OVERVIEW OF CANCER PAIN MANAGEMENT
A PALLIATIVE CARE PERSPECTIVE

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Continuing the Mission of the Sisters of the Little Company of Mary

CANCER PAIN

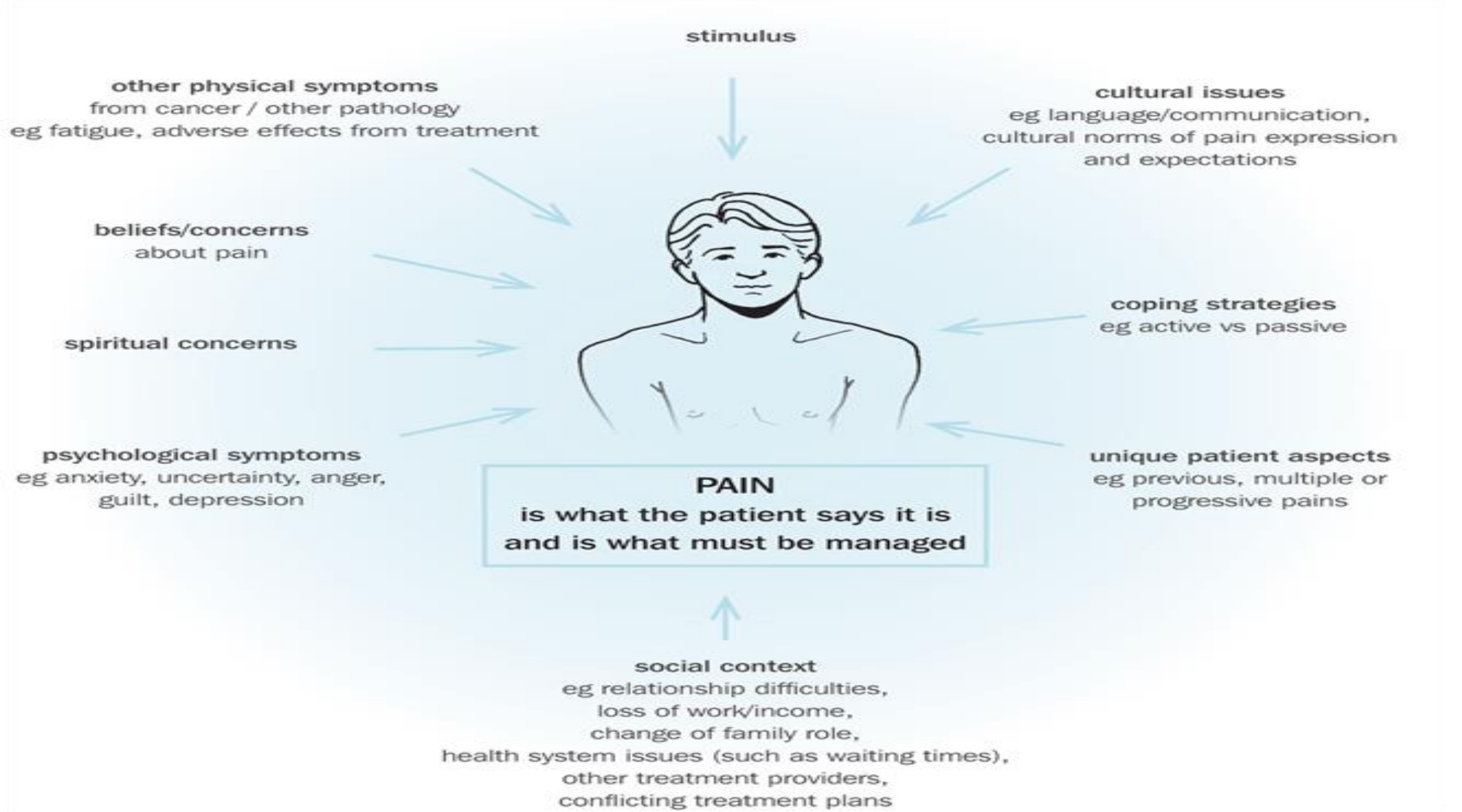
Pain is a frequent complication and it is often multimodal

It can be complex to manage

Why complex?

- Subjective symptom
- Rapid or aggressive disease progression
- Frail baseline (or elderly) population with multiple co-morbidities
- Polypharmacy
- Higher adverse outcomes with pharmacological interventions

Factors influencing perception of pain



CANCER PAIN

Impacts on:

- Activity
- Mood
- Work
- Relationships
- Sleep
- Function

- <u>It affects quality of life</u>

TYPES OF PAIN

Nociceptive – superficial somatic, deep somatic or visceral

Neuropathic

Breakthrough

Incident

Important to identify type(s) of pain as it will influence management strategy

NOCICEPTIVE PAIN

Superficial somatic pain can originate from skin, subcutaneous or oral mucosa involvement, and often described as hot, sharp or stinging

Deep somatic pain can originate from bones, muscles, liver capsule, pleura or peritoneum, and often described as dull, acing or throbbing

Visceral type pain can originate from deep tumour masses or lymph nodes, and often described as dull, deep, gnawing or sensation of pressure

NEUROPATHIC PAIN

Neuropathic pain can originate from tumour compromising on a nerve or a group of nerves

Examples include plexus involvement, spinal cord injury or compromise on peripheral nerves

Often described as altered sensation, tingling, burning, radiating and hyperalgesia

APPROACH TO CANCER PAIN

Wide variability of how cancer pain is treated in practice

Today we will focus on some evidence based and best practice approaches

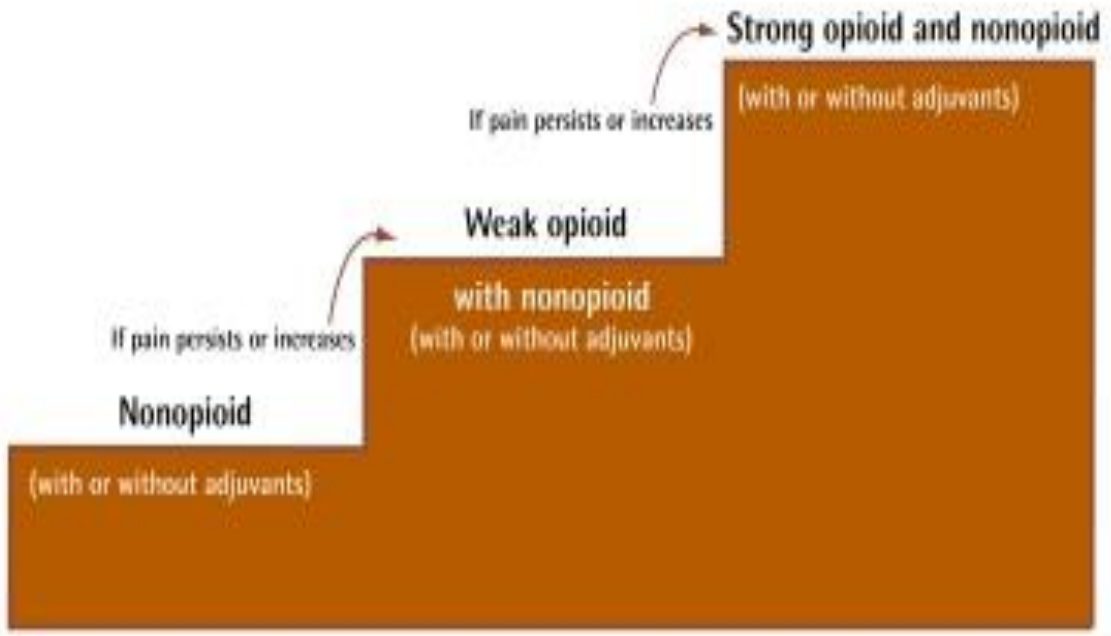
Acknowledge that poorly controlled pain causes significant distress and disability

Back to basics – comprehensive approach begins at diagnosis, should be mechanism based, multimodal and be tailored to the individual patient

Includes pharmacological, allied health input and non pharmacological options

WHO ANALGESIC LADDER 1986

Figure 1. The World Health Organization analgesic ladder for treating cancer pain

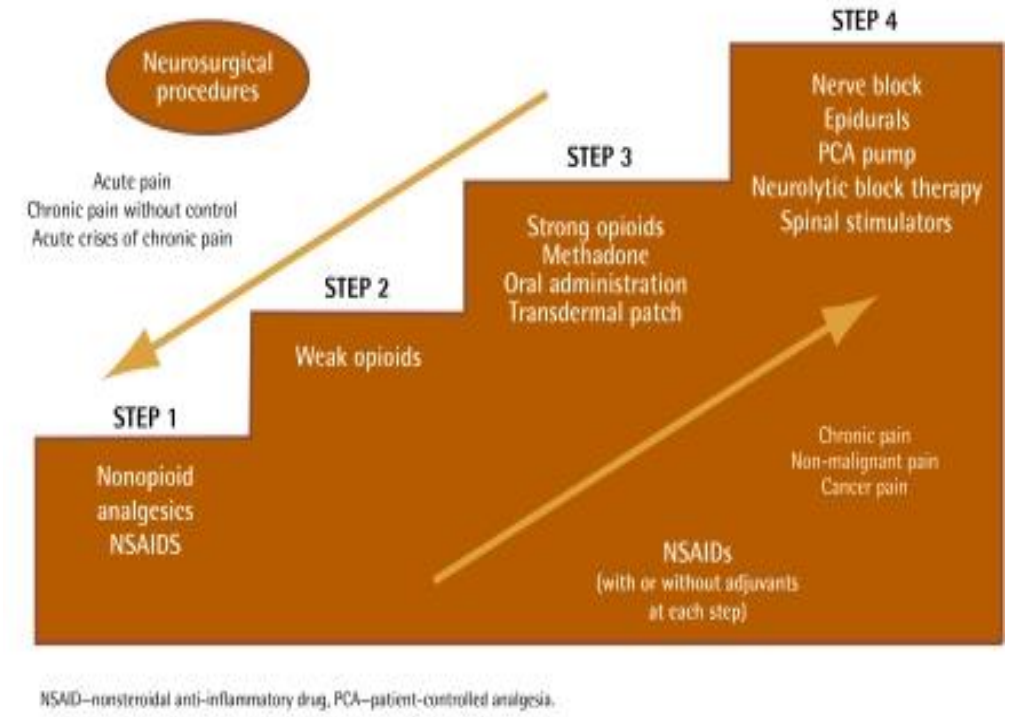


Adapted from the World Health Organization.[1]

PROPOSED ADAPTATION OF ANALGESIC LADDER

Vargas-Schaffer G. Is the WHO analgesic ladder still valid? Twenty-four years of experience. *Can Fam Physician.* 2010;56(6):514-e205.

Figure 2. New adaptation of the analgesic ladder



NSAID—nonsteroidal anti-inflammatory drug, PCA—patient-controlled analgesia.

PARACETAMOL

Analgesic and antipyretic action in the central nervous system

Excellent safety in therapeutic doses justifies recommendation as the 1st line analgesic for mild to moderate pain

Can be used at lower doses as long as liver function is stable

In ESRF max dose is 3g/day – can be dialysed out by haemodialysis but not peritoneal dialysis

PARACETAMOL

Negligible anti-inflammatory effects

Theoretically, used to reduce the overall daily doses of opioids

Note: no strong evidence supporting use of paracetamol in addition to strong opioids in advanced cancer pain

Reference:

Nabal M. The role of paracetamol and nonsteroidal anti-inflammatory drugs in addition to WHO Step III opioids in the control of pain in advanced cancer. A systemic review of the literature. Palliat Med. 2011;26(4) 305-312. Available from pmj.sagepub.com DOI: 10.1177/0269216311428528

NSAIDS

Useful in inflammation, tissue injury, metastatic bone pain, neoplastic fever and postoperative pain

Oral options include ibuprofen, diclofenac, indomethacin, celecoxib and naproxen

There are some topical options

SC options includes ketorolac (non selective COX inhibitor) and parecoxib (selective COX 2 inhibitor)

NSAIDS

Caution with peptic ulcer disease, cardiovascular or cerebrovascular at risk patients, renal impairment and concurrent use of corticosteroids

Note: limited evidence for use in cancer pain

References:

Kenner D, Bhagat S, Fullerton S. Daily Subcutaneous Parecoxib Injection for Cancer Pain: An Open Label Pilot Study. J Palliat Med. 2015; 18(4) 366-372.

Nabal M. The role of paracetamol and nonsteroidal anti-inflammatory drugs in addition to WHO Step III opioids in the control of pain in advanced cancer. A systemic review of the literature. Palliat Med. 2011;26(4) 305-312. Available from pmj.sagepub.com DOI: 10.1177/0269216311428528

WEAK OPIOIDS

Not uncommon for palliative care patients to have been prescribed weak opioids in the early stages of their pain management

Seldom continued as pain increases

In addition, potential drug interactions may become an issue

STRONG OPIOIDS

This is the mainstay of palliative cancer pain management

Many options:

- Morphine (tablet SR, tablet IR, liquid IR, injectable IR)
- Oxycodone (tablet SR, tablet IR, liquid IR, injectable IR)
- Hydromorphone (tablet SR, tablets IR, liquid IR, injectable IR)

STRONG OPIOIDS

- Methadone (tablet, liquid, injectable)
- Buprenorphine patches (topical)
- Fentanyl (patches, buccal lozenges, sublingual, injectable)
- Tapentadol (combination of opioid + NRI) – note: the use of this medication is increasing despite limited evidence in cancer related pain

SELECTING A STRONG OPIOID

Any strong opioid can be used as first line – all have similar efficacy and toxicity profile

Decide on route of administration based on swallowing ability and absorption (CSCI, topical patch, oral – tablet vs liquid)

Take into account metabolism and elimination (liver and renal impairment), as well as onset and duration of action desired

SELECTING A STRONG OPIOID

Think forward – potential dose requirement (eg buprenorphine patch vs tablet hydromorphone SR)

Health economics, cost factors and PBS availability (in Australia)

MONITORING

Once selected:

- Titrate dose to effect
- Observe tolerability
- Observe for opioid toxicity or hyperalgesia

Should rapid dose escalation be required with minimal desired effect and/or the presence of opioid toxicity or hyperalgesia – consider opioid rotation (incorporating a dose reduction), or addition of methadone. Consult your local palliative care team.

SOME SIGNS OF OPIOID TOXICITY

Tremors
Myoclonus
Sedation
Respiratory depression

Sedation score

0 – wide awake
1 – easy to rouse
2 – easy to rouse, but cannot stay awake
3 – difficult to rouse

Aim to keep the sedation score <2; a score of 2 represents early respiratory depression.

OTHER OPIOID RELATED PRACTICES

Availability of ‘as needed’ doses of IR opioids continue to be recommended as best practice for moderate to severe cancer pain

Pre-emptive doses of IR opioids may also be appropriate for predictable episodes of pain (incidental pain)

ADJUVANTS

Gabapentinoids - pregabalin, gabapentin

SNRIs – duloxetine

TCA – amitriptyline (note: side effect burden at higher doses)

References:

McGeeney BE. Adjuvant Agents in Cancer Pain. Clin J Pain. 2008 May;24(4) S14-S20.

Mishra S et al. A comparative efficacy of amitriptyline, gabapentin, and pregabalin in neuropathic cancer pain: a prospective randomized double-blind placebo-controlled study. Am J Hosp Palliat Care. 2012 May;29(3):177-82.

Matsuoka et al. Additive Duloxetine for Cancer-Related Neuropathic Pain Nonresponsive or Intolerant to Opioid-Pregabalin Therapy: A Randomized Controlled Trial. Jpainsymman. 2019 Oct;58(4) 645-653.

ADJUVANTS

Glucocorticoids – dexamethasone

Bisphosphonates for metastatic bone pain

References:

Chow E, et al. Dexamethasone in the prophylaxis of radiation-induced pain flare after palliative radiotherapy for bone metastases: a double-blind, randomised placebo-controlled, phase 3 trial. Lancet Oncol. 2015 Nov;16(15):1463-1472.

Kane CM, Hoskin P, Bennett MI. Cancer induced bone pain. BMJ. 2015 Jan 29;350:h315. doi: 10.1136/bmj.h315. PMID: 25633978.

ADJUVANTS

Benzodiazepines – clonazepam, diazepam, lorazepam

Ketamine infusion – for the NMDA antagonist effect

Ketamine compounded wafers – off label use after other lines have failed

Reference:

Hugel H et al. Clonazepam as an adjuvant in patients with cancer –related neuropathic pain. Jpainsymman. 2003;26(6) 1073-1074.

ADJUVANTS

Lignocaine infusion – could be considered for refractory neuropathic pain where agents with better level of evidence is ineffective (Systemic Review 2018)

Nifedipine - acts as smooth muscle relaxant, may be useful in tenesmus pain

Hyoscine butylbromide - bowel spasmodic pain

ADJUVANTS

Morphine solugel dressings for painful wounds

Ketamine in dressings may help as local anaesthetic effect

Sodium Valproate (limited/poor evidence for cancer related neuropathic pain)

Triptans – theoretical only: restricts cranial blood flow to brain lesions

MEDICINAL CANNABIS

Experimental therapy and lacks evidence for use

High side effect burden and unknown interactions with other drugs or systemic anti-cancer therapy

Should only be used after standard treatments have failed

Expensive (private script)

MEDICINAL CANNABIS

Conditions and approval process varies by state (TGA Online)

Personal experience from limited prescribing:

- No objective improvements in terms of cancer pain
- Patients say things have improved
- Does not appear to have caused much harm
- Most patients sleep better and have less anxiety

Reference:
Guidance for the use of medicinal cannabis in the treatment of palliative care patients in Australia, Version 1, December 2017 published by Australian Government Department of Health – Therapeutic Goods Administration.

Palliative Radiotherapy

Non-invasive

Effective in controlling pain (1/3rd complete response, 1/3rd partial response)

Effect usually at 4-6 weeks after last fraction

Need to monitor progress – may have potential to de-escalate SR opioid doses

Palliative Radiotherapy

Possibility of radiation induced pain flare:

- utilise more frequent ‘as required’ IR opioids
- can consider low dose corticosteroid or NSAIDs

Reference:

Dharmarajan KV et al. Top 10 Tips Palliative Care Clinicians Should Know About Radiation Oncology. J Palliat Med. 2018;21(3) 383-388.

Chow E, et al. Dexamethasone in the prophylaxis of radiation-induced pain flare after palliative radiotherapy for bone metastases: a double-blind, randomised placebo-controlled, phase 3 trial. Lancet Oncol. 2015 Nov;16(15):1463-1472.

PAIN SERVICE

Procedures such as nerve blocks, epidural, temporary intrathecal infusions, percutaneous electrical nerve stimulation (PENS), brain and spinal stimulators

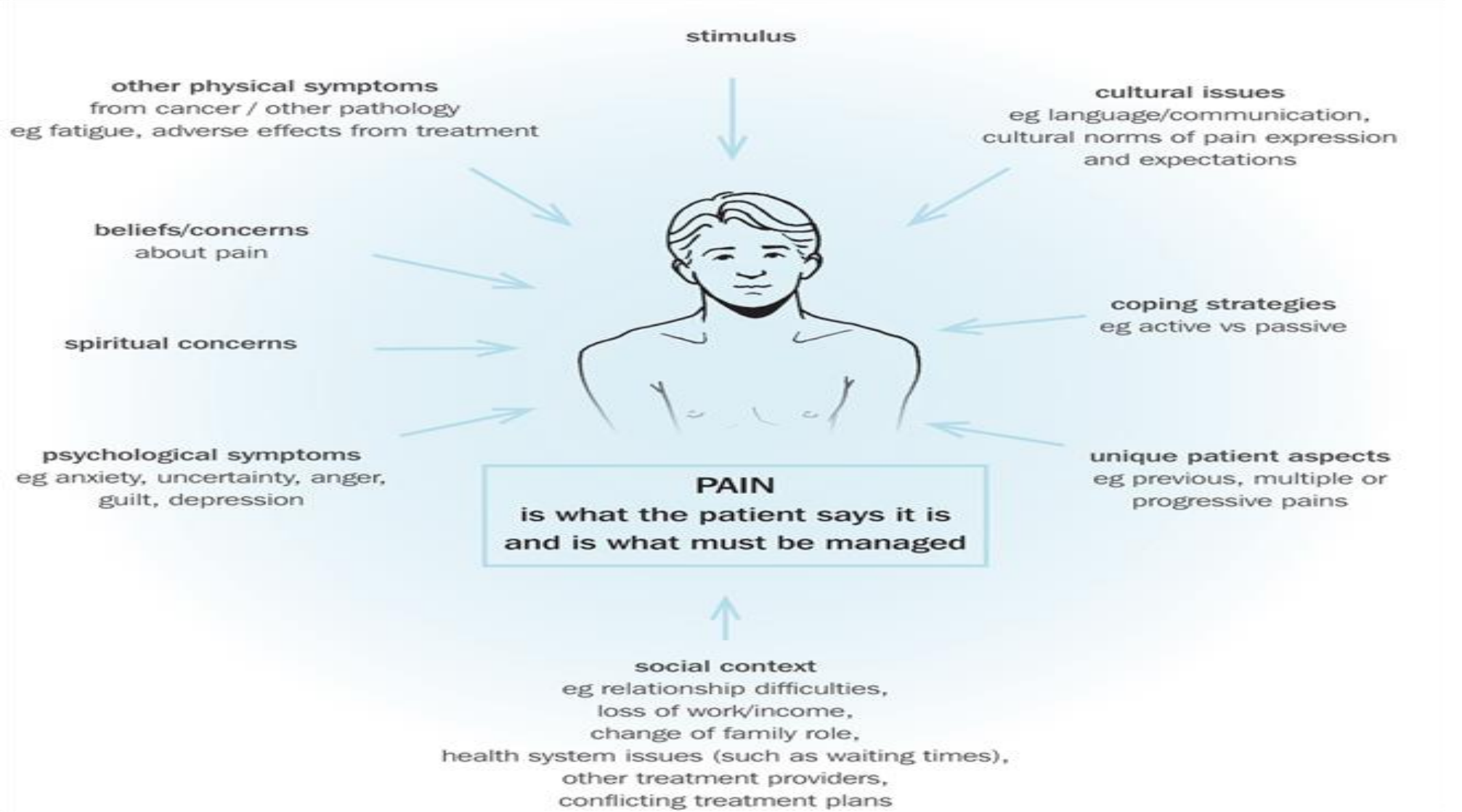
Example: Celiac Plexus Block can dramatically improve visceral epigastric pain in patients with upper gastrointestinal malignancies, leading to a potential decrease in previously stable opioids

Overall aim is to reduce high opioid requirements, opioid sparring effect and / or to avoid significant side effects from systemic opioids

Reference:

Chou CZ et al. Top Ten Tips Palliative Care Clinicians Should Know About Interventional Pain and Procedures. J Palliat Med. 2020;23(10) 1386-1391.

Factors influencing perception of pain



ALLIED HEALTH TEAM

Palliative Care Social worker

Palliative Care Psychologist

Spiritual Support Care Team

Palliative Care Physiotherapist

Occupational Therapist

NON PHARMACOLOGICAL INTERVENTIONS

Should be viewed as an aid in holistic patient care alongside analgesic and procedural interventions

NON PHARMACOLOGICAL INTERVENTIONS

Acupuncture – used despite minimal evidence

Massage therapy – potential positive effect in a systemic review

Music therapy – evidence base is small

Art therapy – used as psychotherapeutic modality, limited studies

Relaxation / Mindfulness therapy – some efficacy, evidence base is small

Touch therapy – review of 24 RCTs inconclusive due to methodology

THINKING OUTSIDE THE BOX

Cancer treatment is evolving, becoming more targeted and increasingly involves the use of immunotherapy combinations

Patients are living (years) longer, hence the need to be aware that approaches to cancer pain need to evolve

THINKING OUTSIDE THE BOX

In the right patient population, do we:

- Go hard, escalating opioid doses (and other pharmacological interventions), risking significant adverse effects and financial burden?

OR

- Plan for early non pharmacological intervention to spare long term opioid burden?

TAKE HOME MESSAGE

Opioids are the mainstay – start low and go slow, but make breakthroughs available and most importantly monitor response

Tailor the analgesic regime to the individual (consider type of pain, metabolism, drug interactions, side effects, absorption, convenience, select patient populations etc)

Use the least amount of drugs required to keep symptoms at bay and escalate appropriately when the clinical situation necessitates

TAKE HOME MESSAGE

Utilise the expertise and experience of your allied health team in the management of cancer pain

Palliative cancer pain management can be complex, so ask for help if it becomes a struggle

‘Palliative care is also about living well’
“As is our understanding of medicine, so is our patient care”

REFERENCES

Care Search Palliative Clinical Evidence On Cancer Related Pain

Reproduced with permission from Pain: assessment in palliative care [published 2016 Jul]. In: eTG complete [digital]. Melbourne: Therapeutic Guidelines Limited; 2019 Dec. <https://www.tg.org.au>

NCBI Can Fam Physicians 2010 Jun 56(6):514-517 Is the WHO Analgesic Ladder Still Valid? 24 Years of Experience

REFERENCES

Nabal M. The role of paracetamol and nonsteroidal anti-inflammatory drugs in addition to WHO Step III opioids in the control of pain in advanced cancer. A systemic review of the literature. Palliat Med. 2011;26(4) 305-312. Available from pmj.sagepub.com DOI: 10.1177/0269216311428528

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McGeeney BE. Adjuvant Agents in Cancer Pain. Clin J Pain. 2008 May;24(4) S14-S20.

REFERENCES

Lee J, Sanderson C, Agar M et al. Lidocaine for Cancer Pain in Adults: A Systemic Review and Meta-Analysis. J Palliat Med. 2018; 1-9. Available from Mary Ann Liebert Inc DOI: 10.1089/jpm.2018.0257

Parlow JL et al. Self-administered nitrous oxide for the management of incident pain in terminally ill patients" a blinded case series. Palliat Med. 2005;19: 3-8.

Guidance for the use of medicinal cannabis in the treatment of palliative care patients in Australia, Version 1, December 2017 published by Australian Government Department of Health – Therapeutic Goods Administration.

REFERENCES

Dharmarajan KV et al. Top 10 Tips Palliative Care Clinicians Should Know About Radiation Oncology. J Palliat Med. 2018;21(3) 383-388.

Berna L et al. Bone pain palliation with strontium-89 in breast cancer patients with bone metastases and refractory bone pain. Eur J Nucl Med. 1995;22(10) 1101-1104.

Sartor O et al. Samarium-153-Lexidronam Complex for Treatment of Painful Bone Metastases in Hormone-Refractory Prostate Cancer. Urology. 2004;63(5) 940-945.

REFERENCES

Hugel H et al. Clonazepam as an adjuvant in patients with cancer –related neuropathic pain. Jpainsymman. 2003;26(6) 1073-1074

Mishra S, Bhatnagar S, Goyal GN, Rana SP, Upadhya SP. A comparative efficacy of amitriptyline, gabapentin, and pregabalin in neuropathic cancer pain: a prospective randomized double-blind placebo-controlled study. Am J Hosp Palliat Care. 2012 May;29(3):177-82. doi: 10.1177/1049909111412539. Epub 2011 Jul 10. PMID: 21745832.

Kane CM, Hoskin P, Bennett MI. Cancer induced bone pain. BMJ. 2015 Jan 29;350:h315. doi: 10.1136/bmj.h315. PMID: 25633978.

REFERENCES

Matsuoka et al. Additive Duloxetine for Cancer-Related Neuropathic Pain Nonresponsive or Intolerant to Opioid-Pregabalin Therapy: A Randomized Controlled Trial. Jpainsymman. 2019 Oct;58(4) 645-653.

Chow E, Meyer RM, Ding K, Nabid A, Chabot P, Wong P, Ahmed S, Kuk J, Dar AR, Mahmud A, Fairchild A, Wilson CF, Wu JSY, Dennis K, Brundage M, DeAngelis C, Wong RKS. Dexamethasone in the prophylaxis of radiation-induced pain flare after palliative radiotherapy for bone metastases: a double-blind, randomised placebo-controlled, phase 3 trial. Lancet Oncol. 2015 Nov;16(15):1463-1472. doi: 10.1016/S1470-2045(15)00199-0. Epub 2015 Oct 18. PMID: 26489389