ISSN: 2181-3337 | SCIENTISTS.UZ VOLUME 5 ISSUE 8 AUGUST 2026

RATIONAL USE OF ANTIPYRETICS (PARACETAMOL AND IBUPROFEN) IN THE MANAGEMENT OF FEVER IN CHILDREN: AN EVIDENCE-BASED NARRATIVE REVIEW

Abdubannobova Dilnavoz
Faculty of Pediatrics, Andijan State Medical Institute, Andijan, Uzbekistan
Email: dilnavozabdubannopova72@gmail.com

DOI: 10.67620/sai.58d0009

ABSTRACT

Fever is among the most frequent reasons for pediatric consultation and a persistent source of caregiver anxiety. Paracetamol (acetaminophen) and ibuprofen are widely used antipyretic agents, yet rational use requires a distinction between lowering temperature and improving clinically meaningful outcomes. This narrative evidence review critically evaluates comparative efficacy, safety, combined or alternating therapy, and caregiver-related determinants of medication use. Current meta-analytic evidence indicates that ibuprofen may produce a slightly greater and longer reduction in temperature than paracetamol in some age groups; however, this pharmacodynamic advantage does not establish universal clinical superiority because evidence for improved comfort and functional outcomes is less consistent. Both agents are generally safe at recommended doses in otherwise healthy children, although ibuprofen warrants particular caution in dehydration, renal impairment, and selected infectious contexts, whereas paracetamol toxicity is strongly associated with supratherapeutic or duplicated dosing. Guidelines consistently recommend treating distress rather than the numerical temperature and do not support antipyretics for prevention of febrile seizures. Combined or alternating regimens can improve short-term defervescence but increase regimen complexity and the potential for dosing errors; therefore, routine dual-agent use is difficult to justify. The central argument of this review is that rational antipyretic therapy should be symptom-centered, individualized, and safety-oriented, with weight-based dosing and caregiver education treated as core therapeutic interventions rather than secondary advice.

ACCEPTED

08.09.26

Keywords: *fever, children, paracetamol, acetaminophen, ibuprofen, antipyretics, rational pharmacotherapy, fever phobia.*

CC BY

Introduction

Fever is one of the most common clinical presentations in childhood and accounts for a substantial proportion of pediatric office and emergency contacts. Contemporary guidance emphasizes that fever is a regulated host response rather than a disease in itself, and its height alone is usually a poor proxy for illness severity outside specific high-risk age groups (National Institute for Health and Care Excellence [NICE], 2021; Niehues et al., 2026). Nevertheless, caregivers frequently interpret fever as intrinsically dangerous and may attempt to normalize temperature rapidly, a pattern historically described as “fever phobia.” Systematic reviews show that misconceptions, anxiety, and inconsistent fever-management practices

remain common across settings and have changed less than expected despite decades of educational activity (Bertille et al., 2018; Purssell & Collin, 2016; Thompson et al., 2020).

Paracetamol and ibuprofen are the two principal antipyretics used in children. The clinically important question, however, is not simply which drug lowers temperature more effectively. A rational pharmacotherapeutic decision must integrate patient comfort, hydration, age, comorbidity, risk of toxicity, regimen simplicity, and caregiver capacity to administer medicines accurately. This review therefore advances the argument that the appropriate endpoint of antipyretic treatment is relief of distress and preservation of safety, not normalization of the thermometer reading. On this basis, a small statistical advantage in temperature reduction should not be interpreted automatically as evidence of superior pediatric care (Sullivan & Farrar, 2011; Tan et al., 2020).

Methods

A focused narrative evidence review was undertaken using PubMed-indexed literature and official guideline repositories. Priority was given to contemporary clinical guidelines, systematic reviews and meta-analyses, randomized controlled trials, pediatric safety studies, and systematic evidence on caregiver knowledge and behavior. Search concepts included childhood fever, paracetamol or acetaminophen, ibuprofen, antipyretics, alternating therapy, combined therapy, febrile seizures, fever phobia, dosing error, and caregiver education. The evidence base was synthesized thematically rather than statistically. Because this was not a preregistered systematic review and did not use duplicate screening or a formal risk-of-bias framework, its conclusions should be interpreted as a critical narrative synthesis rather than as a new systematic review.

Fever as a Therapeutic Target: Distress Rather Than Temperature

The most consistent principle across major guidance is that antipyretic treatment should be considered when a child is distressed, not simply because a measured temperature exceeds a particular threshold. NICE (2021) advises against using antipyretic agents solely to reduce body temperature, while the American Academy of Pediatrics similarly frames the therapeutic objective as improvement of comfort and well-being rather than restoration of normothermia (Sullivan & Farrar, 2011). The 2026 evidence-based outpatient guideline by Niehues et al. (2026) further reinforces this symptom-oriented approach and explicitly discourages routine antipyretic administration in children whose degree of suffering does not warrant drug treatment.

This distinction is academically important because temperature is a surrogate endpoint. A treatment can produce faster defervescence without necessarily improving hydration, activity, sleep, pain, caregiver reassurance, or the underlying illness. Accordingly, comparative trials should be interpreted according to the hierarchy of outcomes: patient-centered benefit and safety carry greater clinical weight than small differences in degrees Celsius. The same reasoning explains why antipyretics should not be used to prevent febrile seizures; multiple guidelines conclude that temperature-lowering treatment does not reliably prevent recurrence of febrile convulsions (Chiappini et al., 2017; NICE, 2021; Sullivan & Farrar, 2011).

Comparative Efficacy of Paracetamol and Ibuprofen

Both paracetamol and ibuprofen reduce fever effectively. Earlier randomized-trial meta-analysis found that ibuprofen produced greater temperature reduction than acetaminophen at several early time points, with broadly comparable safety in the included trials (Perrott et al., 2004). More recent evidence is directionally similar. In a systematic review and meta-analysis of 19 studies including 241,138 children younger than 2 years, ibuprofen was associated with lower temperature at less than 4 hours and between 4 and 24 hours, and with less pain at 4-24 hours, while adverse events were uncommon (Tan et al., 2020).

These findings support the conclusion that ibuprofen may have a modest antipyretic advantage under some conditions, but they do not establish a universal first-line hierarchy. The size of the temperature difference is generally small, and the evidence base is stronger for temperature outcomes than for child comfort. Therefore, the clinically defensible interpretation is that either medicine can be appropriate in an

ISSN: 2181-3337 | SCIENTISTS.UZ

otherwise healthy child, with drug selection individualized to the clinical context rather than driven by a presumption that the agent producing the lowest temperature is necessarily superior (Sullivan & Farrar, 2011; Tan et al., 2020).

Safety and Patient-Specific Risk

At recommended pediatric doses, paracetamol and ibuprofen have broadly comparable short-term safety profiles in generally healthy children. A systematic review of pediatric pain and fever studies found no compelling evidence of a major overall safety difference, although the type of potential harm differs between the two drugs (Southey et al., 2009). Paracetamol has a narrow margin for error when repeated supratherapeutic dosing or unintentional duplication occurs, particularly when caregivers use multiple products containing acetaminophen. Its rational use therefore depends on accurate dose calculation, dosing intervals, and avoidance of ingredient duplication (Sullivan & Farrar, 2011).

Ibuprofen is an NSAID and requires more explicit attention to renal perfusion and hydration. NSAID exposure has been identified as an important cause of acute kidney injury in children, especially in settings in which intravascular volume is reduced (Misurac et al., 2013). Evidence in young infants suggests that short-term ibuprofen can be safe under selected conditions, but age, body weight, and hydration status remain important determinants of appropriate use (Ziesenitz et al., 2017). Guideline panels also advise caution or avoidance in dehydration and in certain infections such as varicella because potential harms may outweigh a modest antipyretic benefit (Chiappini et al., 2017).

Consequently, it is overly simplistic to characterize either agent as universally “safer.” Paracetamol may be preferable when renal perfusion or gastrointestinal risk is a concern, whereas ibuprofen may be reasonable when a longer antipyretic effect is desirable in a well-hydrated child without contraindications. The rational choice is therefore conditional rather than absolute.

Combined and Alternating Therapy: Efficacy Versus Implementation Risk

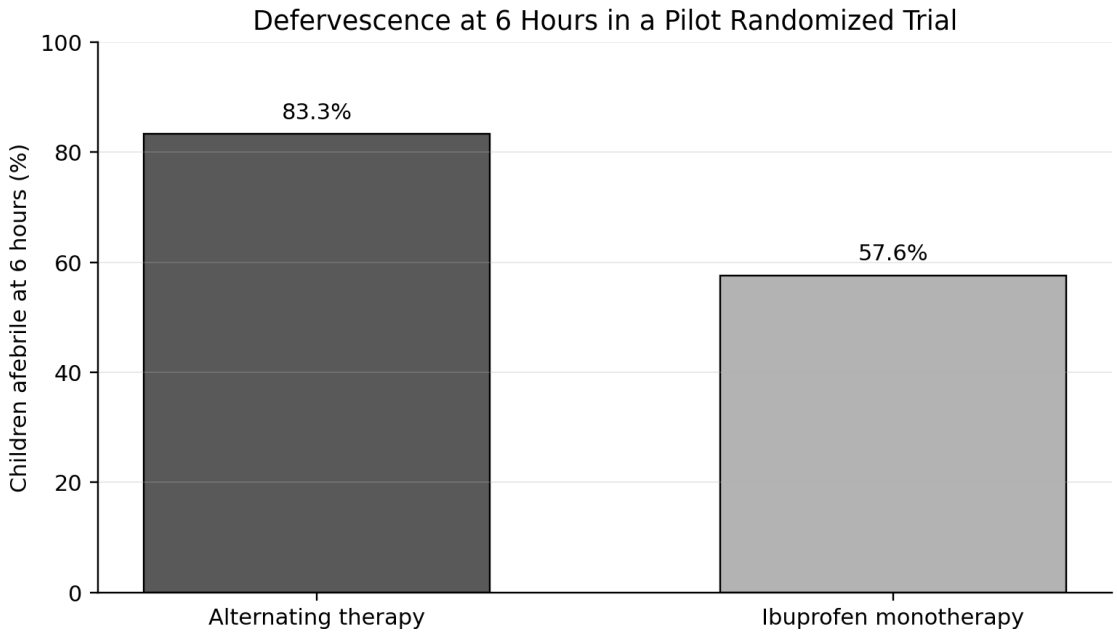
Combined or alternating regimens illustrate the difference between pharmacologic efficacy and rational clinical practice. In the PITCH randomized controlled trial, using paracetamol and ibuprofen together increased time without fever compared with either drug alone in young children managed in the community, although the relationship between additional temperature reduction and sustained improvement in discomfort was less straightforward (Hay et al., 2008). A Cochrane review similarly concluded that combined or alternating therapy can reduce temperature more effectively than monotherapy, but evidence for improved child discomfort was inconclusive and safety evidence was insufficient for confident routine recommendations (Wong et al., 2013).

A pilot randomized study by Nabulsi et al. (2006) provides a useful example of this tension. At 6 hours, 83.3% of children who received alternating ibuprofen and paracetamol were afebrile compared with 57.6% receiving ibuprofen monotherapy. Figure 1 visualizes this statistically significant difference. However, the study enrolled only 70 children, the outcome was defervescence rather than a validated patient-centered measure, and a more complicated schedule may create additional opportunities for dose duplication or interval errors. Therefore, the result supports biological efficacy but does not, by itself, justify routine alternating therapy.

ISSN: 2181-3337 | SCIENTISTS.UZ

Figure 1

Defervescence at 6 Hours in a Pilot Randomized Trial of Alternating Therapy Versus Ibuprofen Monotherapy



Note. Data are from Nabulsi et al. (2006), n = 70. The figure illustrates a surrogate antipyretic outcome and should not be interpreted as evidence that alternating therapy provides superior patient-centered benefit or should be used routinely.

This interpretation is consistent with guideline logic. NICE (2021) advises against simultaneous administration and recommends considering alternation only when distress persists or recurs before the next dose is due. The central safety argument is that a modest incremental reduction in temperature may not compensate for the cognitive burden of maintaining two dosing schedules, particularly in anxious caregivers or households using multiple formulations. Regimen simplicity is therefore a clinically relevant component of medication safety.

Caregiver Behavior, Fever Phobia, and Medication Safety

Fever management occurs largely outside clinical settings, so caregiver behavior is part of the pharmacology of real-world treatment. Systematic evidence demonstrates persistent uncertainty about fever thresholds, variable use of temperature measurement, and frequent reliance on antipyretics even when fever-associated distress is limited (Bertille et al., 2018). A systematic review of 36 studies involving 15,727 participants found that caregivers commonly seek information about pediatric fever while simultaneously reporting misconceptions, anxiety, and heterogeneous management practices (Thompson et al., 2020). Fever phobia has also remained remarkably persistent across time and geography (Purssell & Collin, 2016).

These findings strengthen the argument that caregiver education is not an optional adjunct to prescribing; it is a risk-reduction intervention. A prescription or over-the-counter recommendation that does not communicate the treatment goal, weight-based dose, dosing interval, product concentration, and conditions requiring medical review is incomplete from a rational-pharmacotherapy perspective. Education should explicitly explain that the child's behavior, hydration, breathing, level of responsiveness, and other warning signs are more clinically informative than achieving a "normal" temperature. It should also discourage waking a comfortable sleeping child solely to administer an antipyretic and should emphasize safe storage and avoidance of duplicate acetaminophen-containing products (Sullivan & Farrar, 2011).

Practical Framework for Rational Pharmacotherapy

A rational approach can be organized around four decisions. First, determine whether medication is indicated: the presence of distress or pain, rather than fever alone, should drive treatment. Second, select

ISSN: 2181-3337 | SCIENTISTS.UZ

a single agent according to the child's age, body weight, hydration, renal status, gastrointestinal considerations, prior tolerance, and local labeling. Third, calculate the dose by weight and use an appropriate measuring device. Common guidance supports paracetamol doses of approximately 10-15 mg/kg per dose and ibuprofen doses of approximately 5-10 mg/kg per dose, but maximum daily doses, minimum ages, and dosing intervals vary by jurisdiction and product; local pediatric guidance and product labeling should therefore be followed (Niehues et al., 2026; Sullivan & Farrar, 2011; Ziesenitz et al., 2017). Fourth, reassess the child rather than the thermometer: failure to reach normothermia is not, by itself, treatment failure if distress improves.

Routine simultaneous dual therapy should be avoided. Alternation should be exceptional rather than automatic and should be considered only when clinically meaningful distress recurs before the next dose of the initial agent is due and the caregiver can follow a clear written schedule (NICE, 2021). Nonpharmacologic management should emphasize fluids and avoidance of over-wrapping; routine tepid sponging is not recommended in major guidelines because it can increase discomfort without addressing the therapeutic goal (NICE, 2021).

Academic Synthesis and Argument

The evidence supports a hierarchy of reasoning for pediatric fever management. At the lowest level, temperature reduction is easy to measure and often favors ibuprofen or dual-agent regimens. At a higher clinical level, however, comfort, safety, caregiver comprehension, and recognition of serious illness are more consequential. This creates an important evidence-to-practice gap: interventions can appear "more effective" when efficacy is defined by temperature while being less attractive when effectiveness is defined by patient-centered benefit under real-world conditions. The rational response is not to dismiss comparative antipyretic efficacy, but to place it in its proper clinical context.

Accordingly, this review rejects two oversimplified positions: that paracetamol should always be the first-line drug, and that ibuprofen should be preferred simply because it may lower temperature more strongly. Instead, current evidence supports conditional equivalence: both agents are legitimate options when distress warrants treatment, and the preferred drug is the one that provides adequate symptom relief with the lowest foreseeable risk in the individual child. Similarly, evidence that alternating therapy lowers temperature more effectively does not justify its routine use because the added complexity can undermine medication safety. This interpretation aligns comparative trials with guideline recommendations rather than treating them as competing bodies of evidence (Hay et al., 2008; NICE, 2021; Tan et al., 2020; Wong et al., 2013).

Limitations of the Evidence

Several limitations should temper interpretation. First, many trials prioritize temperature endpoints over validated measures of comfort, activity, hydration, or caregiver-relevant outcomes. Second, the strongest comparative evidence is heterogeneous with respect to age, dose, indication, and follow-up duration. Third, rare adverse events are difficult to quantify in randomized trials and often depend on observational data. Fourth, recommendations on minimum age and maximum dosing vary across jurisdictions and formulations. Finally, this paper is a narrative synthesis rather than a systematic review, so it does not provide a new pooled estimate or formal certainty-of-evidence rating. These limitations reinforce the need for cautious translation of statistical efficacy into clinical recommendations.

Conclusion

The rational management of fever in children is best understood as a symptom-centered and safety-oriented process rather than a pharmacologic attempt to normalize body temperature. Paracetamol and ibuprofen are both effective antipyretics, and ibuprofen may provide somewhat greater or longer temperature reduction in some populations. Yet this difference is not sufficient to establish universal clinical superiority. Drug selection should be individualized, with particular attention to hydration, renal risk, age, comorbidity, previous tolerance, and the possibility of dosing error. Antipyretics should not be

ISSN: 2181-3337 | SCIENTISTS.UZ

used to prevent febrile seizures, and routine simultaneous or alternating dual-agent treatment is not supported by the balance of evidence and implementation risk. The strongest academic and practical conclusion is therefore that correct indication, weight-based dosing, regimen simplicity, and caregiver education are not ancillary aspects of fever management; they are the core components of rational pediatric pharmacotherapy.

REFERENCES

1. Bertille, N., Purssell, E., Hjelm, N., Bilenko, N., Chiappini, E., de Bont, E. G. P. M., Kramer, M. S., Lepage, P., Lava, S. A. G., Mintegi, S., Sullivan, J. E., Walsh, A., Cohen, J. F., & Chalumeau, M. (2018). Symptomatic management of febrile illnesses in children: A systematic review and meta-analysis of parents' knowledge and behaviors and their evolution over time. *Frontiers in Pediatrics, 6*, 279. https://doi.org/10.3389/fped.2018.00279
2. Chiappini, E., Venturini, E., Remaschi, G., Principi, N., Longhi, R., Tovo, P.-A., Becherucci, P., Bonsignori, F., Esposito, S., Festini, F., Galli, L., Lucchesi, B., Mugelli, A., Marseglia, G. L., & de Martino, M. (2017). 2016 update of the Italian Pediatric Society guidelines for management of fever in children. *The Journal of Pediatrics, 180*, 177–183.e1. https://doi.org/10.1016/j.jpeds.2016.09.043
3. Hay, A. D., Costelloe, C., Redmond, N. M., Montgomery, A. A., Fletcher, M., Hollinghurst, S., & Peters, T. J. (2008). Paracetamol plus ibuprofen for the treatment of fever in children (PITCH): Randomised controlled trial. *BMJ, 337*, a1302. https://doi.org/10.1136/bmj.a1302
4. Misurac, J. M., Knoderer, C. A., Leiser, J. D., Nailescu, C., Wilson, A. C., & Andreoli, S. P. (2013). Nonsteroidal anti-inflammatory drugs are an important cause of acute kidney injury in children. *The Journal of Pediatrics, 162*(6), 1153–1159.e1. https://doi.org/10.1016/j.jpeds.2012.11.069
5. Nabulsi, M. M., Tamim, H., Mahfoud, Z., Itani, M., Sabra, R., Chamseddine, F., & Mikati, M. (2006). Alternating ibuprofen and acetaminophen in the treatment of febrile children: A pilot study. *BMC Medicine, 4*, Article 4. https://doi.org/10.1186/1741-7015-4-4
6. National Institute for Health and Care Excellence. (2021). *Fever in under 5s: Assessment and initial management (NICE Guideline NG143)*. https://www.nice.org.uk/guidance/ng143
7. Niehues, T., Krafft, H., Schemmer, J., Schwarz, S., Möhler, R., & Martin, D. (2026). Clinical practice guideline: The outpatient management of fever in children and adolescents. *Deutsches Ärzteblatt International, 123*, 226–230. https://doi.org/10.3238/arztebl.m2026.0002
8. Perrott, D. A., Piira, T., Goodenough, B., & Champion, G. D. (2004). Efficacy and safety of acetaminophen vs ibuprofen for treating children's pain or fever: A meta-analysis. *Archives of Pediatrics & Adolescent Medicine, 158*(6), 521–526. https://doi.org/10.1001/archpedi.158.6.521
9. Purssell, E., & Collin, J. (2016). Fever phobia: The impact of time and mortality—A systematic review and meta-analysis. *International Journal of Nursing Studies, 56*, 81–89. https://doi.org/10.1016/j.ijnurstu.2015.11.001
10. Southey, E. R., Soares-Weiser, K., & Kleijnen, J. (2009). Systematic review and meta-analysis of the clinical safety and tolerability of ibuprofen compared with paracetamol in paediatric pain and fever. *Current Medical Research and Opinion, 25*(9), 2207–2222. https://doi.org/10.1185/03007990903116255
11. Sullivan, J. E., & Farrar, H. C. (2011). Fever and antipyretic use in children. *Pediatrics, 127*(3), 580–587. https://doi.org/10.1542/peds.2010-3852
12. Tan, E., Braithwaite, I., McKinlay, C. J. D., & Dalziel, S. R. (2020). Comparison of acetaminophen (paracetamol) with ibuprofen for treatment of fever or pain in children younger than 2 years: A systematic review and meta-analysis. *JAMA Network Open, 3*(10), e2022398. https://doi.org/10.1001/jamanetworkopen.2020.22398

ISSN: 2181-3337 | SCIENTISTS.UZ

13. Thompson, A. P., Nesari, M., Hartling, L., & Scott, S. D. (2020). Parents' experiences and information needs related to childhood fever: A systematic review. *Patient Education and Counseling, 103*(4), 750–763. https://doi.org/10.1016/j.pec.2019.10.004
14. Wong, T., Stang, A. S., Ganshorn, H., Hartling, L., Maconochie, I. K., Thomsen, A. M., & Johnson, D. W. (2013). Combined and alternating paracetamol and ibuprofen therapy for febrile children. *Cochrane Database of Systematic Reviews, 2013*(10), Article CD009572. https://doi.org/10.1002/14651858.CD009572.pub2
15. Ziesenitz, V. C., Zutter, A., Erb, T. O., & van den Anker, J. N. (2017). Efficacy and safety of ibuprofen in infants aged between 3 and 6 months. *Paediatric Drugs, 19*(4), 277–290. https://doi.org/10.1007/s40272-017-0235-3

ISSN: 2181-3337 | SCIENTISTS.UZ