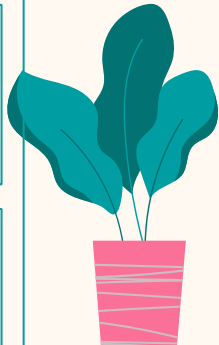


METHADONE REPLACEMENT THERAPY (MRT) IN PRIMARY CARE

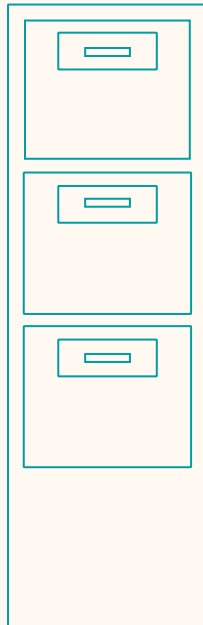
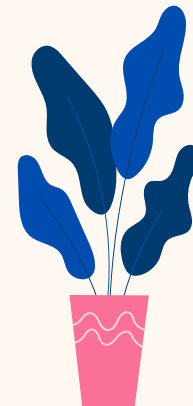


Dr. Siti Nuradliah bt Jamil
Pakar Perubatan Keluarga
Klinik Kesihatan Pasir Gudang



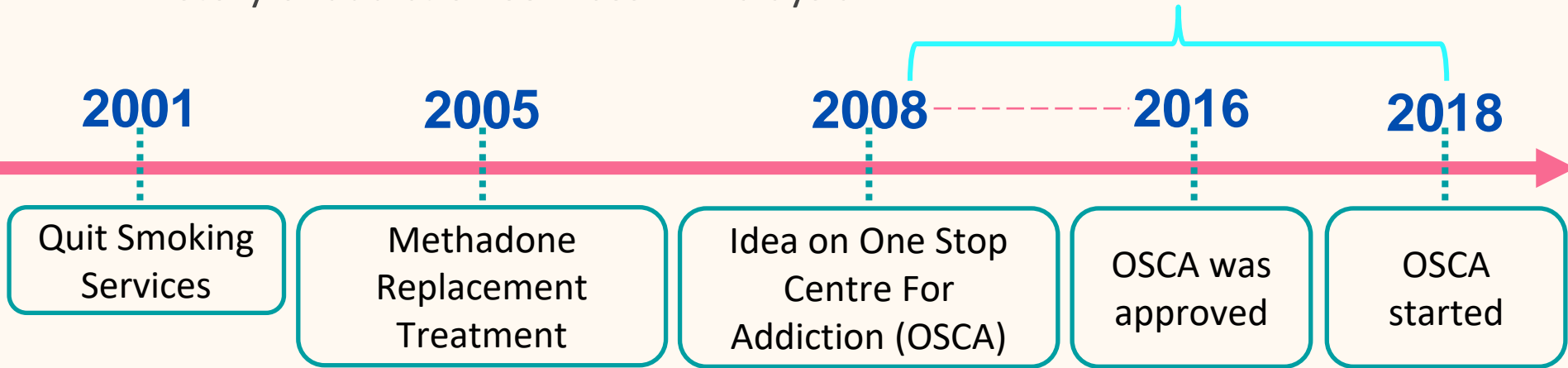
Outline :

- Introduction on MRT in Primary Care
- What is Methadone
- MRT
 - Objective
 - Policy of MRT & selection criteria
 - Compliance of patients receiving MRT
 - Treatment
 - Special situation & special population



Introduction : MRT in Primary Care

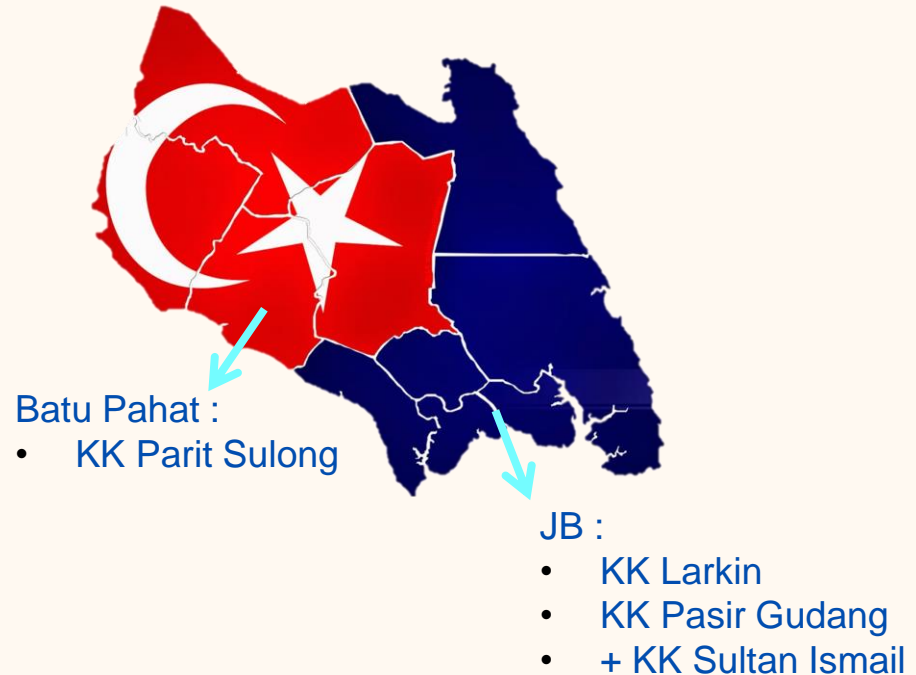
- History of addiction services in Malaysia :



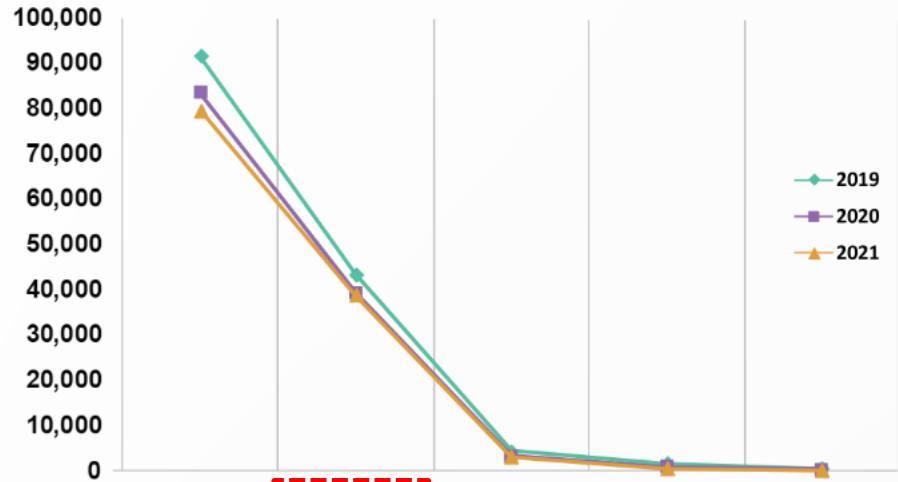
- Methadone replacement therapy : part of harm reduction strategy
- Currently, it is integrated under OSCA services in Primary Care in selected health clinic

Introduction : OSCA in Primary Care & Johor

States (Total: 32)	OSCA location
PERLIS (1)	KK Kuala Perlis
KEDAH (1)	KK Sg Petani
P. PINANG (1)	KK Butterworth*
PERAK (1)	KK Parit
SELANGOR (1)	KK Batu 9, Cheras*
WPKL (7)	KK Jinjang, KK Tanglin, KK Petaling Bahagia, KK Cheras, KK Sg Besi, KK Setapak, KK Kuala Lumpur,
WP PUTRAJAYA (2)	KK Presint 18, KK Presint 9
MELAKA (3)	KK Masjid Tanah* , KK Tengker, KK Merlimau
N. SEMBILAN (2)	KK Tampin, KK Bandar Sri Jempul
JOHOR (3)	KK Pasir Gudang & KK Larkin, KK Parit Sulong
PAHANG (4)	KK Beserah, KK Bandar Tun Razak, KK Benta, KK Bandar Jengka
KELANTAN (1)	KK Pengkalan Chepa
TERENGGANU (1)	KK Kuala Besut*, KK Kuala Abang
SARAWAK (2)	KK Tudan*, KK Petrajaya
SABAH (1)	KK Menggatal*
WP LABUAN (1)	KK Labuan



Jadual 1.8: Jumlah Penyalah Guna dan Penagih Dadah serta Bahan Mengikut Kategori Dadah, 2019 – 2021



KATEGORI DADAH/TAHUN	ATS	OPIAT	GANJA	LAIN-LAIN	PIL PSIKOTROPIK	JUMLAH
2019	91,684	43,578	4,497	1,826	614	142,199
2020	83,698	39,599	3,396	1,063	569	128,325
2021	79,816	39,100	3,179	697	347	123,139
PERBANDINGAN ANTARA TAHUN 2020 & 2021	-4.6%	-1.3%	-6.4%	-34.4%	-39.0%	-4.0%





POLISI DAN PROSEDUR OPERASI PI
**PROGRAM RAWATAN
METHADON**



Bahagian
Kementerian

GARIS PANDUAN

**KAUNSELING
METHADON**



BAHAGIAN PERKHIDMATAN FARMASI
KEMENTERIAN KESIHATAN MALAYSIA

GARIS PANDUAN

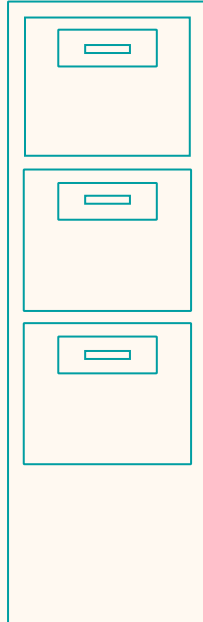
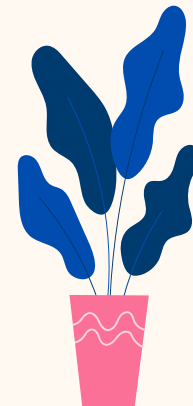
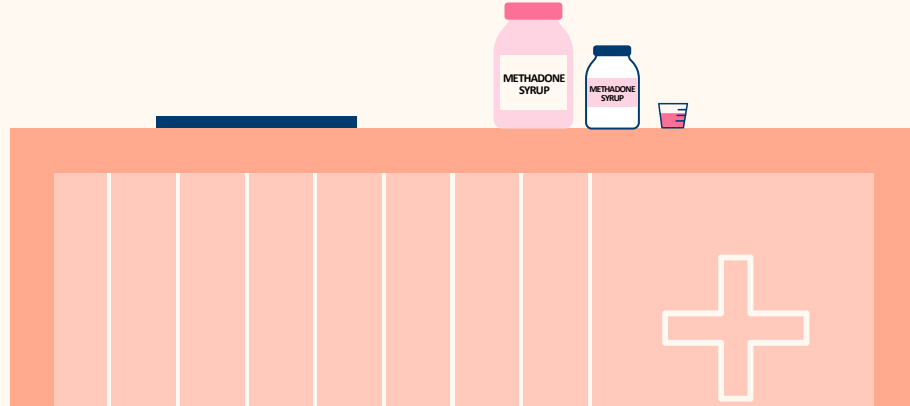
**PENDISPENSAN RAWATAN
TERAPI GANTIAN
METHADONE**



BAHAGIAN PERKHIDMATAN FARMASI
KEMENTERIAN KESIHATAN MALAYSIA

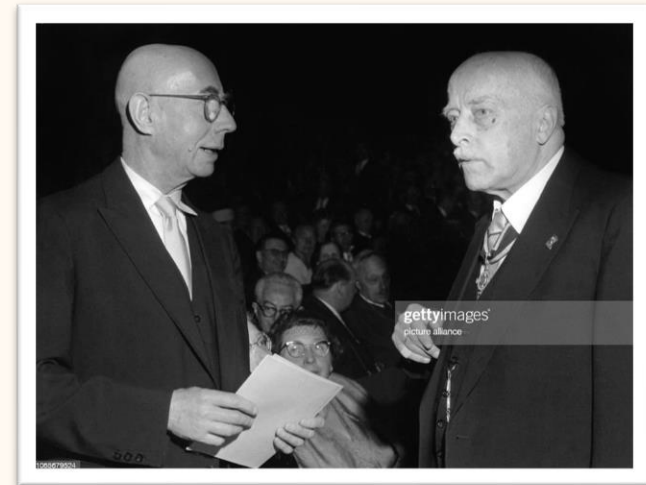
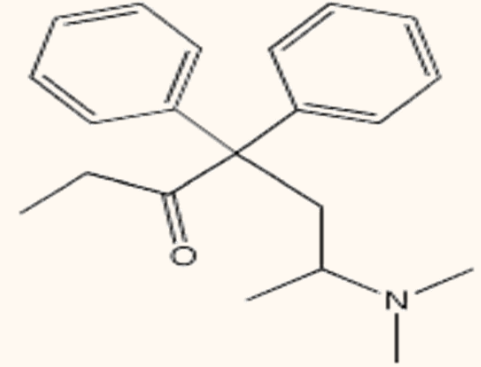
01

Methadone



Methadone :

- It is a long acting synthetic opioid agonist
- Developed by German chemist :
Gustav Ehrhart & Max Bockmühl
- Methadone action :
 - Reduces opioid craving
 - Reduced opioid withdrawal
 - Blunts or blocks the effects of opioids

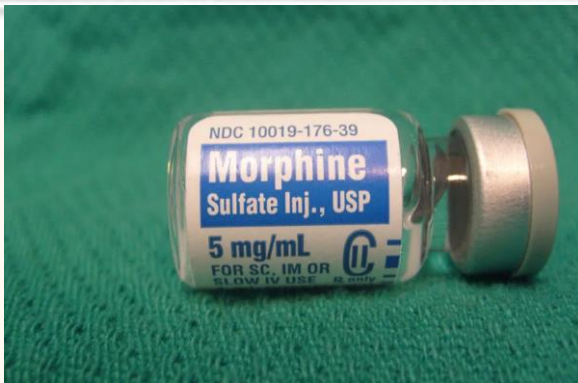


Opioid :

Local street names

Candu, Pink, Ubat, Pek Hoon, Che Putih, Heroin, Morphine, Codeine

Mode of administration: Inhalation ("chasing the dragon"), and intravenous injection



Illicit Opioids

- 'Candu'
- Heroin
- Morphine

Pharmacological Opioids

- Morphine
- Hydromorphone
- Hydrocodone
- Oxycodone & Oxycodone/Naloxone (Targin)
- Oxycontin
- Fentanyl
- Tramadol
- Codeine
- Methadone
- Buprenorphine

Agonis Penuh

- **Heroin**
- **Codeine**
- **Morphine**
- **Pethidine**
- **Methadone**

Agonis Separa

- **Buprenorphine**
(subuxone)

Antagonis

- **Naloxone**
(antidot)
- **Naltrexone**

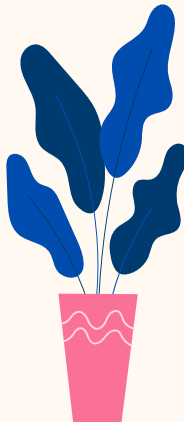
Opioid Receptor Types

Mu Receptor	Associated with opioid addiction
	Mu is for morphine
	Morphine for Morpheus Greek God of Dreams
	Activation produces analgesia, euphoria, Respiratory depression, and pupil constriction

Kappa Receptor	Activation also produces analgesia
	Hope for analgesia with less abuse potential not realized because produces psychosis

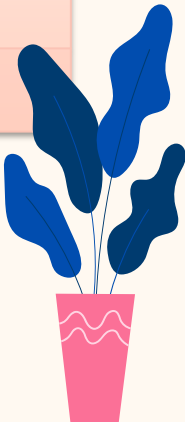
Delta Receptor	Activation in humans not well characterized
---------------------------	---

Affinity towards
mu receptors
Methadone > Heroin



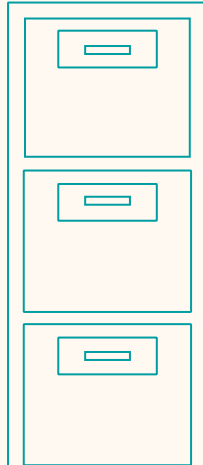
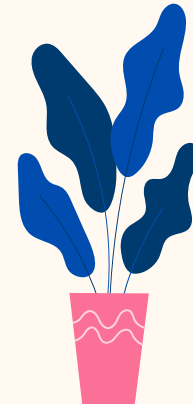
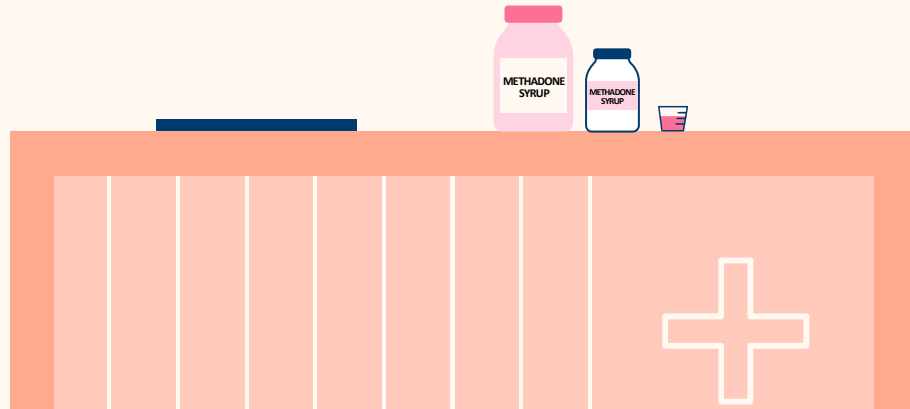
Heroin vs Methadone

	Heroin	Methadone
Route of admistration	IV / chase	Oral
Onset of duration	Immediate	30 minutes
Duration of action	3-6hours	24-36hours
Euphoria	First 1-2hours	None
Withdrawal symptoms	After 3-4hours	After 24hours



02

Methadone Replacement Therapy



Introduction : Objective of MRT

- Objektif Umum :

- Untuk **mengurangkan jangkitan penyakit bawaan darah**
- Merawat pesakit yang mempunyai **masalah penagihan khasnya opiat**
- **Meningkatkan kualiti hidup**

- Objektif Khusus :

- Mengurangkan **risiko dan penyebaran jangkitan HIV, Hepatitis B, Hepatitis C**
- Mengurangkan **penyalahgunaan dadah opiat dan komplikasi sampingan**
- **Mengurangkan kejadian pesakit relaps / menagih semula**
- Meningkatkan **kesihatan mental dan fizikal pesakit**
- Meningkatkan **keupayaan sosio ekonomi pesakit** dan membolehkan mereka mendapatkan pekerjaan
- Meningkatkan kesediaan dan penyesuaian pesakit untuk **kembali ke pangkuan masyarakat**
- Meningkatkan keselamatan masyarakat dan **mengurangkan kegiatan jenayah** yang dikaitkan dengan penagihan
- Mengurangkan **amalan berisiko melalui suntikan dadah**

Policy on Methadone Replacement Therapy

- 1 Setiap pesakit yang mengikuti rawatan methadone, mesti didaftarkan dan direkodkan.
- 2 Tiada had limit pengambilan / pendaftaran pesakit untuk mengikuti rawatan methadone di fasiliti-fasiliti rawatan.
- 3 Rawatan methadone di fasiliti Kerajaan diberikan secara percuma kepada warganegara Malaysia sahaja.
- 4 Methadone hanya boleh dipreskrib oleh pengamal perubatan berdaftar yang telah menjalani latihan dalam rawatan methadone.



Policy on Methadone Replacement Therapy

- 5 Latihan terdiri daripada latihan formal (sekurang-kurangnya 8 jam) oleh KKM/akademia/agensi diiktiraf atau secara sangkutan (*attachment*) di klinik Methadone selama lima (5) hari. Menghadiri kedua-dua latihan adalah digalakkan.
- 6 Preskripsi methadone hendaklah diperbaharui setiap kali rawatan susulan.
- 7 Methadone hendaklah didispens dalam bentuk cecair berkepekatan rendah oleh pengamal perubatan berdaftar, pegawai farmasi atau penolong pegawai farmasi diiktiraf.
- 8 Pendispensan methadone hendaklah dilakukan setiap hari secara *Direct Observation Therapy (DOT)*



Policy on Methadone Replacement Therapy

9 Pemberian dos bawa balik hanya boleh diberikan kepada pesakit yang stabil sahaja dan atas preskripsi serta pertimbangan pengamal perubatan yang merawat.

10 Segala pembekalan, rekod dan penyimpanan ubat methadone mestilah mematuhi semua perkara yang termaktub di dalam Akta Racun 1952 dan Peraturan - Peraturan Racun (Bahan-Bahan Psikotropik) 1989.

11 Rawatan susulan oleh Pengamal Perubatan berdaftar hendaklah dibuat secara berkala mengikut kemajuan pesakit atau sekurang-kurangnya setiap tiga (3) bulan dan setiap penilaian pesakit hendaklah dicatatkan di dalam rekod rawatan pesakit.



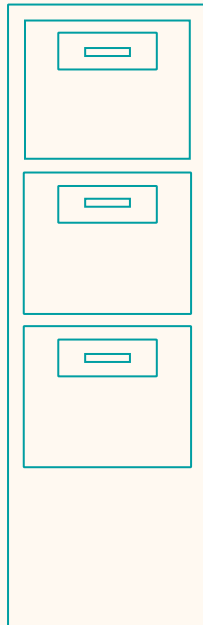
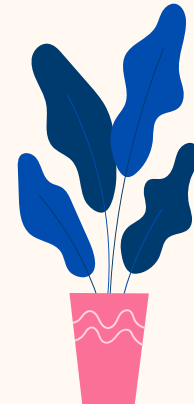
Process of Methadone Replacement Therapy

Patient Selection Criteria : Inclusion & Exclusion criterias

Compliance of Patients Receiving
Methadone Replacement Therapy

Registration, Early assesment including history taking,
physical examination

Dose initiation, titration, detoxification & Monitoring



Patient Selection Criteria for Methadone Replacement Therapy

- Pesakit yang mempunyai kebergantungan (*dependency*) kepada opiat dan mempunyai tempoh pengambilan opiat secara berkala dan berlanjutan.
- Diagnosis kebergantungan kepada opiat perlu dikenalpasti mengikut DSM 5 (*Diagnostic and Statistical Manual of Mental Disorder*) terbitan *American Psychiatric Association* 2015.

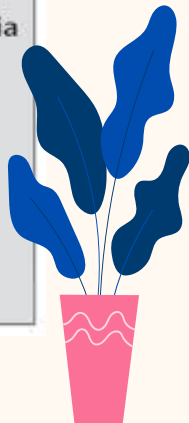
Substance Use Disorder (DSM 5, APA 2015) :

- Conditions arising from the misuse of alcohol, psychoactive drugs, or other chemicals such as volatile substances.
- Two or more substance use disorder criteria within a 12-month period.



DSM 5 : Substance Use Disorders

	DSM-IV Abuse ^a		DSM-IV Dependence ^b		DSM-5 Substance Use Disorders ^c	
Hazardous use	X	} ≥1 criterion	-	} ≥3 criteria	X	} ≥2 criteria
Social/interpersonal problems related to use	X		-		X	
Neglected major roles to use	X		-		X	
Legal problems	X		-		-	
Withdrawal ^d	-		X		X	
Tolerance	-		X		X	
Used larger amounts/longer	-		X		X	
Repeated attempts to quit/control use	-		X		X	
Much time spent using	-		X		X	
Physical/psychological problems related to use	-		X		X	
Activities given up to use	-		X	X		
Craving	-		-	X		



Patient Selection Criteria for **Starting** Methadone Replacement Therapy

- Pesakit yang mempunyai kebergantungan (*dependency*) kepada opiat dan mempunyai tempoh pengambilan opiat secara berkala dan berlanjutan.
- Diagnosis kebergantungan kepada opiat perlu dikenalpasti mengikut DSM 5 (*Diagnostic and Statistical Manual of Mental Disorder*) terbitan *American Psychiatric Association* 2015.



Patient Selection Criteria for Starting Methadone Replacement Therapy

KRITERIA KELAYAKAN (*INCLUSION*) DAN TIDAK LAYAK (*EXCLUSION*)

Sila tandakan (✓) pada kriteria yang berkenaan

(A) Kriteria Layak (Inclusion) Mengikuti Program Rawatan Rawatan methadone



Penagihan utama adalah kepada dadah jenis opiat



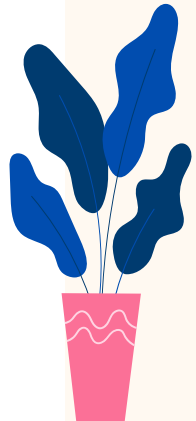
Pergantungan / penagihan dadah mesti disahkan dan tempoh penagihan opiate hendaklah sekurang-kurangnya setahun



Pesakit secara sukarela mengikut program ini



Pesakit mesti mematuhi semua peraturan dan prosedur yang ditetapkan



Patient Selection Criteria for Starting Methadone Replacement Therapy

(B) Kriteria Tidak Layak (Exclusion) Mengikuti Program Rawatan Rawatan methadone



Penagihan utama adalah dadah bukan opiat



Penagihan opiat kurang dari 1 tahun (pengamal perubatan berdaftar perlu mendapatkan konsultasi Pakar Psikiatri / Pakar Perubatan Keluarga bagi memulakan rawatan kepada pesakit sekiranya keadaan memerlukan)



Pesakit mempunyai kegagalan hepatic yang teruk (*clinically decompensated liver disease*)

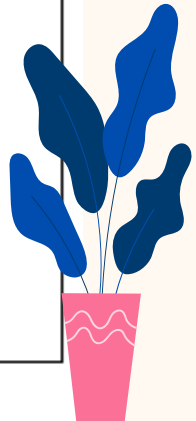


Pesakit mempunyai sejarah hipersensitif kepada methadone



Pesakit mempunyai penyakit mental tidak terkawal (rujuk pesakit untuk nasihat pakar)

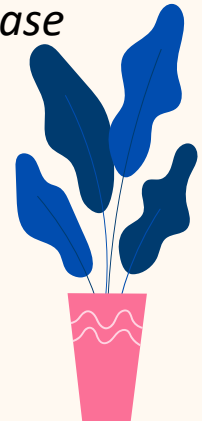
Nota: Kriteria di atas boleh disemak semula oleh Pakar Psikiatri / Pakar Perubatan Keluarga



Patient Selection Criteria for Starting Methadone Replacement Therapy

- ✗ • Masalah perubatan teruk (*Acute Medical Disorders*) - pesakit mempunyai masalah perubatan lain seperti depresi pernafasan yang teruk, asma akut, alkoholism akut, kecederaan kepala dan tekanan intrakranial tinggi (*raised intracranial pressure*), kolitis ulseratif, kekejangan (*spasm*) saluran biliari dan renal, pesakit sedang menerima rawatan *monoamine oxidase inhibitors* atau dalam tempoh 14 hari selepas berhenti rawatan (*monoamine oxidase inhibitors*).
- Pesakit bagaimana pun boleh dirujuk untuk nasihat pakar.

Monoamine oxidase inhibitors (MAOIs)				
Phenelzine	15	30	Hypertensive crisis which has been associated with intracranial bleeding, postural hypotension, arrhythmias, headache, abdominal discomfort, constipation, weight gain, dry mouth, somnolence, erectile dysfunction	B
Moclobemide	150	150 - 600	Hypertensive crisis, tachycardia, dizziness, headache, abdominal pain, nausea, diarrhoea, vomiting, sleep disturbances, constipation, somnolence, agitation, anxiety, increased appetite, blurred vision	B



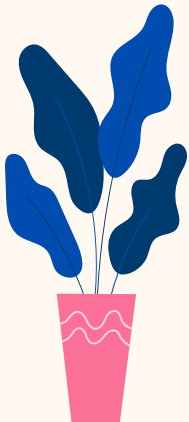
Patient Selection Criteria for **Stopping** Methadone Replacement Therapy

- Pusat rawatan mempunyai bidang kuasa untuk **memberhentikan rawatan** selaras dengan kesihatan.

Nota: Ujian urin positif dadah **BUKANLAH** satu kriteria untuk memberhentikan atau menangguhkan rawatan methadone.

mengganggu perjalanan atau keharmonian klinik.

- **Menjalankan Aktiviti Pengedaran dan Penyalahgunaan Dadah Di Kawasan Fasiliti Rawatan** : Termasuk mengedar, menjual, membeli atau memiliki dan menggunakan sebarang jenis dadah yang dilarang.
- **Penyelewengan Dos Bawa Balik (DBB) Methadone** : Termasuk menjual atau berkongsi dos methadone bawa balik.



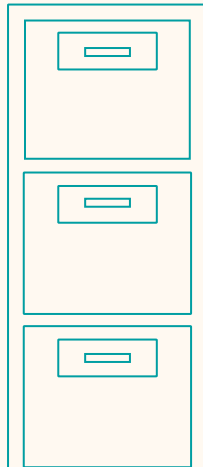
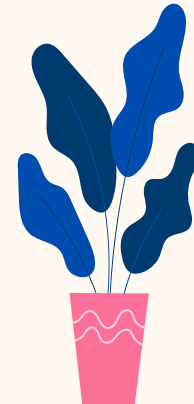
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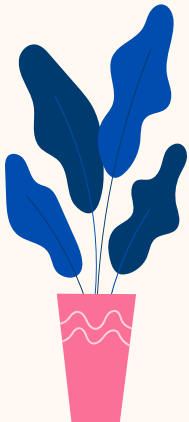
Dose initiation, titration, detoxification & Monitoring



Compliance of Patients Receiving Methadone Replacement Therapy

Pematuhan pesakit yang mengikuti program rawatan methadone Kerajaan hendaklah menandatangani kontrak persetujuan pesakit (Lampiran 2) bagi mengikuti rawatan tersebut dan mematuhi syarat-syarat yang telah ditetapkan:

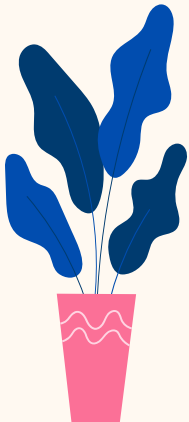
- Memahami bahawa **tujuan rawatan** adalah **sebahagian** daripada **proses pemulihan sepanjang hayat**.
- Pesakit hendaklah **memberi sepenuhnya kerjasama** terhadap program ini dan **mematuhi segala peraturan** yang telah ditetapkan.
- Pesakit hendaklah **menghadiri sesi intervensi psikososial** yang dijadualkan.
- Pesakit hendaklah **menghadiri rawatan di klinik setiap hari sehingga stabil**.



Compliance of Patients Receiving Methadone Replacement Therapy

Kriteria pematuhan pesakit yang mengikuti program rawatan Methadone :

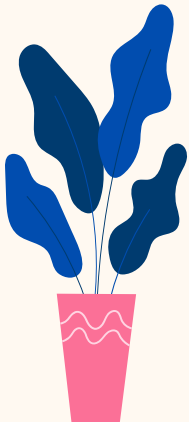
- Memahami bahawa **tujuan rawatan** adalah **sebahagian** daripada **proses pemulihan sepanjang hayat**.
- Pesakit hendaklah **memberi sepenuhnya kerjasama** terhadap program ini dan **mematuhi segala peraturan** yang telah ditetapkan.
- Pesakit hendaklah **menghadiri sesi intervensi psikososial** yang dijadualkan.
- Pesakit hendaklah **menghadiri rawatan di klinik setiap hari sehingga stabil**.



Compliance of Patients Receiving Methadone Replacement Therapy

Kriteria pematuhan pesakit yang mengikuti program rawatan Methadone :

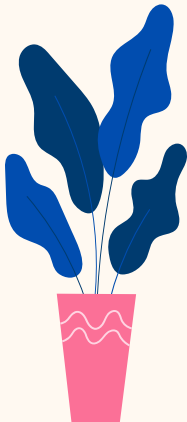
- Pesakit hendaklah menjalani ujian air kencing bagi saringan dadah atau apa-apa ujian yang berkaitan mengikut keperluan.
- Pesakit dinasihatkan berhati-hati sekiranya memandu kenderaan, menunggang motosikal atau mengendalikan sebarang mesin dalam tempoh 3-4 jam selepas minum dos methadone.
- Pesakit tidak digalakkan berkumpul tanpa alasan di fasiliti rawatan setelah mendapatkan rawatan.
- Pesakit digalakkan membawa ahli keluarga terdekat semasa rawatan dijalankan.



Compliance of Patients Receiving Methadone Replacement Therapy

Kriteria pematuhan pesakit yang mengikuti program rawatan Methadone :

- Pesakit hendaklah **memberitahu** petugas fasiliti rawatan jika mengalami **sebarang masalah kesihatan**.
- Pesakit perlu memaklumkan kepada petugas fasiliti rawatan jika **memerlukan rawatan methadone di fasiliti lain atau di luar kawasan**.
- Pesakit **dilarang membuat kacau ganggu di fasiliti rawatan** semasa menghadiri rawatan methadone.
- Pesakit **dilarang mengeluarkan kata-kata kesat atau ugutan** kepada mana-mana pihak.



Compliance of Patients Receiving Methadone Replacement Therapy

Kriteria pematuhan pesakit yang mengikuti program rawatan Methadone :

- **6.13** : Pesakit **tidak boleh mengambil apa juga jenis dadah terlarang yang lain, alkohol atau benzodiazepines seperti nimetazepam (erimin 5), diazepam (valium), midazolam (dormicum / dormi), alprazolam (xanax)** bersama dengan methadone kerana ia boleh membahayakan diri pesakit.

Nota: Penggunaan polisubstan seperti di para 6.13 BUKANLAH satu kriteria untuk memberhentikan atau menangguhkan rawatan methadone.

KRITERIA KELAYAKAN (INCLUSION) DAN TIDAK LAYAK (EXCLUSION)

Sila tandakan (✓) pada kriteria yang berkenaan

(A) Kriteria Layak (Inclusion) Mengikuti Program Rawatan Rawatan methadone

- Penagihan utama adalah kepada dadah jenis opiat
- Pergantungan / penagihan dadah mesti disahkan dan tempoh penagihan opiate hendaklah sekurang-kurangnya setahun
- Pesakit secara sukarela mengikut program ini
- Pesakit mesti mematuhi semua peraturan dan prosedur yang ditetapkan

Sila tandakan (✓) pada kriteria yang berkenaan

(B) Kriteria Tidak Layak (Exclusion) Mengikuti Program Rawatan Rawatan methadone

- Penagihan utama adalah dadah bukan opiat
- Penagihan opiat kurang dari 1 tahun (pengamal perubatan berdaftar perlu mendapatkan konsultasi Pakar Psikiatri / Pakar Perubatan Keluarga bagi memulakan rawatan kepada pesakit sekiranya keadaan memerlukan)
- Pesakit mempunyai kegagalan hepatic yang teruk (*clinically decompensated liver disease*)
- Pesakit mempunyai sejarah hipersensitif kepada methadone
- Pesakit mempunyai penyakit mental **tidak terkawal** (rujuk pesakit untuk nasihat pakar)

*Nota: Kriteria di atas boleh disemak semula oleh Pakar Psikiatri / Pakar Perubatan Keluarga***KONTRAK PERSETUJUAN PESAKIT**

Nama Pesakit : No KP :

Nama Pusat Rawatan : No ID Pesakit :

Saya (Nama Pesakit) bersetuju untuk menyertai Rawatan Rawatan methadone Kementerian Kesihatan Malaysia dan akan mematuhi syarat-syarat berikut :-

1. Saya akan memberi sepenuh kerjasama terhadap program ini dan mematuhi segala peraturan yang telah ditetapkan.
2. Saya bersedia untuk menjalani ujian air kencing apabila diminta.
3. Saya akan menghadiri rawatan Methadone di hospital atau klinik setiap hari sehingga saya betul – betul stabil.
4. Dos yang dibenar bawa balik hanya akan diberikan setelah saya benar-benar stabil dan di bawah kawalan serta memenuhi kriteria yang diberikan sebagaimana yang dipersetujui oleh doktor.
5. Saya akan menghadiri sesi kaunseling seperti yang dijadualkan.
6. Saya akan selalu berkelakuan baik dan tidak akan berkelakuan yang boleh mengganggu atau mendatangkan sebarang kecederaan kepada mana – mana orang samada dari segi fizikal, emosi atau mental.
7. Saya tidak akan mengeluarkan kata-kata kesat atau cercaan kepada mana-mana pihak.
8. Saya tidak akan menjalankan sebarang aktiviti atau kegiatan mengedar, menjual, membeli atau memiliki dan menggunakan sebarang jenis dadah yang dilarang.
9. Saya faham dan saya berikrar akan mematuhi semua perkara di atas sepanjang masa. Kegagalan saya berbuat demikian boleh menyebabkan saya diberhentikan dari menjalani program ini.

.....
(Tandatangan Pesakit).....
Tarikh.....
(Tandatangan Saksi).....
Tarikh

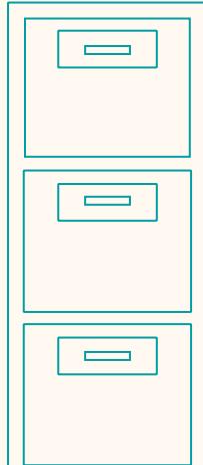
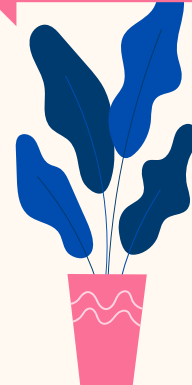
Process of Methadone Replacement Therapy

Patient Selection Criteria : Inclusion & Exclusion criterias

Compliance of Patients Receiving
Methadone Replacement Therapy

Registration, Early assesment including history taking,
physical examination

Dose initiation, titration, detoxification & Monitoring

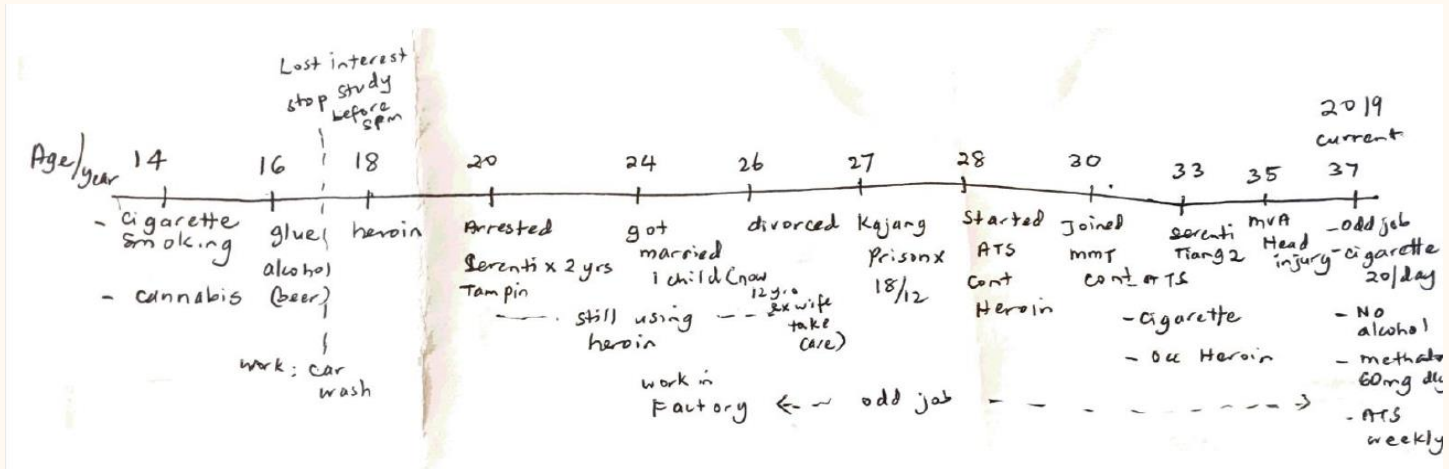


Procedure of Patients Receiving Methadone Replacement Therapy : Registration

- Semasa pendaftaran, penolong pegawai perubatan atau jururawat terlatih akan melengkapkan maklumat-maklumat berikut secara berperingkat:
 - Maklumat peribadi pesakit
 - Opiat Treatment Index – ‘baseline’, tahunan
 - ASSIST.V3 – baseline, tahunan
 - WHO QOL - ‘baseline’, tahunan
 - Kad ID Pesakit akan dikeluarkan kepada pesakit

Procedure of Patients Receiving Methadone Replacement Therapy : Early assessment

- History taking

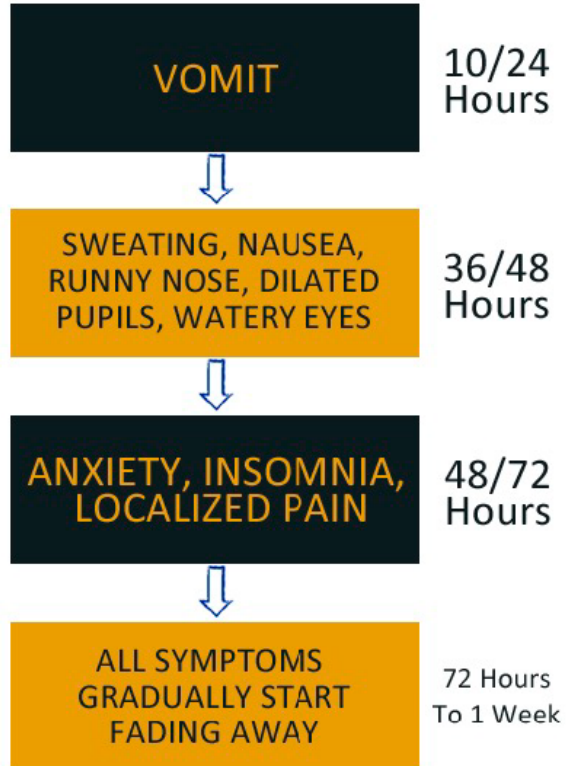


- Physical examination : tattoo, bar code scar, signs of chronic liver diseases

Opioid Withdrawal

- As the body gets used to a regular dose of opioids, it **slows production of natural opioids**
- When the dose is not taken, the body **experiences uncomfortable withdrawal symptoms**

opiate withdrawal timeline



Time since last heroin use	Common symptoms
6 to 12 hours	<ul style="list-style-type: none"> • runny eyes and nose, sneezing, yawning • sweating
12 to 24 hours	<ul style="list-style-type: none"> • agitation and irritability • goosebumps • sweating, hot and cold flushes • loss of appetite
More than 24 hours	<ul style="list-style-type: none"> • strong urges (cravings) to use heroin • stomach cramps, diarrhoea • poor appetite, nausea, vomiting • back pain, pain in joints, legs or arms, headache • poor sleep • lethargy, fatigue • restlessness, irritability, agitation • poor concentration • hot and cold flushes, increased sweating
2nd to 4th days	Symptoms reach their peak
5th to 7th days	Most physical symptoms begin to settle down; appetite returns
Second week	'Physical' discomfort subsiding; may have ongoing problems with poor sleep, tiredness, irritability, cravings, low mood
Weeks to months	Improvements in sleep, levels of activity and mood; and general health, and reduced cravings

Procedure of Patients Receiving Methadone Replacement Therapy : Invx & Monitoring

Investigations	At initial	1 st month	2 nd month	Monthly / Random	Annually
ECG	✓ If dose >100mg	-	-	-	✓
HIV	✓	-	-	-	✓
Hepatitis B	✓	-	-	-	✓
Hepatitis C	✓	-	-	-	✓
LFTs	✓	-	-	-	✓
FBS / FSL / RP	✓	-	-	-	✓
CXR	✓	If symptomatic			
Urine drug	✓	WEEKLY	2-WEEKLY	✓	-

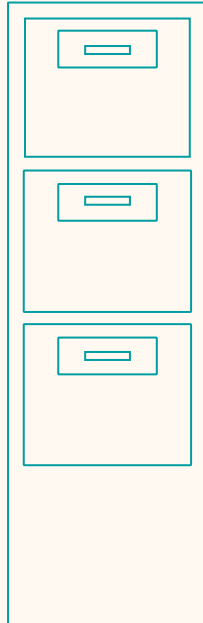
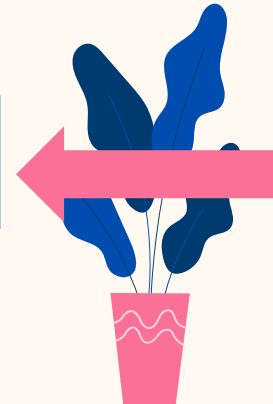
Process of Methadone Replacement Therapy

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physical examination

Dose initiation, titration, detoxification & Monitoring



Procedure of Patients Receiving Methadone Replacement Therapy : Treatment

- Objektif rawatan :
- Mengekalkan pesakit dalam rawatan dengan mengurangkan tanda dan gejala tarikan.
- Memulakan dos dengan kadar yang bersesuaian untuk mengelakkan kesan buruk (*adverse effect*) bagi mencapai dos yang diperlukan.
- Memastikan keselamatan pesakit semasa induksi.
- Kaedah pelaksanaan :
- Memastikan wujud satu hubungan terapeutik yang sesuai.
- Menerangkan dengan teliti kesan-kesan gian yang mungkin dialami semasa fasa induksi dan fasa pengekalan.
- Menggunakan dos yang selamat dan mencukupi.
- Pemantauan yang berterusan dilakukan terhadap pesakit yang mengikuti program ini.

Procedure of Patients Receiving Methadone Replacement Therapy : Treatment

- Pesakit yang telah melepasi pemeriksaan fizikal boleh terus diberikan **dos permulaan antara 20 – 30 mg (tanpa perlu menunggu keputusan ujian makmal).**
- Pesakit **digalakkan untuk dipantau 3 – 4 jam selepas dos permulaan** diberikan (masa dimana methadone menunjukkan kesan puncak) untuk melihat sebarang tanda toksik atau tarikan (*withdrawal*).
- Jika pesakit menunjukkan **gejala tarikan selepas 4 jam dos permulaan, dos suplementari sebanyak 5 mg boleh diberikan.**
- Pengamal perubatan boleh mempertimbangkan pemberian **dos permulaan yang lebih tinggi daripada 30 mg sekiranya perlu tetapi tidak melebihi 40mg.**
- Pesakit hendaklah **dipantau selama 3 – 4 jam selama 3 hari pertama** untuk mengelakkan terlebih dos (*overdose*).

Treatment : Induction

Peningkatan Dos :

- 5-10mg setiap 3 hari (jika tiada tanda tarikan)
- Tidak melebihi 20mg/minggu
- Jumlah dos minggu pertama tidak boleh > 50mg

Tempoh penstabilan

- Masa penstabilan dos biasanya SATU minggu/lebih

Dos Optimum

- 60-80mg/day

Dos Permulaan

- Boleh dimulakan TANPA ujian makmal
- Mula dengan Syrup Methadone 20-30mg/hari
- Pantau 3-4 jam utk kesan toksik atau withdrawal
- Jika ada withdrawal, boleh tambah melebihi dose 30mg (tetapi tidak melebihi 40mg/hari)

Treatment : Optimisation

9.5.3 Sebarang perubahan dos rawatan perlu mengambil kira perkara berikut

- i. Penggunaan semasa opiat mungkin memerlukan dos methadone yang lebih tinggi
- ii. Tahap metabolisma methadone seseorang pesakit
- iii. Penggunaan ubat lain (seperti anti-tibi , arv , psikotropik)
- iv. Kehamilan
- v. Penggunaan polisubstans

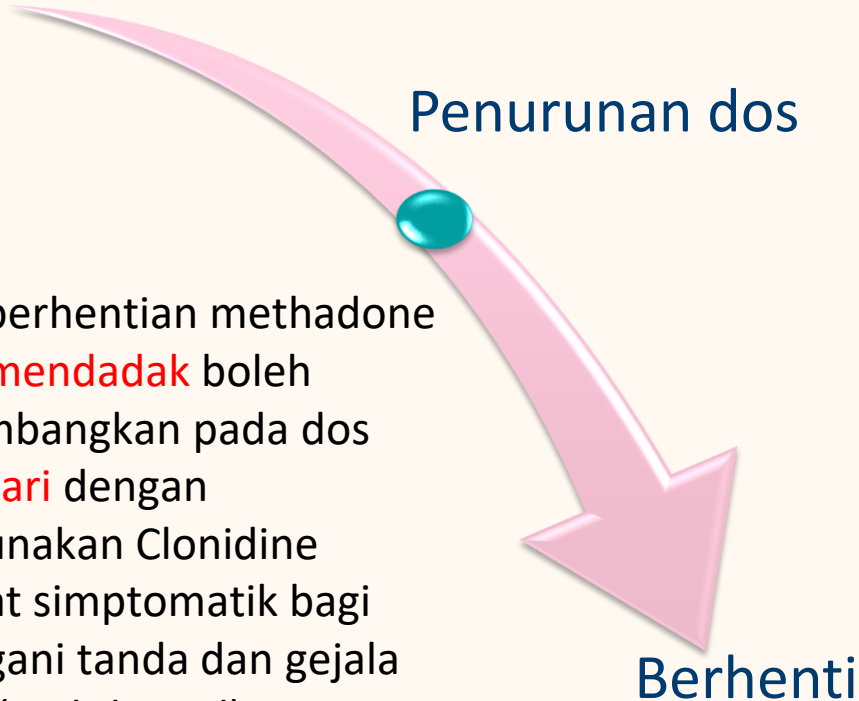
9.5.4 Pematuhan kepada pengambilan methadone setiap hari akan dapat memastikan aras methadone plasma dikekalkan dan dapat mengelakkan simptom / gejala tarikan

Treatment : Detoxification

- Jika pesakit bersedia untuk dan ingin berhenti dari rawatan → rujuk kepada Pakar Perubatan.
- Faktor – faktor yang perlu di nilai antaranya :
 - Sokongan Keluarga
 - Pekerjaan tetap
 - Bebas dari penggunaan dadah
 - Kekuatan sendiri
 - Stabil dalam rawatan
 - Coping mechanism dan pengurusan stress yang baik
 - Tiada masalah perubatan akut
 - Kesihatan mental yang baik

Treatment : Detoxification

Dos Optimum

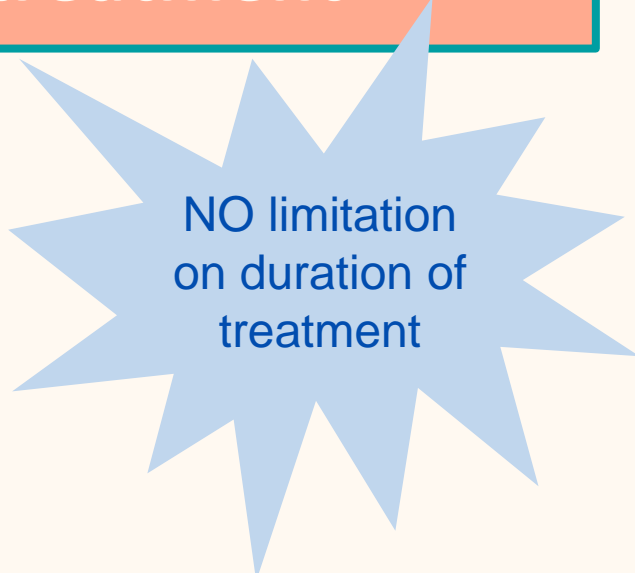


Pemberhentian methadone secara **mendadak boleh dipertimbangkan pada dos **40mg/hari** dengan menggunakan Clonidine dan ubat simptomatik bagi menangani tanda dan gejala tarikan (withdrawal)

- Penurunan yang tidak mendadak bagi mengelakkan kesan pengunduran teruk
- Penurunan / perubahan dos methadone hanya boleh dilakukan sekali seminggu
- 10mg/minggu hingga jumlah dos mencecah 40mg/hari
- Seterusnya 5mg/minggu
- Withdrawal : bawah 20mg/hari
- Kebanyakan 2-3hari selepas pemberhentian dos, sehingga 10-20hari
- Sokongan ubatan/psikologi/ + pemantauan yang berterusan

Treatment : Duration of treatment

- **Lebih lama** = hasil rawatan yang **lebih baik**.
- Dalam tempoh 1 tahun :
 - **Pengurangan ketara penggunaan opia**
 - **Pengurangan penglibatan dalam jenayah**
 - **Hubungan stabil**
 - **Pekerjaan stabil**
- Adalah **disarankan** agar pesakit dapat **kekal dalam rawatan sekurang – kurangnya 12 bulan** selepas mencapai perubahan gaya hidup yang kekal/stabil.



NO limitation
on duration of
treatment

Treatment : Take Away Dose (DBB)

- Diberikan kepada pesakit yg stabil selepas perbincangan bersama pasukan ie MO / FMS.
- DBB maksima: tempoh 3 hari.
- Bagi kes-kes tertentu, DBB boleh dilanjutkan **melebihi 6 hari** mengikut keperluan:
 - ibadah umrah / haji
 - lawatan ke luar negara
 - nelayan laut dalam
 - masalah kesihatan
 - mengikut keperluan pekerjaan
- Jika <3hari : DBB dicairkan dan diberikan dalam unit dos (bagi mengelakkan risiko terlebih dos (overdose) dan penyelewangan secara suntikan).
- Jika > 6hari : Pencairan ubat boleh dikecualikan.

Pesakit hendaklah **menyertakan dokumen pengesahan**

Treatment : Take Away Dose (DBB)

Jenis DBB



Jangka masa pendek

- Pesakit yang **belum stabil** tetapi mempunyai keperluan DBB
- Perlu pemantauan rapi

Jangka masa panjang

- Bagi pesakit yang telah menunjukkan kestabilan

Treatment : Take Away Dose (DBB)

- Penilaian untuk menentukan pesakit stabil bagi DBB → berdasarkan borang *Assessment of Patient's Stability For Take Away Dose* (Lampiran 12).
- Penilaian-penilaian awal sebelum DBB meliputi :
 - i. Penilaian menyeluruh terhadap pesakit sebelum memberi DBB
 - a. Sosial : Pekerjaan, keluarga dan kanak-kanak
 - b. Perubatan : Contoh - masalah ingatan (dementia kerana AIDS), penyakit psikiatri yang tidak stabil
 - ii. Berjumpa dgn wakil ahli keluarga untuk penerangan dan kerjasama dalam pemantauan DBB.

Take Away Dose (DBB) : Syarat-syarat DBB

- Pesakit **stabil dan tidak dalam keadaan intoksikasi**
- Pemantauan **urin bebas** dari sebarang dadah
- Pesakit **mematuhi semua peraturan dan pelan rawatan** yang ditetapkan
- **Kehadiran** pesakit ke pusat rawatan secara harian **mengganggu aktiviti pesakit yang berfaedah** (pekerjaan/kerjaya, pendidikan, masalah kesihatan, rumahtangga atau lain-lain aktiviti harian).
- **Tidak terlibat dengan aktiviti jenayah** termasuk penjualan dan pengedaran dadah
- Pesakit boleh menjamin **DBB boleh disimpan dan dijaga dengan selamat** di rumah (bukan di dalam peti sejuk atau tempat yang boleh dicapai oleh kanak-kanak)
- Pesakit **tidak menyalahguna DBB**
- **Tiada masalah kelakuan yang serius**

Take Away Dose (DBB) : Syarat-syarat DBB

- **Menandatangani Kontrak Perjanjian Persetujuan DBB**
- *DBB boleh diberhentikan sekiranya pesakit tidak patuh kepada syarat atau sekiranya pengamal perubatan yang merawat mempunyai keraguan ke atas pematuhan pesakit terhadap ubat dan mensyaki kemungkinan penyelewengan (diversion).*
- *Sekiranya preskripsi ubat methadone telah tamat tarikh, secara automatik pemberian DBB adalah terbatal.*
- *Semua DBB hendaklah direkodkan dalam preskripsi dan rekod rawatan pesakit.*

Take Away Dose (DBB) : Syarat-syarat DBB

Cadangan tempat selamat untuk penyimpanan:

- i. Mempunyai beg sandang atau 'pouch' untuk menempatkan
- ii. sementara DBB yang baru diperolehi
- iii. Menyimpan DBB di tempat tinggi dan berkunci
- iv. Tidak menyimpan DBB di dalam peti sejuk
- v. Tidak menyalin DBB ke dalam bekas lain yang tidak berlabel
- vi. serta boleh mendatangkan kekeliruan

Take Away Dose (DBB) : Syarat-syarat DBB

Pemantauan DBB :

- Pemeriksaan urin berkala secara rawak.
- Patuh kepada kehadiran pengambilan dos yang ditetapkan
- Lawatan ke rumah untuk memastikan DBB disimpan dengan selamat seperti cadangan di atas
- Peka terhadap maklumat tentang penyalahgunaan DBB dari sebarang sumber dan perlu menyiasat

Pengendalian pesakit yang bermasalah tentang DBB :

- Penyiasatan yang menyeluruh dan adil
- Memberi nasihat
- Memberi bantuan jika perlu dan bersesuaian
- Memberhentikan DBB kepada DOTS
- DBB masih boleh dipertimbangkan semula sekiranya pesakit menunjukkan kestabilan / perubahan yang baik

Missed Dose

1 2 3 4

Hari ke 3 :

- Dose asal >60mg – ½ dari dos asal
- Dos asal 30-60mg – 30mg
- Dos asal < 30mg – bagi dos asal

Hari ke 4 :

- 40mg atau separuh dos asal, yang mana lebih rendah

Pengurusan Kes Tertinggal Dos Methadone

Jumlah Hari		Tindakan
• Satu (1) hari	:	Tiada perubahan dos
• Dua (2) hari	:	Jika tiada tanda intoksikasi, berikan dos asal.
• Tiga (3) hari	:	<ul style="list-style-type: none">• Berbincang dengan pengamal perubatan• Administer separuh dos asal bagi dos melebihi 60mg.• Sekiranya dos asal 30mg – 60mg, administer 30mg.• Sekiranya dos asal kurang daripada 30mg, administer dos asal.
• Empat (4) hari	:	<ul style="list-style-type: none">• Berbincang dengan pengamal perubatan• Bekalkan dos sementara berdasarkan kebenaran pengamal perubatan• Rujuk pesakit kepada pengamal perubatan secepat mungkin• Disyorkan dos 40mg atau separuh dos yang mana lebih rendah
• Lima (5) hari dan lebih	:	Untuk rawatan permulaan semula.

Nota : Peningkatan dos seterusnya adalah 5 – 10 mg setiap tiga (3) hari sehingga mencapai dos asal.

MRT : Monitoring

- Pesakit perlu **dipantau setiap hari** oleh pegawai farmasi/pengamal perubatan (swasta) untuk tujuan penyelarasan dos methadone dan penilaian ke atas sebarang tanda intoksikasi.
- Pesakit perlu dinilai sekurang – kurangnya **dua kali dalam dua minggu pertama** selepas memulakan rawatan.
 - 1st two weeks – weekly review
 - 2weekly for 1month
 - 3monthly

Rawatan Susulan Yang Disarankan	
Tempoh Rawatan	Kekerapan susulan
• Dua minggu pertama (M1 dan M2)	: 2 kali setiap minggu
• Dua minggu kedua (M3 dan M4)	: Sekali seminggu
• Satu bulan seterusnya (M5 – M8)	: 2 kali dalam tempoh sebulan
• Bulan seterusnya	: ikut kemajuan pesakit atau sekurang-kurangnya setiap 3 bulan bagi pesakit yang telah stabil

Setiap kemajuan pesakit hendaklah dicatatkan di dalam rekod rawatan pesakit pada setiap rawatan susulan.

MRT : Monitoring

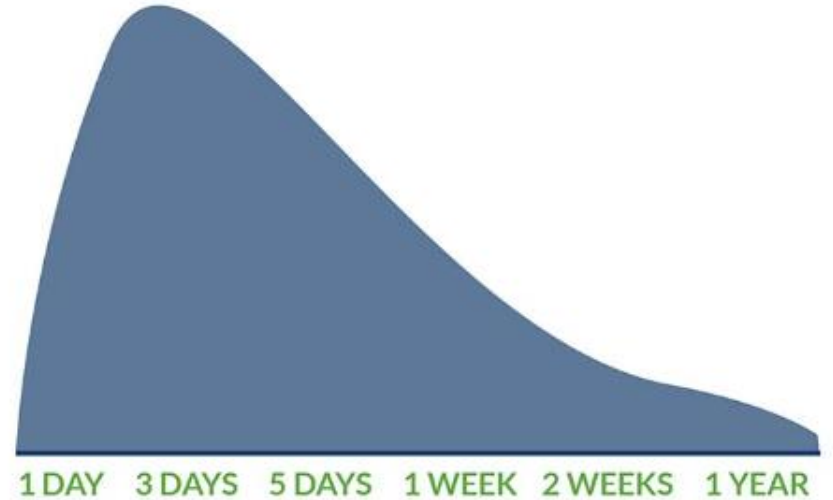
- Penilaian berikut perlu dipertimbangkan semasa pemantauan dalam minggu pertama bagi penyelarasan dos :
 - a. Tahap tarikan (*withdrawal*)
 - b. Intoksikasi
 - c. Penggunaan dadah terlarang
 - d. Penggunaan ubat lain
 - e. Kesan sampingan
 - f. Persepsi pesakit ke atas dos yang cukup
 - g. Pematuhan terhadap program methadone

Methadone withdrawal

METHADONE WITHDRAWAL

- 
- Chills ■
 - Anxiety ■
 - Nausea ■
 - Diarrhea ■
 - Vomiting ■
 - Irritability ■
 - Insomnia ■
 - Exhaustion ■
 - Runny nose ■
 - Muscle aches ■
 - Stomach cramps ■
 - Profuse sweating ■

METHADONE WITHDRAWAL TIMELINE



STAGE 1

Withdrawal symptoms appear within 30 hours and generate mild to moderate symptoms in the majority of users. However, the intensity quickly escalates

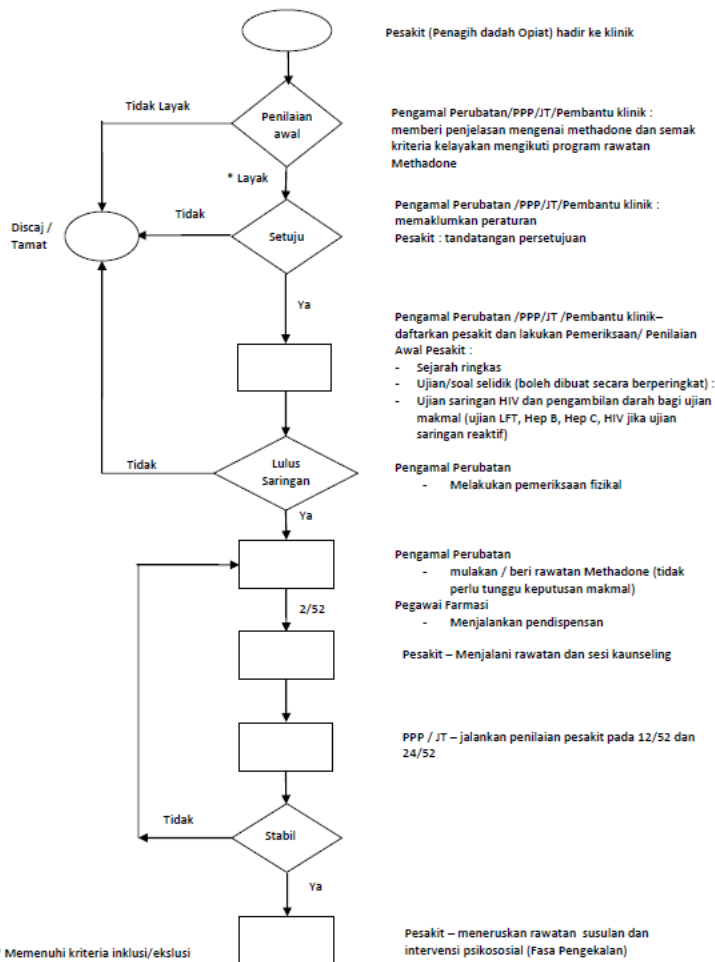
STAGE 2

The peak, or acute, withdrawal phase lasts approximately 1-3 days with the most intense symptoms subsiding within 1-2 weeks

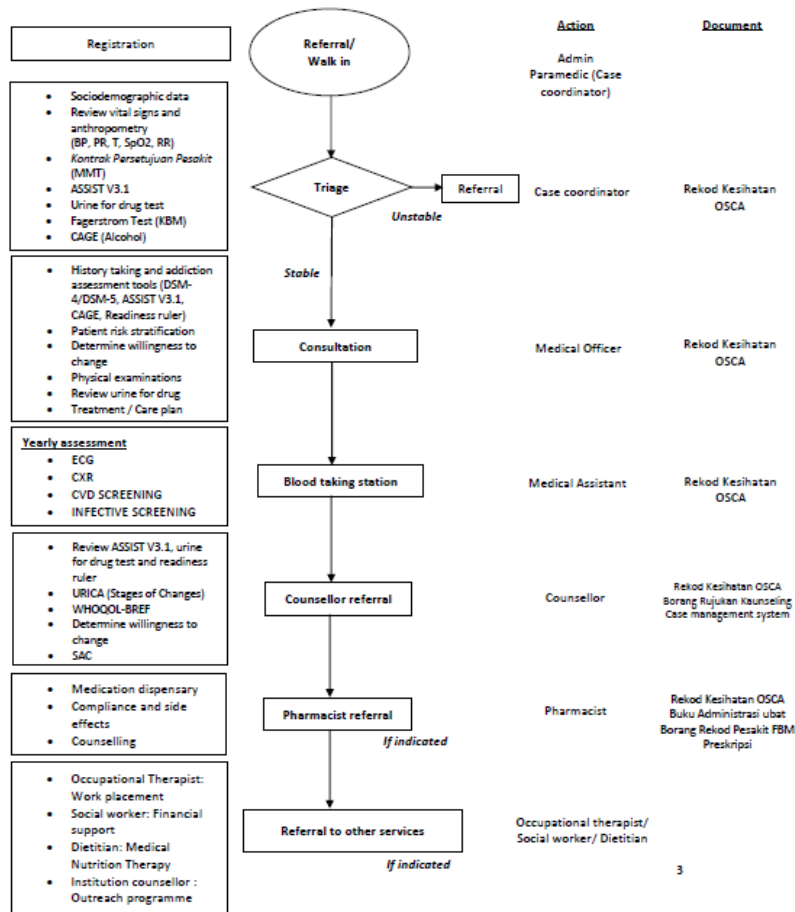
STAGE 3

Post-acute withdrawal syndrome (PAWS) may affect users for months, or even years

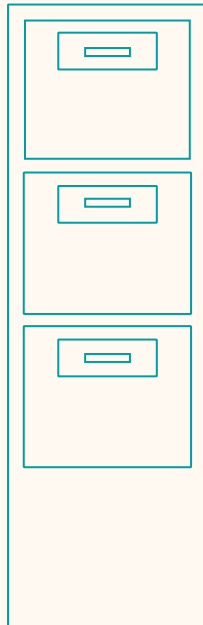
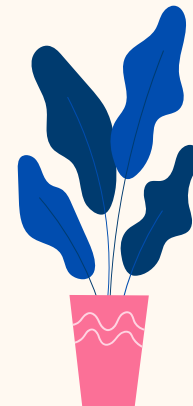
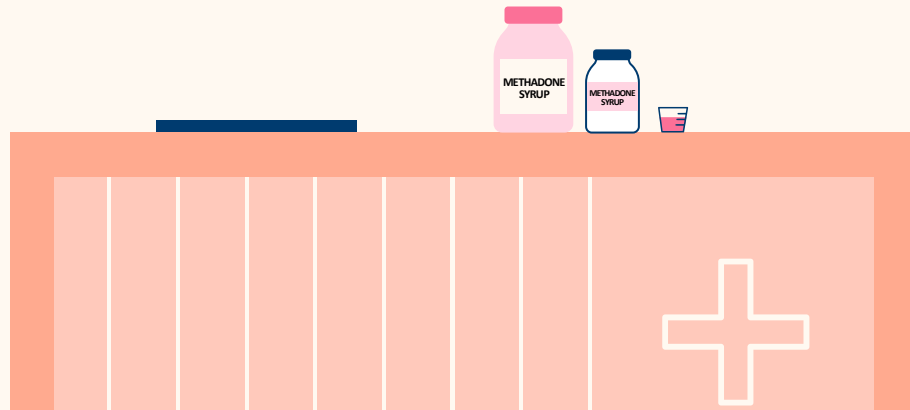
CARTA ALIRAN PROSEDUR RAWATAN METHADONE KERAJAAN



WORK PROCESS ON MANAGEMENT OF CLIENT IN OSCA CLINIC

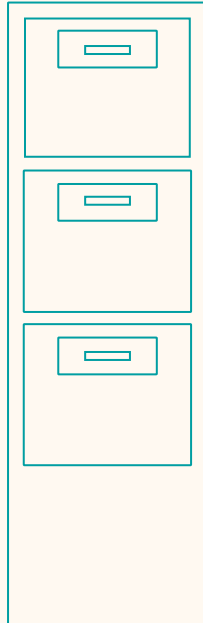
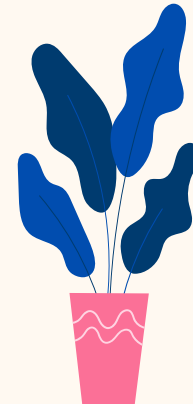
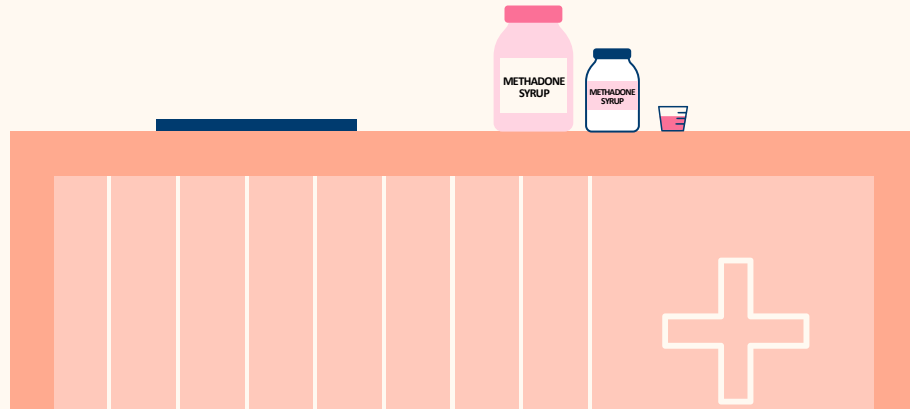


MRT in Special situation and population

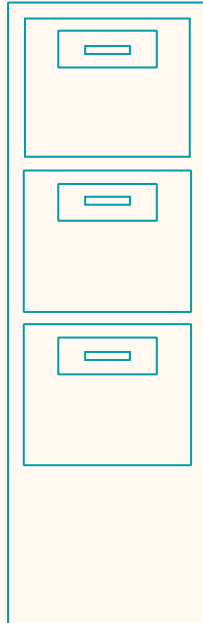
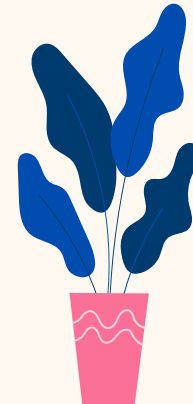
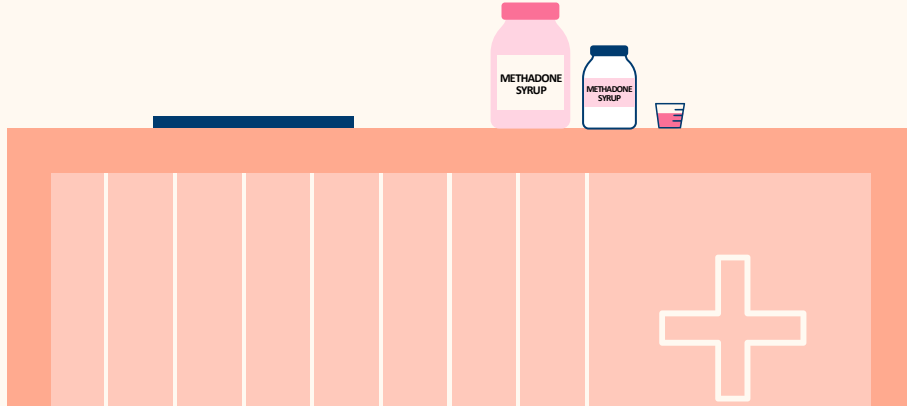


01

MRT in Special situation



MRT in Special situation : change from one pharmacotherapy to Methadone



Buprenorphine / naloxone

- a. Pesakit mengalami kesan sampingan terhadap buprenorphine/naloxone
- b. Respons terhadap rawatan buprenorphine /naloxone yang tidak mencukupi
- c. Penyalahgunaan buprenorphine/naloxone
- d. Ketiadaan buprenorphine/naloxone di pusat rawatan di mana pesakit berpindah masuk.

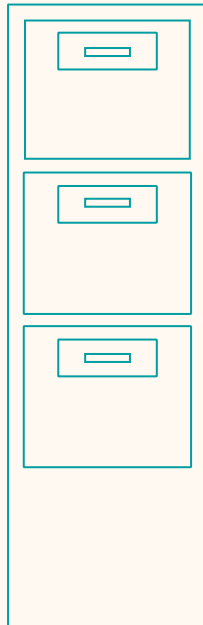
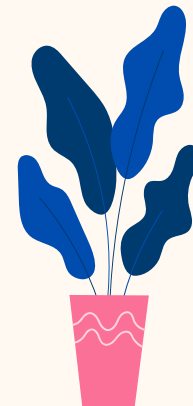
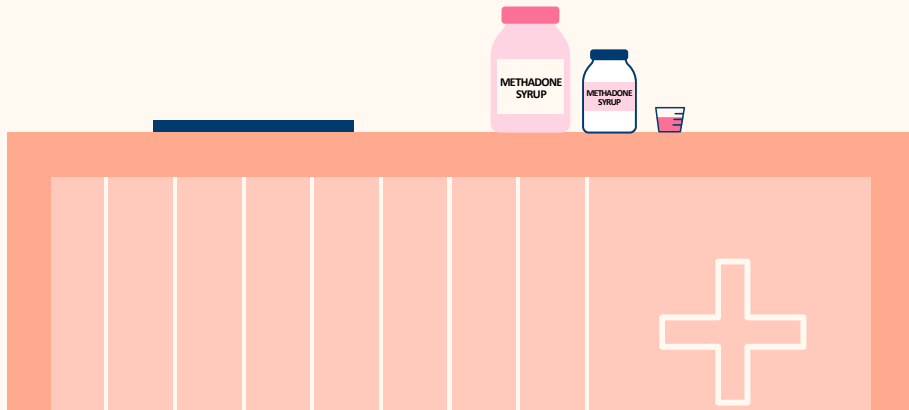
- Stabil dengan Buprenorphine / naloxone
- Kurangkan dos Buprenorphine / naloxone <8mg beberapa hari
- + Methadone 24jam selepas dos terakhir Buprenorphine / naloxone (not more than 40mg)
- Dos methadone yang rendah perlu dimulakan kepada pesakit yang sebelum ini mengambil dos buprenorphine/ naloxone yang rendah (4 mg atau kurang)

Naltrexone

Pertimbangan menukarkan preskripsi ini secara amnya disebabkan oleh relaps kepada opiat, susulan daripada pemberhentian naltrexone.

- JANGAN berikan methadone sehingga sekurang – kurangnya 72 jam selepas dos terakhir Naltrexone.
- Methadone yang dimulakan hendaklah tidak melebihi 20 mg dan perlu diberi secara berhati-hati.

Split Dose

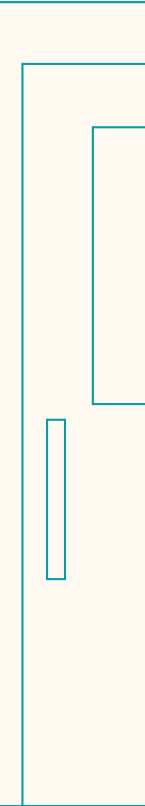
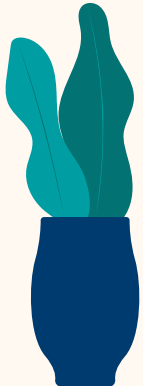


Methadone Split Dose

- Used only for **high doses** of methadone due to drug interaction effects (e.g. ART, anti-TB)
- A split-dosage can only be instituted by a physician and must be clearly defined by the dosage required by the patient, e.g.:

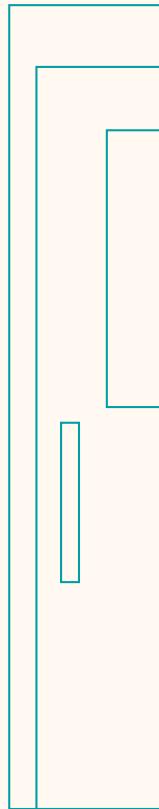
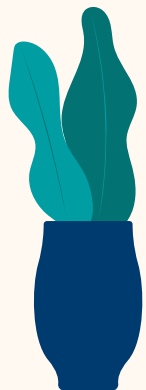
Syrup Methadone 90mg OM, 60mg ON

- A split-dosage for morning and evening needs to be supplied in 2 dose units (2 separate bottles).



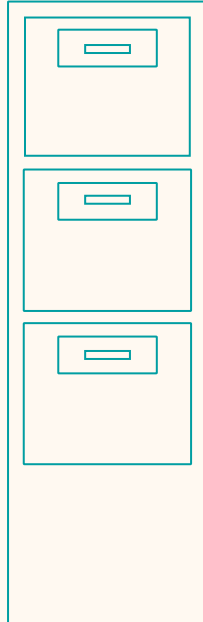
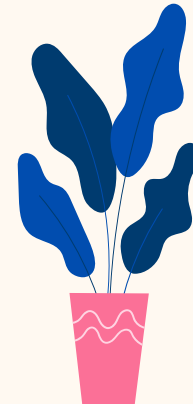
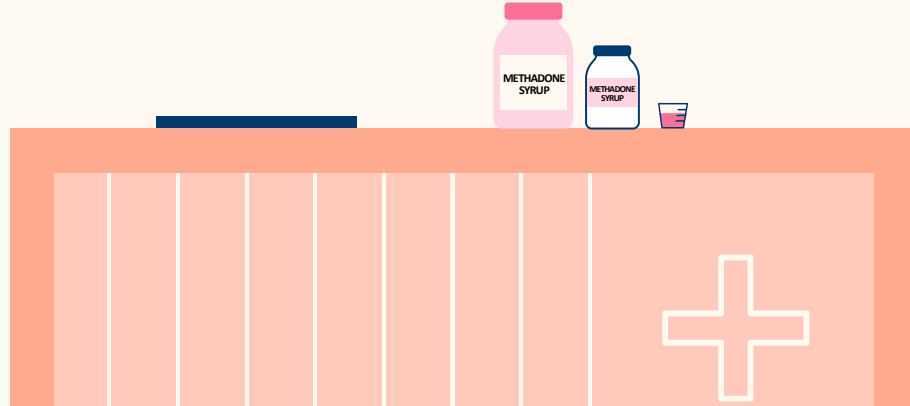
Methadone Split Dose

- The **split dose should be taken in DOTS** and **monitored daily for at least one week** to ensure that patients receive therapeutic dose.
- Any increase in methadone dose for patients who require a 'split-dose', methadone will be **dispensed by DOTS for at least 3 days** to ensure that the patient receives a therapeutic dose.



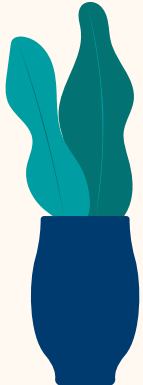
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During intoxication



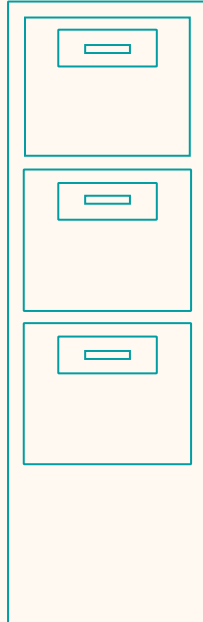
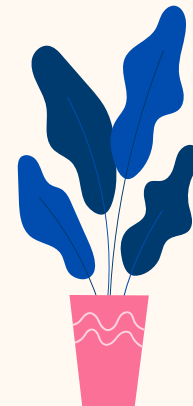
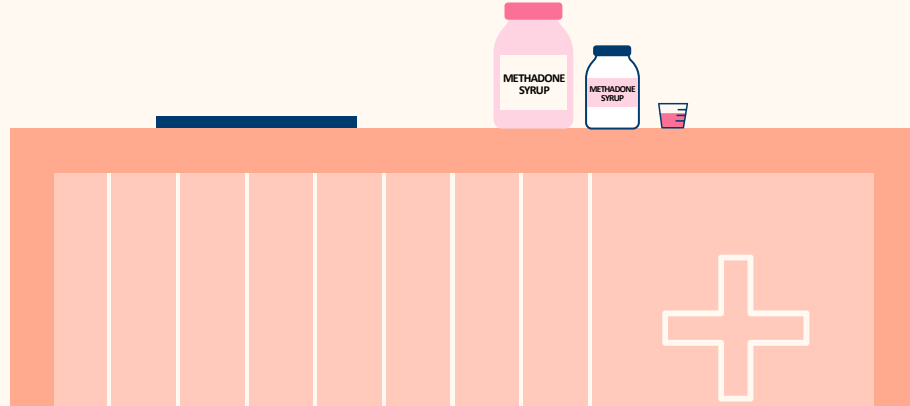
Methadone during Intoxication

- Methadone dispensing should be delayed and referred to the Medical Officer for further evaluation.
- Medical Officers need to get an specialist's opinion regarding the appropriate safe dose.



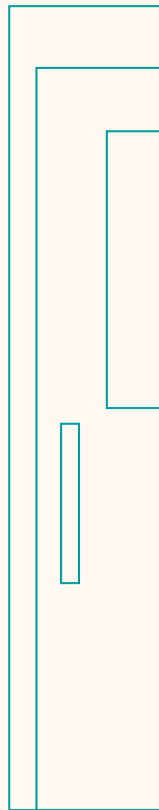
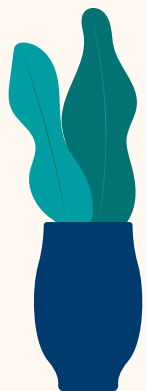
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Methadone Overdose



Methadone Overdose

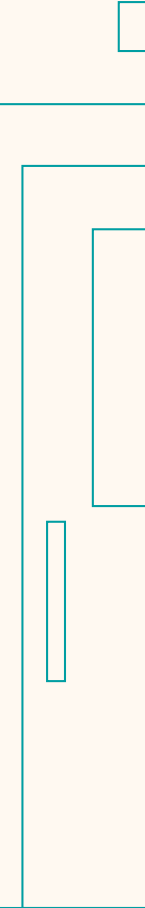
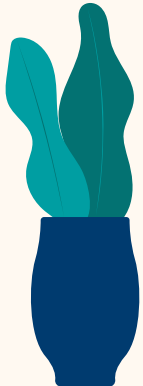
- More than 90% of deaths that occurred during stabilization of methadone treatment involve other drugs.
- Clients should be warned about the risks associated with using other drugs with methadone
 - Death after methadone induction often occurs
 - At home during sleep
 - Hours after peak concentration has occurred
 - Occurs around the third or fourth day of methadone induction



Methadone Overdose

Maybe related to:

- Other drug use (i.e. sedatives such as alcohol and benzodiazepines)
- Tolerance of incomplete evaluations
- Starting dose that is too high
- Lack of understanding regarding cumulative effects
- Inadequate observation and monitoring of dosage
- Variation of methadone metabolism in each individual



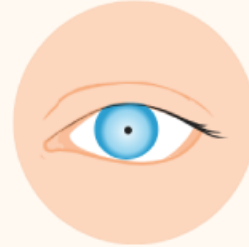
Methadone Overdose: Signs



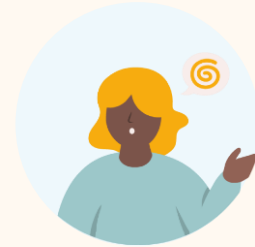
Unresponsive to voice/sound, coma



Feeling intoxicated / sedation / nodding off



Pinpoint pupils



Slurred Speech, Unsteady Gait



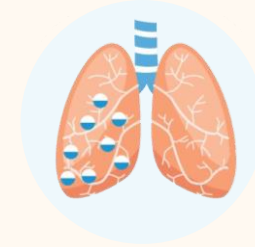
Blue or grey / ashen lips and nails



Bradycardia, Hypotension



Hypoventilation



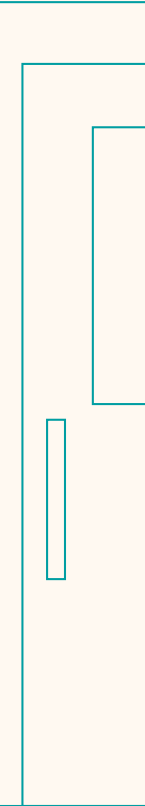
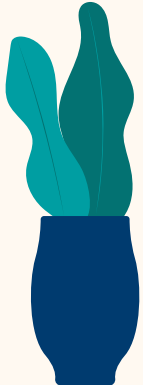
Pulmonary Oedema

Symptoms **can last for 24 hours or more. Death usually occurs as a result of respiratory depression.**

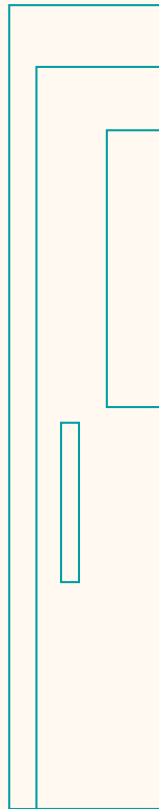
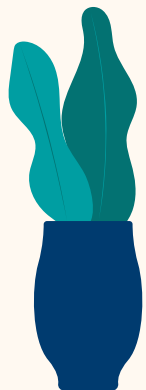
Methadone Overdose: Management

MONITORING

- Check frequently for vital signs, oxygen saturation
- Hold a brief conversation to assess alertness
- ECG and cardiac monitoring to check for prolonged QT interval and ventricular arrhythmias.



Methadone Overdose: Management



Methadone Overdose: Management

NALOXONE

- If the patient has respiratory depression, give 2.0 mg naloxone IV.
- If no respiratory depression, give 0.01 mg/kg body weight to avoid precipitating withdrawal.
- If no response after initial dose, repeat naloxone 2–4 mg every 2–3 min. If there is no response after 10–20 mg naloxone, search for other causes of coma.
- If the patient responds to naloxone, infuse at 2/3 the effective dose per hour.
 - Give a bolus of 1/2 the effective dose 15–20 min after starting infusion.
 - Titrate the dose to avoid withdrawal, while maintaining adequate non-assisted respirations.

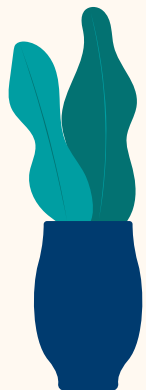


Methadone Overdose: Management

NALOXONE

Precautions:

- Ventricular dysrhythmias and cardiac arrest can occur with naloxone-induced withdrawal, especially if patients are withdrawing from other substances.
- The patient may become agitated and AOR discharge. Intubation avoids these risks.

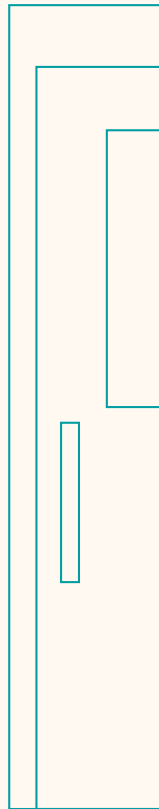
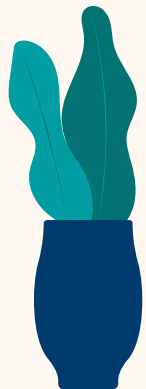


Methadone Overdose: Management

INTUBATION

This avoids risks of naloxone-induced withdrawal. Intubation is necessary if:

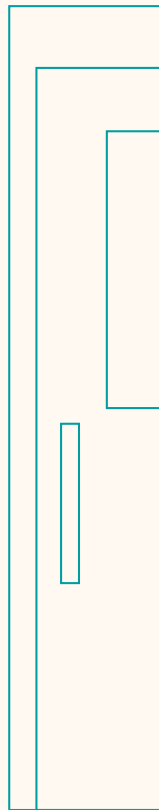
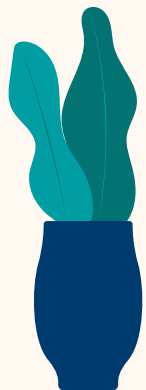
- RR < 12
- Hypercapnia
- Desaturation persists despite supplemental oxygen
- Patient fails to respond to naloxone within 2 min



Methadone Overdose: Management

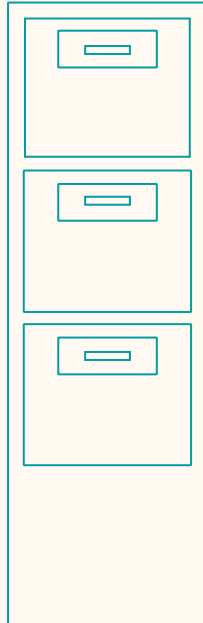
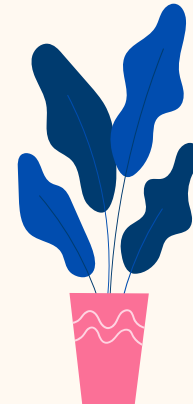
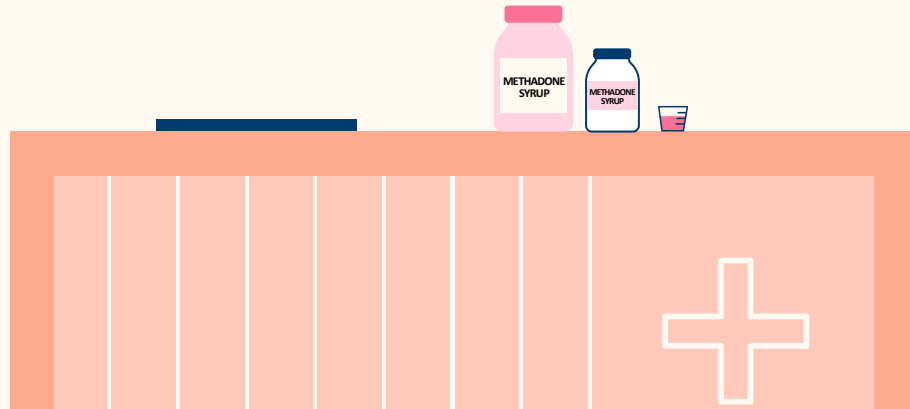
Time intervals for monitoring suspected methadone overdose:

- Observe for at least 10 hours post-overdose.
- Discharge if completely asymptomatic during that time.
- If symptomatic at any time during the 10 hours, observe for at least 24 hours post-overdose.
- If intubated or on naloxone, continue for at least 24 hours post-overdose.
- Monitor for at least 6 hours after naloxone or intubation discontinued.



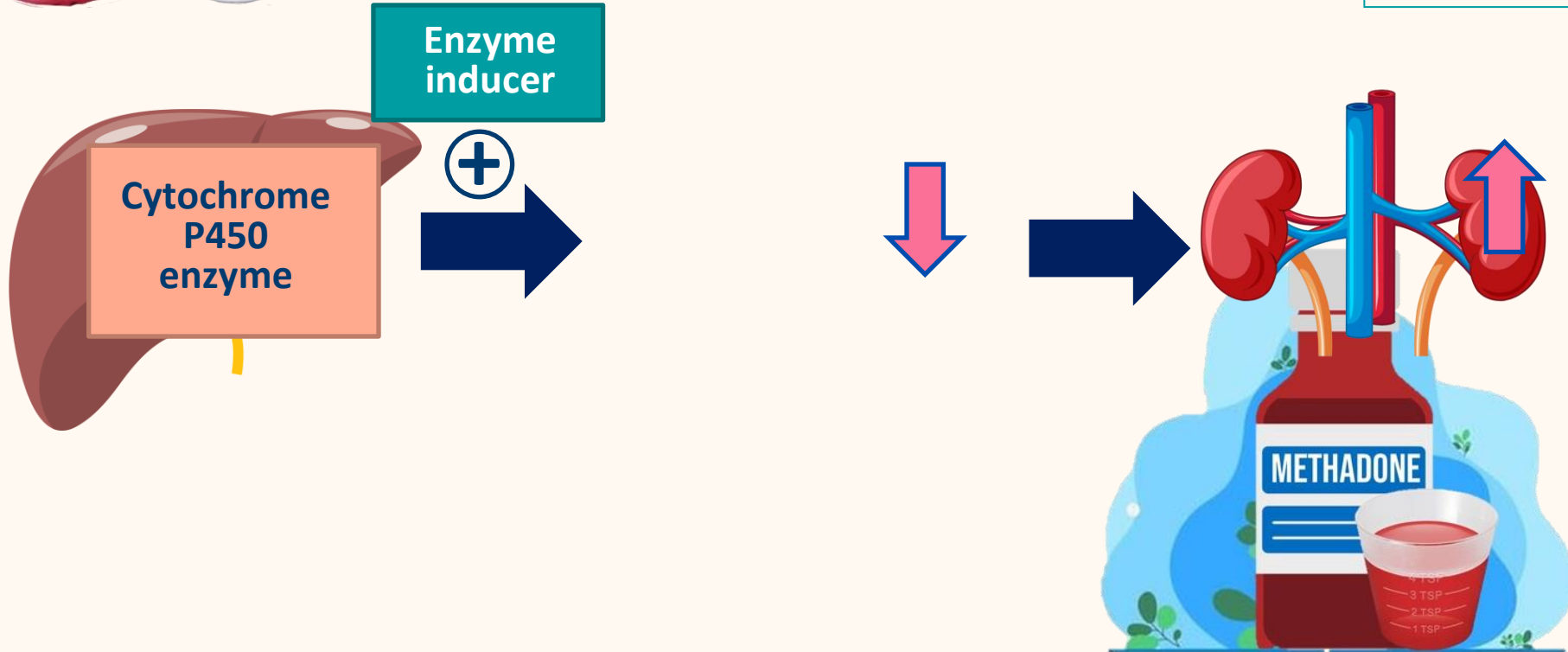
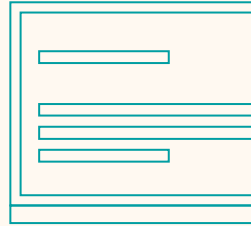
01

MRT in Special population





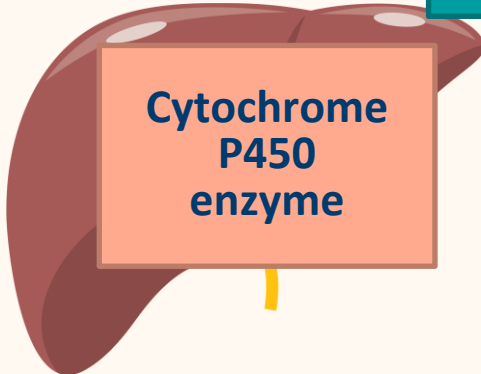
METHADONE Metabolism



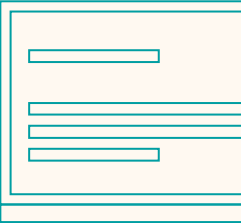
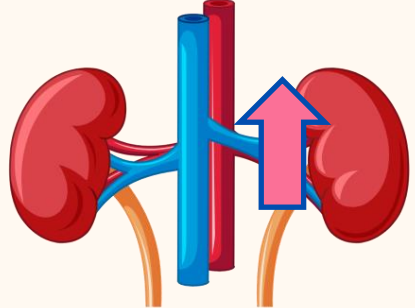
Methadone Metabolism



Enzyme inhibitor



Cytochrome P450 enzyme

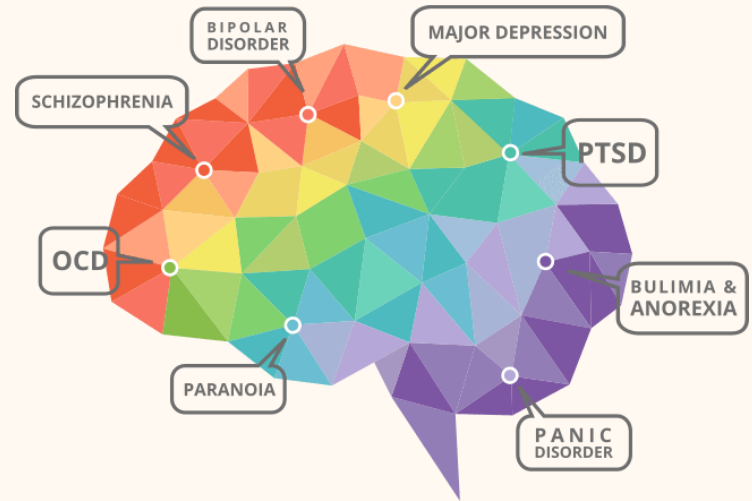


Drug-drug interactions

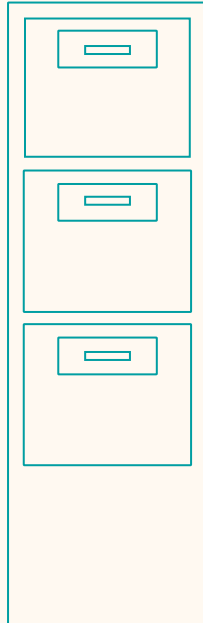
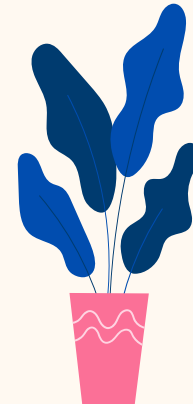
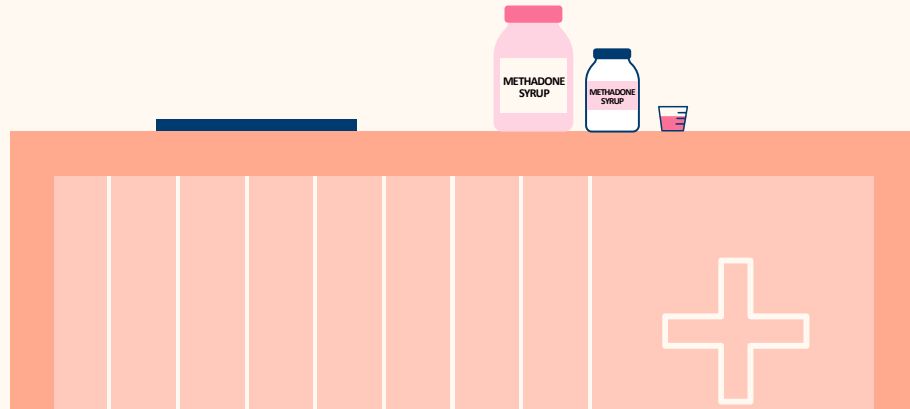
Drug	Effect	Mechanism of action	Clinical importance
Fluconazole ⁴⁸	Increased methadone levels; AUC increases by 35%	Inhibition by fluconazole of cytochrome P450 3A4-mediated methadone metabolism	Respiratory depression has occurred
Paroxetine	Increased methadone levels	Paroxetine is a mild inhibitor of CYP1A2, CYP2C9, CYP2C19, and CYP3A4	
St John's Wort ⁴⁹	Decreased methadone levels	CYP3A4 induction	Has precipitated withdrawal
Voriconazole ⁵⁰	Increased methadone levels	Inhibits CYP3A4-mediated metabolism	None reported
Ciprofloxacin ⁵¹	Increased methadone levels	Inhibits CYP3A4-mediated metabolism	Somnolence reported
Retrovirals ⁵² (except zidovudine)	Decreased methadone levels	CYP3A4 induction; P-glycoprotein?	
Carbamazepine ⁷	Decreased methadone levels	CYP3A4 induction	
Desipramine ⁷	Increased desipramine levels	Unknown	Increased adverse effects from desipramine
Azithromycin	Increased methadone levels	Inhibits CYP3A4-mediated metabolism	
Fluvoxamine ⁶³	Increased methadone levels	Inhibits CYP3A4-mediated metabolism	
Fosphenytoin ⁵⁴	Decreased methadone levels	Decreased methadone trough and AUC	Withdrawal symptom
Desipramine ⁷	Increased desipramine levels	Mechanism unknown	
Didanosine ⁵²	Decreased didanosine levels	Mechanism unknown	
MAO inhibitors ¹¹	Methadone is a serotonin uptake inhibitor		Serotonin syndrome
Ketoconazole	Increased serum methadone levels	Inhibition of CYP3A4	
Nevirapine ^{52,55}		CYP inducer	
Efavirenz ⁵²		CYP inducer	

Psychiatric comorbidities

- High incidence of comorbidities
- Refer to MO / FMS / Psychiatrist / Counsellor if needed
- Anxiety, depression, personality disorders are common
- Psychotherapy may be useful as adjunct

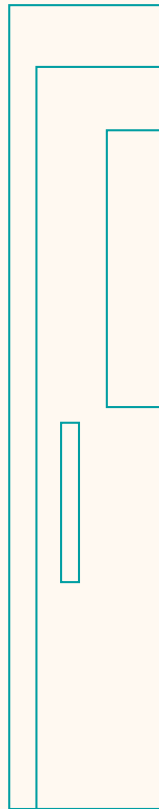


Human Immunodeficiency Virus



Methadone and HIV

- Illicit drug users especially intravenous drug users (IVDU) often have difficulties accessing HIV care.
- They are less likely to receive antiretroviral therapy compared to other populations.
- Evidence indicate that IVDUs benefit significantly from the treatment but mortality remains high compared to non-user HIV patients.
- Factors contributing to mortality include **delayed initiation of treatment, poor adherence to treatment regimen, interruptions in medical care and ongoing drug use.**



Methadone and ART

- Co-administration of ART (NRTI, NNRTI and PIs) with methadone can result in significant reduction in plasma methadone, leading to opioid withdrawal symptoms or increasing ARV drug toxicities.
- Dose titration according to clinical effects.









Anti-retroviral Agent	Effect on Methadone	Comments
Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
Efavirenz (EFV)	Methadone C _{max} ↓ 45% and AUC ↓ 52%	Symptoms of withdrawal may develop after 3–7 days, requiring significant increase in methadone dose
Nevirapine (NVP)	Methadone AUC ↓ 41%	

Methadone and ART

Anti-retroviral Agent	Effect on Methadone	Comments
Nucleoside / Nucleotide Reverse Transcriptase Inhibitors (NRTIs)		
Zidovudine (AZT)	None	AZT AUC ↑ 29–43%. Monitor for AZT adverse effects, in particular bone marrow suppression (especially anaemia).
Abacavir (ABC) ⊕	Methadone clearance ↑ 22%	Monitored for withdrawal symptoms; dose increase unlikely, but may be required in small number of patients
Protease Inhibitors (PIs)		
Lopinavir / ritonavir (LPV/r) ⊕	If boosted with ritonavir, Methadone AUC ↓ 16%–18%;	Opioid withdrawal unlikely but may occur. Adjustment of methadone dose usually not required; however monitor for opioid withdrawal and increase dose as clinically indicated.


Brincidofovir and tecovirimat (antivirals for monkeypox) now included in the comedication list

Looking for interactions with COVID-19 therapies, including Paxlovid? [Click here for covid19-druginteractions.org](#)

HIV Drugs	Co-medications	Drug Interactions
<input type="text" value="Search HIV drugs..."/>	<input type="text" value="Methadone"/>	<input type="checkbox"/> Check HIV/ HIV drug interactions
<input checked="" type="radio"/> A-Z <input type="radio"/> Class <input type="radio"/> Trade	<input checked="" type="radio"/> A-Z <input type="radio"/> Class <input type="radio"/> Trade	Drug Interactions will be displayed here
Selected HIV Drugs will be	<input checked="" type="checkbox"/> Methadone 	
<input type="checkbox"/> Atazanavir alone (ATV) 		
<input type="checkbox"/> Atazanavir/cobicistat (ATV/c) 		
<input type="checkbox"/> Atazanavir + ritonavir (ATV/r) 		
<input type="checkbox"/> Bictegravir/ Emtricitabine/Tenofovir alafenamide (BIC/FTC/TAF) 		
<input type="checkbox"/> Cabotegravir [oral] (CAB oral) 		
<input type="checkbox"/> Cabotegravir PrEP [long acting] (CAB LA, PrEP) 		
<input type="checkbox"/> Cabotegravir/rilpivirine 		

 hiv-druginteractions.org/checker

Welcome Update



UNIVERSITY OF
LIVERPOOL

Liverpool HIV iChart

Providing summary data of HIV drug interactions. Full details available at www.hiv-druginteractions.org

Search For Drug Interactions

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← Back **HIV Drugs** Next

🔍 Search

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B
C
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G
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Bictegravir/FTC/TAF

Cobicistat (with ATV or DRV)

Darunavir

Didanosine (ddl)

Dolutegravir

Efavirenz

Elvitegravir/Cobi/FTC/TAF

Elvitegravir/Cobi/FTC/TDF ✓

Emtricitabine (FTC)

← Back **Co-medications** Next

🔍 Search

A
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Mesalazine

Mesna

Metformin

Methadone ✓

Methamphetamine

Methotrexate

Methyldopa

Methylphenidate

Methylprednisolone

← Back **Results** Restart

Potential Weak Interaction →

Rilpivirine

Methadone

No Interaction Expected →

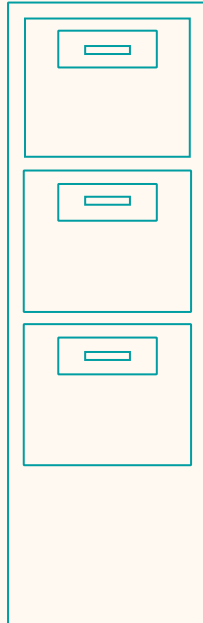
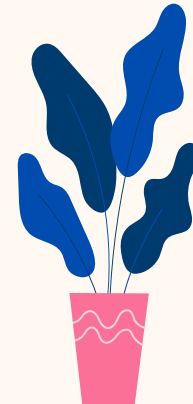
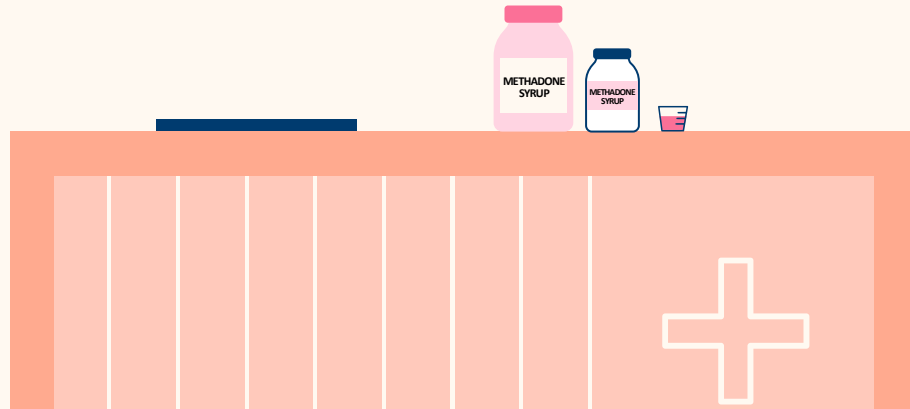
Elvitegravir/Cobi/FTC/TDF

Methadone

No Interaction Expected →

? Results Key i

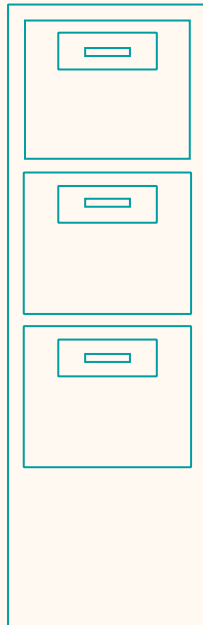
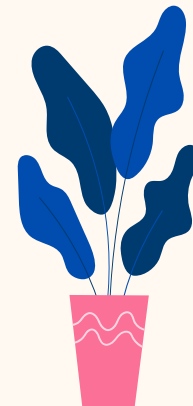
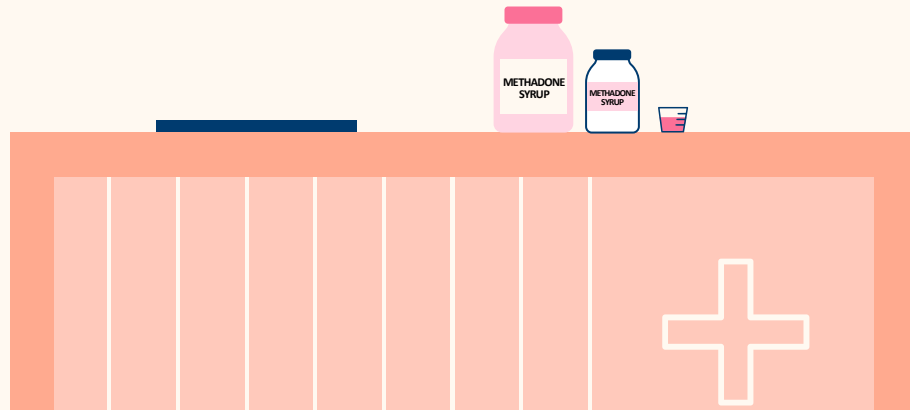
Hepatitis B & C



Hepatitis B & C

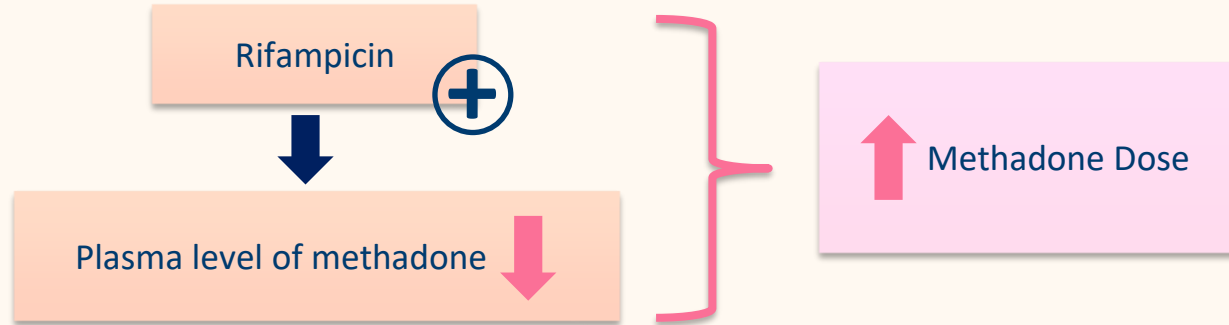
- Refer gastro/ID depending on hospital
- Ensure they are on follow up
- Monitor ALT/AST level (Acceptable up to 3 times normal)
- No dose adjustment necessary unless on treatment –refer drug-drug interaction
- Pt on long term methadone treatment usually does not need dose adjustment.
Unless there is sudden deterioration of liver function

Tuberculosis

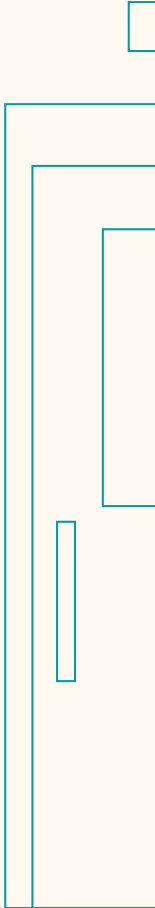
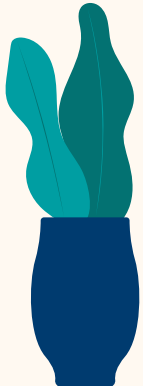


Methadone and Tuberculosis

- Drug interaction between methadone, buprenorphine with rifampicin.



- Dose titration according to clinical effects.
- Patients should inform doctor / pharmacist when anti-TB drug is stopped



Methadone and Common Drugs

CYP450 3A Inducers		CYP450 3A Inhibitors	
Dexamethasone	+	Amiodarone	<i>Lopinavir</i>
Efavirenz		Azoles (Fluco-, Itra-, Ketoco-)	<i>Ritonavir</i>
Phenobarbital		Cimetidine	Verapamil
Phenytoin		Clarithromycin	
Rifampicin		Diltiazem	
St. John's wort		Grapefruit juice	



[Treatments](#) > [Pain](#) > [Methadone](#)[Print](#) [Save](#)

Methadone Interactions

A total of **680 drugs** are known to interact with [methadone](#), categorized as 315 major, 356 moderate, and 9 minor interactions.

Does methadone interact with my other drugs?

- [View all 680 medications](#) that may interact with methadone
- [View alcohol/food interactions](#) (2)
- [View disease interactions](#) (17)

Most frequently checked interactions

View interaction reports for **methadone** and the medicines listed below.

● Major ● Moderate ● Minor ● Unknown

● [Adderall \(amphetamine / dextroamphetamine\)](#)

● [Adderall \(amphetamine / dextroamphetamine\)](#)


● [Ambien \(zolpidem\)](#)


How to Prevent Deadly Drug Interactions


Some mixtures of medications can lead to serious and even fatal consequences.


[Here are 9 ways to stay safe](#)

DRUG STATUS

 Availability

 High potential for abuse

 **Approval History**
Drug history at FDA

 **WADA Class**
Anti-Doping Classification


User Reviews & Ratings

8.7 / 10  [563 Reviews](#)

Related Drugs

[Subutex](#), [Sublocade](#), [Zubsolv](#), [Buprenex](#),
[Probuphine](#), [Bunavail](#), [aspirin](#), [tramadol](#),
[acetaminophen](#), [duloxetine](#)

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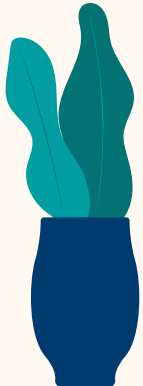
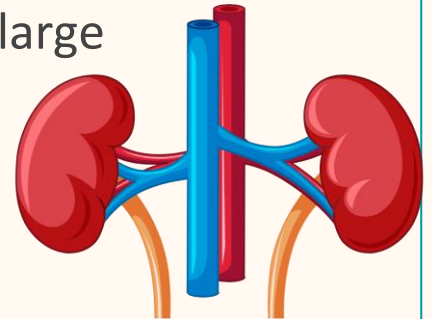


[drugs.com/drug-interactions/methadone.html](https://www.drugs.com/drug-interactions/methadone.html)

Methadone and **Organs Impairment**

Kidney

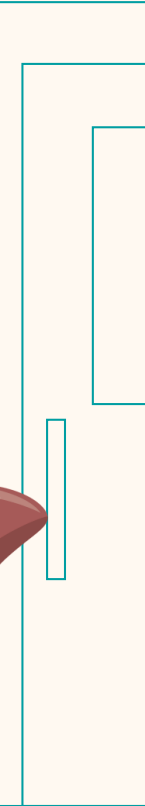
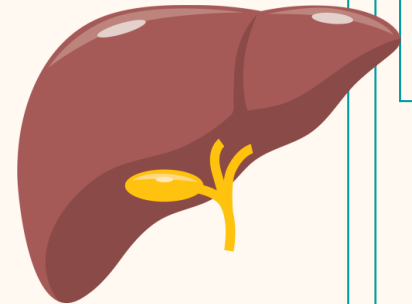
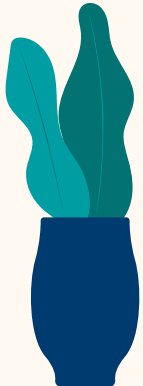
- Methadone and its metabolites are excreted in the urine and faeces.
- For patients with impaired renal function, methadone **clearance via faeces increases and no dose adjustment is required.**
- Removal by **dialysis is not expected to be significant** due to methadone is highly protein bound and has large volume of distribution.



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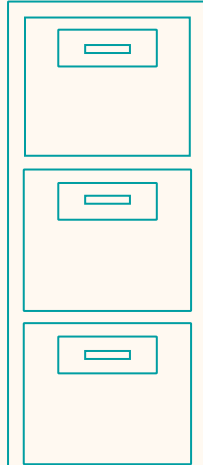
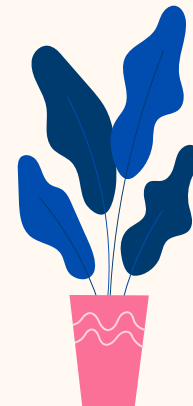
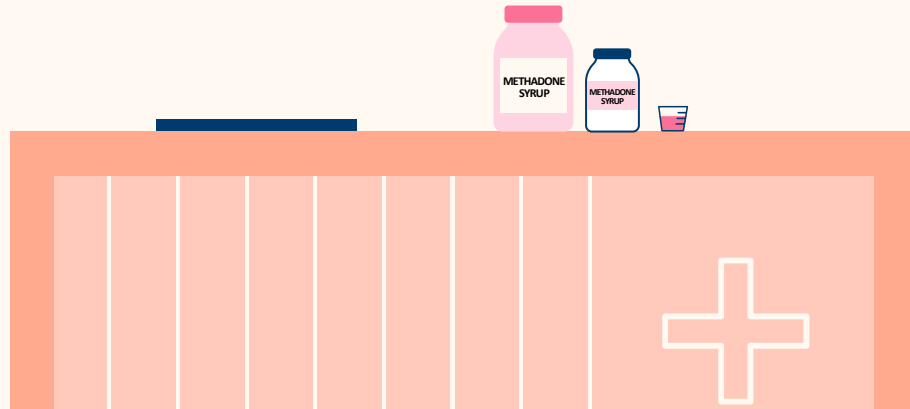
Liver

- Methadone is not hepatotoxic. However, the liver has a central role in methadone metabolism, clearance, and drug storage.
- Therefore, usual methadone doses may be implemented for patient with chronic, stable liver functions but **avoided in patients with progressive failure.**



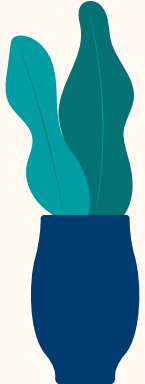
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Pregnancy



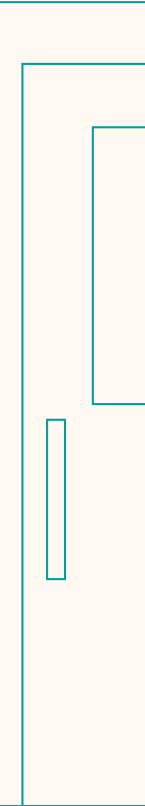
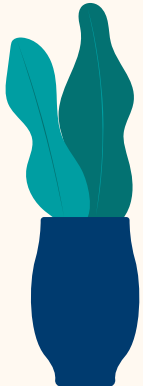


Methadone and Pregnancy

- Opioid agonist treatment is thought to have **minimal long-term developmental impact on children** in relative to the harm resulting from maternal use of heroin and prescription opioids.
 - Studies show that pregnant women with opioid use disorder who are not in treatment should be encouraged to **start** treatment with methadone as **early as possible**.
 - Clinicians should be aware that the pharmacokinetics of methadone are affected by pregnancy.
 - With **advancing gestational age**, plasma levels of **methadone progressively decrease and clearance increases**.
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Methadone and Pregnancy

- Opioid users who become pregnant are given **high priority** to be started on MRT
- Naloxone challenge- **should not** be used as it may precipitate miscarriage
- Pregnant ladies should be **given adequate dose** of methadone to ensure plasma stability
- **May need to increase dose-** increase metabolism in liver, increased plasma volume, to minimize other drug use.
- **Increased or split doses** may be needed as pregnancy progresses.
- **After child birth,** doses may need to be adjusted

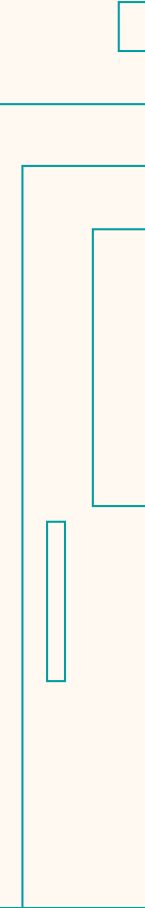
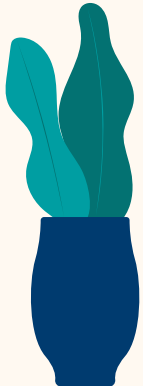


Methadone and Pregnancy

- Pregnant women who are on agonist treatment should be encourage **not to discontinue** treatment while pregnant as withdrawal may cause :

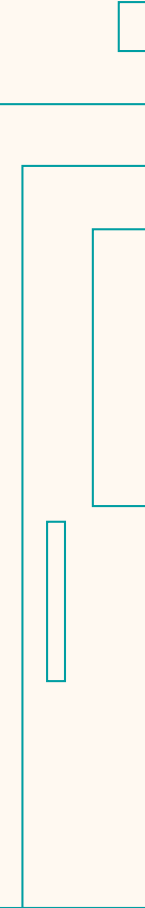
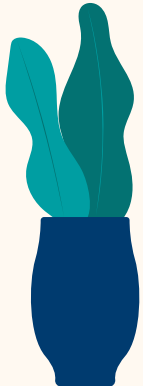
1 st trimester	• Miscarriage
3 rd trimester	• Foetal distress • IUD

- Therefore, methadone, buprenorphine and suboxone are the accepted for use during pregnancy [Pregnancy category C].



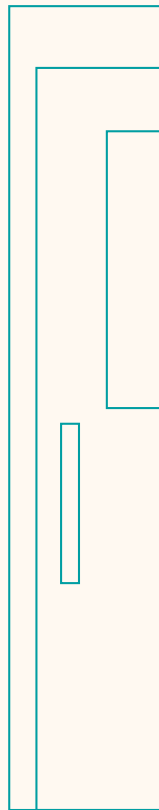
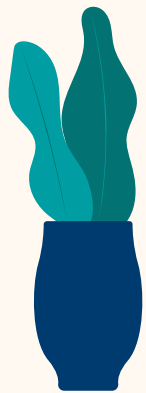
Methadone and Pregnancy

- Dose reduction can be done in 2nd trimester but go low and slow → 2.5-5mg/week
- Pt specific and stable pregnancy
- Methadone can cause respiratory depression but neonatal withdrawal is a major issue as it is unpredictable



Methadone and Breastfeeding

- Small amounts of methadone in breast milk can pass to the baby, but these levels are low.
- Studies have shown amount of buprenorphine metabolites secreted in breast milk are so low that they pose little risk to breastfeeding infants.
- Therefore, mothers receiving methadone and buprenorphine for the treatment of opioid use disorders should be **encouraged to breastfeed**.
- However, breastfeeding from mothers taking **methadone** is considered **safe** for baby but **not safe for HIV positive** mother.





Thank You!

Any Questions?

