



Complex Malignancy Related Symptoms

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Cancer Pain

What makes for difficult to control Cancer Pain ???



Risk factors for Complex Pain

Pathophysiology- eg .neuropathic pain, prolonged unrelieved pain

PHx Chronic non malignant pain

Previous long term opioid use – prescribed or illicit

Illicit substance abuse (other than opioids)

ETOH dependence/ abuse






Benzodiazepine dependence/ abuse

Depression/Anxiety

Cancer Pain

What works for Cancer Pain (and what has not been shown to)?

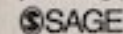
Practice review: Evidence-based and effective management of pain in patients with advanced cancer

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Abstract

Background: Pain of a moderate or severe intensity affects over half of patients with advanced cancer and remains undertreated in at least one-third of these patients.

Aim: The aim of this study was to provide a pragmatic overview of the evidence supporting the use of interventions in pain management in advanced cancer and to identify where encouraging preliminary results are demonstrated but further research is required.

Design: A scoping review approach was used to examine the evidence supporting the use of guideline-recommended interventions in pain management practice.

Data sources: National or international guidelines were selected if they described pain management in adult cancer patients and were written within the last 5 years in English. The Cochrane Database of Systematic Reviews (January 2014 to January 2019) was searched for 'cancer' AND 'pain' in the title, abstract or keywords. A MEDLINE search was also made.

Results: A strong opioid remains the drug of choice for treating moderate or severe pain. Bisphosphonates and radiotherapy are also effective for cancer-related bone pain. Optimal management requires a tailored approach, support for self-management and review of treatment outcomes. There is likely a role for non-pharmacological approaches. Paracetamol should not be used in patients taking a strong opioid to treat pain. Cannabis-based medicines are not recommended. Weak opioids, ketamine and lidocaine are indicated in specific situations only.

Conclusion: Interventions commonly recommended by guidelines are not always supported by a robust evidence base. Research is required to evaluate the efficacy of non-steroidal anti-inflammatory drugs, anti-convulsants, anti-depressants, corticosteroids, some invasive anaesthetic techniques, complementary therapies and transcutaneous electrical nerve stimulation.

Table 3. Summary of recommendations for addressing pain in advanced cancer patients.

	Strength of evidence
Do	
1. Screen for pain	Strong
2. Assess the components of the pain (e.g. neuropathic, nociceptive, inflammatory)	Tentative
3. Agree upon a tailored pain management plan	
(a) Treat moderate or severe pain with a strong opioid, such as morphine	Strong
(b) Consider opioid switching	Moderate
(c) Consider epidural or intrathecal administration of opioids	Moderate
(d) Treat metastatic bone pain with radiotherapy and/or bisphosphonates	Strong
(e) Support patients to use self-management strategies	Strong
(f) Physiotherapy-based interventions	Tentative
(g) Non-pharmacological approaches, for example, music therapy	Tentative
4. Regularly review and evaluate cancer pain treatment outcomes	Moderate
Do not	
1. Routinely use oral paracetamol to treat moderate or severe pain in patients on strong opioids	Moderate
2. Routinely use weak opioids such as codeine	Moderate
3. Routinely use ketamine	Moderate
4. Routinely use intravenous lidocaine	Moderate
5. Use cannabis-based medicines	Strong
Don't know if there is benefit of	
1. Non-steroidal anti-inflammatory drugs	
2. Anti-convulsants, anti-depressants	
3. Corticosteroids	
4. Other anaesthetic interventions, such as coeliac plexus block and spinal cord stimulation	
5. Acupuncture, massage	
6. Transcutaneous electrical nerve stimulation	

The 'DO's' of Cancer Pain Management

- Routinely screen for pain in patients with cancer-
various tools available . There is likely significant
under-reporting of pain
- Routinely assess the characteristics of pain
(neuropathic, nociceptive, inflammatory)

The 'DO's of Cancer Pain Management

- Agree upon a tailored management plan with patient with regular review of effectiveness of interventions
- Use a strong opioid to treat moderate to severe pain
- Consider use of adjuvants (especially in neuropathic pain)
- Consider opioid rotation if rapid escalation of dose with poor control or significant toxicity
- Treat metastatic bone pain with radiotherapy /bisphosphonates

The 'DO's' of Cancer Pain Management

- Encourage Patients to use self-management strategies and don't forget non-pharmacological interventions such as physiotherapy, relaxation, distraction, music therapy, hypnosis (acupuncture)
- Specialist Pain Unit interventions are required in some circumstances

Choosing Your Opioid

Morphine – Avoid if moderate to severe renal impairment. “o” liquid (Ordine), SR tab /capsules MS Contin/ Kapanol . Amps- all on PBS. SR suspension deleted

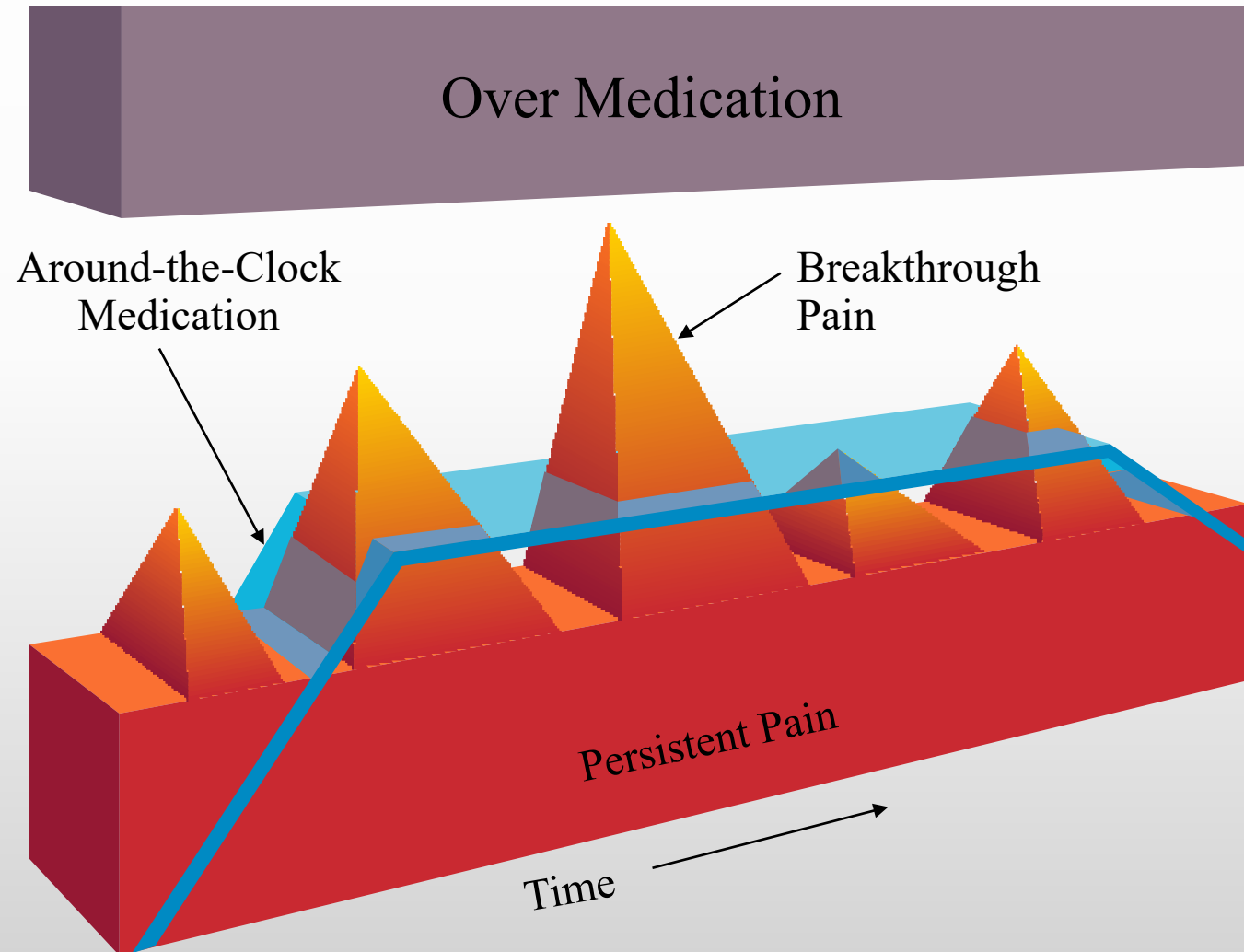
Fentanyl – ok in renal impairment but 12 mcg patch = 43 mg /d ‘o’ morphine so not for opioid naïve patient . Patches clunky to titrate- not ideal in unstable pain. Ampoules not on PBS. S/L preparations are fast onset/quick offset – mimic IV profile- avoid with Hx IVDU. Issue of tachyphylaxis ? Not as effective for bony pain?

Oxycodone – ok in renal impairment . Oral liquid and SR tab on PBS .

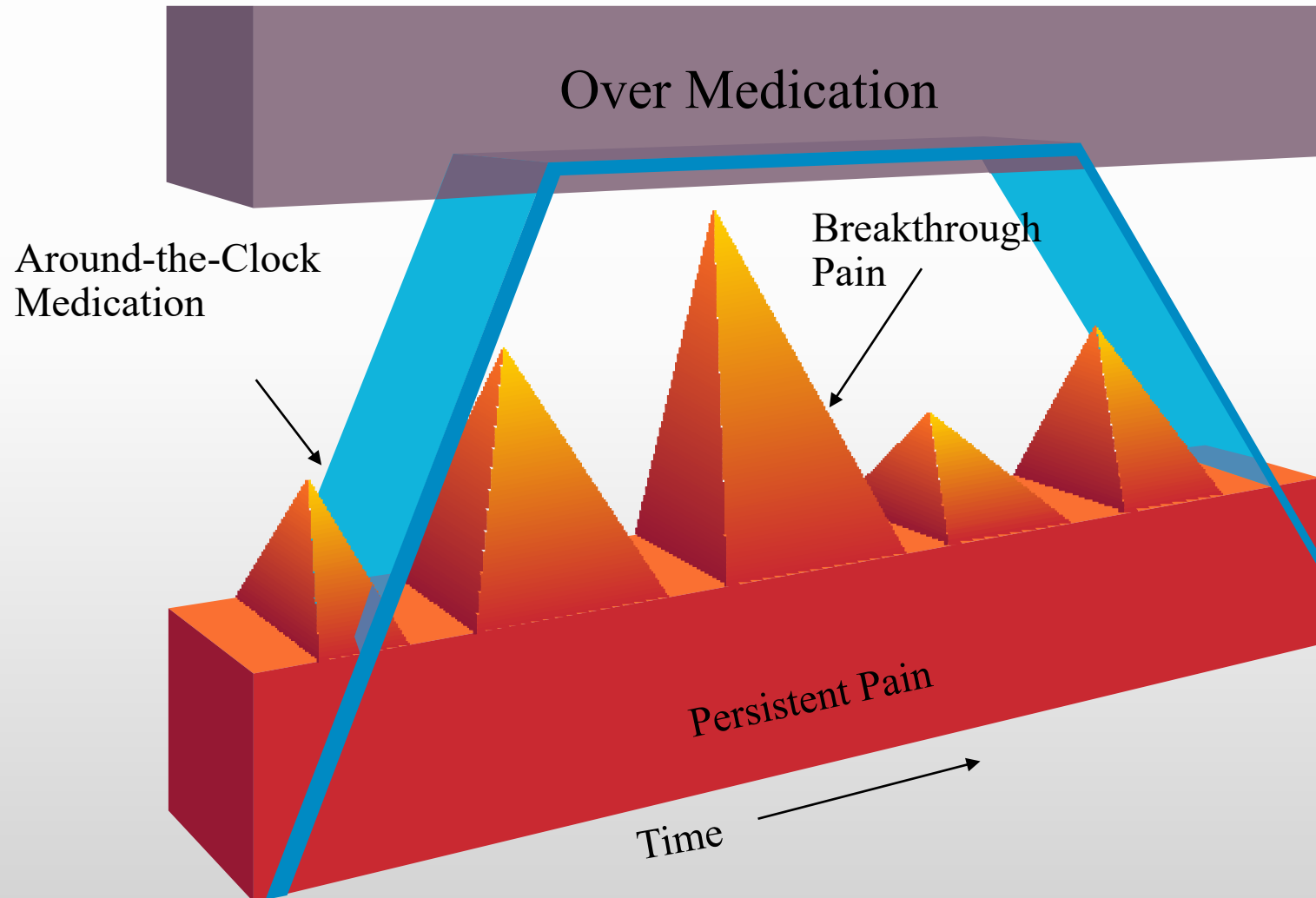
s/c preparation in some IP settings (Oxynorm, endone, Oxycontin , Targin **)

Hydromorphone(x5 potency morphine), – ok in moderate renal impairment (dose reduced and increased interval)- oral IR liquid (Dilaudid)- supply issues , SR once daily tablet(Jurnista), ampoules – all on PBS.

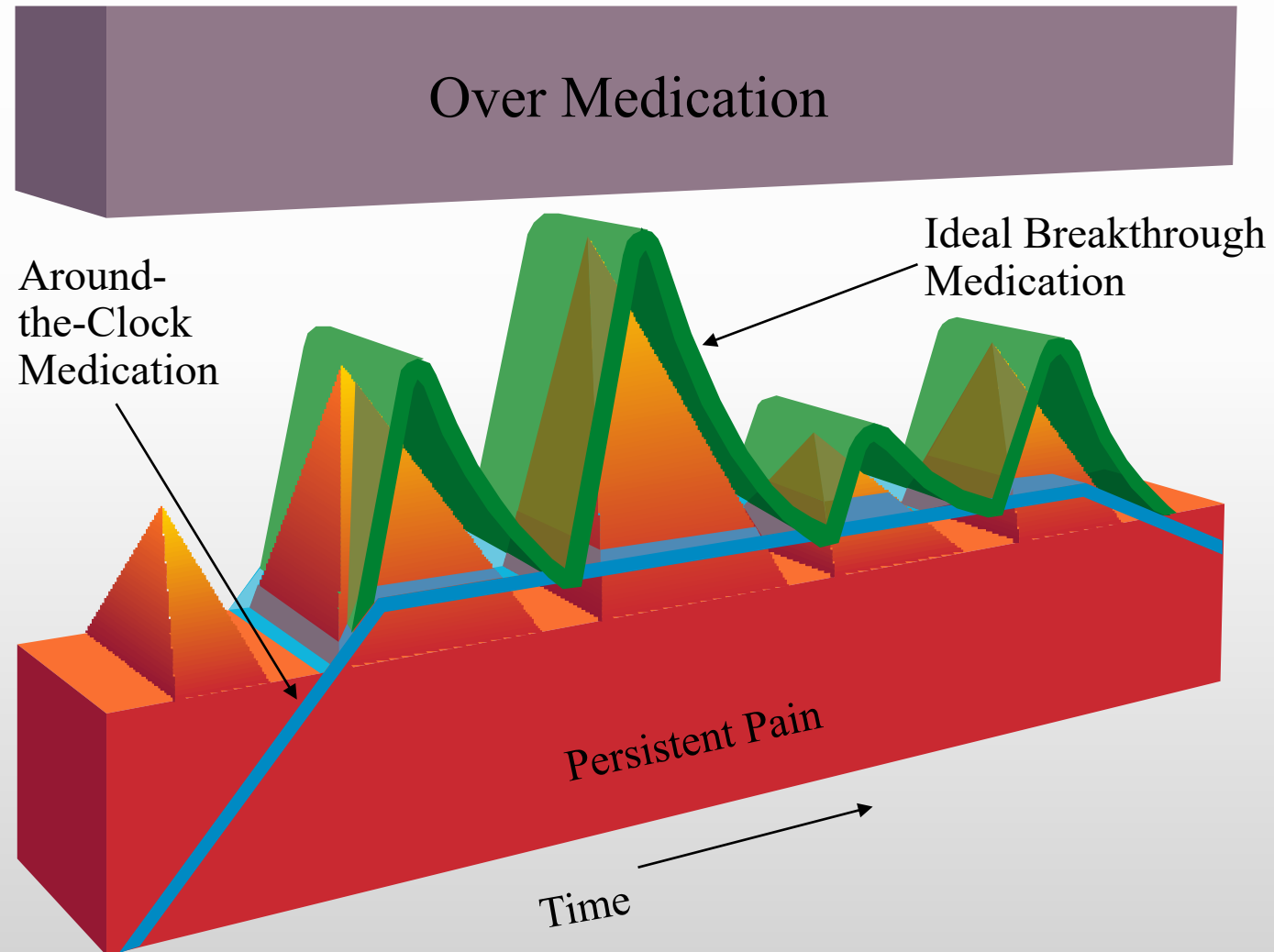
ATC Medications–Shortcomings



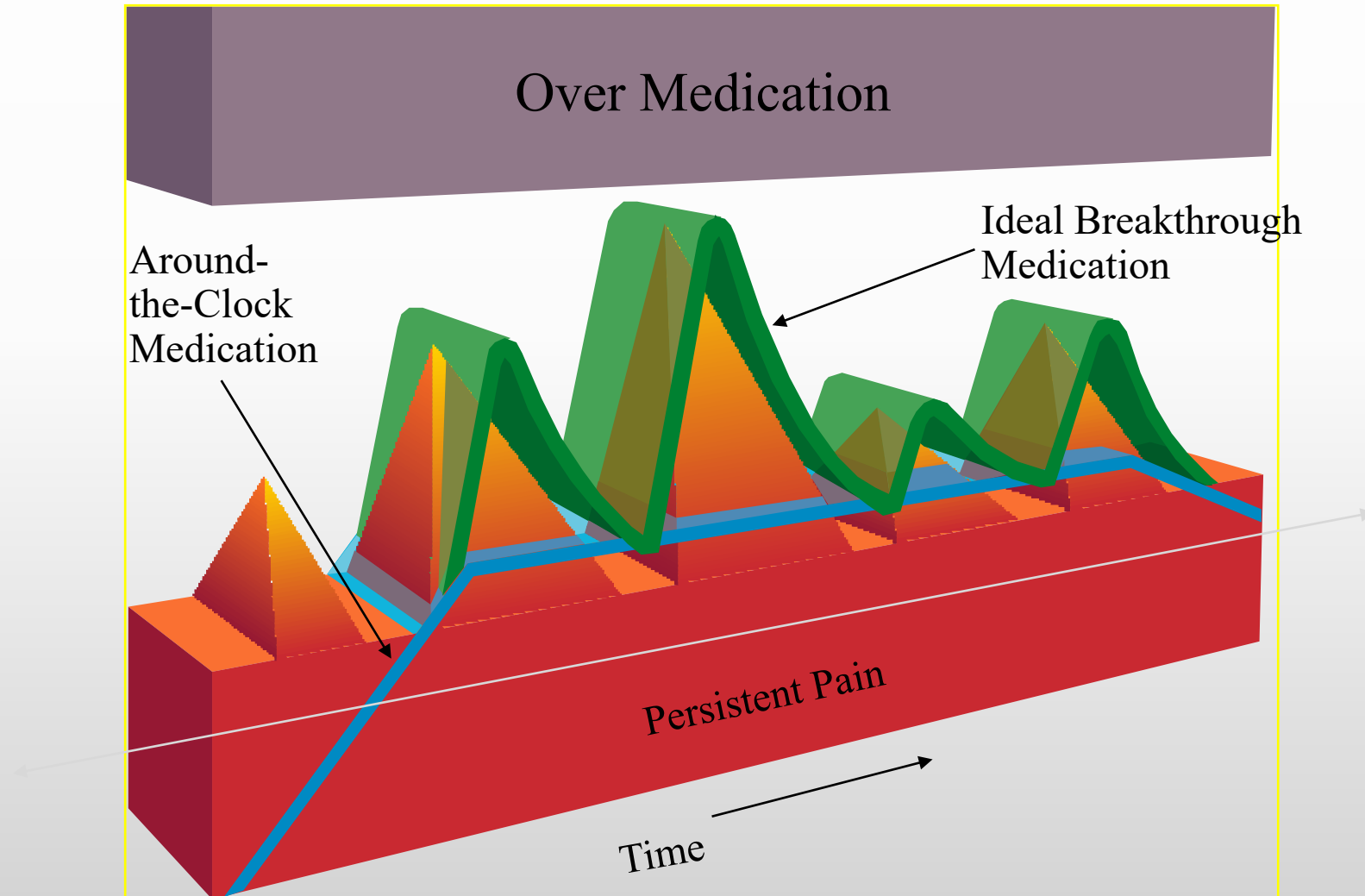
Increasing Dose of ATC Medication— More Side Effects



Treating Cancer Pain—Ideal



IT IS DIFFICULT TO CHARACTERISE BP WHEN BASELINE PAIN IS NOT CONTROLLED



Breakthrough pain prescribing- and the concept of Tmax

- Patients on a regular opioid will require an opioid prescribed as required for breakthrough pain. An appropriate as required dose is typically **1/6th** to **1/10th** of the regular opioid dose.
- The as required dose is usually increased appropriately when the dose of regular opioid is increased.
- For most as required opioids a prescribing interval equivalent to the duration of expected onset of action for the route administered is permitted, particularly if pain is severe to allow for dose titration whilst monitoring for toxicity. **The prescription should also identify that if 3 or more doses have been given within 4 hours with little or no benefit urgent advice or review should be sought.** If more than 6 doses are required in 24 hours advice or review should be requested.

Ref TG

Opioid Toxicity

- Can be precipitated by several factors, including rapid dose escalation, renal impairment, sepsis, electrolyte abnormalities, drug interactions.
- Wide variation in the dose of opioid that can cause symptoms of toxicity.
- Prompt recognition and treatment are needed. Symptoms include:
 - persistent sedation (exclude other causes)
 - vivid dreams/hallucinations; shadows at the edge of visual field
 - delirium
 - muscle twitching/myoclonus/jerking
 - abnormal skin sensitivity to touch (opioid induced hyperalgesia, OIH).
- If the pain is controlled, reduce the opioid dose by a third. Ensure the patient is well hydrated. Seek advice.
- If pain is uncontrolled, consider reducing opioid dose by a third. Consider adjuvant analgesics, alternative opioids or both. Seek advice.
- Naloxone (in small titrated doses) is only needed for life-threatening respiratory depression (Nasal spray on PBS)

Drugs for Neuropathic Pain

GABAPENTIN

PREGABALIN

(Dose reduce in Renal Impairment. ESRF 25 mg pregabalin daily/ alt days)

Amitriptyline

Duloxetine

Therapeutic dose ranges for commonly used adjuvant analgesics

Category based on conventional use	Class	Drugs	Usual starting dose	Usual effective dose range*
Multipurpose analgesics	Glucocorticoids	Dexamethasone	Varies	1 to 2 mg twice daily, orally or IV
		Prednisone	Varies	5 to 10 mg twice daily
	Antidepressants	Desipramine	10 to 25 mg at bedtime	50 to 150 mg at bedtime
		Duloxetine	20 to 30 mg daily	60 to 120 mg daily¶
		Bupropion	75 mg twice daily	300 to 450 mg dailyΔ
		Venlafaxine, sustained release	75 mg once daily	150 to 225 mg daily
		Nortriptyline	10 to 25 mg at bedtime	50 to 150 mg at bedtime
	Alpha-2 adrenergic agonists	Tizanidine	1 to 2 mg at bedtime	2 to 8 mg twice daily
Used for neuropathic pain	Antiseizure medications	Gabapentin	100 to 300 mg twice daily	300 to 1200 mg three times daily
		Pregabalin	50 to 75 mg twice daily◇	150 to 300 mg twice daily
	GABA agonists	Clonazepam	0.5 mg at bedtime	0.5 to 3 mg daily
Used for bone pain	Osteoclast inhibitors	Pamidronate	–	60 to 90 mg monthly, IV
		Zoledronic acid	–	4 mg monthly, IV
		Denosumab	–	120 mg monthly, subcutaneously
Used for bowel obstruction	Anticholinergic drugs	Glycopyrrolate	0.1 mg daily	0.1 to 0.2 mg three times daily, subcutaneously
	Somatostatin analogue	Octreotide	Varies	0.1 to 0.3 mg twice daily, subcutaneously

IV: intravenous; GABA: gamma-aminobutyric acid.

* All doses shown are for adult patients, oral administration, unless otherwise noted.

¶ Randomized trials conducted in patients with diabetic peripheral neuropathy suggest no additional efficacy from 120 mg daily versus 60 mg daily.

Δ Bupropion doses ≥150 mg should be sustained release.

◇ Medically frail patients and those with significantly impaired kidney function are started at 25 mg once daily and titrated more gradually.

Commonly used Adjuvant & other drugs which can prolong QT interval

PAIN :

Amitriptyline

Prochlorperazine

Pregabalin (less of a risk)

Methadone

Other Indications :

Metoclopramide Citalopram

Haloperidol Amiodarone

Clarithromycin Domperidone

- Coeliac plexus blocks useful for upper GI malignancies esp pancreatic
- Hypogastric plexus block can be helpful for pelvic malignancy
- Pudendal or ganglion impar blocks for distal rectal or vaginal cancers
- Epidural infusions can be useful when prognosis very short
- Implantable intrathecal pumps when longer prognosis
- Spinal cord stimulators helpful in chronic pain syndromes
- Botox for pain associated with increase muscle tone and spasticity
- Assess for common nonmalignant MSS pain – for targeted therapies
- Non opioids

Switching between opioids

- Dose reduce on rotation
 - Reduce equianalgesic dose of new opioid by 25-50%
 - Call for advice

What about Targin®?

- Combination prolonged-release oxycodone and naloxone
- Contraindicated in moderate-to-severe liver dysfunction



Targin®

- Normal liver function:
 - Naloxone antagonises the effects of oxycodone in the gastrointestinal tract.
 - Naloxone removed by extensive first pass metabolism by the liver, so does not affect analgesia

What about Targin®?

- abnormal liver function impairs first pass metabolism
- Naloxone bypasses first pass metabolism
- Ends up in systemic circulation
- Poor pain control
- Narcosis on switching from Targin to other opioids



Pain management and SUD

History of substance abuse is predictor of poor pain management

Patient reluctance to take opioids for fear of relapse

Pain difficult to assess

Rapid development of tolerance

Require “higher than normal” doses

Narrowed therapeutic range

Co-existing anxiety and stress

“aberrant” drug seeking behaviour

Concerns about diversion



Epidemiology in palliative care populations

6-15% incidence in general population USA

3% incidence in palliative care population

Kirsh (2006)

27 % incidence of alcoholism in hospice patients

Reisfeld (2009)

46% of new patients referred to palliative care clinic had positive scores on substance abuse assessment tool

Important to screen for HX in all patients when considering initiating ongoing opioid

(Childers, 2014)

Guidelines for management *Kirsh (2006)*

Table 1. Basic principles for prescribing controlled substances to patients with advanced illness and issues of addiction

Choose an opioid based on around-the-clock dosing

Choose long-acting agents when possible

As much as possible, limit or eliminate the use of short-acting or “breakthrough” doses

Use non opioid adjuvants when possible and monitor for compliance with those medications

Use nondrug adjuvants whenever possible (i.e., relaxation techniques, distraction, biofeedback, TNS, communication about thoughts and feelings of pain)

If necessary, limit the amount of medication given at any one time (i.e., write prescriptions for a few days’ worth or a weeks’ worth of medication at a time)

Utilize pill counts and urine toxicology screens as necessary

If compliance is suspect or poor, refer to an addictions specialist

Methadone

Half-life 15-32 hours

Good oral bioavailability

Used in medication assisted treatment of opioid addiction

Impedes withdrawal for significantly longer period than it relieves pain: opioid craving managed with single daily dosing vs 2-3 daily doses required in pain management

PC patient with malignant pain on Methadone maintenance

general approach is to maximize non-opioid options for pain relief. Split methadone dose to BD or TDS and titrate. Other guidelines recommend addition and titration of second opioid eg morphine- *ALL must be done in collaboration with Primary prescriber/ DASSA etc.*

Recommendations for management

Take a complete substance history

Investigate pain appropriately

Treat pain aggressively

Use non-opioid and non-pharmacological measures/ locoregional blocks
/RT

use opioids at appropriate doses – may need larger than usual doses

Consider pharmacology of tolerance – begin slowly and anticipate rapid
dose titration

Manage co-morbid anxiety, stress and psychiatric disorders

Multidisciplinary approach & Liaison with other services e.g. DASSA



Substance use disorder and palliative care – risk mitigation

Scriptcheck

Single prescriber

Limited quantities prescribed

Locked box

Identify family support

Identify those in network who may abuse drugs and pose a threat

Comply with legislation

Constipation

- Intestinal transit
- Poor intake
- Immobility
- Opioids
- 5HT₃ antagonists
- Anticholinergic
- Generalised weakness



Opioid induced constipation

- Stool softening plus stimulant
 - Coloxyl and Senna 1-2 BD
- Osmotic laxatives
 - Movicol 1-2 sachets BD-TDS
 - Lactulose 20ml BD-TDS

Escalation!

- Suppositories/Enemas
 - Bisacodyl suppositories
 - Microlax enemas
- Movicol Jug
 - 6 sachets in 1L water

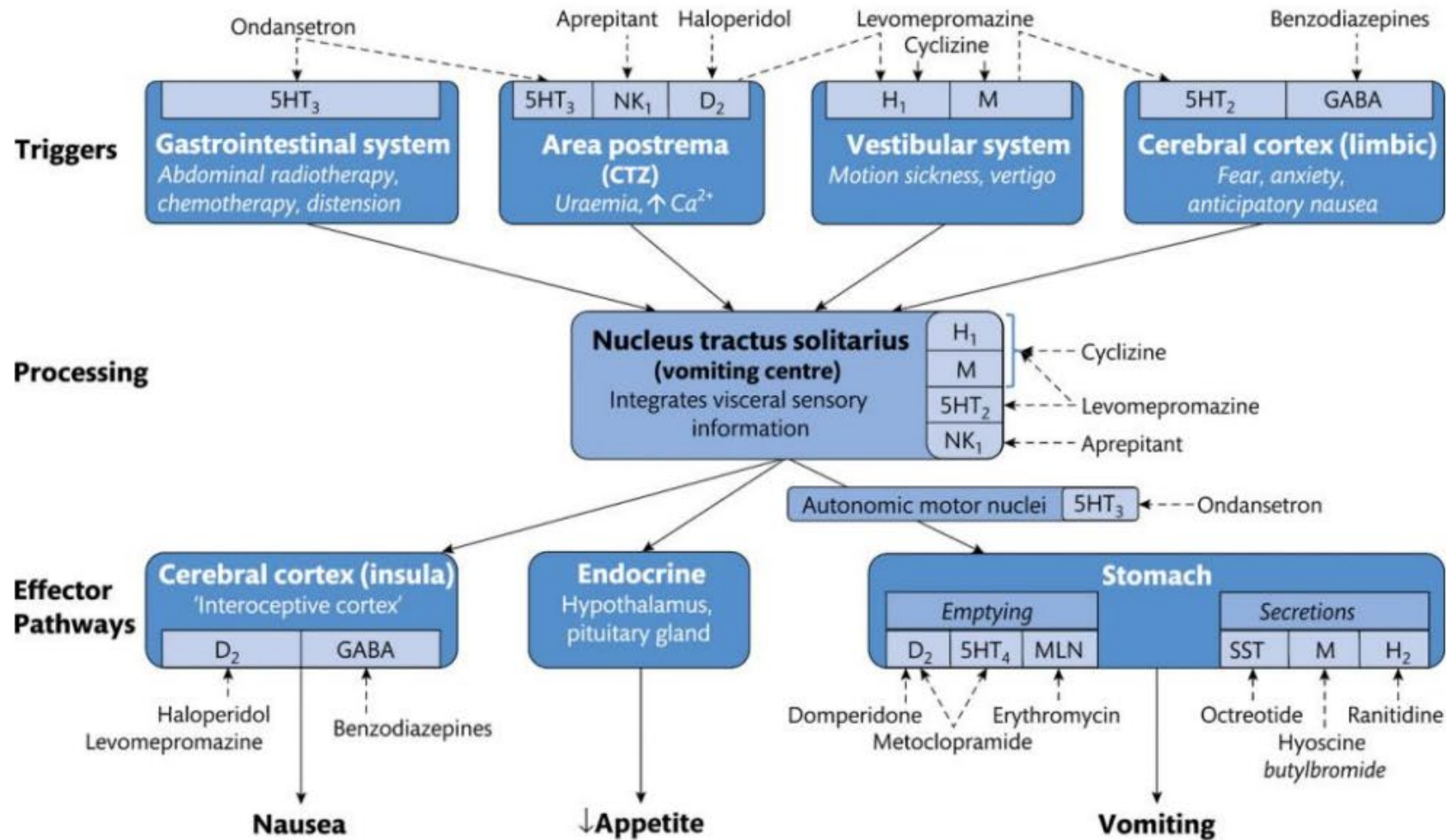




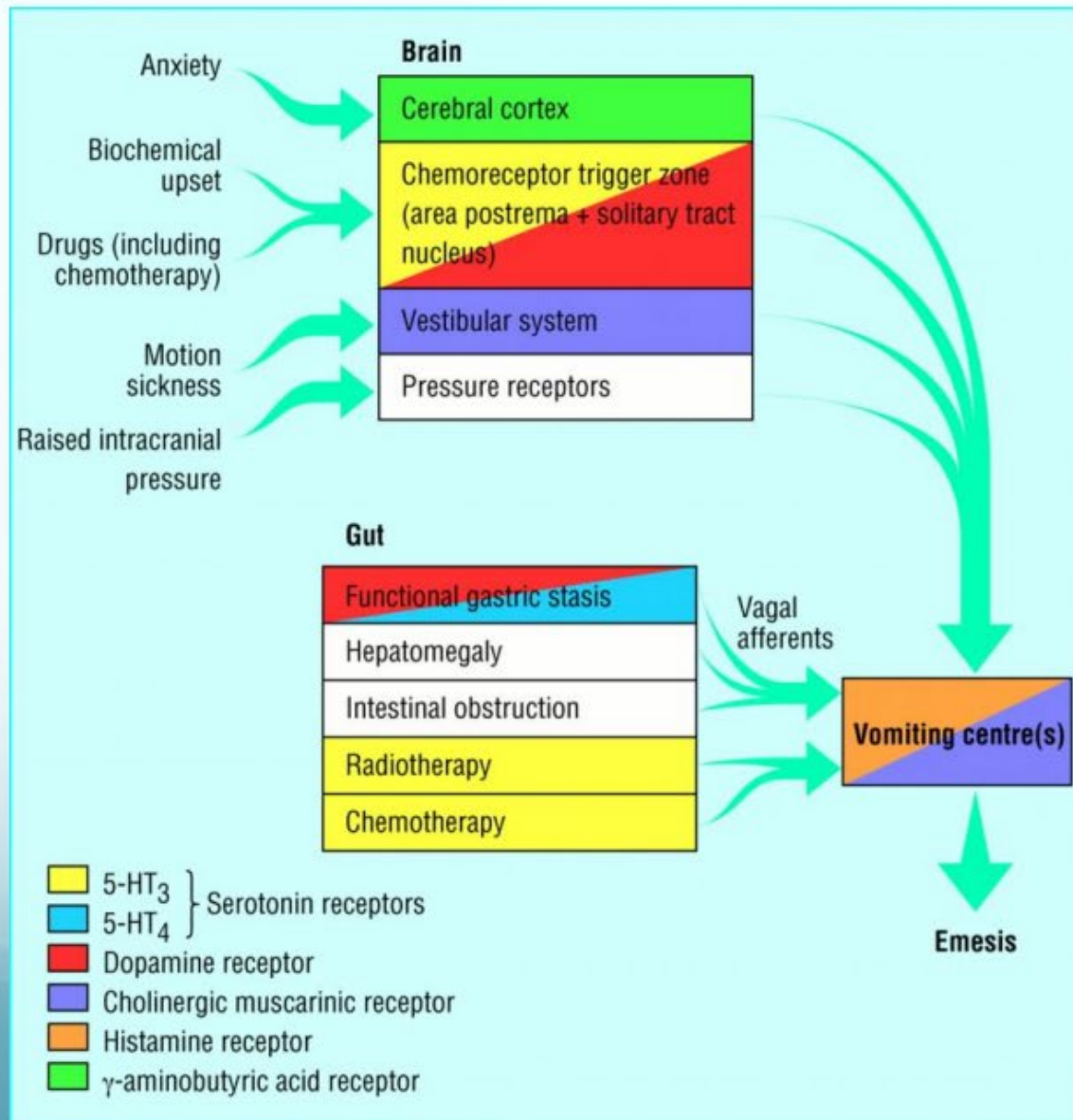
Target anti-emetic
according to most
likely etiology- often
multi-factorial

Nausea

Physiology



Antiemetic Choice



Dominant Cause	Treatment
Drug/toxin	Haloperidol levomepromazine
Chemo/Radiotherapy	Ondansetron/halop Dexamethasone
Vestibular involvement	Prochlorperazine promethazine
Gastric stasis/ileus	Metoclopramide
Mechanical Obstruction	Haloperidol/Cyclizine Dexamethasone
Gastritis	Metoclopramide + F
Cause unknown	Haloperidol
CNS disease/Raised ICP	Dexamethasone Cyclizine
Anxiety	Clonazepam

Medical Management of Malignant Bowel Obstruction / GOO

Avoid pro-kinetics

Dexamethasone 4-8 mg s/c/d

IV PPI vs s/c Ranitidine

Continuous s/c infusion _ Opioid + Hyoscine butylbromide 40-80 mg+ Haloperidol 1.5-5mg/d – substitute Ondansetron in Parkinsonism

?? Octreotide if ongoing large volume vomiting



Medication Management

Paul Tait, Palliative Care Pharmacist

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Deprescribing

- NSW Therapeutic Advisory Group: [Deprescribing Tools](#)
- PHN Tasmania: [Deprescribing Resources](#)
- SA Health: [Medication Cessation Fact Sheet](#)

Dosing

- Australian Medicines Handbook: [AMH](#) [AMH aged care companion](#)
- Caring at Home Project: [palliMEDS](#)
- palliAGED: [For GPs](#) [palliAGEDgp](#)
- SA Health: [Prescribing Guidelines for the Pharmacological Management of Symptoms for Adults in the Last days of Life Clinical Guideline](#)
- Therapeutic Guidelines: [Therapeutic Guidelines: Palliative Care](#)

Drug conversion

Opioid

- Australian and New Zealand College of Anaesthetists (ANZCA): [ANZCA opioid calculator](#)
- Australian Medicines Handbook: [Australian Medicines Handbook \(AMH\)](#)
- eviQ: [Opioid Conversion Calculator](#)
- Therapeutic Guidelines: [Therapeutic Guidelines: Palliative Care](#)

Benzodiazepine

- SA Health: [DASSA Benzodiazepine Equivalence](#)



Education

Caregiver

- Caring at Home Project: [caring@home](#)

GP

- CareSearch: [Palliative Perspectives Blog Series](#)

Funding

- Pharmaceutical Benefits Scheme (PBS): [PBS Prescriber Bag](#) [PBS Palliative Care Items](#)



Human Resources

- Local community pharmacist: [Pharmacist](#)
- SA Health: [Palliative Care Support Line for Clinicians](#)
- RACF Hospice Project Paul.Tait@sa.gov.au, 0481 061 093

Medicinal Cannabis

- Australian government: [Medicinal Cannabis - Consumer Information](#)
- SA Health: [Medicinal Cannabis Patient access pathway for SA](#)



Swallowing Difficulties

- Speak with your local pharmacist
- MIMS: [MIMSonline](https://mims.com.au)



Symptom Assessment

- End of Life Directions for Aged Care (ELDAC): [Common ELDAC Clinical Tools](#)

Conclusion

When caring for people with palliative care needs, there are several medication management challenges that can occur.

These resources may be useful in understanding and responding to these.

Recording - Chronic Pain and Substance Abuse



Palliative Care and Chronic Pain
and Substance Abuse Disorder

Dr Linda Foreman and Dr Emma Burns
Senior Palliative Care Consultants

Recording - Non-Malignant Pain in the Elderly



Session 3
Non-Malignant pain in the elderly
Dr Hima Vanugopal
Pain Physician
Flinders Medical Centre (SALHN)

hima Venugopal

44:21

24 hour Telephone Advice line for GPs-
to Palliative Medicine Consultant:
1300673122