Short title: Acute pain

1. Purpose

1.1 To advance the standards of care related to management of acute pain.

1.2 To develop a framework for provision of high-quality management of acute pain.

2. Scope

This document is intended to apply to specialists of the college (ANZCA and FPM), trainees, and SIMGs managing acute pain. It may be used as a reference by acute pain services as well as all doctors prescribing analgesia for acute pain within hospital settings.

It is intended to apply to the management of all forms of acute pain including non-surgical acute pain.

3. Background

Effective and safe management of acute pain requires individualised treatment regimens which are informed by patients and their carers. It is also dependent on developing and maintaining close liaisons with all involved staff and ensuring that they are trained and skilled.

Formal protocols and guidelines relevant to the circumstances of each institution are of assistance, and formal quality assurance programs to regularly evaluate effectiveness of acute pain management are to be encouraged.

In individualising patient care it is recognised that some patients, or groups of patients, may have special needs that require particular attention. Such demographic groups include: older, paediatric, pregnant or postpartum patients, Aboriginal people, Māori, Pacific and/or Torres Strait Islander people, and non-English speaking people. Patients with the following conditions may need individualised treatment: sleep-disordered breathing, renal or hepatic impairment, opioid tolerance or substance use disorder, cognitive behavioural and/or sensory impairments.

Clinicians may decide to diverge from the recommendations in this position statement to accommodate exceptional situations. However, any decisions to alter management should be guided by evidence, or where this may be deficient, then be guided by consensus. Evidence-based information related to management of acute pain in these patient groups and situations is included in the latest edition of *Acute Pain Management: Scientific Evidence*, Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. https://www.anzca.edu.au/safety-advocacy/advocacy/college-publications.

4. Framework for acute pain management

4.1 Education

4.1.1 Education regarding acute pain management should be part of the medical undergraduate core curriculum. Knowledge should be supplemented at the postgraduate level for all

ANZCA and FPM trainees and other medical staff. Anaesthetists have a key role to play in these education programs.

4.1.2   Nursing staff have a key role in the management of acute pain. Their ongoing education and accreditation are essential. Pharmacists and other associated allied health practitioners, including physiotherapists, also have keys roles and ongoing education is likewise important.

4.1.3   Patient attitudes and beliefs have been shown to modify pain perceptions, analgesic requirements, and response to analgesic therapies, all of which can impact on patient outcomes. Patient and carer education can, therefore, positively influence the outcome of acute pain management. Such education should include setting the expectation of using pain relief to enable good functional recovery as opposed to absence of pain.

4.1.4   The nature of our interactions (verbal and non-verbal language) can influence a patient's experience of pain. For example, language that promotes an appropriate sense of safety and recovery can positively influence a patient's pain experience, while language that promotes a sense of danger or damage can negatively influence that experience.

4.2   Assessment of analgesic efficacy and adverse effects

Regular assessments of adequacy of analgesia, monitoring, and documentation of any adverse effects or complications should be undertaken to safely and effectively individualise treatment regimens.

- Efficacy of analgesia should include assessment of patient function, such as Functional activity scores (FAS), as well as an assessment of pain intensity. Adjustments to analgesic regimens should not be made based on pain scores (assessed both at rest and with activity) alone.

- Unexpected levels of pain despite treatment, or pain that suddenly increases, may signal the development of a new medical or surgical issue, or be the result of pain that is not opioid-responsive. In the latter scenario, alternate analgesia and/or optimisation of nonpharmacological interventions should be considered.

- Anxiety, mood, fear and past experiences contribute to the pain experience. These factors should be acknowledged and inform non-pharmacological interventions. Additional opioids to treat these pain drivers should be avoided.

- All patients given opioids are at risk of developing opioid-induced ventilatory impairment (OIVI) and should be monitored as summarised in the accompanying Analgesic Stewardship appendix. At a minimum, this includes regular assessment of a patient's level of sedation. Factors that increase the risk of OIVI need to be recognised and measures taken to mitigate risk where possible. Instructions for the management of OIVI should be available.

- In addition to OIVI, other risks should be considered when discharging patients who have been prescribed opioids for short-term ongoing management of acute pain. These include persistent post-discharge opioid use, opioid misuse and diversion. Factors that increase these risks need to be recognised and measures taken to mitigate them, where possible.

4.3   Pharmacological therapies

4.3.1   The selection of medications, techniques, and routes for their administration should be evidence-based. Medications that may be used include opioids, paracetamol, non-steroidal

anti-inflammatory drugs, local anaesthetics and ketamine, as well as adjuvant agents such as antidepressants, gabapentinoids and alpha-2 agonists. Other medications may be required for the treatment of analgesia-related side effects.

4.3.2   For many analgesic medications, optimisation of therapeutic effect and minimisation of side effects, should be achieved through careful titration and individualisation of dose regimens.

4.3.3   Multimodal analgesia aims to reduce opioid-related adverse effects by reducing opioid requirements and to improve pain relief. Medications employed as part of multimodal analgesia regimens should not increase the risk of adverse effects or interactions with other analgesic medications. The use of non-opioid analgesic and adjuvant medications and 'opioid-free analgesic techniques' will not avoid the need for opioids in all patients, either in hospital or after discharge, and may not lead to a reduction in patient harm.

4.3.4   Modified-release opioids are associated with increased risk of opioid-related harm and complications compared with immediate-release opioids. Routine prescription of modified-release opioids for the management of acute pain is best avoided unless there is a demonstrated need, close monitoring is available, and a cessation plan is in place.

4.3.5   Analgesic stewardship programs are recommended. More detail about analgesic stewardship is included in the accompanying appendix.

4.3.6   Implementation of established guidelines and order sets (including in electronic medical record systems) are recommended. Such guidelines and order sets will often combine the medication prescription, monitoring requirements and instructions for nurses to follow should a patient develop a medication-related adverse effect. These are especially important for some specialised analgesia delivery techniques which may involve use of complex equipment and require greater medical and nursing knowledge and expertise.

Anaesthetists initiating these forms of analgesia may delegate the management of the techniques to another trained and skilled medical practitioner, or registered nurse, or to a pain service, provided that these personnel have received appropriate training and provided the anaesthetist is satisfied with the competence of the person(s) to whom management has been delegated. Such techniques include but are not limited to:

- Patient-controlled analgesia (PCA).

- Opioid infusions in selected patients where PCA is not appropriate.

- Epidural and intrathecal analgesia.

- Other major regional analgesic procedures.

- Continuous infusions of local anaesthetics and ketamine, and some other analgesic medications (for example Entonox ® and methoxyflurane).

Guidelines and order sets are also recommended for immediate-release opioids ordered on as 'as needed' basis.

4.4   Delivery of safe and effective acute pain management

4.4.1   Hospitals and health facilities should ensure there is the necessary governance, healthcare worker training, staffing, and appropriate clinical documentation wherever opioid medication

and specialised analgesia delivery techniques are used.

4.4.2   Consideration should be given to a multidisciplinary approach in the management of acute pain, such as with an acute pain service, especially where patients have complex medical or psychological comorbidities.

4.4.3   Hospitals that are accredited for training by the college (ANZCA and FPM) are required to have an Acute Pain Service.

4.4.4   Acute pain services should include:

- Staffing by qualified and trained clinicians, particularly anaesthetists and nurses with special expertise in acute pain management.

- Close liaison with pharmacists and other associated allied health practitioners

- Close collaboration with surgical, medical and other specialties involved in any patient's overall care.

- Development of specific policies and protocols for recognition of adverse reactions, as well as their treatment based on ANZCA/FPM guidelines.

- Regular (in most cases at least daily) reviews of all patients under their care and liaison with relevant medical nursing and pharmacy staff.

- Provision of consultation services for patients with acute or acute-on-chronic pain.

- Availability of after-hours acute pain review services with consultant/ specialist level input available.

- Involvement in management plans for analgesia after discharge, where applicable.

4.5   Quality assurance

4.5.1   Regular audits should be instituted to assess effectiveness of treatments and incidence of side effects and adverse events. This should include records of patient demographics, analgesic medications and techniques used, assessment of analgesic efficacy, and any adverse effects that occur.

4.5.2   The outcomes of quality assurance activities, and any adverse events from pain management should be overseen by an appropriately qualified specialist and/or appropriate hospital committee and reviewed, with the mechanism to deal with adverse events clearly identified.

4.5.3   Research, education and participation in trials is encouraged where possible.

Further reading

Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. Acute Pain Management: Scientific Evidence. 5th ed. Melbourne: Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. 2020. Available from: https://www.anzca.edu.au/safety-advocacy/advocacy/college-publications Accessed 30 April 2024.

Also see references listed at the end of the accompanying appendix.

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PS41(G) Appendix 1: Analgesic Stewardship

1. Aims

This document is intended to add to the information in PS41 and summarise current thinking related to analgesic stewardship. It may be used as a reference by acute pain services as well as all doctors prescribing analgesia for acute pain within hospital settings. The principles apply to the management of all forms of acute pain, including from non-surgical aetiologies.

2. Analgesic stewardship

Opioid stewardship has been defined as 'co-ordinated interventions designed to improve, monitor, and evaluate the use of opioids in order to support and protect human health' [1].

Analgesic stewardship includes consideration of opioids as well as other analgesic and adjuvant medications and strives for a balance between analgesia that is sufficient to facilitate patient recovery and restoration of function, and minimisation of analgesia-related harms to the patient and others.

It is recognised that non-pharmacological measures are also important in the management of acute pain. However, discussion about these options is outside the scope of this document. More information is available from *Acute Pain Management: Scientific Evidence* [2].

Safe and effective management of acute pain requires selection of an optimal treatment regimen which is then modified as needed for the individual patient (for example for age or comorbidities) based on assessments of adequacy of analgesia and early recognition and treatment of any adverse effects. Strategies that aim to reduce the risk of both short- and long-term harms from these medications are important.

Education of all staff involved is needed, but as one component only of all interventions aimed at improving opioid-related safety. In the hierarchy of risk-reduction strategies, education alone is one of the weakest and needs to be supplemented by more effective, but harder to implement, high-level system-focused strategies such as forcing functions, barriers, fail-safes and automation, as well as medium-level strategies including standardisation and protocols, warnings, alerts, reminders and checklists [3]. Therefore, while individual practitioners play an important role, effective opioid stewardship needs to involve the healthcare system as a whole at both local and national levels [4].

For more detail on strategies that may be used to promote opioid stewardship within hospitals and the community see Levy et al [4].

Analgesic stewardship includes consideration of the following stages of patient care: [4]

- Prior to admission
- During admission
- At the time of and after discharge

3. Adequacy of analgesia

Pain is a very individual and subjective experience. Patient experiences of pain can be affected by a number of psychological, cultural, social and environmental factors. Predictors of poorer postoperative pain control (higher pain scores and sometimes higher opioid requirements) in the early postoperative period include younger age, female sex, smoking, preoperative anxiety and depression, pain catastrophising, preoperative pain and preoperative opioid use [2,4,5,6,7].

In the mid-1990s, the 'Pain as the 5th Vital Sign' campaign emphasised the need for pain to be measured and recorded on a regular basis, as was done for a patient's vital signs [2]. Commonly used pain measurement tools included unidimensional pain rating scales which were used in many institutions to

determine effectiveness of analgesia and guide opioid titration. The aim was that unrelieved pain or high pain scores would raise a 'red flag' and prompt an escalation of care, including unrestricted titration of opioids doses.

However, 'chasing' unidimensional pain scores with opioids and raising expectations (in patients, carers and staff) that arbitrarily defined 'acceptable' levels of pain, or even elimination of pain, can always be achieved, can lead to prescription of an excessive amount of opioid and increase the risks of opioid-induced ventilatory impairment (OIVI), persistent postdischarge opioid use (PPOU), and opioid misuse and diversion after discharge [4].

Unidimensional pain scores are only one aspect of assessing a patient's pain and their response to treatment. Analgesic medications, especially opioids, should never be titrated according to a patient's pain scores alone. More important is an assessment of how acute pain is affecting the patient's physical function [2,4,8,9]. Functional limitation because of pain means that re-evaluation of therapy is required.

One example of a score used to assess patient function is the Functional Activity Scale – Table 1 [2,10].

Table 1: Functional Activity Scale*	
A	No limitation: the patient is able to undertake the activity** without limitation due to pain
B	Mild limitation: the patient is able to undertake the activity but experiences moderate to severe pain
C	Severe limitation: the patient is unable to complete the activity due to pain
* Adapted from Scott DA & McDonald WM (2008) Assessment, Measurement and History. In: Textbook of *Clinical Pain Management: Acute Pain* 2e. Macintyre PE, Rowbotham D and Walker S (eds). London, Hodder Arnold.	
** Activity assessed is relevant activity related to the cause of the 'new' acute pain – for example ability to take deep breaths and cough after abdominal surgery or injury, or to flex knee after knee surgery	

To assist with the patient's ability to achieve functional goals, timing of the administration of an 'as needed' immediate-release opioid dose so that near maximum effect of that dose occurs at the time of the designated activity (for example physiotherapy, walking), may be beneficial – 'activity-based analgesia'.

Unexpected levels of pain despite treatment, or pain that suddenly increases, may signal the development of a new medical or surgical issue, unrecognised opioid tolerance, or be the result of pain that is not opioid-responsive, and alternative analgesia should be considered.

This does not mean that pain scores should be abandoned, but that **pain score trajectories** (an assessment of pain resolution over time) rather than the actual pain score at any one time, may give a better indication of patient progress. A trajectory that is not decreasing (pain is either not resolving or is increasing) could indicate a new or different cause for the pain, for example, development of a postoperative or post-trauma complication, or the presence of non-opioid-responsive pain such neuropathic pain, or psychological distress [4]. Patient factors such as lower age, female sex, anxiety and a higher number of pain behaviours rather than type of surgery, are related to the likelihood of patients being in the high pain trajectories; those in the high pain trajectories also have higher postoperative opioid requirements [11].

Trajectories that do not decrease over the first few days after surgery have been shown to be a predictor of chronic postsurgical pain [12,13] and could increase the risk of PPOU [14].

Opioid dose trajectories are also good indicators of patient progress. The risk of PPOU is higher in patients whose opioid dose trajectories in the immediate postoperative period are not decreasing, and the

key predictor of this was inpatient opioid requirement; patient psychological comorbidities were not included in the data collected [15].

The presence or absence of side effects from analgesic drugs will also affect what alterations are made to treatment regimens.

4. Potential significant adverse effects: opioids

Potential significant harms related to the use of opioids in acute pain management include those that may occur when the patient is in hospital and those that may arise after discharge. The most important are [4]:

- Opioid-induced ventilatory impairment (OIVI)
- Persistent postdischarge opioid use (PPOU)
- Opioid misuse and diversion

4.1 Opioid-induced ventilatory impairment

4.1.1 Background

OIVI continues to cause patient harm in the acute pain setting, including hypoxic brain damage and death: the peak risk is within 24 hours of surgery and the majority of events are preventable [2].

'OIVI can usually be avoided by careful titration of the dose against effect and careful observation and monitoring' [2]. This applies to all opioids administered for the management of acute pain, regardless of route or technique of administration.

OIVI may result from three main and interlinked mechanisms: [16].

- Depression of respiratory drive with a reduction in alveolar ventilation (respiratory rate and/or depth of breathing) – 'central respiratory depression'.
- Depression of consciousness (and therefore arousal) – 'sedation'.
- Depression of supraglottic airway muscle tone – 'upper airway obstruction'.

The true incidence of OIVI in the acute pain setting is unclear as publications commonly rely on surrogate measures such as respiratory rate and oxygen saturation. Some studies report rates of naloxone administration, but the need for this will depend on the definition used for OIVI in the first place. Respiratory rate and oxygen saturation are *not* direct measures of adequacy of ventilation and there is no good evidence of a reliable correlation with the partial pressure of carbon dioxide in arterial blood ($PaCO_2$) – a direct measure of OIVI [16].

In some cases where patients have come to harm from OIVI, snoring (due to partial upper airway obstruction) was reported prior to the event. Patients who are snoring should not be assumed to be sleeping normally and their level of sedation should still be assessed on a regular basis.

4.1.2 Risk factors for OIVI

Factors that have been reported to be associated with an increased risk of OIVI can be divided into those that are patient-related (largely non-modifiable) and those that are modifiable.

4.1.2.1 Patient-related risk factors

The most frequently reported patient-related risk factors for OIVI are older age, female gender, sleep disordered breathing (SDB), obesity, renal impairment,

pulmonary disease (in particular chronic obstructive pulmonary disease), cardiac disease, diabetes, hypertension, neurologic disease, two or more comorbidities, genetic variations in opioid metabolism, and opioid-tolerance [2,4,17]. The higher risk of OIVI in opioid-tolerant patients is likely related to differential tolerance to opioids [18]. These risks factors are reported associations only and cannot show causation.

It is interesting to note that a significant proportion of patients who were shown not to have SDB before surgery developed moderate to severe SDB in the postoperative period when given opioid analgesia [19].

Importantly, many patients who come to harm have no identifiable comorbidities that would predict an increased risk of OIVI [2,16]. As it is not possible to reliably identify all patients who might come to harm from OIVI, *all patients must be assumed to be at risk*. Any attempts to rely on identification of an 'at-risk' patient will inevitably result in OIVI being missed in other patients.

Therefore, the focus on prevention of harm from OIVI must be on better assessment and monitoring of *all* patients, especially in the high-risk period, and appropriate and rapid responses and interventions when OIVI is detected.

While patient-related factors are largely non-modifiable, it is known that the dose of opioid required to manage acute pain decrease as patient age increases [2,20]. Age-based doses are recommended for the initial opioid prescription in opioid-naïve patients [21,22].

4.1.2.2 Modifiable risk factors

Modifiable risk factors include: [2,4].

- Coadministration of sedatives (for example benzodiazepines, gabapentinoids, antipsychotics and sedating antihistamines).

- Simultaneous use of multiple opioid agents (this does not include verified doses of opioids taken for management of chronic pain, where the patient has developed a tolerance to and physical dependence on these medications).

- Continuous infusions of opioids.

- Initiation of long-acting opioid preparations (including methadone).

- Multiple prescribers.

- Inadequate nursing assessments or responses.

- Reliance on unidimensional pain scores alone to assess adequacy of analgesia, and chasing' pain scores – that is, titrating opioids to pain scores alone to reduce them to a predetermined acceptable number.

- Using opioids for pain that is not opioid-responsive.

The risk of OIVI is less with the atypical opioids tramadol, tapentadol and buprenorphine (patches only) [2].

4.1.3 Mitigation of harm

As reliable identification of patients who are at increased risk of OIVI is not possible, reducing the risk of OIVI relies on:

- Avoidance of modifiable risk factors where possible (see above).

- Appropriate monitoring with appropriate early escalation of care and appropriate

responses when OIVI is first noted.

4.1.3.1 Avoidance of modifiable risk factors

See list of modifiable risk factors above.

4.1.3.2 Monitoring and appropriate responses

In acute care hospitals, 'track and trigger' early warning systems are commonly used. Their aim is to improve detection and subsequent management of a deteriorating patient, with timely and appropriate escalation of care. In many published reports of patient deaths resulting from OIVI, undue reliance has been placed on respiratory rate as a unidimensional measure of OIVI, either without formal assessment of patient sedation, or without recognising the significance of excessive sedation [2,16].

Monitoring

Respiratory rate and oxygen saturation levels are *not* direct measures of adequacy of ventilation [16].

Respiratory rates of less than 8 or 10 breaths per minute in adults are commonly considered to indicate OIVI, although this is known to be a very unreliable measure. There is no good evidence of a reliable correlation with $PaCO_{2;.}$ – a direct measure of OIVI – and respiratory rate, and some patients can maintain a rate that is within acceptable limits even in the presence of severe OIVI [2,16].

Similarly, low oxygen saturation levels are often used to determine the presence of OIVI, but these too may remain within an acceptable range even in the presence of increased $PaCO_2$ levels [2,16].

The use of low-flow supplemental oxygen to help prevent hypoxaemia (which may be indicated in some patients depending on factors such as type of surgery or injury and patient comorbidities) makes the measurement of oxygen saturation levels an even less reliable way to detect OIVI; there may also be reasons other than opioids for hypoxaemia [2,16]. In addition, hypoxemia is commonly worse while the patient is asleep and may be missed if pulse oximetry is used only intermittently, because the patient is roused during measurement [23].

There appears to be a better correlation between a patient's $PaCO_2$ and level of sedation, and regular assessment of a patient's level of sedation is therefore important in all patients receiving any opioid for management of their acute pain [2,8,16,21,24]. In any patient who is given an opioid, oversedation should be considered to indicate OIVI until proven otherwise, regardless of a patient's respiratory rate or oxygen saturation levels.

Sedation scores should be assessed repeatedly at intervals that are appropriate to the route of opioid administration – for example for immediate-release opioids administered as PRN doses either orally or by subcutaneous injection, it would be appropriate to do this at the time of administration and then at the time the peak effect of the dose is expected to be seen – about 1 hour [22].

Supplemental oxygen will not mask increasing sedation resulting from opioid-induced CNS depression and, if OIVI is severe, any additional CNS depression due to high carbon dioxide levels [16].

The AVPU score (A = alert; V = responds to voice; P = responds to pain, and U = unresponsive), based on the more complex 15-point Glasgow Coma Score, is not

able to distinguish between a patient who is 'easy to rouse' and can stay awake and one who is 'easy to rouse but unable to remain awake', and is therefore not sensitive enough to enable to early detection of OIVI.

One example of a commonly used sedation scoring system is in Table 2 [22].

Table 2: Sedation Scores
0 =   wide awake
1 =   easy to rouse
2 =   easy to rouse but unable to remain awake
3 =   difficult to rouse
1.   A score of 2 is taken to indicate early OIVI and therefore the aim should be to titrate an opioid so that a patient's sedation score is always less than 2.
2.   Note that a sedation score (for example 'sedation score less than 2') may be specified in the 'Max Dose/24 hrs' in the PRN section of the ACSQHC *National Inpatient Medication Chart* (NIMC) to indicate the maximum amount to be administered in 24 hrs when prescribing opioids in [25].

It is recommended that a sedation scoring system containing 'S' (meaning the patient is normally asleep but is easy to rouse) is not used as the patient may not be woken properly to have their level of sedation assessed more accurately; they may wake easily, but then either stay awake or have difficulty staying awake, and so the opportunity to recognise and trigger an appropriate intervention before significant patient harm from OIVI has occurred may be lost [16].

It has been suggested that all postoperative patients prescribed opioids should be monitored using continuous pulse oximetry, with the addition of continuous measurement of carbon dioxide levels (end-tidal or transcutaneous measures) in those patients receiving supplemental oxygen [26]. Continuous measurement of a patient's carbon dioxide concentrations is more likely to identify OIVI than continuous pulse oximetry [27].

It is acknowledged that provision of continuous electronic monitoring, especially of carbon dioxide levels, for every patient given an opioid for management of acute pain in every Australian and New Zealand hospital may be desirable but is not possible at present. The ability to measure carbon dioxide is generally limited to settings such as postoperative recovery, intensive care, and some high dependency units.

Even if it was possible to use electronic monitoring equipment for every patient given an opioid for acute pain in every hospital, some patients will be taking opioids at home, maybe for the first time, so some simple clinical observation is still required.

Opioid prescriptions for acute pain management must be linked to monitoring in a robust way, regardless of the route of administration of the opioid. This is important regardless of whether paper or electronic medical record (EMR) systems are used.

Appropriate responses

Guidelines for prescription and monitoring need to be accompanied by standardised orders that outline the appropriate responses to each level of sedation [22].

Acute Pain Services usually use 'standard orders' when prescribing analgesic techniques such as PCA, epidural or regional analgesia, to maximise the effectiveness of pain relief as well as patient safety. These orders aim to guide selection of medicines and their concentrations, dose and dose intervals, monitoring requirements, choice of equipment, and responses to inadequate or excessive analgesic doses, including excessive sedation and other complications [2,22]. The development of 'standard orders' for the safe prescription and administration of all opioids used in acute pain management, including PRN opioids, is likely to add an extra safety dimension by emphasising monitoring of sedation (at times appropriate to the route of administration) and promoting quicker recognition and treatment of opioid-related side effects. Examples of suggested inclusions in 'standard orders', which can be incorporated into EMR systems, are available [22].

4.2 Persistent postdischarge opioid use

4.2.1 Background

Most of the information regarding PPOU comes from the postoperative setting where it has been defined as continuation of opioids prescribed for postoperative pain for longer than 90 days after surgery [4]. Many studies have shown some patients are still taking an opioid for some years after discharge [2]. It has been estimated that PPOU may occur in up to a quarter of patients [4,28].

4.2.2 Risk factors for PPOU

It has been suggested that the risk of PPOU may be higher after certain types of surgical procedures, but this finding is not consistent across studies and patients after all types of surgery must be assumed to be at risk [4].

Factors that have been reported to be associated with an increased risk of PPOU can be divided into those that are patient-related and those that are modifiable.

Similar factors have also been associated with an increased risk of PPOU after trauma.

4.2.2.1 Patient-related risk factors

Patient-related factors that have been associated with a higher risk of PPOU after surgery include psychological comorbidities (anxiety, depression, catastrophic thinking, and post-traumatic stress disorder), preoperative use of benzodiazepines or antidepressants, preoperative tobacco use, alcohol and substance use disorders, pre-existing chronic pain, preadmission opioid use, lower age, female sex, and socioeconomic factors such as lower household income [2,4,22,29].

Some of these factors could be considered modifiable. While this would require appropriate resources and an adequate length of time before surgery, potential benefits have been reported.

For example, one of the strongest predictors of PPOU is pre-existing chronic opioid use, so weaning opioid doses prior to surgery could be of benefit [4]. Possible further advantages in preadmission opioid weaning are discussed in 6.2.

Patients undergoing more minor surgery appear to be just as vulnerable to PPOU as those undergoing major surgery [4].

4.2.2.2 Modifiable risk factors

Modifiable risk factors for PPOU often relate to prescribing practices and

include:[2,4].

- Long-term preadmission opioid use.

- Psychological comorbidities.

- Unrealistic expectations.

- Reliance on unidimensional pain scores alone to assess adequacy of analgesia and 'chasing' pain scores: titrating opioids to pain scores alone to reduce them to a predetermined acceptable number.

- Abnormal pain and opioid dose trajectories: trajectories that are not decreasing.

- Over-reliance on opioid analgesia – in hospital and on discharge.

- Use of modified-release opioid preparations.

- Large numbers of tablets on discharge.

- Repeat opioid prescriptions.

- Lack of deprescribing advice.

4.2.3 Mitigation of harm

Reducing the risk of PPOU will rely on:

- Avoidance of modifiable risk factors where possible (see above).

- Appropriate education of patient and their carers.

- Appropriate communication with the patient's general practitioner.

- Referral to other specialist services if needed (for example chronic pain management, psychology, or addiction medicine).

Use of peripheral regional analgesia has not been shown to reduce the incidence of PPOU [14,30,31].

4.3 Opioid misuse and diversion

The number of opioid tablets prescribed at discharge for ongoing management of acute pain often far exceeds the number used by the patient, and many patients neither store their opioid securely nor dispose of any opioid in excess of requirements [2,4,32]. This reservoir of unused opioid presents significant risks (including unintentional overdose and diversion) to the patient, their family or pets, and to others in the community [2,4,32]. Longer discharge prescriptions of opioids and repeat prescriptions increase both the risk of PPOU and the development of opioid misuse disorders [33].

More than 50% of adults who misuse opioids obtain them from family or friends [2,4].

An assessment of a patient's risk of opioid misuse can be made – see Section 6.1.2 – and education about secure storage of opioids provided [4]. Information about the ways in which excess medication can be disposed of decreases the likelihood of patients keeping leftover opioids [4].

The risk of misuse and diversion is less with the atypical opioids tramadol, tapentadol and buprenorphine (patches only) [2].

5. Potential significant adverse effects: non-opioid and adjuvant medications

Potential harms from non-opioid and adjuvant medications must also be considered. See Section 7 for

information about selected agents.

6. Analgesic stewardship prior to admission

The period prior to admission allows time for patient/carer education, an assessment of whether the patient may be at risk of some specific short- and longer-term opioid-related complications, and, if time allows, weaning of preoperative opioids. Some patients may also benefit from referral to chronic pain management and/or addiction medicine services.

6.1 Patient and carer education

Education about the surgical procedure and postoperative care has been shown to reduce preoperative anxiety and postoperative pain [7]. Education should include information about the preadmission, in-hospital and postdischarge stages of treatment, such as [4,7]:

- Anticipated levels of pain and discomfort and functional impairment, and expected resolution over time.

- Realistic expectations about pain relief after surgery – that the aim of pain relief is to assist with functional recovery after surgery or trauma and while pain will be reduced, it is not likely to be eliminated.

- Reassurance that reduction of pain and discomfort and achievement of functional goals is also a priority for the staff who will be caring for them.

- The medications and techniques (including non-pharmacological) that are likely to be used.

- Risks and side effects of opioids including the potential for inadvertent, long-term use, misuse and addiction.

- Risks and side effects of other analgesic medications and analgesic techniques.

- Analgesic agents that might be provided after discharge and, if opioids are prescribed, that the aim is for short-term use only (ideally less than one week in most cases) and progressive dose decreases as the patient recovers.

6.2 Assessment of potential risk factors

6.2.1 Psychological co-morbidities

Psychological co-morbidities such as anxiety, depression and catastrophic thinking as well as pre-existing chronic pain and long-term preadmission opioid use are associated with higher risks of PPOU, persistent postsurgical and post-trauma pain, and opioid misuse [2,4]. Psychological comorbidities as predictors of high pain scores and opioid requirements are covered in Section 3.

Early identification of vulnerable individuals may offer the opportunity to target modifiable risk factors – for example, initiation of psychological interventions aimed at reducing anxiety, depression and catastrophic thinking [2,4]. This has been described by some centres following the development of transitional pain services, acute pain service outpatient services, and the perioperative surgical home, where selected patients can be seen prior to elective surgery and/or after discharge can reduce the risks of postdischarge chronic pain and excessive opioid use [22].

6.2.2 Risk of opioid misuse

Scoring systems have been developed to assess the risk of opioid misuse in the chronic pain setting. While not validated for patients with acute pain, one that is very simple and

quick to used is the *Revised Opioid Risk Tool – Modified* (ORT-R) [34].

The ORT-R includes a number of questions which relate to a personal or family history of abuse of alcohol, illegal drugs, or prescription drugs, as well as the patient's age and whether they have a diagnosis of attention-deficit disorder, obsessive-compulsive disorder, bipolar disorder, or schizophrenia. A diagnosis of depression is scored separately. A score of 2 or lower indicates low risk of future opioid use disorder (OUD); a score ≥3 indicates a high risk.

When considering the risk of OUD after discharge, it may be reasonable to widen the definition of 'family' and consider the friends with whom a patient may be living and will be returning to with these medications [22].

6.3   Weaning long-term opioid doses

Compared with opioid-naïve patients, patients who are opioid-tolerant prior to admission are more likely to report higher pain scores after surgery or trauma, have higher opioid requirements, and to be at greater risk of OIVI [2] and PPOU, including longer use of any additional opioid prescribed for management of postoperative pain [4]. Opioid tolerance may also be accompanied by opioid-induced hyperalgesia and physical dependence leading to increased pain sensitivity and risk of opioid withdrawal if their opioid is abruptly ceased or reduced in dose [2].

Long-term opioid use prior to admission has also been associated with an increased risk of less well-recognised adverse outcomes after a number of different types of surgery. These include an increased risk of surgical site and periprosthetic infections, higher early revision rates for major joint arthroplasty and spinal fusion, longer hospital stays, a greater chance of non-home discharge, higher numbers of postdischarge emergency department visits and readmission rates, and higher healthcare costs; in some studies, the risks are reported to be proportional to opioid dose [2,35].

There is some evidence that these risks may be reduced, even to levels similar to opioid-naïve patients, if opioids can be reduced in dose or ceased some months prior to admission [2,35].

If opioids are to be weaned, sufficient time prior to surgery is required and weaning should be slow, achievable, and patient patient-centred; rapid or forced tapers may risk precipitating mental health crises in vulnerable patients, illicit drug use and suicide [35]. There is evidence to show that tapering of opioid doses in patients with chronic pain most commonly leads to a reduction in their level of pain or no change in their pain, rather than a worsening of pain [22,35].

Information for clinicians related to opioid tapering been published by the Therapeutic Goods Administration of Australia [36].

7.   Analgesic stewardship during admission

Analgesic stewardship includes consideration of opioids as well as other analgesic and adjuvant medications and strives for a balance between pain relief that is sufficient to facilitate patient recovery and restoration of function, and minimisation of analgesia-related harms to the patient and others.

Regular assessments of adequacy of analgesia, monitoring, and documentation of any adverse effects or complications should be undertaken to safely and effectively individualise treatment regimens.

Safe and effective management of acute pain requires selection of an appropriate treatment regimen which is then modified as needed for the individual patient, based on assessments of adequacy of analgesia, monitoring for the onset of any analgesic-related adverse effects, and early recognition and treatment of any adverse effects that arise.

The selection of analgesic medications should be evidence-based and also take into account any fixed patient-related or modifiable risk factors that may impact upon their use. Medications that may be used include opioids, paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) and ketamine, as well as adjuvant agents including antidepressants and gabapentinoids. Other medications may be required for the

treatment of analgesia-related side effects.

Opioids still play a key role in the management of moderate or severe acute opioid-responsive pain in many patients, However, non-opioid and adjuvant analgesia medications included as components of multimodal analgesia can offer significant benefits [2].

Multimodal analgesia aims to reduce opioid-related adverse effects by reducing opioid requirements and to improve pain relief. Medications employed as part of multimodal analgesia regimens should not increase the risk of adverse effects or interactions with other analgesic medications. The use of non-opioid analgesic and adjuvant medications and 'opioid-free' analgesic techniques will not avoid the need for opioids in all patients, either in hospital or after discharge, and may not lead to a reduction in patient harm.

Regional analgesic techniques are also important components of multimodal analgesia for some patients. For information refer to the ANZCA professional document *PG03(A) Guideline for the management of major regional analgesia (PS03)*.

7.1   Opioid medications

In adults, age is a better predictor of opioid requirements than patient weight, with requirements decreasing as age increases [20]. It is likely primarily a result of increased brain sensitivity to opioids rather than age-related changes in pharmacokinetics [2].

Therefore, in opioid-naïve adults, initial opioid doses should be based on patient age [2,21]. Additional adjustments may be required (or a particular opioid avoided) based on patient comorbidities (for example renal impairment) [2].

7.1.1.   Long-acting opioids

Some patients, for example those who have sustained significant multiple traumatic or burns injuries, may have demonstrated prolonged opioid needs. In these cases, it may sometimes be appropriate to introduce a long-acting opioid on a temporary basis and after careful assessment. Communication with the primary service (including rehabilitation services) or general practitioner about the temporary basis of this prescription is essential. If long-acting preparations are used, atypical opioids should be considered as they are associated with a lower risk of OIVI and of misuse/diversion than conventional opioids [2].

Patients who are already taking a long-acting opioid prior to admission, including those in opioid- substitution programs, are tolerant to and physically dependant on that opioid. After independent confirmation of the drug and dose, their long-acting opioid should usually be continued [2].

Spinal morphine (intrathecal or epidural) is also long acting. It has been recommended for use in patients undergoing Caesarean Section [47,48] and has also been used for analgesia after other types of surgery, whether added to a spinal local anaesthetic or given alone in patients also having a general anaesthetic [2]. As with other more specialised analgesia delivery techniques (see Section 4.3.6 of PS41), guidelines and order sets which often combine the medication prescription, monitoring requirements and instructions for nurses to follow should a patient develop a medication-related adverse effect, are important when spinal morphine is used. The patient remains the responsibility of the anaesthetist administering the spinal morphine, or patient management may be delegated to another trained and skilled medical practitioner, or registered nurse, or to a pain service.

Routine prescription of long acting opioids for the management of acute pain should be avoided unless there is a demonstrated need, close monitoring is available, and a cessation plan is in place. This recommendation is consistent with those made by many national and international (USA, Canada and the UK) professional bodies and guidelines [4,8,21,37,38,39,40,41,42,43].

This is also in line with the approved indications for long-acting opioids listed by regulatory authorities including the Therapeutic Goods Administration in Australia, Medsafe in New Zealand, and the Food and Drug Administration (FDA) in the US.

Modified-release opioids, also known as controlled-release, extended-release, sustained-release preparations and slow-release, used for the management of acute pain have been shown in comparison to immediate-release preparations to [4,44,45]:

- Provide less effective pain relief.

- Increase the risk of OIVI and other opioid-related adverse events.

- Increase the risk of PPOU.

The Australian Commission on Safety and Quality in Health Care *Opioid Analgesic Stewardship in Acute Pain Clinical Care Standard*, endorsed by ANZCA/FPM, notes that the use of slow-release oral opioids '…should be exceptional and not routine' [42].

Interpersonal variation in pharmacokinetics and response to opioids make predicting a dose of modified-release in an opioid naïve person impossible[2], and if side effects are encountered, they may be of sustained duration. In addition, the slow onset and offset of these opioid preparations makes rapid and safe titration impossible and down titration as pain resolves, more difficult [2]. It is also known that addition of a 'background infusion' to opioid administration by IV PCA markedly increases the risk of OIVI [2]. Administration of a new long-acting opioid in addition to IV PCA or PRN oral opioids is essentially the same as adding such a background infusion.

Immediate-release preparations are able to be titrated for each patient when ordered on an 'as needed' basis and therefore, better match the changes in pain intensity that occur in the postoperative and post-trauma periods as well as promote dose-to-dose assessment of the patient. Note that regularly scheduled administration of any opioid increases the risk of OIVI [46].

7.1.2 Opioid-sparing and opioid-free analgesia

There is good evidence of benefit for using an opioid-sparing analgesic regimen [2].

Increasing concerns that opioids used for the management of acute pain contribute to in-hospital adverse events (including OIVI), and to risks after discharge including PPOU and opioid misuse and diversion and thus contributing to the opioid 'epidemic', have led to an increasing focus on the concept of opioid-free anaesthesia and analgesia (OFAA). These good intentions fail to note that intraoperative and immediate postoperative opioid use has not been implicated as contributing to the opioid epidemic [49].

OFAA techniques are currently poorly defined, with limited good evidence to support the technique and the adjuvants recommended, or their optimal doses [14,49,50]. In addition, the non-opioid and adjuvant agents tend to be administered with little variation in the doses used; only limited if any titration is possible based on patient needs as further increases in dose can often confer no additional benefit but increase the risk of adverse effects [14].

Most studies also look at the effects of OFAA during in the early postoperative period only, and some patients may later be given an opioid [14].

While use of OFAA leads to a reduction in nausea and vomiting [50], there is, as yet, no evidence to show that OFAA leads to clinically significant benefits in terms of pain relief and opioid use after surgery, or affects discharge opioid prescribing or the rates of PPOU, including when peripheral regional analgesia is used [14,30,31]. Evidence to show that OFAA has any greater benefits than an opioid-sparing analgesic regimen is also lacking [14].

7.2 Non-opioid and adjuvant analgesic medications

In general, the same non-opioid analgesic and adjuvant drugs are used in both opioid-sparing and OFAA regimens. The evidence to support their use is variable.

Selected comments for some of the agents used are given below – for more detail refer to *Acute Pain Management: Scientific Evidence 5e* [2].

Paracetamol

There are very few contraindications to the use of paracetamol and the risk of adverse effects is minimal if recommended doses are used [2].

Non-steroidal antiinflammatory drugs (NSAIDs)

NSAIDs are still often underused because of concerns about adverse effects. There is evidence that [2,51]:

- They are opioid-sparing and may decrease the incidence of postoperative nausea and vomiting when used in multimodal analgesic regimens.

- Gastrointestinal ulceration risk is lower with COX2-selective NSAIDs.

- Non-selective NSAIDs especially may cause bronchospasm in patients with NSAID-exacerbated respiratory disease.

- Non-selective NSAIDs but not COX2-selective NSAIDs interfere with platelet function .

- Short-term use of NSAIDs does not appear to increase the risk of serious cardiovascular adverse events after non-cardiac surgery.

- There appears to be no clinically significant adverse effect on bone and enteral anastomoses healing, at least when NSAIDs are used for a short period (for example 2 weeks).

- The risk of adverse effects is reduced with short-term use (for example less than 5 days).

In patients at risk of haemodynamic instability, or who have postoperative or post-traumatic haemodynamic instability, it has been suggested that NSAIDs be avoided in patients who have an eGFR less than 80 mL/min [21].

Gabapentinoids

Once commonly recommended for inclusion in multimodal analgesia regimens, it is now recognised that the benefits of these medications have been over-estimated and potential harms under-estimated [52,53].

Their use leads to [2,53,54,55]:

- Statistically but not clinically significant reductions in postoperative pain and postoperative opioid requirements, and a lower risk of postoperative nausea and vomiting.

- No reduction in the incidence of chronic postsurgical pain.

- An increased risk of dizziness, visual disturbances and OIVI.

- Risk of abuse and misuse.

Routine use in the management of acute pain is therefore no longer recommended [52,53].

Lidocaine

Evidence of any benefit from lidocaine infusions is limited [56,57]:

- Reported benefits, including reductions in postoperative pain, opioid requirements, and postoperative nausea and vomiting, and earlier return of bowel function, are not supported by

good quality evidence.

- Reports of patient harm and 'near-misses' associated with perioperative administration have raised concerns about the risks.

Dexmedetomidine

Intraoperative use of dexmedetomidine is associated with, in the postanaesthesia recovery unit (PARU), lower rates of postoperative nausea and vomiting, shivering, cough and emergence agitation as well as lower pain scores. The incidence of hypotension is increased but not the incidence of sedation or bradycardia, and length of stay in PARU is not increased [58].

Ketamine

Ketamine is commonly used in the acute pain setting and is considered to be safe and effective, especially in the low doses commonly used [2].

Perioperative low-dose use leads to [2,59]:

- Reduced postoperative pain intensities and opioid requirements.
- Clinically small reductions in postoperative nausea and vomiting.
- An incidence of central nervous system adverse events that is little different from controls.
- A lower risk of chronic postsurgical pain after some operations.

Magnesium

Low-quality evidence related to perioperative use of magnesium shows [60]:

- A statistically significant but small reduction in postoperative opioid requirements .
- No reduction in postoperative pain scores or postoperative nausea and vomiting.

7.3 Assessment of analgesic efficacy and adverse effects

Efficacy of analgesia should include assessment of patient function such as FAS, as well as patient self-reported pain scores. Adjustments to analgesic regimens should not be made based on pain scores (assessed both at rest and with activity) alone. See Section 3.

Regular monitoring, and documentation of any adverse effects or complications should be undertaken to safely and effectively individualise treatment regimens. For monitoring related to OIVI see Section 4.1.

7.4 Guidelines and order sets

Implementation of established guidelines and order sets (including in electronic medical record systems) for analgesic medications are recommended, especially those that link opioid prescribing and monitoring [4]. Such guidelines and order sets will often combine the medication prescription, monitoring requirements and instructions for nurses to follow should a patient develop a medication-related adverse effect [22]. These are especially important for some specialised analgesia delivery techniques which may involve use of complex equipment and require greater medical and nursing knowledge and expertise. However, they are also recommended for immediate-release opioids ordered on as 'as needed' basis; examples are available [22].

7.5 Preparation for discharge

Preparation for discharge should start soon after admission and include daily review of a patient's pain score and opioid dose trajectories. Patients who are not following an expected trajectory should be assessed as this may signify postoperative or post-trauma complications, neuropathic pain or psychological distress; even before discharge, opioid weaning strategies should commence [4].

Referral to an addiction or pain medicine specialist should be considered if the patient is taking two or more psychoactive drugs in combination, a combination of opioids and benzodiazepines, has a significant psychiatric illness, uses illicit drugs, or shows evidence of high-risk behaviours [2].

Tolerance to opioids and development of a physical dependence likely takes 7 to 10 days [21] and so, after short-term use of a few days only, opioids can be reduced in dose quite rapidly without adverse consequences. If the patient requires opioids for longer than this a slower wean may be needed if the dose trajectory has not been decreasing spontaneously. See Section 6.3.

8. Analgesic stewardship at and after discharge

8.1 Analgesic prescriptions

Multimodal analgesia should continue after discharge [2]. If an opioid is required [2,4]:

- Avoid modifiable risk factors for OIVI where possible (see Section 4.1.2.2).

- Avoid modifiable risk factors for PPOU where possible (see Section 4.2.2.2).

- Reassess patient for risk of opioid misuse.

- The number of opioid tablets used at home is better predicted by the number of tablets taken the day before discharge and patient age. Therefore, doses prescribed on discharge are best based on the patient's opioid requirement in the 24 hours before leaving hospital rather than the type of surgery alone. Patients who have used no opioid in the day before discharge should not be given an opioid at discharge.

- Where oral liquid opioid preparations are used, prescribe and dispense the smallest volume possible. This is particularly relevant when prescribing for children, as commercially produced oral liquid opioid preparations are only available in large volume bottles that typically far exceed the patient's opioid requirements. Pharmacies should be encouraged to dispense smaller volumes as appropriate.

- Avoid use of long-acting opioids and prescribe immediate-release opioids (if required) to promote functional recovery rather than eliminate pain; promote 'activity-based analgesia'.

- Limit the number of tablets and duration of first prescription. Ideally this should be less than 7 days.

- In some patients, 'interval dispensing' of an opioid (for example, at one- or two-day intervals) may be required.

8.2 Patient/carer education

Discussion with patients and carers and written information given at discharge should include the following points [2,4,22].

- That the aim of pain relief is to restore functional activity and not abolish all pain; activity-based analgesia should be the aim. That is, the patient should be encouraged to take their opioid, if needed, prior to periods of activity.

- The PRN dose intervals for discharge opioids are often labelled by the pharmacist according to the prescription received (for example '4 hourly PRN'). However, patients and carers must be told that this does not mean they need to be taken every 4 hours; using as little as possible to achieve functional goals is the aim.

- The opioid is not to be used to aid sleep.

- If opioids are prescribed, the aim is for short-term use only (ideally less than one week in most

cases) and progressive dose decreases as the patient recovers.

- Expected duration of treatment; how to taper and then cease opioids.

- Information about the importance of any non-opioid and adjuvant analgesics prescribed and how to wean and then cease these medications; opioids should be ceased before other analgesic medications.

- The use of non-pharmacological analgesic measures.

- Recognition of and reducing the risk of OIVI (the need to avoid benzodiazepines, gabapentinoids, alcohol or cannabis); Patients prescribed opioids to take at home, and their family or carers, should be educated about the significance of sedation and the steps to take should excessive sedation be noted.

- The risks of opioid misuse and addiction.

- Opioids should only be taken by the person for whom they are prescribed, for the reason for which they have been prescribed, and in doses no higher than prescribed.

- Opioids must be stored securely and excess medications disposed of safely: leftover opioid along with unsafe storage increases the risk of accidental poisoning (including children and pets), diversion and misuse.

- Prescription opioid use is associated with a significantly increased risk of fatal crash involvement. Opioids impair driving skills and cognitive reasoning in a similar manner to alcohol. Driving risk may be increased in the first few weeks following initiation of a prescription opioid (for example, for management of their acute pain) and, while long-term opioids in stable doses appear to have no significant impact on driver-related psychomotor skills, psychomotor impairment returns if the dose is increased. Advice should be given about the dangers and the legal implications of driving while under the influence of an opioid; patients should be cautioned against driving while still taking an opioid prescribed for ongoing management of acute pain after surgery or injury. The same advice would apply to performing other complex tasks or making key decisions.

- The need to see their doctor should significant pain continue.

Written material (print or electronic) used to supplement verbal information should be available in a language and reading level appropriate to the patient and others.

8.3 Communication with the patient's treating doctors

Communication with the patient's general practitioner or other treating doctors when the patient is discharged is essential and the advice given should mirror that given to the patient. There should be a clear plan for analgesia reduction after discharge, and robust systems for communication with usual treating practitioners in the community will assist in avoiding unintended dose escalation or prolonged duration of opioid use [2].

The following information should be considered [2,4,22]:

- Opioid use should be short-term only and that daily dose trajectories should be trending downwards.

- Repeat prescriptions for an opioid are a major modifiable risk factors for PPOU and also increase the risk of opioid misuse.

- Patients who request more opioid should be reviewed and, if they are still taking an opioid beyond what would be considered the usual healing time for their surgery or injury, or if they have been taking opioids for longer than 90 days after discharge, may benefit from specialist review.

- The opioid should only be continued if needed (still ceasing within an overall short timeframe) after exclusion of other causes such as neuropathic pain or postoperative/post-trauma complications, and assessment of relevant psychosocial factors.

- Even if some patients have developed chronic postsurgical or post-trauma pain and require medication(s) for its management, adjuvant analgesic agents rather than opioids may be more appropriate if medications are needed.

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