
2. Management of Alcohol & benzodiazepine dependence
3. Psychostimulants
4. Volatile substances, cannabis and new psychoactive substances
At the end of this workshop you will be able to:

► Understand acute and chronic effects of psychostimulants

► Identify the medical and psychiatric dangers associated with intoxication, overdose and withdrawal

► Describe drug interactions with other substances as well as the psychostimulant dependence treatment model

► Explain about empirically supported methods available for treatment of stimulant-use disorders
Psychostimulants: amphetamine type stimulants & cocaine
Stimulants

Description:
► A group of synthetic and plant-derived drugs that increase alertness and arousal by stimulating the central nervous system. Although MDMA (ecstasy) has some hallucinogenic properties, it is often classified as a stimulant.

Medical uses:
► Short-term treatment of obesity, narcolepsy, and hyperactivity in children

Method of use:
► Intravenous, intranasal, oral, smoking
# Types of stimulant drugs

<table>
<thead>
<tr>
<th>Amphetamine type stimulants (ATS)</th>
<th>Cocaine group</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Amphetamine</td>
<td>• Cocaine</td>
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<tr>
<td>• Dexamphetamine</td>
<td>• Crack cocaine</td>
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<tr>
<td>• Methcathinone</td>
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<tr>
<td>• Ecstasy-type substances (e.g., MDMA)</td>
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<tr>
<td>• Methamphetamine “speed,” “crystal,” “ice,” “yaba,” “shabu”</td>
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<tr>
<td>• Methylphenidate</td>
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Stimulants: acute and chronic health effects
### Acute stimulant effects

<table>
<thead>
<tr>
<th>Psychological</th>
<th>Physical</th>
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<tbody>
<tr>
<td>• Increased energy</td>
<td>• Increased heart rate</td>
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<tr>
<td>• Increased clarity</td>
<td>• Increased pupil size</td>
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<tr>
<td>• Increased competence</td>
<td>• Increased body temperature</td>
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<tr>
<td>• Heightened feelings of sexuality</td>
<td>• Increased respiration</td>
</tr>
<tr>
<td>• Increased sociability</td>
<td>• Cardiac arrhythmias</td>
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<tr>
<td>• Improved mood</td>
<td>• Constriction of small blood vessels</td>
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<tr>
<td>• Powerful rush of euphoria – freebase and intravenous only</td>
<td>• Decreased appetite</td>
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<td></td>
<td>• Decreased need for sleep</td>
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</tbody>
</table>
Chronic stimulant effects

Psychological

► Severe anxiety
► Paranoia
► Psychosis
► Irritability
► Confusion
► Desire to isolate
► Memory impairment
► Inability to concentrate
► Loss of control
► Aggressiveness
Chronic stimulant effects

Physical

► Weight loss/anorexia
► Sleep deprivation
► Respiratory system disease
► Cardiovascular disease
► Headaches
► Severe dental disease
► Needle marks and abscesses – intravenous only
► Seizures
Long-term effects of stimulants

- Strokes, seizures, and headaches
- Irritability, restlessness
- Depression, anxiety, irritability, anger
- Memory loss, confusion, attention problems
- Insomnia
- Paranoia, auditory hallucinations, panic reactions
- Suicidal ideation
- Sinus infection
- Loss of sense of smell, nosebleeds, chronic runny nose, hoarseness
- Dry mouth, burned lips
- Worn teeth (due to grinding during intoxication)
- Problems swallowing
- Chest pain, cough, respiratory failure
- Disturbances in heart rhythm and heart attack
- Gastrointestinal complications (abdominal pain and nausea)
- Loss of libido
- Malnourishment, weight loss, anorexia
- Weakness, fatigue
- Tremors
- Sweating
- Oily skin, complexion
Stimulant withdrawal symptoms

- Depression
- Difficulty concentrating
- Increased need for sleep / insomnia
- Memory dysfunction
- Anxiety
- Decreased sex drive
- Low energy
- Irritability
- Headache
- Craving
Amphetamine type stimulants – ATS
Amphetamine-type stimulants (ATS) are a group of substances comprised of synthetic stimulants, including amphetamine, methamphetamine, methcathinone and ecstasy-type substances (e.g. MDMA and its analogues)
ATS prevalence

ATS are attractive to millions of drug users in all regions of the world because they are affordable, convenient to the user and often associated with a modern and dynamic lifestyle. Their risks are often underestimated in public perception.
Use of amphetamines* and prescription stimulants in 2014 (or latest year available)
Amphetamine and ecstasy groups
global prevalence

- **Americas:** The proportion of people in treatment for cocaine use has decreased over the past decade.

- **Latin America and the Caribbean:** The number of people in treatment for cocaine use is quite high and makes nearly a half of all people in treatment for drug use disorders.

- **Asia:** Increase in treatment for the use of ATS, and a decrease in treatment for opioid dependence.

- **East and South-East Asia:** Increase in the use of amphetamines.
Expert perception of trend changes in the use of amphetamines*, 2014 or latest year available backward to 2010
Injecting ATS use growing and ↑ the risk of BBV (HIV)

Emergence of analogue substances falling outside of international control in established ATS markets

Substances such as mephedrone or methylenedioxypyrovalerone (MDPV) sold as ‘bath salts’ or ‘plant food’ and act as substitutes for illicit stimulant drugs such as cocaine or ecstasy
Total ATS seizures reported worldwide 2006-2014

Global seizures of amphetamines-group substances\(^{(a)}\) : 2005-2013

<table>
<thead>
<tr>
<th>Year</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
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<tr>
<td>Ton equivalents(^{(b)})</td>
<td>53</td>
<td>50</td>
<td>51</td>
<td>68</td>
<td>88</td>
<td>141</td>
<td>139</td>
<td>134</td>
<td>163</td>
</tr>
</tbody>
</table>

\(^{(a)}\) Amphetamine, methamphetamine and related non-specified amphetamines.

\(^{(b)}\) This quantity reflects the bulk weight of seizures, with no adjustment for purity. Seizures reported by volume (litres, millilitres, etc.) are converted to kg equivalents by assuming a weight of 1 kg per litre. Seizures of amphetamines-group substances reported in tablets or similar units are converted using assumed bulk tablet weights between 90mg and 300 mg, depending on the region and specific drug type, and based on information currently available to UNODC. Further details on conversion factors are given in the methodology section accompanying the World Drug Report.
What is methamphetamine?

Methamphetamine is a synthetic drug that is usually manufactured in illegal laboratories. Methamphetamine comes as a powder, tablet or as crystals that look like shards of glass. It can be swallowed, sniffed/snorted, smoked or injected.

Also called Crystal Meth, Crack Meth, Ice, Tik, Shabu, Yaba
How does methamphetamine affect users?

Methamphetamine stimulates a feeling of physical and mental well being, as well as a surge of euphoria and exhilaration. Users experience a temporary rise in energy, often perceived to improve their performance at manual or intellectual tasks. Users also experience delayed hunger and fatigue.
Risks associated with methamphetamine use

► **Short term:** impaired appetite, tachypnea, tachycardia, hypertension, increased body temperature and sweating

► **Large doses:** restlessness, irritability, panic attacks

► **Excessive dose:** convulsions, respiratory failure, CVA / heart failure

► **Long-term:** malnutrition, weight loss and the development of psychological dependence

► **Discontinuation of c/c use:** depression and increased somnolence

► **Other:** may trigger aggressive, violent & bizarre behaviour
Serious and permanent scars caused by scratching in a Methamphetamine user
Methamphetamine use

Scars from infected injection sites are often referred to as “tracks”
Methamphetamine use leads to severe tooth decay

“Meth Mouth”
Prenatal MA exposure

Preliminary findings on infants exposed prenatally to methamphetamine (MA) and non-exposed infants suggest…

► Prenatal exposure to MA is associated with an increase in SGA (small for gestational size)

► Neurobehavioural deficits at birth were identified in NNNS (Neonatal Intensive Care Unit Network Neurobehavioral Scale) neurobehaviour, including dose response relationships and acoustical analysis of the infant’s cry
Methamphetamine: psychiatric consequences

- Paranoid reactions
- Protracted memory impairment
- Depressive / dysthymic reactions
- Hallucinations
- Psychotic reactions
- Panic disorders
- Rapid addiction
Let’s think!

Case study

► What brief intervention would you suggest for Rory?

Rory, a 24-year-old student, presents with persistent headache, lethargy, and unexplained weight loss. He is “burning the candle at both ends,” working in a bar and studying, and states that “life is pretty hectic” at present. Speed helps him get things done.
What is MDMA?

3,4-Methylenedioxymethamphetamine

► Derivative of amphetamine & member of phenethylamine family

► MDMA & analogues: 3,4-methylenedioxyamphetamine (MDA) and 3,4-methylenedioxyethylamphetamine (MDEA), together called ecstasy-group substances

► MDMA hydrochloride, a white or off-white powder or crystals, is the most common salt form and is soluble in water

MDMA powder known by street names “Molly” or “Mandy”
Ecstasy: is it same as MDMA?

- MDMA was the original chemical found in ecstasy and the 2 terms were used interchangeably.
- Now, “ecstasy” pills contain varying products with MDMA alone/MDMA mixed with other psychoactive substance or no MDMA at all.
- MDMA is usually made into brightly coloured pills or capsules and sold as ecstasy for oral use. It is also snorted or injected.
- Ecstasy use has made its way into the mainstream culture in certain countries especially among young people.

“Ecstasy” also known by street names “E”; “X”; “XTC”; “Rolls”; “Beans”; “Adam” + imprinted logo in the pills, e.g. “Mitsubishi”, “Playboy”, “Rolex”, and many others.
Ecstasy: how does it affect users?

- Ecstasy can heighten users' empathy levels and induce a feeling of closeness to people around them.
- It is often used at "rave parties" to increase participants' sociability and energy levels.
- Ecstasy also clouds the user's judgment and increases the chance of him or her making bad choices, such as having unprotected sex. Thus, the user risks contracting HIV/AIDS, hepatitis and other infectious diseases.
Risks associated ecstasy use

- **Immediate effects:** dehydration, dizziness, exhaustion and impaired thermoregulation

- **Large doses:** restlessness, anxiety, visual / auditory hallucinations

- **Longer-term:** severe depression and memory loss, hepatic & renal dysfunction, convulsions & heart failure

- **Other risks:** tablets or pills that are sold as "ecstasy" may contain other potentially dangerous substances which can vary widely in strength and effects
Where are we so far?

► What are stimulants and how are they used?
► Can you give examples of ATS group stimulants?
► What is MDMA and how is it different from ecstasy?
► Can you give some examples of short-term and long-term effects of stimulants?
Break
Cocaine

Crack/Bazooka/Blanche/Cake/Coke/Lady
Coca bush
What is cocaine?

Cocaine is a fine white or off-white powder that acts as a powerful stimulant. It is extracted from the leaves of the coca plant. On the street, it can be diluted or “cut” with other substances to increase the quantity.

Crack is cocaine that has been further processed with ammonia or sodium bicarbonate and looks like small flakes or rocks.

► Cocaine → powder-sniffed, injected, smoked on foil
► Crack → smoked
Cocaine

- Alkaloid from plant leaf of Erythroxylon coca
- Known as Coke, Charlie, Snow, Okey Doke
- Central nervous system stimulant with local anaesthetic actions
- Also stimulates the sympathetic nervous system
- Blocks reuptake of dopamine, noradrenaline, and serotonin

Cocaine  Crack  Crack in vials
Chronic use of cocaine impact on neurochemistry
Cocaine: symptoms of withdrawal

- Dysphoria (rather than depression), which may persist (up to 10 weeks). Plus at least two of:
  - Fatigue
  - Insomnia / hypersomnia
  - Psychomotor agitation
  - Craving
  - Increased appetite
  - Vivid unpleasant dreams

- Withdrawal tends to peak 2–4 days following cessation of use
Cocaine free base
Cocaine: metabolism

- Rapid onset of action (2–8 minutes respectively)
- Peak blood levels occur in 5–30 minutes
- Action is brief:
  - half-life of 15–30 minutes if injected
  - half-life of up to 30 minutes if snorted
- Metabolised by liver, 1%–2% excreted unchanged in urine
- Inactive metabolites can be detected in:
  - blood or urine for 24–36 hours after use
  - hair for weeks to months after use
Risks associated with cocaine use

► **Short-term:** low appetite, tachypnea, tachycardia, increased body temperature; bizarre, erratic and sometimes violent behaviour

► **Excessive doses:** convulsions, CVA, heart failure

► **Long-term:** sniffing – damage nose tissue; smoking – respiratory problems; injection – abscesses & infectious diseases. Strong psychological dependence, malnutrition, weight loss, disorientation, apathy and a state similar to paranoid psychosis

► **Other:** mixing cocaine with alcohol is a dangerous cocktail and can greatly increase the chances of sudden death
Cocaine: acute and chronic effects as compared to methamphetamine

Since the half-life of cocaine is much shorter, in comparison to methamphetamine there is:

- Somewhat less severe neurotoxicity
- Somewhat lower frequency of drug-induced psychosis
- Somewhat shorter protracted withdrawal symptoms
Methamphetamine vs. Cocaine

► **Half-life:**
  - Cocaine: 2 hours
  - Methamphetamine: 10 hours

► **Paranoia:**
  - Cocaine: 4 - 8 hours following drug cessation
  - Methamphetamine: 7-14 days

► **Methamphetamine psychosis** – may require medication/hospitalisation and may not be reversible

► **Neurotoxicity:** Appears to be more profound with amphetamine-like substances
Cocaine epidemiology

- Global cultivation: 132,300 ha
- Global seizures: 655 tons
- Global production: 746,843 tons
- Global number of users: 18.3 million
Cocaine epidemiology

Global cultivation
- Most recent estimate (2014): 132,300 ha
- Change from previous year: 185,300 x 10%

Global seizures
- Stable
- Cocaine as seized: 655 tons

Global production
- 746-943 tons
- Pure cocaine
- Change from previous year: 38%

Global number of users
- 18.3 million
- 2014
Use of cocaine 2014

Use of cocaine* in 2014 (or latest year available)

* Cocaine includes cocaine salt, crack cocaine and other types of cocaine such as coca paste, cocaine base, basuco, paco and merla.
Cocaine global trends

- Cocaine use still concentrated in the Americas, Europe and Oceania
- Practically all of the world’s cocaine is produced in 3 countries in South America
- Expert opinion is that there may be pockets of emerging cocaine use in Africa & Asia, due to increase in trafficking through Africa, increase in affluence
- The most problematic use of cocaine is in the Americas
- In North America, cocaine use has been declining since 2006, partly due to a sustained shortage. However, more recently, a slight increase in prevalence has been observed in the United States, as has an increase in maritime seizures
Stimulants: pharmacology & clinical properties
Stimulants: synaptic activity

dopamine

dopamine receptor
Cocaine: neurobiology
Meth / Amphetamine effects: onset and duration

- **Amphetamine**
  - Injection: 1 min
  - Intranasal: 3 min
  - Swallowed: 6 hours

- **Cocaine**
  - Injection: 1 min
  - Intranasal: 3 min
  - Swallowed: 20 min

Duration of effect:
- 1 min
- 3 min
- 60 min
- 30 min
- 20 min
# Amphetamine effects

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Toxic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feel good Alert</td>
<td>Feel great Increased libido</td>
<td>Extreme agitation Incoherence</td>
</tr>
<tr>
<td>Alert Energy Confidence</td>
<td>Increased stamina No need for sleep</td>
<td>Increased temperature Dehydration</td>
</tr>
<tr>
<td>Sleeplessness Reduced appetite Dry mouth</td>
<td>Crash Suspicion Headache Teeth grinding Anxiety</td>
<td>Thought disorder Violent aggression Stroke Heart attack</td>
</tr>
</tbody>
</table>
“Typical” pattern of use

<table>
<thead>
<tr>
<th>Symptom Severity</th>
<th>Using</th>
<th>Stopping</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>‘Run’</td>
<td>Crash</td>
</tr>
<tr>
<td></td>
<td>Intoxication</td>
<td>Withdrawal</td>
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<tr>
<td>Low</td>
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<td>20</td>
<td>25</td>
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<tr>
<td>Days</td>
<td></td>
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</tr>
</tbody>
</table>

- Thought disorder
- Agitation
- Insomnia
- Suspicion
- Increased energy
- Feel good
- Exhaustion
- Depression
- Oversleeping
- Overeating
- No craving
- Anhedonia
- Lack energy
- Anxiety
- Sleepless
- High craving
- Flat mood
- Emotionally fragile
- Episodic craving to cues
Psychostimulants management
Assessment points

- Occupation
- Age
- Social activities
- Alcohol and drug (AOD) use history
  - patterns of use, drug type, route, other drug use
- Physical health (e.g., stability of weight)
- Mental health (emotional lability, psychosis / paranoia)
- Current level of intoxication/evidence of withdrawal
- Laboratory investigations
Management of toxic reactions

Priorities are:

- Maintain airway, circulation, breathing
- Control elevated body temperature (hydration, cold water, ice)
- Control seizures (IV diazepam)
- Manage psychotic symptoms (antipsychotics)
- Reassurance, support, comfort, minimal stimulation

Treatment depends on patient’s condition on presentation.
## Psychostimulant withdrawal

<table>
<thead>
<tr>
<th>Crash (days 1-3)</th>
<th>Peak Symptoms (days 2-10)</th>
<th>Residual Symptoms (from 1-8 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Exhaustion</td>
<td>• Dysphoria</td>
<td>• Episodic craving</td>
</tr>
<tr>
<td>• Depression</td>
<td>• Lack energy</td>
<td>• Insomnia</td>
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<tr>
<td>• Oversleeping</td>
<td>• Increased appetite</td>
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<tr>
<td>• No cravings</td>
<td>• Generalised aches and pains</td>
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<td></td>
<td>• Re-emergence of mild psychotic features, including: misperceptions, paranoid ideation,</td>
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<tr>
<td></td>
<td>hallucinations, anxiety</td>
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<td></td>
<td>• Sleeplessness</td>
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<td>• High craving</td>
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<td>• Episodic craving</td>
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<td>• Insomnia</td>
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<td>• Fluctuating</td>
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<td>• Irritability</td>
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<td>• Agitation</td>
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<td>• Restlessness</td>
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<tr>
<td></td>
<td></td>
<td>• Dysphoria</td>
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<td></td>
<td>• Lethargy</td>
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<td></td>
<td></td>
<td>• Amotivation</td>
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</tbody>
</table>
Withdrawal treatment

► Immediate withdrawal treatment
  – Setting (outpatient or inpatient)
  – Supportive environment, information, and reassurance
  – Provide ongoing monitoring
  – Plan long-term management strategies

► Planning for prolonged withdrawal
  – Anticipate it will be prolonged (i.e., affecting sleep, mood, cravings)
  – Plan for lapse and relapse
A staged treatment and a treatment that combines medication with therapy appropriate for the particular stage of treatment may have the best results.

Sufficient doses and medication compliance are of central importance.

- **Psychoactive dependence treatment model**

  - **Ablinence-Induction**: COCAINE, Amphetamines, Modafinil, Disulfiram, Methylphenidate, MetAMPH, Methylphenidate, Mirtazapine.
  - **Relapse-Prevention**: COCAINE, MetAMPH, Topiramate, Methylphenidate, Topiramate, naltrexone, bupropion.

  - **ACTIVE USE** → **INITIAL ABSTINENCE** → **SUSTAINED ABSTINENCE**

  - Contingency Management → Cognitive Behavioural Therapy for Relapse Prevention
Psychostimulant interventions

- Be non-judgemental, do not insist on abstinence
- Engage and retain patient in treatment
- Understand patient’s treatment goals
- Tailor intervention to suit patient, including level and intensity of referrals
- Offer flexible service delivery, consistent with a patient’s changing goals and needs
- Provide psychosocial support
- Address concurrent mental health needs, e.g., anxiety, bipolar, or attention deficit disorders are common with cocaine use
Low threshold treatment services

Low threshold treatment services for Stimulant users, especially Methamphetamine users

► Street outreach and field workers in clubs and bath houses
► Needle exchange
► Drop-in centres for food, medical services
► Housing for homeless methamphetamine users
► HIV risk reduction groups employing peer and professional counselling
► No empirical evidence at this point
Psychosocial interventions for the treatment of stimulant-use disorders

- Cognitive-Behavioral Therapy (CBT)
- Community Reinforcement Approach
- Contingency Management
- 12-Step Facilitation
- Brief Cognitive Behavioral Therapy
- Matrix Model

All have demonstrated efficacy for the treatment of cocaine and/or methamphetamine dependence.
Pharmacotherapy for psychostimulant withdrawal

- Aim is to decrease discomfort
- Non-stimulating/non-threatening environment
- Possible suicide precautions
- Medications to be given in combination with behavioral treatments (synergistic effect)
Medications with some level of evidence to support use in treating psychostimulant dependence

**COCAINE**
- Amphetamine
- Modafinil
- Disulfiram
- Methylphenidate

**AMPHETAMINE**
- Methylphenidate
- Mirtazapine
- Bupropion
Antagonist approach

- Peripheral blockers
  - Vaccine

- Indirect antagonists
  - Topiramate, Tiagabine, Gabapentin, Vigabatrin, Baclofen (↑GABA)
  - Naltrexone (↓Opiate)
  - Doxazosin (↓NA)

- Presynaptic DA depletion
  - Reserpine

- DA receptor blockers
  - Olanzapine, Aripiprazole
Disulfiram for treatment of cocaine dependence

- Disulfiram: reduce the rewarding effects of cocaine use
- Disulfiram beneficial when given with Inter Personal Therapy (IPT) or CBT
- Combination of Disulfiram & Naltrexone effective in abstinence from both alcohol & cocaine in their concurrent dependence
- In trials with comorbid alcohol and cocaine dependence, higher dose of Disulfiram, 500 mg/day used
Pharmacological treatment of stimulant drugs: current evidence base

- Psychosocial interventions – CBT & CM mainstay of treatment
- Use of dopamine agonists, anti-depressants or anticonvulsants, not recommended
- Disulfiram is not yet an established treatment for cocaine use, but current small evidence base is of interest
- No clear evidence to support substitute prescribing of dexamphetamine for treatment of cocaine or amphetamine dependence
- There is new promising indication for the effectiveness of psychostimulants (amphetamines, methylphenidate) for the treatment of amphetamine and cocaine abuse and dependence
Let’s think!

Case study

► How would you incorporate an alcohol and other drug history into your consultation?

► What triggers may lead you to suspect psychostimulant use?

Kylie, a 33-year-old lawyer, recently discovered she was pregnant. She has an active work and social life, and consequently, tends to eat poorly. The pregnancy was unplanned. She is concerned about the health of her baby and her lifestyle that precludes regular eating habits.
Questions
What are the stages of psychostimulant withdrawal?

Can you describe the psychostimulant dependence treatment model?

What kind of empirically supported methods are there for treatment of stimulant-use disorders?

Why and how to use pharmacotherapy for psychostimulant withdrawal?
Thank you for your time!
End of workshop 3