

# Current concepts in management of pain in children in the emergency department

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Pain is common in children presenting to emergency departments with episodic illnesses, acute injuries, and exacerbation of chronic disorders. We review recognition and assessment of pain in infants and children and discuss the manifestations of pain in children with chronic illness, recurrent pain syndromes, and cognitive impairment, including the difficulties of pain management in these patients. Non-pharmacological interventions, as adjuncts to pharmacological management for acute anxiety and pain, are described by age and development. We discuss the pharmacological management of acute pain and anxiety, reviewing invasive and non-invasive routes of administration, pharmacology, and adverse effects.

## Introduction

Pain is a common symptom in children presenting to emergency departments. Under-treatment of pain (commonly labelled oligoanalgesia) has been frequently reported particularly in younger children, those with cognitive impairment, and children in developing countries. Organisations such as the Joint Commission International have made pain assessment and management a priority issue.<sup>1</sup> Initiatives include recording of pain scores, staff education, and quality improvement processes.<sup>2-5</sup> Such efforts have fostered advances in the pharmacological and non-pharmacological treatment of pain in children. We review the state of emergency-department pain management in children, including recognition, assessment, and non-pharmacological and pharmacological treatment.

## Recognition and assessment of pain

Pain as a presenting complaint for episodic illnesses, acute injuries, or exacerbation of chronic conditions, accounts for up to 78% of emergency department visits.<sup>6</sup> Musculoskeletal injuries are common;<sup>7-9</sup> 27–42% of children sustain a fracture before the age of 16 years.<sup>10,11</sup> Other common causes include headache, otalgia, sore throat, and abdominal distress.<sup>7,12-14</sup> About half of patients report their pain as moderate to severe.<sup>7,15,16</sup> A visit to a noisy, crowded emergency department can be a frightening experience for a child with acute pain, especially if he or she should need a diagnostic or therapeutic procedure. Early and aggressive treatment of pain is recommended, because uncontrolled or severe pain stimuli can lead to hyperalgesia—an enhancement of the pain response (figure 1).<sup>17</sup>

Recognition and assessment of pain in infants and young children can be difficult because these patients cannot verbalise their pain experience (panel). Spinal reflex responses to mechanical stimulation are exaggerated in young infants, but facial expression is a weak indicator.<sup>18</sup> In preverbal children, excessive crying, irritability, poor feeding, position and movement of the arms and legs, and sleep disturbance can indicate pain.<sup>17-19</sup> Altered facial expression is also suggestive.<sup>19</sup> Physiological variables can also indicate acute pain.<sup>19,20</sup>

Tools to grade children's pain are widely recommended;<sup>20</sup> they include: physiological measures (heart and respiratory rates, blood pressure), observational and behavioural measures (grading of facial expression, leg movements, activity, crying), self-reporting measures,<sup>20,21</sup> and parents' report.<sup>22</sup> No single element is reliable alone, including pain scoring, so a combination of measures is generally used clinically.<sup>23</sup> Physiological measures reflect stress reactions that are not generally correlated with self-reported pain. Behavioural measures can reflect fear and anxiety rather than pain.<sup>24</sup> Accordingly, most physicians regard patients' self-reporting of pain as the gold standard for children old enough to comply effectively.<sup>25,26</sup>

Several behavioural scales are widely used for infants and non-verbal children, including the face, legs, activity, cry, and consolability scale<sup>27</sup> and the Children's Hospital of Eastern Ontario pain scale.<sup>28</sup> Numerical scales are not suitable for younger children, and pictorial-based pain scales are used, such as the

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## Search strategy and selection criteria

We searched the Cochrane Library, Medline, PubMed, and relevant specialty journals (all from 1980 to January, 2014). We used the search terms "pediatric pain", "pain assessment", "pain management", "chronic pain", "pain scores", "pain protocols", and "emergency department". We selected publications from the past 15 years with an emphasis on the past 3 years, but we did not exclude commonly referenced and influential older publications. We also searched references of articles identified by our search strategy for related articles. We included four types of studies: randomised controlled trials, observational studies, retrospective studies, and meta-analyses but excluded abstracts and case reports. However, we searched all types of publications, including abstracts and case reports, to find out whether a specific adverse event or complication had been reported. Several review articles, editorials, and book chapters were included because they provide comprehensive overviews that are beyond the scope of this Review.

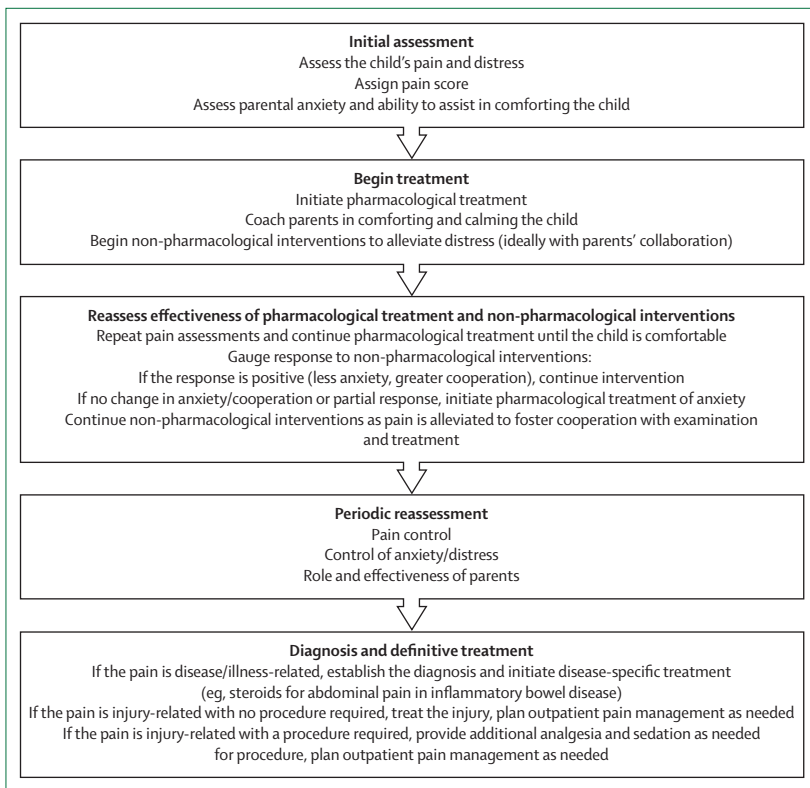


Figure 1: Stepwise integrated pharmacological and non-pharmacological approach to pain management

### Panel: Signs and symptoms of pain in infants and young children

#### Physiological changes

- Increase in heart rate, respiratory rate, blood pressure, muscle tone
- Oxygen desaturation
- Sweating
- Flushing
- Pallor

#### Behavioural changes

- Change in facial expression (grimacing, furrowing of the brow, nasal flaring, deep nasolabial groove, curving of the tongue, quivering of the chin)
- Finger clenching
- Thrashing of limbs
- Writhing
- Back arching
- Head banging
- Poor feeding
- Sleep disturbance
- Pseudoparalysis

Wong-Baker FACES, and OUCHER pain scales. Children older than about 8 years can generally comply with visual analogue scales and verbal numerical scales, the tools used in adults.<sup>20</sup>

## Pain in children with special needs

### Pain in children with chronic illness

Acute pain is common in children with chronic illnesses such as sickle cell disease, haemophilia, juvenile idiopathic arthritis, inflammatory bowel disease, hereditary angioedema, cancer, Mediterranean fever, Fabry disease, and Gaucher disease. Some typical features of acute pain (eg, tachycardia, diaphoresis, facial expression) might not manifest in these children, as they attenuate with time in chronic pain.<sup>29</sup> These children and their families often have heightened fear and anxiety related to pain sensitisation<sup>30,31</sup> from repeated experiences during which pain was not adequately controlled.<sup>31–34</sup> Effective analgesia should be initiated while specific disease-related treatments are sought.

### Chronic conditions with recurrent pain

Headache is the most common chronic or recurrent pain in children, followed by abdominal pain and musculoskeletal pain.<sup>35</sup> Migraine occurs in up to 10·6% of children between the ages of 5 years and 15 years, and up to 28% of older adolescents.<sup>36</sup> Recurrent abdominal pain affects 9–15% of children,<sup>37,38</sup> while constipation has a worldwide prevalence of 7–30%<sup>39</sup> and is a frequent cause of emergency department visits for abdominal pain.<sup>40</sup> Chronic pain can substantially affect the life of the child and family through school absences, poor grades, social withdrawal, and adverse family interactions. Complex regional pain syndrome is a chronic painful disorder characterised by neurogenic inflammation with increased tissue levels of mediators, enhanced peripheral adrenergic sensitivity, with reorganisation of sensory and motor cortex. Most of the scientific literature on complex regional pain syndrome is in adults. This disorder is best treated by interdisciplinary treatment programmes based on a combination of medications (anti-neuropathic drugs such as gabapentin, local anaesthetics, acetaminophen, non-steroidal anti-inflammatory agents, tramadol, and low-dose ketamine), somatic and sympathetic blocks, and cognitive-behavioural and physical therapies. Children admitted with acute on chronic flares should be managed by a paediatric pain management expert.<sup>41,42</sup>

### Pain in children with cognitive impairment

Children with cognitive impairment (eg, cerebral palsy, metabolic syndromes, genetic diseases) frequently have pain related to specific conditions such as gastro-oesophageal reflux disease with oesophagitis, spasticity with muscle spasm or contractures leading to joint subluxations and dislocations, constipation and faecal impaction, osteopenia with pathological fractures, and dental disease; they can also have pain from trauma, infections, headache, teething, and menses.<sup>43</sup> Maladaptive behaviour, decreased functioning, and sleep disorders often result. Cognitively impaired children seem to experience pain more frequently than healthy

children, with the more severely impaired experiencing the most pain.<sup>44,45</sup> Severely affected children cannot verbalise their pain and can present with atypical pain responses, such as a full-blown smile (with or without laughter) or the freezing phenomenon (the face not moving for several seconds). Reduced interaction, search for comfort or physical closeness, shivering, pallor, sweating, sharp breath, and breath-holding are common manifestations of pain in this population.<sup>46</sup> Some pain features are particular to specific syndromes. Children with Down's syndrome can show delayed expression of pain and have difficulty in localising it.<sup>47,48</sup> Children with autism spectrum disorders respond in the same way as non-autistic children do to noxious stimuli, but they tend to recover more slowly.<sup>49,50</sup> Facial and leg movements can be impaired in cerebral palsy, and recognition of pain is therefore complex.

Specific measurement tools that take into account idiosyncratic pain behaviours, such as verbal outbursts, tremors, increased spasticity, jerking movements, and changes in respiratory pattern, can be used for this population. The non-communicating child's pain checklist–postoperative version,<sup>46,51</sup> an observational scale based on manifestations that are deemed to be physiological or behavioural indicators of pain, is widely used for children from age 3 years up to 18 years. Although regarded by experienced operators to be the most reliable and easiest scale to use for children with cognitive impairment,<sup>52</sup> it can be time-consuming and difficult to administer by staff unfamiliar with its use.

Analgesic therapy in children with cognitive impairment and cerebral palsy should take into account factors that could alter doses, duration of treatment, and side-effects. Spasticity-related pain is treated with baclofen or diazepam.<sup>53</sup> Malnutrition and dehydration can increase the risk of adverse effects from paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs).<sup>54</sup> Some anticonvulsants (carbamazepine, phenobarbital, phenytoin, primidone) can increase the risk of paracetamol toxicity. Opioid adverse effects can exacerbate motor impairment, spasticity, constipation, and chronic lung disease.<sup>43,55</sup>

### **Somatisation**

Psychosomatic symptoms account for 8–10% of primary care visits and are a common reason for assessment in the emergency department.<sup>56</sup> A somatoform disorder is characterised by symptoms that suggest physical illness but cannot be explained by a general medical condition and are not attributable to a specific mental disorder.<sup>57</sup> Somatoform disorders are most common in adolescents, and patients perceive their pain as real and recurrent. Suspicion of somatoform pain is strengthened by the presence of vague and changeable description and location of pain, selective avoidance of unpleasant activities, a temporal relation to a stressful event, related anxiety and depression, difficulties at school, and a

family history of somatisation disorders. School refusal, bullying, depression, child abuse, and eating disorders can all present as somatoform pain.<sup>58</sup> Suspicion of somatisation should prompt consultation with the primary-care provider and a plan for outpatient follow-up; in some cases, hospital admission with social work and psychiatric assessment might be necessary.

### **Malingering**

Malingering is defined as feigning an illness, or consciously exaggerating symptoms of a real illness, to derive personal gain; it should be suspected when there is a discrepancy between history and findings on physical examination or between symptoms and the patient's anxiety.<sup>57</sup> Suspicion is raised by the presence of a symptom shown during the medical examination, a secondary benefit, a loss of school days, an association with a stressful event, or poor compliance with investigations and treatment. Clinicians should consider malingering in their differential diagnosis to avoid unnecessary investigations (eg, CT for abdominal pain). Malingering should prompt consultation with the primary care provider and a plan for outpatient follow-up.

## **Non-pharmacological approaches for acute pain and anxiety**

### **Physical comfort measures and distracting activities**

Psychological, behavioural, and physical interventions, stratified by age and development, can be used as adjuncts to pharmacological management.<sup>59–64</sup> In children, disorders causing acute pain are often accompanied by anxiety and distress. A stepwise approach to managing acute pain and anxiety combines pharmacological and non-pharmacological interventions as integrated treatment (figure 1).

Non-pharmacological approaches can be divided into two general categories: physical comfort measures and distracting activities (figure 2).<sup>64</sup> Physical comfort measures are specific interventions for neonates, infants, and young children. Neonates and infants have a positive physiological response (lowering of pain scores, cry duration, and heart rate variation) to oral stimulation as well as physical contact or touch during painful procedures (venepuncture, heel lancing).

Preschool children benefit from touch and various distracting activities. Application of heat or cold for minor injuries or burns is appropriate for school-age and older children and adolescents, but it should be carefully supervised by parent or clinician in preschool children and those who are non-verbal or have difficulty in communicating.

Passive and interactive distracting activities can be used in children of all ages and developmental levels; they include bubble blowing, lighted wands, sound and music, controlled deep breathing, art, puppets, imitation play, interactive games, books, guided imagery, and hypnosis.

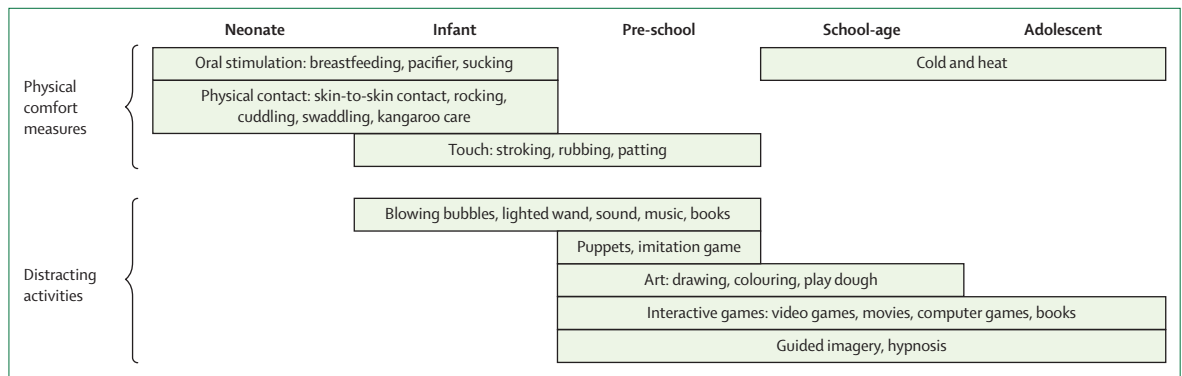


Figure 2: Non-pharmacological interventions

Non-pharmacological interventions are especially helpful when cooperation is necessary but pharmacological management is not feasible. Physical examination and common procedures such as venepuncture and intravenous cannulation can be difficult to accomplish in distressed young children because they cannot control their apprehension.<sup>65-67</sup> Topical anaesthetics control pain but have little effect on distress in a child expecting a needle. Forceful immobilisation, widely used for young children when pharmacological intervention is not practicable, can be frightening and can further escalate the already high degree of anxiety, leading to apprehension of medical staff and future medical treatment.<sup>68,69</sup>

Understanding of neurodevelopmental principles provides a practical framework for clinicians to manage acute anxiety and distress in young children (aged 2–5 years) because the ability to control distress necessitates the maturation of specific neural structures.<sup>65,66,70</sup> Young children have difficulty in gaining control of fear because the connectivity between frontal-lobe structures and the rest of the brain is not fully mature; this connectivity facilitates the control of intense affective states.<sup>65,66,71,72</sup> Young children who are fearful have compromised ability to use the language of others to reassure themselves and therefore have difficulty cooperating.<sup>67,73-76</sup> Furthermore, young children have difficulty in relating their past experience to what is happening in the present.<sup>67</sup> To understand the meaning of such phrases as “it will only hurt for a minute” or “almost done”, the child has to recall past events with a short duration. Thus, young children are not able to use this information to control their distress.

Because young children are cognitively immature, physical comfort measures and distraction activities are more effective than is verbal reasoning in helping to control their distress. Children do not have sufficient cognitive development to understand the perspective of strangers trying to reassure them until the age of 5–7 years.<sup>65-67,77,78</sup>

### Role of parents

Parents can be active participants in helping their child to cope with procedures and can assist the clinician by

engaging the child in an activity of interest, shifting attention away from the examination or procedure. However, parents’ ability to assist the clinician depends on their own level of anxiety. A very anxious parent, or one who has other children to take care of, will find it difficult to assist in helping the sick child to cope with the examination or procedure.

Strategies for managing parents vary according to their degree of anxiety: having parents leave the room before the start of the examination or procedure (for those who are extremely anxious or emotionally distraught); having parents simply observe the procedure; or having parents actively assist by helping comfort and calm their child. Some parents independently manage their child’s anxiety—eg, the clinician arrives to find the child on a parent’s lap with the parent reading a book or playing a game with the child. Play therapists and child life specialists can be especially helpful in working with the parents and the child to relieve anxiety and improve cooperation.

Clinicians should be aware of parental input (to the child) before arrival in hospital and be prepared to recognise, and undo if necessary, counterproductive parental suggestions, especially if they result in a high degree of anxiety and distress. Many parents, in an attempt to lessen the child’s anxiety and increase coping capability, will tell the child that he or she will be getting a small needle and the procedure will only hurt for a minute (or words to that effect). In this situation, the clinician might be greeted by the child in obvious distress about the possibility of an injection.

Parents should be prepared and coached. Clinicians should discuss with parents, before the examination or procedure and out of earshot of the child, what will happen and how the parents can help their child to cope. Parents should be instructed in the use of language-based coping skills (use of developmentally specific words and phrases, encouragement, praise) and distraction activities and to avoid vague or negative language, apology, global reassurance, criticism, or the use of potentially frightening terms (figure 3).<sup>62,63</sup> Assignment of these tasks to parents serves as a

distraction for them, probably lessening the personal anxiety that they transmit to the child. Words or phrases that are helpful to one child might be threatening to another; parents and health-care providers should select their language carefully.<sup>62</sup>

## Pharmacological treatment of acute pain

### Analgesic therapy

Analgesic therapy is warranted whenever non-pharmacological approaches are insufficient, or when they are unlikely to achieve the needed pain relief when given alone. We present various recommended options in tables 1 and 2. Inhaled nitrous oxide and parenteral ketamine are often administered for sedation and analgesia during procedures; however, we do not discuss these drugs further here given the limited published experience for non-procedural analgesia in children.

### Routes of administration

The oral and intranasal routes are fast and well tolerated for initial pain therapy, if they are not contraindicated by the clinical situation (ie, if fasting is indicated or the child has nasal trauma or obstruction). The intranasal route has the advantage of quicker onset and higher bioavailability. Severe pain is best treated intravenously, because the ability to titrate to pain relief rapidly generally outweighs the additional stress and pain caused by achieving intravenous access.

### Mild pain

Paracetamol is extremely safe at therapeutic doses<sup>96</sup> and can readily be used for mild pain alone or with other agents for moderate to severe pain. On the basis of pharmacokinetics, a higher initial loading dose can be considered (table 1),<sup>97</sup> as long as continued therapy will not exceed the daily maximum dose. In some countries, an intravenous form of paracetamol is available and is particularly valuable when a child is vomiting.

Alternatives to paracetamol for mild pain are NSAIDs such as ibuprofen and naproxen. NSAIDs can cause adverse gastrointestinal and renal effects; however, they are uncommon in children.<sup>98,99</sup> Owing to its association with Reye's syndrome, aspirin should be avoided as an analgesic except for specific rheumatological disorders.

Coadministered paracetamol and ibuprofen can be superior to either agent alone.<sup>100</sup> Some parents and clinicians administer paracetamol and ibuprofen simultaneously in alternating doses; this practice seems safe but might not provide superior pain relief to either agent alone.

Oral sucrose decreases crying time in infants aged 1–12 months who are undergoing needle-related procedures, and it is of course safe.<sup>101,102</sup> Sucrose does not seem to be effective in children older than a year.<sup>103</sup>

Tramadol, an opioid-related analgesic, has not been well studied in children. It seems to be less potent than traditional opioids, but it causes less respiratory

Language to avoid	Language to use
You will be fine; there is nothing to worry about (reassurance)	What did you do in school today? (distraction)
This is going to hurt/this won't hurt (vague; negative focus)	It might feel like a pinch (sensory information)
The nurse is going to take some blood (vague information)	First, the nurse will clean your arm, you will feel the cold alcohol pad, and next... (sensory and procedural information)
You are acting like a baby (criticism)	Let's get your mind off of it; tell me about that film... (distraction)
It will feel like a bee sting (negative focus)	Tell me how it feels (information)
The procedure will last as long as... (negative focus)	The procedure will be shorter than... (television programme or other familiar time for child) (procedural information; positive focus)
The medicine will burn (negative focus)	Some children say they feel a warm feeling (sensory information; positive focus)
Tell me when you are ready (too much control)	When I count to three, blow the feeling away from your body (coaching to cope; distraction limited control)
I am sorry (apologising)	You are being very brave (praise; encouragement)
Don't cry (negative focus)	That was hard; I am proud of you (praise)
It is over (negative focus)	You did a great job doing the deep breathing, holding still... (labelled praise)

Figure 3: Suggested language for parents and health-care providers<sup>62</sup>

depression and sedation as well as other adverse effects than other opioids do. It can lower the seizure threshold and has been associated with serotonin syndrome. It should be avoided in patients with a history of epilepsy and those receiving stimulant or serotonergic drugs.<sup>81,104</sup>

### Moderate pain

Moderate pain warrants more potent therapy than paracetamol or NSAIDs alone, such as an oral opioid. Intranasal diamorphine or fentanyl can also provide similar initial pain relief to intravenous opioids.<sup>85–89,105</sup> Codeine is no longer recommended owing to its differential metabolism, with low efficacy in poor metabolisers and rare reports of life-threatening or fatal respiratory depression in ultra-rapid metabolisers.<sup>106,107</sup>

### Severe pain

In children with severe pain, intravenous access should be established as soon as possible; titrated opioids should then be given. Oral or nasal opioids can be given before intravenous cannulation. Inhaled methoxyflurane (available in the UK, Australia, and New Zealand) has also been used for rapid pain relief in the prehospital setting and seems to be safe.<sup>108,109</sup>

Should opioid therapy result in drowsiness or mild respiratory depression, further doses should be withheld and the child monitored carefully and stimulated as needed. Serious respiratory depression is unlikely when intravenous opioids are titrated carefully with standard doses; however, whenever they are administered, resuscitation and monitoring equipment should be immediately available, as should the reversal agent naloxone.

Route and dose	
<b>Mild pain</b>	
Paracetamol	Intravenous <sup>79</sup> <10 kg: 7.5 mg/kg every 4–6 h, maximum 30 mg/kg daily ≥10 kg: 15 mg/kg every 6 h, maximum 60 mg/kg daily or 4000 mg/day  Oral <sup>80</sup> <60 kg: 10–15 mg/kg every 4 h, maximum 100 mg/kg daily* ≥60 kg: 650–1000 mg every 4 h, maximum 4000 mg/day
Ibuprofen	Oral <sup>80,81</sup> Infants: 4–10 mg/kg every 6–8 h, maximum 40 mg/kg daily <60 kg: 6–10 mg/kg every 6–8 h, maximum 40 mg/kg daily ≥60 kg: 400–800 mg every 6–8 h, maximum 3200 mg/day
Naproxen	Oral <sup>80,81</sup> >2 years: 5–7 mg/kg every 8–12 h <60 kg: 5–7 mg/kg every 12 h, maximum 24 mg/kg daily ≥60 kg: 250–500 mg every 12 h, maximum 1000 mg/day
<b>Moderate pain</b>	
Hydrocodone (with paracetamol)	Oral <sup>81</sup> <50 kg: 0.1–0.2 mg/kg every 4–6 h ≥50 kg: 5–10 mg every 4–6 h
Oxycodone	Oral <sup>80,81</sup> ≤6 months: 0.025–0.05 mg/kg every 4–6 h <50 kg: 0.1–0.2 mg/kg every 4–6 h ≥50 kg: 5–10 mg every 4–6 h
Hydromorphone	Oral <sup>80,81</sup> Infants >6 months and >10 kg: start 0.03 mg/kg every 4 h Children <50 kg: 0.03–0.08 mg/kg every 3–4 h Children ≥50 kg: 2–4 mg every 3–4 h
Ketorolac	Oral <sup>82</sup> ≥50 kg: 20 mg initially, then 10 mg every 4–6 h, maximum 40 mg/day  Intravenous ≥1 month and <2 years: 0.5 mg/kg every 6–8 h 2–16 years: 0.5 mg/kg up to 15 mg every 6 h >16 years: 0.5 mg/kg up to 30 mg every 6 h
Tramadol	Oral <sup>83</sup> 4–16 years: 1–2 mg/kg up to 100 mg every 4–6 h, maximum the lesser of 8 mg/kg daily or 400 mg/day ≥16 years: 50–100 mg every 4–6 h, maximum 400 mg/day  Intravenous <sup>82,84</sup> ≥4 years: 2 mg/kg up to 100 mg every 4–6 h
Diamorphine	Nasal <sup>85,86</sup> ≥6 months: 0.1 mg/kg aerosol
Fentanyl	Nasal <sup>87–89</sup> ≥6 months: 1.5–2 µg/kg up to 50 µg aerosol (volumes >0.2 mL divided between nostrils)
<b>Severe pain</b>	
Morphine	Intravenous <sup>90,90</sup> ≤6 months: titrate to pain control, with usual effective dose 0.025–0.030 mg/kg; typically repeat every 2–4 h >6 months and <50 kg: titrate to pain control, with usual effective dose 0.2–0.5 mg/kg; typically repeat every 3–4 h ≥50 kg: titrate to pain control, with usual effective dose 2.5–5 mg; typically repeat every 3–4 h
Fentanyl	Intravenous <sup>90,81</sup> <6 months: titrate to pain control, with usual effective dose 1–4 µg/kg; typically repeat every 2–4 h ≥6 months and <50 kg: titrate to pain control, with usual effective dose 1–2 µg/kg; typically repeat every 30–60 min ≥50 kg: titrate to pain control, with usual effective dose 50–100 µg; typically repeat every 1–2 h
Hydromorphone	Intravenous <sup>90,81</sup> Infants >6 months and >10 kg: titrate to pain control, starting with 0.01 mg/kg every 3–6 h Children <50 kg: titrate to pain control, with usual effective dose 0.015 mg/kg; typically repeat every 3–6 h Children ≥50 kg: titrate to pain control, with usual effective dose 1 mg; typically repeat every 2–3 h
Changes in dosing might be indicated according to the clinical situation. Intravenous doses should be administered slowly. Patients with chronic pain might need more frequent and higher doses. All doses are shown for immediate-release preparations. Optimum dosing strategies for obese children remain undefined; some clinicians calculate on the basis of ideal bodyweight whereas others select a point somewhere between ideal and actual bodyweight. *Maximum 75 mg/kg daily in infants, 60 mg/kg daily in term neonates.	
<b>Table 1: Systemic pharmacological management of acute pain in children</b>	



Adverse effects of the histamine-releasing opioids (morphine, hydromorphone), including nausea, vomiting, and pruritus, can be treated with antiemetics and antihistamines. Decreases in blood pressure from morphine or hydromorphone are generally not clinically significant in otherwise healthy children. Meperidine is no longer used in most settings, because it has no advantages over other opioids and has a metabolite that can cause seizures.

### Prehospital pain

Management of paediatric pain in ambulances is constrained by provider training and experience, limited available analgesic agents, and the competing management priorities of transport to the hospital.

### Acute exacerbations of chronic pain

Many children with sickle-cell disease, cancer, or other recurrent or chronic pain syndromes have opioid tolerance, and intravenous administration is preferred so that the higher doses generally needed for pain relief can be rapidly titrated. In patients with sickle-cell vaso-occlusive crisis necessitating hospital admission, patient-controlled analgesia can be initiated in the emergency department after initial pain control has been achieved.

### Topical anaesthesia

Topical anaesthetics applied to intact skin can effectively diminish the pain of phlebotomy, intravenous cannulation, or lumbar puncture (table 2). Tetracaine works faster than lidocaine plus prilocaine (EMLA cream) and seems to provide superior pain relief.<sup>110</sup> Ethyl chloride (coolant) spray has shown mixed results for topical anaesthesia and is not preferred to the agents in table 2.<sup>111,112</sup>

A locally prepared solution or gel containing lidocaine, epinephrine, and tetracaine (table 2) can be applied directly onto small wounds to provide partial or complete local anaesthesia.<sup>94,95</sup>

### Procedures

Children with painful conditions that necessitate procedures (eg, displaced fractures, abscesses, joint effusions) should first receive effective analgesia by one of the routes discussed (table 1). Many will also need procedural sedation with midazolam, nitrous oxide, ketamine, propofol, or other agents; such sedation practice has been detailed elsewhere and is beyond the scope of this review.<sup>113–115</sup>

### Standing protocols

Nurse-driven triage protocols for pain assessment and management allow rapid initiation of pharmacological pain relief along with non-pharmacological measures such as distraction activities, positions of comfort, ice, and immobilisation.<sup>116</sup> We encourage the adoption of standing protocols to permit triage nurses to administer analgesics rapidly to children in pain, and to apply

	Dose	Notes
<b>Intact skin</b>		
Lidocaine 2.5% and prilocaine 2.5% (EMLA cream) <sup>91</sup>	<3 months old or <5 kg: 1 g 3–12 months and >5 kg: 2 g 1–6 years and >10 kg: 10 g 7–12 years and >20 kg: 20 g	60 min is needed to achieve maximum effect; cover cream with an occlusive dressing
Lidocaine 70 mg and tetracaine 70 mg (Synera patch) <sup>92</sup>	Age ≥3 years: apply patch	20–30 min needed to achieve maximum effect
Tetracaine 4% (Ametop) <sup>93</sup>	>1 month and <5 years: apply 1 tube of gel (1 g) >5 years: apply up to five tubes of gel (5 g)	30 min before venepuncture; 45 min before intravenous cannulation
<b>Wounds</b>		
Lidocaine, epinephrine, tetracaine (LET) solution or gel <sup>94,95</sup>	Age ≥1 year: apply to wound	20 min needed for maximum effect
* Also referred to as ALA on the basis of alternative names for the constituents: adrenaline, lignocaine, amethocaine. These mixtures are locally made by hospital formularies, with a common formula being lidocaine 4% plus epinephrine 0.1% plus tetracaine 0.5%. The cocaine-based formulation was historically avoided on wounds of digits, ears, penis, nose, mucous membranes, close to the eye, or deep wounds involving bone, cartilage, tendon, or vessels. The lidocaine-based formulation can be used in such settings.		
<b>Table 2: Topical pharmacological management of acute pain in children</b>		

topical anaesthesia to appropriate skin locations for those likely to need laceration repair, intravenous cannulation, or lumbar puncture.<sup>2–5,80,90,117,118</sup>

### Future directions

Future initiatives in emergency-department paediatric pain management will focus on developing condition-specific protocols to optimise pain recognition, assessment, and management, especially for children with cognitive impairment, recurrent pain syndromes, and chronic illness. How can we know when we have successfully provided sufficient analgesia, and when our efforts remain inadequate? When does anxiety predominate over pain such that anxiolytic agents might be more effective than analgesics? What are safe and effective methods of providing rapid pain relief on arrival in the emergency department by use of nurse-driven triage protocols? How can we safely improve the efficacy of non-invasive routes of administration (oral, sublingual, intranasal)? Is there a role for tramadol or ketorolac in the management of acute pain in children? How can we apply pharmacogenomics to individualise treatment and decrease related adverse events? Can we safely expand the use of patient-controlled analgesia to selected populations (eg, sickle-cell disease, cancer-related pain)?

#### Contributors

BSK, LC, SMG, and EB contributed equally to drafting and revising the report, including the scientific literature search, figures, tables, and references. BSK takes responsibility for the review as a whole.

#### Declaration of interests

We declare no competing interests.

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## References

- 1 The Joint Commission 2009 Requirements that Support Effective Communication, Cultural Competence, and Patient-Centered Care: Hospital Accreditation Program (HAP). The Joint Commission. Available at: [http://www.jointcommission.org/Advancing\\_Effective\\_Communication/](http://www.jointcommission.org/Advancing_Effective_Communication/) (accessed July 14, 2014).
- 2 Boyd RJ, Stuart P. The efficacy of structured assessment and analgesia provision in the paediatric emergency department. *Emerg Med J* 2005; **22**: 30–32.
- 3 Eisen S, Amiel K. Introduction of a paediatric pain management protocol improves assessment and management of pain in children in the emergency department. *Arch Dis Child* 2007; **92**: 828–29.
- 4 Somers LJ, Beckett MW, Sedgwick PM, Hulbert DC. Improving the delivery of analgesia to children in pain. *Emerg Med J* 2001; **18**: 159–61.
- 5 Todd KH, Ducharme J, Choiniere M, et al, and the PEMI Study Group. Pain in the emergency department: results of the pain and emergency medicine initiative (PEMI) multicenter study. *J Pain* 2007; **8**: 460–66.
- 6 Grant PS. Analgesia delivery in the ED. *Am J Emerg Med* 2006; **24**: 806–09.
- 7 Kennedy RM, Luhmann JD, Luhmann SJ. Emergency department management of pain and anxiety related to orthopedic fracture care: a guide to analgesic techniques and procedural sedation in children. *Paediatr Drugs* 2004; **6**: 11–31.
- 8 Downing A, Rudge G. A study of childhood attendance at emergency departments in the West Midlands region. *Emerg Med J* 2006; **23**: 391–93.
- 9 Cooper C, Dennison EM, Leufkens HG, Bishop N, van Staa TP. Epidemiology of childhood fractures in Britain: a study using the general practice research database. *J Bone Miner Res* 2004; **19**: 1976–81.
- 10 Migita RT, Klein EJ, Garrison MM. Sedation and analgesia for pediatric fracture reduction in the emergency department: a systematic review. *Arch Pediatr Adolesc Med* 2006; **160**: 46–51.
- 11 Hryhorczuk AL, Mannix RC, Taylor GA. Pediatric abdominal pain: use of imaging in the emergency department in the United States from 1999 to 2007. *Radiology* 2012; **263**: 778–85.
- 12 Eslick GD. Epidemiology and risk factors of pediatric chest pain: a systematic review. *Pediatr Clin N Am* 2010; **57**: 1211–19.
- 13 Walker DM, Teach SJ. Emergency department treatment of primary headaches in children and adolescents. *Curr Opin Pediatr* 2008; **20**: 248–54.
- 14 Galinski M, Picco N, Hennequin B, et al. Out-of-hospital emergency medicine in pediatric patients: prevalence and management of pain. *Am J Emerg Med* 2011; **29**: 1062–66.
- 15 Pitts SR, Niska RW, Xu J, Burt CW. National Hospital Ambulatory Medical Care Survey: 2006 emergency department summary. *Natl Health Stat Rep* 2008; **7**: 1–38.
- 16 Fitzgerald M, Howard RF. The neurobiologic basis of pediatric pain. In: Schechter NL, Berde CB, Yaster M. Pain in infants, children and adolescents, 2nd edn. Philadelphia: Lippincott Williams and Wilkins, 2003: 19–42.
- 17 Johnston CC, Stevens BJ, Boyer K, Porter FL. Development of psychologic responses to pain and assessment of pain in infants and toddlers. In: Schechter NL, Berde CB, Yaster M. Pain in infants, children and adolescents, 2nd edn. Philadelphia: Lippincott Williams and Wilkins, 2003: 105–27.
- 18 Liebelt EL. Assessing children's pain in the emergency department. *Clin Pediatr Emerg Med* 2000; **1**: 260–69.
- 19 Drendel AL, Kelly BT, Ali S. Pain assessment for children: overcoming challenges and optimizing care. *Pediatr Emerg Care* 2011; **27**: 773–81.
- 20 Chiaretti A, Pierri F, Valentini P, Russo I, Gargiullo L, Riccardi R. Current practice and recent advances in pediatric pain management. *Eur Rev Med Pharmacol Sci* 2013; **17** (suppl 1): 112–26.
- 21 Association of Paediatric Anaesthetists of Great Britain and Ireland. Good practice in postoperative and procedural pain management, 2nd edn. *Paediatr Anaesth* 2012; **22** (suppl): 11–79.
- 22 Finley GA, MacLaren Chorney G, Campbell L. Not small adults: the emerging role of pediatric pain services. *Can J Anesth* 2014; **61**: 180–87.
- 23 Gaffney A, McGrath PJ, Dick B. Measuring pain in children: Developmental and instrument issues. In: Schechter NL, Berde CB, Yaster M. Pain in infants, children and adolescents, 2nd edn. Philadelphia: Lippincott Williams and Wilkins, 2003.
- 24 Bauman BH, McManus JG Jr. Pediatric pain management in the emergency department. *Emerg Med Clin North Am* 2005; **23**: 393–414, ix.
- 25 Voepel-Lewis T, Burke CN, Jeffreys N, Malviya S, Tait AR. Do 0-10 numeric rating scores translate into clinically meaningful pain measures for children? *Anesth Analg* 2011; **112**: 415–21.
- 26 Ramelet AS, Abu-Saad HH, Rees N, McDonald S. The challenges of pain measurement in critically ill young children: a comprehensive review. *Aust Crit Care* 2004; **17**: 33–45.
- 27 Manworren RC, Hynan LS. Clinical validation of FLACC: preverbal patient pain scale. *Pediatr Nurs* 2003; **29**: 140–46.
- 28 Goldman A, Frager G, Pomietto M. Pain and palliative care. In: Schechter NL, Berde CB, Yaster M. Pain in infants, children and adolescents, 2nd edn. Philadelphia: Lippincott Williams and Wilkins, 2003: 539–62.
- 29 Schechter NL, Zeltzer LK. Pediatric pain: new directions from a developmental perspective. *J Dev Behav Pediatr* 1999; **20**: 209–10.
- 30 Tsao JC, Evans S, Seidman LC, Zeltzer LK. Experimental pain responses in children with chronic pain and in healthy children: how do they differ? *Pain Res Manag* 2012; **17**: 103–09.
- 31 Porter FL, Grunau RE, Anand KJ. Long-term effects of pain in infants. *J Dev Behav Pediatr* 1999; **20**: 253–61.
- 32 van Staa A, Jedeloo S, van der Stege H, and the On Your Own Feet Research Group. "What we want": chronically ill adolescents' preferences and priorities for improving health care. *Patient Prefer Adherence* 2011; **5**: 291–305.
- 33 Barbi E, Gerarduzzi T, Marchetti F. Managing chronic pain in children and adolescents: procedural sedation should be considered. *BMJ* 2003; **327**: 681.
- 34 Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JAM, et al. Pain in children and adolescents: a common experience. *Pain* 2000; **87**: 51–58.
- 35 Balottin U, Poli PF, Termine C, Molteni S, Galli F. Psychopathological symptoms in child and adolescent migraine and tension-type headache: a meta-analysis. *Cephalalgia* 2013; **33**: 112–22.
- 36 Di Lorenzo C, Colletti RB, Lehmann HP, et al, and the American Academy of Pediatrics Subcommittee on Chronic Abdominal Pain, and the NASPGHAN Committee on Abdominal Pain. Chronic abdominal pain in children: a clinical report of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr* 2005; **40**: 245–48.
- 37 Primavera G, Amoroso B, Barresi A, et al. Clinical utility of Rome criteria managing functional gastrointestinal disorders in pediatric primary care. *Pediatrics* 2010; **125**: e155–61.
- 38 Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology* 2006; **130**: 1527–37.
- 39 Diamanti A, Bracci F, Reale A, Crisogianni M, Pisani M, Castro M. Incidence, clinical presentation, and management of constipation in a pediatric ED. *Am J Emerg Med* 2010; **28**: 189–94.
- 40 Goldschneider KR. Complex regional pain syndrome in children: asking the right questions. *Pain Res Manag* 2012; **17**: 386–90.
- 41 Perez RS, Zollinger PE, Dijkstra PU, et al, and the CRPS I task force. Evidence based guidelines for complex regional pain syndrome type 1. *BMC Neurol* 2010; **10**: 20.
- 42 Massaro M, Pastore S, Ventura A, Barbi E. Pain in cognitively impaired children: a focus for general pediatricians. *Eur J Pediatr* 2013; **172**: 9–14.
- 43 Breau LM, Camfield CS, McGrath PJ, Finley GA. The incidence of pain in children with severe cognitive impairments. *Arch Pediatr Adolesc Med* 2003; **157**: 1219–26.
- 44 Parkinson KN, Dickinson HO, Arnaud C, Lyons A, Colver A, and the SPARCLE group. Pain in young people aged 13 to 17 years with cerebral palsy: cross-sectional, multicentre European study. *Arch Dis Child* 2013; **98**: 434–40.
- 45 Breau LM, Burkitt C. Assessing pain in children with intellectual disabilities. *Pain Res Manag* 2009; **14**: 116–20.
- 46 Hennequin M, Morin C, Feine JS. Pain expression and stimulus localisation in individuals with Down's syndrome. *Lancet* 2000; **356**: 1882–87.
- 47 Mafrica F, Schifilliti D, Fodale V. Pain in Down's syndrome. *ScientificWorldJournal* 2006; **6**: 140–47.



- 48 Rattaz C, Dubois A, Michelon C, Viellard M, Poinso F, Baghdadli A. How do children with autism spectrum disorders express pain? A comparison with developmentally delayed and typically developing children. *Pain* 2013; **154**: 2007–13.
- 49 Nader R, Oberlander TF, Chambers CT, Craig KD. Expression of pain in children with autism. *Clin J Pain* 2004; **20**: 88–97.
- 50 Zelter LK, Krane EJ. Pediatric pain management. In: Kliegman RM, Stanton BF, St Geme JW III, Schor NF, Behrman RE. Nelson textbook of pediatrics, 19th edn. Philadelphia: Elsevier, 2011.
- 51 Massaro M, Ronfani L, Ferrara G, et al. A comparison of three scales for measuring pain in children with cognitive impairment. *Acta Paediatr* 2014; published online July 15. DOI:10.1111/apa.12748.
- 52 Hoving MA, van Raak EP, Spincemaille GH, Palmans LJ, Becher JG, Vles JS, and the Dutch Study Group on Child Spasticity. Efficacy of intrathecal baclofen therapy in children with intractable spastic cerebral palsy: a randomised controlled trial. *Eur J Paediatr Neurol* 2009; **13**: 240–46.
- 53 Misurac JM, Knoderer CA, Leiser JD, Nailescu C, Wilson AC, Andreoli SP. Nonsteroidal anti-inflammatory drugs are an important cause of acute kidney injury in children. *J Pediatr* 2013; **162**: 1153–59, e1.
- 54 American Academy of Pediatrics. Committee on Drugs. Acetaminophen toxicity in children. *Pediatrics* 2001; **108**: 1020–24.
- 55 Rask CU. Functional somatic symptoms in 5–7 year old children: assessment, prevalence and co-occurrence. *Dan Med J* 2012; **59**: B4537.
- 56 American Psychiatric Association. Task Force on DSM-IV. (2000). Diagnostic and statistical manual of mental disorders. behavenet.com/apa-diagnostic-classification-DSM-IV-TR (accessed Feb 22, 2015).
- 57 Sonneveld LP, Brilleslijper-Kater SN, Benninga MA, Hoytema van Konijnenburg EM, Sieswerda-Hoogendoorn T, Teeuw AH. Prevalence of child sexual abuse in pediatric patients with chronic abdominal pain. *J Pediatr Gastroenterol Nutr* 2013; **56**: 475–80.
- 58 Hearst D. The Runaway Child: managing anticipatory fear, resistance and distress in children undergoing surgery. *Paediatr Anaesth* 2009; **19**: 1014–16.
- 59 Duff AJA. Incorporating psychological approaches into routine paediatric venepuncture. *Arch Dis Child* 2003; **88**: 931–37.
- 60 Young KD. Pediatric procedural pain. *Ann Emerg Med* 2005; **45**: 160–71.
- 61 Mednick L. Preparation for procedures. In: Shaw RJ, DeMaso DR, eds. Textbook of pediatric psychosomatic medicine, 1st edn. Washington, DC: American Psychiatric Publishing, 2010.
- 62 Cohen LL. Behavioral approaches to anxiety and pain management for pediatric venous access. *Pediatrics* 2008; **122** (suppl 3): S134–39.
- 63 Kuttner L. A child in pain. Wales: Crown House Publishing, 2010.
- 64 Konner M. The evolution of childhood: relationships, emotion, mind. Cambridge, MA: Belknap Press of Harvard University Press, 2010.
- 65 Kagan J, Herschkowitz N. A young mind in a growing brain. Mahwah, NJ: Lawrence Erlbaum Associates, Inc, 2005.
- 66 White SH. The child's entry into the age of reason. In: Sameroff AJ, Haith MM, eds. The five to seven year shift: the age of reason and responsibility. Chicago: University of Chicago Press, 1996.
- 67 Cohen LL, Blount RL, Cohen RJ, Ball CM, McClellan CB, Bernard RS. Children's expectations and memories of acute distress: short- and long-term efficacy of pain management interventions. *J Pediatr Psychol* 2001; **26**: 367–74.
- 68 Frank NC, Blount RL, Smith AJ, Manimala MR, Martin JK. Parent and staff behavior, previous child medical experience, and maternal anxiety as they relate to child procedural distress and coping. *J Pediatr Psychol* 1995; **20**: 277–89.
- 69 LeDoux JE. Emotion circuits in the brain. *Annu Rev Neurosci* 2000; **23**: 155–84.
- 70 Morgane PJ, Mokler DJ. The limbic brain: continuing resolution. *Neurosci Biobehav Rev* 2006; **30**: 119–25.
- 71 Heimer L, Van Hoesen GW. The limbic lobe and its output channels: implications for emotional functions and adaptive behavior. *Neurosci Biobehav Rev* 2006; **30**: 126–47.
- 72 Flavell JH, Green FL, Flavell ER, Grossman JB. The development of children's knowledge about inner speech. *Child Dev* 1997; **68**: 39–47.
- 73 Flavell JH, Flavell ER, Green FL. Development of children's understanding of connections between thinking and feeling. *Psychol Sci* 2001; **12**: 430–32.
- 74 Nelson K. Memory development from 4 to 7 years. In: Sameroff AJ, Haith MM, eds. The five to seven year shift: the age of reason and responsibility. Chicago: University of Chicago Press, 1996.
- 75 Pillow BH. Development of children's understanding of cognitive activities. *J Genet Psychol* 2008; **169**: 297–321.
- 76 Tomasello M, Kruger AC, Ratner HH. Cultural learning. *Behav Brain Sci* 1993; **16**: 495–552.
- 77 Weisner TS. The 5 to 7 transition as an ecocultural project. In: Sameroff AJ, Haith MM, eds. The five to seven year shift: the age of reason and responsibility. Chicago: University of Chicago Press, 1996.
- 78 Piaget J. The psychology of intelligence. London: Routledge & Kegan Paul, 1950.
- 79 Lavonas EJ, Reynolds KM, Dart RC. Therapeutic acetaminophen is not associated with liver injury in children: a systematic review. *Pediatrics* 2010; **126**: e1430–44.
- 80 Marzuillo P, Guarino S, Barbi E. Paracetamol: a focus for the general pediatrician. *Eur J Paediatr* 2013; **173**: 415–25.
- 81 Mak WY, Yuen V, Irwin M, Hui T. Pharmacotherapy for acute pain in children: current practice and recent advances. *Expert Opin Pharmacother* 2011; **12**: 865–81.
- 82 Neri E, Maestro A, Minen F, et al. Sublingual ketorolac versus sublingual tramadol for moderate to severe post-traumatic bone pain in children: a double-blind, randomised, controlled trial. *Arch Dis Child* 2013; **98**: 721–24.
- 83 Marzuillo P, Calligaris L, Barbi E. Tramadol can selectively manage moderate pain in children following European advice limiting codeine use. *Acta Paediatr* 2014; published online June 29. DOI:10.1111/apa.12738.
- 84 Murthy BV, Pandya KS, Booker PD, Murray A, Lintz W, Terlinden R. Pharmacokinetics of tramadol in children after i.v. or caudal epidural administration. *Br J Anaesth* 2000; **84**: 346–49.
- 85 Wilson JA, Kendall JM, Cornelius P. Intranasal diamorphine for paediatric analgesia: assessment of safety and efficacy. *J Accid Emerg Med* 1997; **14**: 70–72.
- 86 Cole J, Shepherd M, Young P. Intranasal fentanyl in 1–3-year-olds: a prospective study of the effectiveness of intranasal fentanyl as acute analgesia. *Emerg Med Australas* 2009; **21**: 395–400.
- 87 Borland M, Milsom S, Esson A. Equivalency of two concentrations of fentanyl administered by the intranasal route for acute analgesia in children in a paediatric emergency department: a randomized controlled trial. *Emerg Med Australas* 2011; **23**: 202–08.
- 88 Kendall JM, Reeves BC, Latter VS, and the Nasal Diamorphine Trial Group. Multicentre randomised controlled trial of nasal diamorphine for analgesia in children and teenagers with clinical fractures. *BMJ* 2001; **322**: 261–65.
- 89 Saunders M, Adalgais K, Nelson D. Use of intranasal fentanyl for the relief of pediatric orthopedic trauma pain. *Acad Emerg Med* 2010; **17**: 1155–61.
- 90 Berde CB, Sethna NF. Analgesics for the treatment of pain in children. *N Engl J Med* 2002; **347**: 1094–103.
- 91 Akorn. EMLA cream, US package insert. [http://www.akorn.com/documents/catalog/sell\\_sheets/63323-289-55.pdf](http://www.akorn.com/documents/catalog/sell_sheets/63323-289-55.pdf) (accessed March 13, 2015).
- 92 Synera. Synera patch, US package insert. [http://www.synera.com/wp-content/uploads/2014/05/SYNERA\\_PI.pdf](http://www.synera.com/wp-content/uploads/2014/05/SYNERA_PI.pdf) (accessed June 16, 2015).
- 93 Smith & Nephew. Ametop 40mg/g gel, UK product insert. <http://www.smith-nephew.com/global/assets/pdf/products/wound/api-ametop-uk-aug-2012.pdf> (accessed March 13, 2015).
- 94 Resch K, Schilling C, Borchert BD, Klatzko M, Uden D. Topical anesthesia for pediatric lacerations: a randomized trial of lidocaine-epinephrine-tetracaine solution versus gel. *Ann Emerg Med* 1998; **32**: 693–97.
- 95 Eidelman A, Weiss JM, Baldwin CL, Enu IK, McNicol ED, Carr DB. Topical anaesthetics for repair of dermal laceration. *Cochrane Database Syst Rev* 2011; **6**: CD005364. DOI:10.1002/14651858.CD005364.pub2.
- 96 Gibb IA, Anderson BJ. Paracetamol (acetaminophen) pharmacodynamics: interpreting the plasma concentration. *Arch Dis Child* 2008; **93**: 241–47.
- 97 Bianciotto M, Chiappini E, Raffaldi I, et al, and the Italian Multicenter Study Group for Drug and Vaccine Safety in Children. Drug use and upper gastrointestinal complications in children: a case-control study. *Arch Dis Child* 2013; **98**: 218–21.

- 98 Misurac JM, Knoderer CA, Leiser JD, Nailescu C, Wilson AC, Andreoli SP. Nonsteroidal anti-inflammatory drugs are an important cause of acute kidney injury in children. *J Pediatr* 2013; **162**: 1153–59.
- 99 Merry AF, Gibbs RD, Edwards J, et al. Combined acetaminophen and ibuprofen for pain relief after oral surgery in adults: a randomized controlled trial. *Br J Anaesth* 2010; **104**: 80–88.
- 100 Smith C, Goldman RD. Alternating acetaminophen and ibuprofen for pain in children. *Can Fam Physician* 2012; **58**: 645–47.
- 101 Kassab M, Foster JP, Foureur M, Fowler C. Sweet-tasting solutions for needle-related procedural pain in infants one month to one year of age. *Cochrane Database Syst Rev* 2012; **12**: CD008411.
- 102 Michiels EA, Hoyle JD. Systematic Review Snapshot: Sweet solutions and needle-related pain in infants. *Ann Emerg Med* (in press).
- 103 Harrison D, Yamada J, Adams-Webber T, Ohlsson A, Beyene J, Stevens B. Sweet tasting solutions for reduction of needle-related procedural pain in children aged one to 16 years. *Cochrane Database Syst Rev* 2011; (10): CD008408.
- 104 Lexi-Drugs drug database, Lexicomp, Wolters-Kluwer Health, Hudson, OH, USA. www.lexi.com (accessed Feb 22, 2015).
- 105 Borland M, Jacobs I, King B, O'Brien D. A randomized controlled trial comparing intranasal fentanyl to intravenous morphine for managing acute pain in children in the emergency department. *Ann Emerg Med* 2007; **49**: 335–40.
- 106 Ciszkowski C, Madadi P, Phillips MS, Lauwers AE, Koren G. Codeine, ultrarapid-metabolism genotype, and postoperative death. *N Engl J Med* 2009; **361**: 827–28.
- 107 Racoosin JA, Roberson DW, Pacanowski MA, Nielsen DR. New evidence about an old drug—risk with codeine after adenotonsillectomy. *N Engl J Med* 2013; **368**: 2155–57.
- 108 Grindlay J, Babl FE. Review article: Efficacy and safety of methoxyflurane analgesia in the emergency department and prehospital setting. *Emerg Med Australas* 2009; **21**: 4–11.
- 109 Bendall JC, Simpson PM, Middleton PM. Effectiveness of prehospital morphine, fentanyl, and methoxyflurane in pediatric patients. *Prehosp Emerg Care* 2011; **15**: 158–65.
- 110 Lander JA, Weltman BJ, So SS. EMLA and amethocaine for reduction of children's pain associated with needle insertion. *Cochrane Database Syst Rev* 2006; (3): CD004236.
- 111 Costello M, Ramundo M, Christopher NC, Powell KR. Ethyl vinyl chloride vapocoolant spray fails to decrease pain associated with intravenous cannulation in children. *Clin Pediatr (Phila)* 2006; **45**: 628–32.
- 112 Farion KJ, Splinter KL, Newhook K, Gaboury I, Splinter WM. The effect of vapocoolant spray on pain due to intravenous cannulation in children: a randomized controlled trial. *CMAJ* 2008; **179**: 31–36.
- 113 Green SM, Roback MG, Kennedy RM, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update. *Ann Emerg Med* 2011; **57**: 449–61.
- 114 Krauss B, Green SM. Procedural sedation and analgesia in children. *Lancet* 2006; **367**: 766–80.
- 115 O'Connor RE, Sama A, Burton JH, et al. Procedural sedation and analgesia in the emergency department: recommendations for physician credentialing, privileging, and practice. *Ann Emerg Med* 2011; **58**: 365–70.
- 116 Taylor SE, Taylor DM, Jao K, Goh S, Ward M. Nurse-initiated analgesia pathway for paediatric patients in the emergency department: a clinical intervention trial. *Emerg Med Australas* 2013; **25**: 316–23.
- 117 Priestley S, Kelly A-M, Chow L, Powell C, Williams A. Application of topical local anesthetic at triage reduces treatment time for children with lacerations: a randomized controlled trial. *Ann Emerg Med* 2003; **42**: 34–40.
- 118 Corwin DJ, Kessler DO, Auerbach M, Liang A, Kristinsson G. An intervention to improve pain management in the pediatric emergency department. *Pediatr Emerg Care* 2012; **28**: 524–28.