Appropriate use of opioids to address cancer-related pain

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How should we assess and manage cancer-related pain?

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What are the key chronic pain syndromes that can result from cancer?

Main types of cancer-related chronic pain syndromes

Treatment-related pain[1]

All cancer treatment modalities have the potential to cause pain, including:

- Surgery
- Radiation
- Hormone therapy
- Chemotherapy
- Steroids
- Bisphosphonates
- Stem cell transplantation

Cancer-related pain[2]

- Neuropathic pain (nerve lesion or damage)
- Nociceptive pain (visceral and somatic)
- Mixed pathophysiology, including both a nociceptive and a neuropathic component

1. Glare PA, et al. *J Clin Oncol.* 2014;32:1739–47; 2. Caraceni A, Shkodra M. *Cancers (Basel)*. 2019;11:510.

How do you screen patients for pain resulting from malignancy or cancer treatments?

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Examples of cancer-related pain assessment tools

Numerical rating scale (NRS) for pain intensity[1]

Pain rated on a scale of 0 (no pain) to 10 (worse pain)

Edmonton Classification System for Cancer Pain (ECS-CP)[2]

Incorporates:

Pain mechanism
Incident pain
Psychological distress
Addictive Behaviour
Cognitive function

Cancer Pain Prognostic Scale (CPPS)[3]

Incorporates:

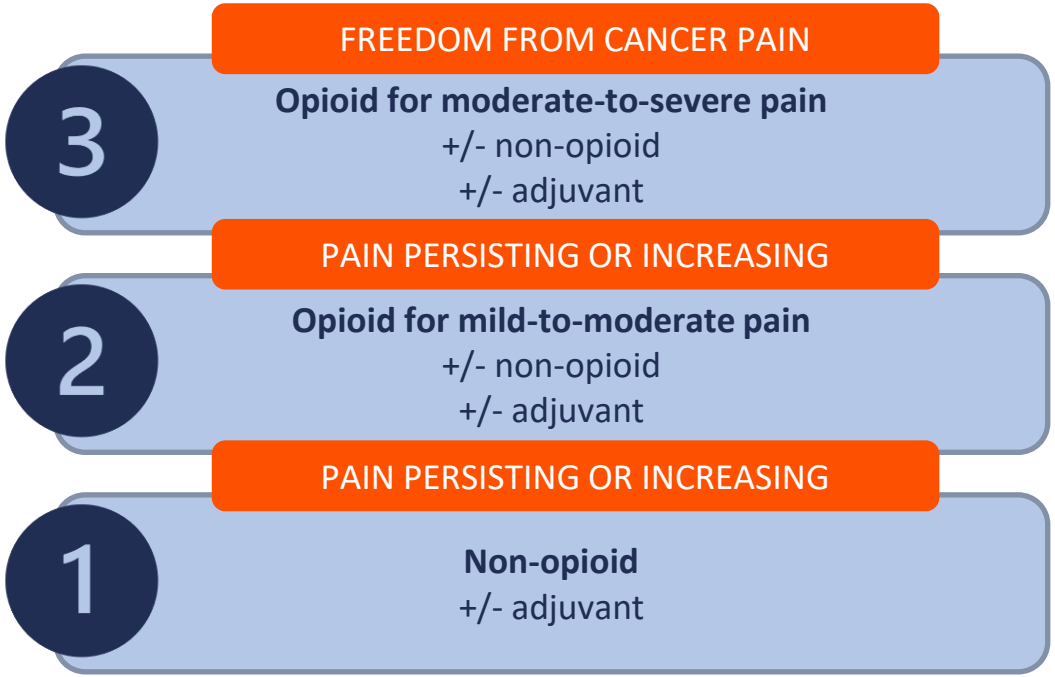
Worst pain severity
Emotional wellbeing
Daily opioid use
Pain characteristics

Initial and ongoing assessment of pain should be an integral part of cancer care,[1] and it should recognize that individuals experience and express pain differently[4]

1. Fallon M, et al. *Ann Oncol.* 2018;29(Suppl. 4):iv166–91; 2. Fainsinger RL, Nekolaichuk CL. *Support Care Cancer.* 2008;16:547–55;
3. Caraceni A, Shkodra M. *Cancers (Basel).* 2019;11:510; 4. WHO guidelines. 2019. Available at: www.who.int/publications/i/item/9789241550390 (accessed 17 April 2022).

How should current guidelines for the management of cancer-related pain be applied in practice?

WHO three-step analgesic ladder



- Provides a general guide to pain management based on pain severity
- It should not replace individualized therapeutic planning based on careful assessment of each patient's pain

WHO, World Health Organization.
WHO guidelines. 2019. Available at: https://www.who.int/publications/i/item/9789241550390 (accessed 25 March 2022).

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What are the principles of opioid titration for the management of cancer-related pain?

Principles of opioid titration

Opioid-naïve patients receiving non-opioid analgesic drugs	Start at 20–30 mg of oral morphine/equivalent dose of other opioids and titrate until pain control is achieved[1,2]
Patients previously receiving opioids for moderate pain	Initial starting dose of 60 mg of oral morphine equivalents[2]
Patients with worsening analgesia during the course of illness	Dose increments of 30–50%[2]

1. NICE. CG140. May 2012. Available at: https://www.nice.org.uk/guidance/cg140 (accessed 17 April 2022); 2. Mercadante S, et al. *Eur J Pain*. 2007;11:823–30.

What are the principles of opioid switching and dose conversion for the treatment of cancer-related pain?

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Opioid switching

Indications for opioid switching[1]

- Poor analgesic efficacy
- Intolerable adverse effects
- Drug-drug interactions
- Different route of administration needed
- Change in clinical status/setting
- Financial/drug availability considerations

Practical considerations[2]

Requires comprehensive assessment, including the underlying clinical situation, comorbidities and concomitant drugs

Exclude any possible pharmacokinetic factor that could limit effectiveness of certain drugs

Refer to evidence-based recommendations for conversion ratios during opioid switching

1. Fine PG, Portenoy RK. *J Pain Symptom Manage*. 2009;38:418–25; 2. Fallon M, et al. *Ann Oncol.* 2018;29(Suppl. 4):iv166–91.

How can we implement proactive treatments to mitigate common opioid-induced side effects for patients with cancer-related pain?

Prof. Marie Fallon

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What adverse effects may be associated with the use of opioids for cancer-related pain?

Possible adverse effects associated with opioids[1,2]

- Dry mouth
- Bowel dysfunction (most commonly constipation)
- CNS toxicity

- Nausea and vomiting
- Pruritus
- Respiratory depression (rare[3])

Every assessment should include a review of side effects

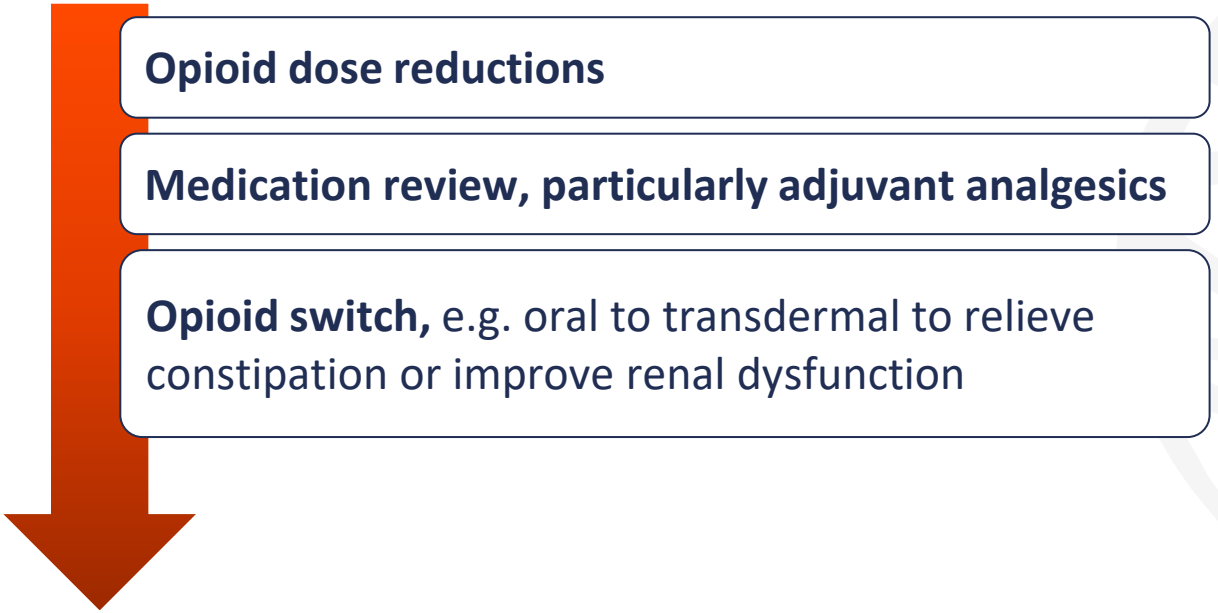
CNS, central nervous system.

1. Fallon M, et al. *Ann Oncol.* 2018;29(Suppl. 4):iv166–91; 2. Sarrió RG, et al. *BMC Palliat Care*. 2021;20:1; 3. Bruera E, Paice JA. *Am Soc Clin Oncol Educ Book.* 2015;e593–9.

What is best practice for assessing a patient's risk of opioid-induced side effects?

When should opioid adjustments occur in patients with cancer in order to manage side effects?

Opioid adjustment for side-effect management



Swegle JM, Logemann C. *Am Fam Physician*. 2006;74:1347-54.

What therapeutic options can be considered to manage common and persistent opioid-induced side effects?

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Management strategies for opioid-induced constipation

Prophylaxis and management

- Combination stimulant and softener laxative[1]
- Dose titrated for each individual patient[2]

Persistent opioid-induced constipation[3]

- Peripherally acting μ-receptor antagonists (PAMORAs)

1. Fallon M, et al. *Ann Oncol.* 2018;29(Suppl. 4):iv166–91; 2. Walters JB, Montagnini M. *J Opioid Manag.* 2010;6:435–44; 3. Crockett SD, et al. *Gastroenterology*. 2019;156:218–26.

Which newer analgesic approaches may have fewer side effects than opioids?

Newer analgesic approaches to manage cancer-related pain

Adjuvant analgesics for pain with a neuropathic component[1]

- **Anticonvulsants**
  (e.g. gabapentin, pregabalin)

  May cause cognitive side effects[2]
- **Antidepressants**
  (e.g. duloxetine)

  Be aware of anticholinergic effects[1] and possible drug–drug interactions[3]

Combination therapies

- Oxycodone + naloxone helps with reducing opioid-induced constipation[4]

1. WHO guidelines. 2019. Available at: www.who.int/publications/i/item/9789241550390 (accessed 25 March 2022); 2. Park SP, Kwon SH. *J Clin Neurol.* 2008;4:99–106;
3. Bleakley S. *Prog Neurol Psychiatry.* 2016;20;21–7; 4. Fallon M, et al. *Ann Oncol.* 2018;29(Suppl. 4):iv166–91 .

How can we prevent the misuse of opioids in patients with cancer-related pain?

Prof. Frank Elsner

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What are the key points for clinicians regarding the safe use of opioids?

Key considerations for clinicians on the safe use of opioids

Establish correct indication for use of opioid therapy[1]

Assess risks and benefits of opioid treatment[2]

Discuss the risks and benefits of opioid treatment with patients and caregivers[2]

1. WHO guidelines. 2019. Available at: www.who.int/publications/i/item/9789241550390 (accessed 22 April 2022);
2. Pergolizzi JV Jr, et al. *Front Pain Res (Lausanne)*, 2021;2:691720.

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What universal precautions can be taken to minimize the possible adverse consequences of opioid use?

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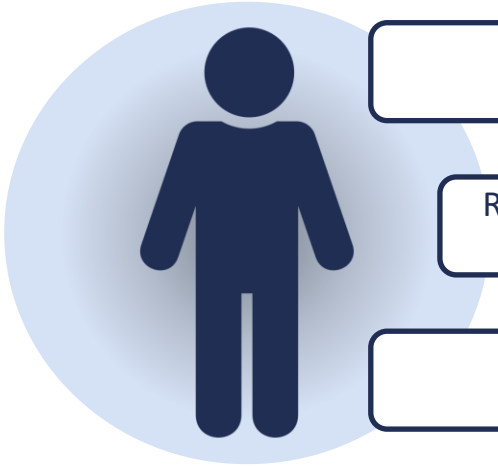
Universal precautions to minimize the possible adverse consequences of opioid use



- Comprehensive assessment of the patient, including the patient's risk factors for misuse[1,2]
- Regular monitoring of all patients (more frequent follow-up for patients at high risk of non-medical opioid use)[3]
- Use of prescription drug monitoring programmes (where available)[2]

1. WHO guidelines. 2019. Available at: www.who.int/publications/i/item/9789241550390 (accessed 22 April 2022); 2. Paice JA. *Oncologist.* 2019;24:1294–8;
3. Dalal S, Bruera E. *Am Soc Clin Oncol Educ Book*. 2019;39:24–35.

How should patients at risk of opioid use disorder be identified?

Addictive behaviours and opioid use in chronic pain

- Population-based study using data from the Danish Health Survey and the Danish health and socioeconomic registers
- 13,281 individuals analysed to assess association between chronic non-cancer pain (≥6 months), opioid use, health behaviour and body mass index

Six potential addictive behaviours identified:

Daily smoking	Obesity
High alcohol intake	Long-term use of benzodiazepines
Illicit drug use in the past year	Long-term use of benzodiazepine-related drugs

Højsted J, et al. *Pain*. 2013;154:2677–83.

What is best practice regarding monitoring patients for potential opioid dose reduction or discontinuation?

Assessment of a patient with pain

Initial and ongoing assessment of pain should be an integral part of cancer care

Adequate assessment of the patient with pain should include, but not be limited to:

- Regular assessment of the use of analgesics and their effectiveness and tolerability
- Spending time with the patient and their family to understand their needs

Fallon M, et al. *Ann Oncol.* 2018;29(Suppl. 4):iv166–91.