Opioid Rotation – What is the role and How do I choose?

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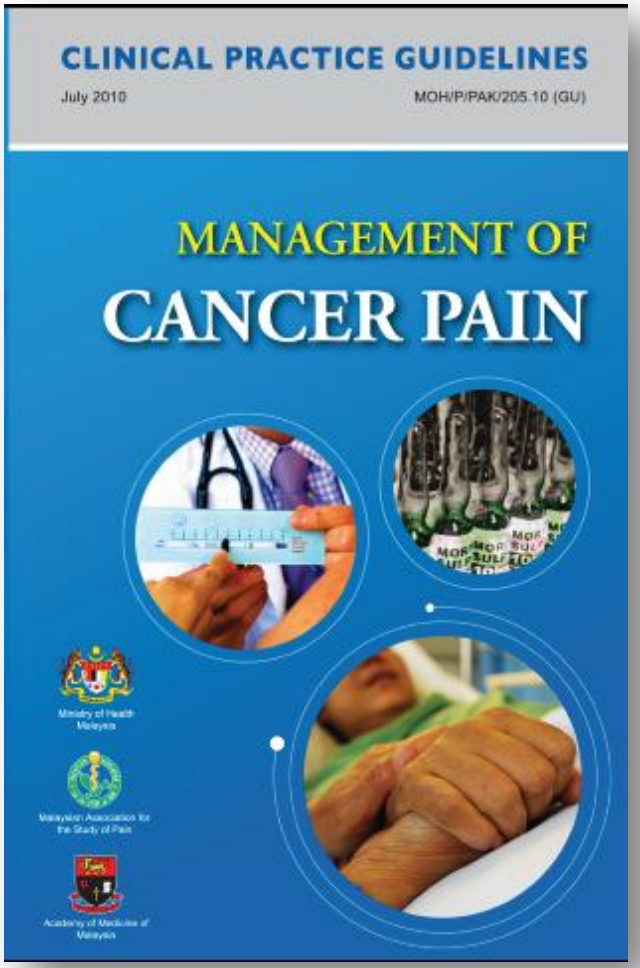
Introduction

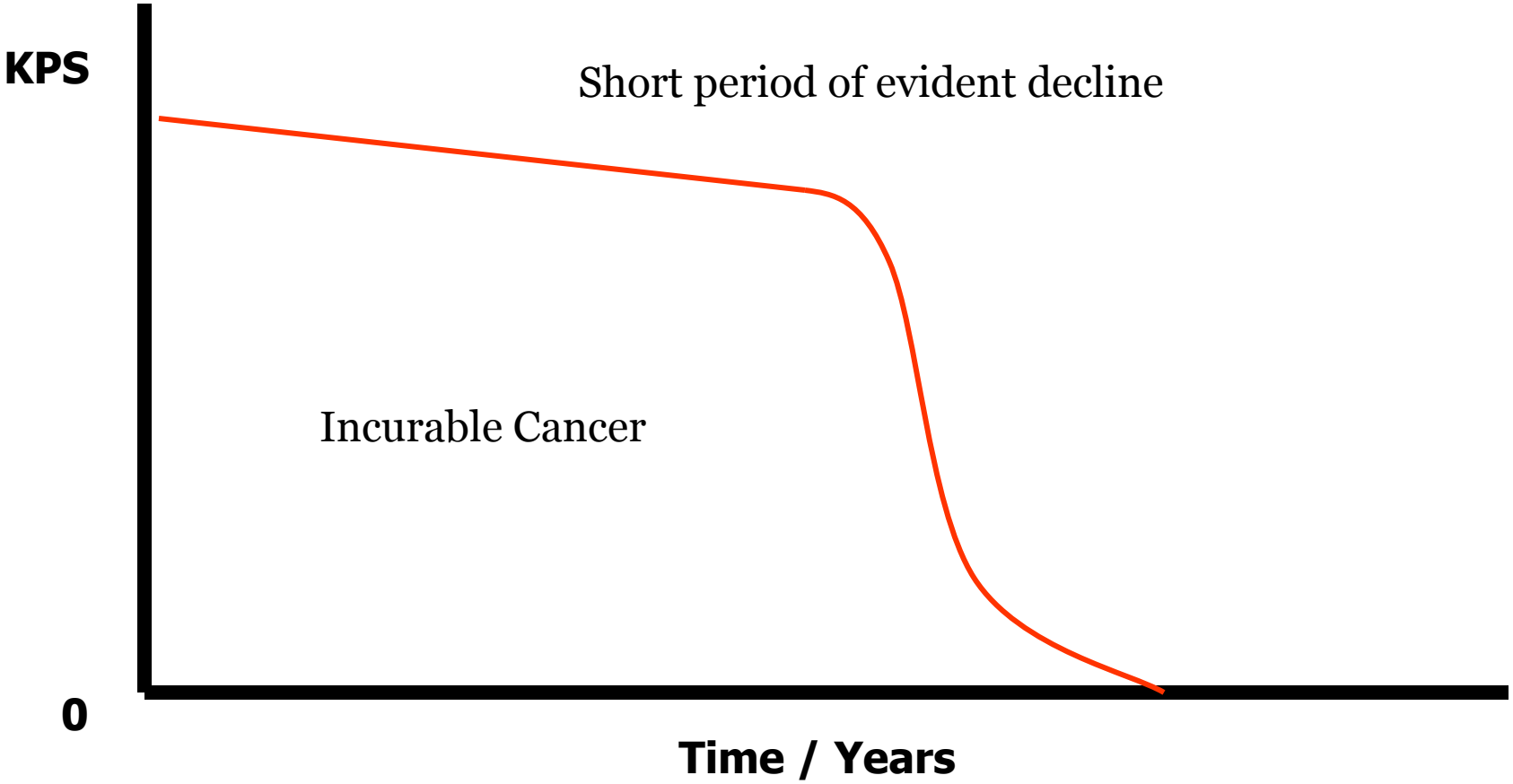
- WHO states that 70-90% of cancer pain can be relieved by drug therapy.
- Opioid therapy is the mainstay of management for moderate to severe cancer pain
- Oral Morphine is the drug of choice for the management of moderate to severe cancer pain.



Chronic Cancer Pain – a dynamic process

- Pt's pain changing
- Pt's condition changing
- Pt's goals of care changing

Disease Trajectory



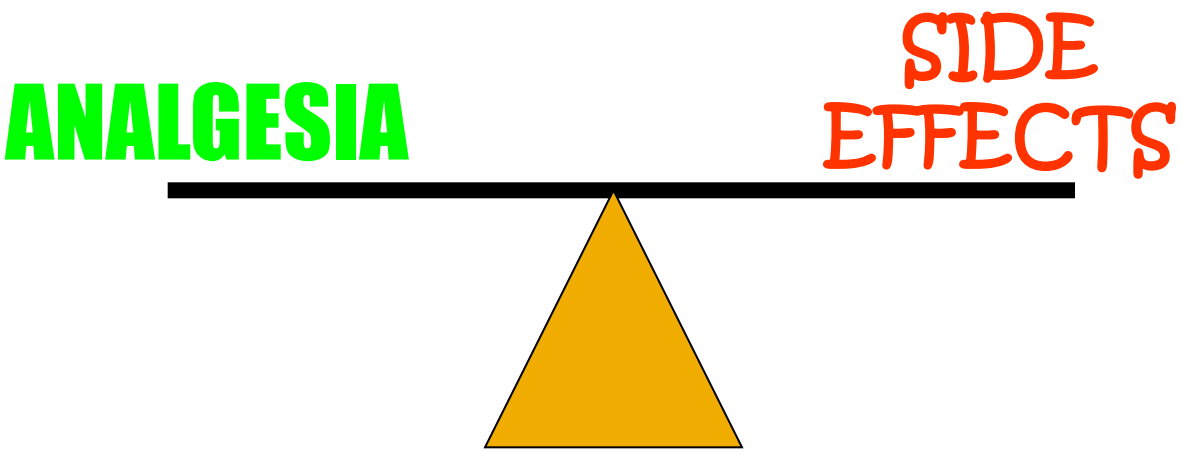
Challenge of Chronic Cancer Pain Management

- Controlling Pain
- Controlling Side Effects
- Providing most appropriate route of administration and ensure compliance
- Do no harm

What is Opioid Rotation ?

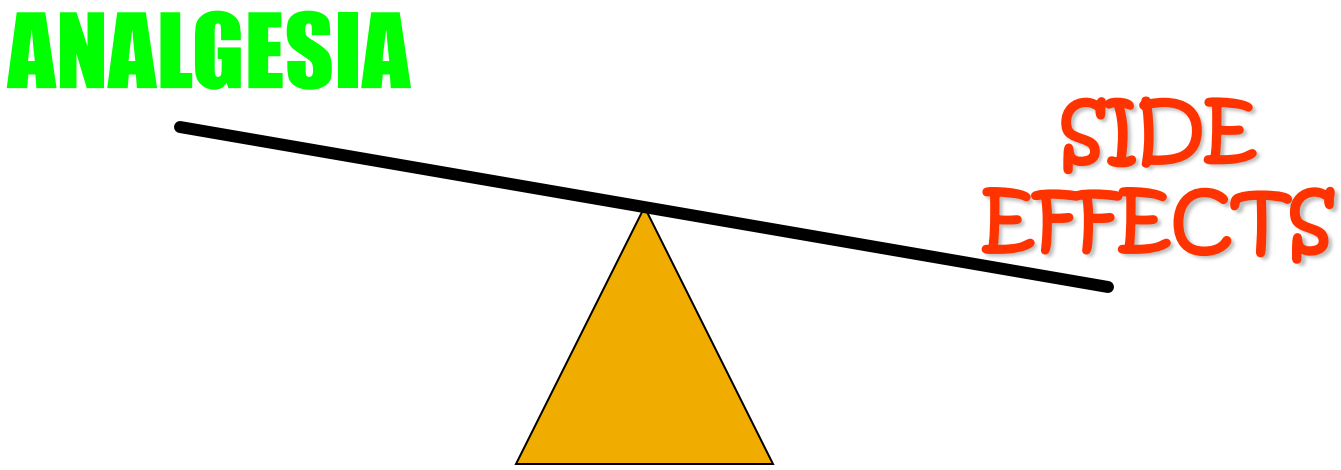
Opioid Responsiveness

- The degree of analgesia achieved as the dose is titrated to an **endpoint** defined either by intolerable side effects or the occurrence of acceptable analgesia.



Opioid Rotation

- Concept whereby opioid is changed to another in order to improve the balance between analgesia and side effects.



Opioid Rotation

- May also refer to changing from one route of administration to another route using the same opioid. Eg. Oral morphine to s/c morphine or Intrathecal morphine

- Also known as “opioid switching”

Rationale of Opioid Switching

- Opioid responsiveness for different opioids may vary in each individual.
- Factors interfering with an opioid's response
  - Progression of the disease
  - Development of tolerance
  - Appearance of intractable side effects
  - Type and temporal pattern of pain
  - Metabolites and excretion
  - Pharmacokinetic and pharmacodynamic factors

Vadalouca A, et al. J Opioid Manage 2008;4(4):213

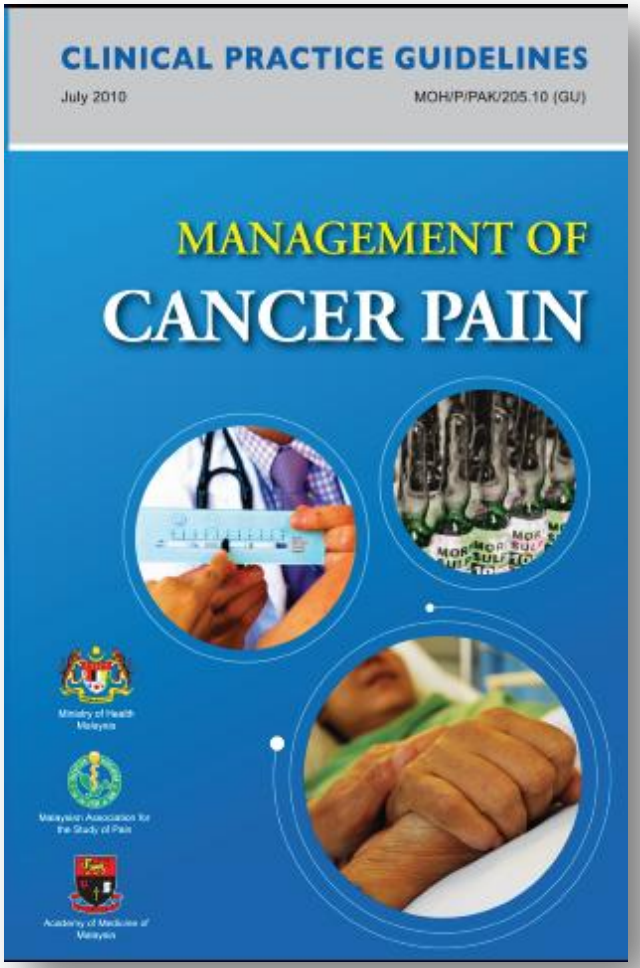
Indications for opioid switching

- Inadequate pain relief despite appropriate dose titration of the initial opioid.
- Intolerable side effects (sedation, nausea, vomiting and constipation)
- Renal impairment
- Practical considerations (patient preference, inability to swallow, etc.)

MOH Cancer Pain Management CPG

Recommendation

- Oral morphine should be the **first line** therapy for moderate to severe cancer pain.
- Oxycodone & fentanyl are alternatives to morphine for moderate to severe cancer pain.



So how do I choose?

Surely a patch is better because it is easier for patient!

Fentanyl is safer than morphine!

Fentanyl is more effective than morphine!

More expensive so must be much better!

Transdermal Fentanyl

ADVANTAGES

- Useful for patients who cannot swallow or have bowel obstruction.
- Better compliance – change every 72 hours
- Safer to use in renal failure

DISADVANTAGES

- Fixed dose – cannot be used in opioid naive
- Difficult to adjust dose as increases must follow patch strength.
- Breakthrough analgesia requires using IR morphine or IR oxycodone.

Newer compared to morphine so must be better!

Stronger than morphine so must be better relief!

Not as notorious as morphine so must be safer and no problems with addiction!

Oxycodone

ADVANTAGES	DISADVANTAGES
▪ Similar to morphine in terms of onset and duration of action as well as titration. ▪ Easy to convert for patients who can take oral medication. ▪ Has full range of tablet, injection and liquid preparations. ▪ Targin is useful for constipation.	▪ More potent hence starting dose may be too high for opioid naive if using oxynorm capsules. ▪ Requires full range of preparations to be most useful.

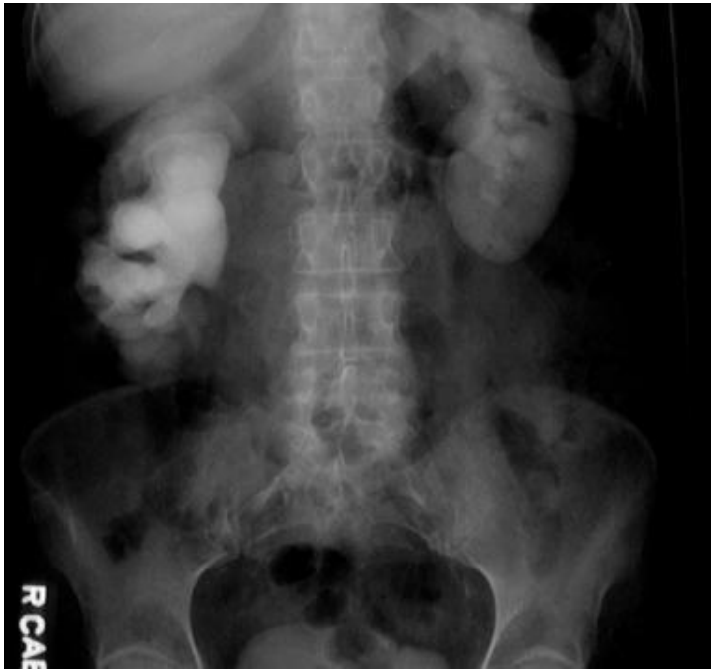
Factors to consider

- Can the patient take oral medication?
- Is the renal function normal ?
- What is available in the pharmacy?

When do I use Fentanyl

Patients who cannot swallow due to bowel obstruction or head and neck cancer.

Patients with renal impairment or where I anticipate worsening renal function.



Other reasons to consider fentanyl

Patients who cannot tolerate both morphine and oxycodone due to side effects.

Patient in terminal phase wanting to go home and requires continuation of opioid therapy.

Conversion factor for fentanyl

- Total daily dose of opioid in morphine equivalents = **60** mg

- Converted dose of transdermal fentanyl
  = **60** ÷ **3**
  = **20** mcg/h of transdermal fentanyl

Table 3. Suggested dose conversion ratio in the direction specified

From \ To	Codeine mg/day	Oral morphine mg/day	SC morphine mg/day	Oxycodone mg/day	Fentanyl TD mcg/h
Oral codeine mg/day		8	20	12	24
Oral morphine mg/day	8		2.5	1.5	3
SC morphine mg/day	20	2.5		0.6	1.2
Oxycodone mg/day	12	1.5	0.6		2
Fentanyl TD mcg/h	24	3	1.2	2	

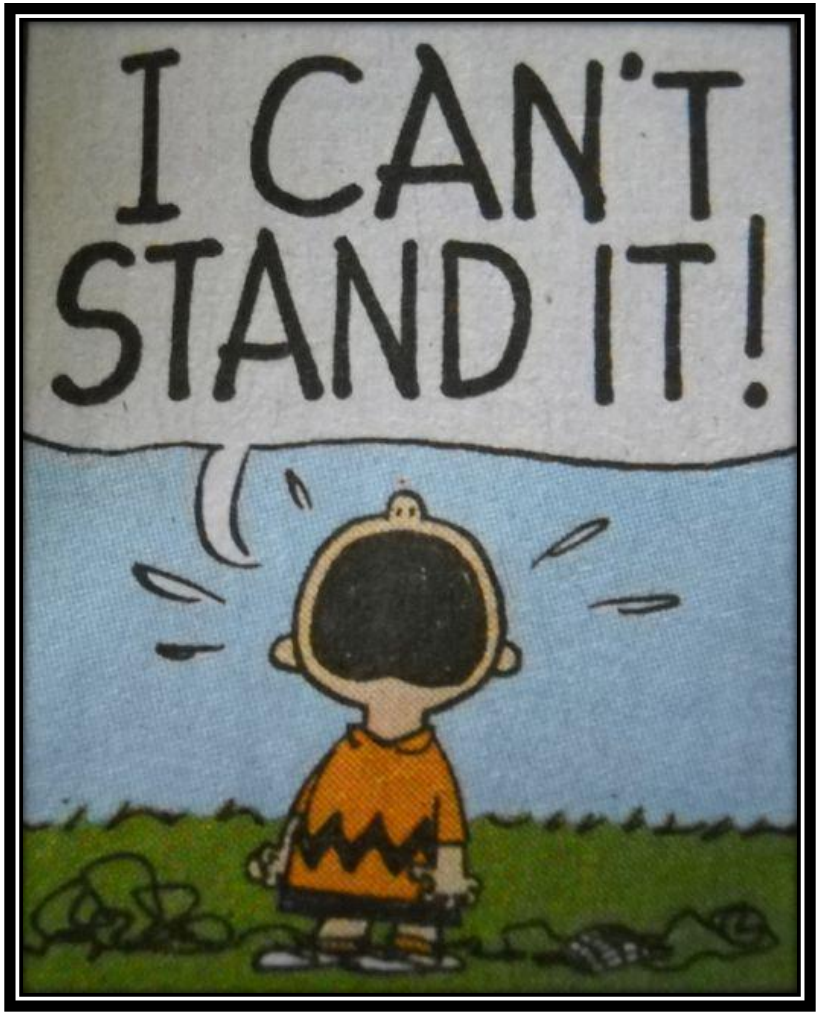
MULTIPLY

DIVIDE

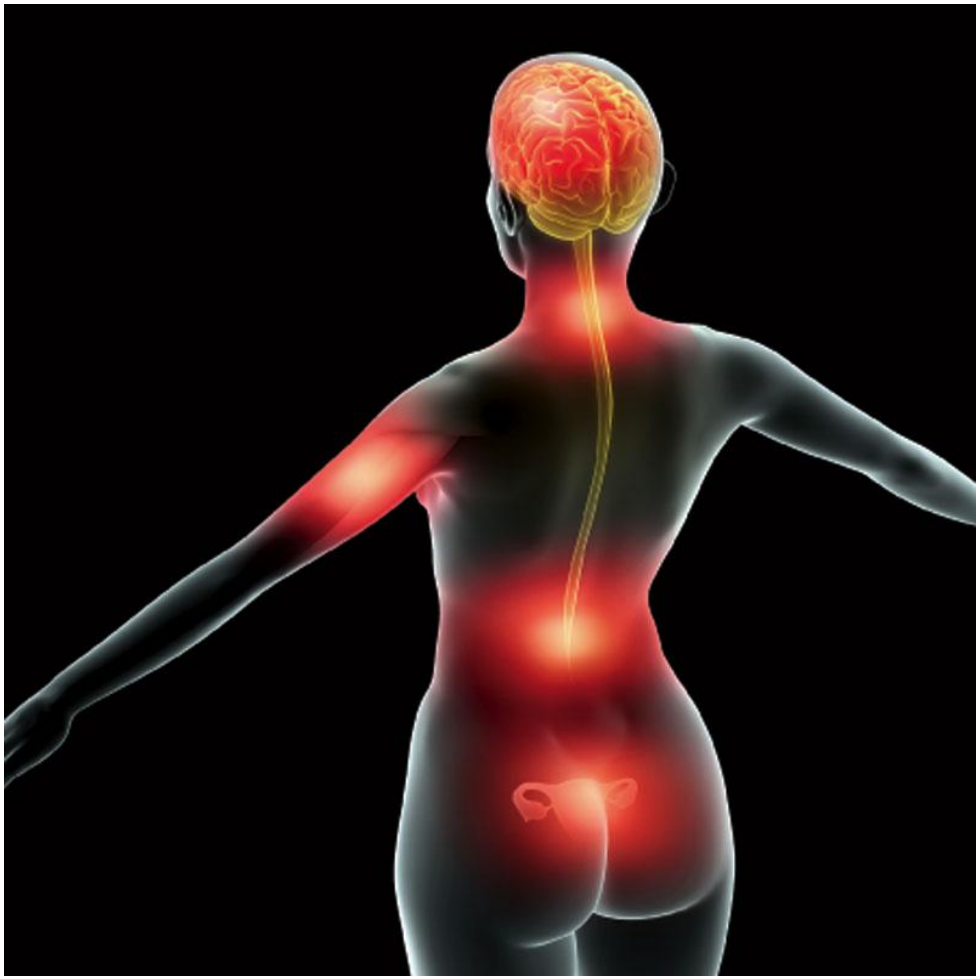
When do I use Oxycodone

Intolerant to morphine but normal renal function and tolerating oral meds

Not getting enough relief with morphine



Mixed nociceptive and neuropathic pain



Severe Constipation

Morphine Phobia

Conversion Factor for Oxycodone

- Oxycodone is **1.5 x** more potent than morphine
- Total daily morphine usage = 60 mg
- Converted oxycodone dose = 60 ÷ 1.5

  = **40mg**

** May then dose reduce further by 25-30% to take into account incomplete cross tolerance.*

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MULTIPLY

DIVIDE

Range of Oxycodone Preparations

Immediate release (4-6 hourly)

1. OxyNorm® oral solution (5 mg/5 mL)
2. OxyNorm® capsules (5 and 10 mg)
3. OxyNorm® injection (10 mg/mL)

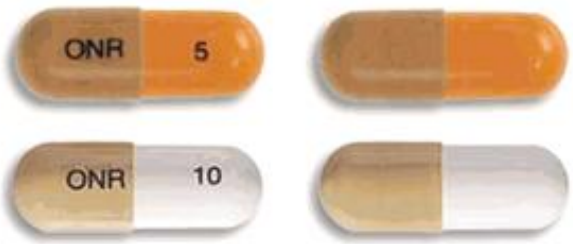
Prolonged release (12-hourly)

1. OxyContin® (10, 20 and 40 mg)

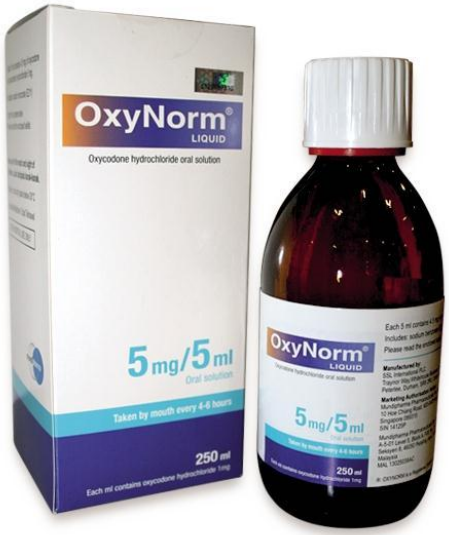
   **New formulation – abused deterrence*

1. Targin® (oxycodone + naloxone: 5, 10, 20mg)

Oxynorm:
Immediate Acting Preparations



C. oxynorm



Oxynorm solution

Inj. oxynorm

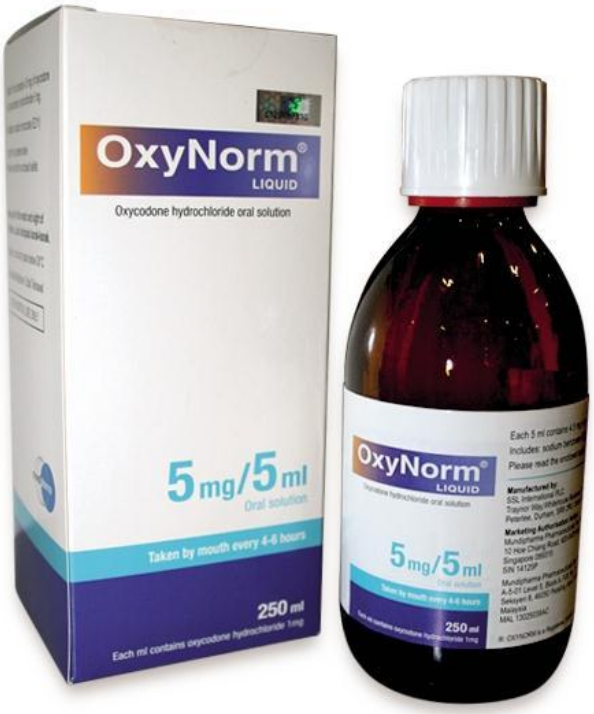
Oxycontin: Prolonged Release Preparation

T. Oxycontin

T. Targin (Oxycontin + Naloxone)

The role of various oxycodone preparations in managing cancer pain

Small starting doses



Liquid oxynorm 1mg/ml

Targin 5/2.5mg

Case study 1

- Mr. H, 62 y.o. Gentleman with advanced colon cancer and liver metastasis.
- c/o pain in the abdomen and right hypo-chondrium with PS 7/10
- Was given aq. Morphine 3mg 4 hourly and prn to titrate analgesia.
- Develop severe nausea and vomiting as well as drowsiness.
- Refused further morphine

Case study 1

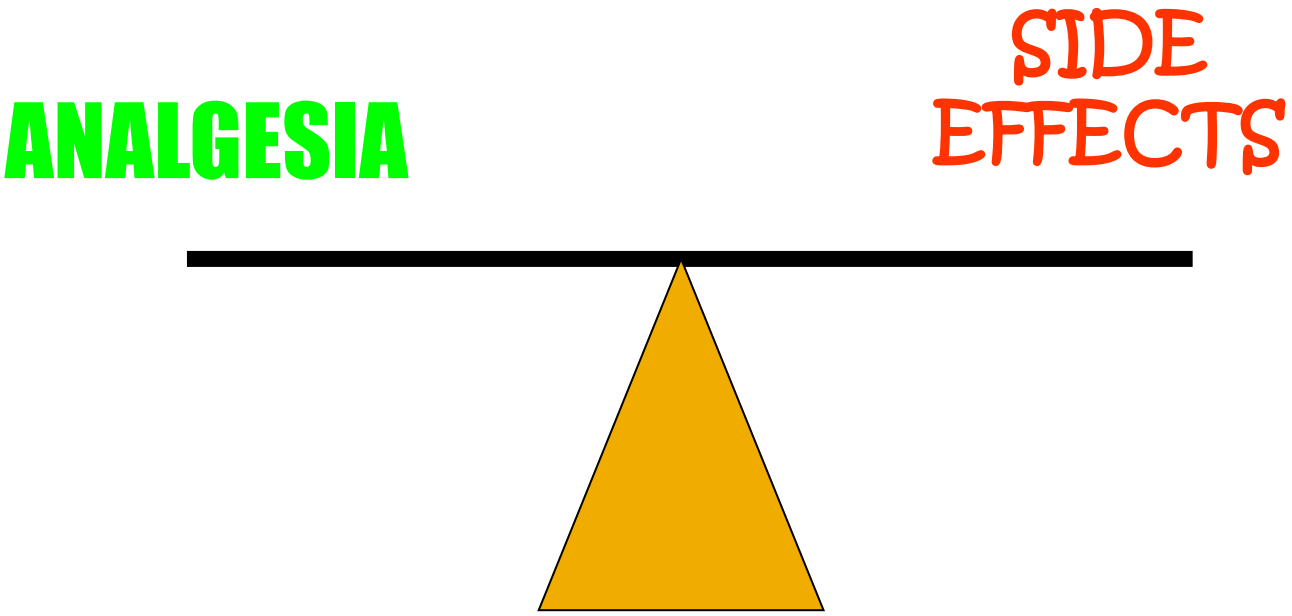
- Started on oxynorm solution 1mg 4 hourly and prn.
- Tolerated oxynorm solution well and took additional doses of 1mg x 3 with pain score reducing to 3-4/10.
- Pain fairly stable with dose of 10-12mg oxynorm daily.

Case Study 1

- Converted to T. Targin 5mg bd and oxynorm solution 2mg prn

- Conclusion:
  - Oxynorm solution can be useful for small dose titration in cancer pain and small prn doses.
  - Targin 5mg is useful for low dose oxycodone requirements for maintenance analgesia.

Opioid rotation and mixed nociceptive and neuropathic pain



Case Study 2

- En P, 73 case of advanced hormone refractory prostate cancer with extensive bony metastasis in the spine and bony pelvis.
- c/o severe back pain with pain score of 6-7/10 in the lower back worse on movement.
- Also c/o pain radiating down from pelvis to right lower limb associated with numbness and dysaesthesia. Very severe and spontaneous at times.

Case study 2

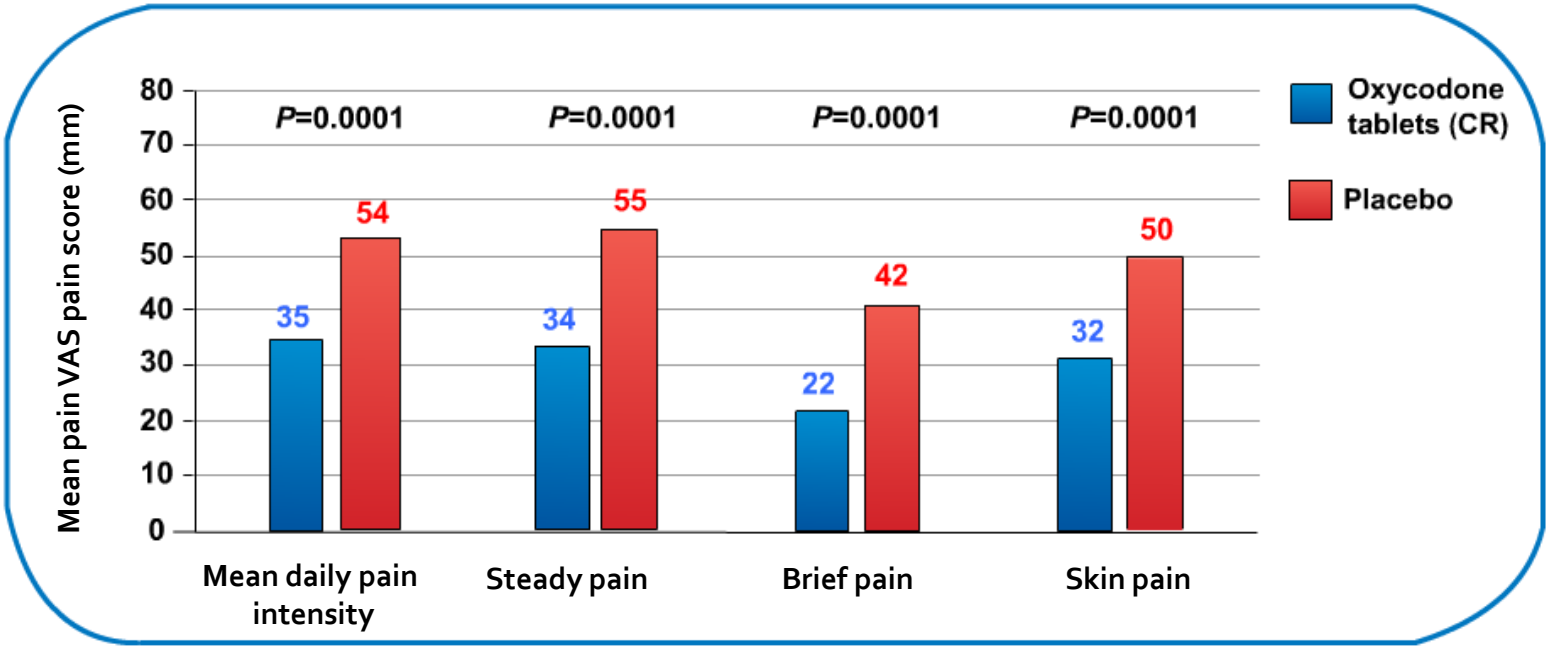
- Was started on aq. Morphine and titrated dose up to SR morphine 180mg bd with Aq morphine 50mg prn. Pain score still 4-5/10.
- Was not drowsy and tolerated morphine well however pain score not reducing with further breakthrough doses.
- Also spontaneous pain radiating from pelvis to right lower limb persistent.

Case Study 2

- Opioid rotation to oxycontin 120mg bd and oxynorm capsule 30mg prn.
- Pain score reduced to 2-3/10 with less spontaneous neuropathic pain.

Efficacy of oxycodone controlled-release tablets in postherpetic neuralgia

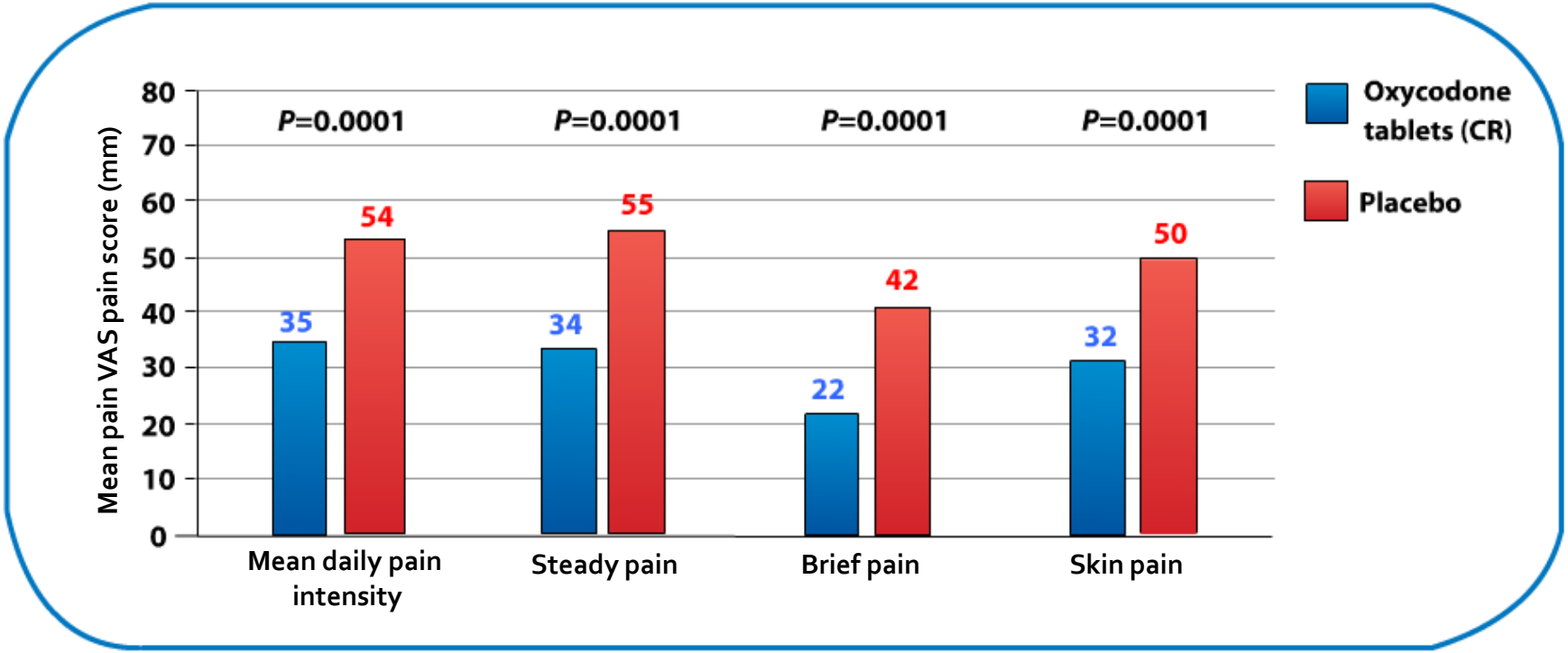
The mean daily dose of oxycodone controlled-release tablets during the final week of treatment was 45mg



Oxycodone controlled-release tablets are effective for the relief of overall, steady, brief and skin pain in patients with post-herpetic neuralgia, when compared with placebo

Watson C and Babul N. *Neurology* 1998;50(6):1837-1841.

Efficacy of oxycodone controlled-release tablets in painful diabetic neuropathy



Oxycodone controlled-release tablets are effective in the relief of neuropathic pain in diabetic neuropathy, when compared with active placebo

Watson CP *et al. Pain* 2003;105(1-2):71-78.

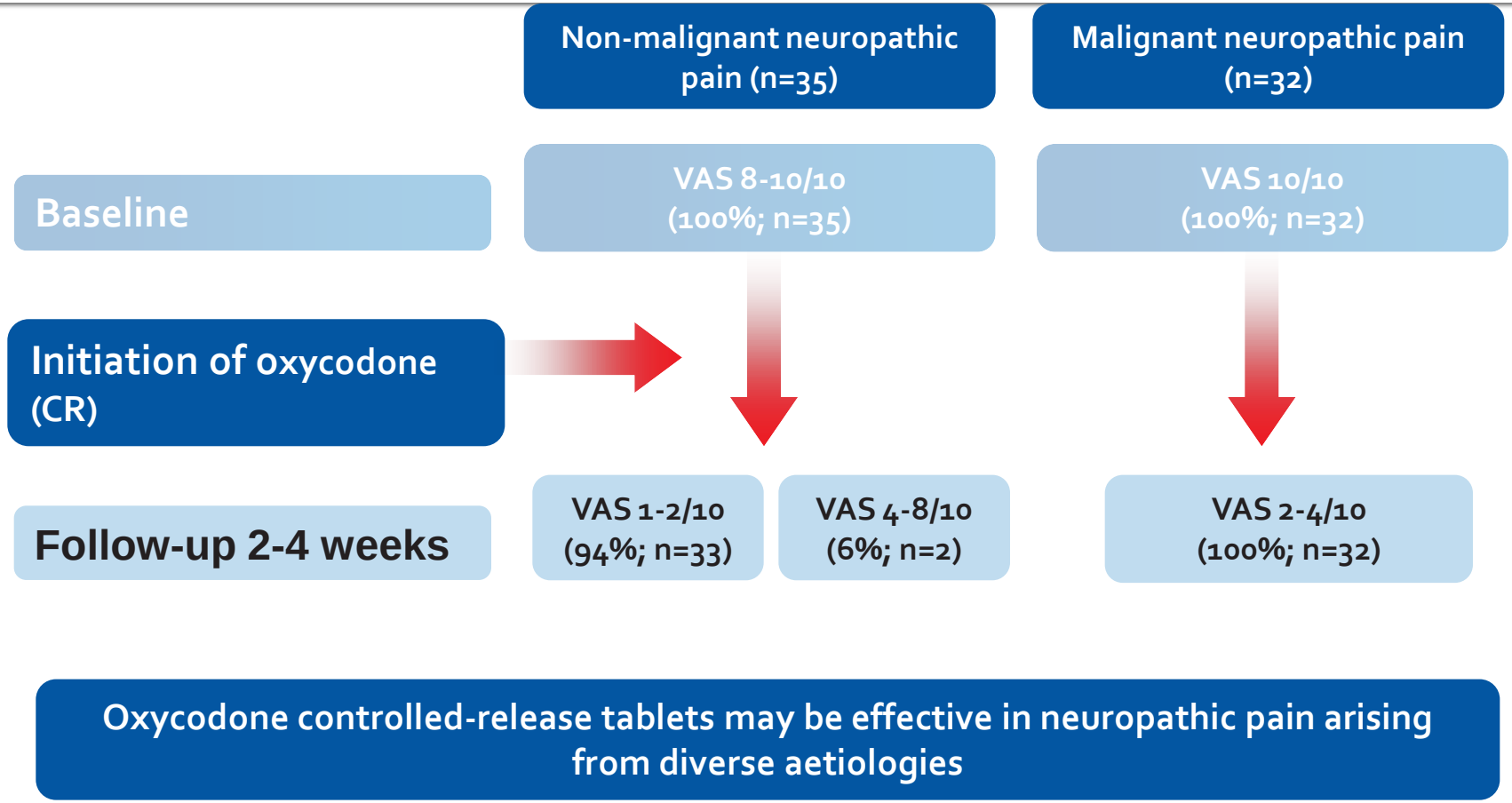
Analgesic therapy in postherpetic neuralgia

Intervention	NNT (95% CI)
Oxycodone prolonged release tablets	2.50 (1.74 - 4.41)
Tricyclic antidepressants	2.64 (2.1 - 3.54)
Combined opioids	2.67 (2.07 - 3.77)
Gabapentin	4.39 (3.34 - 6.07)
Tramadol	4.76 (2.61 - 26.97)
Pregabalin	4.93 (3.66 - 7.58)

Tricyclic antidepressants, opioids, gabapentin, tramadol and pregabalin can be considered effective treatments for postherpetic neuralgia

Hempenstall K *et al.* Analgesic therapy in postherpetic neuralgia: a quantitative systematic review. *PLoS Med 2005;2:e164.*

Efficacy of oxycodone controlled release tablets in managing neuropathic pain



Oxycodone controlled-release tablets may be effective in neuropathic pain arising from diverse aetiologies

Ong EC. *Oncology* 2008;74(Suppl.1):72-75.

Severe Constipation

TARGIN

Combined Oxycontin + Naloxone tablets

5/2.5mg
10/5mg
20/10mg

Case Study 3

- Pn. T, 48 y.o. Lady with metastatic ca lung and severe chest pain.
- On T. Morphine SR 30mg bd and aq morphine 10mg prn
- Pain fairly well controlled but 2 weeks later readmitted for poor pain control and severe constipation.
- Was already on Sy. Lactulose 15mls tds

Case Study 3

- Was converted to s/c morphine 5mg 4 hourly and prn to control pain.
- Later bowels cleared using oral fleet x 1 and continued with lactulose and bisacodyl.
- Once pain controlled, coverted to T. Targin 20/10mg bd and oxynorm 5mg prn.
- Pain well controlled and no further issues with constipation.

Using Targin

- Remember:
  - This is a prolonged release oxycodone exactly like oxycontin but with naloxone combined.
  - Dosing is similar to using oxycontin.
  - Maximum dose of Targin is limited by the Naloxone component.
    - Not more than 40/20mg bd (this may change with newer data)

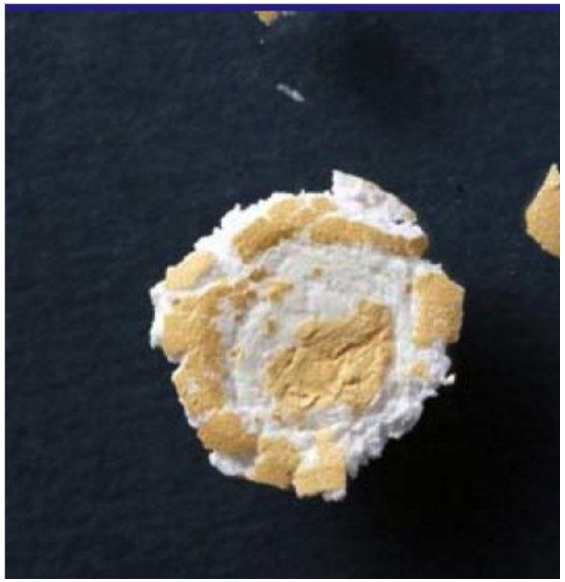
Using Targin

- Same principle applies – do not cut crush or chew targin tablets
- Once maximum targin given but if pain still not optimal, to top up oxycodone dosing with T. Oxycontin.
  - Eg. If total oxycontin dose is 120mg bd then give Targin 40/20mg bd + Oxycontin 80mg bd
- Breakthrough medication is using oxynorm prn at 1/6 -1/12 of the total 24 hour requirement

Oxycontin Prolonged Release – new abuse deterrent formulation

Abuse deterrent oxycontin

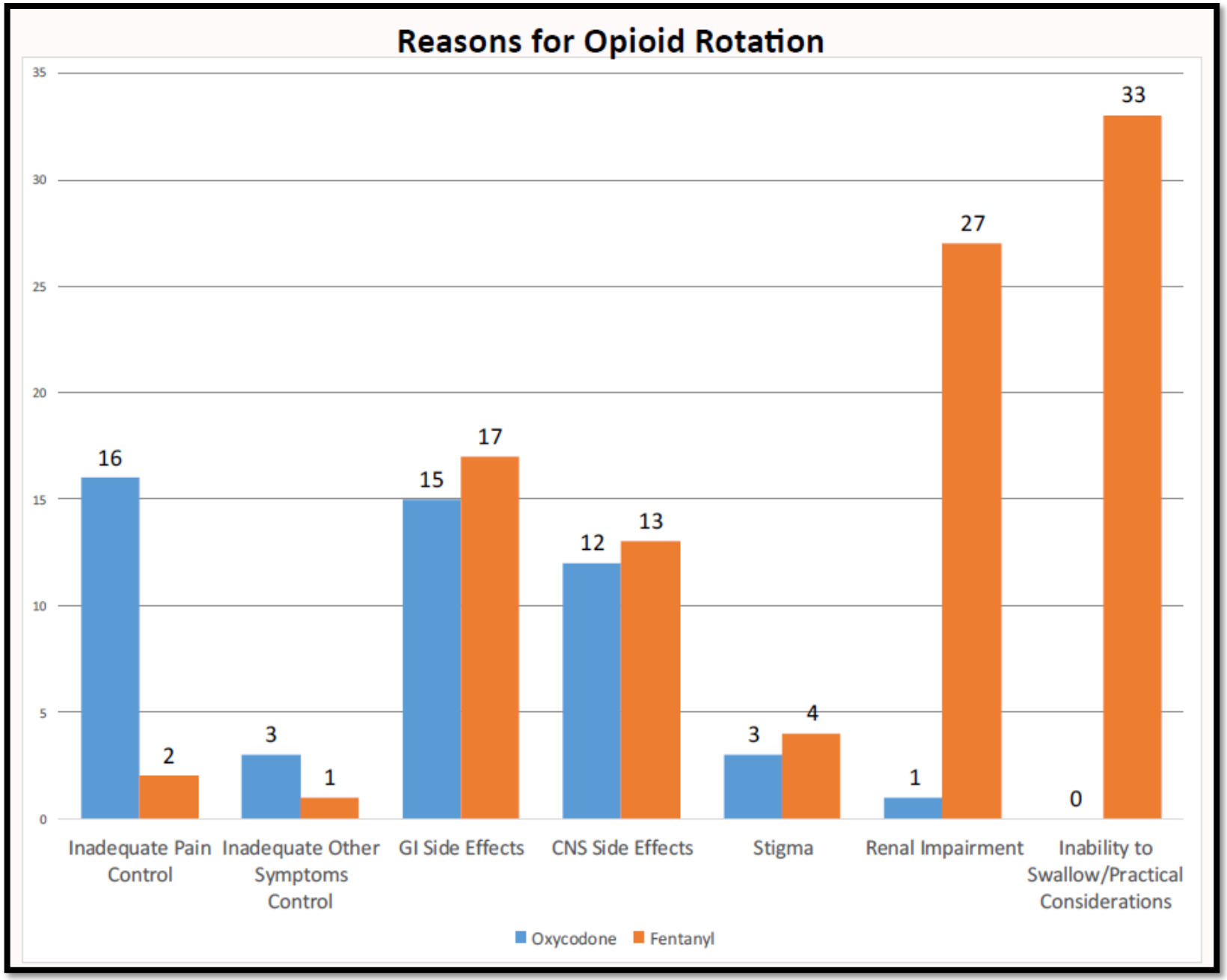
- Difficult to crush hence no powder to inhale.
- Forms a gel when wet and does not dissolve so cannot inject.



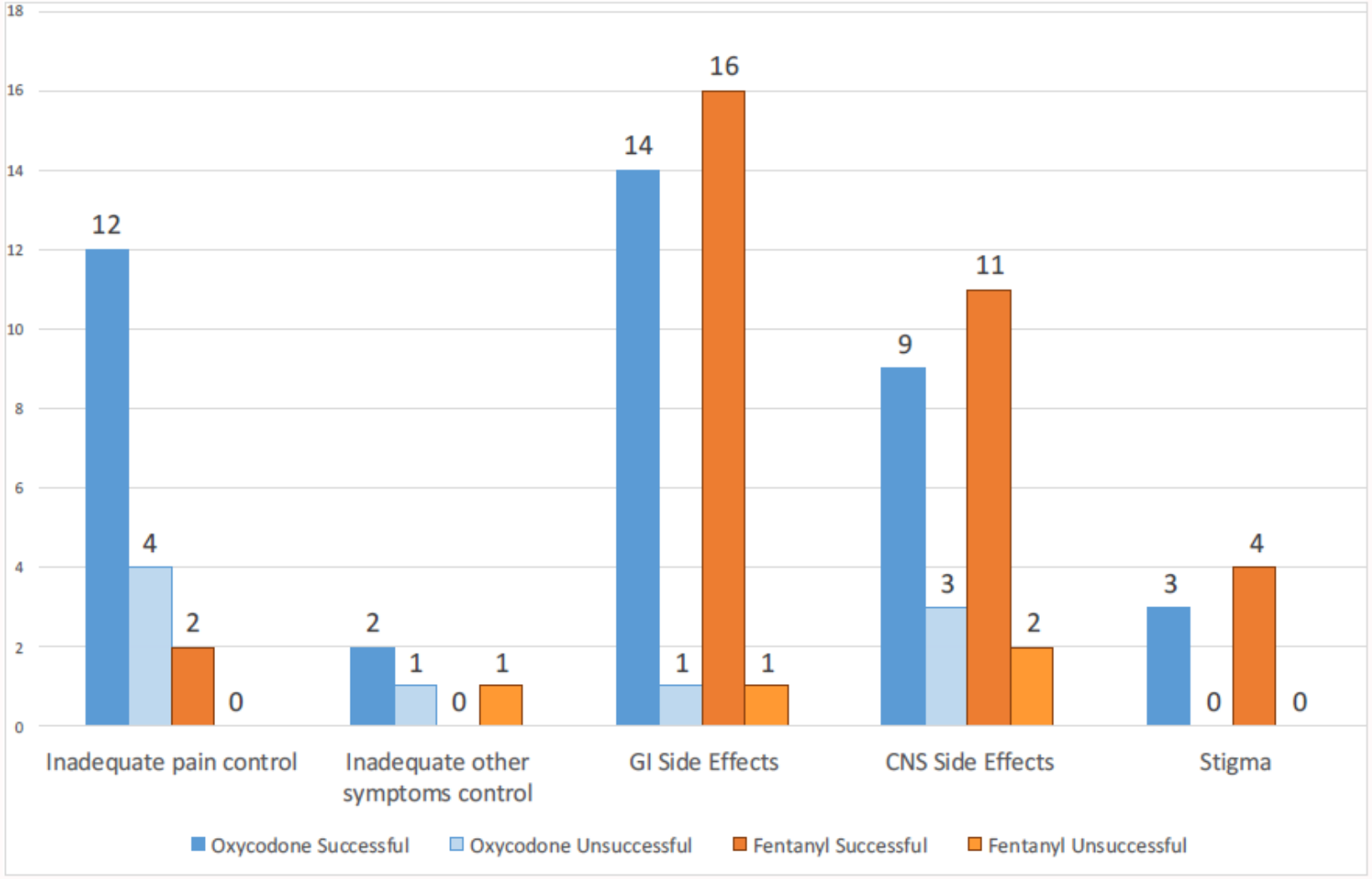
Abuse Deterrent Oxycontin

Opioid Rotation – The IKN Experience 2015

- A total of 135 patients (55%) from 243 treated for cancer pain required opioid rotation.
- 97 patients (71%) rotated to fentanyl
- 38 patients (29%) rotated to oxycodone
- Reason for using fentanyl
  - Inability to take oral medication
  - Renal impairment
- Reason for using Oxycodone
  - Poor pain control with morphine
  - Intolerable side effects with morphine


Reasons for Opioid Rotation
35
30
25
20
15
10
5
0
16
2
3
1
15
17
12
13
3
4
1
27
0
33
Inadequate Pain Control
Inadequate Other Symptoms Control
GI Side Effects
CNS Side Effects
Stigma
Renal Impairment
Inability to Swallow/Practical Considerations
Oxycodone
Fentanyl

OUTCOMES of Opioid Rotation by Indication
(except for indication of practical considerations/inability to swallow)



Conclusion

- Opioid rotation is a useful strategy to optimise cancer pain management.
- Morphine is still the first choice for management of cancer pain but opioid rotation may be necessary almost 50% of the time.
- Selection of alternative opioids should be based on specific reasons and indications rather than randomly.

THANK YOU