Palliative Care ECHO

Pain Management - Opioids

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Pain Management Caresearch

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- Over 50% of seriously ill patients experience pain
- Palliative care patients continue to experience unacceptably high levels of pain
- Effectively treated using a multimodal approach
- Under assessment more likely in non-cancer, RACFs, cognitive impairment & ethnic minorities
- Pain should be actively identified, carefully assessed & treated promptly
- Use validated assessment tools
- Base choice of opioid on access, patient history, cost

Total pain – subjective + multifactorial

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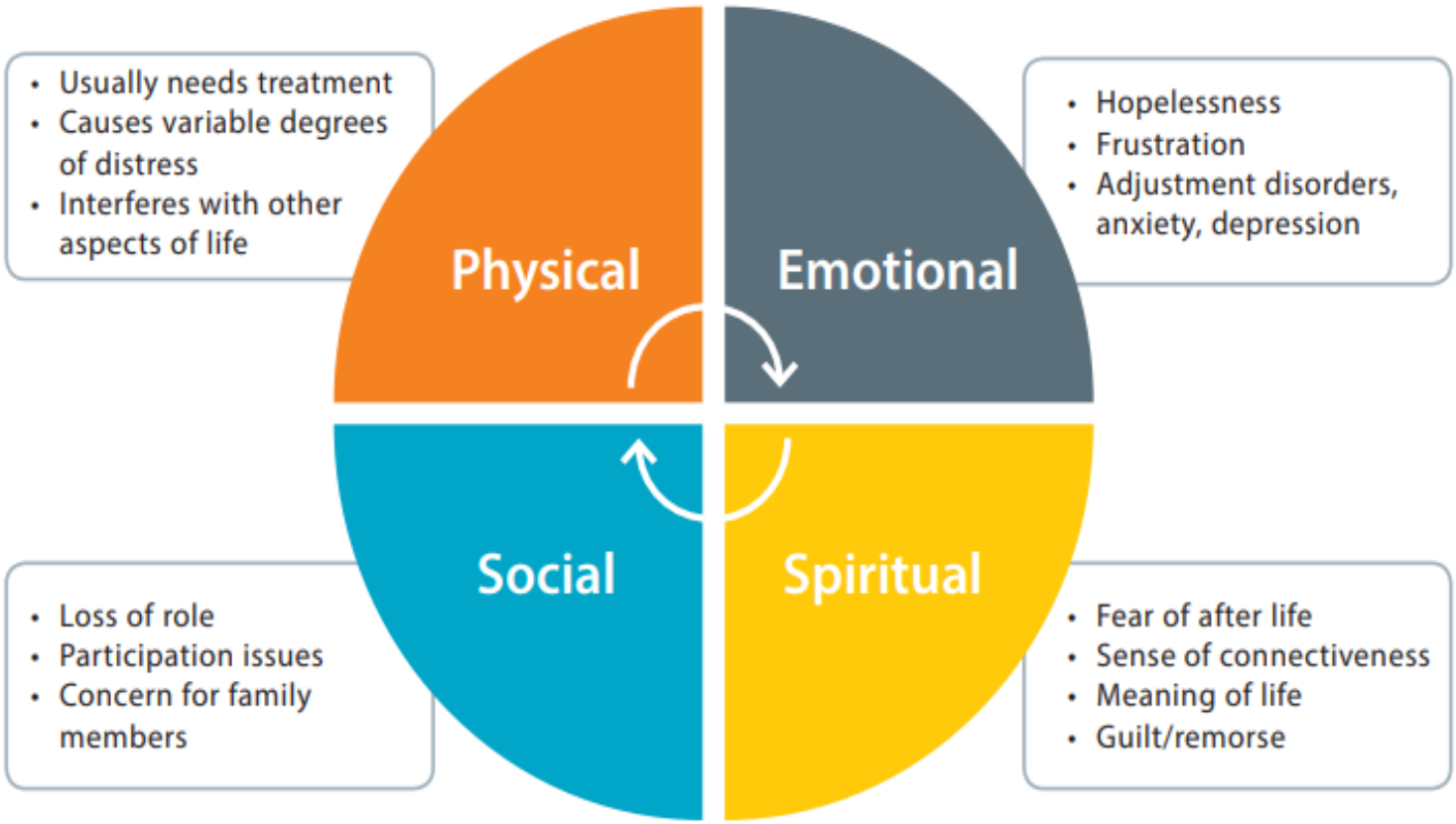

PSA Palliative Care Essential CPE

Pain in different diseases

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Disease	Possible causes of pain
Advanced cancer	Malignant diseases e.g. primary tumour, bone, liver or brain metastases –tumour infiltration, nerve compression
	Treatments e.g. surgery, chemo or radiotherapy
Advanced heart failure	Ischaemia/angina
	Oedema e.g. leg swelling, ascites
	Non-angina chest pain (dull pressing pain
Motor neurone disease	Musculoskeletal eg weakness, immobility and stiffness
Unrelated to primary disease	Arthritis, infection

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Opioids in Palliative Care

Chemical Classification*

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Phenanthrenes	Phenylpiperidines	Diphenylheptanes
tapentadol	fentanyl	methadone
buprenorphine	sufentanyl	
morphine		
hydromorphone		
oxycodone		

*Knowledge of different classes of value when dealing with intolerance

Opioid analgesics

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Opioid subclass	Mechanism of action			Efficacy	Pharmacokinetics
	μ	δ	κ		
Opioid agonists • Morphine • Hydromorphone • Oxycodone • Methadone* • Fentanyl • Sufentanil	 +++ +++ ++ +++ +++ +++	 + +	 + + +	Strong opioids	First-pass effect – duration 1-4h Duration Methadone 4-6h, long variable t1/2
Mixed agonist antagonist • Buprenorphine	+ -	-	-	Can antagonize agonist effect – weak opioid	Duration of action 4-8h
Mixed** Opioid Tapentadol	++			Strong opioid	Duration 4-6h

*NMDA antagonist, presynaptic 5HT & NA reuptake inhibitor ** Noradrenaline reuptake inhibitor

- Oral morphine, oxycodone and hydromorphone all have similar efficacy and toxicity in opioid naïve patients.
- Mainstay of treatment for moderate to severe pain

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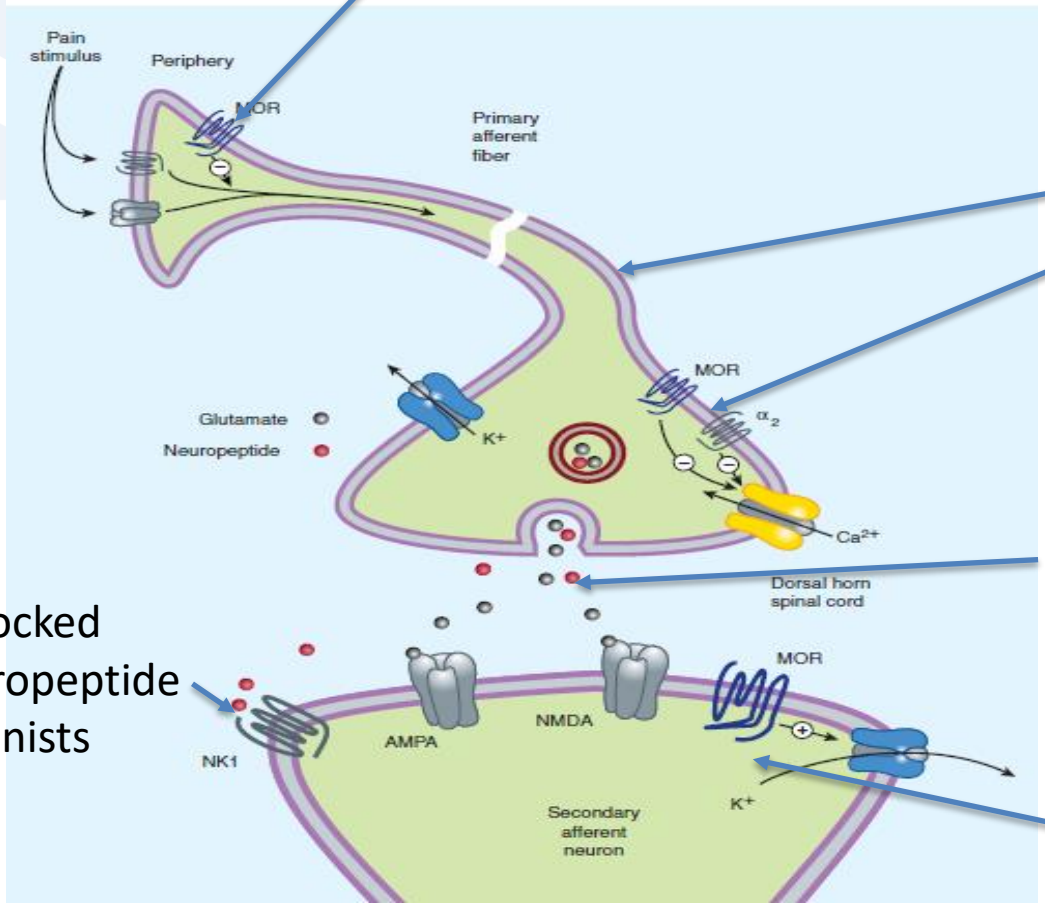
Pain blocked by opioids at MOR at periphery under inflammatory conditions



Primary afferent neurone

Pain blocked at presynaptic ending by opioids, CCB, α agonists & NRI

glutamate & neuropeptide synapse with secondary neurone

Pain blocked by neuropeptide antagonists

Pain blocked by opioids at post synaptic MOR

Barriers to Good Pain Control

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Patient factors include:

anxiety and depression
fear of addiction
fear of becoming tolerant to medications
fear of adverse effects of therapy
an inability to comply with complicated programs
an inability to understand dosing guidelines
communication difficulties (language differences, cultural issues, intellectual impairment).

Clinician factors include:

lack of pain assessment skills
lack of knowledge of current therapeutic approaches
insufficient knowledge of, and uncertainty about the role of opioid treatment
overestimation of the risks of addiction and concern about drug tolerance
concern about the management of adverse effects
concern about the regulations for controlled prescription drugs.

Managing Pain in the Dying patient. Philip S et al. Am Fam Physician 2000 Feb 1:61 (3);755-764

Comprehensive Pain Assessment

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Cause
disease or treatment?

Treat reversible causes

Prognosis goals of care

Duration
Acute or chronic?

Assess response to current analgesia

benefit vs adverse effects?

signs of
tolerance
hyperalgesia
allodynia?

optimal route formulation?

assess compliance health literacy

=

agree a pain management plan

regular review

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Pain assessment

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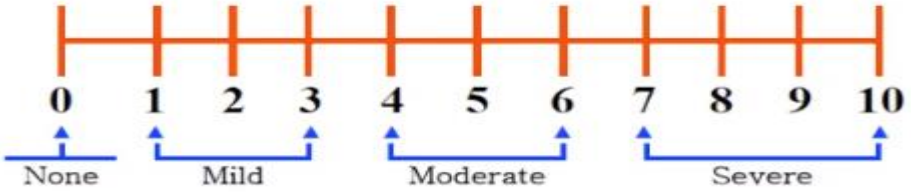
- Site, quality, duration, severity, triggers, response to current analgesia – is it opioid-responsive?
- Description of pain – use validated tools



Wong-Baker FACES Pain Rating Scale

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Opioid-induced hyperalgesia

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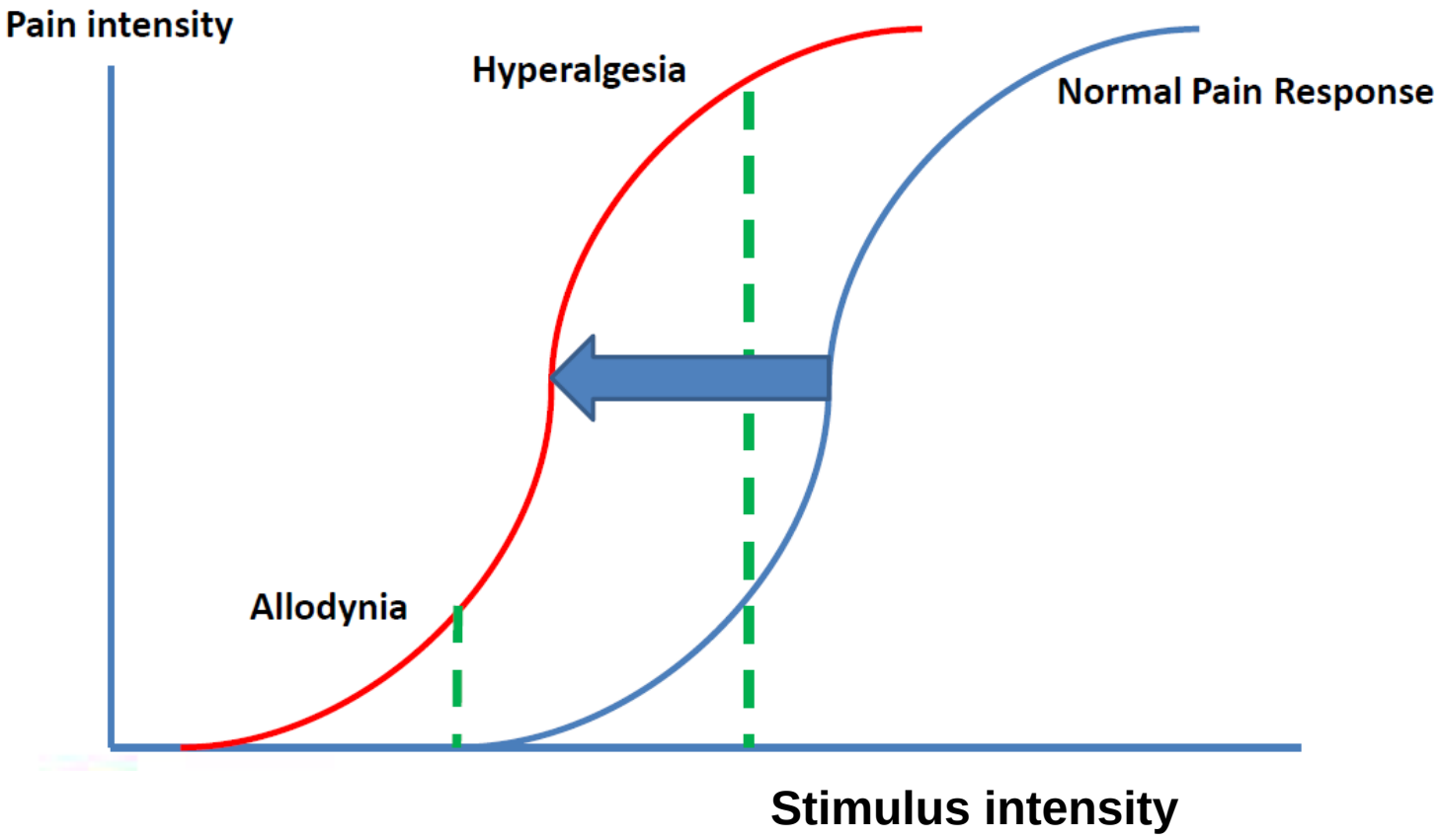
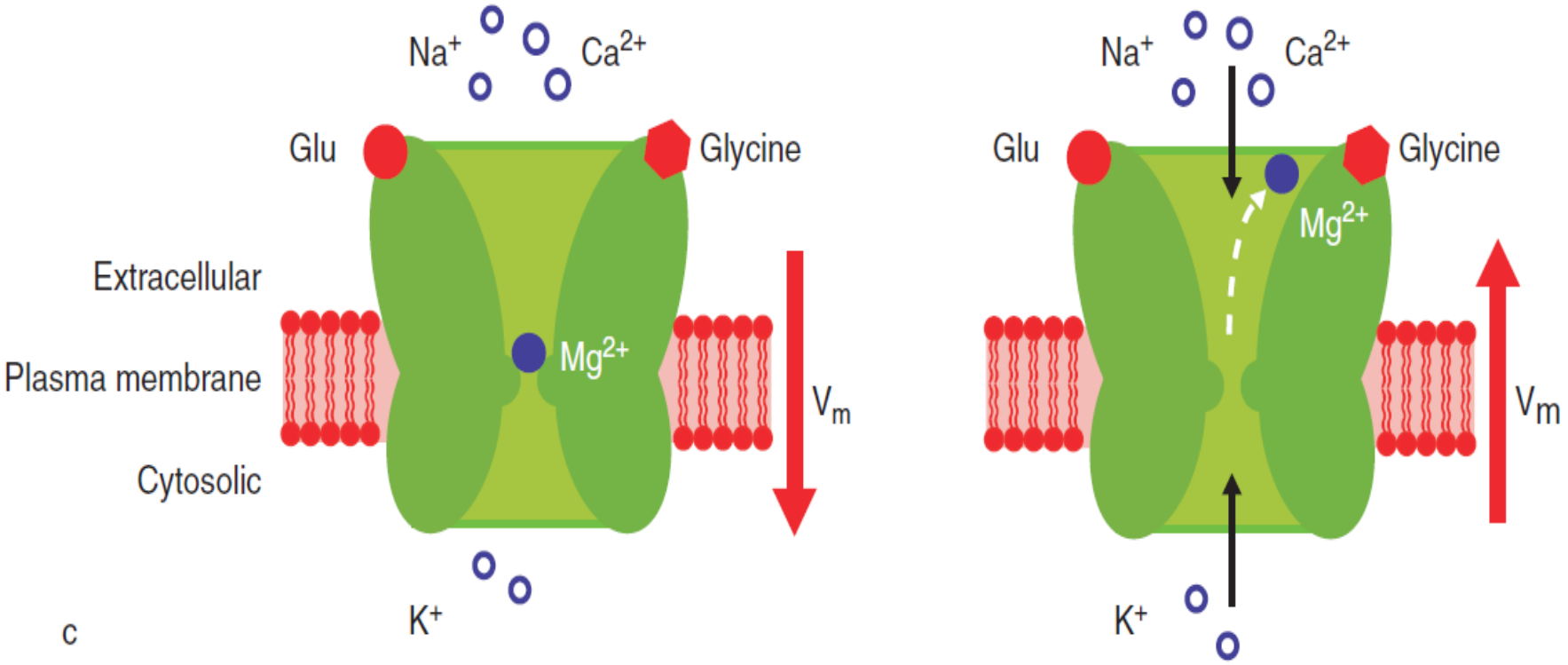
- Increased pain sensitivity caused by opioid exposure
- Appears to involve the overactivation & stimulation of NMDA receptor
- Via activation of glial cells which play a role in inflammation, pain signal transmission, pain hypersensitivity and opioid tolerance eg M3G can activate these cells
- Pain experienced may be similar or different to underlying pain
- More commonly seen in high, escalating opioid doses
- Consider OIH if opioid fails to address pain
- Distinguish from tolerance – decreased drug efficacy which can be overcome with an increased dose
- In contrast OIH can worsen pain due to increased sensitisation

Central Sensitisation



NMDA-receptor



NMDA-receptor activation = inflammatory & neuropathic pain
Mg2+ block relieved secondary hyperalgesia

Treatment options

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- reduce opioid dose
- swap to a different opioid
- supplement with non-opioid analgesics
- hospital admission to trial alternative analgesics such as methadone and/or ketamine

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Changing opioid and/or route

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- TD patch – poor adhesion, consider appropriate alternative route PO or CSCI – NIKKI & Surefuser guide, CADD (coming soon)
- NIKI T34, T34 & BodyGuard T syringe pumps (caresearch.com.au)
- Surefuser Infusion Device (caresearch.com.au)
- Consider timing of change of new opioid
- Consider dose – palliMEDS app, FPM app
- Apps for health professionals (caringathomeproject.com.au)
- Management plan for pain

Timing of change of opioid: eTG

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Changing to →	Transdermal buprenorphine	Transdermal fentanyl	Twice-daily modified-release opioid	Once-daily modified-release opioid	Continuous subcutaneous opioid infusion
Changing from ↓					
Transdermal buprenorphine	-	Apply fentanyl patch 24 hours after removing buprenorphine patch.	Give first dose 24 hours after removing patch.	Give first dose 24 hours after removing patch.	Start CSCI 12 to 18 hours after removing patch (NB2).
Transdermal fentanyl	(NB3)	-	Give first dose 8 to 12 hours after removing patch.	Give first dose 4 to 8 hours after removing patch.	Start CSCI 6 to 8 hours after removing patch (NB2).
Twice-daily modified-release opioid	(NB3)	Apply patch at the same time as last dose.	Give first dose 12 hours after last dose (NB4).	Give first dose 12 hours after last dose.	If pain is well controlled, start CSCI 2 to 4 hours before next opioid dose would have been given.
Once-daily modified-release opioid	(NB3)	Apply patch 18 hours after last dose.	Give first dose 24 hours after last dose.	Give first dose 24 hours after last dose (NB4).	If pain is uncontrolled, CSCI may need to be started earlier, seek specialist palliative care advice.
Continuous subcutaneous opioid infusion	Stop infusion 12 to 18 hours after applying patch (NB5)	Stop infusion 6 to 8 hours after applying patch.	Stop infusion 2 to 4 hours after first oral dose.	Stop infusion 4 to 6 hours after first oral dose.	-

CSCI = continuous subcutaneous infusion
NB1: When changing opioid formulation or route of administration, calculate the total amount of opioid taken in the previous 24 hours (ie sum of all regular and breakthrough opioid doses {do not include doses taken for incident pain}). Convert this does to the equivalent morphine does, see Table 1.27, then convert to the appropriate dose for the new route of administration.
NB2: For patients in the terminal phase, to avoid potentially inaccurate dose conversion, treatment with transdermal patch can be continued and extra analgesia added by infusion, as required.
NB3: Advice not given because in practice this change is unlikely. Seek specialist palliative care advice.
NB4: Advice for changing between different modified-release opioids and different brands of modified-release opioids.
NB5: Be aware that it may take up to 3 days for buprenorphine to reach steady state.

Key points for opioid use

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- Treat persistent pain promptly
- Use a stable regimen - regular & prn opioid
- Provide written pain management plan
- Confirm with patient/carer
- Reassess regularly – encourage pain diary
- Medicines-diary-WEB.pdf (caringathomeproject.com.au)
- Consider opioid rotation if pain uncontrolled despite dose titration or alternative adjuvants
- Monitor for signs of tolerance or hyperalgesia

Links & Resources

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- PallConsult | Metro South Health
- Home (caringathomeproject.com.au)
- 1-s2.0-S0304395909001250-gr1.jpg (530×707) (els-cdn.com) McGill Pain Questionnaire
- Brief Pain Inventory (Short Form) (nsw.gov.au)

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Case Study

Charleville GP Clinic

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- Male with metastatic SqCC who had multiple sources of pain and was complex to manage
- Chest wall pain (original SCC site)
- Back pain intermittently with radiation down legs (had some known spinal mets plus from pathological fractures)
- He also had poor self-management and tolerance of pain so that we were often chasing the pain (rather than pre-empting the pain) leading to overall an unsatisfactory pain control for quite some time.
- This was compounded by tolerance of opiates and constipation (?cauda equina which he would not go away to get investigated).

Management of complex pain and pain crises: the options

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treating team not comfortable with high level opiates or alternative pain control strategies, requested guidance on pain management options:

- Opiate therapy: usual doses, pitfalls at high doses, when you would change to a different opiate type
- Adjunct therapy
- Methadone as adjuvant or switch
- Non-pharmacological therapy
- Ketamine use
- PCA use for pain crisis

Pain medication

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- Ms Contin 80mg bd
- Sevredol 30mg q2h prn (6-8 doses per day)
- Pregabalin 300mg bd
- Amitriptyline 50mg nocte
- Naproxen 500mg bd (stat ketorolac sc)
- Lidocaine 5% patch 1-2 daily (for back pain)
- Paracetamol 1g qid

- Normal renal function

Admitted to Charleville Hospital

to consider ketamine infusion or methadone rotation

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changed *MS Contin* to CSCI:

- Morphine 70mg
- Midazolam 10mg
- Metoclopramide 30mg
- Glycopyrrolate 800microg

Methadone: indications

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- *first-line strong opioid:* uncommon in Australia
- *second-line strong opioid* (when it is not possible to switch to another easier-to-use opioid) in the following circumstances:
  - neurotoxicity with morphine (e.g. myoclonus, allodynia, hyperalgesia) that does not respond to a reduction in dose
  - end-stage renal failure (ESRF; not first-line choice)
- *adjuvant analgesic:* morphine poorly-responsive pain, e.g. mixed nociceptive–neuropathic pain despite additional use of NSAID + adjuvant analgesics. Probably the commonest indication in palliative care.

Chose adjuvant use:

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Addition of methadone po 5mg mane

Dose titrated up to 10mg bd over 22 days

Day 22 changed to methadone 20mg CSCI

Continued with morphine CSCI

Use of prn analgesia

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- Morphine 10mg subcut q2h prn
  (using 2-3 doses/day for breakthrough pain)
- Fentanyl sublingual 300microg q2h prn
  (using for incident pain – preferred to morphine)
- Trialled clonidine prn
- Cauda equina? To consider radiotherapy