

# Clinical Considerations for OTC Antipyretic-Analgesics among 2-12 Year Old Children

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# Disclosures

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- Ian Paul has served as a paid consultant in the past 20 years for the Consumer Healthcare Products Association and several OTC drug manufacturers including Pfizer, GSK, McNeil, J&J, P&G, and Perrigo.

# Common Uses for OTC Pediatric Analgesic-Antipyretic Drugs

- **Fever**
- **Pain from mild, common conditions** – Common cold, sore throat, ear pain, body ache, tooth pain, headache
- **Musculoskeletal pain** – injuries, sprains, strains, fractures, bruises



# OTC Analgesic-Antipyretics for Children 2-<12 Years Old

**TABLE 1** Antipyretic Information

Variable	Acetaminophen	Ibuprofen
Decline in temperature, °C	1–2	1–2
Time to onset, h	<1	<1
Time to peak effect, h	3–4	3–4
Duration of effect, h	4–6	6–8
Dose, mg/kg	10–15 every 4 h	10 every 6 h
Maximum daily dose, mg/kg	90 mg/kg <sup>a</sup>	40 mg/kg
Maximum daily adult dose, g/d	4	2.4
Lower age limit, mo <sup>b</sup>	3	6

[www.pediatrics.org/cgi/doi/10.1542/peds.2010-3852](http://www.pediatrics.org/cgi/doi/10.1542/peds.2010-3852)

- Naproxen – also available OTC; no label dosing for children <12 years old

# Benefits of Currently Available Drugs/Products for Children

- Available in numerous formulations to suit child ability/preference
  - Liquid, chewable, tablet/capsule, suppository
- Generally effective at reducing fever and pain at recommended OTC doses for common self-limited conditions
- Generally good side effect profile when taken at recommended doses for recommended duration of time
- Clinical experience suggests generally low-risk of masking severe illnesses



# Limitations of Currently Available Drugs/Products for Children

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- Generally short duration of action of ~6-8 hours that might not cover entire school day, overnight sleep duration
- Even with current formulations, some children struggle to swallow medication.



# Are We Missing Something We Need to Treat Fever/Pain?

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- On January 9, 2007 Apple introduced the first iPhone. Did you know you needed a smartphone then? Did you realize how important it would be for daily life?



# New Options for Children 2-<12?

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- Naproxen, with a longer duration of action, has a similar efficacy/safety profile as ibuprofen for pain, just no dosing and formulations available OTC for children
- Combination product: Acetaminophen-Ibuprofen combination currently FDA approved and marked for pain relief for those 12 years and older
- No naproxen-acetaminophen combination available in the US
- Without pediatric combination product, co-administration of acetaminophen and ibuprofen is common by caregivers (Wright AD et al. *Clin Pediatr*, 2007) and commonly recommended by pediatricians (Mayoral CE et al. *Pediatrics*, 2000)
- Would caregivers like a combination product if available?

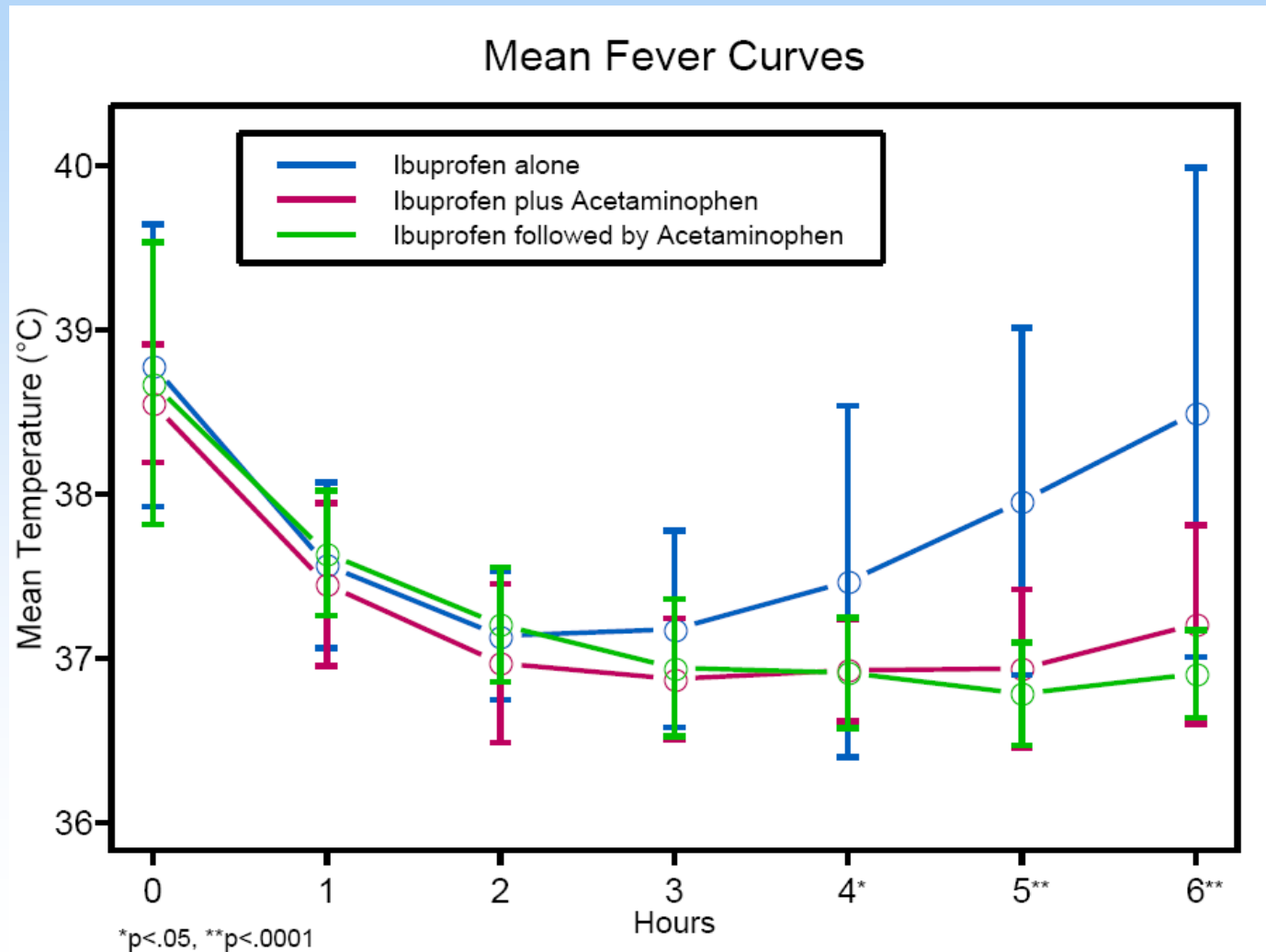


# Advantages with Alternating/Combined Use?

- Objective: To compare the antipyretic effect of three treatment regimens over a 6-hour observation period in children ages 6 months to 7 years (N=60) (Paul IM et al. *Clin Ther*, 2010)
  - Patients were children with common conditions: upper respiratory infections, acute otitis media
  - Ibuprofen dosed at 10 mg/kg, Acetaminophen at 15 mg/kg

Treatment Group	Time (hours)		
	0	3	6
A	Ibuprofen		
B	Ibuprofen + Acetaminophen		
C	Ibuprofen	Acetaminophen	

# Better Antipyresis with Alternating/Combined Dosing



# Meta-Analysis Published in *Pediatrics*: September 2024

## Short-term Dual Therapy or Mono Therapy With Acetaminophen and Ibuprofen for Fever: A Network Meta-Analysis

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**RESULTS:** We included 31 trials (5009 children). We found that combined (odds ratio [OR], 0.19; confidence interval [CI], 0.09–0.42) and alternating therapies (OR, 0.20; CI, 0.06–0.63) may be superior to acetaminophen, whereas ibuprofen at a high dose may be comparable (OR, 0.98; CI, 0.63–1.59) in terms of proportion of afebrile children at the fourth hour. These results were similar at the sixth hour. There were no differences between ibuprofen (low or high dose), or alternating, or combined with acetaminophen in terms of adverse events.

**LIMITATIONS:** We only evaluated the efficacy and safety during the first 6 hours.

**CONCLUSIONS:** Dual may be superior to single therapies for treating fever in children. Acetaminophen may be inferior to combined or alternating therapies to get children afebrile at 4 and 6 hours. Compared with ibuprofen, acetaminophen was also inferior to ibuprofen alone at 4 hours, but similar at 6 hours. PROSPERO registration: CRD42016035236.

\*Notable that literature has focused on fever for children, not pain. Issues include assessment/outcome measures and statistical power may be challenging



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