Guidelines for the management of acute pain in emergency situations

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Author contributions

Professor Saïd Hachimi-Idrissi developed the premise of the acute pain management guideline.

All authors had full access to all data and evidential materials and take responsibility for the integrity of the guideline and the accuracy of analyses. All authors were involved in the concept, and design of the guidelines, drafting of the guideline handbook manuscript and critical revision of all manuscript drafts.

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Foreword

Despite advances in pain management, oligoanalgesia remains a significant part of ours and our patients' lives in the emergency setting. Indeed, pain is categorised as one of the primary reasons patients call upon emergency services either in Emergency Departments (ED) or pre-hospital services.

The reasons for oligoanalgesia are diverse and result from a limited analgesic availability, fear of opioid dependence or potential for diversion and abuse, ability of personnel to prescribe, set up of pre-hospital settings, for example presence of emergency physicians or not, failure to follow pain management guidelines, overcrowding in the ED and lack of pain management knowledge or resources. Effective pain management is a particular challenge in children where anxiety may be heightened and venous access difficult. Whilst guidelines exist within some countries across Europe no pan-European guidelines or recommendations exist. Under the auspices of the European Society for Emergency Medicine (EUSEM), the European Pain Initiative seeks to address this unmet need. From this initiative a comprehensive handbook comprising seven chapters has been developed, including guidelines for manging acute pain in both adults and children. It is intended to provide a robust, systematic aid to making clinical decisions with respect to acute pain for our patients. This handbook clarifies where evidence and expert consensus support clinical practice recommendations and our hope is that it will be useful to healthcare professionals in the emergency setting.

I want to thank the excellent European Pain Initiative committee who conducted this work, ably led by Professor Saïd Hachimi-Idrissi and supported by colleagues from across Europe. I commend these guidelines to all our colleagues managing acute pain in emergency settings to improve the lives of our patients.

Professor Luis Garcia-Castrillo Riesgo

President

European Society for Emergency Medicine

Preface

This Handbook has been developed to support improvements in the assessment and management of acute pain in Emergency settings across Europe. These guidelines, supported by an unrestricted educational grant from Mundipharma International Limited, outline the unmet needs existing for acute pain, assessment of pain and recommendation for pain management by first responders, paramedics and Emergency Department physicians. They have been developed following a rigorous review of available clinical evidence and analysis of current management practices across Europe through EUSEM members. It is our hope that these guidelines will provide healthcare professionals with evidence-based practical information that will help them manage their patient's pain as effectively as possible.

As Chair of the European Pain Initiative developed under the auspices of EUSEM I would like to acknowledge the hard work and commitment of my fellow Committee members and the valuable input received from many colleagues.

Professor Saïd Hachimi-Idrissi

University of Ghent, Belgium

Overview

Pain management is a vital component of patient care, particularly in the emergency setting where pain can hinder the opportunities to treat and manage pain causing conditions. Pain remains one of the primary reasons for patients to seek emergency medical care, yet despite this it often remains under-acknowledged, -assessed and -treated.[1,2] Acute pain is of itself very distressing, and if unresolved can lead to complications and, in the longer-term, the generation of chronic pain. Effective and rapid treatment of pain is therefore essential.[2,3]

Emergency care systems are different across the European countries. The differences across health care systems and education within Europe, as well as the care and the cure of patients varies dramatically. Likewise, the management of acute events is also different across Europe depending on the emergency setting patients find themselves in e.g. hospital Emergency Department (ED) or pre-hospital setting and whether the patient is admitted into a teaching or a general hospital.

The organisational quality of the process of managing an acute event appears to be a fundamental driver of clinical quality. In many settings the term "clinical quality" has been operationalised into so called "key performance indicators". One of the most frequently used key performance indicators in emergency care is "pain". Pain is the most common reason for seeking medical care but is frequently under-treated despite the consequences. On a systemic level, these consequences include enormous healthcare cost, loss of productivity and decreased ability to work, whilst for individuals, the adverse effects of pain include increased oxygen demand, increased blood pressure and intracranial pressure and the risk of chronification.[3,4]

Under the auspices of the European Society for Emergency Medicine (EUSEM) a programme – the European Pain Initiative (EPI) – was launched to provide information, advice and guidance on pain management in the emergency setting, both EDs and pre-hospital settings. As there are no well-defined emergency medicine guidelines at a European level, EUSEM identified that European acute pain management guidelines, particularly for the pre-hospital setting, would be useful for day to day patient management and for providing guidance to trainees and non-emergency medicine physicians. No previous initiative to develop such European guidelines has been undertaken before.

A multi-disciplinary steering committee Chaired by Professor Saïd Hachimi-Idrissi was assembled at the annual EUSEM congress in 2017 and over the intervening period this committee developed a peer-reviewed handbook to provide detailed insight into the assessment and management of acute pain as well as providing algorithms for pain management for adaptation nationally and locally.

The objective of the EPI was to develop a practical guideline that would have pan-European relevance across prescribing environments to combat acute pain in the emergency setting. The aim was to provide prescribers, including clinicians and nurses or paramedics with prescribing capabilities, with a flexible algorithm to treat acute pain including non-pharmacological and pharmacological methods, being mindful of special patient populations. Implementation of non-pharmacological pain control methods can be found in Chapter 4 (page 25) and pharmacological analgesic options in Chapter 5 (page 33). Treatment algorithms that consider pharmacological pain control in partnership with non-pharmacological methods and their application across patient groups can be found in Chapter 7 (page 67). The hope is that the resulting handbook based on evidence and clinical practice will provide practitioners in the emergency setting useful, practical information that will help them manage their patient's pain as effectively as possible. As a result, information in this handbook covers conventional and traditional medications and routes of delivery as well as emerging practice in analgesia.

Informing the content of the handbook and guidelines

When the idea of this handbook and guidelines was conceived it was believed, based on published literature and anecdote, that practice across Europe would differ and that oligoanalgesia was likely to continue to be problematic. To inform the requirements for the handbook a survey of the EUSEM membership was developed and circulated in early 2019.

More than 100 EUSEM members completed the survey with most respondents being physicians working within EDs (62%) or across both EDs and pre-hospital settings (28%). It was clear from respondents that pain assessment is embedded within routine clinical practice with 90% of all respondents undertaking assessments with the Visual Analogue Scale (VAS) and Numerical Rating Scale (NRS) the most popular, perhaps a reflection of their ease of implementation. There was a wide variety of pain scales used among participants reflecting individual patient populations and depth of information detail perhaps, or institution guidelines. Among children the FACES scale is the scale overwhelmingly used (40%)[5] followed by the Faces, Legs, Activity, Cry, Consolability (FLACC) Scale[6] and the modified FLACC-R scale for children with cognitive impairment,[7] possibly reflecting their potential for use among younger children including those who are, as yet, non-verbal. Among neonates and infants the COMFORT[8] and CRIES[9] scales are most commonly used. However, it is clear across Europe that, for some, pain assessments are undertaken from clinical impressions of physicians, often based on patient vital signs, or asking patients if they believe they need analgesia rather than the use of validated pain score tools.

For those patients with cognitive impairment or the elderly VAS and NRS remain the most commonly used tools, with some use of scales such as the Pain Assessment in Advanced Dementia (PAINAD)[10] and Pain Assessment Checklist for Seniors with Limited ability to Communicate (PACSCLAC).[11] However, within this population there is a greater emergence of reliance on patient vital signs, patient facial expression and yes/no questioning to guide analgesic administration. It would be interesting to explore if this approach is a possible cause of why older patients are less likely to receive analgesia.[12-14]

It is clear from respondents that pain assessment is most commonly undertaken at first interaction with patients, whether that be in the pre-hospital or ED setting, and reassessments of pain are routinely undertaken.

When it comes to pain management, it is clear that for more than half of all respondents the WHO pain ladder is used as a guide to analgesia. The WHO analgesic ladder was developed in 1986 specifically to address cancer pain and advocates a transition from simple analgesics to non-opioids through to opioids plus adjuvants.[15] No pain ladder for acute pain has ever been formally developed. Even in chronic pain the role of the WHO ladder is being questioned and suggestions made that it be reviewed in light of new knowledge and available clinical trial data,[16] but it is recognised that any updates need to be balanced with, and cognizant of, the original ladder's simplicity that has led to its enduring use across all pain types, not just cancer pain.[17] Apart from WHO guidelines, it is clear that analgesic decisions are informed evenly by a range of material influence including institution derived guidelines, regional guidelines, as well as national and societal guidelines, but more than 25% of respondents do not have guidelines that are being followed, indicating a need for evidence based guidelines. Given the diversity of analgesic approaches across Europe, including the use and availability of medications, as shown in the EUSEM survey, it is clear that any guidelines developed need to be adaptable, in a credible way, to suit the needs of individual institutions and units.

Methods

To develop this handbook, relevant publications were identified via a literature search performed using PubMed to search the MEDLINE online database on 30 November 2018, and via concomitant searches on Cochrane, Google Scholar and EMBASE. Search terms were used to follow the strategic methodology and relevant publications were identified via a literature search performed using MEDLINE, Cochrane database, Google Scholar and EMBASE online databases using search terms: trauma pain OR trauma AND acute pain; analgesia OR analgesic OR analgesics; wound OR wounds injury OR injuries; therapeutics; pain therapy OR drug therapy; pain assessment; pre-hospital; ladder of treatment; routes of administration OR intravenous OR intranasal OR inhaled OR intramuscular; non-pharmacological treatments; pharmacological treatment OR ketamine OR morphine OR fentanyl OR sufentanil OR paracetamol OR nitrous oxide OR ibuprofen OR diclofenac OR ketorolac OR celecoxib OR dipyrone OR metamizole OR etoricoxib OR parecoxib OR methoxyflurane; pharmacological treatment OR opioids; emergency medical technicians OR evidence based emergency medicine OR emergency medicine OR emergency nursing OR emergency medical services; guidelines.

English-language articles published within the past 10 years returned by this search were used as basis for the handbook. At this point >20,000 publications were returned, and these were screened for relevance using the criteria established by PRISMA[18] and against the inclusion/exclusion criteria presented in **Table 1**.

Table 1 Inclusion/exclusion criteria for publications returned after literature searches

Inclusion	Exclusion
Randomised controlled trials (RCTs)	Individual case reports
Clinical trials without randomisation e.g. open label, observational, retrospective	Treatment methods not found in the ED e.g. acupuncture
Meta analyses	Older than 10 years
Case series/case-controlled studies	Non-English language
Systematic reviews	

All publications were reviewed and a working document package of 800 results was obtained from which the handbook has been developed, of which >200 have been used to develop recommendations. Where required there have been further inclusions of older literature sources as some analgesics in the emergency setting were first made available for use many years ago and for whom newer literature does not exist, and some newly published data that emerged after the cut-off date that were applicable to the practical implementation of analgesia in Chapters 5 and 6 and recommendations in Chapter 7. In tandem with the literature search, a survey of EUSEM members to explore current clinical practice was undertaken and responses from practitioners along with published literature were used to inform the handbook and develop treatment algorithms.

The resulting handbook developed by the Committee has been peer-reviewed by EUSEM. Its purpose is to be a practical, evidence-based guide for use by those with appropriate prescribing rights within their scope of professional practice who are able to accept clinical/legal responsibility for their prescribing decisions, and as such detailed information of anatomy and analgesic techniques have not been included. Suggested doses and treatment regimens are provided to enable practitioners to adopt a flexible, pragmatic multi-modal analgesic approach. However, doses are advisory only and should be adapted according to local requirements and analgesic availability. Whilst the best efforts of the Committee and EUSEM have been used to provide accurate information at the time of development responsibility for any errors or omissions is disclaimed.

The success of any clinical guideline or recommendation requires successful implementation. Barriers to implementation are typically focused on knowledge, attitude and external barriers. In an attempt to pre-emptively address possible barriers this handbook has been developed to include a comprehensive overview of scientific and clinical evidence supporting acute pain management in the emergency setting, as well as the real-world perspectives of emergency medicine practitioners at all levels. In order to address external barriers, the recommendations for acute pain management have been developed to provide users with options in terms of recommended medications. This is done to reflect the availability for medication across Europe and also the differences in prescribing capability and responsibility among emergency personnel. In this way, it is hoped that the recommendations developed will be applicable to both the pre-hospital and ED settings across all appropriate personnel with the necessary prescribing rights including clinicians, paramedics and nurses.

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GUIDELINES FOR THE MANAGEMENT OF ACUTE PAIN IN EMERGENCY SITUATIONS

CHAPTER 1:

The current state of acute pain management in emergency situations in Europe

Prevalence of acute pain in emergency situations

Pain is defined by the International Association for the Study of Pain (IASP) as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.'[1] Acute pain is typically of sudden onset and of limited duration and is provoked by a specific injury or disease.[2] It is highly prevalent, with up to 70% of patients in the pre-hospital setting[3,4] and between 60% and 90% of patients entering the Emergency Department (ED) reporting pain.[5-7] Pain is a primary complaint in half of all ED visits.[6] Extrapolating the prevalence of acute pain to the national scale using available data from Europe on the annual number of ED visits suggests that millions of people in Europe suffer from acute pain every year,[8-11] making its management a massive undertaking and of great importance.

This chapter provides an overview of the current situation in Europe as regards the unmet needs and current practice in the management of acute pain in the pre-hospital and ED settings, and outlines the guidelines that are available to advise emergency medicine professionals.

Oligoanalgesia in emergency settings: pre-hospital

Acute pain is often poorly assessed and inadequately treated in the pre-hospital setting.[4,12-17] Initial and final assessment of pain does not take place in one-third to almost one-half of cases, and when pain assessment does take place, many patients reporting moderate to severe pain do not receive analgesia.[14] In an Australian study of 333 patients aged over 65 years attended to by an ambulance following a fall resulting in suspected bone fracture, initial and final pain assessment was undertaken at the scene in around half of cases, and only 60% of all patients with suspected fracture received analgesia.[14] Similarly, a retrospective chart review of 1,407 ambulance patients in the Netherlands found that while 70% of patients reported pain, only 31% had a systematic pain assessment and only 42% received analgesia.[3]

Oligoanalgesia may result from a lack of availability of analgesics to pre-hospital personnel. A study in Italy reported that 12% of all ambulances do not carry strong analgesics such as opioids, and 10% of all ambulances carry no analgesic medication at all, despite 42% of patients reporting moderate to unbearable pain.[12] In Switzerland, a ten-year retrospective review of 1,202 patients attended by air ambulance found oligoanalgesia in 43% of cases.[18] In this study, predictors of undertreated pain included male gender, pain score NRS>4, no analgesia and lack of experience of the attending physician. Oligoanalgesia was due to insufficient analgesic dosing in 75% of cases and a complete lack of analgesia administration in 25%.[18] In contrast, a study in France showed that 90% of paediatric patients who reported pain received analgesia while being transported by mobile intensive care units (MICU). It was

noted that this unusually high figure may be related to the fact that the medical team on board the MICU included a trained ambulance driver, an emergency physician, a nurse anaesthetist, and sometimes a medical student, compared with other countries where ambulances are generally staffed by paramedics or ambulance staff.[19]

Oligoanalgesia in emergency settings: ED

In addition to the issues seen in pre-hospital emergency analgesia, there are unmet needs associated with acute pain management in the ED setting. The problem of oligoanalgesia in the ED was first acknowledged in the late 1980s.[20] Since then, a considerable number of studies have shown that pain is assessed in some, but by no means all, patients and that even when pain is assessed and documented many patients do not receive analgesia.[21,22] In a prospective study carried out in a Norwegian university hospital ED in 2015, 77% of 764 patients were evaluated for pain on arrival, and of those with moderate to severe pain, only 14% were given analgesics.[21] In a prospective, observational study of 2,838 patients visiting an urban ED in Italy, 71% presented with pain, but only one-third (32%) received pharmacological pain relief.[23] Of these, 76% rated their pain as severe and 19% as moderate.[23] Pain may also persist after the patient has left the ED. Of 582 consecutive patients presenting at an ED with pain, 37% of patients had ongoing pain a week after discharge, despite being prescribed analgesic therapy.[24]

Barriers to effective pain management in the ED are varied and include poor assessment of pain, limited availability of opioids, resistance among healthcare providers to prescribe opioids, fear of opioid dependence or potential for diversion and abuse, failure to follow pain management guidelines, overcrowding in the ED and lack of pain management knowledge or resources.[12,13,22,24-29]

Oligoanalgesia in the ED can affect any patient, but is a particularly well-recognized issue in paediatric patients.[30] Pain assessment can be more difficult to perform in children,[30] and this group is often more challenging to manage than adults, for reasons such as heightened anxiety and difficulties in obtaining intravenous (IV) access.[28,31] Even when pain scores are documented, only two-thirds of children in pain in the ED may receive analgesia.[32]

Current practice in analgesia in emergency situations

No single standard of care currently exists for the treatment of pain in an emergency situation. The choice of analgesic depends on severity of pain, nature of injury and local protocols. In general, those with mild pain tend to receive paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs), those with moderate pain receive paracetamol, NSAIDs, nitrous oxide or weak opioids, while IV morphine or ketamine are reserved for those with severe pain.[33-35] Paracetamol and NSAIDs are more common in the ED setting than the pre-hospital setting; ketamine is mainly used in the pre-hospital setting and nitrous oxide and opioids are used in both.[28]

A range of personnel may be involved in the care of a patient with acute pain in an emergency situation, including emergency services (ambulance, mountain rescue, fire department, coast guard, police), triage nurses and physicians. As noted earlier, the type of analgesia available to a patient at different stages of care may be limited by the prescribing rights of the emergency services personnel or nurses treating them, or the availability of an analgesic on scene (particularly opioids and ketamine).

Current European guidelines

There are currently no European guidelines for the management of acute pain in an emergency situation, but a number of national guidelines are available. Evidence suggests that implementing guidelines for the management of acute pain in the emergency setting (including providing multichannel education on those guidelines to ED staff) promotes improved pain management, increased administration of analgesia and greater patient satisfaction.[36]

In 2010, the French Society for Emergency Medicine published guidelines on the safe and effective provision of analgesia and sedation in emergency medicine. Their key recommendations are the use of local and/or regional analgesia for pain management when indicated and feasible, with the use of nitrous oxide for slight trauma and

IV morphine given immediately for severe pain, alone or as part of multimodal analgesia (**Figure 1.1**).[37] After opioid titration, analgesia should be given again before recurrence of pain. They state that nurses should be able to assess and treat pain as part of a known service protocol, provided that an emergency physician can intervene without delay and at any time.[37]

An intersociety consensus conference including seven Italian interdisciplinary and interprofessional societies related to pain and emergency medicine was held in 2010 to discuss the assessment and treatment of pain in the emergency setting. In 2015, the recommendations of this consensus group were published. The Italian Intersociety recommendations on pain management in the ED setting state that the use of IV paracetamol should be considered for its opioid-sparing properties and reduction of opioid-related adverse events (AEs) (**Figure 1.2a,b**).[38] Oral paracetamol and NSAIDs are recommended for mild pain; NSAIDs, IV paracetamol and paracetamol in combination with weak oral opioids for moderate pain; and morphine and fentanyl for severe pain. They note that pain relief and the use of opioids in patients with acute abdominal pain do not increase the risk of error in the diagnostic and therapeutic pathway in adults, so such concerns should not delay analgesia.

The Netherlands Association for Emergency Nurses has published guidelines on pain management for trauma patients in the chain of emergency care. The recommendations include two algorithms for measuring pain and providing pharmacological analgesia one for ambulance pre-hospital settings or out of hours general practitioner services and one for helicopter emergency services, (**Figure 1.3**).[39,40] According to the guidelines, pain scores must be documented (NRS is recommended) and should be assessed at a minimum of three times: at arrival, after intervention and at the end of the medical visit. Paracetamol is the treatment of choice, with additional use of NSAIDs or opioids if necessary. Fentanyl and morphine are the preferred options for severe pain during emergency care.

In Slovakia, national guidelines have been issued by the Ministry of Health that provides a scope of practice for healthcare professionals, including pre-hospital personnel.[41] For pre-hospital personnel, the Ministry recommends the administration of non-opioid analgesics and tramadol to patients intramuscularly (IM), IV or by inhalation (INH) as needed.

In the United Kingdom (UK), guidance from the Joint Royal Colleges Ambulance Liaison Committee and the Ambulance Service Association, issued in 2017, advises that all patients with pain should have a pain severity score undertaken, with a simple 10-point verbal scale usually being the most appropriate. Pain assessment should be repeated after each intervention. Balanced analgesia with a multimodal approach is recommended, utilising analgesics with different mechanisms of action. The recommendations further state that relief of pain is one of the most important clinical outcomes in paramedic practice, and that there is no reason to delay pain relief as it does not affect later diagnostic efficacy and may in fact facilitate prompt diagnosis.[42]

Also in the UK, earlier recommendations from the Royal College of Emergency Medicine best practice guideline on management of pain in adults, published in 2014, state that recognition and alleviation of pain should be treated as a priority (**Figure 1.4**).[43] This should start at triage, include monitoring of pain during the ED visit and finish with ensuring that adequate analgesia is provided at, and if appropriate beyond, discharge. For moderate and severe pain, analgesia should be provided within 20 minutes of arrival in the ED.

In the Republic of Ireland, clinical practice guidelines have been developed by the Pre-Hospital Emergency Care Council (PHECC) that cover the range of clinical scenarios encountered by pre-hospital personnel, including pain in adults and children and have been recently updated (**Figures 1.5a and 1.5b**).[44] The guidelines recommend the assessment of pain using an analogue or visual pain scale and the consideration of non-pharmacological pain management techniques such as splinting, psychological support, heat or cold therapy and patient positioning. If pain relief is inadequate, then it is recommended that mild pain is treated with oral paracetamol or ibuprofen and moderate pain is managed with inhaled methoxyflurane or nitrous oxide and/or oral paracetamol and ibuprofen. For severe pain, patients should receive intranasal (IN) fentanyl as first-line therapy and IV fentanyl or IV morphine second line; if pain persists, the addition of IV paracetamol or IV ketamine should be considered.[44] Similar guidelines, with

differences in route of administration and dosing, are recommended for children aged 15 years or younger, with the possibility to add in additional IV ondansetron if nausea occurs.

State of workforce education and quality assurance

A diverse range of barriers preclude effective emergency pain management in the ED as identified in an American study, including bias relating to race, ethnicity, gender and age; ED physicians' inadequate knowledge and formal training in the management of acute pain; prejudice against the use and prescription of opioids; and the ED environment (such as overcrowding and interruptions) and culture (such as language barriers between patients and staff, lack of health insurance and frustration with waiting times).[22]

Inadequate pain management in the pre-hospital setting is associated with a number of factors, including lack of knowledge and confidence of personnel, underestimation of pain, unwillingness to administer strong doses of opioids, suspicion of potential drug-seeking behaviour in patients, and fear of side effects or injuries being masked.[13-15,18,45]

Pain management education rarely forms part of healthcare professionals' training,[22,46] and changing the practice, attitudes and behaviour of established physicians may be difficult.[22] Achieving change in practice may require the use of multifaceted strategies incorporating a range of different methods.[46] Interventions to improve pain management within the ED may need to be tailored to an individual department in order to fully address the challenges, and should be developed following an analysis of the needs and barriers to pain management that exist.[46] Currently, the knowledge of pre-hospital and ED staff about the management of acute pain is limited,[22,47,48] and many EDs don't have pain management guidelines or pain quality management programmes in place.

The current state of acute pain management in emergency situations in Europe: take-home messages

- **Acute pain is highly prevalent in emergency situations, both pre-hospital and in the ED.**

- **Acute pain is often poorly assessed and treated in both the pre-hospital and ED settings, and all too often acute pain is not assessed and therefore not treated.**

- **Barriers to adequate pain management are multifactorial and include lack of knowledge and training, reluctance to give opioids, and concerns about drug-seeking behaviour or abuse.**

- **Pain education of ED and pre-hospital staff is limited and there is a lack in systematic quality management programmes for acute pain management.**

- **There is no single current standard of care for the treatment of pain in an emergency, with management based on severity of pain, injury and local protocols.**

- **There are currently no European Guidelines for the management of acute pain in an emergency situation, but national guidelines agree that pain management should be made available to all patients and implemented with the assistance of standardised scales and tools.**

- **Changing practices, attitudes and behaviour can be difficult, and improvements and interventions should be developed with barriers to pain management and the needs of the individual ED in mind.**

Figure 1.1 French Society for Emergency Medicine guidelines for trauma pain in spontaneously breathing adults[37]
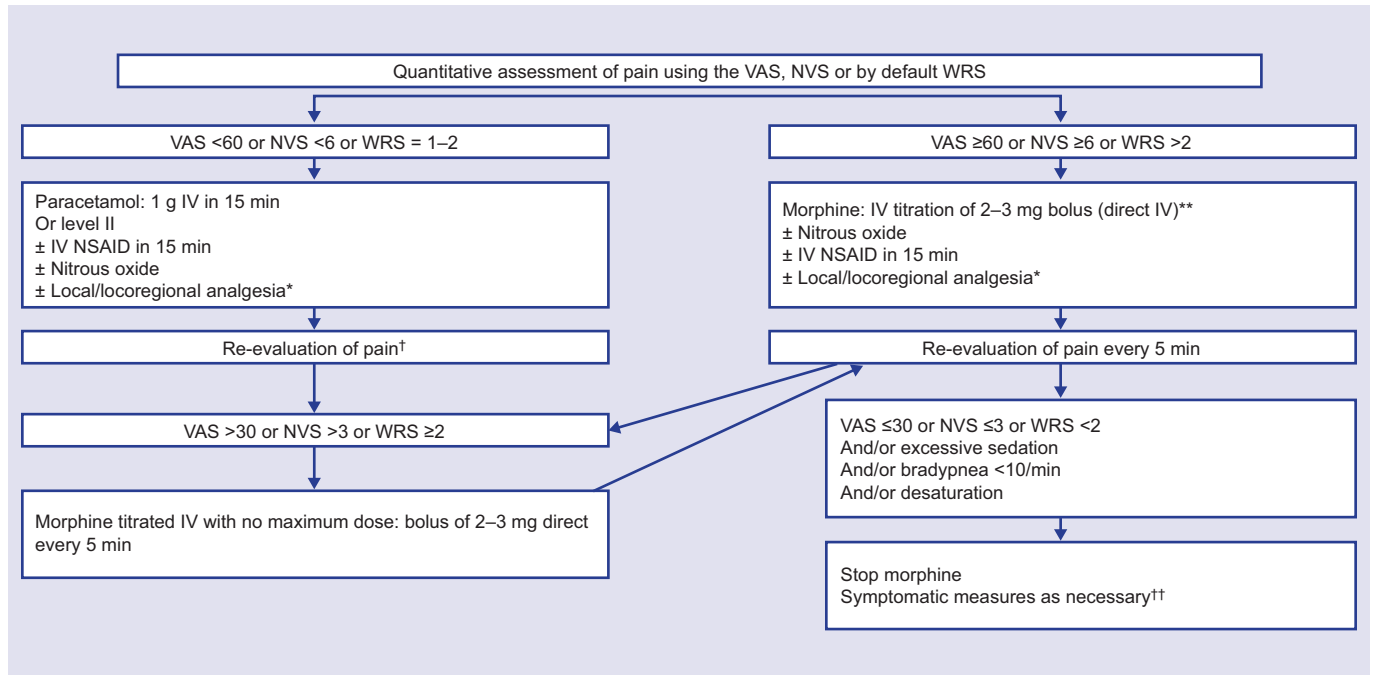
VAS, visual analogue scale; NVS, numerical value scale; WRS, word-graphic rating scale.
*Respecting contraindications of each molecule and/or technique
**Possible loading dose of morphine under constant medical supervision: initial bolus of 0.05-0.10 mg/Kg IV direct, adapted to the age and background of the patient; †Period for re-evaluation of pain dependant on the type of analgesic administered; ††Stimulation and/or ventilator support and/or IV naloxone
Reproduced with permission from *French Society for Emergency Medicine. Sédation et Analgésie en Structure d'Urgence*.[37]

Figure 1.2a Italian Intersociety recommendations on pain management in the ED setting[38]
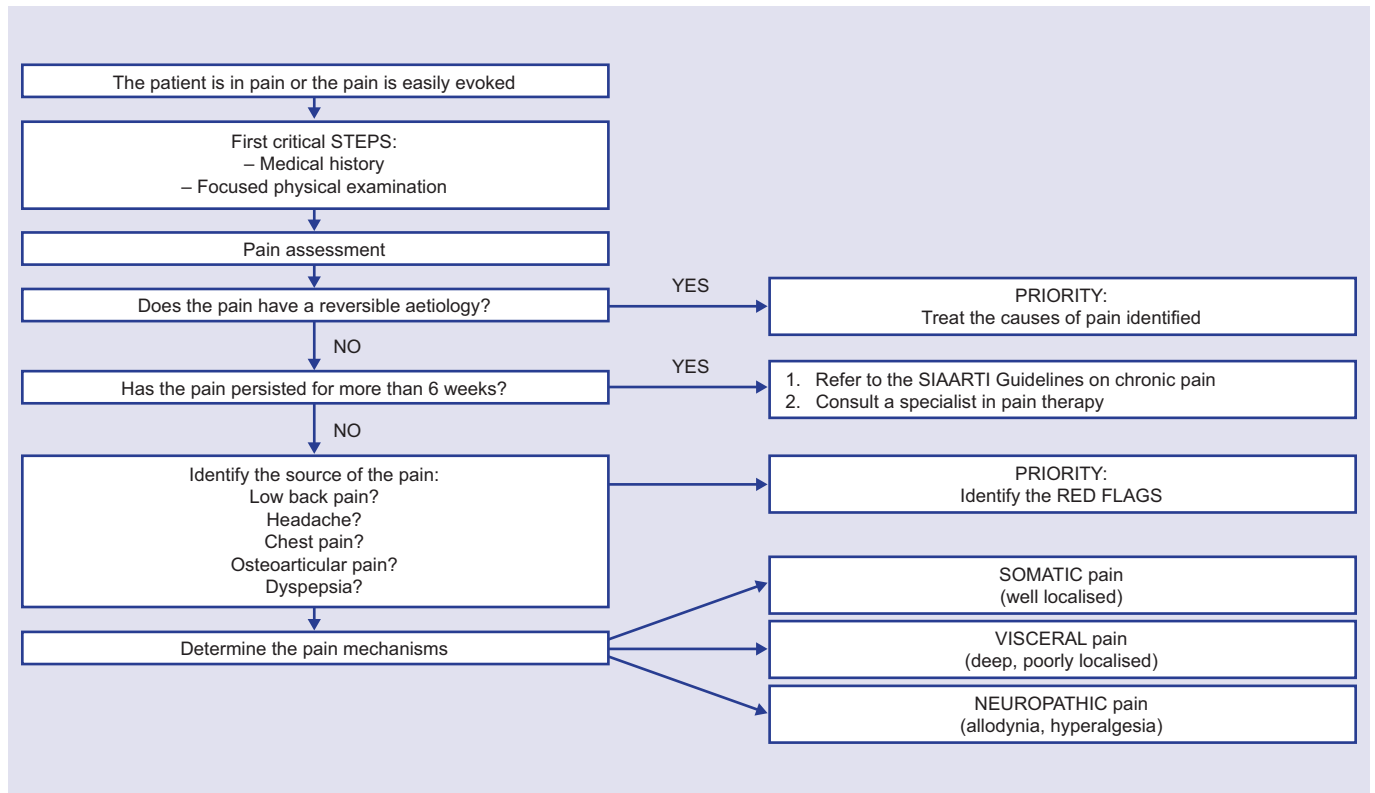
SIAARTI, Italian Society of Anaesthesia, Analgesia, Resuscitation, Intensive Care.
Reprinted with permission of Edizioni Minerva Medica from *Savoia et al. Minerva Anestesiol* 2015;81:205-25.[38]

Figure 1.2b Analgesic recommendations

| Level of pain	Analgesic treatment
NRS 1–3	**Adult patient** Oral/orodispersible paractetamol (1 g max 3 g per day) NSAIDs

	Pediatric patient (1–10 years)
	
	Paracetamol
	  – syrup (30 mg per 1 mL) 10–15 mg/Kg (repeatable every 6 hours)
	  – suppositories 10–15 mg/Kg (repeatable every 6 hours)
	
	Ibuprofen 4–10 mg/Kg (repeatable every 6 hours)

NRS 4–6	**Adult patient**
	
	Paracetamol IV 1 g (max 4g per day)
	
	Paracetamol in combination with weak opioids orally
	  – paracetamol/codeine 500/30 mg (repeatable every 6 hours)
	  – paracetamol/tramadol 325/37.5 mg (repeatable every 6 hours)
	
	NSAIDs

	Pediatric patient (1–10 years)
	
	Paracetamol IV 15 mg/Kg (repeatable every 6 hours). The maximum dose must not exceed 60 mg/Kg (not to exceed 2 g per day).
	
	Paracetamol/codeine:
	  – syrup (25/1.5 mg per 1 mL) 1 mL per 4 Kg of body weight (repeatable every 6 hours)
	  – suppositories 200/5 mg (repeatable every 8–12 hours)
	
	Tramadol (choose the lowest effective analgesic dose)
	  – drops (2.5 mg per drop) 1–2 mg/Kg. The maximum daily dose must not exceed 8 mg/Kg (not to exceed 400 mg per day)
	  – 1–2 mg/Kg IV

NRS 7–10	**Adult patient**
	
	Opioids
	  – morphine (initial dose 4–6 mg IV)
	  – fentanyl (initial dose 50–100 µg IV)

	Pediatric patient (1–10 years)
	
	Opioids
	  – morphine IV 0.05–0.1 mg/Kg (perform titration to the lowest effective dose
	  – fentanyl IV 1–2 µg/Kg

NRS, Numerical Rating Scale.
Reprinted with permission of Edizioni Minerva Medica from *Savoia et al. Minerva Anestesiol* 2015;81:205-25.[38]

Figure 1.3 Netherlands Association for Emergency Nurses algorithm for managing pain in the chain of emergency care in pre-hospital settings[39,40]
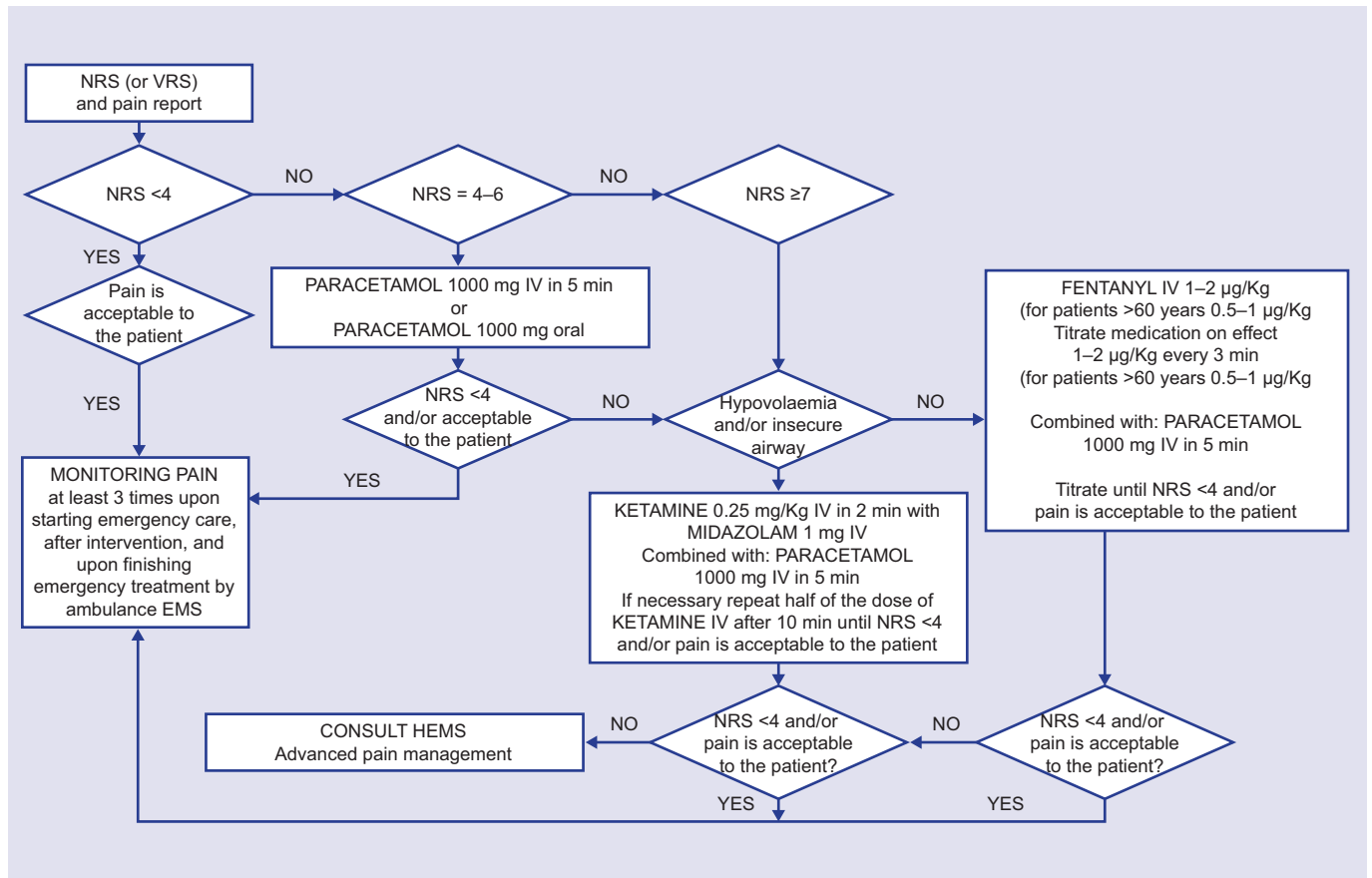
EMS, emergency medical services; HEMS, helicopter emergency medical services; NRS, Numerical Rating Scale.
Reproduced with permission from *Berben et al*.[39]

Figure 1.4 UK Royal College of Emergency Medicine best practice guideline on management of pain in adults[43]
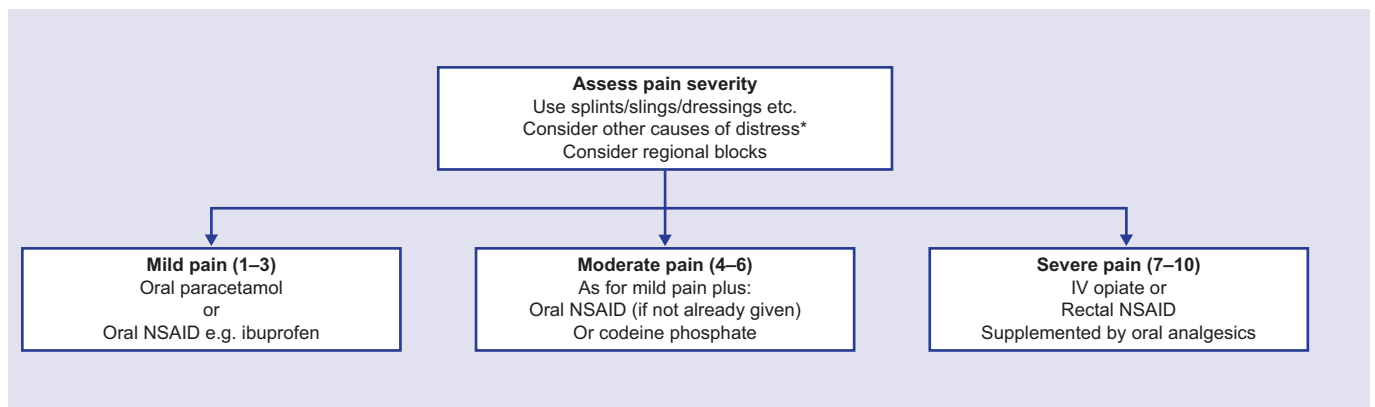
*For example, fear of the unfamiliar environment, needle phobia, fear of injury severity
IV, intravenous; NSAID, non-steroidal anti-inflammatory drug.
Reproduced with permission from *The Royal College of Emergency Medicine*.[43]

Figure 1.5a Republic of Ireland Pre-hospital Emergency Care Council clinical practice pain management guideline for adults for implementation by emergency technicians, paramedics and advanced paramedics[44]

| 4/5/6.2.6 Version 6, 07/2019 | Pain Management – Adult | EMT · P · AP |

Pain → Pain assessment

Analogue or Visual Pain Scale
0 = no pain……..10 = unbearable

Consider non pharmacological pain management techniques
- Splinting
- Psychological support
- Heat or cold therapy
- Positioning

Adequate relief of pain
- Yes or best achievable → Go back to originating CPG
- No → Implement pharmacology strategy at appropriate level on the pain ladder

If pain management not resolved — Request ALS

Consider Medical Support
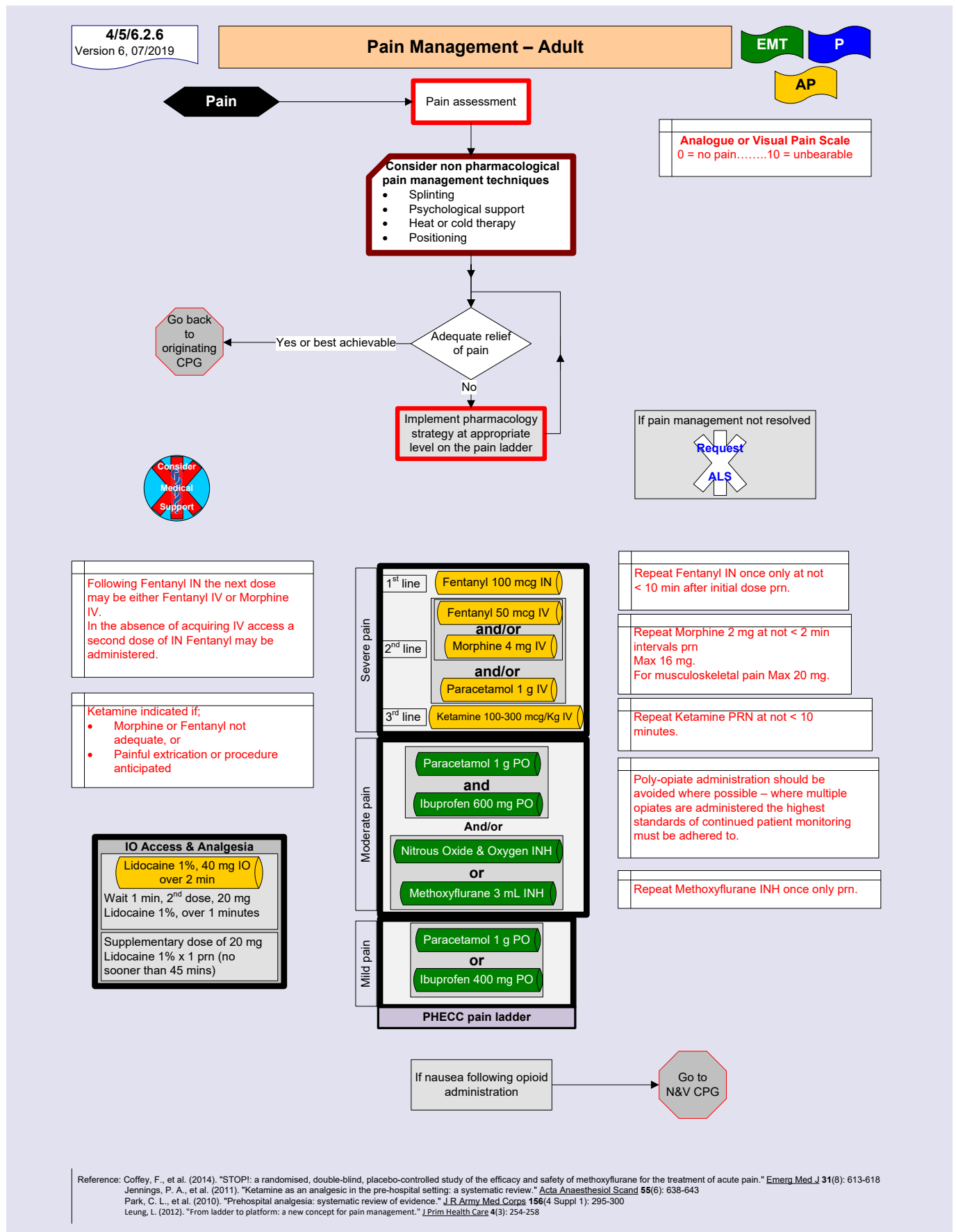
Following Fentanyl IN the next dose may be either Fentanyl IV or Morphine IV.
In the absence of acquiring IV access a second dose of IN Fentanyl may be administered.

Ketamine indicated if;
- Morphine or Fentanyl not adequate, or
- Painful extrication or procedure anticipated

IO Access & Analgesia
Lidocaine 1%, 40 mg IO over 2 min
Wait 1 min, 2nd dose, 20 mg Lidocaine 1%, over 1 minutes
Supplementary dose of 20 mg Lidocaine 1% x 1 prn (no sooner than 45 mins)

Severe pain
- 1st line: Fentanyl 100 mcg IN
- 2nd line: Fentanyl 50 mcg IV **and/or** Morphine 4 mg IV **and/or** Paracetamol 1 g IV
- 3rd line: Ketamine 100-300 mcg/Kg IV

Moderate pain
- Paracetamol 1 g PO **and** Ibuprofen 600 mg PO
- **And/or**
- Nitrous Oxide & Oxygen INH **or** Methoxyflurane 3 mL INH

Mild pain
- Paracetamol 1 g PO **or** Ibuprofen 400 mg PO

PHECC pain ladder

Repeat Fentanyl IN once only at not < 10 min after initial dose prn.

Repeat Morphine 2 mg at not < 2 min intervals prn
Max 16 mg.
For musculoskeletal pain Max 20 mg.

Repeat Ketamine PRN at not < 10 minutes.

Poly-opiate administration should be avoided where possible – where multiple opiates are administered the highest standards of continued patient monitoring must be adhered to.

Repeat Methoxyflurane INH once only prn.

If nausea following opioid administration → Go to N&V CPG

Reference: Coffey, F., et al. (2014). "STOP!: a randomised, double-blind, placebo-controlled study of the efficacy and safety of methoxyflurane for the treatment of acute pain." Emerg Med J **31**(8): 613-618
Jennings, P. A., et al. (2011). "Ketamine as an analgesic in the pre-hospital setting: a systematic review." Acta Anaesthesiol Scand **55**(6): 638-643
Park, C. L., et al. (2010). "Prehospital analgesia: systematic review of evidence." J R Army Med Corps **156**(4 Suppl 1): 295-300
Leung, L. (2012). "From ladder to platform: a new concept for pain management." J Prim Health Care **4**(3): 254-258

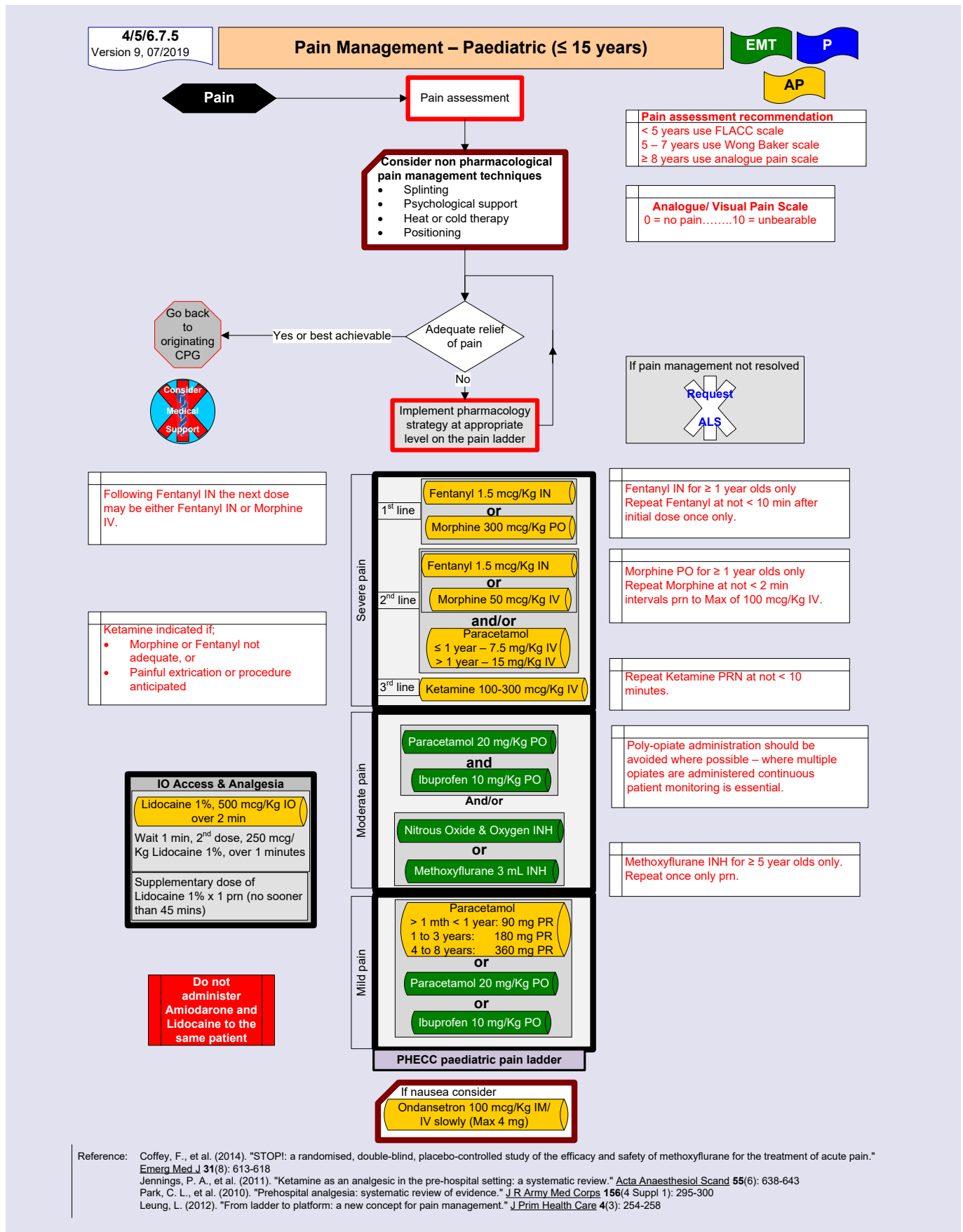ALS, advanced life support; AP, Advanced Paramedic; CPG, clinical practice guideline; EMT, emergency medical technician; IN, intransally; INH, inhaled; IO, intraosseous; IV, intravenously; N&V, nausea and vomiting; P, paramedic; PHECC, (Republic of Ireland) Pre-hospital Emergency Care Council; PO, orally (per os); PRN, as needed (pro re nata).
Reproduced with permission from the *Pre-Hospital Emergency Care Council*.[44]

Figure 1.5b Republic of Ireland Pre-hospital Emergency Care Council clinical practice pain management guideline for children for implementation by emergency technicians, paramedics and advanced paramedics[44]

4/5/6.7.5
Version 9, 07/2019

Pain Management – Paediatric (≤ 15 years)

EMT   P

AP

Pain

Pain assessment

Pain assessment recommendation
< 5 years use FLACC scale
5 – 7 years use Wong Baker scale
≥ 8 years use analogue pain scale

Consider non pharmacological pain management techniques
• Splinting
• Psychological support
• Heat or cold therapy
• Positioning

Analogue/ Visual Pain Scale
0 = no pain……..10 = unbearable

Go back to originating CPG

Consider Medical Support

Adequate relief of pain

Yes or best achievable

No

If pain management not resolved
Request ALS

Implement pharmacology strategy at appropriate level on the pain ladder

Following Fentanyl IN the next dose may be either Fentanyl IN or Morphine IV.

Severe pain

1st line
Fentanyl 1.5 mcg/Kg IN
or
Morphine 300 mcg/Kg PO

Fentanyl IN for ≥ 1 year olds only
Repeat Fentanyl at not < 10 min after initial dose once only.

2nd line
Fentanyl 1.5 mcg/Kg IN
or
Morphine 50 mcg/Kg IV
and/or
Paracetamol
≤ 1 year – 7.5 mg/Kg IV
> 1 year – 15 mg/Kg IV

Morphine PO for ≥ 1 year olds only
Repeat Morphine at not < 2 min intervals prn to Max of 100 mcg/Kg IV.

Ketamine indicated if;
• Morphine or Fentanyl not adequate, or
• Painful extrication or procedure anticipated

3rd line Ketamine 100-300 mcg/Kg IV

Repeat Ketamine PRN at not < 10 minutes.

Moderate pain

Paracetamol 20 mg/Kg PO
and
Ibuprofen 10 mg/Kg PO
And/or
Nitrous Oxide & Oxygen INH
or
Methoxyflurane 3 mL INH

Poly-opiate administration should be avoided where possible – where multiple opiates are administered continuous patient monitoring is essential.

IO Access & Analgesia
Lidocaine 1%, 500 mcg/Kg IO over 2 min
Wait 1 min, 2nd dose, 250 mcg/ Kg Lidocaine 1%, over 1 minutes
Supplementary dose of Lidocaine 1% x 1 prn (no sooner than 45 mins)

Methoxyflurane INH for ≥ 5 year olds only. Repeat once only prn.

Mild pain

Paracetamol
> 1 mth < 1 year: 90 mg PR
1 to 3 years: 180 mg PR
4 to 8 years: 360 mg PR
or
Paracetamol 20 mg/Kg PO
or
Ibuprofen 10 mg/Kg PO

Do not administer Amiodarone and Lidocaine to the same patient

PHECC paediatric pain ladder

If nausea consider
Ondansetron 100 mcg/Kg IM/ IV slowly (Max 4 mg)

Reference: Coffey, F., et al. (2014). "STOP!: a randomised, double-blind, placebo-controlled study of the efficacy and safety of methoxyflurane for the treatment of acute pain." Emerg Med J **31**(8): 613-618
Jennings, P. A., et al. (2011). "Ketamine as an analgesic in the pre-hospital setting: a systematic review." Acta Anaesthesiol Scand **55**(6): 638-643
Park, C. L., et al. (2010). "Prehospital analgesia: systematic review of evidence." J R Army Med Corps **156**(4 Suppl 1): 295-300
Leung, L. (2012). "From ladder to platform: a new concept for pain management." J Prim Health Care **4**(3): 254-258

ALS, advanced life support; AP, Advanced Paramedic; CPG, clinical practice guideline; EMT, emergency medical technician; FLACC, Face, Legs, Activity, Cry, Consolability (scale); IM, intramuscularly; IN, intransally; INH, inhaled; IO, intraosseous; IV, intravenously; P, Paramedic; PHECC, (Republic of Ireland) Pre-hospital Emergency Care Council; PO, orally (per os); PR, per rectum; PRN as needed (pro re nata). Reproduced with permission from the *Pre-Hospital Emergency Care Council*.[44]

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GUIDELINES FOR THE MANAGEMENT OF ACUTE PAIN IN EMERGENCY SITUATIONS

CHAPTER 2:

Principles of acute pain management

Principles of acute pain management

The proper and effective management of pain is generally understood to be both a right for all patients, and integral to the ethical practice of medicine.[1] The underlying causes of acute pain should always be treated first (where possible). The primary aim of acute pain management is to provide treatment that reduces a patient's pain with minimal adverse effects while allowing them to maintain function. A secondary aim is to prevent the chronification of pain.[2]

Both of these aims can be more effectively achieved if pain is adequately understood and assessed. Clinician validation of a patient's pain is invaluable to assessment of pain thereby contributing to effective analgesic planning. Assessment and proper evaluation of pain is associated with more effective treatment in the pre-hospital setting.[3] Assessment methods should be relevant to the individual patient; selection of a pain measurement tool should take into account any relevant developmental, cognitive, emotional, language and cultural factors.[1] Due to the subjective nature of pain, self-reporting should be used whenever it is appropriate. However, where this is not possible – for example when patients are unable to communicate verbally – this should not be interpreted as if the individual is not experiencing pain and does not require appropriate pain-relieving treatment.[4]

Pain should be addressed as early as possible, and always within a reasonable time frame.[5] What is considered 'reasonable' will vary according to the severity of pain, but ideally no more than 20 to 25 minutes should elapse from initial evaluation to the provision of pain relief (where appropriate).[5,6] Reassessment of pain should take place at a frequency guided by the patient's pain severity, with more frequent assessments as pain severity increases.[7] Particular care should be taken when assessing and treating paediatric and geriatric patients. Both groups are often subject to oligoanalgesia, primarily due to challenges in assessing pain (especially in very young children and older patients with dementia). In addition, difficulties in obtaining intravenous (IV) access in children and concerns about potential adverse events (AEs) in the elderly are also a concern.[5] With these groups, as with pain management in any patient, the personnel involved in care must successfully liaise and communicate efficiently in order to provide safe and effective acute pain management.[1]

At all stages during the acute pain management process, it is imperative for clinicians to reassure patients that their pain is understood and will be taken seriously. Relief of pain facilitates patient care, since severe pain can make it more difficult to perform important tasks related to clinical management such as taking a history or performing a physical examination. Amelioration of pain also has its own medical benefits, such as reducing pain-related tachycardia in a patient with cardiac complaints.[5]

Pathophysiology of pain

While unpleasant, the sensation of acute pain serves a useful function, providing a warning of actual or potential tissue damage resulting from a specific injury or disease. It is typically of limited duration.[8] Pain is the result of the

activation of free nerve endings by tissue damage or disease.[9] Mechanical, thermal or chemical mediators such as bradykinin, substance P, histamine and prostaglandins are released from the injury site, resulting in the generation of action potentials which travel along afferent nerves to the dorsal horn of the spinal cord. There they result in the release of neurotransmitters and neuropeptides that enable the action potentials to cross into the spinothalamic tract and then ascend to the thalamus and midbrain (**Figure 2.1**).[9-11] Nociceptive signals from the thalamus are transmitted to other areas of the brain including the cortex, limbic system and frontal and parietal lobes, and it is here that the action potentials are perceived as pain.[9] The experience of pain is subjective, and can be affected by emotional factors. Stress, anxiety and apprehension – all inherently associated with trauma situations – can enhance the perception of pain.[12]

Importance of effective pain management

Providing effective management of acute pain is important from the human perspective because one is providing

Figure 2.1 The pain pathway

relief from suffering. Improving patient comfort is an endpoint in itself.[5] Another, more pragmatic reason why providing appropriate analgesia is important, is that untreated or undertreated acute pain is associated with significant negative consequences, including the risk of pain chronification, delayed recovery (with an associated increased risk of infection), impaired sleep, reduced mobility and poorer quality of life.[13] Other potential outcomes of delayed or ineffective analgesia include impaired immunity, increased hospital re-admission rates, psychological impacts such as post-traumatic stress disorder, tachycardia, hypertension, increased myocardial oxygen demand, hyperglycaemia, insulin resistance, changes in fat and protein metabolism, and coagulopathies.[1,9,10,13] Control of acute pain after an initial injury can prevent the transition from normal peripheral acute pain to maladaptive sensitisation of the nervous system, which could otherwise result in chronic pain syndromes that may persist for years.[14] The chronification of pain in patients with acute pain is not rare – it occurs with varying prevalence in different categories of trauma patient, from 11% in patients with simple distal fractures of the radius, to as high as 96% in patients with spinal cord injury.[14] Avoiding the transition from acute to chronic pain is therefore an important goal. Where appropriate, a multimodal analgesic approach, using different targeted pharmacological therapies (including both opioid and non-opioid analgesics) at various time points with varying mechanisms of action and differing delivery routes, may optimise outcomes in the treatment of acute pain and help to prevent chronic pain.[15]

In addition to prevention of chronic pain, evidence has consistently shown that effective pain management can improve other short- and long-term outcomes in the ED, including sleep, physical function, quality of life and prevent the development of longer term chronic pain.[13,16,17] It is important that analgesia be provided promptly, minimal delays in analgesic administration are known to be associated with shorter ED stays.[18] In a Canadian post-hoc analysis of real-time data, patient stay in the ED was dependent on the interval length between admission and analgesic administration. Length of stay could be shortened by a median of 1.6 hours if analgesia was received within 90 minutes compared with time after ≥90 minutes, regardless of whether patients were subsequently discharged (p<0.001) or admitted to hospital from the ED (p<0.05).[18]
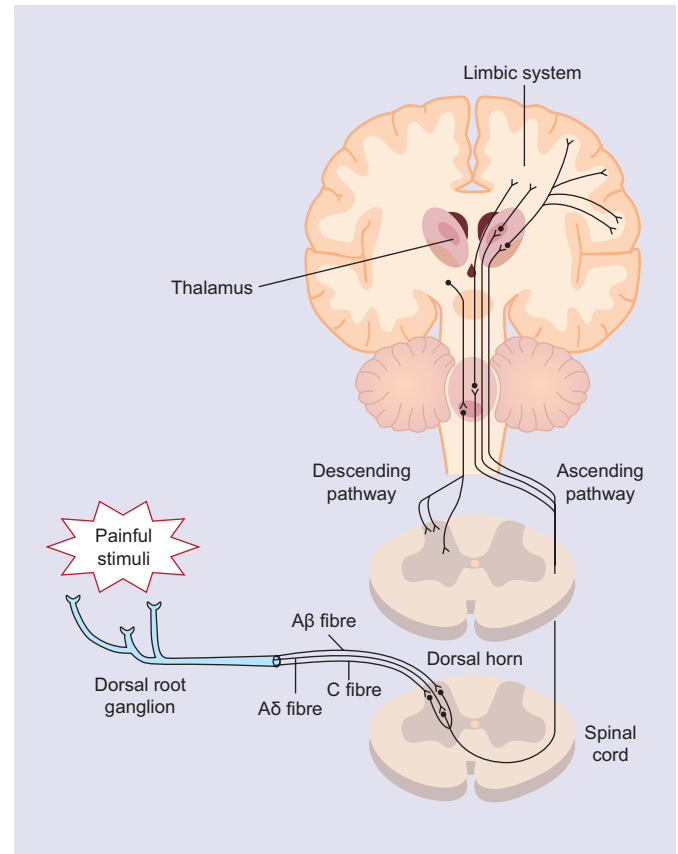
Management of pain according to the World Health Organisation (WHO) pain relief ladder

Evidence suggests that implementation of guidelines for management of acute pain in the emergency setting leads to improved pain management.[19] In a Swiss interventional study, the frequency of pain assessment, the frequency of use of analgesia and the total dose of analgesia administered all increased following the adoption of simple clinical guidelines on the treatment of pain from any cause by ED staff, resulting in higher levels of pain relief and patient satisfaction with pain management.[19]

However, in the absence of relevant or specific guidelines, the WHO pain relief ladder, which was originally designed for cancer pain, is widely accepted as a guide for the management of acute pain (**Figure 2.2**).[20,21] The WHO pain relief ladder provides a stepped approach to the management of cancer pain in which, if pain occurs, there should be prompt oral administration of drugs until the patient is free of pain.[20] Adjuvants (including antidepressants, anticonvulsants and glucocorticoids) can be used in conjunction with analgesics for pain management or to mitigate physiological processes that can perpetuate or exacerbate pain, such as oedema, swelling, anxiety and muscle contraction or spasticity.[21] To maintain freedom from pain, drugs should be given at regular intervals in accordance with their pharmacological characteristics – a 'by the clock', rather than an 'on demand as pain arises' administration. Surgical intervention on appropriate nerves may be used to provide further pain relief if drugs are not entirely effective.[20]

Since the initial publication of the WHO pain relief ladder in 1986, a number of modifications have been proposed to adapt the ladder to different types of pain, such as acute pain, and to take into account recent developments in analgesia such as nerve block techniques and sublingual and transdermal opioids.[22,23] In patients with acute pain it may be more appropriate to use the pain relief ladder in reverse, so that patients in severe acute pain begin with strong opioids, then as the pain resolves analgesia is reduced to weak opioids, and finally to non-opioids until pain is managed.[23]

Figure 2.2 The World Health Organization pain relief ladder[20]
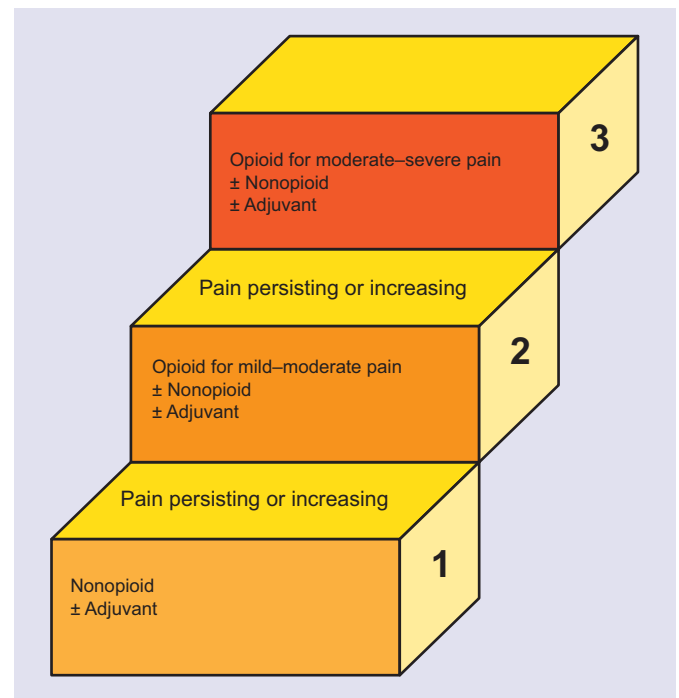
Principles of acute pain management: take-home messages

- **Proper and effective pain management is a right of all patients experiencing pain. The key aim is to reduce pain, maintain function and minimise adverse effects.**

- **Acute pain is generally associated with injury and is of limited duration. It results from the activation of nerve endings at the site of tissue damage.**

- **Appropriate and adequate validation of the patient's pain and pain assessment is vital to effective pain management.**

- **Effective pain management can improve long-term outcomes, while untreated or undertreated acute pain is associated with significant negative impact. Long-term chronic pain may result if acute pain is not adequately controlled.**

- **The WHO pain relief ladder provides a general guide to pain management, though further modifications to the original model may be required to make it fully applicable to acute pain management.**

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GUIDELINES FOR THE MANAGEMENT OF ACUTE PAIN IN EMERGENCY SITUATIONS

CHAPTER 3:

Assessment of pain

Importance of effective pain assessment

Reliable and accurate assessment of acute pain is necessary to allow the provision of safe, effective and individualised pain management. It assists the diagnosis of the source of the pain, the selection of an appropriate analgesic and the monitoring of the response to that therapy.[1]

Pain perception is subjective and individual, which can present a challenge to healthcare professionals when it comes to understanding the degree of pain that a patient is experiencing. Self-reporting of pain should be used where possible, as proxy ratings of pain have been shown to underestimate high pain levels in some studies.[2] When selecting the pain measurement tool(s) to be used in assessing pain, the healthcare provider should take into consideration all relevant factors relating to the individual patient: developmental, cognitive, emotional, language and cultural.[1]

Reassessment of pain is as important as the initial assessment, and should take place at a frequency guided by the patient's pain severity.[3] Patients in the ED prefer pain assessment to take place approximately every 15 minutes, with more frequent assessments when pain is severe.[4] Automated pain tracker devices based on tablet computers provided to patients in the ED may be helpful to promote regular pain assessment, with a pilot project suggesting that these automated systems can improve pain care, efficiency and pain assessment documentation, and that patients find them easy to use.[5] It is important that pain assessment is done in real time, as it has been shown that patients do not accurately recall their pain levels retrospectively, even just one to two days after acute trauma.[6]

This chapter reviews the tools and scales used to assess and monitor pain in patients with acute pain in an emergency setting.

Effective patient pain history

The first element to effective pain assessment and management is an effective patient history. As a first step, clinicians should reassure patients that their pain will be taken seriously and that the impact of their pain and its requirement for treatment is understood. Respectful validation of a patient's suffering is invaluable to assessment and will lead to effective analgesic planning. It is important to ensure that careful attention is paid to the patient's reported symptoms in order to direct the process of the physical examination and lead towards a pain differential diagnosis. During the pain history, an understanding of the following is required: location of pain; temporal characteristics; aggravating and alleviating factors; impact of pain on function and quality of life; past treatment and reports; and also patient expectations and goals for their pain *(for more information see Chapter 6 – Pain Management, Table 6.1, see page 61)*.

Categorical pain scales

Categorical scales use words to convey the degree of pain or pain relief. A verbal descriptor scale is the most commonly used type of categorical pain scale.[1] This type of scale typically includes four to five descriptors from 'no pain' through to 'excruciating/agonising pain' (or similar terminology), which can be converted to numeric scores for the purposes of recording a pain rating and comparison of a patient's pain over time. Pain relief (rather than pain intensity) can also be graded using a verbal descriptor scale. The benefit of categorical scales is that they are quick and simple to use; however, they are less sensitive than numerical scales due to the reduced number of possible options.[7,8] They also rely on the patient correctly interpreting and understanding the descriptor words, so may not be suitable for all patients, particularly where there is a language barrier.

Numeric rating scales

Numeric rating scales (NRS) can be delivered verbally or in a written format. In either format, patients are asked to rate the intensity of their pain according to an 11-point scale of 0 (no pain) to 10 (worst pain imaginable) (**Figure 3.1**).[8,9] Mild pain would be considered as a pain score of 1–3, moderate pain a score of 4–7 and severe pain a score of >7.[10] Patients may be asked to rate their average pain over the past 24 hours or week, but the results are most accurate when the scales are used to record the patient's impression of their current pain intensity.[6]

Figure 3.1 The numeric rating scale (NRS-11)

0 1 2 3 4 5 6 7 8 9 10

0 = no pain   10 = worst pain imaginable

Visual analogue scale

The visual analogue scale (VAS) is the most commonly used scale for rating pain intensity in clinical trials.[1] It takes the form of a 100 mm/10 cm horizontal line, the left end of which is defined as 'no pain' and the right end as 'worst possible pain', with no other tick marks along the length of the line (**Figure 3.2**)[9]. The patient marks the point along the line that they feel corresponds to the level of pain that they are experiencing, and the pain score is recorded as the measurement in millimetres or centimetres from the left end of the scale to the patient's mark. The VAS has similar sensitivity to the NRS when comparing acute postoperative pain intensity, and a greater sensitivity than a 4-category verbal descriptor scale.[7] A VAS rating of more than 70 mm is predictive of the need for a high (e.g. >0.15 mg/Kg) morphine dose to achieve pain relief, and can be considered indicative of severe pain.[11] A reduction in pain intensity of 30%–35% on the VAS has been rated as clinically meaningful by patients with acute pain in the ED.[12] When the VAS is used in clinical practice in the ED, displaying a patient's changing pain scores as a graph over time, it may lead to increased physician awareness of pain scores and the need for earlier analgesia, as well as greater patient satisfaction with pain care.[13]

Figure 3.2 The visual analogue scale (VAS)

Least possible pain   100 mm/10 cm   Worst possible pain
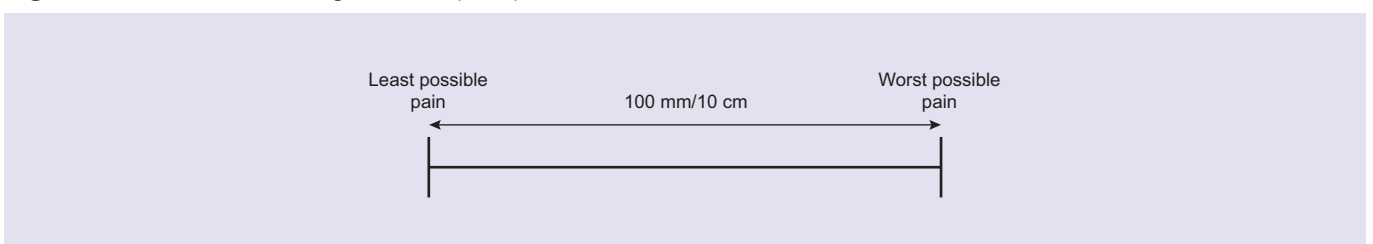
Assessments of functional impact of pain

The functional activity scale (FAS) is a simple 3-level categorical score used to assess whether a patient can undertake appropriate activity at their current pain level and trigger retreatment if activity is curtailed by pain.[1] The patient is asked to complete a particular activity or is assisted in doing so, and their ability to do so is assessed as A (no limitation due to pain), B (mild limitation, with the patient able to complete the activity but experiencing moderate to severe pain in the process) or C (significant limitation, where the patient is unable to complete the activity due to pain). The patient's FAS score can then be used to assess the effectiveness of pain treatment on function. However, this scale has not yet been independently validated.[1]

Assessment of pain in special situations

It is important to recognise that impaired or limited ability – or indeed, complete inability – to communicate verbally does not mean that an individual is not experiencing pain and in need of appropriate pain-relieving treatment.[14] Special consideration must therefore be given to the assessment of acute pain in babies and young children, the elderly (particularly those with dementia) and unconscious or sedated patients.[14] Other circumstances that pose a particular challenge when assessing pain include breakthrough pain in cancer patients or those with chronic non-cancer pain, and in patients with a history of, or current, drug misuse.

Paediatric patients
Evidence suggests that children who present to the ED receive suboptimal assessment and relief of pain, partly due to a failure to use appropriate pain assessment tools.[15] However, a range of paediatric pain rating scales have been developed and are available for use in children from neonates up to adolescence (at which stage adult rating scales can be used).[16]

Scales for the assessment of the intensity of acute pain in neonates include the Premature Infant Pain Profile (PIPP), the CRIES (C-Crying; R-requires increased oxygen administrations; I-increased vital signs; E-expression; S-Sleeplessness) the Neonatal Facial Coding Scale (NFCS).[16] Since such young babies are unable either to communicate verbally or to understand and follow instructions, these scales rely on observations of variables such as the presence or absence of crying, facial expression, heart rate and other vital signs.[16] Another commonly used pain scale which does not rely on the ability of the patient to communicate with the assessor is the FLACC scale. This can be used to assess pain in children between the ages of two months and seven years, in children with cognitive impairment,[17] or in individuals of any age that are unable to communicate their pain.[18] The FLACC scale has 5 criteria (facial expression, position/movement of legs, overall activity, presence/degree of crying, and ability to be consoled or comforted) which are each assigned a score of 0, 1 or 2, giving a total score in the range of 0–10, with 0 representing no pain.[18] A modified version of the FLACC scale, FLACC-R has been developed for children with cognitive impairment.[19]

For those patients with some, albeit limited, ability to communicate, such as young children, the FACES pain scale (FPS) can be very useful (**Figure 3.3**).[20] Patients are shown a range of faces showing varying degrees of distress, and asked to select the expression that corresponds to the amount of pain that they are currently experiencing.[20]

### *Geriatric or cognitively impaired patients*
Pain is generally underreported in the elderly, even those with normal cognition.[21] Identifying and measuring pain in cognitively impaired elderly individuals is an even greater challenge.[22] Nonetheless, it is of great importance since it is estimated that up to one-half of people with cognitive impairment also suffer from pain,[23] and untreated pain in the elderly leads to increased disability and decreased quality of life.[21,24]

Evidence is available to support the reliability and validity of many assessment tools that use patient self-reporting, even in older people with mild-to-moderate cognitive impairment,[25-27] and it is recommended that these should be used wherever possible.[23] Opinion is divided as to whether self-reporting tools can be successfully used in those with advanced cognitive impairment.[22,28] Several of the pain scales used in younger adult populations or children are

Figure 3.3 Wong-Baker FACES scale (FPS)[20]
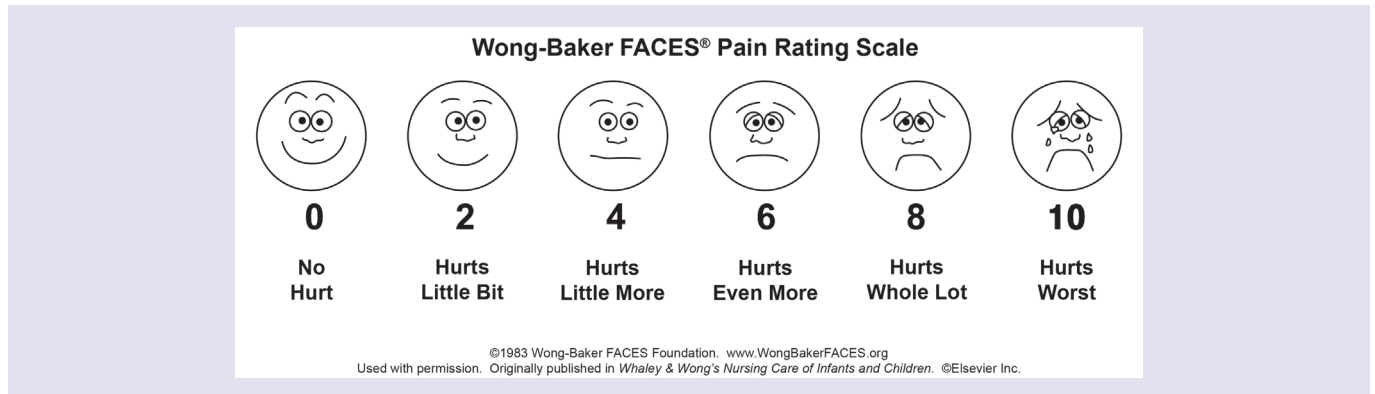
Reproduced with permission from Wong-Baker FACES Foundation http://www.WongBakerFACES.org.[20]

appropriate in elderly patients, including verbal descriptor scales, the NRS and the FPS. Of these, verbal descriptor scales have been shown to be most sensitive and reliable in older adults, including those with mild-to-moderate cognitive impairment.[29]

A number of different specialist pain assessment tools are available for use in non-verbal older adults with dementia.[30] The PAINAD scale is an observer-rated tool for assessing pain-related behaviour, and is partly based on the FLACC scale. It consists of five items: breathing, negative vocalisation, facial expressions, body language and consolability. Each item can be rated from 0 to 2, to generate a score ranging from 0 to 10.[24] Other physiological signs that can give a useful indication of the presence of pain in elderly patients – particularly those with cognitive impairment – include hypertension, tachycardia or bradycardia, sweating and increased muscle tone.

Sedated or unconscious patients

Assessing pain in patients who are critically ill is a challenge, particularly where patients are non-verbal due to sedation or lack of consciousness.[31] This is especially true in the pre-hospital setting, where altered mental state is the main risk factor for patients receiving no pain assessment.[32] The behavioural pain scale (BPS) has been validated for use in critically ill, sedated and mechanically ventilated patients (**Table 3.1**). The BPS score is calculated as the sum of three subscales (facial expression, upper limb movements and compliance with mechanical ventilation), each with a score ranging from 1 to 4.[31] Of the pain scales developed for use in adult patients under intensive care, the BPS is considered to be one of the most valid and reliable.[31,33]

Table 3.1 The behavioural pain scale (BPS)[31]

Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (e.g. brow lowering)	2
	Fully tightened (e.g. eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation for most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

Reproduced with permission from *Payen et al*.[31]

Breakthrough pain

Breakthrough pain is defined as 'a transient exacerbation of pain that occurs either spontaneously or in relation to a specific predictable or unpredictable trigger despite relative stable and adequately controlled background pain'. It occurs in patients with cancer at a rate of ~60%,[34] but evidence relating to its prevalence in chronic non-cancer pain is currently lacking. Breakthrough pain impacts patients' ability to function, as well as their mood and quality of life.[35] A diagnostic algorithm has recently been developed to diagnose breakthrough cancer pain,[36] but tools such as these should be used in conjunction with detailed clinical assessment and, importantly, with information from patients and their carers.[37,38]

Pain in patients with active or previous drug misuse

A challenge in the ED is patients seeking opiates who report pain. For these patients, it is essential to differentiate between the patient with genuine pain and those falsely reporting pain only to gain medication. It is recognised that patients who are seeking opiates will present with very plausible pain symptoms and discriminating the patient's report from the patient's clinical symptomology can be difficult. Features of patients seeking opiates falsely reporting pain may include: repeated visits to the ED; cutaneous signs of drug abuse (e.g. skin tracks from IV or subcutaneous [SC] injections); assertive or aggressive patients who may be emotionally labile; current intoxication; an unusual level of knowledge about controlled substances; a very 'textbook' medical history or evasiveness/vagueness in response to questioning; reluctance to provide additional information (e.g. primary care practitioner details); and requests for a specific controlled drug with no interest in or reluctance for other suggested medications. Clinical judgement, experience and careful observation – particularly when the presenting patient believes that they are not being observed by healthcare professionals – can help to distinguish between genuine patients and opiate-seeking individuals.

Other assessments in patients in the ED

Besides pain intensity, a number of other factors can affect a patient's requirement for analgesia; for example, the degree of consciousness or level of agitation. In order to determine the analgesic needs of patients with trauma pain within the ED, several scales assessing factors other than pain are often used to evaluate patients. The Glasgow Coma Scale (GCS) was developed to assess the depth and duration of impaired consciousness and coma. It evaluates consciousness and neurological function using a numerical scale for a range of behavioural parameters (eye opening, verbal response, motor response).[39] The Ramsay Scale includes six levels of sedation, three relating to a conscious patient, and three to a sleeping patient. Patients are scored according to their levels of alertness and agitation, from level 1 (patient awake, anxious, agitated or restless) to level 6 (patient asleep, with no response to stimulus).[40] The Richmond Agitation Sedation Scale (RASS) is a 10-point sedation scoring system which evaluates patients based on observation of their level of alertness and behaviour, and according to their responses to verbal cues and (if unresponsive to verbal cues) physical stimulation. Scores range from +4 (combative, violent) to −5 (unrousable, unresponsive), with a score of 0 indicating an individual demonstrating alert calm.[41]

Assessment of pain: take-home messages

- **Regular, accurate assessment of pain is required to improve acute pain management.**

- **For adults and children able to verbalise their pain NRS and VAS pain scales are recommended.**

- **In patients who are non-verbal, such as young children age appropriate observational scales can be used for example Wong-Baker FACES scale, FLACC and CRIES and for those with cognitive impairment FLACC-R.**

- **In adult patients with mild cognitive impairment patient self-reporting should be considered. In patients with more severe impairment observational scales such as Wong-Baker FACES scale may be appropriate but consider the use of specific scales such as PAINAD which is based on the FLACC scale and is fully validated.**

- **In unconscious or sedated patients, the use of the observational BPS should be considered – this scale was developed and validated for use in critically ill, sedated, mechanically ventilated patients.**

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GUIDELINES FOR THE MANAGEMENT OF ACUTE PAIN IN EMERGENCY SITUATIONS

CHAPTER 4:

Non-pharmacological therapies in acute pain

Current non-pharmacological therapeutic options in acute pain

While pharmacological analgesics are essential for the management of pain in the ED, the place and importance of non-pharmacological treatments should not be overlooked.[1] Such therapies are increasingly being used alone or in combination with pharmaceutical agents as part of a multimodal approach to managing pain. This chapter reviews the main non-pharmacological therapies currently available to manage acute pain. Published clinical evidence on the use of these therapies in a pre-hospital or ED setting is limited in some cases; what evidence is currently available is presented in **Table 4.1** (*see page 29*).

Psychological interventions

Sharing information

Providing patients with procedural information (a summary of what will happen during a treatment) and sensory information (a description of the sensory experiences that a patient might feel during treatment) appears to positively affect outcomes and leads to reductions in reported pain and pain medication requirements, improvements in postoperative recovery, and reductions in length of hospital stay.[2,3] A Cochrane review of studies testing preoperative psychological interventions such as sharing information included a meta-analysis of 38 studies measuring the effect of these strategies on postoperative pain. Psychological preparation techniques were associated with lower postoperative pain, with similar results across all techniques used.[2] However, the level of evidence available was low with a high potential for bias, and it came primarily from studies in adults undergoing elective surgery, rather than the emergency setting.[2]

It should also be considered that, for some patients, receiving too much detailed information may increase anxiety, so the approach to sharing information might have to be adjusted according to the individual patient's coping strategy.[4]

Relaxation (stress and tension reduction)

The use of relaxation training can help patients to reduce stress and tension through techniques such as focussing on breathing patterns, concentrating on mental imagery of relaxing scenes and gradually releasing of muscle tension throughout the body. Music often forms an important part of the relaxation process. There is some evidence to suggest that the use of relaxation techniques can reduce anxiety and pain,[5-10] although once again the setting for these studies is generally postoperative pain relief rather than emergency analgesia. Indeed, relaxation techniques generally require practice on the part of the patient,[4] and may therefore have limited immediate use in an emergency situation. They may, however, be of value later when the patient is recovering.

Hypnosis

Hypnosis has a long history of use in acute pain conditions.[11] In the past, the design of studies on the use of hypnosis in acute pain lacked scientific rigour. However, there are some randomised clinical trials (RCTs) that report a significant

effect of hypnosis on acute procedural pain as well as chronic pain conditions.[12] A review on the use of hypnosis to relieve pain in clinical settings (including invasive medical procedures, burns wound care, labour and bone marrow aspiration) provided moderate support for the use of hypnosis in the treatment of acute pain.[12] In 12 of 19 studies reviewed, hypnosis was more effective in reducing pain scores than the comparator treatments which included no treatment, standard care or other psychological interventions.[12]

Similarly, a meta-analysis of 18 studies of hypnotically induced analgesia, that included 933 participants, revealed a moderate to large effect of hypnosis on pain, supporting the efficacy of hypnotic techniques for pain management.[13] Types of pain included burn, coronary pain and headache, as well as experimental pain stimuli such as cold and focal pressure.[13]

Evidence from studies in paediatric cancer patients undergoing lumbar puncture and venepuncture suggests that the addition of hypnosis to the use of analgesic cream results in less pre-procedural anxiety and less procedural pain and anxiety.[14,15] However, an RCT in children with acute burns undergoing dressing changes found that although hypnosis was able to decrease pre-procedural anxiety and heart rate it did not significantly reduce pain intensity or accelerate wound healing.[16]

Attention control methods

Attention-based techniques to control pain include distraction techniques, concentration on imagined scenes or sensations, focus on external stimuli such as music or odours, or techniques to change the patient's emotional state to a more peaceful and comfortable one.[4] Attention control techniques including the use of imagery, music and jaw relaxation have demonstrated benefits in acute postoperative pain in a number of older studies.[17-19] In a laboratory-based study, distraction led to lower intensity of acute pain induced by a thermode in 109 female participants.[20] In a systematic review of 42 RCTs, distraction using music reduced perioperative pain and anxiety in approximately half of the studies included.[21]

In children, distraction therapy can be very effective and is a technique often used in paediatric medicine. Distraction may include controlled breathing (blowing an imaginary balloon or feather or using physical items like blow pipes), books appropriate to the child's age, games and puzzles, either listening to or singing along with music, and toys, such as touch and feel toys or finger puppets.[21-24] A systematic review of 59 studies with 5,550 participants concluded that distraction is effective in needle-related procedure-related pain in children and adolescents aged between 2 and 19 years.[24]

For babies, breastfeeding or bottle feeding of sugar sweetened water can be effective, as can non-nutritive sucking on pacifiers or non-lactating nipples. In older children, distraction may be possible through coaching or coping statements, watching video, playing video games or virtual reality.[25] Interactive distractions such as playing video games are more beneficial than passive distractions like watching videos.[25] Virtual reality is emerging as a potentially effective technique to distract patients from pain.[26] It has been used successfully in an RCT in endoscopic urological surgery and found to be comparable to midazolam sedation in mitigating pain during surgery.[22]

Cognitive behavioural intervention

Cognitive behavioural therapy (CBT) is a psychological technique that includes cognitive and behavioural modifications of specific activities to reduce the impact of pain and disability and overcome barriers to physical and psychosocial recovery.[27] Interventions aim to reduce the distressing or threatening nature of pain and enhance a patient's sense of confidence to cope with it.[4] In chronic pain conditions such as subacute chronic neck pain and lower back pain, CBT is commonly used and there evidence of moderate strength to suggest that it has beneficial effects on pain, disability and quality of life in these conditions.[27,28] The intervention has also been successfully used in the management of postoperative and procedural pain.[4] However, there is currently little evidence on the use of CBT to address acute pain in a pre-hospital or ED setting.

Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation (TENS) is a treatment that relieves pain by administering pulsed electrical currents across the intact surface of the skin to selectively stimulate non-noxious, low-threshold afferent peripheral nerve fibres in the skin. This is claimed to inhibit transmission of nociceptive information at the level of the spinal cord.[29] While a 1996 systematic review concluded that TENS did not have a significant analgesic effect on acute postoperative pain,[30] there is more recent evidence from a meta-analysis that high-intensity TENS can significantly reduce requirements for postoperative analgesia.[31] This analysis included 21 randomised, placebo-controlled trials with a total of 1,350 patients, and reported that the mean reduction in analgesic consumption following treatment was 26.5% less than placebo. In 11 of the 21 trials (n=964), high intensity stimulation was used, and in this subgroup of studies the mean reduction in analgesic consumption following treatment was 35.5% less than placebo.[31]

A Cochrane review of TENS for acute pain of less than 12 weeks' duration, including procedural pain and acute trauma such as sprains or fractures, included 19 studies and 1,346 participants.[29] The review indicated that TENS, administered as a stand-alone treatment for acute pain in adults, reduced pain intensity more than that see with placebo. Patients receiving TENS were nearly four times more likely to achieve at least a 50% reduction in pain than those given placebo.[29] However, the quality of the data was poor, and there was significant heterogeneity between trials and high risk of bias and unblinding.

A systematic review and meta-analysis of the effectiveness and safety of TENS administered to patients with acute pain in the pre-hospital setting analysed data from four RCTs in acute renal colic, acute lower back pain, traumatic hip pain and pelvic pain.[32] All studies included found that TENS led to statistically and clinically significant reductions in pain severity (pooled data: reduction in the mean VAS pain severity of 38 mm; p<0.0001). TENS also resulted in reduced patient anxiety.[32]

Acupuncture and related techniques

Acupuncture is a well-known traditional therapy that has been used in China for pain and other conditions for over 3,000 years.[33] More recently, acupuncture has demonstrated effectiveness versus sham for acute postoperative pain in a systematic review of RCTs, in terms of pain intensity, opioid use and some opioid-related side effects.[33] Fifteen trials comparing acupuncture with sham control in the management of acute postoperative pain were included. Significant differences on the visual analogue scale (VAS) were seen at 8 hours and 72 hours, and the weighted mean difference for cumulative opioid analgesic consumption for acupuncture versus sham was −9.14 mg at 72 hours.[33]

There are no studies on the use of acupuncture in the pre-hospital setting. This is likely to be due to obvious logistical concerns around transporting and handling patients undergoing the procedure. The related technique of acupressure (applying pressure to specific relaxation points) has, however, been demonstrated to reduce pain and anxiety during ambulance transport after minor trauma in two randomised, double-blind studies by the same group.[34,35] In the first of these trials, patients being transported to hospital for minor trauma were randomised to 'true' acupressure, acupressure using sham pressure points and no acupressure. Upon arrival at the hospital, pain and anxiety scores were significantly lower in the true acupressure group, and overall satisfaction was higher.[34] The second trial focussed on patient anxiety, and found that patients receiving acupressure during ambulance transport were less anxious, anticipated less pain from treatment at hospital and were more optimistic about their outcomes.[35]

Other approaches

Ultrasound

Ultrasound consists of high frequency sound waves directed at a specific site on the body to produce an image or to stimulate the tissue for therapeutic purposes. Ultrasound is frequently used in an emergency setting, but more often in a diagnostic or therapy-guiding capacity (e.g. ultrasound-guided nerve block) than in a therapeutic one.[36,37] While evidence exists on the use of ultrasound in the treatment of pain with acute fractures, a systematic review of 12 studies

reported no difference in pain scores between ultrasound and placebo groups at eight weeks.[38] In addition, it was noted that the quality of the studies varied considerably in terms of design, quality and risk of bias, making it difficult to draw conclusions from the analysis.[38]

Cold and heat

Cryotherapy is defined as the therapeutic application of a substance (e.g. ice pack or coolant spray) to the body that removes heat from the body, resulting in decreased tissue temperature, while heat therapy is the therapeutic application of a substance (e.g. heat wrap, bath) to the body that adds heat, resulting in increased tissue temperature.[39] The physiological effects of cryotherapy include reductions in pain, oedema, inflammation and muscle spasm, while the physiological effects of heat therapy include relief from pain and increases in blood flow and elasticity of connective tissues.[40]

There is limited evidence from RCTs to support the use of cryotherapy following acute musculoskeletal (MSK) injury.[40] In one pilot study, patients with an acute tear to the gastrocnemius muscle were randomised to receive either repeated application of crushed ice or no ice treatment. No significant differences in functional capacity, convalescence time, absence from work or pain score were seen between groups.[41] There is limited evidence to support the use of heat therapy in general; however, studies have shown heat-wrap therapy to provide short-term reductions in pain and disability in patients with acute low back pain.[40]

Traction and bracing

Skeletal traction is a common method for preoperative fracture stabilisation and pain control in patients with femoral shaft, acetabular and unstable pelvic fractures. In a prospective study of adult trauma patients, pain scores during immobilisation of isolated femur fractures were lower in patients placed in skeletal traction than patients who were splinted.[42]

Bracing may be useful to reduce pain and protect the neck, back and joints from further injury in trauma patients. However, mobilisation of joints such as the elbow should be started early following trauma to avoid long-term stiffness.[43]

Patient positioning

A systematic review of evidence for bed rest and exercise in patients recovering from acute lower back pain concluded that bed rest compared with advice to stay active has, at best, no effect, and at worst may have slightly harmful effects on acute lower back pain.[44]

In non-complex fractures it has long been established that appropriate positioning, for example with a back slab for wrist/arm fractures can alleviate pain and this is recommended widely.[45] Likewise, splints or slings may be helpful in patients with soft tissue injury in the early post-injury period in order to reduce pain and promote healing. In these instances, elevation and ice may also be of benefit.

Non-pharmacological therapies in acute pain: take-home messages

- **A number of different non-pharmacological approaches are increasingly being used alone or in combination with pharmaceutical agents as part of a multimodal approach to managing pain.**

- **The goals of non-pharmacological intervention in pain management are to decrease fear, distress and patients' anxiety.**

- **Non-pharmacological interventions often require few minimal resources and can be implemented in busy emergency settings (EDs or pre-hospital settings) and are proven effective in mitigating patients anxiety, stress and pain levels.**

- **Non-pharmacological interventions should be implemented early with patients, either alone or in combination with pharmacological options.**

- **Non-pharmacological interventions that should be considered include positioning of patients using traction or bracing, stress reduction techniques, attention control e.g. distraction, TENS and acupressure, all of which are supported by clinical evidence.**

Table 4.1 Evidence for non-pharmacological therapies for the treatment of acute pain in emergency situations

Evidence levels: IA, meta-analysis of randomised clinical trials; IB, randomised clinical trial; IIA, non-randomised clinical trial; IIB, other study; III non-experimental descriptive study; IV, expert opinion.

Therapy	Use in acute pain	Evidence	Level of evidence
Psychological interventions			
Sharing information	Postoperative pain	No evidence available in an emergency setting	N/A
Relaxation (stress and tension reduction)	Postoperative pain	No evidence available in an emergency setting	N/A
Hypnosis	Procedural pain, renal colic	In a case of pain caused by severe renal colic not relieved by pethidine, hypnosis was used to suggest that the pain felt by the patient was diminished to a mild itch. Upon exiting the hypnotic trance, the patient did not complain of any further pain while waiting to be seen by a urologist.[11]	IV
Attention control methods	Postoperative pain, procedural pain	No evidence available in an emergency setting	N/A
CBT	Postoperative pain, procedural pain	No evidence available in an emergency setting	N/A
TENS	Procedural pain, acute trauma pain, renal colic	A Cochrane review of studies of TENS for acute pain, including acute trauma such as sprains and fractures, reported a mean difference on a 100 mm VAS of −24.62 mm in favour of TENS versus placebo.[29]	IA
		A systematic review and meta-analysis of studies of TENS in the pre-hospital setting included four studies and reported that TENS produced a mean VAS reduction of 38 mm (p<0.0001) in patients with moderate to severe acute pain, and pain scores significantly lower than placebo (p<0.0001).[32]	IA
Acupuncture and related techniques	Trauma pain	In an RCT of patients with minor trauma in the pre-hospital setting, 60 patients were randomised to acupressure, acupressure using sham points and no acupressure. On arrival at hospital, patients in the acupressure group had significantly less pain and anxiety, lower heart rate and greater overall satisfaction (p<0.01).[34]	IA
Ultrasound	Fracture	A systematic review of ultrasound in the treatment of fracture concluded that the benefits (including improvements in pain scores) could not be ruled out, but that the current evidence was insufficient to support its use.[38]	IA
Cold and heat	MSK injury	Patients with an acute tear to the gastrocnemius muscle were randomised to receive either repeated application of crushed ice (n=10) or no ice treatment (n=9) within six hours of injury. No significant differences in pain score were seen between groups.[41]	IB
Traction and bracing	Fracture	Patients with femoral shaft, acetabular and unstable pelvic fractures were placed into distal femoral skeletal traction (n=85) or a long-leg splint (n=35).	IIB
		Pain scores during immobilisation of isolated femur fractures were lower in patients placed in skeletal traction than patients who were splinted. There was no difference in pain score following mobilisation.[42]	
Patient positioning	Back pain, fracture	A systematic review of nine trials including 1,435 patients with acute lower back pain or sciatica concluded that bed rest has either no effect or a slightly harmful effect on acute lower back pain compared with remaining active.[44]	IA

CBT, cognitive behavioural therapy; RCT, randomised controlled trial; TENS, transcutaneous electrical nerve stimulation; MSK, musculoskeletal; VAS, visual analogue scale.

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GUIDELINES FOR THE MANAGEMENT OF ACUTE PAIN IN EMERGENCY SITUATIONS

CHAPTER 5:

Pharmacological therapies in acute pain

Current pharmacological therapeutic options in acute pain

A wide range of analgesic agents are currently available for use in the ED and pre-hospital settings, including both opioid and non-opioid options with a number of different formulations and routes of administration. However, there is great variation in the availability and use of non-opioid analgesics as well as opioids across Europe.[1] In addition, emergency setting personnel providing pain relief across Europe vary in terms of educational level, training and job specification (e.g. nurses, paramedics, emergency physicians) which can determine their ability/authority to provide analgesics for patients in pain.[2-4]

Determining which analgesic is the most appropriate to use in patients will to some extent depend on the setting, whether the patient is presenting at the ED or if treatment is taking place in one of a wide range of potentially hostile environments in the pre-hospital setting. Other factors include the ability of the treating healthcare personnel to administer various analgesics, the pain intensity of the patient as determined by pain assessment and recommendations on the class of analgesic as provided by the WHO ladder.[5]

This chapter reviews the main pharmacological therapies currently used to treat acute pain in emergency situations. Clinical evidence on the use of these agents in the pre-hospital and ED settings is presented in **Table 5.1** *(see page 44)*.

Nitrous oxide

Nitrous oxide has a long history of use as an analgesic and is commonly used to relieve moderate pain in ED and pre-hospital settings.[6-8] Inhaled nitrous oxide is provided in a cylinder as a pressurised gas usually comprising a 50/50 mixture of nitrous oxide and oxygen. It is typically self-administered by the patient via a mask or mouthpiece (by adults and children most typically aged >5 years) or in young children (≤4–5 years) can be administered by mask by healthcare professionals. The patient controls their own intake with a demand-valve device, which discontinues the flow of gas if the patient loses consciousness.[6]

Nitrous oxide has both analgesic and anxiolytic effects,[6] and is a weak anaesthetic, with a concentration of about 70% required to produce unconsciousness.[9] It has a rapid onset and offset of effect of approximately three to five minutes,[10] and thus does not mask signs and symptoms of illness and injury that may help provide a definitive diagnosis.[11] Side effects of nitrous oxide can include euphoria, disorientation, sedation, nausea, vomiting, dizziness and generalised tingling,[9] but the incidence of significant adverse events (AEs) is low.[11] Nevertheless, nitrous oxide is contraindicated in patients at risk of pneumothorax, bowel obstruction, head injuries with impaired consciousness, faciomaxillary injuries and decompression sickness, as it can diffuse into gas-filled cavities (e.g. intestine, thorax and middle ear) and increase volume and pressure.[6,9]

There are very limited recent data supporting the use of nitrous oxide for pre-hospital or ED pain, and even fewer

comparative studies of nitrous oxide and placebo or other analgesics in the pre-hospital setting.[11] One of the few more recent studies was a double-blind, randomised controlled trial published in 2013, in which 60 patients with moderate acute pain being transported by ambulance received either 50/50 nitrous oxide/oxygen (n=30) or medical air (n=30). At 15 minutes, 67% of the patients in the nitrous oxide group had a numerical rating scale (NRS) score of 3 or lower versus 27% of those in the medical air group (p<0.001).[12] The median NRS score in the nitrous oxide group at 15 minutes was 2, versus 5 in the medical air group.[12] Another recent observational study included 85 patients in the ED with moderate to severe pain (defined as ≥30 mm on a 100 mm visual analogue scale [VAS]) who used a portable device to self-administer 50/50 nitrous oxide and oxygen.[13] Patients reported significant reductions in pain scores at 20 minutes that were sustained over the 60 minutes of observation. Levels of patient and nurse satisfaction were high.[13]

Paracetamol

Commonly used for treating mild to moderate acute pain, paracetamol can be administered intravenously (IV), per rectum (PR) or by oral routes.[14] Paracetamol is often used in combination with opioids, and may decrease opioid requirements by up to 20%.[15] The maximum recommended adult dose of paracetamol is 4,000 mg/day and is considerably lower for paediatric patients (toxic dose 150 mg in single dosing and maximum 80 mg/Kg per day), with a risk of hepatotoxicity at higher doses.[14,16] It should be used with caution in the following individuals: alcoholics; those at risk of hepatic dysfunction or with hepatic impairment; patients with cirrhosis; and those with renal impairment.[16] Potential side effects include hypersensitivity including skin rash, erythema, flushing, pruritus and tachycardia.[17,18] Paracetamol is contraindicated in severe hepatic impairment or severe active liver disease.[18,19]

Paracetamol has been demonstrated to provide analgesia as effectively as many non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin.[16] Studies comparing oral paracetamol with NSAIDs for acute blunt minor musculoskeletal (MSK) extremity trauma,[20] traumatic or inflammatory pain to the extremities (paracetamol in combination with codeine),[21] acute MSK pain[22] and pain caused by ankle sprain[23] found pain treatment with paracetamol to be at least as effective as NSAIDs. Paracetamol IV has also demonstrated similar analgesic effects to IV morphine in patients with isolated limb trauma in a pilot study carried out in an ED in the UK.[24] In another study, IV paracetamol plus oral oxycodone was found to be as effective as IV morphine in relieving pain from acute bone fracture, although the combination was associated with more side effects (namely nausea and itching) than morphine.[25] However, a systematic review of evidence for analgesics in acute trauma pain showed clinically significant pain relief in only two out of four studies with paracetamol (including the UK study mentioned above).[26] In addition, paracetamol does not have the anti-inflammatory properties of NSAIDs,[14,16] and has a slow speed of onset and less efficacy when taken orally.[10]

NSAIDs

NSAIDs such as ibuprofen, diclofenac, ketorolac and naproxen are commonly used in both the pre-hospital and ED settings for mild to moderate pain, particularly with an inflammatory component.[10] They are most commonly administered via the oral or IV routes.[10,27] NSAIDs inhibit the cyclooxygenase 1 (COX-1) and cyclooxygenase 2 (COX-2) enzymes in order to produce analgesic, antipyretic and anti-inflammatory effects.[16] They may decrease opioid requirements and therefore opioid-related side effects.[28] However, they may also contribute to decreased fracture healing and infection that is a limitation to their use.[16,28] Recommendations suggest NSAIDs should not be used within the first three days of soft tissue injuries such as sprains or fracture to avoid potential delays to healing.[29,30] They are also associated with a number of serious adverse events (SAEs), including gastritis, bleeding and renal failure,[28,31-33] and should be avoided in the elderly or those with renal issues. NSAIDs are contraindicated in patients with active peptic ulceration or those with stomach bleeding, uncontrolled hypertension, significant renal disease or impairment, those with inflammatory bowel disease such as Crohn's disease or ulcerative colitis and those who have experienced a previous transient ischaemic attack or stroke (apart from aspirin).[32,34,35]

In spite of concerns regarding renal AEs with NSAIDs, a systematic review and meta-analysis has recommended NSAIDs as the preferred analgesic option for patients presenting to the ED with renal colic.[36] Comparing the safety

and efficacy of NSAIDs with opioids and paracetamol for the management of acute pain due to renal colic, NSAIDs were equivalent to opioids or paracetamol in the relief of acute pain at 30 minutes, with less vomiting than opioids and fewer requirements for rescue analgesia compared with opioids and paracetamol.[36] In a prospective, double-blind study, the NSAIDs ketorolac, diclofenac and etoricoxib showed similar, significant reductions in acute pain caused by ankle fracture over 24 hours.[37] Ketorolac is used extensively in the ED for acute pain management and in a study has demonstrated efficacy for acute MSK pain, although osteopathic manipulation provided significantly superior relief.[38] Ketorolac is effective in renal colic, however it has been shown to be most effective in combination with morphine rather than when either medication was used alone,[39] a result replicated in a second study,[40] and ketorolac is likely to be less effective than ketamine.[41] In acute low back pain ketorolac demonstrated comparable analgesia to naproxen but was associated with a faster onset of analgesic action within 60 minutes of administration (24.2% of ketorolac treated patients vs 6.5% of naproxen treated patients [p=0.049]).[42] Recent studies, however have demonstrated an analgesic ceiling dose of 10 mg with no additional analgesic benefits observed at higher doses; as a result it is recommended to use ketorolac at does of 10 mg or below.[43] These findings are important as a study indicated that in more than 95% of cases ketorolac was prescribed above its analgesic ceiling dose increasing NSAID associated risks for no analgesic benefit.[44] Whilst ketorolac is not indicated for use in children, IV ketorolac is used widely in paediatric post-operative pain with the ability to reduce opioid use, length of stay in hospital and reduced hospital costs.[45] Sublingual ketorolac has been compared with sublingual tramadol in children with severe post-traumatic bone pain due to fractures and dislocations.[46] In this study in 342 children aged 4–17 years, both ketorolac and tramadol significantly reduced pain by 110 min from baseline (p<0.001) which was not significantly different; however children receiving ketorolac required significantly less rescue medication than those treated with tramadol (p=0.098).[46] In a second study in abdominal pain in children presenting to the ED, sublingual ketorolac 0.5 mg/Kg provided analgesia comparable to sublingual tramadol 2 mg/Kg and sublingual paracetamol 20 mg/Kg.[47] There is limited published experience for the use of ketorolac for acute pain in children in the ED, and a Cochrane review suggests the strength of evidence for ketorolac in children for acute post-operative pain is uncertain.[48] Ketorolac, along with other medications such as IV parecoxib and inhaled methoxyflurane, may provide paediatric physicians non-opiate analgesic options which is to be welcomed.[49] Unfortunately, a systematic review of analgesics in the emergency care setting suggested an inconclusive benefit for NSAIDs.[26] Across five studies of NSAIDs that were included in this review, no clinically meaningful reductions of pain greater than 20 mm on the VAS or 2 points on the NRS were reported; NSAIDs were therefore not recommended for pre-hospital use.[26]

Topical NSAIDs (most commonly diclofenac, administered via patches, plasters and gels) have been successfully used to provide relief in acute pain due to soft tissue injury[50-55] and ankle sprain.[56-60] There is some evidence that the degree of analgesia provided by topical NSAIDs can be comparable to oral NSAIDs.[52] Topical administration of NSAIDs also has the advantage of limiting the risk of systemic side effects associated with other routes, although this also limits their usefulness to more superficial pain. They are also not appropriate for use on broken skin.[61]

COX-2 inhibitors

COX-2 inhibitors are a type of NSAID most typically used for the treatment of pain in arthritis and ankylosing spondylitis. COX-2 inhibitors act to reduce pain and inflammation either by inhibiting COX-2 preferentially over the constitutive COX-1 or by inhibiting COX-2 only.[62,63] Currently, only four COX-2 inhibitors are available – etoricoxib, celecoxib, parecoxib and meloxicam – all of which inhibit COX-2 to a greater extent than COX-1, but none are exclusively selective for COX-2 alone. Inhibitors with exclusive selectivity for COX-2, like rofecoxib, have been associated with fatal cardiovascular (CV) side effects and withdrawn from use.[62,64] Whilst there is extensive evidence for COX-2 inhibitors in chronic pain conditions, there is limited published evidence for their use in acute pain conditions as might be experienced in the pre-hospital or ED setting.

Etoricoxib is a COX-2 inhibitor available as an oral preparation in doses ranging from 30 to 120 mg[65] which has demonstrated efficacy in acute tendinopathy[66] and postoperative pain,[67] for example MSK pain; etoricoxib has been shown to be as effective as diclofenac.[37] Similar results have been observed in renal colic, although data are only available in abstract form.[68]

Celecoxib is a selective orally available COX-2 inhibitor licensed in Europe for rheumatoid arthritis, osteoarthritis and ankylosing spondylitis,[69] where it has shown efficacy.[70-72] In the United States of America (USA) it is also licensed for use in primary dysmenorrhoea and adenomatous colorectal polyps.[73] Celecoxib has proven efficacy in postoperative pain[74-78] where it has been suggested that it might reduce postoperative opioid requirements,[78] although data in this regard appear equivocal.[79] In addition, celecoxib has been used effectively pre-emptively before surgery to reduce postoperative pain scores.[80]

No recent studies on the use of celecoxib in the ED exist, but an older study of acute MSK pain in an ED suggested that celecoxib 200 or 400 mg was as effective as ibuprofen 600 mg,[81] which suggests that its use in the ED is limited in preference to ibuprofen. Given data such as these, celecoxib is suggested for use as second line medication for acute pain behind paracetamol and NSAIDs such as ibuprofen.[82] However, it is clear from practising clinicians in the ED that celecoxib is used, on occasion, despite its cost compared with NSAIDs.

Parecoxib is an injectable COX-2 inhibitor licensed for post-operative analgesia in adults where it has shown efficacy.[83,84] It has also demonstrated efficacy in renal colic, where it was shown to be as effective as ketoprofen,[85] and in a study of abdominal pain against IV morphine in the ED where there was a significant reduction in pain comparable to that of morphine.[86]

Meloxicam, available as oral and orodispersible preparations,[87,88] inhibits both COX-1 and COX-2 with preference for COX-2 and is used almost exclusively for chronic pain conditions such as rheumatoid arthritis,[89] with some evidence for its use in postoperative pain.[90] It has a half-life of 20 hours and only reaches peak plasma concentrations after approximately 10 hours, rendering it of little use for emergency pain scenarios.[89]

Dipyrone (metamizole)

Dipyrone (metamizole) is an analgesic with minimal anti-inflammatory effects, in common with paracetamol.[91] It can be administered orally, by IV infusion or subcutaneous (SC) injection. It is used in some countries for the treatment of acute pain including postoperative pain, colic, cancer and migraine,[92] but is banned in others due to its association with life-threatening blood disorders such as agranulocytosis, which are thought to have a possible association with patient ethnicity.[93,94] Dipyrone is recommended to be administered as a single dose by infusion of 1,000 to 5,000 mg, with a maximum dose of 5,000 mg.[95] Onset of effect can be anticipated within 20- to 30-minutes and the risks of hypotension can be mitigated by short infusion over 15 minutes.[95]

Dipyrone has demonstrated efficacy in renal colic and acute pancreatitis pain.[96,97] In a pilot study of 16 patients randomised to receive SC morphine 10 mg/4 hours (n=8) or dipyrone 2 g/8 hours (n=8) for acute pancreatitis pain, 75% of dipyrone-treated patients achieved pain relief compared with 37.5% of morphine-treated patients with a faster onset of pain relief.[96] While this study failed to demonstrate superior efficacy of dipyrone over morphine, dipyrone-treated patients had lower pain scores than those treated with morphine; dipyrone may thus provide an alternative to morphine. A randomised, double-blind study compared dipyrone with dexketoprofen in renal colic.[98] Dipryone 2 g was effective in reducing pain comparable with dexketoprofen 50 mg. The most common AEs recorded were gastrointestinal (GI) disorders, dizziness, headache and abdominal pain.[98]

Efficacy in severe migraine and primary headache has also been demonstrated, although the number of studies is small.[99] Across all studies dipyrone was not associated with agranulocytosis, and side effects were mild to moderate. Case studies of agranulocytosis related to dipyrone use do appear in the literature, however.[100] Clinical signs for agranulocytosis include fever, tonsillitis and aphthous stomatitis.

Opioids

Overview

Opioids are a large class of drugs that act on opioid receptors, primarily within the central nervous system, to produce an analgesic effect. They are commonly used for treating moderate to severe acute pain,[6] with weak opioids such as

codeine or tramadol typically used for moderate pain, and strong opioids such as morphine and fentanyl typically used for severe pain.[5] Opioids have proven efficacy in providing pain relief in emergency settings.[26]

Opioids can be administered via the IV, intramuscular (IM), intranasal (IN), oromucosal (OM)/sublingual (SL), sub-cutaneous (SC) or oral routes, with the choice of opioid and route of administration depending on the severity of the pain and the condition and comorbidities of the patient.[5] Opioids are associated with a number of side effects (particularly in opioid-naive patients), such as nausea and vomiting, sedation and respiratory depression, and itching and anaphylactoid reactions.[16,101] Generally, opioids are contraindicated or should be used with caution in patients with severe respiratory instability, acute psychiatric instability or uncontrolled suicide risk, those receiving drugs capable of eliciting life-limiting drug–drug interactions, and those seeking opioids for addiction purposes.[102,103] In order to decrease opioid requirements, while also improving analgesia, opioids may be used in combination with other agents, such as paracetamol, NSAIDs or alpha-2 agonists (e.g. clonidine).[5,104] A meta-analysis of 17 randomised clinical trials (RCTs) showed that patients receiving an opioid in combination with an NSAID had significantly lower pain scores and opioid requirements.[104]

Codeine

Codeine is indicated for the management of acute moderate pain in children aged over 12 years and adults whose pain is not relieved by analgesics such as paracetamol or ibuprofen.[106] It is used primarily in primary care or as an analgesic on discharge from the ED.[105] Published evidence of its use in the pre-hospital setting is not available.

Codeine is available as an oral formulation in tablets and suspension form.[106] It is available as combination therapy with paracetamol in a few countries, most notably the UK, Australia and New Zealand. In some parts of Europe codeine is available as an over-the-counter medication for sale to the public, but in many it is restricted to prescription-only status. Improved understanding of codeine's pharmacogenomics and the risk of ultra-fast metabolism has raised concerns about its safety and it is contraindicated in children aged less than 12 years.[107,108]

Two cross-sectional, observational prospective studies have been performed to compare codeine in combination with paracetamol with ketorolac in the ED setting.[21,109] The first study included patients with polytrauma (defined as injuries of at least two long bone fractures, or one life-threatening injury and at least one additional injury, or severe head trauma and at least one additional injury) treated with either paracetamol/codeine or ketorolac. No significant differences in analgesia between paracetamol/codeine or ketorolac were observed.[109] However, in the later, larger study by the same group in patients with acute pain, fractures or MSK pain, the combination was significantly superior to ketorolac for pain relief in fractures or muscular pain and acute pain, with a duration of effect that exceeded two hours.[21] The authors suggest that paracetamol/codeine may be equivalent to ketorolac in non-traumatic or post-traumatic acute pain, but is superior for patients with fractures or muscular pain,[21] and the combination may be useful in patients at risk of cerebral haemorrhage or GI effects.[109]

In an RCT, paracetamol/codeine was compared with two other paracetamol combinations with oxycodone and hydrocodone in patients with acute extremity pain.[110] In this study, all combinations reduced the NRS from a baseline score of 8.7, with no significant differences between groups at two hours. Numerically, codeine/paracetamol was the least effective (pain reduction: codeine/paracetamol 3.9; paracetamol/oxycodone 4.4; paracetamol/hydrocodone 3.5) compared with ibuprofen or paracetamol alone (4.3).[110] The same group demonstrated in a separate study that paracetamol/codeine can reduce baseline pain by half in patients discharged from the ED and was more effective than a paracetamol/hydrocodone combination.[111]

Tramadol

Tramadol is a weak opioid analgesic typically used to relieve moderate to severe pain. It has successfully been used in the treatment of postoperative pain, pain associated with labour and acute myocardial infarction, as well as for trauma pain in both the pre-hospital and ED settings.[112] Tramadol is available in IV, SC, IM and oral formulations.[112] In terms of side effects, tramadol is associated with low rates of respiratory depression, unlike some other opioids. Nausea, vomiting and dizziness may occur with tramadol; however, these can be reduced by slower IV infusion.[112]

Piritramide

Piritramide is a strong opioid available in Austria, Belgium, Czech Republic, Germany and the Netherlands and can be administered via the IM, IV or SC routes.[113] It is indicated for use in the treatment of severe pre- and postoperative pain or during surgery in adults and children aged over five years,[113] although it also has some use across Europe in the emergency setting. For postoperative pain, piritramide is dosed at 0.2 to 0.3 mg/Kg IM to an average dose for adults of 20 mg (approximately 2 mL).[113] As with many other opioids, piritramide is associated with respiratory depression and the summary of product characteristics recommends that a μ-opioid receptor antagonist is always kept available in case of breathing difficulty.[113]

The efficacy of piritramide in postoperative pain has been established and has been shown to be comparable with other opioids such as morphine or remifentanil,[114-116] although evidence is limited and its use has been questioned.[117]

In the English language published literature, there is little data regarding the use of piritramide in the emergency setting. One prospective, open-label single-blind study published in 2000 demonstrated significant reductions in pain from baseline ($p<0.01$) for piritramide at 60 minutes but not at 30 minutes, compared with pro-paracetamol (the pro-drug of paracetamol), tramadol and diclofenac that demonstrated significant pain relief from baseline within 30 minutes ($p<0.02$).[118] Piritramide was also associated with significantly more side effects than the comparator drugs ($p<0.05$).[118]

Morphine

Morphine is a strong opioid commonly used for severe pain in the ED and pre-hospital settings,[119] and can be administered via IV, SC, IM and oral routes.[10,26] Many international guidelines recommend IV morphine as the standard analgesic for management of severe acute pain in emergency settings.[120-124] Morphine is associated with nausea, vomiting and dizziness, but these effects can be reduced and managed by administering the drug by a slower IV infusion.[10] Using two doses of morphine, 30 minutes apart, is another approach that may provide improve analgesia with no increase in the rate of AEs.[119]

Patient-controlled analgesia (PCA), generally IV morphine administered on demand with a lockout between doses, has been used for many years, and studies suggest that it provides greater patient satisfaction than physician-managed analgesia.[125-127] In an RCT of patients with acute abdominal pain in the ED, patients receiving morphine via PCA had significantly greater reductions in NRS score from 30 to 120 minutes than those who received physician-managed analgesia alone.[125] More patients in the PCA arms reported that they wanted the same pain management in the future, and fewer required further analgesics at 120 minutes.[125] Another RCT comparing morphine given via PCA and as titrated boluses found that patients who were in control of their analgesia had greater reductions in pain score while consuming similar amounts of morphine. These patients were also more satisfied with their method of pain relief.[127]

Oxycodone

A strong opioid used for treating severe pain in the ED, oxycodone is available in oral and IV formulations.[26] Oxycodone may be a preferred opioid for the elderly due to its short half-life and the fact that it does not form toxic metabolites.[128] It is often combined with paracetamol to enhance analgesia, and there is evidence that this combination has equivalent analgesic efficacy to fentanyl in an ED setting.[129]

A single dose of oral oxycodone has demonstrated equivalent effectiveness to the NSAID naproxen in soft tissue injuries in the ED, although more patients in the oxycodone arm than the naproxen arm required additional analgesia in the first 24 hours after discharge (16.0% versus 6.6%). In addition, the safety profile for oxycodone was significantly worse than that of naproxen (the most common AEs being nausea and vomiting).[130]

Fentanyl

Fentanyl is a strong opioid routinely used in the USA for treating severe pain in the ED and pre-hospital settings, and is commonly administered as IN, OM or IV formulations.[10] In the European Union, fentanyl is licensed only for the treatment of breakthrough cancer pain.[131] Fentanyl delivered intranasally can be associated with epistaxis, accidental swallowing and blocked nose, which can result in suboptimal drug delivery and reduced analgesia.[132]

Fentanyl provided via the IV route has demonstrated comparable efficacy to IV morphine in the pre-hospital and ED settings, with a faster onset of action.[133,134] In a review of medical charts from 2,348 patients treated with IV fentanyl by ambulance personnel in Denmark, fentanyl provided pain reductions of >2 points on the NRS for 79.3% of patients, but moderate to severe pain was still reported by 60% of patients on arrival at hospital.[135]

Fentanyl is also available as an OM formulation, which can provide relief of acute orthopaedic pain in the ED in 10 minutes.[136] Oromucosal fentanyl can also be combined with nitrous oxide for fracture reduction in the ED.[10] Similarly, nebulised fentanyl has been shown to provide rapid and effective analgesia in patients with acute limb pain in the ED.[137]

Intranasal fentanyl provides a fast onset of action and is easily administered, making it particularly useful in children,[138] but further rigorous evidence to support its use in the ED and pre-hospital settings is required.[132] Of the limited evidence available, some studies report analgesic non-inferiority of IN fentanyl to IV morphine while others show inferiority of IN fentanyl, although it is generally acknowledged as easier to use than IV morphine.[10,132]

Sufentanil

Sufentanil is a synthetic opioid, like fentanyl, but with five to eight times the potency.[139] Given by the IV route, sufentanil has similar effectiveness to IV morphine, with a faster onset of action and a shorter duration of action.[120] Sufentanil has been successfully used via the IN route to treat patients with moderate to severe pain in the extremities,[139,140] and in children in a pre-hospital setting,[141] but is unlicensed for use in children so should not be used in children aged ≤18 years.

Oromucosal sufentanil tablets have demonstrated significant effects on moderate to severe acute pain in the ED, with few AEs.[142] A PCA device that dispenses OM sufentanil according to a prespecified lockout system is now available, which may address some of the concerns related to IV PCA, such as problems related to the invasive route of delivery and pump errors, and may provide greater patient satisfaction than IV-based systems.[143,144]

Ketamine

Ketamine is an N-methyl-D-aspartate antagonist widely used in emergency acute pain[10] and commonly used in combat scenarios.[145] It is given via IV, IM and IN routes.[146,147] At full doses (1.5–2.0 mg/Kg IV), ketamine is used as an anaesthetic, while at lower sub-dissociative doses (0.5 mg/Kg) it provides analgesia that can be opioid sparing.[10] It is as effective as morphine[10] but with a faster onset of action.[148] Ketamine has a wide therapeutic index, cardiovascular stability and no incidence of respiratory depression.[10,148] Haemodynamically, it is associated with increases in heart rate and blood pressure (BP), but it is not associated with raised intracranial pressure.[10] It is worth considering that, in emergency acute pain, increases in BP may be useful to support normalised BP. Ketamine is contraindicated in patients with eclampsia or pre-eclampsia, uncontrolled hypertension, severe cardiac disease or when stroke or cerebral trauma are suspected.[149] Because of fears of possible AEs and the need for patient monitoring[10] it is not used in all European countries.

Vomiting can occur in up to 30% of patients given ketamine,[150] therefore co-administration of an anti-emetic such as ondansetron is recommended.[10] In adults, ketamine is also often co-administered with a benzodiazepine to prevent emergence effects (e.g. hallucinations, vivid dreams, floating sensations and delirium), although there is no evidence to support emergence effects at lower doses of ketamine.[10,146] Recent guidelines published in 2018 have suggested that ketamine may be moderately useful in patients with opioid tolerance or dependence, or for those at risk of respiratory problems such as those with obstructive sleep apnoea, although only limited evidence exists.[151]

A number of studies have been carried out which support the use of sub-dissociative doses of ketamine in a pre-hospital or ED setting.[152-154] In an RCT comparing IV ketamine (40.6 mg) plus IV morphine (5 mg) (n=70) and IV morphine (14.4 mg) (n=65) demonstrated superior analgesia for combination therapy (VRS change from baseline -5.6 (95% CI -6.2, -5.0) vs morphine alone -3.2 (95% CI -3.7, -2.7).[154] Adverse events were more common in the combined therapy group 39% (95%CI 27%, 51%) vs morphine alone 14% (95%CI 6%, 25%). In a study of patients

with orthopaedic trauma, IN ketamine was found to be as effective as IV ketamine in reducing pain, with AEs mild and transient in both groups. Given these data, IN ketamine may have a role where IV access is difficult, or may be of use, as the authors suggest, in crowded EDs to facilitate prompt, effective analgesia.[155]

Intranasal ketamine has shown comparable efficacy and safety to IV and IM morphine in patients with moderate to severe acute pain in the ED.[156] In a randomised double-blind study, IN ketamine was compared with IV morphine in patients in renal colic.[157] At five minutes IV morphine was more effective than ketamine, but at 30 minutes both groups had comparable pain relief, despite the significantly higher baseline pain in the ketamine group.[157] The incidence of AEs were comparable across both groups.[157]

In a study comparing IN ketamine with IN fentanyl in children with suspected extremity fractures, similar pain relief was observed at 20 minutes with both groups requiring a similar level of opioid rescue therapy, and whilst there were more AEs reported for ketamine, all were mild.[158] In the Pain Reduction with Intranasal Medications for Extremity Injuries (PRIME) study, children were randomised to either IN ketamine or IN fentanyl.[159] After 30 minutes, pain reduction was comparable with both ketamine and fentanyl. While AEs were higher in the ketamine group, these were mild and transient and it is suggested that IN ketamine could be considered for children for whom opioids would be problematic.[159] These results mirror those seen in the earlier Pain in Children Fentanyl or Ketamine (PICHFORK) study.[160] Similar data are also seen in smaller studies.[161]

Intranasal ketamine has been recommended by American joint society guidelines as beneficial for acute pain management, particularly in patients where IV access is difficult or in children undergoing procedures.[151] However, it is notable that all studies of IN ketamine to date have used ketamine for injection solution, as there is currently no ketamine formulation specifically designed for IN delivery available.[155-161]

Methoxyflurane

The inhalational analgesic low-dose methoxyflurane has been used extensively in emergency settings in Australia and New Zealand for over 40 years, and has been approved in some European countries (Belgium, France, Ireland, Switzerland and the UK) for emergency relief of moderate to severe pain in conscious adult patients with trauma and associated pain.[162,163] Licenced indications for methoxyflurane differ in Europe and Australasia.[164,165] In Europe, as of 2020, methoxyflurane is only licensed for use in trauma pain in conscious adults, whilst in Australasia methoxyflurane is licensed for the management of acute pain in adults and children. It is clear from real-world experience that methoxyflurane is being used in a wide variety of patients and it is included in guidelines for acute pain in both adults and children.[166]

Methoxyflurane is self-administered in analgesic doses at a maximum of 2 x 3 mL vials in a single administration via a single-use, handheld inhaler. It provides rapid, short-term pain relief within six to ten inhalations.[164] In anaesthetic doses, methoxyflurane is associated with hepatotoxicity and nephrotoxicity, but no significant AEs have been reported at analgesic doses.[167] It is contraindicated in patients sensitive to fluorinated anaesthetic agents, patients with known or genetic susceptibility to malignant hyperthermia, patients with liver damage as a result of previous methoxyflurane or halogenated anaesthetic use, significant renal impairment, altered levels of consciousness and clinically evident CV instability or respiratory depression.[164]

Methoxyflurane has been reported to provide similar rapid pain relief to nitrous oxide in patients with acute pain, though it may offer additional benefits in emergency situations in terms of greater ease of administration and portability.[162]

In a retrospective observational study of patients with visceral pain being transported by ambulance, methoxyflurane provided a more rapid onset of action than IN fentanyl, though fentanyl provided greater pain reduction by the time of arrival at hospital.[168] Another retrospective study, this time in paediatric patients with moderate to severe acute pain in a pre-hospital setting, compared the effectiveness of IV morphine, IN fentanyl and inhaled methoxyflurane. Methoxyflurane was less effective than morphine and fentanyl in terms of reducing pain score by ≥30%, but still provided effective analgesia in the majority (78%) of patients.[169]

In a Phase III study, methoxyflurane was effective and well tolerated for the management of acute pain due to minor trauma, with a rapid onset of analgesia.[170,171] Pain intensity was significantly improved at all time points compared with placebo (p<0.0001), and onset of pain relief occurred rapidly, within six to ten inhalations. The median time to first pain relief was four minutes, and significantly less rescue medication use was required with methoxyflurane than with placebo (p=0.0002); comparable results were found in the adult sub-group analysis of this study.[170,171] Two Phase III studies have demonstrated efficacy of methoxyflurane versus standard of care (SoC) analgesics.[172,173] In the first, an open label Phase III study in Spain comparing methoxyflurane with SoC analgesia (determined by the prescribing physician), the primary endpoint was change in pain from baseline. Over 20 minutes methoxyflurane provided a significantly greater reduction in pain intensity of 2.5 points compared with SoC of 1.4 points (p<0.001).[173] Reduction in pain was not related to baseline pain and methoxyflurane was as effective in severe pain (NRS ≥7) as in moderate pain (NRS ≤7) and greater pain reductions compared with SoC were maintained. Pain reduction with methoxyflurane was also greater than SoC regardless of whether SoC was an opioid or non-opioid analgesic. The majority of patients achieved a 30% improvement (87.9%) compared with SoC (57.7%) by 20 minutes[173] which is considered clinically important. In the second randomized, active-controlled study in Italy, patients with fracture, dislocation, crushing or contusion were treated with methoxyflurane or SoC analgesics (NRS <7 SoC = IV paracetamol or IV ketoprofen; NRS ≥7 SoC = IV morphine) with a primary endpoint of change in pain score from baseline.[172] Over the course of ten minutes change in pain intensity VAS across the entire patient cohort was greater for methoxyflurane than SoC (ΔVAS -5.94 mm; 95% CI: -8.83 mm, -3.06 mm p<0.001) demonstrating that it was both comparable to SoC as it met non-inferiority margins but also superior in exceeding non-inferiority.[172] In patients with moderate pain specifically, methoxyflurane was non-inferior to SoC at all time points up to ten minutes, but for patients with severe pain non-inferiority of methoxyflurane with SoC was observed at three minutes, but with superior analgesia at five minutes. Effective and superior analgesia was maintained up to 25 minutes post-administration. Satisfaction with methoxyflurane was greater than with SoC and both treatments were well tolerated.[172]

Nerve blockade

Local and regional nerve blockade, using local anaesthetic agents injected directly onto or near the nerve (either as a single injection, multiple injections, or a continuous infusion), is increasingly being employed for a wide range of painful injuries and illnesses.[174,175] The absence of systemic sedation with nerve block analgesia makes it easier to monitor the mental status of patients with head injuries, and can ease the transport and supervision of patients with acute trauma.[176]

The disadvantages of nerve blockade techniques are the complexity and the invasive nature of the procedures and the training required to achieve and maintain proficiency. Adverse effects are rare, but include infection, nerve injury and intravascular injection.[176] Local anaesthetics are contraindicated in patients with heart block or severe sinoatrial block with no pacemaker fitted, serious adverse reactions to previous local anaesthetic administration, concurrent treatment with Class 1 antiarrhythmic agents (e.g. quinidine), and prior use of amiodarone hydrochloride.[177] In addition, local anaesthetics in nerve blocks are often co-administered with epinephrine in order to slow the rate of anaesthetic absorption, and epinephrine is contraindicated in patients with pheochromocytoma, hyperthyroidism, severe hypertension or severe peripheral vascular occlusive disease.[178]

Single nerve block procedures are often used by surgeons or emergency medicine physicians in the preoperative phase, while more complex techniques such as plexus blockade are more commonly reserved for use by anaesthesiologists for control of pain during or after surgery.[176] Single-injection blocks are mainly performed for anaesthesia, whereas continuous peripheral nerve blocks are predominantly used for perioperative analgesia.[179] Continuous nerve block techniques have also been successfully used in military medical care for treating soldiers wounded in combat, as well as for trauma to the upper and lower extremities and to the chest (most commonly for rib fracture).[179,180]

An RCT of individuals with hip fracture in the ED compared conventional analgesics with ultrasound-guided, single-injection, femoral nerve block administered at admission followed by placement of a continuous fascia iliaca block

within 24 hours. Two hours after presentation at the ED, pain scores were significantly lower in the nerve block group compared with the control group, and at six weeks after the procedure participants in the nerve block group reported better walking and stair climbing ability.[181] Systematic reviews of the literature on the use of peripheral nerve block as analgesia for patients with hip fracture conclude that it provides rapid reduction in pain (within 30 minutes) with a low risk of AEs,[182-184] whilst reducing the requirement for opioids.[184]

Other types of nerve blockade are also widely used in the management of acute pain. Fascia iliaca block is also often used in the acute management of proximal femoral fractures, and is routinely performed in over 60% of UK NHS trusts.[175] Brachial plexus blockade has been used in patients undergoing surgery for acute distal radius fractures, and resulted in significantly better pain scores at 2 hours post-surgery than general anaesthesia, although some delayed rebound pain at 12 and 24 hours was reported.[185] In some EDs, epidural administration may be used, but published evidence of its use in this setting is lacking.

Lidocaine

Lidocaine is a local anaesthetic which can be given via topical, IV and intra-articular routes. Data to support the use of IV lidocaine for acute trauma pain in the ED are currently limited.[174] Two studies investigating IV lidocaine to relieve pain from renal colic in the ED either alone or as an adjuvant to opioids reported positive outcomes with lidocaine.[186,187] A randomised, double-blind study reported no significant difference in reduction in pain score between IV lidocaine and IV morphine in ED patients with acute limb trauma.[188]

Several studies have shown that intra-articular lidocaine is not significantly different compared with IV analgesia and/ or sedation for reduction of acute shoulder dislocation in the ED in terms of pain relief or patient satisfaction, with shorter duration of hospitalisation and lower risk of complications.[189-191] Meanwhile, topical lidocaine, delivered as a patch, has shown effectiveness in treating rib fracture pain.[192]

Pharmacological therapies in acute pain: take-home messages

- A wide range of analgesic agents are currently available for use in the ED and pre-hospital settings to manage pain from mild to severe intensities.

- Nitrous oxide is an appropriate analgesic for acute pain management in most patients as it has a long history of use as an analgesic and has very rapid on- and offset of effect, does not mask injury, and can be self-administered by patients with no significant adverse events observed.

- Paracetamol and NSAIDs are commonly used for treating mild to moderate acute pain and represent good choices for use in mild to moderate pain in the emergency setting. However, NSAIDs are associated with a number of SAEs when given systemically and should be avoided in elderly patients or those with renal issues and are contraindicated in patients with gastrointestinal bleeding, uncontrolled hypertension and significant renal disease.

- Dipyrone (metamizole) is an analgesic with minimal anti-inflammatory effects with demonstrated efficacy in renal colic and acute pancreatitis, however it is associated with life threatening agranulocytosis and is banned in some countries and subjected to restrictions in others.

- Opioids are a proven mainstay of analgesia for moderate to severe pain in the pre-hospital and ED settings and can be administered by a wide range of routes; they are associated with AEs such as nausea and respiratory depression and should be used within institution protocols and monitoring procedures.

- Ketamine, given at low doses, provides effective analgesia that can be opioid sparing and its use intranasally is useful when IV access is difficult and is as effective as IN fentanyl in children.

- Methoxyflurane provides rapid, effective pain relief which is well tolerated providing an analgesic that can be administered quickly as a bridge to other analgesics e.g. while IV access for other drugs is established, the handheld inhaler provides easy self-administration of analgesia by patients and portability.

- Nerve block provides effective pain relief with a low risk of AEs, which can be opioid sparing, it has established proven efficacy in the ED but administration procedures are complex and invasive.

- Lidocaine may provide useful anlagesia in the ED, but evidence to support this is currently limited.

Table 5.1 Evidence for pharmacological analgesics for the treatment of acute pain in the pre-hospital and ED settings

Evidence levels: IA, meta-analysis of randomised clinical trials; IB, randomised clinical trial; IIA, non-randomised clinical trial; IIB, other study; III non-experimental descriptive study; IV, expert opinion.

Therapy	Route	Evidence	Level of evidence
Nitrous oxide	**Inhaled**		
		Of 47 patients with abdominal or chest pain, MSK trauma or burns treated by a mobile unit, 44 (93.6%) achieved partial or complete pain relief with nitrous oxide.[8]	III
		In patients with moderate acute pain being transported by ambulance, 67% of 30 patients treated with nitrous oxide had NRS ≤3 at 15 minutes versus 27% of 30 patients treated with medical air (p<0.001).[12]	IB
		Significant reductions in mean pain scores at 20 minutes, sustained to 60 minutes, were reported in 85 patients in the ED with moderate to severe pain who self-administered nitrous oxide.[13]	IIB
Paracetamol	**IV, PR, oral**		
		In a double-blind RCT of adult ED patients with acute MSK pain randomised to oral paracetamol (n=30), oral ibuprofen (n=30) or combination (n=30), pain scores decreased over the 1-hour study period for all groups, with no significant differences between groups in terms of pain reduction or need for rescue analgesics.[22]	IB
		In patients with localised traumatic or inflammatory pain of the extremities treated with oral paracetamol and codeine (n=87) or oral ketorolac (n=113), paracetamol and codeine was equivalent to ketorolac in non- and post-traumatic pain, but superior in acute, fracture and muscular pain.[21]	IIA
		Patients with isolated limb trauma and in moderate to severe pain were randomised to IV paracetamol (n=27) or IV morphine (n=28). There were no significant differences between groups in terms of analgesic effect at any time point measured or rescue analgesia required, but there were significantly more adverse reactions in the morphine group.[24]	IIB
		A systematic review of pain relief in emergency care in the Netherlands included 4 studies in which paracetamol was used. Pain reduction was seen in all 4 studies, but effective pain relief of more than 20 mm on the VAS or 2 points on the NRS was reported in only 2 of the 4 studies.[26]	IV
		Patients with acute ankle sprain were randomised to receive oral paracetamol (n=45) or oral diclofenac (n=45). There was more ankle oedema in the diclofenac group at Day 3 but not at Day 0, but no difference in pain reduction between groups.[23]	IIB
		Patients with acute blunt minor MSK extremity trauma randomised to paracetamol (n=182), diclofenac (n=183) or combination therapy (n=182) showed no significant differences in NRS reduction at 90 minutes, either at rest or with movement.[20]	IB
		In patients with acute bone fracture randomised to IV morphine (n=74) or oral oxycodone plus IV paracetamol (n=79), pain scores were lower in the morphine group at 10 minutes, but similar at later time points. Nausea and itching were seen significantly more frequently in the oxycodone/paracetamol group.[25]	IB
NSAIDs	**Oral, IM, IV, topical**		
Systemic NSAIDs		A systematic review of 36 RCTs including 4,887 patients with acute renal colic reported a marginal benefit of NSAIDs over opioids in terms of pain reduction at 30 minutes; fewer rescue treatments were required and rates of vomiting were lower with NSAIDs than with opioids. Compared with paracetamol, NSAIDs showed no difference in pain reduction at 30 minutes but a reduced requirement for rescue treatments.[36]	IV
		A systematic review including 5 studies of NSAID use in emergency care reported no clinically meaningful reductions of pain >20 mm on the VAS or 2 points on the NRS.[26]	IV

Therapy	Route	Evidence	Level of evidence
		Patients with acute pain due to ankle fracture (n=60) were randomised to oral ketorolac, diclofenac, or etoricoxib. Reductions in levels of pain were similar between groups (74.5%, 74.3% and 70.9%, respectively).[37]	IIA
		Patients (n=58) with acute neck pain of <3 weeks duration were randomised to osteopathic manipulation or 30 mg IM ketorolac and pain evaluated one-hour post-dosing on a 5-point Likert scale. Both groups had reductions in pain intensity, but pain relief was significantly superior with manipulation rather than ketorolac (pain reduction 2.8±1.7 vs 1.7±1.6, p=0.02).[38]	IIA
		Patients with renal colic (n=300) were randomised to IV morphine and ketorolac (0.1 mg/Kg and 30 mg, n=100) or IV ketorolac alone (30 mg, n=100) or IV morphine alone (0.1 mg/Kg, n=100) in an RCT. Pain intensity significantly superior with combination therapy compared with IV morphine alone (3.01±0.98 vs 3.66±1.02, p=0.012) and compared with IV ketorolac alone (3.01±0.98 vs 3.68±0.88, p=0.018). Patients receiving combination therapy also required significantly less rescue analgesia than those receiving morphine alone (16% vs 20%, p=0.041) or ketorolac alone (16% vs 24%, p=0.012).[39]	IIA
		Patients with acute renal colic (n=126) were randomised to IV ketamine 0.6 mg/Kg (n=62) or IV ketorolac 30 mg (n=64). Both treatments reduced pain, with the onset of pain relief with ketamine faster than ketorolac (at 5 minutes pain reduction with ketamine superior to ketorolac p<0.001). At all other time points pain reduction was comparable.[41]	IIA
		Children with supracondylar humerus fracture received ketorolac as peri-operative analgesia (n=114) vs those who did not (n=228).[45] Mean pain rating 0-29 minutes was significantly lower in patients receiving ketorolac (VAS=0.7) compared with the control group (VAS=1.4) (p=0.017) and remained significantly lower at 30 minutes up to 120 minutes (p=0.036). Patients who received ketorolac required significantly lower doses of oxycodone (1.0 vs 1.2 doses, p=0.003), and postoperative stay in hospital was 50% shorter (13.6 hours vs 20.4 hours, p<0.001). As a result, hospitalisation costs were 40% lower for ketorolac treated patients.[45]	IIA
		In acute low back pain ketorolac over 10 days has proven to be non-inferior to naproxen, but had a faster onset to analgesia at 60 minutes for 24.2% ketorolac treated patients vs 6.5% naproxen treated patients (p=0.049).[42]	IB
		In children (4-17 years of age) with fractures or dislocations, sublingual ketorolac (n=64) was compared with sublingual tramadol (n=67).[46] Baseline pain score was IQR 8 in both groups. At 100 minutes both groups had significant reductions in pain compared with baseline that were comparable to each other ketorolac IQR=4, tramadol IQR=5 (p<0.001). Use of rescued medication was significantly higher in tramadol treated patients (12.3%) vs ketorolac treated patients (3.3%) (p=0.098). Rates of adverse events were not significantly different between groups, but adverse events were numerically higher in the tramadol group (4.6%) vs 0% in the ketorolac group and included 2 children with vomiting and 1 with vomiting and dry mouth.[46]	IIA
		Sublingual preparations of ketorolac 0.5 mg/Kg (n=70), tramadol 2 mg/Kg (n=70) and paracetamol 20 mg/Kg (n=70) in children with abdominal pain in the ED indicated comparable reductions in pain from baseline at 2 hours.[47] Median IQR pain scores at 2 hours were 2 for ketorolac and 3 for tramadol and paracetamol which was not significantly different. However, children treated with tramadol experienced significantly more adverse events (n=8) compared with paracetamol (n=1) or ketorolac (n=0).[47]	IIA
Topical NSAIDs		Patients with acute ankle sprain in the ED were randomised to a diclofenac/heparin (n=142), diclofenac (n=146) or placebo (n=142) plaster. The diclofenac/heparin plaster was associated with a significantly greater mean reduction in pain on movement after 3 days than the diclofenac only plaster, and both active treatments provided significantly greater pain relief than placebo.[56]	IB

Therapy	Route	Evidence	Level of evidence
		In patients with acute pain due to clinically significant minor soft tissue injury randomised to diclofenac (n=207) or placebo (n=211) patch, patients treated with the diclofenac patch had an 18% greater reduction in mean pain score versus placebo, and median time to pain resolution was 2 days shorter in the diclofenac patch group.[50]	IB
		A systematic review of 8 studies of the diclofenac patch reported reductions in VAS pain scores ranging from 26% to 88% on Day 7 and 56% to 61% on Day 14. Median time to pain resolution was 3 days less than with placebo.[51]	IV
		Patients with minor soft tissue injury occurring within 72 hours of study entry were randomised to diclofenac (n=192) or placebo (n=192) patch. Reduction in pain on movement after 7 days was significantly greater in the diclofenac plaster group than with placebo, with the difference in efficacy evident after 1 day.[55]	IB
		A review of published data on the use of topical NSAIDs in the treatment of acute soft tissue injuries reported that topical NSAIDs are significantly more effective than placebo in relieving acute pain. Topical NSAIDs provided comparable pain relief to oral NSAIDs, but with fewer AEs.[52]	IV
		Patients with acute ankle pain caused by a minor sprain were randomised to the diclofenac patch (n=68) or placebo (n=66) daily for 7 days. Patients treated with the diclofenac patch experienced a significantly greater reduction in pain compared with placebo, beginning 4 hours into treatment (p=0.02).[59]	IB
		Post-hoc analysis of an RCT comparing the diclofenac patch (n=60) with placebo (n=60) in pain due to acute traumatic stress injury revealed that diclofenac patch was consistently superior to placebo in providing relief from pain on movement, with mean differences in VAS score versus placebo greatest on Day 2 and Day 3 of the 7-day study (both p<0.0001).[53]	IB
		An RCT comparing diclofenac spray gel (n=118) with placebo (n=114) in the treatment of acute uncomplicated ankle sprain found a significantly greater proportion of patients achieved at least a 50% decrease in ankle swelling in the diclofenac arm. Spontaneous pain VAS scores were significantly lower in the diclofenac group than the placebo group at all time points.[57]	IB
		Patients with acute ankle sprain were treated with diclofenac gel x2 (n=80) or x3 times per day (n=80), or with placebo (n=82). At Day 5, the reduction in pain on movement on the VAS in both diclofenac groups was almost double that with placebo (p<0.0001).[58]	IB
		A Cochrane review of the use of topical NSAIDs in acute pain in 47 studies and 3,455 participants reported a number needed to treat to achieve 50% pain relief versus placebo was 4.5 for 6 to 14 days.[61]	IA
		An RCT comparing ketoprofen gel (n=50) with placebo (n=50) in the treatment of pain due to ankle sprain reported greater reduction in VAS score in the ketoprofen arm at 15 and 30 minutes.[60]	IB
COX-2 inhibitors			
Etoricoxib		In 28 athletes with acute Achilles tendinopathy, oral etoricoxib provided significant relief of tendon pain over a 7-day treatment period versus baseline (p<0.001).[66]	IIB
		(*)A Cochrane review of 6 studies of single dose oral etoricoxib for acute postoperative pain reported that 66% of participants prescribed etoricoxib and 12% given placebo reported at least 50% pain relief over 6 hours.[67]	IA
Celecoxib		An RCT comparing oral celecoxib 200 mg (n=34) and 400 mg (n=32), and ibuprofen 600 mg (n=39) for acute pain found no significant difference between the groups at 5 hours in terms of change of categorical pain intensity or VAS scores, though the latter approached significance favouring ibuprofen.[81]	IB
Parecoxib		Patients with acute renal colic who received IV parecoxib (n=174) achieved equivalent reductions in pain at 30 minutes to those who received IV ketoprofen (n=164).[85]	IIB

Therapy	Route	Evidence	Level of evidence
		In patients in the ED with acute traumatic pain of NRS ≥6, there was no significant difference in pain relief between IV parecoxib (n=18) and IV morphine (n=14), though there was a non-significant trend towards superiority of morphine. Dizziness was observed in 43% of patients given morphine versus none given parecoxib.[86]	III
Dipyrone (metamizole)	**Oral, IV, SC**		
		In patients with acute pancreatitis pain randomised to receive morphine (n=8) or IV dipyrone (n=8), 75% of dipyrone-treated patients achieved pain relief within 24 hours compared with 37.5% of morphine-treated patients, with a faster onset of pain relief (10 hours versus 17 hours).[96]	IIB
		A randomised, double-blind study compared IV dipyrone (n=103) with IV dexketoprofen 25 mg (n=101) or 50 mg (n=104) in patients with moderate to severe pain due to renal colic. Reductions in VAS score were comparable between dipyrone and dexketoprofen 50 mg groups, though the onset of analgesia was slower, with greater reductions in pain in the first 30 minutes in the dexketoprofen groups.[98]	IIB
Opioids	**Oral, IV, SC, IM, IN**		
Codeine		In patients with polytrauma treated with either paracetamol/codeine (n=30) or ketorolac (n=30), no significant differences in VAS score between paracetamol/codeine or ketorolac were observed at any time point.[109]	IIA
		Oral codeine in combination with paracetamol (n=87) was equivalent to oral ketorolac (n=113) in non- and post-traumatic pain of the extremities, but superior in acute pain (p=0.002) and fracture and muscular pain (p=0.044).[21]	IIA
		Patients with acute extremity pain were randomised to oral ibuprofen/ paracetamol, oral oxycodone/paracetamol, oral hydrocodone/paracetamol or oral codeine/paracetamol (n=104 in each group). At 2 hours, there were no significant differences between groups in reduction of NRS score.[110]	IB
Piritramide		Patients with single peripheral injury in the ED randomised to IV pro-paracetamol (n=40), IV tramadol (n=40) and IV diclofenac (n=40) achieved significant reductions in VAS score from baseline within 30 minutes (p<0.02). Patients who were randomised to IM piritramide (n=40) achieved significant reductions in VAS score from baseline within 60 minutes (p<0.01).[118]	IIB
Morphine		In an RCT, patients in the ED with acute abdominal pain received an initial dose of IV morphine followed by physician-managed analgesia as needed. Patients randomised to PCA dosing also received either 1 mg (n=69) or 1.5 mg (n=72) morphine on demand with a 6-minute lockout between doses, while the non-PCA arm (n=70) did not. All 3 groups had similar, significant reductions in NRS scores to 30 minutes, after which NRS scores in the PCA groups continued to decline (to 120 minutes) while those in the non-PCA group did not (p=0.004).[125]	IB
		In an RCT in patients with limb trauma in the ED, IV morphine (n=100) or placebo (n=100) was given 30 minutes after an initial dose of IV morphine. Patients in the morphine arm had significantly reduced pain at 1 hour compared with placebo (p<0.05), with no significant difference in the rate of AEs.[119]	IB
		Patients with acute pain presenting to two EDs were randomised to morphine given either via PCA (n=24) or as titrated boluses (n=23). Patients in the PCA group had a significantly greater reduction in pain on the VAS than the bolus group (p<0.001), with similar consumption of morphine.[127]	IB
		In an RCT, patients with acute traumatic pain of VAS score ≥7 presenting to the ED were randomised to morphine given either via PCA (n=47) or as titrated boluses (n=49). Patients in the PCA group had lower mean VAS scores than the bolus group at all time points, and were more satisfied with their care.[126]	IB

Therapy	Route	Evidence	Level of evidence
Oxycodone		In an RCT in ED patients with simple MSK injury with no complicating factors, there were no significant differences in terms of respect to time-to-analgesia, analgesic efficacy, side effects, and patient satisfaction between oral oxycodone with paracetamol (n=34) and OM fentanyl (n=38).[129]	IB
		Patients in the ED with soft tissue injuries were randomised to a single dose of either oral oxycodone (n=75) or oral naproxen (n=75). Pain scores were similar between groups at all time points assessed, although more patients given oxycodone than naproxen required additional analgesia in the first 24 hours after discharge (16.0% versus 6.6%).[130]	IB
Fentanyl		In an RCT comparing nebulised fentanyl (n=47) with IV morphine (n=43) in ED patients with moderate to severe acute limb pain, fentanyl and morphine provided similar reductions in pain of >3 points on the NRS. Patient satisfaction in both groups was similar and no adverse effects were reported in the fentanyl group.[137]	IB
		An RCT performed in a children's hospital ED randomised paediatric patients aged 3 to 15 years with fractures to standard (n=98) or high concentration (n=91) IN fentanyl. There was no statistically significant difference in median pain score between the 2 groups at any of the study time points. Within groups, patients in the standard concentration group with weight <50 Kg had a significantly greater reduction in pain score than those weighing ≥50 Kg. There was no significant difference by weight group within the high concentration arm.[138]	IB
		Patients receiving OM fentanyl for orthopaedic extremity pain in the ED (n=30) had a faster onset of pain relief than those who received oxycodone/paracetamol (n=30) (median 10 versus 35 minutes). Patients in the fentanyl arm also achieved a greater magnitude of pain relief and lower rescue medication rate.[136]	IB
		Of 2,348 patients treated with IV fentanyl in a pre-hospital setting, 79.3% achieved pain reductions of NRS >2, but moderate to severe pain was still reported by 60% of patients on arrival at hospital.[135]	III
		In a retrospective cohort study of IV fentanyl versus IV morphine, 168 patients with trauma pain in the ED achieved similar analgesia regardless of receipt of fentanyl or morphine (a reduction of NRS 2, not significant [NS]).[134] Baseline pain score in the IV fentanyl group was higher (NRS 10, IQR 8–10)) than IV morphine treated patients (8, IQR 4–10). Time to lowest pain score was faster with IV fentanyl (22 vs 47 minutes; p<0.001). Adverse event profiles in both groups were comparable, although the use of prophylactic anti-emetics was significantly higher in morphine treated patients (21.4% vs 0%; p<0.001).[134]	III
Sufentanil		Patients with acute severe trauma pain were randomised to IV sufentanil (n=54) or IV morphine (n=54). At 15 minutes, 74% of patients in the sufentanil group achieved pain relief (defined as NRS ≤3) versus 70% of those in the morphine group. Duration of analgesia was longer in the morphine group.[120]	IB
		IN sufentanil was given to 15 ED patients with acute extremity injuries. Over 30 minutes, mean pain score decreased by 4.3 points and 8 patients achieved a final pain score of ≤3. Average patient satisfaction was 4.5 out of 5.[139]	III
		Patients presenting with acute extremity injuries (most commonly upper extremity dislocations) to a ski resort clinic (n=40) were given IN sufentanil. Mean reduction in pain score was 4.7 at 10 minutes and 5.7 at 30 minutes. Five patients (12.5%) required more than 1 dose of sufentanil, and 78% of patients were very satisfied with their treatment.[140]	III
		Patients presenting at the ED with pain ≥4 on the NRS due to trauma or injury received either a single (n=40) or multiple (n=36) doses (up to 3 additional doses at least 60 minutes apart) of OM sufentanil 30 µg. In both groups, reduction in pain was clinically meaningful within 30 minutes, and pain levels had dropped by 36% at 60 minutes. 75% of patients in the multiple dose cohort required only one dose of sufentanil in total.[142]	IIB

Therapy	Route	Evidence	Level of evidence
		(*)A hand-held PCA device dispensing sufentanil OM tablets (with a lockout period of 20 minutes) was used for postoperative pain relief in 280 patients undergoing major surgery. OM sufentanil use provided effective analgesia in 90% of patients, with NRS scores <4 in 75% of patients. Over 70% of patients were highly satisfied with the system.[144]	III
		(*)Patients undergoing major elective surgery were randomised to a hand-held PCA device dispensing sufentanil OM tablets with a 20-minute lockout (n=177) or IV PCA morphine with a 6-minute lockout (n=180) for the treatment of acute postoperative pain. Successful analgesia (according to Patient Global Assessment) was achieved in 78.5% of patients receiving sufentanil and 65.6% of those receiving morphine.[143]	IB
Ketamine	IM, IV, IN		
		An RCT of patients with acute pain in the ED compared low-dose IV ketamine (n=24) with IV morphine (n=21). There were no significant differences in NRS reduction between groups at any time point. Time to achieve maximum NRS reduction was 5 minutes for ketamine and 100 minutes for morphine.[148]	IB
		Patients with long bone fractures were randomised to IV morphine (n=63) or low-dose IV ketamine (n=63). Pain scores decreased significantly in both groups at 10 minutes, with no significant differences between groups.[152]	IB
		In an RCT comparing IN ketamine (n=77) with IV ketamine (n=77) in patients with orthopaedic trauma, IN ketamine was found to be as effective as IV ketamine in reducing pain at 30 minutes. Rescue analgesia was required in 20% of patients (with no difference between groups). Adverse events were mild and transient in both groups.[155]	IB
		Patients with renal colic (n=40) received IV morphine (n=20) or IN ketamine (n=20) in a double-blind RCT. At baseline pain scores were higher in the morphine group vs that in the ketamine group (VAS: morphine = 7.40±1.18; ketamine 8.35±1.30) (p=0.021). At 5 minutes post-administration, pain relief with morphine was superior to ketamine, VAS scores were 6.07±0.47 for morphine and 6.87±0.47 for ketamine (p=0.025). At 15 minutes and 30 minutes, pain scores for both groups were comparable. At 15 minutes: morphine 5.24±0.49 morphine, ketamine 5.60±0.49 – mean difference –0.36; at 30 minutes: morphine 4.02±0.59, ketamine 4.17±0.59, mean difference –0.15.[157]	IB
		Children aged 4 to 17 years with suspected extremity fractures were randomised to IN ketamine (n=43) or IN fentanyl (n=44). Similar pain relief was observed at 20 minutes between groups, with both groups requiring a similar level of opioid rescue therapy (16% versus 18%).[158]	IB
		Children aged 8 to 17 years presenting to the ED with moderate to severe pain due to traumatic limb injuries were randomised to either IN ketamine (n=45) or IN fentanyl (n=45). After 30 minutes pain reduction was comparable between groups (−30.6 and −31.9 mm on 100 mm VAS). The need for rescue analgesia was similar between groups.[159]	IB
		Patients in the ED with moderate to severe acute traumatic pain were randomised to IN ketamine (n=34), IV morphine (n=26) or IM morphine (n=30). Pain relief 1 hour after treatment was significant and comparable between groups. IN ketamine was clinically comparable to IV morphine in terms of time to onset (14.3 versus 8.9 minutes) and time to maximum pain reduction (40.4 versus 33.4 minutes).[156]	IB
		Patients with pain due to trauma in the pre-hospital setting were randomised in an open-label study to morphine or morphine plus ketamine. All patients received IV morphine 5 mg, and were then randomised to ketamine (mean total dose 40.6 ± 25 mg) or morphine (mean total dose 14.4 ± 9.4 mg). Mean change in pain score from baseline was –5.6 (95% CI –6.2 to –5.0) for ketamine and –2.4 (95% CI –3.7 to –2.7) for morphine. AEs were more commonly reported in patients treated with ketamine (n=27/70, 39%), the most common of which was disorientation, vs morphine (n=9/65, 14%), the most common of which was nausea.[154]	IIA

Therapy	Route	Evidence	Level of evidence
Methoxyflurane	**Inhaled**		
		In a Phase III study of patients presenting to the ED with minor trauma (including 90 individuals aged 12 to 17 years), those randomised to methoxyflurane (n=150) reported significantly greater reductions in pain severity at all time points tested than those randomised to placebo (n=150) (p<0.0001). Onset of pain relief occurred within 6 to 10 inhalations and the greatest treatment effect with methoxyflurane (of −18.5 mm) was seen at 15 minutes.[170]	IB
		In the adult subgroup of the above Phase III study, mean change from baseline was greater for methoxyflurane than placebo at all time points (−34.8 versus −15.2 mm on 100 mm VAS at 20 minutes). Median time to first pain relief was 5 minutes, versus 20 minutes with placebo, and 79.4% of patients in the methoxyflurane arm experienced pain relief within 1 to 10 inhalations.[171]	IB
		Adult trauma patients treated with methoxyflurane (n=135) or SoC analgesia (n=135; NRS ≥4-6 IV paracetamol/IV ketoprofen; NRS ≥7 IV morphine) had a greater reductions in VAS over 10 minutes than SoC (ΔVAS -5.94 mm; 95% CI: -8.83 mm, -3.06 mm p<0.001).[172] Over 10 minutes comparable results were observed in patients with moderate baseline pain (ΔVAS -5.97 mm; 95% CI: -9.55 mm, -2.39 mm p=0.001) where SoC was IV paracetamol or IV ketoprofen and severe baseline pain where patients received IV morphine (ΔVAS -5.54 mm; 95% CI: -10.49 mm, -0.59 mm p=0.029). Median time to onset of first pain relief was 9 minutes (95% CI, 7.72 minutes, 10.28 minutes) with methoxyflurane compared with 15 minutes (95% CI, 14.17 minutes, 15.83 minutes) for SoC.[172]	IIA
		In adult trauma patients treated with methoxyflurane (n=156) or SoC (n=149), change from baseline pain was greater over 20 minutes for methoxyflurane than SoC 2.5 points vs 1.4 points (p<0.001).[173] Significant reductions in pain were demonstrated for methoxyflurane regardless of baseline pain, and pain reduction with methoxyflurane was greater than SoC even if SoC contained opioids. Onset to pain reduction was 3 minutes for methoxyflurane compared with 10 minutes for SoC (p<0.001).[173]	IIA
		In paediatric patients with moderate to severe acute pain in a pre-hospital setting, effective analgesia (defined as a reduction in NRS pain score of at least 30%) was achieved in 78.3%, 87.5% and 89.5% of patients given methoxyflurane, morphine and fentanyl, respectively.[169]	IIB
		In a retrospective observational study of 1,024 patients with visceral pain who received methoxyflurane (n=465), IN fentanyl (n=397) or both (n=162) in the pre-hospital setting, methoxyflurane provided more rapid onset of action than IN fentanyl (VAS 2.0 versus 1.6 at 5 minutes), although fentanyl provided greater pain reduction by arrival at hospital (3.2 versus 2.5).[168]	IIB
Nerve blockade	**Injection, infusion**		
		In an RCT including individuals with hip fracture in the ED, patients were randomised to receive femoral nerve block at admission followed by continuous fascia iliac block within 24 hours (n=79) or conventional analgesics (n=82). Pain scores 2 hours after presentation at the ED favoured the nerve block group over the control group (3.5 versus 5.3, p=0.002). At 6 weeks, participants who received nerve block reported better walking and stair climbing ability (mean Functional Independence Measure locomotion score of 10.3 versus 9.1, p=0.04).[181]	IB
		A systematic review of pain management in hip fracture included 32 studies on nerve blockade, and concluded that nerve blockades are effective for relieving acute pain and reducing delirium.[182]	IV
		A review of 7 studies of femoral nerve block in hip fracture reported decreased rescue analgesia requirements in 6 studies and no AE.[184]	IV

Therapy	Route	Evidence	Level of evidence
		A national observational study in the UK received responses from 77% of all acute medical trusts in the UK. Of these, 62% of routinely provide fascia iliac compartment block for the management of pain caused by proximal femoral fracture.[175]	III
		Patients undergoing surgery for fixation of acute closed distal radius fractures were randomised to brachial plexus blockade (n=18) or general anaesthesia (n=18). Patients who received nerve block had lower pain scores at 2 hours after surgery (1.4 versus 6.7), but higher scores at 12 hours (6.0 versus 3.8) and 24 hours (5.3 versus 3.8).[185]	IIB
Lidocaine	**IV, IA, topical**		
		A meta-analysis of 9 RCTs including 438 patients compared IA lidocaine with IV analgesia and sedation. IA lidocaine was not significantly different compared with IV analgesia and/or sedation for reduction of acute shoulder dislocation in the ED in terms of pain relief or patient satisfaction, but did have a shorter duration of hospitalisation (p=0.03) and lower risk of complications (p<0.00001).[189]	IA
		A Cochrane review of 5 studies (n=211) comparing IA lidocaine with IV analgesia with or without sedation for manual reduction of acute anterior shoulder dislocation in adults reported no significant difference between lidocaine and analgesia/sedation with regard to pain during the procedure and post-reduction pain relief. Lidocaine may be associated with fewer adverse effects and a shorter recovery time.[190]	IA
		IA lidocaine (n=32) was compared with IV pethidine and diazepam (n=31) for the relief of pain during reduction of acute anterior shoulder dislocations. There was no significant difference between groups in terms of pain relief or patient satisfaction, and patients in the lidocaine group had a shorter duration of hospitalisation and fewer complications.[191]	IB
		Patients presenting to the ED with renal colic (n=110) were randomised to IV morphine plus IV lidocaine or IV morphine alone. Patients in the combination group had a reduced length of time to becoming pain free (87 versus 100 minutes) and nausea free (27 versus 58 minutes).[186]	IIB
		Patients referred to the ED due to renal colic were randomised to IV lidocaine (n=120) or IV morphine (n=120). Patients in the lidocaine group had significantly greater pain relief than those in the morphine group at 30minutes (p=0.0001).[187]	IIB
		In a randomised study, patients with acute traumatic extremity pain were given either IV lidocaine (n=25) or IV morphine (n=25). Pain scores decreased significantly in both groups over 1 hour, with no significant differences between groups.[188]	IIB
		A retrospective analysis compared patients with rib fracture treated with lidocaine patch (n=29) with a matched control cohort (n=29). In the 24 hours after receiving lidocaine, patients in the active treatment group had a greater decrease in pain scores than controls (p=0.01). At 60 days, patients in the lidocaine group had a lower McGill Pain Questionnaire score, even though only 1 patient was still using a patch at this time point.[192]	IIB

AE, adverse event; ED, emergency department; IA, intra-articular; IM, intramuscular; IN, intranasal; IQR, inter quartile range; IV, intravenous; MSK, musculoskeletal; NRS, numeric rating scale; NSAIDs, non-steroidal anti-inflammatory drugs; OM, oromucosal; PCA, patient-controlled analgesia; PR, per rectum; RCT, randomised controlled trial; SC, sub-cutaneous; VAS, visual analogue scale.
(*) Study undertaken in patients with post-operative pain.

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GUIDELINES FOR THE MANAGEMENT OF ACUTE PAIN IN EMERGENCY SITUATIONS

CHAPTER 6:

Management of pain in the pre-hospital and hospital settings

The successful management of patients' pain is one of the most important contributions that can be made by emergency care practitioners, not least because undertreated acute pain can have damaging long-term consequences[1-3] but also because providing effective pain relief is an important endpoint in itself.[3] In this chapter we will focus on issues relating to the assessment and management of pain in the pre-hospital and acute hospital settings.

Pre-hospital management of acute pain

Emergency pre-hospital care can be required in a wide range of settings, from the home and roadside to remote locations such as mountainsides or coastal areas, and can involve a wide range of personnel, including paramedics, mountain rescue, fire department, water rescue and police with differing access to, and experience with, the provision of analgesia. In some cases, physical access to the patient may be restricted. All of these factors can have an impact on how the assessment and management of pain might be optimally provided.

Assessment

Acute pain is often poorly assessed in the pre-hospital setting,[4-10] with initial and final pain assessment absent in up to half of all cases.[6] In practice, whether pain is assessed or not in the pre-hospital setting tends to be associated with the clinical condition and level of alertness of the patient, rather than the type of personnel present at the scene.[9] Tools are available, however, that are both simple and quick to use to assess pain in the pre-hospital setting, especially in those patients who are able to communicate verbally. The numerical rating scale (NRS) (which has been shown to correlate highly with the visual analogue scale [VAS]; r=0.94)[11] is the assessment tool most often used in adult patients in the pre-hospital setting (Level III)[9] (*see Table 7.1, page 69*). In addition, recording pain at the scene of the emergency and on arrival at the ED has been shown to be feasible using the VAS and verbal descriptor scales, as well as the NRS.[12,13] Following the adoption of a universal pre-hospital pain assessment protocol (which included use of a four-category verbal descriptor scale and the NRS), a retrospective review of 1,227 emergency medical services patient records found that pain assessment was successfully performed per protocol in 84% of patients (Level III).[13] In a prospective, observational study, paramedics were asked to record patients' pain severity using the VAS at two time points during initial assessment and on arrival at hospital (Level III).[12] Results revealed a mean improvement in pain score of 18.2 mm during the assessment period, although a deterioration in pain score was recorded in 18% of patients. The investigators noted the importance of having data available from a valid and reliable measurement tool in order to make it possible to audit and make improvements to clinical practice.[12]

Management of acute pain

An important aim of best-practice acute pain management should be, wherever possible, for patients to receive adequate treatment for their pain before reaching the ED. Management of pre-hospital analgesia often includes providing pain relief for procedures carried out at the scene of the emergency, most commonly limb realignments in

the case of dislocations and splinting in the case of fracture, which often result in intense to severe pain and must be managed accordingly (Level IIB).[14] However, acute pain is often undertreated in the pre-hospital setting,[4-10] with many patients reporting moderate to severe pain receiving no analgesia at all.[6] In one example, in patients aged over 65 years with suspected fractures attended by paramedics, the median initial pain intensity was 8 on a 10-point NRS, and yet only 60% of individuals received analgesia (Level III).[6]

Debate about optimal analgesic care of patients with acute pain in the pre-hospital setting continues, and there is wide variation in clinical practice.[15] For example, the type of analgesia available to a patient at the scene of the emergency may be limited by the prescribing rights of emergency services personnel or nurses, or by availability of the drug according to the health authority in that country. In the UK, opioids have been available for use by paramedics for the management of pain since the early 1990s, but this may not be the case elsewhere.[9] In Italy, a tenth of all ambulances carry no analgesic medication at all, despite over 40% of the patients they transport reporting moderate to unbearable pain (Level III).[4] In France, around 40% of patients with acute pain cared for on board a mobile intensive care unit receive paracetamol (Level III),[8] while this is rarely used in the pre-hospital setting in other European countries such as the UK (Level III).[9]

Ketamine, nitrous oxide and opioids are commonly used in the pre-hospital setting.[3,15] Ketamine is often combined with morphine in patients with acute trauma pain, and can reduce morphine requirements in these individuals (Level IB).[15] Ketamine is particularly useful in a pre-hospital setting as, in addition to its opioid-sparing effect, it provides effective analgesia without respiratory depression and has little effect on blood pressure and pulse rate (Level IIB).[16]

According to a retrospective review of ambulance service records performed in the UK, nitrous oxide is the most commonly used analgesic in patients with fracture, while opioids are likely to be prescribed for conditions such as acute myocardial infarction (Level III).[9] While morphine (and fentanyl in the United States of America [USA]) is widely used in the pre-hospital setting,[3,16] the potential for excessive sedation, respiratory depression and nausea with the use of opioids may be a concern in patients with severe acute pain (Level IV).[16] In addition, the time taken to administer IV opioids can delay transfer to hospital, increasing patient distress as well as impacting on patient flow and resource utilisation.[3,17] Moreover, IV access can be difficult to achieve in a range of situations such as confined spaces (e.g. an accident victim trapped in a car), cold conditions, in very young or very old patients or in those with needle phobia. In such cases, inhaled analgesics have distinct advantages. The inhalational analgesic low-dose methoxyflurane is used extensively within a number of ambulance services and armed forces in Australia and New Zealand,[18] though currently it is less widely used in Europe. The methoxyflurane inhaler is compact, highly portable and easy to use, all useful qualities for use in the pre-hospital setting. For this reason it has been proposed as an ideal analgesic for remote emergency settings such as at high altitudes (Level III).[19]

Whichever analgesic agent is selected for pre-hospital pain management, monitoring the effects of that analgesic on the patient is vital, and should include electrocardiogram, breathing and heart rate, pulse oximetric oxygen saturation, blood pressure (BP) and (optionally) capnography. Emergency equipment for airway management, ventilation, suction and resuscitation must be available in case of an adverse response (Level IA).[20]

In addition to the pharmacological options for pain management in the pre-hospital setting, non-pharmacological management techniques can also be considered, as long as they do not prolong total rescue time in the case of life-threatening injury (Level IA).[20] In injuries of the extremities, positioning and splinting can help to relieve pain until the patient reaches the ED, as well as helping to prevent further damage and maintain local perfusion (Level IA).[20] There is also evidence to suggest that acupressure (Level IA) and TENS (Level IA) may reduce pain severity and patient anxiety in the pre-hospital setting.[21-23]

ED management of acute pain

The primary aim of acute pain management is to reduce the patient's pain with minimal AEs while allowing them to maintain function.[24] Successful management of acute pain requires close liaison of all personnel involved in the care of the patient,[2] and an efficient clinical handover between pre-hospital and ED staff plays a vital role in patient care.[25]

Assessment

Evaluation of acute pain

Once a patient reaches the hospital ED, their pain should be assessed as quickly as possible. The assessment of acute pain should include a thorough general medical history and physical examination, a specific history of the pain under evaluation (**Table 6.1**), and an assessment of any associated functional impairment.[2] As discussed in more detail in Chapter 3, self-reporting of pain should be used whenever appropriate, as pain is a personal and entirely subjective experience. The choice of pain measurement tools must reflect the individual patient in terms of developmental, cognitive, emotional, language and cultural factors.[2] The inability to communicate verbally does not mean that an individual is not in pain and in need of analgesia, and a number of validated tools are available to assess patients in these circumstances.[26]

Table 6.1 Fundamental components of a pain history[2]

Site of pain	• Primary location of pain – description and diagram of pain location • Radiation of pain from primary location
Circumstances associated with pain onset	• Including details of trauma or surgical procedures
Character of pain	• Descriptors of sensation – sharp, burning, throbbing etc. • McGill Pain Questionnaire – sensory and affective descriptors • Characteristics of neuropathic pain using specific neurapathic pain questionnaires e.g. NPQ, DN4, LANSS, PainDETECT, ID pain

Intensity of pain	Intensity in different situations
	• At rest
	• On movement
	• Other temporal factors
	  – Pain duration
	  – Pain over time: current, last week, highest intensity
	  – Characteristic of pain – continuous, intermittent

Associated symptoms	• Other symptoms e.g. nausea
Effect of pain on activities and sleep	• Interruptions to sleep, ability to undertake normal activities
Treatment	• Current and previous medications including dose, frequency, efficacy, side effects • Other treatment for pain • Which healthcare professionals have been consulted in relation to pain
Relevant medical history	• Prior or coexisting pain conditions and treatment outcomes • Prior or coexisting medical conditions
Factors affecting patients' symptomatic treatment	Understand non-medical factors including • Belief concerning the causes of pain • Understanding, knowledge, expectations and preference for pain management treatment • Expectations of outcome of pain treatment • The reduction in pain required for patient satisfaction • The patient's typical coping strategies for stress and pain (understand if patient has anxiety, depression or psychiatric disorders present) • Family/carer expectations and beliefs about pain, stress and management course

DN4, Douleur Neuropathique en 4 Questions; NPQ, Neuropathic Pain Questionnaire; LANSS, Leeds Assessment of Neuropathic Symptoms and Signs

Regular reassessment of pain is as important as the initial assessment, in order to monitor the effectiveness of pain management and the changing analgesic requirements of the patient. It should take place at a frequency guided by the patient's pain severity.[3]

Unidimensional measures of pain intensity such as the VAS, NRS and verbal descriptor scales are more commonly used to quantify pain in the acute pain setting than multidimensional measures, which are often used in the assessment of chronic pain to provide further information about the characteristics of the pain and its impact on the individual, such as associated disability.[2]

In adult patients who are alert, communicative and without cognitive impairment, the VAS and NRS provide a more sensitive measurement of pain than verbal descriptor scales (Level III).[27,28] Of the two, the NRS may be more practical than the VAS in a busy ED in that it is generally easier for patients to understand and also doesn't require patients to have clear vision and manual dexterity, or for a pen and paper to be provided.[28] For the assessment of patients who fall outside of this alert, verbally communicative profile, the Face, Legs, Activity, Cry and Consolability (FLACC) scale and FACES pain scale (FPS) are recommended for use in young children with no and limited abilities to communicate, respectively (Level III).[29-31] The methods of assessing pain in elderly individuals should be driven by the presence and degree of cognitive impairment. While cognitively intact elderly individuals can be assessed in the same way as younger adults, a range of specialised tools are available for individuals with cognitive impairment and advanced dementia (see Chapter 3).[32-34]

Other clinical assessments

Many patients with acute pain in the ED undergo other clinical assessments to provide additional information on the cause of their acute pain, which can in turn help to determine the optimal analgesic approach. Radiography, ultrasonography and computed tomography (CT) are common in the management of acute abdominal pain, and provide a reasonable to good degree of sensitivity for the diagnosis of urgent conditions (88% for radiography, 70% for ultrasonography and 89% for CT; (Level III).[35] Electrocardiograms, radionuclide myocardial perfusion, magnetic resonance imaging, CT and biomarker analysis can all be useful to provide further information in patients with acute chest pain (Level IV).[36] Ultrasound, sonography and CT are commonly used in female patients with acute pelvic pain in the ED (Level IV).[37]

Management of acute pain

Selection of analgesic approach

Following assessment of a patient's pain, the appropriate analgesic must be selected, taking into account its benefits and risks with reference to the individual patient and considering both pharmacological and non-pharmacological approaches. Once analgesia has been provided, patients must be reassessed to ensure that their pain is being successfully managed, and their pain relief regimen should be re-evaluated regularly during their stay in the ED (Level IV).[38] Any barriers to pain management should be discussed with the patient and family member in order to identify potential solutions.[38]

A wide range of analgesic agents are used to treat acute pain in the ED, including paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), opioids and nitrous oxide.[3] Although opioids are commonly used in this setting, a number of considerations should be taken into account when deciding whether to administer opioids to a patient with acute pain. These include the high associated administrative burden, including the requirement for patient monitoring after receiving an opioid (from ≥1 hour to an overnight stay, dependent on local protocols); the burden of managing analgesia given via the IV route; and the special regulations, staff training and certification requirements, and storage and prescribing procedures associated with controlled substances.[3] In addition, opioids are associated with a higher incidence of adverse reactions than some other analgesic options, particularly in opioid-naive patients.[39] Notable side effects of opioids include nausea and vomiting, sedation and respiratory depression, itching and allergic reaction.[39-41]

The use of multimodal analgesia, an approach involving the combination of opioid and non-opioid analgesics acting at different sites within the pain pathway to provide an additive or synergistic effect, may help to optimise outcomes in the treatment of acute pain, reduce opioid-related side effects and prevent chronic pain (Level IV).[42] The administration of rapidly acting IV agents in small doses at frequent intervals until pain relief is achieved is recommended to allow the determination of the patient's individual requirements before long-acting medications or patient-controlled analgesia (PCA) are initiated (Level IV).[38]

While pharmacological analgesics are essential for the management of pain in the ED, the importance of non-pharmacological treatments should not be overlooked.[43] Psychological interventions such as the sharing of information about the procedure and what the patient might expect to feel during it,[44,45] and distraction techniques such as the use of imagery, music and relaxation, may be most appropriate to acute pain in the ED,[46-48] although robust clinical evidence specific to this setting is currently lacking.

Logistical considerations

Patient-controlled delivery of analgesia should be considered where appropriate and possible, since it provides a rapid response to patients' changing requirements for pain relief and removes some of the burden of management from hospital staff.[49] Evidence suggests that PCA also results in greater patient satisfaction than physician-managed analgesia (Level IB),[50-52] and reducing delays in analgesic administration may lead to patients leaving the ED faster.[53] A short time to analgesia, rather than provision of adequate pain relief, has been associated with a shorter length of ED stay in a post-hoc analysis of real-time data (Level III).[53]

The chances of patients receiving adequate, timely analgesia are related to time and resources within the ED.[54-56] A greater delay in a patient receiving their first analgesia has been significantly correlated with larger EDs, the absence of a triage nurse, older patients and moderate initial pain intensity (Level IIB).[57] High levels of ED crowding and long wait times are common in some European countries as demand for services increases: in France, visits to the ED increased by 64% from 1995 to 2005, while in Italy the number of ED visits has recently been increasing by 5% to 6% per year (Level IV).[58] Overcrowding contributes to delays in patients receiving analgesia.[55] In a retrospective cohort study of patients presenting with severe pain to the ED, 70% experienced delay between triage and analgesia and 49% experienced delayed analgesia after placement in a room/cubicle in the ED (Level III).[55] Delays in treatment were independently associated with overcrowding parameters (number of waiting rooms and inpatients, and occupancy rates) and increased as the ED became busier.[55]

Discharge from the ED

Effective communication between the physician and patient is required for optimal management of the patient after discharge from the ED (Level IV).[59] Written discharge instructions can improve communication and patient management when used to complement verbal instructions.[59] These can come in a variety of formats, from simple written notes to pre-formatted instruction sheets with spaces for patient details and instructions to be added (**Figure 6.1**). The latter are recommended as they can include standardised language that has been reviewed for clarity and simplicity, and the provision of subheadings can help to prompt ED personnel to provide adequate information that covers all relevant topics.[59] Published recommendations also include the establishment of policies to

Figure 6.1 Sample discharge patient instruction sheet

Discharge Information Sheet

Patient name………………………………………………………………………………….
This form provides information about your medical care following discharge from hospital.
Please keep this form and take it with you in case you need further care from your primary care physician or hospital.

You were seen today by Drs…………………………………………………………………..
…………………………………………………………………………………………………

Your diagnosis………………………………………………………………………………..
What you might expect……………………………………………………………………….
Potential complications which may occur……………………………………………………………………
Return to the Emergency Department if the following occurs…………………………………………………………..

Prescribed medication (name, dose, frequency of administration, reason for prescribing)
1………………………………………………………………………………………………..
2………………………………………………………………………………………………..
3………………………………………………………………………………………………..
What to do with your current medication……………………………………………………………………….

Follow up with…………………………………………….. Contact details………………………………………
Follow up within (days/weeks)…………………………………………………………………………………..

Instructions given by
Name……………………………………………….. Signature…………………………………………..

I, the patient, have read and understood these instructions
Name……………………………………………….. Signature…………………………………………..
Date…………………………………………………..

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promote best practice in communication in the ED, including systems to ensure that discharge instructions are given to all patients upon leaving the ED.[59]

Over half of patients who arrive at the ED in pain will still have moderate to severe pain at discharge.[60] Emergency physicians therefore have an important role in helping patients to manage pain, even after they have left the ED. Over 20% of patients discharged with fractures or non-fracture musculoskeletal (MSK) diagnoses (e.g. sprains and back pain) leave the ED without an analgesic prescription (Level III).[60] Around three quarters of patients discharged from the ED with a prescription for medication state that they are satisfied with their pain relief (Level III).[61] However, 13% of patients with prescribed analgesics never collect their medication, and – unsurprisingly – these patients report the least satisfaction with their pain control.[61]

Management of pain in the pre-hospital and hospital settings: take-home messages

- **The NRS is the most commonly used pain scale in adult patients in the pre-hospital setting.**

- **The analgesic agents available to a patient at the scene of an emergency varies by country and in some cases according to the personnel attending the scene.**

- **From those that are available, the most appropriate agents to use will depend on the severity and cause of pain, as well on any limitations imposed by the emergency setting (e.g. restricted access where a patient is trapped in a vehicle).**

- **In the ED, effective assessment and regular reassessment of pain are important. The initial assessment should include a general and a pain-specific medical history.**

- **The choice of analgesic agent should take into account its benefits and risks, considering the specific needs of the individual patient.**

- **Overcrowding in the ED contributes to delays in receiving analgesia, which in turn can affect patient outcomes.**

- **Effective communication is required for optimal management of the patient after discharge from the ED.**

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GUIDELINES FOR THE MANAGEMENT OF ACUTE PAIN IN EMERGENCY SITUATIONS

CHAPTER 7:

Pharmacological management of acute pain symptoms – recommendations

In the pre-hospital or ED setting pain management should be straightforward to administer and be patient- and condition-specific. In all cases it should be preceded by pain assessment and recording of pain scores.

This guideline handbook, and in particular this chapter, have been developed in order to provide clear guidance on pain management approaches for both adults and children. The recommendations in this chapter do not cover palliative care or discharge analgesia from either the ED or pre-hospital setting.

This chapter provides an overview of treatment options for patients experiencing acute pain. An overview of the principles of acute pain management, prescribing caveats for special populations and implementation of non-pharmacological and pharmacological analgesia for both adult and paediatric patients is provided. The content contained in this Chapter is intended for use by all emergency personnel including ED physicians, nurses and paramedics who have relevant prescribing authority. The treatment algorithms give an overview of all potential analgesic medications that may be used to manage pain by its severity. Practitioners should choose medication within their appropriate prescribing rights and within their scope of professional practice and accept clinical/legal responsibility for their prescribing decisions.

Given the variety of medication availability across Europe the algorithms have been developed with a range of flexible alternative options to meet the needs of individual institutions and settings. Before using the algorithms in this chapter it is incumbent on the user to review their analgesic choices against the needs and characteristics of the individual patient. Dosing considerations for special populations are provided.

Principles of effective pain management

- Evaluate how distress is contributing to a patient's pain experience, take measures to address their pain empathically, acknowledging it and demonstrating a willingness to understand their experience.
- In all cases consider the use of non-pharmacological analgesic strategies to achieve pain relief. This may involve techniques such as splinting, immobilisation, heat/cold, distraction, etc. and for children additional distraction techniques such as play *(see Chapter 4 for an overview of non-pharmacological analgesia)*.
- If pharmacological analgesia is required, ensure that there are no contraindications to medications before administration and ensure that all medications administered are clearly documented *(see Chapter 5 for an overview of pharmacological analgesia)*.
- Analgesics should be administered orally where possible and, whatever route is used, titrated, if possible, until adequate pain management is achieved.
- Pain should be reassessed, and if analgesia is found to be inadequate stronger analgesics should be used, in conjunction with non-pharmacological methods.

Patient considerations

Elderly

Providing effective analgesia to older patients is a common challenge faced by emergency physicians. Older patients have been shown to be at greater risk of oligoanalgesia[1,2] and in the ED are up to 20% less likely to receive treatment than younger patients.[3]

Studies have also indicated that detecting, assessing and managing pain in elderly patients with cognitive impairment are challenging[4] and require a broader approach to include appropriate observation tools and involvement of family/carers. Analgesia should be selected based on patient-specific risks (e.g. polymorbidities, chronic abuse of analgesics, impaired renal or hepatic function) and preferences, alongside frequent reassessment and treatment titration as needed.

Children

The management of pain in children presents issues relating to assessment and intervention. Among children, evaluation of pain may be suboptimal and, even when pain is assessed, for many patients this may not lead to analgesic intervention.[5,6]

The most robust analysis of pain in children and young people is self-report using VAS or NRS scales similar to adults. In children unable to articulate their pain, observational scales can be used, including PIPP,[7] CRIES,[7] FACES[8] and FLACC scales[9] and for those with cognitive impairment the FLACC-R scale[10,11] - but all of these are limited by being an observation of an outsider rather than a report of the patient.

Barriers to pain management in children are multifactorial and include patient volume, staffing issues, lack of non-pharmacological interventions, inadequate pain assessment and lack of analgesic availability at triage.[12] Optimal pain management in children should focus on non-pharmacological interventions, environment and pharmacological interventions.

Studies have demonstrated value in non-pharmacological interventions in children including distraction therapy e.g. controlled breathing, physical distraction with toys/books, or non-nutritive sucking with sucrose solution in the very young through to interactive distraction with video games or virtual reality in older children and adolescents.[13-18] Other interventions to reduce fear and anxiety in children and adolescents include those relating to the ED environment including placing children in child-friendly rooms away from the noise and chaos of the ED, explaining to patients the procedures that might happen and treatment flow and, where possible, include child specialists such as Child Life Specialists.[19,20] The primary focus of paediatric pharmacological pain management is timely intervention via an appropriate route with an appropriate agent. Establishing IV access may be difficult in children and oral or rectal preparations of paracetamol or NSAIDs should be considered for those with mild or moderate pain. For those with severe pain the aim of analgesia should be to establish IV access, and topical anaesthetic administered at point of triage may be helpful to facilitate this. For instances where IV access cannot be established other routes of administration should be considered and the use of IN preparations including IN ketamine and IN fentanyl are increasing in use.[21-25]

Pregnancy

Analgesic prescribing during pregnancy is challenging and whilst many analgesics may be considered safe to use there are specific considerations to be noted.[26] Non-pharmacological treatment should always be considered before analgesic medications are used. Paracetamol is regarded as the analgesic of choice for pregnant patients with no risks noted for congenital abnormalities or spontaneous abortion.[27] Non-steroidal anti-inflammatory drugs (NSAIDs) may be considered in early- and mid-pregnancy[27] but should be avoided in the third trimester because of the risk of premature closure of the ductus arteriosis.[28] Evidence for opioids in pregnancy is largely limited to pregnant patients abusing opioids, which is associated with adverse neonatal outcomes. Short-term use of opioids for pain in pregnancy does not, however, appear to be problematic for patients or foetuses.[26] Although nitrous oxide is not absolutely contraindicated in pregnancy it should be used with caution.

Patients receiving opioids for chronic pain

Any patient in receipt of analgesia for chronic pain conditions presenting with new acute pain needs to be assessed on a case-by-case basis to ascertain the cause. In patients currently receiving opioids, the amount of opioid used daily prior to the onset of the new pain must be determined and adequate doses of opioid need to be prescribed to treat baseline pain in combination with short-acting opioids to address the new acute pain.[29]

Drug-seeking behaviour

There will be occasions when patients presenting with a chief complaint of pain may raise concerns of drug-seeking behaviour, an issue that is likely to increase as concerns regarding opioid prescribing emerge in Europe. A careful history and patient review are required to balance the risk of supplying drugs inappropriately with denying effective analgesia to patients with genuine pain. Until more information is available, unless there is strong evidence to the contrary, an assumption must be made that the patient is in real pain and appropriate analgesia supplied,[30] given that a primary role for clinicians is the alleviation of patients' pain. In patients addicted to opioids who are reporting genuine pain, consider the use of non-opioid approaches such as steroid injections, radiofrequency neurotomy, nerve blocks or non-pharmacological approaches.[31]

Drug seeking individuals may display characteristics including, but not limited:[32]

- Inconsistent behaviour from the triage/waiting room to the treatment area
- Appearing to be in less pain when think not being observed
- Presenting with specific, often subjective complaints e.g. back pain, headache
- Excessively talkative, friendly or helpful
- Suggesting specific medications or dosages
- Claims of extraordinarily rapid relief from injectable medications
- Claiming allergies to non-narcotic medications.

Development of the EUSEM Acute Pain Management Guideline - process

The handbook and the resulting recommendations outlined on the following pages were informed and developed with:

1. A survey of EUSEM members to benchmark the unmet needs and current practice of acute pain management in emergency settings in European countries
2. A comprehensive systematic literature review based on strategic methodology,[33] the results of which were ascribed graded levels of evidence (**Table 7.1**) to assist in developing management recommendations.

Evidence-based data and the real-world experience of EUSEM colleagues across Europe, alongside clinical expertise and experience of the EUSEM European Pain Initiative Steering Committee were then used to develop management recommendations.

Table 7.1 Levels for grading evidence utilised in developing the EUSEM Acute Pain Guidelines

Level IA	Evidence from meta-analyses or systematic review of multiple well-designed randomised controlled clinical studies (RCT)
Level IB	Evidence from at least one published RCT conducted in line with recognised Good Clinical Practice (GCP) standards
Level IIA	Evidence from non-randomised clinical studies including open-label studies, and observational studies
Level IIB	Other study types e.g. retrospective cohort studies
Level III	Non-experimental descriptive study e.g. case series, case-controlled studies
Level IV	Expert opinion derived from respected authorities or clinical evidence

In recognition that variations in practice, drug availability and capability to prescribe differ across Europe, and as an aim to reduce barriers to adoption of these recommendations options are provided within the following treatment algorithms to allow regional and local variation. Recommendations have been made so that acute pain management

is viable for all appropriate personnel in the emergency setting within their appropriate prescribing rights and their scope of professional practice and who are able to accept clinical/legal responsibility for their prescribing decisions.

Algorithms for treatment of undifferentiated acute pain in the emergency setting

Guidance on pain management approaches for consideration in adults and children is provided in **Figure 7.1a,b** and **Figure 7.2a,b**, respectively.

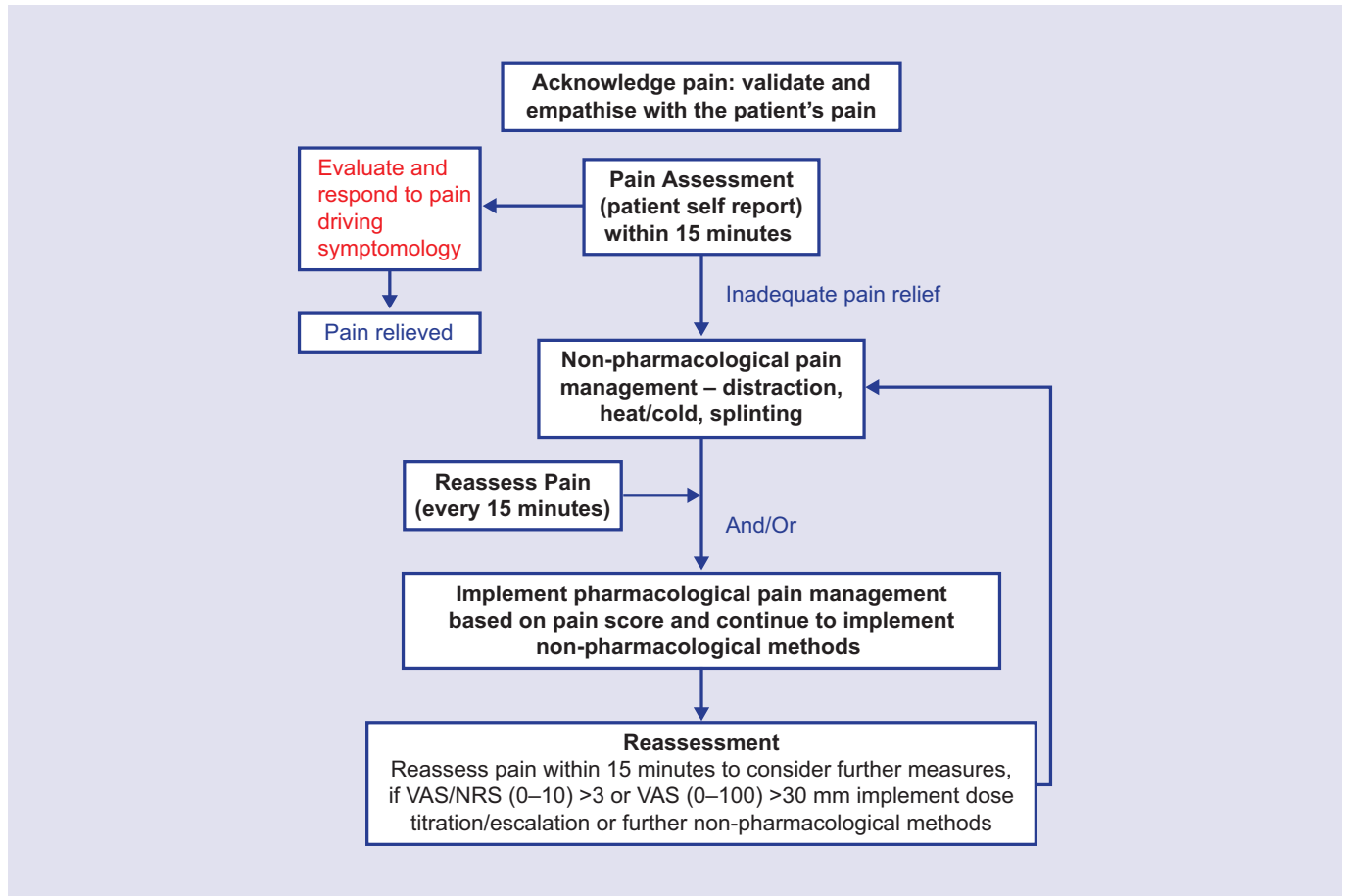**Figure 7.1a** Management of acute pain symptoms – adults

Figure 7.1b Pharmacological management of acute pain symptoms – adults

Pharmacological pain management based on pain score		
Mild pain – NRS 1–3/VAS 1–3/0–30	**Moderate pain – NRS 4–6/VAS 4–6/40–60**	**Severe pain – NRS 7–10/VAS 7–10/70–100**
Paracetamol PO 1 g Paracetamol SL 2 × 0.5 g **OR** Ibuprofen PO 400 mg Naproxen PO 500 mg Diclofenac PO 50 mg Celecoxib PO 200 mg[b]	**Inhaled therapy (as other analgesia established)** Nitrous oxide/oxygen INH Methoxyflurane INH 1 × 3 mL vial (max daily dose 2 × 3 mL vials) **AND** Paracetamol PO 1 g Paracetamol SL 2 × 0.5 g Paracetamol IV 1 g **AND** Ibuprofen PO 400 mg Naproxen PO 500 mg Diclofenac PO 50 mg Ibuprofen IV 400–800 mg (max daily dose 3,200 mg) Diclofenac IV 75 mg (max daily dose 150 mg) Ketorolac IV 0.25 mg/Kg to max 10 mg[a] Celecoxib PO 200 mg[b] **AND** Metamizole 8–16 mg/Kg PO as a single dose **OR** 1 g slow IV infusion (max daily dose 2 g) **AND** Codeine phosphate PO 30–60 mg Tramadol PO 50 mg	**Inhaled therapy (as other analgesia is established)** Nitrous oxide/oxygen INH Methoxyflurane INH 1 × 3 mL vial (max daily dose 2 × 3mL vials) **1st line treatment** Morphine IV 2–3 mg (titrate at not <2 min intervals at 0.1 mg/Kg IV) Fentanyl IV 0.05 mg Fentanyl IN 50–100 µg (repeat dose <10 minutes)[c] Fentanyl SL 100 mg (only for use in patients with opioid tolerance) Sufentanil IV 1.5–2.5 µg/Kg (via PCA) Sufentanil IN 0.5 µg/Kg (option for subsequent dose × 2 at 10 and 20 min of 0.15 µg/Kg as required) Sufentanil SL 15 µg (subsequent doses not to be administered <20 min after previous) **2nd line treatment** Paracetamol IV 1g **AND** Codeine phosphate PO 30–60 mg Tramadol PO 50 mg Oxycodone PO 10 mg **3rd line treatment** Ketamine IV 0.1 mg/Kg (repeat dose × 1 after >10 min) Ketamine IN 0.7 mg/Kg initial dose (subsequent dosing 0.3–0.5 mg/Kg not <15 min) Ketamine IM 0.5–1 mg/Kg (repeat dose × 1)

IM, intramuscular; IN, intranasal; INH, inhaled; IV, intravenously; NRS, numerical rating scale; PCA, patient controlled analgesia; PO, orally (per os); SL, sublingual; VAS, visual analogue scale.

(a)Ketorolac IV 0.25 mg/Kg to a maximum dose of 10 mg may be used in individuals aged >16 years (b)COX-2 inhibitors are used in some countries for acute pain relief, but are avoided in others because of the potential for increased risk of cardiovascular events; (c) titrate fentanyl to effective analgesia or maximum doses recommended in your country/institution

NOTE: for each recommendation within a group, for example Paracetamol PO 1 g, Paracetamol SL 2 × 0.5 g, Paracetamol IV 1g , practitioners should choose only one option. If analgesia is insufficient practitioners should consider adding 1 drug from another group, for example ibuprofen PO 400 mg followed by codeine phosphate PO 30-60 mg if pain severity requires an increase in analgesia. Drugs from within the same group should not be used in combination e.g. diclofenac and ibuprofen or morphine and fentanyl.

Ensure that naloxone reversal is available and ready for use when opioids are administered.

Assess the presence of contraindications for all drugs, including simple analgesics. Consult Summary of Product Characteristics for each medication as required for further information.

General principles

- Do not use intravenous (IV) opioids in combination with other IV opioids because of the risks of sedation and respiratory depression.
- When administering opioids ensure that naloxone is available for reversal and ready to use as required if clinically significant sedation or respiratory depression occurs.
- Only prescribe second line NSAID analgesia (e.g. diclofenac or ketorolac) in patients who have not received previous NSAIDs e.g. ibuprofen.

Dosing considerations for adults

- **Codeine:** indicated for use in patients aged ≥12 years, in adults oral doses of 30–60 mg may be considered up to maximum adult dose of 240 mg/day which must not be exceeded.[34,47]
- **Fentanyl:** for intranasal (IN) or IV administration dosing should be started at 50 µg if possible and may be repeated after initial dosing to a maximum dose of 200 µg or by continuous infusion according to local protocols; if IN fentanyl (50–100 µg) proves insufficient follow with IV fentanyl or IV morphine.[35]
- **Ketamine:** indicated for use when opioids such as morphine or fentanyl prove insufficient or painful extrication from the emergency scene is required; IV dosing of 0.1 mg/Kg is recommended which can be repeated but not more frequently than 10 minutes, IN dosing of 0.7 mg/Kg can be considered with the potential to provide subsequent dosing of 0.3–0.5 mg/Kg at not more than 15 minutes or intramuscular (IM) dosing of 0.5–1 mg/Kg with the option to repeat dosing one. Please note that ketamine is associated with salivation so careful airway management is important.[34,36,37] Avoid use in pregnancy.[36,37]
- **Metamizole:** may be administered as an adjunct to paracetamol in moderate pain at an oral dose of 8–16 mg or slow IV infusion of 1 g, but the risks of serious adverse events mean it cannot be considered for first line treatment in severe pain.[34,38] Serious adverse events include severe agranulocytosis, allergy and anaphylaxis, but its use may be beneficial in emergency care in hostile environments such as entrapment or inhospitable environments such as mountain rescue.
- **Methoxyflurane:** indicated for use in adult patients with moderate to severe acute trauma, one bottle of methoxyflurane in the Penthrox inhaler will provide up to 30 minutes analgesia with continuous use and longer with intermittent use.[39] A second bottle may be added to the Penthrox inhaler if required for extended analgesia, further dosing is contraindicated within 24 hours.[39] The use of methoxyflurane should be considered in inhospitable environments where patients are difficult to reach e.g. mountain rescue, entrapment or multiple casualties.
- **Morphine:** For IV administration at doses of 2–3 mg titrated with subsequent dosing not <2 minute intervals as needed may be administered at doses of 0.1 mg/Kg.[34]

Considerations in special populations and contraindications

- **Codeine:** doses in elderly patients should be reduced. Codeine is a prodrug and will not be effective in patients deficient in CYP2D6 (7% to 10% of the population). Codeine is contraindicated in patients with liver disease and patients at risk of increased intracranial pressure. Codeine must not be used in patients known or suspected of being CYPD26 ultra-rapid metabolisers (1% to 2% of the population) owing to high risk of toxicity. Codeine is not to be used in breastfeeding patients, or in those aged ≤12 years.[34,40]
- **Fentanyl:** indicated for use in patients with opioid tolerance. Data in the elderly are limited but the lowest possible dose should be used. Fentanyl should be used with caution in patients with impaired renal or hepatic function and those at risk of increased intracranial pressure.[35] Fentanyl may produce bradycardia and patients given fentanyl IN should be monitored and caution is advised in patients with previous or pre-existing bradyarrhythmias. As with

all opioids, fentanyl should be used with caution in patients with hypotension or hypovolaemia.[35]

- **Ketamine:** contraindicated for use in patients where an increase in blood pressure (BP) would be hazardous. No studies in pregnancy have been undertaken and the use in pregnancy has not been established and is not recommended except for during surgery or infant delivery (vaginal or abdominal). Dose reductions in patients with hepatic impairment should be considered.[34,36,37]

- **Ketorolac:** IV ketorolac administered by bolus infusion over no less than 15 seconds, recommended maximum dose for adults is 10 mg that may be repeated not less than two hours later. Reduce dosage in adults weighing <50 Kg. In the elderly, use the lowest dose possible and do not exceed a maximum daily dose of 60 mg. Ketorolac is contraindicated in patients with active or historical GI bleeding, heart failure, severe hepatic or renal failure.[41]

- **Methoxyflurane:** contraindicated for use in patients with clinically significant renal or hepatic impairment, cardiac insufficiency or respiratory depression, known or suspected susceptibility to malignant hyperthermia, history of previous serious adverse events (SAEs) with fluorinated anaesthetic agents.[39] Use in pregnancy for emergency analgesia has not been established but methoxyflurane has historically been used for obstetric analgesia; minimum doses of methoxyflurane should be used in this patient group.[39]

- **Metamizole:** use in the third trimester of pregnancy is contraindicated.[34]

- **Morphine:** morphine doses should be reduced in the elderly, and the lowest possible dose to achieve analgesia used; morphine is contraindicated in patients with moderate or severe renal impairment, liver failure, patients at risk of increased intracranial pressure, patients with biliary or renal tract spasm, and patients in receipt or have received monoamine oxidase inhibitors within two weeks. As with all opioids, morphine should be used with caution in patients with hypotension or hypovolaemia and monitor for signs of sedation or respiratory depression.[34]

- **Nitrous oxide/oxygen:** contraindicated for use in patients with head injuries or impaired consciousness, pneumothorax, air embolism, suspicion or evidence of decompression sickness, severe bullous emphysema, gross abdominal distension, intoxication and patients with maxillofacial injuries.[42,43] Use with caution in patients with substance abuse.[43]

- **NSAIDs:** assess the presence of contraindications to prevent gastrointestinal (GI) bleeds, avoid use in patients with asthma. NSAIDs are contraindicated in patients with active or previous GI ulcers, and patients with severe hepatic or renal failure. In the elderly use the lowest possible dose because of the risk of GI bleeding. NSAIDs are contraindicated in the last trimester of pregnancy.[44]

- **Oxycodone:** dose adjustments in the elderly are not usually required. In patients with renal or hepatic impairment dosages of oxycodone should be reduced by 50%.[45] It is not recommended for use in pregnancy, and should not be used in breastfeeding women.[45]

- **Tramadol:** dose reduction in the elderly is not usually required, unless hepatic or renal impairment is present. Consider dose reductions in patients with mild or moderate renal or hepatic insufficiency but tramadol is contraindicated in patients with severe renal or hepatic impairment and those in receipt of, or have received within the previous 2 weeks, monoamine oxidase inhibitors.[34]

- **Sufentanil:** dose reductions in the elderly should not be required, however regardless of administration route, elderly patients should be observed closely for adverse reactions to sufentanil.[46] If IN sufentanil is an option it may be followed by IV opioids as required. Do not use in children aged <18 years. Use with caution in patients with moderate or severe renal or hepatic impairment.[46] Sufentanil is contraindicated in patients with significant or clinically evident respiratory depression.[46]

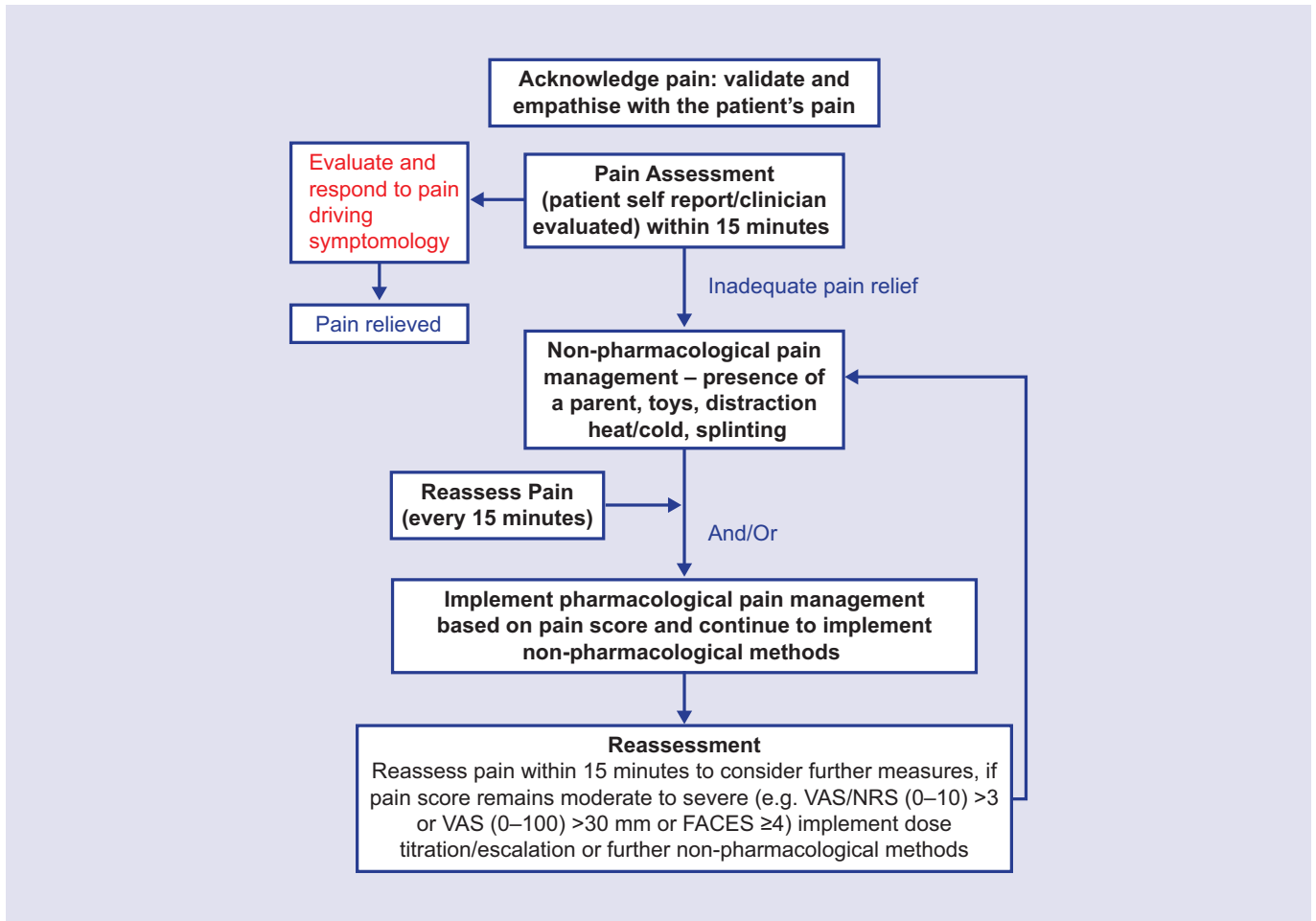**Figure 7.2a** Management of acute pain symptoms – children (>1 year, ≤15 years)

Acknowledge pain: validate and empathise with the patient's pain

Evaluate and respond to pain driving symptomology

Pain Assessment (patient self report/clinician evaluated) within 15 minutes

Pain relieved

Inadequate pain relief

Non-pharmacological pain management – presence of a parent, toys, distraction heat/cold, splinting

Reassess Pain (every 15 minutes)

And/Or

Implement pharmacological pain management based on pain score and continue to implement non-pharmacological methods

Reassessment
Reassess pain within 15 minutes to consider further measures, if pain score remains moderate to severe (e.g. VAS/NRS (0–10) >3 or VAS (0–100) >30 mm or FACES ≥4) implement dose titration/escalation or further non-pharmacological methods

Figure 7.2b Pharmacological management of acute pain symptoms in children (aged >1–15 years)

Pharmacological pain management based on pain score

Mild pain – NRS 1–3, VAS 1–3/10–40, FACES 2 and 4	Moderate pain – NRS 4–6, VAS 4–6/40–60, FACES 4 and 6	Severe pain – NRS 7–10, VAS 7–10/70–100, FACES 8 and 10
Paracetamol PO 20 mg/Kg loading dose followed by subsequent doses 10–15 mg/Kg Paracetamol PR 40 mg/Kg loading dose followed by subsequent doses 20 mg/Kg **OR** Ibuprofen 10 mg/Kg PO	**1st line treatment (option 1)** Nitrous oxide/oxygen INH (until analgesia with other medications established) **AND** Paracetamol PR 15–20 mg/Kg followed by PR doses 20 mg/Kg Paracetamol PO 15–20 mg/Kg followed by PR doses 10–15 mg/Kg Ibuprofen 10 mg/Kg PO	**Inhaled therapy (as other analgesia is established)** Nitrous oxide/oxygen INH (until analgesia with other medications established)
	1st line treatment (option 2) Paracetamol PR 10–15 mg/Kg Paracetamol PO 20 mg/Kg **AND** Diclofenac PO 1 mg/Kg (unless ibuprofen already administered)[a] Diclofenac PR 1 mg/Kg (unless ibuprofen already administered)[a] Ketorolac IV 0.5–1 mg in children >2 years (repeat every 6 hours up to 48 hours)[a] (see NOTE 2)	**1st line treatment** Nitrous oxide/oxygen INH (until analgesia with other medications established) **AND** Fentanyl IN 0.0015 mg/Kg[b] Morphine PO 0.3 mg/Kg
	2nd line treatment Paracetamol PO 10–15 mg/Kg Paracetamol PR 20 mg/Kg Ibuprofen PO 10 mg/Kg **AND** Diclofenac PO 1 mg/Kg (only in children >14 years) (unless ibuprofen already administered)[a] Diclofenac PR 1 mg/Kg (only in children >14 years) (unless ibuprofen already administered)[a] **AND/OR** Codeine phosphate PO 1 mg/Kg (only in children >12 years) Morphine PO 0.2–0.5 mg/Kg	**2nd line treatment** Fentanyl IN 0.0015 mg/Kg Fentanyl IV 0.001 mg/Kg Morphine IV 0.05 mg/Kg (titrate at not <2 min intervals at 0.01 mg/Kg IV. Max dose 01 mg/Kg) Ketamine IN 0.1–0.3 mg/Kg **AND** Paracetamol IV 15 mg/Kg
		3rd line treatment Ketamine IV 0.1 mg/Kg (repeat dose × 1 after >10 min) Ketamine IM 2.5 mg/Kg (a further dose of 1 mg/Kg IM may be administered as required)
		Consider local anaesthetic cream/gel (lidocaine/prilocaine or tetracaine) to facilitate IV administration, requires up to 60 minutes lead time **Ensure availability of naloxone if opioids are used** **Consider anti-emetics as adjunct to opioids: Ondansetron**

IM, intramuscular; IN, intranasal; INH, inhaled; IV, intravenously; NRS, numerical rating scale; PO, orally (per os); PR, per rectum; VAS, visual analogue scale.
(a) More than one NSAID should not be administered so for example diclofenac is contraindicated in patients who have already received ibuprofen; (b) titrate fentanyl to effective analgesia or maximum doses recommended in your country/institution

1. For each recommendation within a group, for example in children with severe pain receiving nitrous oxide, practitioners who wish to provide additional analgesia should choose only one additional option e.g. IN fentanyl 0.0015 mg/Kg OR PO morphine 0.3 mg/Kg NOT both. If analgesia is insufficient practitioners should consider adding 1 drug from another group, for example in children with severe pain treated with nitrous oxide plus IN fentanyl 0.0015 mg/Kg, consider the addition of ketamine (IV or IN) rather than another opioid such as morphine. Drugs from within the same group/class should not be used in combination e.g. diclofenac and ibuprofen.

2. In children aged >16 years ketorolac may also be considered at an IV dose of 0.25 mg/Kg to a max of 10 mg – see Pharmacological management of acute pain symptoms in adults

Ensure that naloxone reversal is available and ready for use when opioids are administered.

Assess the presence of contraindications for all drugs, including simple analgesics. Consult Summary of Product Characteristics for each medication as required for further information.

General principles

- Do not use intravenous (IV) opioids in combination with other IV opioids because of the risks of sedation and respiratory depression.
- When administering opioids ensure that naloxone is available for reversal and ready to use as required if clinically significant sedation or respiratory depression occurs.
- Only prescribe second line NSAID analgesia (e.g. diclofenac or ketorolac) in patients who have not received previous NSAIDs e.g. ibuprofen.

Dosing considerations for children aged >1 year <15 years

- **Codeine:** is indicated for use in patients aged ≥12 years, dosing should be based on body weight (0.5–1 mg/Kg) and the maximum dose of 240 mg/day must not be exceeded.[47]
- **Diclofenac:** not recommended for children aged <14 years, 1 mg/Kg administered by the oral or per rectum routes is recommended. Diclofenace is contraindicated in patients who have already received ibuprofen.[34,48]
- **Fentanyl:** dosing of fentanyl by the intranasal (IN) route 0.0015 mg/Kg or IV route 0.001 mg/Kg may be repeated but not before >10 minutes have elapsed after initial dosing. If IN fentanyl proves insufficient, follow with IV fentanyl or IV morphine.
- **Ketamine:** ketamine IV 0.1 mg/Kg dosing may be repeated once only not <10 minutes after initial dosing as needed.
- **Ketorolac:** whilst ketorolac is not indicated for use in children, IV ketorolac is used widely in paediatric post-operative pain with the ability to reduce opioid use.[49,50] In children aged >2 years IV ketorolac 0.5–1 mg/Kg can be administered by bolus infusion over no less than 15 seconds.[41] IV dosing of ketorolac may be repeated every six hours up to 48 hours.
- **Morphine:** for IV administration of morphine 0.05 mg/Kg subsequent dosing at not <2 minutes intervals as needed may be delivered to a maximum dose of 0.1 mg/Kg.
- **Paracetamol:** a first dose of paracetamcol 20 mg/Kg PO for pain (not fever) may be administered with subsequent dosing of 10–15 mg/Kg up to maximum daily dosing.[51-53]

Other considerations

- **Ondansetron:** it is recommended in cases of opioid-induced nausea and vomiting to use an anti-emetic such as ondansetron. Administer as a single dose based on 0.15 mg/Kg by slow IV (over 30 seconds) to a maximum dose of 8 mg.[54]
- Where non-urgent venepuncture access is required, consider the use of topical local anaesthetic gel/cream (lidocaine/prilocaine or tetracaine) overlaying a suitable vein and the area covered with an occlusive dressing for a minimum of 20 minutes up to 60 minutes.[55,56] Lidocaine 2.5%/prilocaine 2.5% is licensed for use in children aged >1 year.[55]

Considerations in special populations and contraindications

- **Codeine:** codeine is indicated for use in children aged ≥12 years.[47] The maximum daily dose for codeine in children is 240 mg/day that is based on body weight (0.5–1 mg/Kg). It is contraindicated for use in children <12 years due to its unpredictable metabolism and risk of opioid toxicity. Codeine is a prodrug and will not be effective in patients deficient in CYP2D6 (7%–10% of the population). Codeine is contraindicated in patients with liver disease, patients at risk of increased intracranial pressure. Codeine must not be used in patients known or

suspected of being CYPD26 ultra-rapid metabolisers (1%–2% of the population) owing to the high risk of toxicity.[34,40,47] Use with caution at reduced doses in patients with asthma or decreased respiratory reserve, and avoid use in patients with renal or hepatic impairment.[47]

- **Fentanyl:** use with caution in patients with impaired renal or hepatic function and those at risk of increased intracranial pressure. Fentanyl may produce bradycardia and patients given fentanyl either by IV or IN routes should be monitored; caution is advised in patients with previous or pre-existing bradyarrhythmias.[35] IV fentanyl may be used following IN fentanyl but multiple opioids administered intravenously should not be used because of the risks of sedation and respiratory depression. Ensure that naloxone reversal is available and ready to use as required.

- **Ketamine:** contraindicated for use in patients where an increase in blood pressure would be hazardous; consider dose reductions in patients with hepatic impairment.[34,36,37]

- **Morphine:** contraindicated in patients with moderate or severe renal impairment, liver failure, patients at risk of increased intracranial pressure, patients with biliary or renal tract spasm, and patients who have been administered monoamine oxidase inhibitors within two weeks.[57] Do not use IV morphine in combination with other IV opioids, such as fentanyl because of the risks of sedation and respiratory depression. Ensure that naloxone reversal is available and ready to use as required.

- **Nitrous oxide/oxygen:** contraindicated for use in patients with head injuries or impaired consciousness, pneumothorax, air embolism, suspicion or evidence of decompression sickness, severe bullous emphysema, gross abdominal distension, and patients with maxillofacial injuries.[42,43]

- **NSAIDs:** contraindicated in patients with active or previous GI ulcers, and patients with severe hepatic or renal failure.[34,48] Diclofenac is contraindicated in children <14 years of age.[48] Ketorolac is contraindicated in children <16 years of age.[41] Use of combination NSAIDs e.g. ibuprofen and diclofenac or ketorolac is not advised.

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