

Management of Acute Pain and Fever in Children: A guideline for pharmacists

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Title of the guideline

Management of acute pain and fever in children: a guideline for pharmacists

Purpose

The community pharmacy guideline for the management of pain and fever in children utilising non-prescription medicines and non-pharmacological interventions has been developed by the Australasian College of Pharmacy to help guide pharmacists providing care in their primary health setting. Community pharmacy is an accessible and affordable primary health care provider and is often the first health provider consulted when a child has pain and/or fever.

The guideline provides evidence-based advice for the pharmacist to utilise when recommending non-prescription medicines and providing advice to a caregiver requesting a product and/or guidance on the management of pain and/or fever in children, including lifestyle advice and when the child should be referred for medical assessment.

Definitions

Pain - 'Pain is an unpleasant sensory and emotional experience associated with or resembling that associated with actual or potential tissue damage.' The International Association for the Study of Pain (IASP) 2020⁽¹⁻⁴⁾

Acute pain - pain of recent onset and probable limited duration. It usually has an identifiable temporal and causal relationship to injury or disease.^(1,5) Pain that is associated with significant tissue damage and inflammatory response but does not involve damage to peripheral and central neurons.⁽³⁾

Antipyretic - reduces fever⁽⁵⁾

Caregiver - a family member or paid helper who regularly looks after a child

Fever - a temporary rise in body temperature above average, as part of an immunological response, usually caused by an infection.⁽⁶⁾ An average fever is defined as a measurement of >37.5°C in the axilla or >38°C from the tympanic area of the ear.^(7,8)

Key search terms

Acute pain, fever, children, paediatrics, paracetamol, ibuprofen

How to use the Guideline

This guideline was developed following a comprehensive literature review covering acute pain and fever in children (see Appendix 1 for a summary of the included evidence). The evidence was graded using a modified version of the National Health and Medical Research Council (NHMRC) Grades for Recommendations for Developers of Guidelines 2009 (see below for a summary of the evidence grading and Appendix 2 for further details) and guided by expert opinion. The evidence grading resulted in the development of six recommendations for the management of acute pain and fever in children within community pharmacy. The recommendations cover the following:

- 1. Clinical assessment
- 2. Lifestyle considerations
- 3. Criteria for management
- 4. Therapeutic options
- 5. Counselling
- 6. When to refer

Each recommendation covers the management of both acute pain and fever in children within community pharmacy.

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Overview

The guideline can be used to support pharmacists' role in the management of acute pain and fever in children. The guideline discusses assessment of pain and fever in children in community pharmacy, some criteria for management, the safe and effective use of non-prescription medicines (ibuprofen and paracetamol), non-pharmacological interventions, counselling for caregivers, and when to refer for medical advice.

Basic principles of pain management in children include:(1,3,9)

- Regular pain assessment
- Use of non-pharmacological techniques
- Using appropriate medicines at the correct dose and at the correct time, for the correct duration
- Careful management of adverse effects

Where possible, assessment of pain and fever in children involves consideration of both verbal and non-verbal cues.^(1,2,10) While there are many validated tools for assessing pain in children, a community pharmacy environment may not be conducive to using these effectively. Therefore, taking an appropriate history from the child and/or their caregiver/s is key to determining a course of action. (see Appendix 3 for models to be used in pharmacy for appropriate history taking)⁽¹¹⁾

As the carer often initially presents to the pharmacy assistant, the information gathering tools listed in Appendix 3 primarily guide pharmacy assistant referral to the pharmacist (CARER, WHAT STOP GO, ASK ASSESS ADVISE). However, pharmacist referral to a doctor is also outlined in WHAT STOP GO. Recommendation 6 provides details on when the pharmacist should refer the carer for medical advice.

Pharmacy staff providing guidance to the caregiver must determine the caregiver's ability to comprehend and act on the advice given.^(2,3) The recommendation is to consider using a language of lower schooling level when counselling caregivers and also when providing written advice.⁽¹²⁾ When exploring decision-making with regard to child health, studies suggest caregiver behaviours are dynamic and impacted on by three distinct drivers: 1) emotional state, such as vulnerability and anxiety, 2) practicalities of the child and family context, and 3) level of knowledge relating to the childhood condition (fever and/or pain)^(2,9,10,12)

Caregivers often overestimate the risk of harm associated with childhood symptoms such as fever, and can struggle to make health decisions during a child's illness.⁽¹²⁾ Cultural and linguistic diversity can also cause barriers to the caregiver understanding their role in the management of pain and fever in the child.⁽⁹⁾ For Aboriginal and/or Torres Strait Islander peoples, yarning in the clinical setting builds rapport and trust, and is key to effective communication and patient centred care.⁽¹³⁾ Yarning involves:⁽¹³⁾

- 1. the social yarn where one tries to find common ground.
- 2. the *diagnostic yarn* where the patient or caregiver is encouraged to tell their health story as an open-ended dialogue. The health professional's role is to unpack the relevant information and interpret the story through their biomedical lens to inform management.
- 3. the *management yarn* where the health professional provides clear information but may use metaphors and stories connected to the patient's life to assist understanding of their condition and advice provided.

While time constraints may limit yarning, the First Nations caregiver will benefit from the practitioner adopting a less traditional consultation style. Pharmacy staff need to take cultural diversity and health literacy into consideration when taking a patient history, providing advice and presenting the caregiver with a clear action plan to follow.⁽¹²⁾ If any barriers that may put the child at risk are identified, an alternative caregiver or support person may need to be tasked to assist in managing the child's health.^(9,12)

Non-pharmacological approaches to the management of pain and fever in children are highly valuable. Caregivers should be given strategies to manage the child's stress, anticipation, and acceptance of pain, including procedural, physical, and psychological interventions appropriate to the child's age.^(1,9) Surveillance, rest, loose clothing, and hydration are core non-pharmacological management practice for fever in children.^(5,9) Pharmacy staff should ensure caregivers are skilled at monitoring fever in a child, understand the acceptable ranges of body temperature, and actions to take if these are exceeded.⁽⁸⁾

Temperature measurements

The World Health Organisation (WHO) defines equivalent rectal temperature ≥38°C or axillary temperatures of ≥37.5°C as indicative of fever in both adults and children.⁽⁸⁾

The Royal Children's Hospital Melbourne guideline for measuring fever uses the following guideline:⁽⁷⁾

- Axillary temperature: recommended for infants <3 months of age. For a more accurate reading, the thermometer should be placed over the axillary artery for 3 minutes.
- Tympanic temperature: recommended for children >3 months of age. For an accurate measurement, the pinna must be retracted to straighten the external auditory meatus and the instrument should be directed at the tympanic membrane.
- Skin temperature: forehead or infrared thermometers are unreliable
- Rectal temperature: in neonates, screen first with axillary temperature, then consider performing a rectal temperature if a fever is still suspected

Non-prescription pharmacological management for pain and fever includes ibuprofen or paracetamol, both of which have analgesic and antipyretic action, with anti-inflammatory action in the case of ibuprofen.^(9,14,15) Ibuprofen and paracetamol have comparable efficacy in the treatment of acute pain and fever in children and similar tolerability profiles when used at recommended doses over short periods.^(9,16-18)

Microbial toxins and tissue damage induce synthesis and release of pyrogenic cytokines into the systemic circulation. These cytokines (interleukins, prostaglandins) travel to the anterior hypothalamus and stimulate prostaglandin E2 synthesis. Fever occurs when warm-sensitive neurons, normally responsible for triggering heat loss, are inhibited by prostaglandins, mainly prostaglandin E2, which can potentially raise the thermostatic set point in the hypothalamus to febrile levels.⁽¹⁹⁾

Antipyretic agents reduce brain prostaglandin E2 levels and may be beneficial in a child with fever who is distressed. While ibuprofen (and other NSAIDs) inhibits prostaglandin synthesis by competing with arachidonic acid for the cyclo-oxygenase (COX) binding site, paracetamol has several pharmacodynamic targets within the brain. In addition to COX inhibition, paracetamol reduces prostanoid (cyclooxygenase metabolites of arachidonic acid) formation by acting at the COX peroxidase site.⁽¹⁶⁾ However, due to the large amounts of hydroperoxide present in inflammatory environments, the anti-inflammatory activity of paracetamol is reduced.⁽¹⁶⁾ The mechanisms of the analgesic action of these medicines are also thought to differ. In addition to COX inhibition, paracetamol analgesia also appears to be associated with the descending, serotonergic pain control system.⁽¹⁶⁾ Despite these mechanistic differences, in a child with elevated body temperature or pain who is otherwise well and happy, the use of an antipyretic is not required.⁽¹⁶⁾ There is a lack of evidence to support that antipyretics prolong or shorten illness duration in acute upper and lower respiratory tract infection (RTI).⁽²⁰⁾ Therefore, if the fever is well tolerated in the child with a RTI the use of an antipyretic must be weighed against their adverse effect profile.⁽²⁰⁾

A child with fever under the age of three months should be referred for medical advice due to the risks of undiagnosed infection. A malnourished or dehydrated child should be referred for medical advice due to the risk of inappropriate dosing of paracetamol and ibuprofen in this patient cohort.

Management of Acute Pain and Fever in Children

Contraindications for ibuprofen and paracetamol should be considered before recommending their use. Both paracetamol and ibuprofen should be contraindicated in malnourished and/or dehydrated children.⁽¹⁾

Dosing of ibuprofen and paracetamol should be based on weight.^(1, 7, 9, 14) When calculating the dose for overweight or obese children, ideal body weight should be used.^(1,15) Timing of ibuprofen and paracetamol dosing does not require adjustment in relation to food.^(1,7,4) Caregivers should be advised that delaying a dose of ibuprofen or paracetamol until the child has eaten is not necessary and may lead to underdosing and cause unnecessary distress for the child.^(1,3,15-17,21)

Other considerations that are important in relation to doses of ibuprofen and paracetamol include:(1,14,16,17,21,22)

- only using a calibrated device,
- the caregiver recording of the dose and time given,
- the caregiver assessing the efficacy of the previous dose,
- the caregiver determining the need for further dosing,
- the caregiver realising when to seek medical advice about the child's condition.

If the child is refusing the liquid dose an alternate method of dosing can be trialled. Paracetamol suppositories or dissolving tablets are available for ibuprofen and paracetamol and may be used depending on the age of the child. ^(1,14,15,23) The caregiver may need to disguise the medicine in another liquid or give an ice block to freeze the taste buds before medicine time. The use of a straw to suck up the medicine may avoid the taste buds in the tongue and the effort of sucking on the straw makes the medicine go down the throat quickly. At times it may be necessary to resort to bribery with the promise of a treat if the medicine is swallowed.⁽⁹⁾

Different brands of ibuprofen and paracetamol have different flavours. The pharmacy staff should recommend a product that requires the minimal amount of liquid to be swallowed to enhance the ability of the child to successfully swallow the liquid without gagging or vomiting.

Simultaneous administration of ibuprofen and paracetamol for acute pain and fever in children is not currently supported by evidence.^(12,18) Alternating doses of ibuprofen and paracetamol remains controversial and should not be routinely recommended due to insufficient evidence. This strategy should only be used if there is breakthrough in pain or fever before the next scheduled dose is due and the maximum daily dose of each medication is not exceeded (i.e. Do not give more than 4 doses of paracetamol in 24 hours. Do not give more than 3 doses of ibuprofen in 24 hours).^(18,24) Caregivers should be advised how to record the medicine given, the doses, and the times given, to help avoid errors and overdosing. Importantly, caregivers should be advised to assess the child for improvement or deterioration before administering the next dose, and how to determine if medical attention is required.

Children should be referred for further assessment if they exhibit red flags (see Recommendation 6: When to refer) or there is poor or no response to simple analgesia and/or antipyretics or non-pharmacological interventions for pain and/or fever.⁽⁹⁾

Recommendations RECOMMENDATION 1: CLINICAL ASSESSMENT

Evidence grade: A

Where possible assess pain and/or fever in the child using appropriate verbal and non-verbal cues to guide a management plan.^(1,2,10) Use caregiver pain and/or fever behaviour knowledge for children with cognitive impairment or difficulty communicating. Investigate the history of the child that has led to the pain and/or fever occurrence.^(9,10,25,26)

Implications for practice

History taking requires discussion with primary caregivers, as unwell children are not always present or capable of providing accurate responses. The ability to accurately measure pain in children is limited due to confounders such as the child's age, developmental level, cognitive and communication skills, previous pain experiences, and associated beliefs.^(1,2,10,25) The evidence indicates the effectiveness of validated pain screening tools varies for different age groups.⁽¹⁾ The accurate application of validated pain screening tools in a community pharmacy setting may be challenging.⁽¹⁾ Therefore, pharmacy staff use questioning and history taking techniques e.g. Ask, Assess, Advise, What-Stop-Go or CARER, (see Appendix 3)⁽¹¹⁾ to determine the appropriate management recommendations for acute pain in children. Recommendation 6 provides details on when the pharmacist should refer the carer for medical advice.

Three main methods are used to assess pain in children:(1,2,9,10,25)

- 1. Self-reporting of pain
- 2. Behaviour in relation to pain
- 3. Physiological assessment

Where possible, pain is assessed using verbal and non-verbal cues.⁽⁹⁾ The child requires a certain level of cognition and communication development to understand and reliably respond to assessment protocols.^(1,26) As children age, their ability to describe pain improves.^(1,26) Children with cognitive and developmental challenges and non-verbal children may be difficult to assess. Behavioural assessments such as crying, facial expressions, body postures, and hampered movement can be used to overcome these limitations.^(1,2,6)

Physiological measures related to pain assessment such as heart rate, blood pressure, respiration, oxygen saturation, sweating, and neuro-endocrine responses cannot be reliably monitored in a community pharmacy setting. The same physiological responses may be observed when the child is otherwise distressed, and therefore it can be difficult to differentiate between pain and other stresses.⁽¹⁰⁾

In a community pharmacy setting, staff rely on the caregivers' interpretation of children's behaviour to determine their level of and potential cause of pain. While some children will display the above behaviour/s, others may become withdrawn and resistive to communicating their pain status.⁽¹⁰⁾ The caregiver is relied upon to facilitate assessment as they possess the most reliable knowledge of their child.

Points to consider when performing a pain assessment:^(1,2,9,10,26,27)

- Pain history
- Location of pain
- Intensity of pain
- Cognitive development and understanding of pain
- Identification of red flags

Using behaviour cues is not always valid, as children react differently to pain due to their previous pain experiences, caregiver responses to managing pain, and developmental restrictions.^(9,10,25)

Pain in children can be difficult to differentiate from anxiety and stress, especially in a pre-verbal or non-verbal child.^(1,2,10) Therefore, the child's cognitive ability to communicate pain location and intensity must be considered.^(1,2,10) The child's environment and cause of pain (e.g. inflammatory versus non-inflammatory) should be considered when determining the pain management plan.^(1,10) Circumstances that may influence pain perception and coping strategies include social history/issues, cultural and religious beliefs, past pain experiences, and the first pain experience.^(2,10,25,26) In addition, the family's response to their child's pain can have a negative or positive influence on the child.^(1,10)

Points to consider when performing a fever assessment:

- Recent ill health
- Recent contact with other unwell people
- Engagement in vigorous activity prior to presenting with fever

The caregiver should be counselled on the acceptable body temperatures for children at their age and when to seek further medical advice.⁽¹²⁾ An average fever is defined as a measurement of >37.5°C in the axilla or >38°C from the tympanic area of the ear.^(7,8) (see the Royal Children's guideline above for how to manage fever in children) In most children fever alone does not require intervention unless the child appears distressed.^(12,16,19) Often surveillance, rest, and hydration are adequate management approaches for fever.

RECOMMENDATION 2: LIFESTYLE CONSIDERATIONS

Evidence grade: A

Teach caregivers how to manage the child's stress, anticipation, and acceptance of pain.^(9,10,25) Use of the 4 P's of pain management (procedural, pharmacological, physical, and psychological interventions appropriate to the age of the child) is effective in pain management.⁽⁹⁾ Lifestyle interventions of surveillance, rest, and hydration to manage fever in children are supported by robust evidence of efficacy.^(5,728,29)

Implications for practice

The 4 P's of pain management are summarised as:

- 1. Procedural minimising the number of painful events e.g. by combining vaccines, finding alternate routes of administration e.g. nasal spray versus injection, using a wider bore needle gives a faster injection rate, longer needles are associated with less pain and less local reaction.^(9,30) It is recommended to give the most painful vaccine last if more than one vaccine is being given.⁽³⁰⁾
- 2. Pharmacological using a local anaesthetic patch/gel applied to the area for a suitable time before injecting.^(9,30)
- 3. Psychological cognitive and behavioural techniques to reduce fear and anxiety. These techniques need to be taught to the caregiver and it is important that the caregiver does not transfer their own fears and anxiety to the child. Techniques such as distraction, explanation of the procedure including sensory information as to what will happen, how it will feel, and what can be done to minimise the discomfort.^(9,30)
- 4. Physical breastfeeding before and during the procedure, non-nutritive sucking on a dummy, swaddling, holding the child upright and close to the parent with direct eye contact with a calm parent, tactile stimulation of the injection site, application of ice after an injection, using a device that combines cold and vibration to decrease the sensation of pain through distraction.^(9,30)

Recommendations for lifestyle management of pain include the caregiver using psychological techniques to reduce the child's anxiety and fear.^(9,30) These techniques involve child and parent directed training.^(9,30) Administering sweetened fluids before a painful injection, reading a story, watching an activity on a digital device, breathing exercises, blowing bubbles, playing with toys and games, comfort and cuddling from the caregiver are all suggested.^(9,30) Teaching the caregiver how to reduce their own anxiety and fears is important to prevent them transferring these onto the child⁽³⁰⁾

The management of fever in children requires education for caregivers that a raised body temperature (>38°C) is not always reason for referral for medical advice.^(5,28) However, a child younger than three months of age with a body temperature above 38°C should be referred.

Counselling on how to monitor body temperature appropriately is advisable.^(5,28) Recommendations from the Royal Children's Hospital Melbourne for taking a child's temperature include:⁽²⁸⁾

- Axillary temperature: recommended for infants younger than 3 months of age. For a more accurate reading, the thermometer should be placed over the axillary artery for 3 minutes.
- Tympanic temperature: recommended for children older than 3 months of age. For an accurate measurement, the pinna must be retracted to straighten the external auditory meatus and the instrument should be directed at the tympanic membrane.
- Skin temperature: forehead or infrared thermometers are unreliable.
- Rectal temperature: in neonates, screen first with axillary temperature, then consider performing a rectal temperature if a fever is still suspected.

Caregivers need to understand other factors that may have elevated the child's temperature (e.g. vigorous activity, being in a hot environment, being anxious, and crying). Surveillance, rest, and hydration are core management practice for fever in children. The caregiver should understand the time frame and body temperature readings that warrant referral for medical advice.^(5,28)

The Royal Children's Hospital Melbourne recommends the following guide as to when to seek medical advice:⁽²⁸⁾

Immediate care should be sourced from a doctor or hospital emergency department for the following:⁽²⁸⁾

- If the baby is under three months old and has a fever above 38°C, even if they have no other symptoms.
- If the child is immunocompromised (has a weakened immune system) for any reason and has a fever above 38°C.

For all other children, carers should seek medical advice if their temperature is above 38°C and they have any of the following symptoms:⁽²⁸⁾

- a stiff neck or light is hurting their eyes
- vomiting and refusing to drink much
- a rash
- more sleepy than usual
- problems with breathing
- pain that doesn't get better with pain relief medication
- have had any fever for more than two days and there's no obvious cause
- seem be getting more unwell
- have had a febrile seizure

Counselling should explain that dehydration can lead to fever in children and that hydration with an oral hydration solution (ORS) suitable for a child should be used rather than sugary liquids or juices. Water is the preferred liquid if ORS is not available.

RECOMMENDATION 3: CRITERIA FOR MANAGEMENT

Evidence grade: A

Treatment with ibuprofen or paracetamol is contraindicated in the malnourished. and/or dehydrated child. These children should be referred for medical advice immediately.^(28,29)

Contraindications for ibuprofen include gastrointestinal issues, kidney injury, asthma, and cardiovascular conditions. Contraindications for paracetamol include asthma and reduced hepatic function.^[14,15]

There is no evidence that ibuprofen or paracetamol must be administered with food to improve safe use.^[14,15] While both ibuprofen and paracetamol should ideally be administered without food to optimise absorption, the medications can be taken with food without significant clinical impact if it improves medication acceptance by the child or caregiver.

Age restrictions listed on the product for paracetamol and ibuprofen should inform therapy choice in infants; paracetamol dosing range starts from one month of age while ibuprofen from three months of age.^[14–16]

The child with fever who appears well and happy, with no confounding factors, may not require treatment.⁽¹²⁾ Fever where the child is distressed may benefit from treatment. Fever in a child under three months of age requires referral for medical advice.^(28,31)

The caregiver requires counselling on using an appropriate device for accurate measurement of the dose based on the weight of the child, or ideal body weight for overweight or obese children.^(12,14,15) The caregiver should maintain a record of the medicine given, the dose, the time the dose was administered, and the response of the child to the dose.

Counselling should include the need for surveillance of the response to treatment and what to do if the child does not respond or partially responds. If the child does respond and the pain and/or fever resolves the treatment can be ceased.⁽¹²⁾

Implications for practice

Both ibuprofen and paracetamol are first-line pharmacotherapy options for the management of acute pain and fever in children.^{(1,9,14-16,3)-34}) They have different mechanisms of action. Paracetamol is analgesic but has limited antiinflammatory activity.^(16,33) Ibuprofen has both analgesic and anti-inflammatory activity.⁽³⁴⁾ The choice of paracetamol or ibuprofen should be informed by the age of the child and the underlying cause of the child's pain and/or fever. ^(1,3,16,28,29) Paracetamol dosing range starts from one month of age.^(14–16) Ibuprofen dosing range starts from three months of age.^(14,15,34)

Ibuprofen and paracetamol demonstrate similar gastrointestinal tolerability when managing pain in children older than 3 months.^(34–37)

Ibuprofen and paracetamol should ideally be administered without food.^[14,15] Food has been shown to delay paracetamol absorption and the onset of action, and maximum plasma concentration of ibuprofen.^[34] There is a lack of evidence to prove that food is gastroprotective against the adverse effects of NSAIDs.^[34] There is also a risk that the caregiver may delay necessary dosing until food can be given and therefore undertreat the child's pain and/or fever and cause unnecessary distress.^[34]

The research states that administration of an antipyretic to reduce fever in a child who is displaying no other symptoms of distress or illness is not warranted.^(12,34) Ibuprofen or paracetamol can be used for a child with fever who appears distressed. Antipyretics do not prevent febrile convulsions and should not be used for this indication.⁽³⁴⁾

There is ongoing debate over the use of analgesics prior to immunisation. The use of topical anaesthetic agents prior to injection and appropriate injection techniques to minimise pain and distress are the current recommendations.^(9,29) Topical application of ice after injection if the site is painful, is also recommended.^(9,30) Ibuprofen or paracetamol can be administered if the child develops fever and pain post injection.^(9,14,15,28,38)

Reducing the risk of under- or over-treatment of children's pain and fever due to inappropriate medicine use requires education for caregivers on the correct dose, to be given at the correct time, using the correct measuring device. Caregivers should be helped to understand how to document this to help prevent inefficient and unsafe dosing. Caregivers also require education on appropriate dosing techniques and how to assess whether further doses are required or when the child should be referred for medical advice.

Measuring dose

- Base dose on the child's weight (or ideal weight for children who are overweight or obese)⁽¹⁵⁾
- Use a **calibrated syringe** for the most accurate measurement

Appropriate dosing interval

- Ibuprofen dosing interval every **6-8** hours as necessary; paracetamol dosing interval every **4-6** hours as necessary^[14,15]
- Assess/reassess efficacy before administering the next due dose

Maximum daily dose

- Ibuprofen up to **3 times** a day; paracetamol no more than **4 doses** in 24 hours^(14,15)
- Short term use (for less than 7 days) of ibuprofen or paracetamol has equally good safety and tolerability profiles.^(26,34) The length of treatment should be informed by the response of the child to treatment.⁽³³⁾ Poor response requires referral for medical advice.⁽²⁶⁾

If the child does not respond or only partially responds to treatment, they require investigation by a medical practitioner.

Despite the widespread use of ibuprofen and paracetamol, the rate of severe toxicity in children remains rare. ^(9,34,35) Meta-analyses confirm that the safety and tolerability profiles of paracetamol and ibuprofen in managing children's pain and fever are comparable and that both medicines are associated with specific yet rare adverse events.^(9,16,34,35) These are difficult to detect and quantify in all but the largest clinical trials.⁽³⁴⁾ Pharmacists can be confident in the safety and efficacy of non-prescription doses of ibuprofen and paracetamol for short term use and separate potential adverse effects from those attributable to higher doses and/or longer-term use that can cause toxicity.^(9,34,35)

RECOMMENDATION 4: THERAPEUTIC OPTIONS

Evidence grade: A

Ibuprofen and paracetamol have comparable efficacy in the treatment of acute pain and fever in children. (3.5.9.14,16,17,21,24,31)

Simultaneous administration of ibuprofen and paracetamol for acute pain and fever in children is not currently supported by evidence.^(12,18)

Alternating doses of ibuprofen and paracetamol should only be used if there is breakthrough in pain or fever before the next scheduled dose is due.⁽¹⁸⁾ Caregivers should be advised how to record the medicine given, the doses, and the times given, to help avoid errors and overdosing.

When used at the recommended dose for a short duration, the adverse effects associated with the use of paracetamol and ibuprofen are mild and self-limiting and the occurrence of adverse effects can be minimised by accurate dosing and adherence to dosing schedule.^(16,37) Serious, rare adverse effects related to overdose require immediate medical attention.⁽³⁷⁾

Counselling should address accurate dosing methods, dosing schedule, how to reassess the outcome of the previous dose⁽¹⁶⁾, and when to refer. Counselling should also include what to do if a child vomits back the dose.^(12,21)

Implications for practice

Immediate release formulations of paracetamol and ibuprofen generally start to work within an hour and the effect usually lasts several hours.⁽³⁷⁾ Paracetamol and ibuprofen have comparable efficacy in the management of acute pain and fever in children.^(9,14,15,34-37)

The caregiver should be counselled about how to assess the child's response to treatment and to change to another agent if the response to the first agent is insufficient.

Assessment of response to treatment involves determining whether:⁽¹²⁾

- the pain and/or fever has resolved
- the child's distress has resolved, and
- whether the child is now comfortable and returning to their normal routine.

Vomiting after a child receives a dose of antipyretic for pain or fever is common. This may be due to the pain or infection; it could also be the result of the child's distress in being administered a medicine, or an allergic reaction. Both immediate release dose forms of paracetamol and ibuprofen achieve peak plasma concentrations within 30 to 60 minutes. If a child vomits after a dose of these antipyretics, the recommended action is generally not to readminister the dose, especially if the time interval is greater than 15- 20 minutes. However, if the child spits out the dose within the first 5 minutes of dose administration, the dose absorbed would be minimal and the dose could be repeated.

The caregiver is the person best placed to assess whether the child has returned to good health as they are in contact with the child constantly and know them best.

There is no evidence that simultaneous administration of paracetamol and ibuprofen is of benefit in the treatment of pain or fever in children.^(16,18) Combining doses of paracetamol and ibuprofen increases the risk of hyper-dosing due to differences in duration of action and dosing schedules of the two actives. Only consider alternating doses of paracetamol and ibuprofen if distress recurs before the next dose is due.⁽¹⁶⁾

High quality studies used doses of ibuprofen (10mg/kg) or paracetamol (15mg/kg), which corresponds to the recommended dosing schedule in Australia.^(9,14,15,17) Studies indicate that the risk of overdose or repeated supratherapeutic doses of paracetamol use continues to rise in Australia, predominantly in Australian women.⁽¹⁶⁾ The risk of paracetamol overdose includes hepatotoxicity and possible death in adults.^(4,39) The risk is confounded by the number of non-prescription products containing paracetamol for management of pain, fever, cough, cold, and flu.⁽³⁹⁾ Unintentional ingestion of supra-therapeutic doses of paracetamol do occur in Australia leading to hospital admissions, toxic liver disease, and deaths.⁽³⁹⁾ Despite the widespread use of ibuprofen and paracetamol, the rate of severe toxicity in children remains rare.⁽⁷⁾

Management of Acute Pain and Fever in Children

Safety considerations for the treatment of pain and fever in children relate to the following:

- Malnourishment and dehydration can increase the risk of adverse effects from paracetamol and/or ibuprofen
- Accuracy of dose clearly communicate the dose and advise the caregiver on the use of a calibrated measure
- Timing of dose clearly communicate the dosing schedule and urge the caregiver to record the medicine, dose, and time the dose was given
- Counselling the caregiver to observe the response to the dose. This will be useful in determining:
 - efficacy of treatment
 - whether further dosing is required
 - whether a change of medicine is required
 - whether referral to a medical practitioner is required.

RECOMMENDATION 5: COUNSELLING

Evidence grade: A

Dosing of ibuprofen and paracetamol should be based on weight. Calculate the dose for overweight and obese children based on ideal body weight using a standard formula.⁽¹⁵⁾

Ibuprofen and paracetamol dosing time does not require adjustment in relation to food.(34,35)

Treatment with ibuprofen or paracetamol is contraindicated in malnourished and/or dehydrated children. These children should be referred for medical advice immediately.^(28,29)

A calibrated dose device should be used for each dose.

Caregivers should record the medicine, dose, and the time given and the response of the child to the previous dose.

Caregivers should establish a dosing schedule and reassess the child before each dose is given to determine efficacy of the previous dose and whether further dosing is required.

If response is poor to the dose given, an alternate analgesic can be trialled. If response is poor to both ibuprofen and paracetamol, or if the pain and/or fever continues for 48 hours (in the absence of additional red flags such as dehydration, altered alertness and/or vomiting), caregivers should seek medical advice. The use of ibuprofen or paracetamol for longer than 7 days without medical intervention is not backed by research and evaluation.⁽³⁵⁾

Implications for practice

Pharmacy staff advising the caregiver must consider their ability to understand the advice given. The caregiver must understand that consideration of the child's weight is an important factor in managing pain and fever in children.⁽¹⁵⁾

Cultural and linguistic diversity can hinder caregivers' understanding of their role in managing pain and fever in children. Health literacy and cognitive ability of the caregiver can also be a barrier to optimal care of the child. If any barriers that may put the child at risk are identified, an alternative caregiver or support person may need to assist in managing the child's health.

RECOMMENDATION 6: WHEN TO REFER

Evidence grade: B

Pharmacists should take a medical history (using one of the protocols listed in Appendix 3) and use other observations to determine if a child requires referral for medical advice.⁽²¹⁾

Children should be referred for further assessment if they exhibit red flags or there is poor or no response to analgesics, antipyretics, or non-pharmacological interventions for pain and/or fever.^(5,7,2)

Children who are malnourished and/or dehydrated should be referred for medical advice.^(28,29)

Children with fever younger than three months of age should be referred for medical advice.⁽⁷⁾

All immunocompromised children with a body temperature above 38°C should be referred for medical advice.⁽⁷⁾

Implications for practice

Deciding when to refer a child with pain and/or fever requires a detailed history from the caregiver as to the severity of the child's pain and/or fever, how long the pain and/or fever has been present, and any other comorbidities or health conditions the child may have or medicines they take.^(1,2,10,21)

Minor pain of short duration can be managed with non-prescription medicines and non-pharmacological treatment plans.^(21,34-37)

The caregiver must be counselled to seek medical advice if the pain persists or worsens, or the treatment plan is ineffective. The research defines the time period for safe use of over-the-counter products as less than 7 days.⁽³⁷⁾

For fever, the severity of the illness cannot be predicted by the degree of fever. Fever is an indicator of an immune response by the body.^(5,7,34,35)

The rapidity of onset of the fever, the response to antipyretics, the presence of febrile seizures, and the general appearance and activity level of the child are the most useful indicators for when referral is required.^(5,7,17,34,35)

In infants less than three months of age, hypothermia or temperature instability can be signs of serious bacterial infection (or other serious illness). All children younger than three months of age exhibiting fever should be referred for medical advice.^(7,28)

All immunocompromised children with a fever above 38°C should be referred for medical advice.^(7,28)

Refer to Table 1 for a list of observations that should be referred for medical advice.^(7,28)

Table 1: Observations in children with fever requiring referral for medical advice.

COLOUR	ACTIVITY	RESPIRATORY
Pallor Mottled Blue/cyanosed	Lethargic or decreased activity Not responding normally to social cues Does not wake or only with prolonged stimulation, or if roused, does not stay awake Weak, high-pitched or continuous cry	Grunting Tachypnoea Increased work of breathing Hypoxia
NEUROLOGICAL	OTHER	CIRCULATION AND HYDRATION

Examples of red flags for pain in children requiring referral for medical advice.^[3,31]

- Earache*
- Stomach pain
- Migraine
- Pharyngitis
- Viral infections of the mouth
- Pain from an injury
- Post major surgery
- Pain from an unknown source
- Pain that is associated with other symptoms (e.g. bacterial infection, pneumonia, meningitis)
- Pain that is present for a sustained period
- Pain that is unresponsive to non-prescription analgesics
- Pain that may be associated with abuse/bullying
- Severe period pain and period pain that reoccurs and causes loss of school/work/leisure time.
- *Where state and territory legislation allow, appropriately-trained pharmacists may be authorised to manage specified acute conditions including acute diffuse otitis externa and acute otitis media.

Appendix 1

GRADING THE RECOMMENDATIONS

The College uses modified National Health and Medical Research Council (NHMRC) Grades of Recommendations (2009) to determine recommendations for the guideline.⁽⁹⁾ In the absence of published evidence, expert or author opinion was considered.

Each recommendation is based on rating 5 key components of the body of evidence for the recommendation. These are:

- 1. The evidence base, in terms of the number of studies, level of evidence and quality of studies (risk of bias), or expert opinion.
- 2. The consistency of the study results.
- 3. The potential clinical impact of the proposed recommendation.
- 4. The generalisability of the body of evidence to the target population for the guideline.
- 5. The applicability of the body of evidence to the Australian healthcare context.

The level of evidence (hierarchy) for intervention studies is ranked by the study type (Table 2).

TABLE 2: NHMRC GRADES OF RECOMMENDATIONS 2009⁽⁹⁾

GRADE	DESCRIPTION	BODY OF EVIDENCE
A	Body of evidence can be trusted to guide	• one or more level I studies with a low risk of bias or several level II studies with a low risk of bias
	practice	• all studies consistent
		• very large clinical impact
		 population/s studied in body of evidence are the same as the target population for the guideline
		 directly applicable to Australian healthcare context
В	Body of evidence can be trusted to guide	• one or two level II studies with a low risk of bias or a systematic review/several level III studies with a low risk of bias
	practice in most	 most studies consistent and inconsistency may be explained
	situations	• substantial clinical impact
		 population/s studied in the body of evidence are similar to the target population for the guideline
		 applicable to Australian healthcare context with few caveats
С	Body of evidence provides some	 one or two level III studies with a low risk of bias, or level I or II studies with a moderate risk of bias
	support for	• some inconsistency reflecting genuine uncertainty around clinical question
	but care should	• moderate clinical impact
	be taken in its application	• population/s studied in body of evidence differ to target population for guideline, but it is clinically sensible to apply this evidence to target population (e.g. applying adult data to paediatric population)
		• probably applicable to Australian healthcare context with some caveats
D	Body of evidence	• level IV studies, or level I to III studies/systematic reviews with a high risk of bias
	is weak, and	• evidence is inconsistent
	must be applied with	• slight or restricted clinical impact
	caution	• population/s studied in body of evidence differ to target population and hard to judge whether it is sensible to generalise to target population
		not applicable to Australian healthcare context
	Author opinion	May be added to Grade, where appropriate

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TABLE 3: NHMRC EVIDENCE HIERARCHY⁽⁹⁾

LEVEL	STUDY TYPE
I	A systematic review of level II studies
П	A randomised controlled trial
111-1	A pseudo-randomised controlled trial e.g. another means of allocating participants
III-2	A comparative study with concurrent controls e.g. non-randomised trial, cohort study, case-control study, interrupted time series with a control group
III-3	A comparative study without control e.g. historical control study, two or more single arm study, interrupted time series without a control group
IV	Case series with either post-test or pre-test/post-test outcomes

Appendix 2

EVIDENCE SUMMARY

RECOMMENDATION 1: CLINICAL ASSESSMENT

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Management of acute pain in children: safety and efficacy of a nurse-controlled algorithm for pain relief	Falanga IJ, Lafrenaye S, Mayer SK, Tétrault JP.	Acute Pain 2006;8(2):45-54	2 groups each of 56 children between 5-17 years of age admitted for trauma	Prospective, comparative (pre-post-) study	Level III-2	Study evaluated the efficacy and safety of regular versus combined analgesia (paracetamol, naproxen, and morphine) to improve pain relief in the first 2 days following admission following surgery or trauma. Analgesia was given by nurses in accordance with patients' visual analogue scale (VAS) of 0= no pain and 10=worst imaginable pain. A standardised algorithm resulted in better analgesic outcomes.	No children under 5 years were in the study. Assessment of analgesic response and side effect was undertaken by different nursing personnel. Study assessed the efficacy of the algorithm rather than efficacy of individual analgesics
Pain in children: Assessment and non- pharmacological management	Srouji R, Ratnapalan S, Schneeweiss S.	International Journal of Paediatrics 2010;2010:474838. doi:10.1155/2010/474838		Literature review	Author opinion	Review of tools for assessment of a child's pain and the various non-pharmacological techniques that can be used to lower the pain experienced. It is an extensive article reviewing all levels of childhood from neonates to adolescence with recommendations for each level of child maturity.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Pain in children: neglected, unaddressed and mismanaged	Mathews L.	Indian Journal of Palliative Care 2011;175(Suppl) :S70-3		Literature review	Author opinion	Review of guidelines, teaching material and articles; addresses long-term effect on children of mismanaged pain that moves from acute to chronic. Paper discusses that using pain measurement tools is limited in early childhood due to communication and interpretation issues. Paper describes the role of the caregiver in determining whether the child is in pain as they may not display typical pain cues.	While the paper is limited by the authors interpretation of the references that were used, the basic discussion points raised were cognisant with published material in Australian guidelines from the Children's hospitals.
Acute pain management (2020)	The Royal Children's Hospital Melbourne. Victoria	https://www. rch.org.au/ clinicalguide/ guideline_index/ Analgesia_and_ sedation/		Guideline	Grade A	Based on a systematic review of Level 1-IV studies and research papers	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Pain assessment and measurement (2022)	The Royal Children's Hospital Melbourne. Victoria	https://www.rch. org.au/rchcpg/ hospital_clinical_ guideline_ index/Pain_ Assessment_ and_ Measurement/		Guideline	Grade A	Based on Systematic review of Level 1-IV studies and research papers	
Managing paediatric pain in general practice	Yuhico AM, Collins J.	Medicine Today 2014;15(10):26-32		Literature review	Author opinion	Article addresses issues relevant to the ACP Guideline search criteria. Basic discussion of the validated tools that are accessible for assessing pain.	
Febrile child (2022) Information replicated for consumers in <i>Kids Health</i> <i>Information-</i> <i>Fever in Children</i> (Fact Sheet)	The Royal Children's Hospital Melbourne. Clinical Practice Guidelines	https://www. rch.org.au/ clinicalguide/ guideline_index/ Febrile_Child/		Guideline	Grade A	Guideline based on literature review which is regularly reviewed and updated. Focus is the parameters that define fever at all age levels of childhood; it identifies the causes, red flags, management guidelines and when to refer. It discusses underlying causes and the need to recognise the seriously unwell neonate and young infant.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Fever in under 5s: assessment and initial management. 2021	National Institute for Health and Care Excellence (NICE) guideline NG143	https://www.nice.org.uk/ guidance/ng143/chapter/ Recommendations#antipyretic- interventions		Guideline	Grade A	Recommendations for assessment, management, red flags, care at home and referral	
Children's pain and fever management.	Robinson MB	Australian Journal of Pharmacy 2019;Feb:82-7. <u>https://ajp-emag.partica.online/ australian-journal-of-pharmacy/</u> <u>february-2019/flipbook/82/</u>		Literature review	Author opinion	Review of the evidence including a Cochrane review and good quality studies to address the questions posed.	
Fever, fever patterns and disease called 'fever'- a review	Ogoina D	Journal of Infection and Public Health 2011;4(3):108-124		Literature review	Author opinion	Review highlighted the pathophysiology of the febrile response and provided descriptors of fever types and patterns, including their clinical significance. The review also discussed the various medical illnesses described as 'fever'	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Parent's experiences and information needs related to childhood fever: a systematic review	Thompson AP, Nesari M, Hartling L, Scott SD	Patient Education and Counseling 2020;103(4):750-63	15,727 participants	Systematic review	Level III-3 (mainly cross-sectional studies included in the systematic review	Review synthesised the current evidence about experiences and information needs of parents/caregivers managing paediatric fever	
'Yarn with me': applying clinical yarning to improve clinician-patient communication in Aboriginal health care	Lin I, Green C, Bessarab D	Australian Journal of Primary Health 2016;22:377-82		Literature review	Author opinion	Discusses how clinical yarning uses a patient- centred approach to marry aboriginal cultural communication preferences with biomedical understanding of health and disease.	
Pathophysiology and management of fever	Dala S, Zhukovsky D	Journal of Support Oncology 2006;;4(1):9-16		Literature review	Author opinion	Review of the basic pathophysiology of fever, its contributing aetiologies and the management approaches that are based on current evidence.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Recent advances in paediatric use of paracetamol in fever and pain management	De Martino M, Chiarugi A	Pain therapy 2015;4:149- 68		Systematic literature review	Author opinion Grade B	Review article with a systematic literature search (including systematic reviews and meta-analyses). It identified the analgesic and antipyretic doses of paracetamol that are associated with safety and efficacy in children.	
Cochrane in context: Combined and alternating paracetamol and ibuprofen therapy for febrile children.	Wong T, et al	Evidence Based Child Health (2014) (3): 730-2		Systematic review	Level I	Cochrane review of the literature.	
A clinical and safety review of paracetamol and ibuprofen in children	Kanabar DJ.	Inflammaphamacology 2017;25(1):1-9 doi: 10.1007/ s10787-016-0302-3		Literature review	Author opinion	A review of the safety and clinical effectiveness of paracetamol and ibuprofen in the management of inflammation, pain and fever.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Systemic review and meta-analysis of the clinical safety and tolerability of ibuprofen compared with paracetamol in paediatric pain and fever.	Southey ER.	Current Medical Research and Opinion 2009;25(9):2207-22 doi: 10.1185/03007990903116255	2,937 systemic adverse effects reviewed	Systematic review & meta- analysis	Level II and III-1	24 RCTs and 12 other studies examined either ibuprofen and/ or paracetamol versus placebo for adverse effect (AE) data. There was no significant difference between the two groups.	
An assessment of the safety of paediatric ibuprofen	Lesko SM, Mitchell AA.	JAMA 1995;273:929-33	84,192 children	Practitioner based randomised clinical trial	Level II	Randomised double- blind trial in children who received either 12 mg/kg of paracetamol, 5 mg/kg of ibuprofen, or 10 mg/kg of ibuprofen, or 10 mg/kg of ibuprofen. Risk of hospitalisation for gastrointestinal bleeding, renal failure, or anaphylaxis was not increased following short- term use of ibuprofen in children.	No information on the risks of less severe outcomes or the risks of prolonged ibuprofen use were provided.

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Comparison of acetaminophen (paracetamol) with ibuprofen for treatment of fever and pain in children younger than 2 years.	Tan E, Braithwaite I, Mckinlay CJD, Dalziel S.	JAMA Network Open 2020;3(10): e2022398	Number of participants in studies ranged from 40 to 459, with 14 studies of >200 patients.	Systematic review & meta- analysis	Level I (all included studies were placebo- controlled RCTs	Included studies of any design to compare paracetamol with ibuprofen for the short- term treatment of fever or pain in children younger than 2 years.	
Does the use of antipyretics prolong illness? A systematic review of the literature and meta-analysis on the effects of antipyretics in acute upper and lower respiratory tract infections.	Nicolas M, Sun S, Zorzi F, Deplace S, Jaafari N, Boussageon R.	Infectious Diseases Now 2023;53(5):104716. doi: 10.1016/j. idnow.2023.104716	1,466 references	Systematic review & meta- analysis	Level I	Use of antipyretics does not prolong or shorten illness duration in acute upper and lower RTI. Symptomatic efficacy of antipyretics must be weighed against their adverse effects, particularly when fever is well-tolerated.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Children's forgetting of pain- related memories.	Marche TA, Briere JL, von Baeyer CL.	J Pediatr Psychol. 2016 Mar;41(2):220-31.	86 children, 7-15 years old	Descriptive single group study using survey & validated tools	Grade IV or below (there is no comparator group)	Study described confounding factors that contribute to the child's memory of pain and described multiple studies and papers describing techniques to assist a child to reduce their memory of pain. Understanding children's memory of painful experiences may assist pain management and improve their ability to cope with the painful experience. Review of the use of 'Retrieval-Induced Forgetting' by psychologists and the impact this therapy has on children's experience of pain.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Are teething gels safe or even necessary for our children?	Teoh L, Moses GM.	J Paediatrics Child Health. 2020;56(4):502-5. doi:10.1111/ jpc.14769		Literature review	Author opinion	Review of Australian and International evidence of the safety, efficacy and use of topical lidocaine teething gels. It links toxicity issues to use of teething and compounded gels and describes their inappropriate use for relief of mouth and throat pain in children. It recommends use of regular pain relief for painful mouth conditions in children. Also recommends use of cold teething rings as a topical soother and the use of analgesia for self-limiting pain of teething.	An important area for community pharmacists who are regularly requested to supply/ compound these products by medical practitioner recommendation.
Managing Paediatric Pain in general practice	Yuhico AM, Collins J.	Medicine Today 2014; 15(10): 26-32.		Literature review	Author opinion	Article addresses the key search criteria. Discussion of lifestyle and non- pharmacological interventions was extensive.	Some of the question asked in the College guideline review are touched on but the answers were minimal and appeared to be the authors viewpoint.

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Fever in under 5s: assessment and initial management (year).	National Institute for Health and Care Excellence NICE guideline NG143	https://www.nice.org.uk/ guidance/ng143/chapter/ <u>Recommendations</u> #antipyretic-interventions		Guideline	Grade A	Recommendations for assessment, management, red flags, care at home and referral included.	
Pain management strategies for childhood immunisation 2015	RACGP Handbook of Non-drug Interventions (HANDI)	https://www.racgp.org. au/clinical-resources/ clinical-guidelines/handi/ conditions/children/pain- management-strategies- for-childhood-immunisat		Guideline	Grade A NHMRC Level 1 Evidence	Handbook discusses interventions for childhood immunisations (e.g. distraction techniques and the pre-counselling of the caregiver to minimise stress and pain sensation for the child.)	
Kids Health Information-Fever in Children (2021)	Royal Children's Hospital Melbourne	https://www.rch.org.au/ kidsinfo/fact_sheets/fever_ in_children/#:~:text=If%20 your%20baby%20is%20 under%20three%20 months%20old%20 and%20has,doctor%20 or%20hospital%20 emergency%20 department		Caregiver Fact Sheet	Grade A	A fact sheet for caregiver to assist them to manage fever in their child at home.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Pathophysiology and management of fever.	Dala S, Zhukovsky D.	Journal of Support Oncology 2006 ;4(1):9-16.		Literature review	Author opinion	Review of the basic pathophysiology of fever, its contributing aetiologies and the management approaches that are based on current evidence.	

RECOMMENDATION 3: CRITERIA FOR TREATMENT

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Recent advances in paediatric use of paracetamol in fever and pain management.	De Martino M, Chiarugi A.	Pain therapy 2015;4:149-68.		Systematic literature review	Author opinion Grade B	Review article with a systematic literature search (including systematic reviews and meta-analyses). It discussed the proposition that at repetitive doses for consecutive days paracetamol shows lower risk of adverse effects than NSAIDs.	
Febrile child Information replicated for consumers in <i>Kids Health</i> <i>Information-Fever</i> <i>in Children</i> (Fact Sheet).	The Royal Children's Hospital Melbourne. Clinical Practice Guidelines	https://www.rch. org.au/clinicalguide/ guideline_index/ Febrile_Child/		Guideline	Grade A Guideline based on literature review. Regularly reviewed and updated	Guideline on the parameters that defines fever at all age levels of childhood; identified the causes, red flags, management guidelines and when to refer. Discusses underlying causes and the need to recognise the seriously unwell neonate and young infant.	
Fever in under 5s: assessment and initial management. 2021	National Institute for Health and Care Excellence NICE guideline NG143	https://www.nice. org.uk/guidance/ ng143/chapter/ Recommendations #antipyretic- interventions		Guideline	Grade A	Recommendations for assessment, management, red flags, care at home and referral included.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Children's pain and fever management.	Robinson MB.	2 Australian Journal of Pharmacy2019; Feb:82-7. <u>https://ajp-emag.</u> <u>partica.online/</u> <u>australian-journal-</u> <u>of-pharmacy/</u> <u>february-2019/</u> flipbook/82/		Literature review	Author opinion	Paper uses good quality studies including a Cochrane systematic review to address the questions posed.	
Ibuprofen versus paracetamol in paediatric fever: objective and subjective findings from a randomised, blinded study.	Autret-Leca E, Gibb IA, Goulder MA.	Current Medical Research and Opinion 2007;23(9):2205-11 <u>https://doi.</u> <u>org/10.1185/</u> 030079907X223323	304 patients	Double- blind, double- dummy, parallel group, randomised, single-dose trial	Level II	Children from 3 months to 12 years with a fever of non-serious origin were randomised to receive either a single dose of ibuprofen ibuprofen 10mg/kg or paracetamol 15mg/kg. Both drugs showed equivalent efficacy and tolerability in children with fever.	Discussed that previous studies have at times misrepresented the strength of the study findings and doses used in practice. This may be due to differences in dosing guidelines between countries.
Fever, fever patterns and disease called 'fever'- a review.	Ogoina D.	Journal of Infection and Public Health 2011; 4:108-24.		Literature review	Author opinion	Review highlighted the pathophysiology of the febrile response and provided descriptors of fever types and patterns, including their clinical significance. The review also discussed the various medical illnesses described as 'fever'.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Pathophysiology and management of fever.	Dalal S, Zhukovsky D.	Journal of Support Oncology 2006 ;4(1):9-16.		Literature review	Author opinion	Review of the basic pathophysiology of fever, its contributing aetiologies and the management approaches that are based on current evidence.	
Recent advances in paediatric use of paracetamol in fever and pain management.	De Martino M, Chiarugi A.	Pain therapy 2015;4:149- 68.		Systematic literature review	Author opinion Grade B	Review article with a systematic literature search (including systematic reviews and meta-analyses). It identified the analgesic and antipyretic doses of paracetamol that are associated with safety and efficacy in children.	
A clinical and safety review of Paracetamol and Ibuprofen in children.	Kanabar DJ.	Inflammaphamacology 2017;25(1):1-9. doi: 10.1007/ s10787-016-0302-3		Literature review	Author opinion	Review of the safety and clinical effectiveness of paracetamol and ibuprofen in the management of inflammation, pain and fever.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
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An assessment of the safety of paediatric ibuprofen.	Lesko SM, Mitchell AA.	JAMA 1995;273:929- 33.	84,192 children	A practitioner based randomised clinical trial.	Level II	Randomized double- blind trial in children who received either 12 mg/ kg of paracetamol, 5 mg/ kg of ibuprofen, or 10 mg/ kg of ibuprofen. Risk of hospitalisation for gastrointestinal bleeding, renal failure, or anaphylaxis was not increased following short-term use of ibuprofen in children.	No information on the risks of less severe outcomes or the risks of prolonged ibuprofen use were provided.
Comparison of acetaminophen (paracetamol) with ibuprofen for treatment of fever and pain in children younger than 2 years.	Tan E, Braithwaite I, Mckinlay CJD, Dalziel S.	JAMA Network Open 2020;3(10): e2022398	Participants ranged from 40 to 459, with 14 studies of >200 patients.	Systematic review & meta- analysis	Level I (all included studies were placebo- controlled RCTs)	Included studies of any design to compare paracetamol with ibuprofen for the short-term treatment of fever or pain in children younger than 2 years.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Does the use of antipyretics prolong illness? A systematic review of the literature and meta-analysis on the effects of antipyretics in acute upper and lower respiratory tract infections.	Nicolas M, Sun S, Zorzi F, Deplace S, Jaafari N, Boussageon R	Infectious Diseases Now 2023;53(5)::104716. doi:	1,466 references	Systematic review & meta- analysis	Level I	Use of antipyretics does not prolong or shorten illness duration in acute upper and lower RTI. Symptomatic efficacy of antipyretics must be weighed against their adverse effects, particularly when fever is well-tolerated.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Are teething gels safe or even necessary for our children? A review of the safety, efficacy and use of topical lidocaine teething gels.	Teoh L, Moses GM.	J Paediatrics and Child Health 2020;56(4):502-5. doi:10.1111/jpc.14769		Literature review	Author opinion	Review of Australian and International evidence of the safety, efficacy and use of topical lidocaine teething gels. It links toxicity issues to use of teething and compounded gels and describes their inappropriate use for relief of mouth and throat pain in children. It recommends use of regular pain relief for painful mouth conditions in children. Also recommends use of cold teething rings as a topical soother and the use of analgesia for self-limiting pain of teething.	An important area for community pharmacists who are regularly requested to supply/ compound these products by medical practitioner recommendation.
Managing paediatric pain in general practice	Yuhico AM, Collins J.	Medicine Today 2014;15(10): 26-32.		Literature review	Author opinion	Article addresses the key search criteria. It discusses that where inflammation is the primary cause of pain, ibuprofen is the better agent and addresses that ibuprofen not approved for children under three months of age.	Some of the question asked in the College guideline review were touched on but the answers were minimal and appeared to be the authors viewpoint.

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Advances in paediatric use of oral paracetamol in fever and pain management therapy.	De Martino M, Chiarugi A.	Pain Therapy 2015;4(2):149-68.		Systematic literature review	Author opinion Grade B	Review article with a systematic literature search (including systematic reviews and meta- analyses). It discussed the proposition that at repetitive doses for consecutive days paracetamol shows lower risk of adverse effects than NSAIDs. It also discussed the different mechanisms of action of paracetamol and NSAIDs in pain and fever pathways.	
Analgesic efficacy of rectal acetaminophen and ibuprofen alone or in combination for paediatric day-case adenoidectomy	Viitanen H, Tuominen N, Vääräniemi H, Nikanne E, Annila P.	British Journal of Anaesthesia 2003 ;91(3):363-7.	159 children (1-6 years) with 4 groups: paracetamol (n = 40), ibuprofen (n = 41), combination (n = 40), placebo (n =38)	Randomised controlled trial	Level II	Compared either paracetamol 40 mg/kg, ibuprofen 15 mg/kg, their combination, or placebo rectally. Prophylactically administered rectal paracetamol combined with ibuprofen does not improve analgesia after adenoidectomy in the immediate post-operative period compared with either drug alone but does decrease the need for analgesia at home. Study demonstrated a small improvement in pain scores post discharge when used in combination. Ibuprofen caused less sedation in children post discharge.	Used rectal formulations.

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Children's pain and fever management.	Robinson MB.	Australian Journal of Pharmacy 2019; Feb:82-7. <u>https://ajp-emag.partica.</u> <u>online/australian-journal-</u> <u>of-pharmacy/february-2019/</u> <u>flipbook/82/</u>		Literature review	Author opinion	Paper uses good quality studies including a Cochrane systematic review to address the questions posed. It discussed RCH Melbourne guidelines (i.e. there is no evidence of detriment of companion or alternating dosage but there is a danger of overdosage if records of dosing are not undertaken).	
Ibuprofen versus paracetamol in paediatric fever: objective and subjective findings from a randomised, blinded study.	Autret-Leca E, Gibb IA, Goulder MA.	Current Medical Research and Opinion 2007;23(9):2205-11 <u>https://doi.org/10.1185/</u> <u>030079907X223323</u>	304 patients	Double- blind, double- dummy, parallel group, randomised, single-dose trial.	Level II	Children from 3 months to 12 years with a fever of non-serious origin were randomised to receive either a single dose of ibuprofen 10mg/kg or paracetamol 15mg/kg. Both drugs showed equivalent efficacy and tolerability in children with fever.	It discussed that previous studies have at times misrepresented the strength of the study findings and the strength of the doses used in practice. This may be due to differences in dosing guidelines between countries.

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Fever, fever patterns and disease called 'fever'- a review	Ogoina D.	Journal of Infection and Public Health 2011;4: 108- 24.		Literature review	Author opinion	Review highlighted the pathophysiology of the febrile response and provided descriptors of fever types and patterns, including their clinical significance. The review also discussed the various medical illnesses described as 'fever'.	
Pathophysiology and management of fever.	Dala S, Zhukovsky D	Journal of Support Oncology 2006;4(1):9-16.		Literature review	Author opinion	Review of the basic pathophysiology of fever, its contributing aetiologies and the management approaches that are based on current evidence.	
Recent Advances in Paediatric Use of Paracetamol in fever and pain management.	De Martino M, Chiarugi A	Pain therapy 2015 4:149- 68.		Systematic literature review	Author opinion Grade B	The article reviewed the current literature and identified the analgesic and antipyretic doses of paracetamol that guarantee safety and efficacy in children.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Cochrane in context: Combined and alternating paracetamol and ibuprofen therapy for febrile children.	Wong T, et al	Evidence Based Child Health (2014) (3): 730-2		Systematic review	Level I	Cochrane review of the literature.	
Prescribing Controversies: An Updated Review and Meta-Analysis on Combined/ Alternating Use of Ibuprofen and Paracetamol in Febrile Children	Trippella G, Ciarcia M, de Martino M, Chiappini E.	Frontiers in Pediatrics 2019;7(217):1-14	9 studies involving 2,026 children	Systematic review	Level I	Studies evaluated the efficacy and safety of combined or alternating use of ibuprofen and paracetamol in children. Combined or alternating therapy was more effective than monotherapy in reducing body temperature. However, the benefit appeared modest and probably not clinically relevant. The effect on child discomfort and number of doses of medication was also modest.	Evidence not robust enough to encourage combined or alternating paracetamol and ibuprofen instead of monotherapy to treat febrile children, reinforcing the current recommendation of most of the international guidelines.
A clinical and safety review of Paracetamol and Ibuprofen in children.	Kanabar DJ.	Inflammaphamacology 2017;25(1):1-9 doi: 10.1007/s10787-016- 0302-3		Literature review	Author opinion	A review of the safety and clinical effectiveness of paracetamol and ibuprofen in the management of inflammation, pain and fever.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Systemic review and meta-analysis of the clinical safety and tolerability of ibuprofen compared with paracetamol in paediatric pain and fever.	Southey ER	Current Medical Research and Opinion 2009;25(9):2207-22 doi: 10.1185/03007990903116255	2,937 systemic adverse effects reviewed	Systematic review & meta- analysis	Level II and III-1	24 RCTs and 12 other studies examined either ibuprofen and/ or paracetamol versus placebo for adverse effect (AE) data. There was no significant difference between the two groups.	
An assessment of the safety of paediatric ibuprofen.	Lesko SM, Mitchell AA	JAMA 1995;273:929-33	84,192 children	A practitioner based randomised clinical trial.	Level II	Randomised double- blind trial in children who received either 12 mg/kg of paracetamol, 5 mg/kg of ibuprofen, or 10 mg/kg of ibuprofen. Risk of hospitalisation for gastrointestinal bleeding, renal failure, or anaphylaxis was not increased following short-term use of ibuprofen in children.	No information on the risks of less severe outcomes or the risks of prolonged ibuprofen use were provided.
Comparison of acetaminophen (paracetamol) with Ibuprofen for treatment of fever and pain in children younger than 2 years.	Tan E, et al	JAMA Network Open 2020;3(10):e2022398	Number of participants in studies ranged from 40 to 459, with 14 studies of >200 patients.	Systematic review & meta- analysis.	Level I (all included studies were placebo- controlled RCTs	Included studies of any design to compare paracetamol with ibuprofen for the short- term treatment of fever or pain in children younger than 2 years.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Does the use of antipyretics prolong illness? A systematic review of the literature and meta-analysis on the effects of antipyretics in acute upper and lower respiratory tract infections.	Nicolas M, Sun S, Zorzi F, Deplace S, Jaafari N, Boussageon R	Infectious Diseases Now 2023;53(5):104716. doi: 10.1016/j. idnow.2023.104716	1,466 references	Systematic review & meta- analysis	Level I	Use of antipyretics does not prolong or shorten illness duration in acute upper and lower RTI. Symptomatic efficacy of antipyretics must be weighed against their adverse effects, particularly when fever is well-tolerated.	

RECOMMENDATION 5: COUNSELLING

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Advances in paediatric use of oral paracetamol in fever and pain management therapy.	De Martino M, Chiarugi A.	Pain Ther 2015; 4(2):149- 68		Systematic literature review	Author opinion Grade B	Review article with a systematic literature search (including systematic reviews and meta- analyses). It discussed the proposition that at repetitive doses for consecutive days paracetamol shows lower risk of adverse effects than NSAIDs. It discussed the proposition that at repetitive doses for consecutive days paracetamol shows lower risk of adverse effects than NSAIDs.	
Children's pain and fever management.	Robinson MB.	Australian Journal of Pharmacy 2019; Feb: <u>https://ajp-emag.partica.</u> <u>online/australian-</u> <u>journal-of-pharmacy/</u> <u>february-2019/</u> <u>flipbook/82/</u>		Literature review	Author opinion	Review of the evidence including a Cochrane review and good quality studies to address the questions posed. It discussed that pharmacy intervention is for short term management and the need for reassessment and referral protocols should be included in counselling.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Ibuprofen versus paracetamol in paediatric fever: objective and subjective findings from a randomised, blinded study.	Autret-Leca E, Gibb IA, Goulder MA.	Current Medical Research and Opinion 2007;23(9):2205-11 <u>https://doi. org/10.1185/030079907X223323</u>	304 patients	Double- blind, double- dummy, parallel group, randomised, single-dose trial.	Level II	Children from 3 months to 12 years with a fever of non- serious origin were randomised to receive either a single dose of ibuprofen 10mg/kg or paracetamol 15mg/kg. Both drugs showed equivalent efficacy and tolerability in children with fever.	It discussed that previous studies have, at times, misrepresented the strength of the study findings and the strength of the doses used in practice. This may be due to differences in dosing guidelines between countries. It discussed that parents state they prefer ibuprofen over paracetamol based on the dosing schedule being less frequent.
Pain Management -CWH (2021) No: 2006-8215 v17	The Children's Hospital at Westmead	https://www.schn.health.nsw. gov.au/_policies/pdf/2006-8215. pdf		Practice Guideline	Grade B	Comprehensive document of pain management in and children, primarily designed for use in a hospital setting.	Many interventions listed are beyond community pharmacy, but areas of assessment, management and early intervention are relevant. No references to support statements provided.

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Moderate, acute nociceptive pain.	In Analgesic Guidelines, eTG- Therapeutic Guidelines	Last updated Dec 2020		Guideline	Grade B	Guideline for the management of acute pain in children.	
Fever, fever patterns and disease called 'fever'- a review.	Ogoina D.	Journal of Infection and Public Health 2011;4:108- 24.		Literature review	Author opinion	Review highlighted the pathophysiology of the febrile response and provided descriptors of fever types and patterns, including their clinical significance. It also discussed the various medical illnesses described as 'fever'.	
Parent's experiences and information needs related to childhood fever: a Systematic review	Thompson AP, Nesari M, Hartling L, Scott SD	Patient Education and Counseling 2020;103:750-63.	15,727 participants	Systematic review	Level III-3 (mainly cross-sectional studies included in the systematic review.	Review synthesised the current evidence about experiences and information needs of parents/caregivers managing paediatric fever.	
'Yarn with me': applying clinical yarning to improve clinician-patient communication in Aboriginal health care.	Lin I, et al.	Australian Journal of Primary Health 2016,22,377-382		Literature review	Author opinion	Discusses how clinical yarning uses a patient- centred approach to marry aboriginal cultural communication preferences with biomedical understanding of health and disease.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Pathophysiology and management of fever.	Dala S, Zhukovsky D.	Journal of Support Oncology 2006;4(1):9-16		Literature review	Author opinion	Review of the basic pathophysiology of fever, its contributing aetiologies and the management approaches that are based on current evidence.	
A clinical and safety review of Paracetamol and Ibuprofen in children	Kanabar DJ	Inflammaphamacology 2017;25(1):1-9 doi: 10.1007/ s10787-016-0302-3		Literature review	Author opinion	A review of the safety and clinical effectiveness of paracetamol and ibuprofen in the management of inflammation, pain and fever.	
Systemic review and meta-analysis of the clinical safety and tolerability of ibuprofen compared with paracetamol in paediatric pain and fever.	Southey ER	Current Medical Research and Opinion 2009;25(9):2207-22. doi: 10.1185/03007990903116255	2,937 systemic adverse effects reviewed	Systematic review & meta- analysis	Level II and III-1 (both RCTs and other designs included)	24 RCTs and 12 other studies examined either ibuprofen and/ or paracetamol versus placebo for adverse effect (AE) data. There was no significant difference between the two groups.	

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
An assessment of the safety of paediatric ibuprofen	Lesko SM, Mitchell AA	JAMA 1995;273:929-33.	84,192 children	A practitioner based randomised clinical trial	Level II	Randomised double- blind trial in children who received either 12 mg/kg of paracetamol, 5 mg/kg of ibuprofen, or 10 mg/kg of ibuprofen. Risk of hospitalisation for gastrointestinal bleeding, renal failure, or anaphylaxis was not increased following short-term use of ibuprofen in children.	No information on the risks of less severe outcomes or the risks of prolonged ibuprofen use were provided.
Comparison of acetaminophen (paracetamol) with ibuprofen for treatment of fever and pain in children younger than 2 years	Tan E, Braithwaite I, Mckinlay CJD, Dalziel S.	JAMA Network Open 2020;3(10):e2022398	Number of participants in studies ranged from 40 to 459, with 14 studies of >200 patients.	Systematic review & meta- analysis	Level I (all included studies were placebo- controlled RCTs)	Included studies of any design to compare paracetamol with ibuprofen for the short- term treatment of fever or pain in children younger than 2 years.	
Does the use of antipyretics prolong illness? A systematic review of the literature and meta-analysis on the effects of antipyretics in acute upper and lower respiratory tract infections	Nicolas M, Sun S, Zorzi F, Deplace S, Jaafari N.	Infectious Diseases Now 2023; 2;104716. doi: 10.1016/j. idnow.2023.104716	1,466 references	Systematic review & meta- analysis	Level 1	Use of antipyretics does not prolong or shorten illness duration in acute upper and lower RTI. Symptomatic efficacy of antipyretics must be weighed against their adverse effects, particularly when fever is well- tolerated.	

RECOMMENDATION 6: WHEN TO REFER

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Managing Paediatric Pain in general practice.	Yuhico AM, Collins J	Medicine Today 2014; 15(10): 26-32		Literature review	Author opinion	Article addresses the key search criteria. It discussed that where inflammation is the primary cause of pain, that ibuprofen is the better agent and addressed that ibuprofen not approved for children under three months of age.	Some of the question asked in the College guideline review were touched on but the answers were minimal and appeared to be the authors viewpoint.
Children's pain and fever management.	Robinson MB.	Australian Journal of Pharmacy 2019; Feb:82-7. https://ajp-emag.partica. online/australian-journal- of-pharmacy/february-2019/ flipbook/82/		Literature review	Author opinion	Literature review uses quality studies to address the questions posed. It discussed the fact that pharmacy provides short term options and that there is a need for counselling to include how to assess the management of pain and whether to consider dosing or to seek further medical care. Counselling is needed to ensure the caregiver understands when to take the child for further medical advice.	

RECOMMENDATION 6: WHEN TO REFER - CONTINUED

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Fever, fever patterns and disease called 'fever'- a review.	Ogoina D.	Journal of Infection and Public Health 2011;4:108- 24.		Literature review	Author opinion	The review highlighted the pathophysiology of the febrile response and provided descriptors of fever types and patterns, including their clinical significance. The review also discussed the various medical illnesses described as 'fever'.	
Parent's experiences and information needs related to childhood fever: a Systematic review	Thompson AP, Nesari M, Hartling L, Scott SD.	Patient Education and Counseling 2020;103(4):750-63.	1, 727 participants	Systematic review	Level III-3 (mainly cross-sectional studies included in the systematic review.	Review synthesised the current evidence about experiences and information needs of parents/caregivers managing paediatric fever.	

RECOMMENDATION 6: WHEN TO REFER - CONTINUED

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
Pathophysiology and management of fever.	Dala S, Zhukovsky D.	Journal of Support Oncology 2006;;4(1):9-16		Literature review	Author opinion	Review of the basic pathophysiology of fever, its contributing aetiologies and the management approaches that are based on current evidence.	
A clinical and safety review of Paracetamol and Ibuprofen in children.	Kanabar DJ.	Inflammaphamacology 2017;25(1):1-9 doi: 10.1007/ s10787-016-0302-3		Literature review	Author opinion	A review of the safety and clinical effectiveness of paracetamol and ibuprofen in the management of inflammation, pain and fever.	
Systemic review and meta-analysis of the clinical safety and tolerability of ibuprofen compared with paracetamol in paediatric pain and fever.	Southey ER	Current Medical Research and Opinion 2009;25(9):2207-22. doi: 10.1185/03007990903116255	2,937 systemic adverse effects reviewed.	Systematic review & meta- analysis.	Level II and III-1	24 RCTs and 12 other studies examined either ibuprofen and/ or paracetamol versus placebo for adverse effect (AE) data. There was no significant difference between the two groups.	

RECOMMENDATION 6: WHEN TO REFER - CONTINUED

TITLE	AUTHOR/S	PUBLICATION	N=	DESIGN	EVIDENCE HIERARCHY LEVEL &/OR GRADE OF RECOMMENDATION	OUTCOMES	LIMITATIONS
An assessment of the safety of paediatric ibuprofen.	Lesko SM, Mitchell AA.	JAMA 1995;273:929-33	84,192 children	A practitioner based randomised clinical trial.	Level II	Randomised double- blind trial in children who received either 12 mg/kg of paracetamol, 5 mg/kg of ibuprofen, or 10 mg/kg of ibuprofen. Risk of hospitalisation for gastrointestinal bleeding, renal failure, or anaphylaxis was not increased following short- term use of ibuprofen in children.	No information on the risks of less severe outcomes or the risks of prolonged ibuprofen use were provided.
Comparison of acetaminophen (paracetamol) with ibuprofen for treatment of fever and pain in children younger than 2 years.	Tan E, Braithwaite I, Mckinlay CJD, Dalziel S.	JAMA Network Open 2020;3(10):e2022398	Number of participants in studies ranged from 40 to 459, with 14 studies of >200 patients.	Systematic review & meta- analysis	Level I (all included studies were placebo- controlled RCTs).		

Appendix 3

INFORMATION GATHERING TOOLS USED IN COMMUNITY PHARMACY⁽⁴⁰⁾

The assessment of pain and/or fever in children can be integrated into the current tools used in community pharmacy



CARER protocol for providing Pharmacy Medicines and Pharmacist Only Medicines

Your pharmacy's protocols should indicate when the pharmacy assistant must refer to the pharmacist.



This resource was produced as part of The Quality Use of Pharmacy Medicines and Pharmacist Only Medicines Initiative by The Pharmacy Guild of Australia and the Pharmaceutical Society of Australia.

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What-Stop-Go protocol for providing Pharmacy Medicines and Pharmacist Only Medicines



This resource was produced as part of The Quality Use of Pharmacy Medicines and Pharmacist Only Medicines Initiative by The Pharmacy Guild of Australia and the Pharmaceutical Society of Australia.

This protocol was adapted from those originally developed by Prof. Charlie Benrimoj (University of Sydney) and Assoc. Prof. Andy Gilbert (University of South Australia) which were published in the Standards for the Provision of Pharmacist Only and Pharmacy Medicines



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