CLINICAL PRACTICE GUIDELINES FOR BUPRENORPHINE AND METHADONE BASED OST

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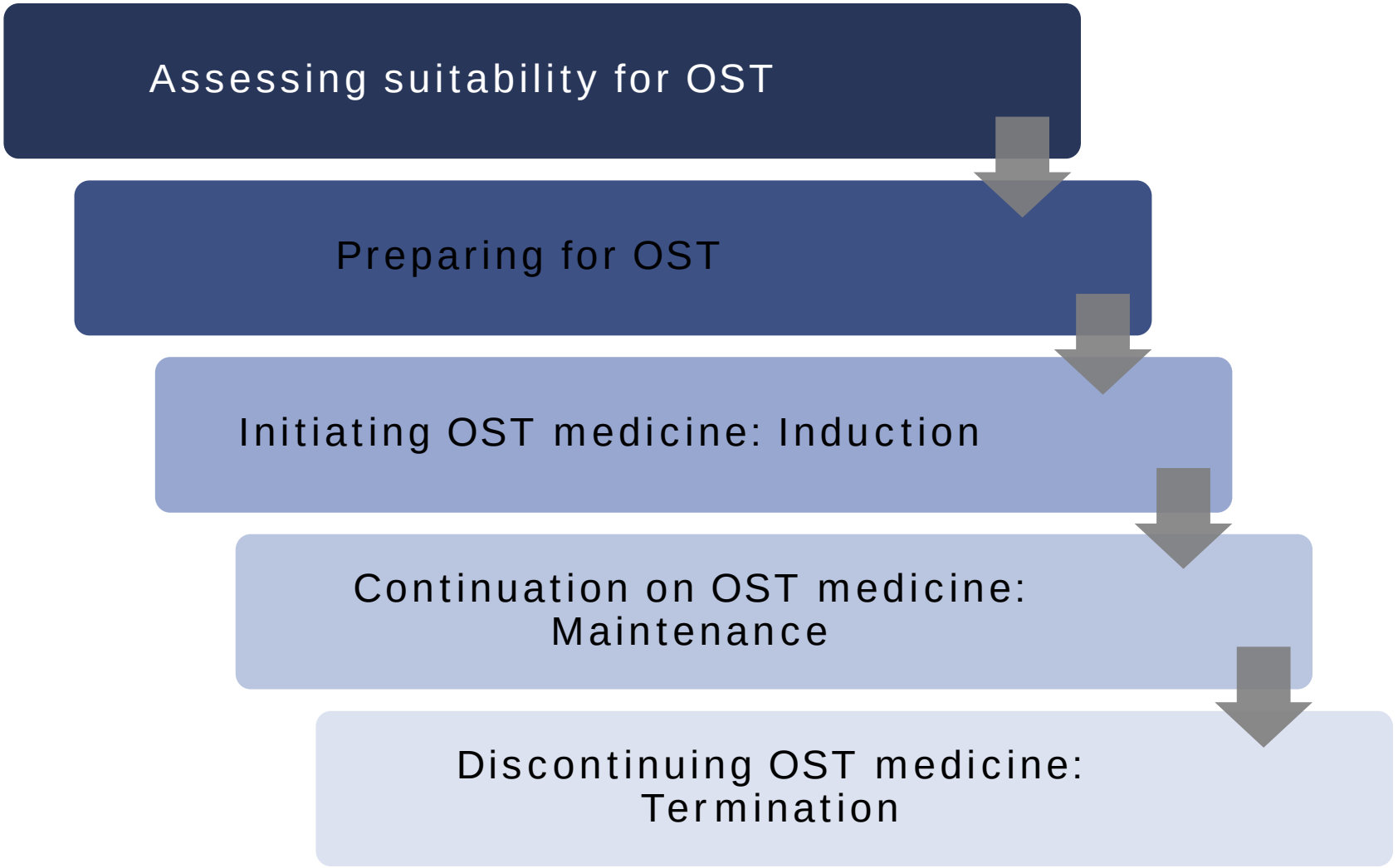
STEPS IN OST DELIVERY



SUITABILITY CRITERIA FOR OST

- Diagnosis of Opioid Dependence
- Capable / ready to provide informed consent
- Willing to follow clinic procedures/rules

ESSENTIAL CRITERIA

SUITABILITY CRITERIA FOR OST

- Age>18 years
- Long history of opioid use
- Poor psychosocial functioning
- High risk behaviour, esp. injecting
- H/O failed abstinence

NON-ESSENTIAL CRITERIA

CONTRA-INDICATIONS FOR OST INITIATION

Absolute

- **Hypersensitivity to OST medicines**
- **Incapability to provide informed consent**

Relative

- **Hepatic impairment**
- **Respiratory dysfunction**
- **Severe dependence on other depressants**
- **Renal / biliary spasms**
- **Ulcerative colitis**

ASSESSMENT FOR OST SUITABILITY

ASSESSMENT MODALITIES

Interaction with the client

Interaction with family members (if present during assessment)

Review of previous treatment records, if available

Observation and physical examination of the client

ASSESSMENT FOR OST SUITABILITY

ASSESSMENT AREAS

- Socio-demographic details
- Psychoactive substance use details
  - Complications
  - Injecting and other high risk behaviours
- Past abstinence attempts
- History of medical illnesses
- Current psychosocial support and living arrangement
- Current status of occupational and family functioning
- Evidence of
  - current opioid withdrawals / intoxication
  - Evidence of injection / other physical consequences of substance use (injection marks, abscesses, scars, etc.)

PREPARING CLIENTS FOR OST

Nature of illness

- ODS is a chronic relapsing medical illness
- Relapse: part of recovery process and strategies available to minimize

Nature of treatment

- OST is a long term treatment (at least an year or more)
- Periodic counseling required

Need for active involvement

- Dispel common myths/misconceptions regarding OST
- Better outcome with family involvement

INFORMED CONSENT

Consent, why?

ENSURES

- **Patient understands the implications of being on treatment and do's and don'ts**
- **Patient accepts the terms and conditions voluntarily**
- **The signed consent acts as a therapeutic contract between patient and service providers**

LAB INVESTIGATIONS BEFORE OST?

NOT ESSENTIAL to perform any lab investigations before OST initiation

If **History / Examination** reveals

- **No abnormality:** OST can be safely started without any need of investigation
- **Some findings:** Relevant investigations

If the center has facilities → routine investigations is a good practice

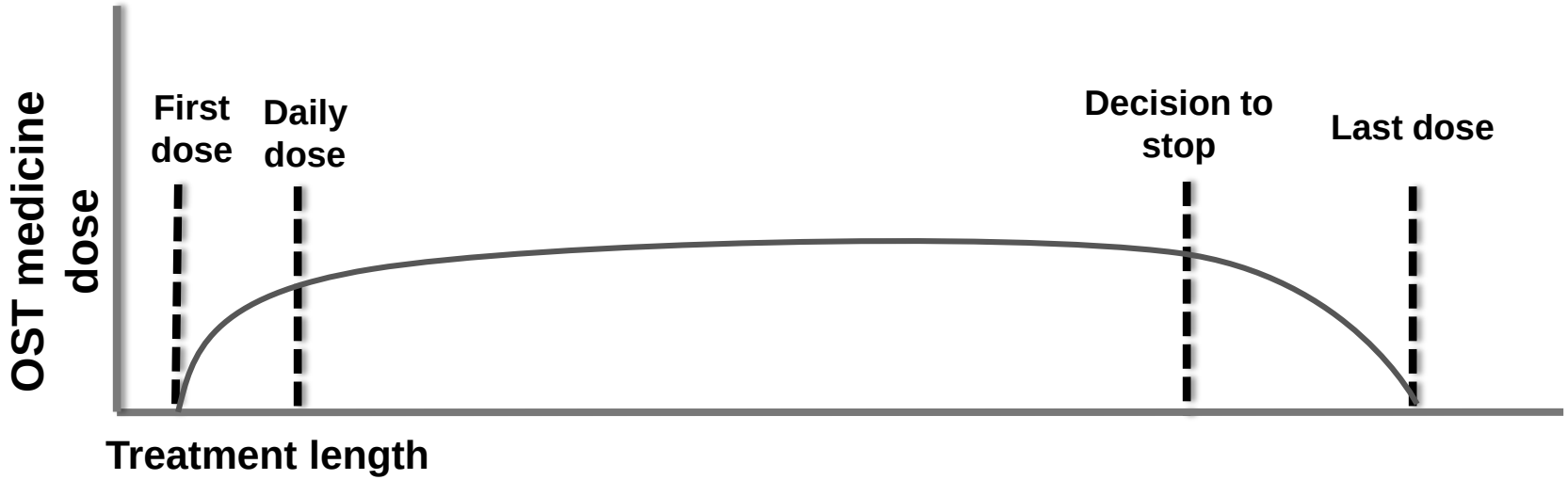
OST PHASES

INDUCTION

MAINTENANCE

TERMINATION

TREATMENT PHASES



INDUCTION

MAINTENANCE

TERMINATION

OST PHASES

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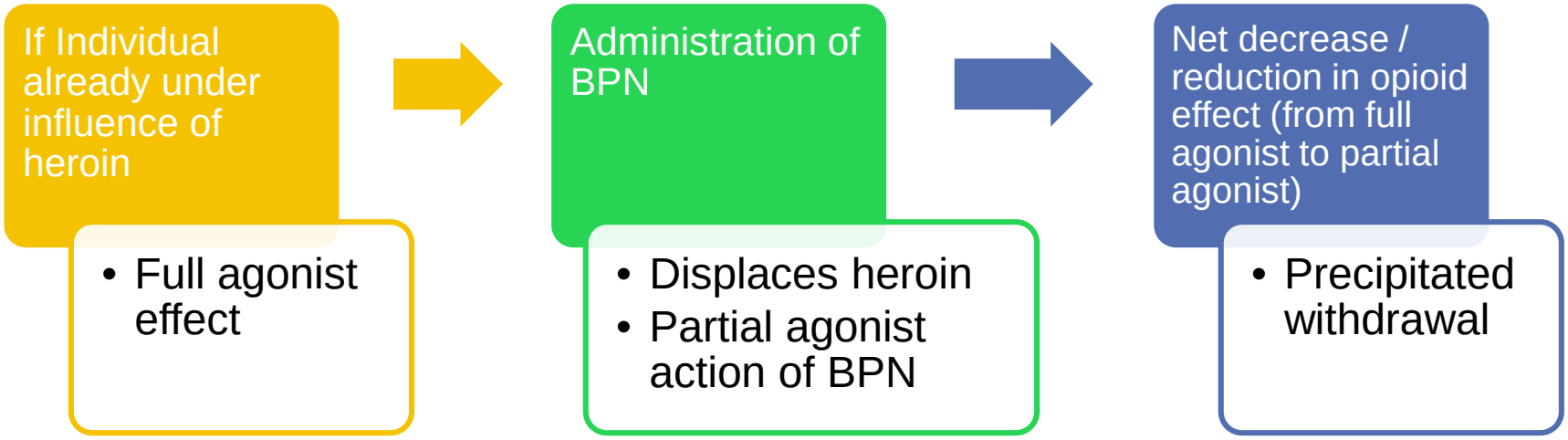
INDUCTION PHASE

GOALS OF INDUCTION PHASE

- Determine the correct dose of OST medicine
- To address any medical or psychosocial crisis
- To establish rapport with the client

INDUCTION PHASE - BUPRENORPHINE

- **Usually lasts for 2-3 days, maximum by 7-10 days**
- Before the first dose
  - Ensure the last dose of illicit opioids used (either injection / inhalational / oral) is 4-6 hours before



HOW TO START BPN?

FIRST DAY:

- Patient is started on 2-4mg/day BPN on first day
- Monitor the patient for 2 hours
- If withdrawal symptoms persist, give another 2-4 mg (max 8 mg)
- If patient is comfortable, review the next day

INDUCTION PHASE - BPN

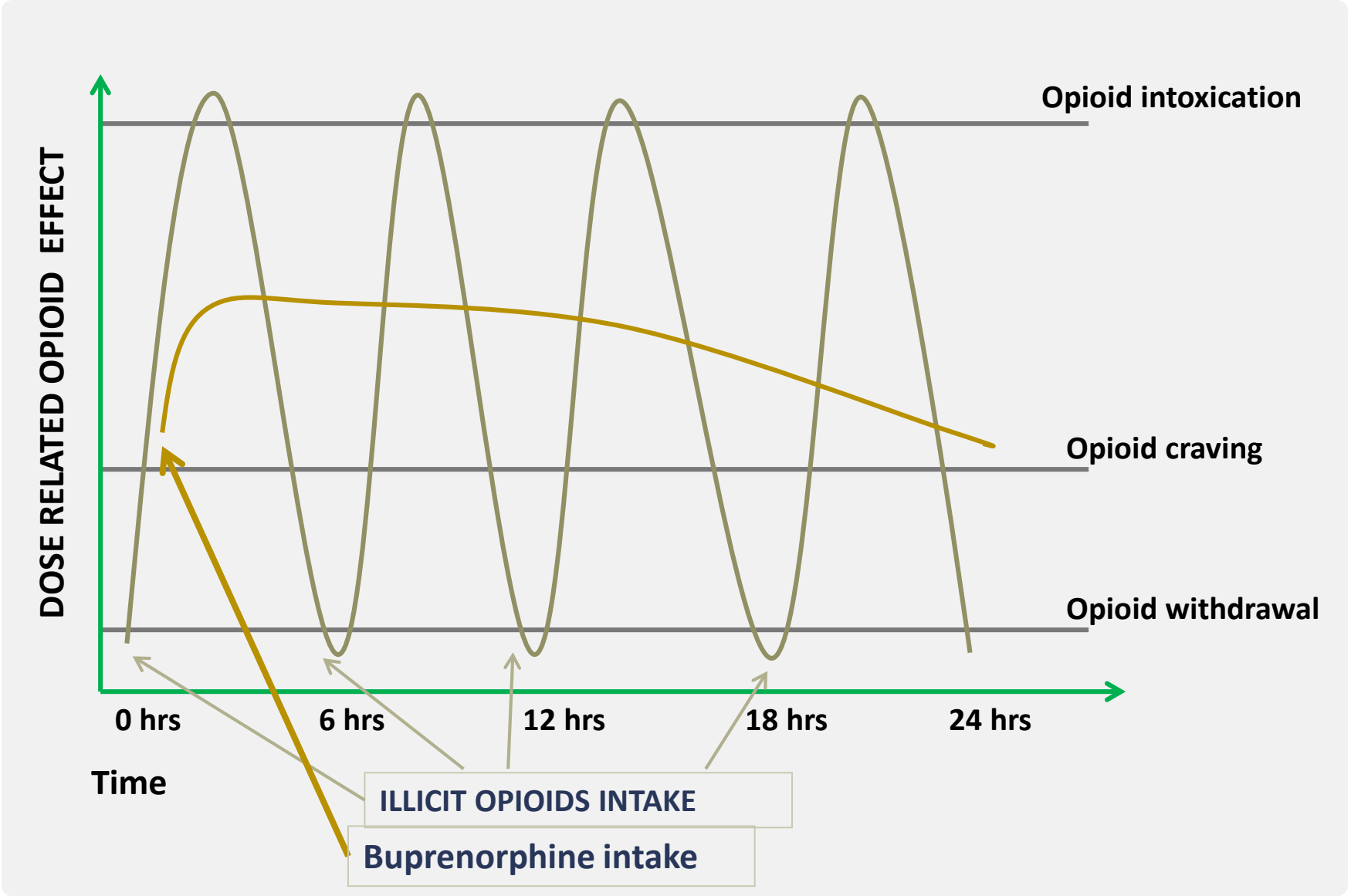
Assessment during next day visit:

- Was the BPN dose on ‘Day-one’ able to control craving and withdrawal for 24-hour period?

- Did the client experience any intoxication-effects of BPN?

☹ **Under-medicated patients:**	▪ craving or withdrawal between doses
😐 **Over-medicated patients:**	▪ buprenorphine intoxication
☺ **Properly medicated patients:**	▪ neither of these experiences

PICTORIAL REPRESENTATION OF LEVELS OF OPIOIDS IN BLOOD AT DIFFERENT TIME POINTS IN 24-HOURS CYCLE



FLOW-CHART ON BPN INDUCTION: DAY TWO

Client returns to the OST center 24 hours after the last BPN dose on DAY TWO

↓

Did the client experience withdrawals and/or craving in the past 24 hours? Did the client take opioids in the past 24 hours and felt a 'high'?

NO → **DAILY DOSE ESTABLISHED Continue with the previous day's dose of BPN**

↓ **YES**

Increase the BPN dose by 2 – 4 mg depending on the severity of withdrawals / craving and ask him to follow up next day (Maximum dose of BPN on DAY TWO not to exceed 12 mg/day)

FLOW-CHART ON BPN INDUCTION: DAY THREE AND BEYOND

Client returns to the OST center 24 hours after the last BPN dose on DAY THREE AND BEYOND

Did the client experience withdrawals and/or craving in the past 24 hours? Did the client take opioids in the past 24 hours and felt a 'high'?

NO

DAILY DOSE ESTABLISHED
Continue with the previous day's dose of BPN

YES

Increase the BPN dose by 2 – 4 mg every day depending on the severity of withdrawals / craving and ask him to follow up next day
(Maximum dose of BPN not to exceed 20–24 mg/day)

INDUCTION PHASE – METHADONE

- **Usually lasts for 2 – 3 weeks**
  - Greatest period of overdose
  - **START LOW, GO SLOW**

- **Patient education**
  - *It takes time to complete induction with methadone*
  - *Will experience increasing effects from methadone over the first few days of treatment even if the dose is not increased*

- Wait for withdrawals to appear / 4-6 hours after last dose of opioid consumed

INDUCTION PHASE – METHADONE

- **First day dose: 10 – 20 mg**

- **Monitor for 3 – 4 hours after the first dose**
  - Intoxication – further observation warranted
  - If withdrawals persistent: additional 5 mg?
    - Not indicated (at present)

A dose of less than or equal to 20 mg is safe, even in opioid-naïve users as this is the lowest dose at which toxicity appears

INDUCTION PHASE – METHADONE

- **First day dose not to exceed >30 mg/day**
- **Continue same dose for 3 – 4 days**
- **Increase by 5 mg every 3 – 4 days**
- **Maximum dose at the end of first week should not exceed 40 mg/day**
- **Total weekly increase should not exceed 20 mg**

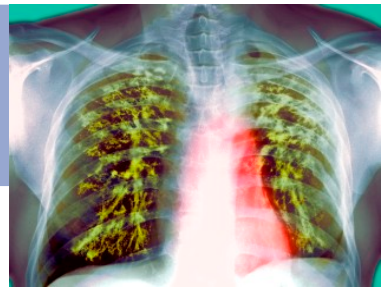
INDUCTION PHASE: OTHER ISSUES

Enhance client's motivation

- to stop/reduce illicit opioids and continue OST

Address any medical priorities.

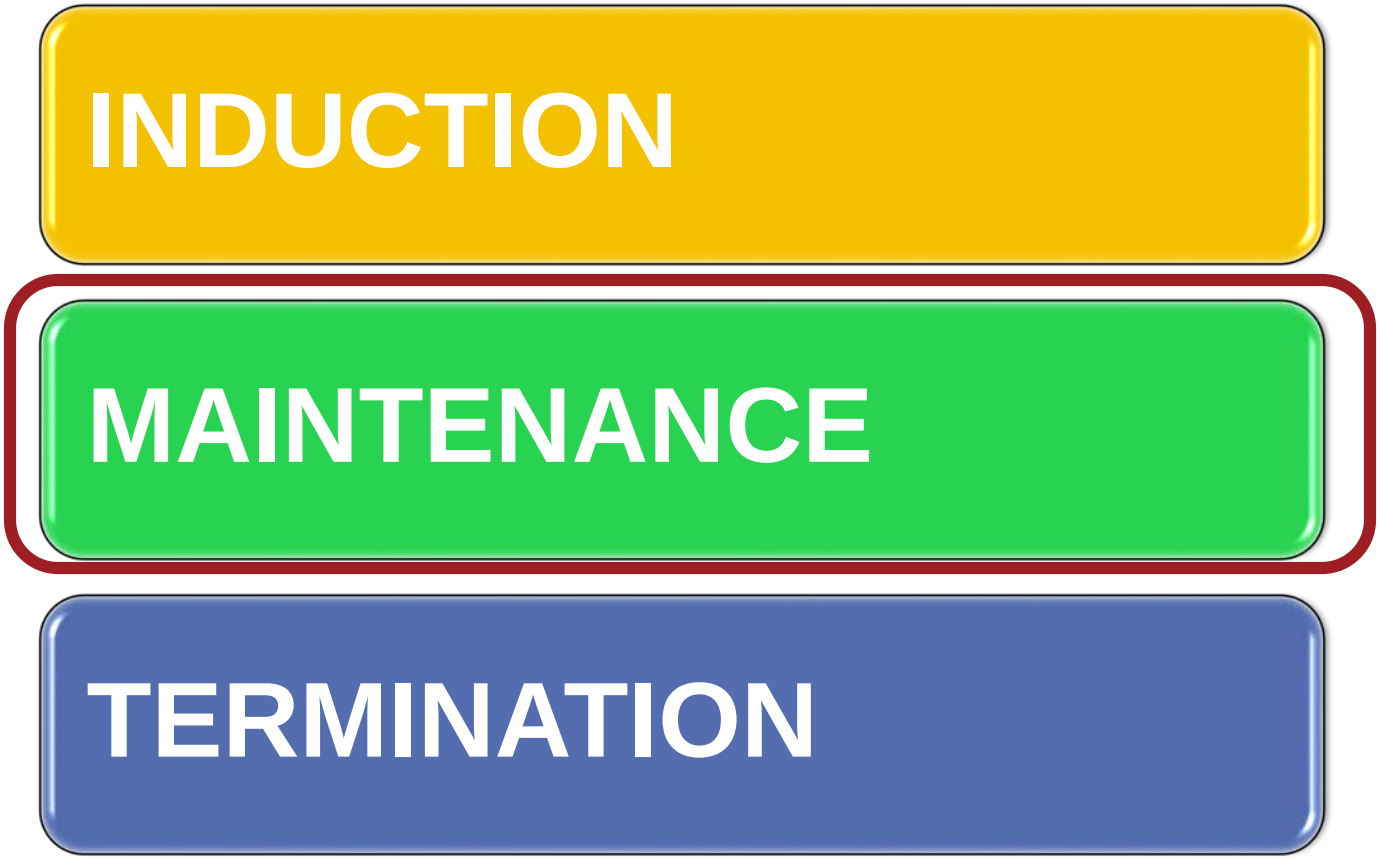
- Open abscess, active tuberculosis, etc.



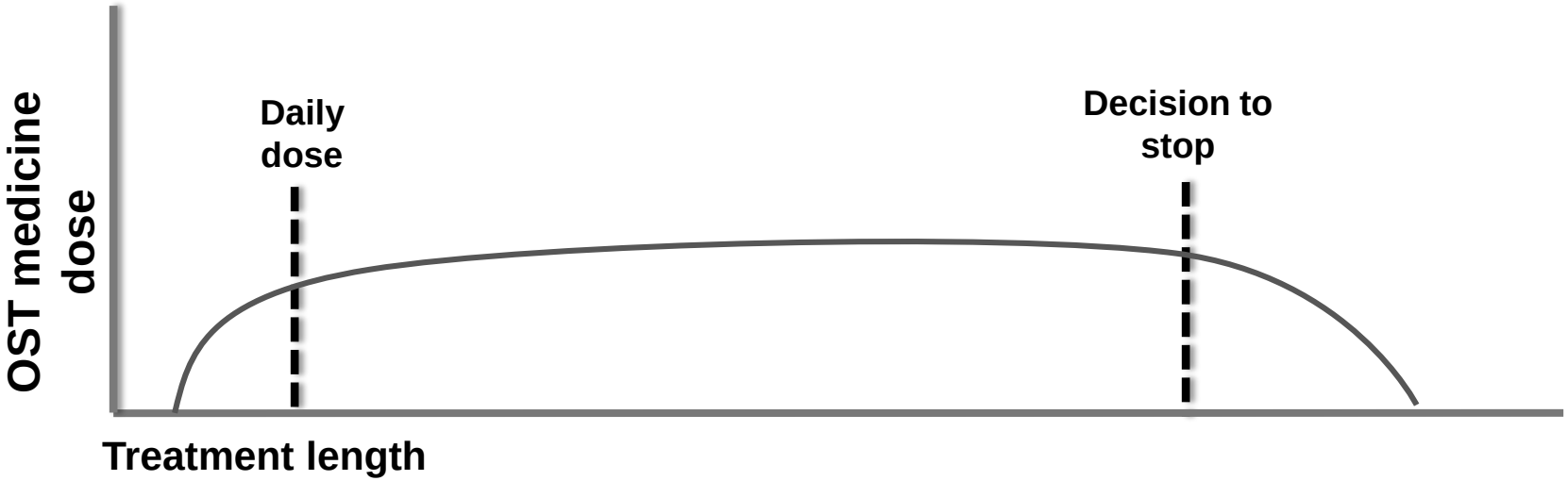
Address any psychosocial crisis.

- Recent homelessness, impending legal crisis, etc.

OST PHASES



TREATMENT PHASES



MAINTENANCE

MAINTENANCE PHASE – GOALS

Maintenance on adequate dose of OST medicine

Ensure treatment retention and prevent opioid relapse

Address other substance use

Occupational, financial and familial Rehabilitation

Motivate and refer the client for other services

MAINTENANCE ON ADEQUATE DOSE

- Focus during induction phase: **Withdrawals and craving of opioids**
- Additional focus during maintenance phase: **No euphoria with illicit opioids consumed**
- Different mechanism for BPN and methadone
  - BPN: Opioid Blockade
  - Methadone: Cross-tolerance

OPIOID BLOCKING EFF

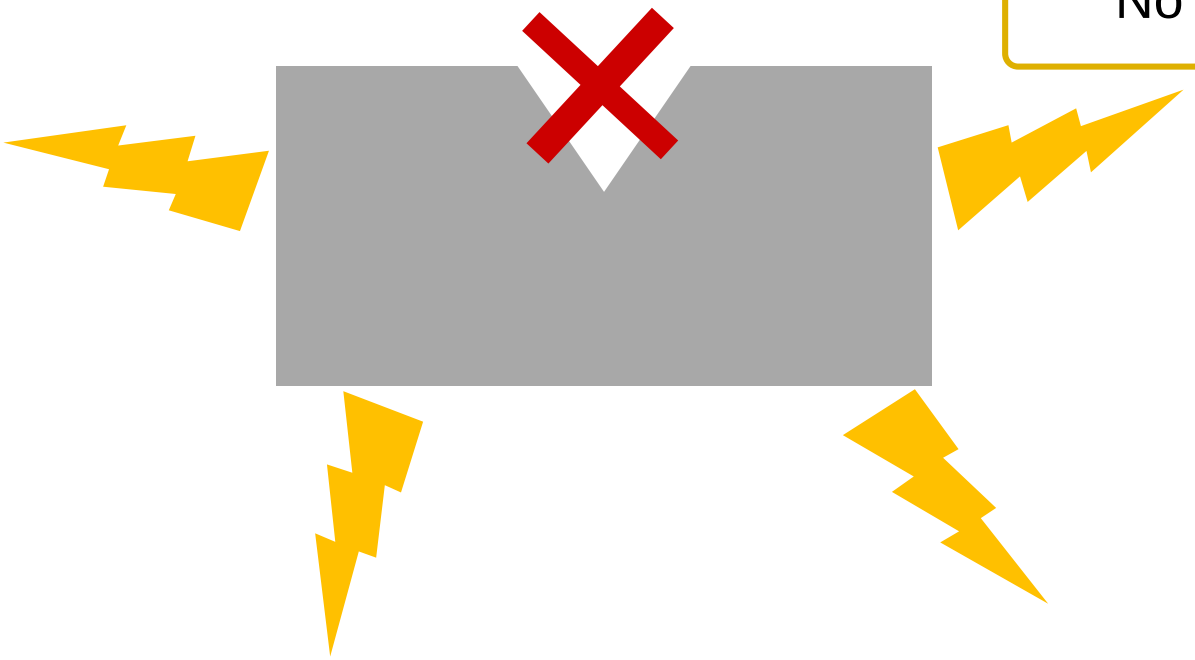
Adequate dose of buprenorphine

Buprenorphine

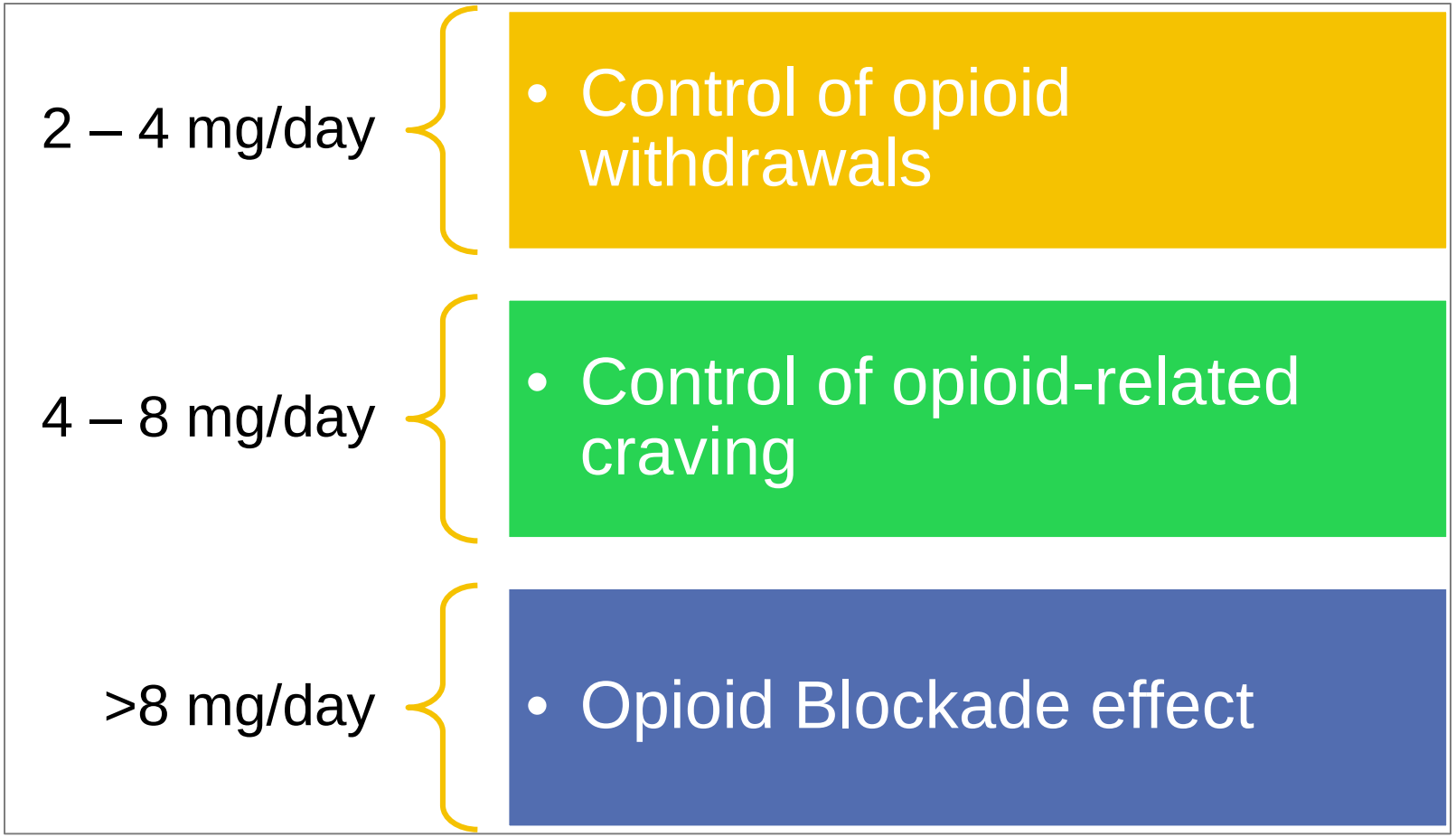
All opioid receptors blocked

No receptors free for heroin to act

No effect of heroin



ADEQUATE MAINTENANCE DOSE: BPN



OPIOID BLOCKING EFFECT – HOW TO ASSESS?

The client used any other opioids/injections while on his current BPN dose?

Does the client experience euphoria while using other opioids/injections?

Euphoria present? → Need to increase buprenorphine dose

WHAT IS ADEQUATE BPN MAINTENANCE DOSE?

- Usual Dose: 12-16 mg/day
- Max. Dose: 32 mg/day

Western Data

- Usual dose: 8 – 12 mg/day
- Maximum dose: 20-24 mg/day

Indian Experience

ADEQUATE MAINTENANCE DOSE: METHADONE

- Lower dose: Withdrawal & Craving
- Higher dose: cross-tolerance for other opioids
- Maintenance dose recommendations

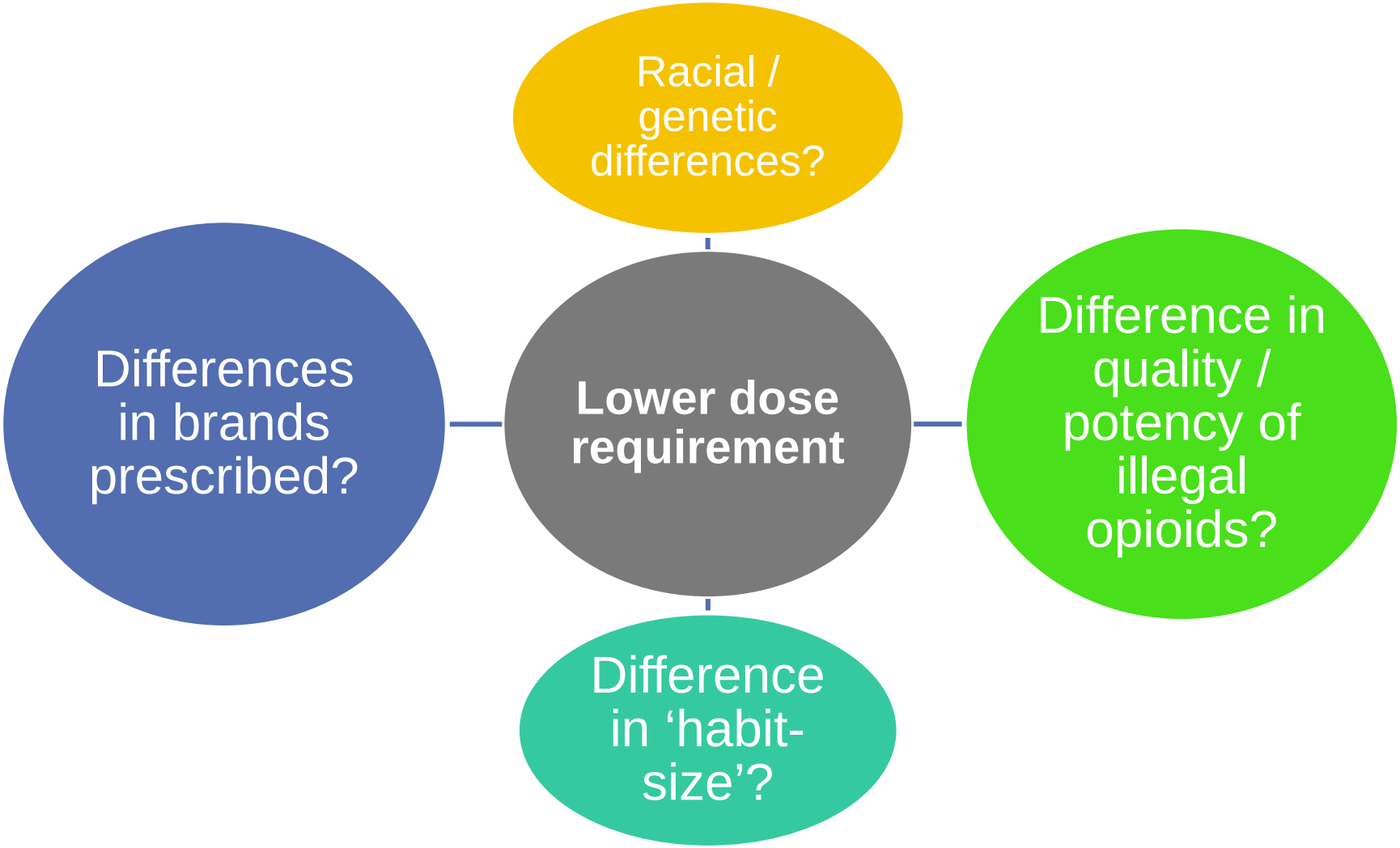
Western Data

- Minimum effective dose: 60 mg/day
- Usual Dose: 60–90 mg/day
- Max. Dose: 120 mg/day

Indian Experience

- Usual dose: 40–60 mg/day
- Maximum dose: ?90 mg/day

REDUCED DOSE IN INDIANS?



SHOULD OST DOSE BE ALTERED DURING MAINTENANCE PHASE?

Reduction?

- No reduction in dose necessary

SAME DOSE AS USED IN INITIAL STAGE SHOULD BE CONTINUED

- Unless: client c/o side-effects of BPN/methadone

Increase?

Can be done/required in some conditions

- Resumption of work (esp. physical labor)
- Onset of co-morbid pain condition
- Re-emergence of craving

DISPENSING – BPN

- Directly observed treatment – DOT?
- Take-home?

Prior to administering the medication, the dispensing staff (nurse) must

- Confirm patient's identity and patient's current prescription
- Confirm that the patient is not intoxicated
- Administer sub-lingually
- Crushing of tablets?

Observe for at least 7-10 minutes after administration – ensure dissolution

DISPENSING – METHADONE

- Directly observed treatment – DOT?
- Take-home?

Prior to administering the medication, the dispensing staff (nurse) must

- Confirm patient's identity and patient's current prescription
- Confirm that the patient is not intoxicated
- Administer Orally

FOLLOW-UP DURING MAINTENANCE

Regular follow-up essential

Assessment during follow-up

- Adequacy of dose
- Any adverse effect
- Compliance to OST
- Use of other substances
- Co-morbid illness
- Progress in socio-occupational functioning

MAINTENANCE PHASE: OTHER ISSUES

Co-morbid substance use

- Other substances use may start/increase
  - Can lead to relapse to opioid use
  - Can increase the risk of respiratory depression
- Enquiry must be made during follow-up
- Treatment must be provided
  - At centre
  - Through referral to a psychiatrist/ drug treatment centre

MAINTENANCE PHASE: OTHER ISSUES

Referral to other services

- HIV testing & referral to ART centre (if positive)
- Screening for Tuberculosis, Hepatitis & referral if required

Relapse prevention

Re-integration

- Repair ties with family and society
- Resume/improve occupational functioning

OST PHASES

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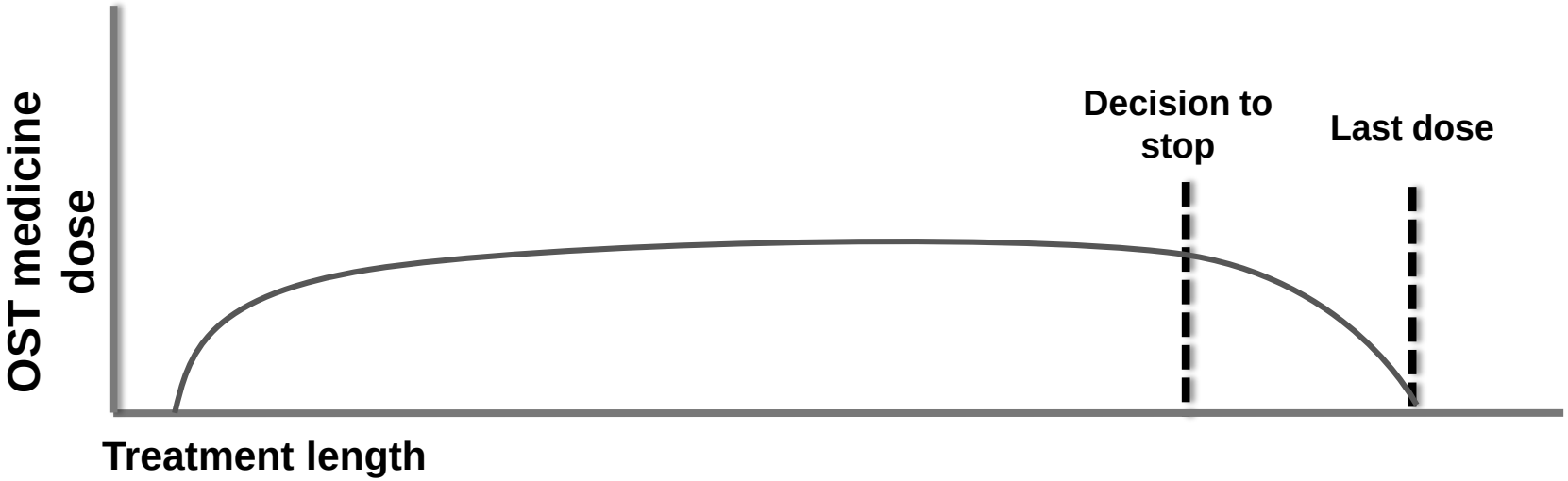

TERMINATION

HOW TO DECIDE WHEN TO STOP?

- Duration **IS NOT** the criteria for considering tapering
- Stopping opioid use is **NOT THE ONLY** criteria for considering tapering
- Varies from one client to another
- Deciding criteria should be :

‘Attainment of treatment goals’

Indicators for CONSIDERING termination

- Cessation of opioid use
- Cessation of illegal activities
- Improved ties with family
- Strong psychosocial support
- Well-maintained occupational functioning
- **CLIENT'S READINESS TO LEAD A MEDICATION-FREE LIFE**

Indicators for NOT CONSIDERING termination

- Continued drug use
- Continued illegal activities
- Poor occupational functioning
- Poor social support (including homelessness)
- Risk of relapse

CAN BE MAINTAINED FOR MONTHS TO YEARS

- *Without any physical / mental adverse effect of BPN/Methadone*

TERMINATION PHASE

Goals	To ensure minimal discomfort during taper
	To support and prevent relapse
	To help make decision on further treatment
	To motivate for continued follow-up after stopping OST medicine

TERMINATION PHASE

Termination should be planned and mutual

- Prepare patient well-in-advance
- Involve family members

Tapering regime

- Never stop abruptly
- No fixed regime
- Gradual decrease in dose – patient's comfort guiding factor
- Can be done on outpatient basis: weeks-months
- Faster taper possible in inpatient setting: days-weeks

AFTER OST: WHAT NEXT?

Possible Alternatives

- Drug-free
  - Continued follow-up for 4-6 month period essential

Naltrexone

- Initiated after an opioid-free period
- Retention better compared to western settings

COMMON & SPECIAL CLINICAL SITUATIONS

COMMON CLINICAL SITUATIONS DURING OST

- **VOMITING**
- **CONSTIPATION**
- **MISSED DOSE**
- **SLEEP DISTURBANCES**
- **SEXUAL PROBLEMS**

SPECIAL CLINICAL SITUATIONS

- **HIV/AIDS**
- **TUBERCULOSIS**
- **ADOLESCENTS**
- **FEMALE DRUG USERS**

VOMITING

- **Uncommon symptom with BPN; common with methadone**
- **Present during the initial weeks of BPN / Methadone treatment**
  - Subsides on its own
- **Intolerable vomiting**
  - Anti-emetics orally half hour before buprenorphine

VOMITED DOSE - METHADONE

- Do not replace unless staff has observed emesis
- Guidelines for replacing vomited methadone dose

Emesis <15 minutes of dose administration	Consider replacing 50-75% of dose
Emesis 15-30 minutes of dose administration	Consider replacing 25-50% of dose
Emesis >30 minutes of dose administration	No need for replacement

CONSTIPATION

- **Common side-effect of OST**
  - Occurs during maintenance phase

- **Causes?**
  - Co-morbid physical illness?
  - Changes in lifestyle after OST initiation?
  - True side-effect of BPN/methadone?

CONSTIPATION

- **Management**
  - R/O other causes of constipation
  - Lifestyle modification – physical exercise, dietary changes
  - Laxatives
  - Decrease BPN/methadone dose if constipation intractable

MISSED DOSE

- **If missed for three days or more: loss of tolerance possible**
- **Reintroduction**
  - Assess for signs of intoxication/withdrawals before recommencement
  - Guidelines

No. of days missed	Recommended strategy
One day	No change in dose
Two days	If no intoxication, same dose
Three – four days	Administer Half-dose
Five days or more	Regard as new induction

SLEEP DISTURBANCE

- **Common problem encountered during the course of OST**
  - Delayed initiation of sleep; frequent waking up at night

- **Reason?**
  - Protracted withdrawal symptom of opioids
  - Cocktail injection of benzodiazepines (diazepam) along with opioids
  - Co-occurring benzodiazepine abuse/dependence

SLEEP DISTURBANCE

- **Management**
  - Treatment of benzodiazepine withdrawal, if dependent on benzodiazepines
  - Initial treatment
    - Sleep hygiene

SLEEP HYGIENE

- Fix the time for going to bed and getting up in the morning
- Avoid afternoon naps
- Have meals 2 hours before sleep
- Avoid stimulants such as coffee, tea or nicotine after sunset
- Avoid stimulating activities such as watching television before going to sleep
- Take light exercise in the evening
- Have a bath with warm water before going to sleep
- Do light reading or listening to music before sleep
- Use the bed only for sleep

SLEEP DISTURBANCE

- If no improvement: low dose benzodiazepines / other sleep inducing medications

Medicine	Dose
Diazepam / Nitrazepam	5–20 mg at night
Mirtazepine	7.5–15 mg at night
Trazadone	25–50 mg at night

SEXUAL PROBLEMS

- **Common during maintenance phase of OST**
- **Types**
  - Pre-mature ejaculation (most common)
  - Erectile dysfunction
  - Anorgasmia
- **Reason?**
  - Protracted withdrawals of opioids
  - Myths/misconceptions

SEXUAL PROBLEMS

- **Management**
  - Assurance: Improvement with passage of time
  - Education regarding normal sexual process
  - Focus on other aspects of marital life, rather than sexual alone
  - Focus on deriving sexual pleasure by non-penetrative methods
  - Refer to psychiatrist

HIV/AIDS: CONSIDERATIONS DURING OST

- **Assess for high risk behaviour**
  - Injection related
  - Sex related
- **Counsel the patient**
  - Pre-test counseling
- **Referral for HIV testing**
  - Post test counseling
    - HIV negative
    - HIV positive

HIV/AIDS: CONSIDERATIONS DURING OST

- If HIV positive and eligible for ART

Initiate first on OST

Stabilise the dose of OST

Initiate ART

Titrate the dose of OST depending on the ART medication

BPN: DRUG – DRUG INTERACTIONS

Anti-retroviral medicine	Effect on buprenorphine	Buprenorphine effect on ART medicine	Clinical considerations
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)			
No majo			
Efavi Nevir			
Ataza			
Riton Indina			s
Integrase Inhibitors			
No major interactions observed/reported			

- Some drug-drug interactions are observed between BPN and ART medications
- often not clinically significant to warrant change in dose of either BPN or ART medicines
- Guided by the clinical signs and symptoms for changing the dose of OST

METHADONE: DRUG-DRUG INTERACTION

Increase in methadone dose required when given with

Anti-retroviral drugs:
Abacavir
Lopinavir,
Nelfinav

Barbi
Phen

Anticon
Carbar
Phe

Anti-tubercular drugs:
Rifampicin

Antibiotics
Ciprofloxacin

Anti-fungal drugs:

Clinically, the dose of methadone need to be changed, if one observes either symptoms of withdrawal or intoxication soon after introduction of another medication to the patient

Decrease in methadone dose required when given with

Drugs contraindicated with methadone

Opioid analgesics:
hine,
ine,
nol,
ramadol

onists:
aloxone,
ne

Monoamine Oxidase Inhibitors

TUBERCULOSIS

- **Opioid dependent individuals are at increased risk of TB**
  - Poor living conditions
  - General debility
  - Nutritional deficiency
- **Often, symptoms of TB attributed to drug use**
  - Cough: concomitant smoking
  - Weight loss: poor nutrition

ATT–OST INTERACTION

- **ATT considerations**
  - Isoniazed: may cause liver toxicity; need to monitor LFT
  - Drug – Drug Interaction
    - Rifampicin:
      - **Increase clearance, resulting in poor analgesia and may precipitate withdrawal**

- **However, suspected tuberculosis or current anti-tubercular treatment by themselves do not preclude withholding or delaying initiation of ost**

ADOLESCENTS

- **Are adolescents using drugs same as adults drug users?**
  - Duration of opioid use: shorter?
  - Exposure to other treatment options: none-minimal?
  - Degree of damage due to opioids: lesser?
  - Psychosocial support: better?

CONFLICTING VIEWS

Detoxification followed by antagonist treatment should be tried initially, and if this strategy fails, agonist medications should be considered

Adolescents also have a high risk of sharing, overdose and other opioid-related complications, and hence, OST should be considered

- Detoxification and antagonist treatments are not available everywhere
- Not possible to wait for a trial of antagonist in every adolescent

ADOLESCENTS

For IDU Client less than 18 years

OST should not be denied straightaway.

Careful assessment

Duration of opioid use

High risk behaviour, (e.g. Sharing)

Available psychosocial support

If long h/o opioid use, presence of high risk behaviour, Poor support

OST must be considered

FEMALE DRUG USERS

- **Issues in Female drug users**
  - Hidden problem
  - Dependence on male partner for drug use
  - Greater chance of selling sex for sustaining drug habit
  - Greater stigma and discrimination
  - Greater inaccessibility to treatment programmes

CONSIDERATIONS FOR PROVIDING OST

- Special efforts to make the OST clinic/centre female friendly

- Ensure that female IDU is examined and interviewed in the presence of a female staff

Specific enquiry

- High-risk sexual behaviour (including selling sex)
- Signs/symptoms of STI
- Last menstrual period (to rule out pregnancy)
- Child-bearing history
- Presence of male drug-using partner

CONSIDERATIONS FOR PROVIDING OST

- Priority to female IDUs – assessment, dispensing and follow-up
- Presumptive STI treatment
- Contraceptives for those in the child-bearing period
- Access to other psychosocial supportive services
- OST for male partner

PREGNANCY

- **OPIOID SUBSTITUTION THERAPY IS RECOMMENDED FOR PREGNANT WOMEN DEPENDENT ON OPIOIDS**

- The process of induction and maintenance is the same as for other patients.

- Termination should not be attempted in first and third trimester

- Regular ANC check-up and Institutional delivery

PREGNANCY

- BPN/Methadone dose
  - Dose may need increase in third trimester
  - Continued throughout the labour
  - Dose may need reduction after delivery
- Breast-feeding to be continued
- Possibility of opioid withdrawal in new-born child soon after delivery – Neonatal Abstinence Syndrome (NAS)
  - Prior liaison with pediatrician
  - Very few will require morphine elixir

Critical issues in OST Programme

Appropriate selection of patients

Adequate Dose

Adequate Duration

Adequate Dispensing procedures

Critical issues in OST Programme

- **Providing psychosocial interventions and ancillary services**
- **Careful monitoring**
- **Attitude of staff**
- **Stock management and record maintenance**

THANK YOU…..