

### Clinical Question:

A father brings his 2 year old child in to your pediatric office stating that the child woke up with a 103 degree F fever this morning. He asks which medication is better to give to his child to reduce the fever- ibuprofen or acetaminophen?

### PICO Question:

Identify the PICO elements – this should be a revision of whichever PICO you have already begun in a previous week

<b>P</b>	<b>I</b>	<b>C</b>	<b>O</b>
Infant with fever	ibuprofen	acetaminophen	Lower fever
Baby with fever	ibuprofen	acetaminophen	Effective fever reduction
Child with fever	ibuprofen	acetaminophen	Safe fever reduction
			Reduced temperature

Is ibuprofen more effective than acetaminophen in reducing fever in otherwise healthy infants?

### Search Strategy:

- 1) **Google Scholar: Ibuprofen vs acetaminophen to reduce fever in children review- 11,900 results** → since 2017- **3,510 results**- this was still a lot, so I went through the first few pages and looked at the titles to help me decide which one to click on. Also, I only used articles that had a downloadable PDF on the side, and tried my best to find articles that were systematic reviews and meta-analyses.
- 2) **Pubmed- Ibuprofen vs acetaminophen fever children- 23 results- since 2014- 11 results**
- 3) **Chocrane Review- Ibuprofen vs acetaminophen children- 39 results- since 2015-19 results**
- 4) **Science Direct- ibuprofen vs acetaminophen fever children- 673 results- since 2017- 159 results**

Articles Chosen (4 or more) for Inclusion

### 1) **Comparison of Acetaminophen (Paracetamol) With Ibuprofen for Treatment of Fever or Pain in Children Younger Than 2 Years** A Systematic Review and Meta-analysis

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2772373>

Tan E, Braithwaite I, McKinlay CJD, Dalziel SR. 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 Netw Open*. 2020;3(10):e2022398. doi:10.1001/jamanetworkopen.2020.22398

### Abstract:

**Importance** Acetaminophen (paracetamol) and ibuprofen are the most widely prescribed and available over-the-counter medications for management of fever and pain in children. Despite the common use of these medications, treatment recommendations for young children remain divergent. **Objective** To compare acetaminophen with ibuprofen for the short-term treatment of fever or pain in children younger than 2 years. **Data Sources** Systematic search of the databases MEDLINE, Embase, CINAHL, and the Cochrane Central Register of Controlled Trials and the trial registers ClinicalTrials.gov and the Australian New Zealand Clinical Trials Registry from inception to March 2019, with no language limits. **Study Selection** Studies of any design that included children younger than 2 years and directly compared acetaminophen with ibuprofen, reporting antipyretic, analgesic, and/or safety outcomes were considered. There were no limits on length of follow-up. **Data Extraction and Synthesis** Following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline, 2 authors independently extracted data and assessed quality. Data were pooled using a fixed-effects method if  $I^2$  was less than 50% and using a random-effects method if  $I^2$  was 50% or greater. **Main Outcomes and Measures** The primary outcomes were fever or pain within 4 hours of treatment onset. Safety outcomes included serious adverse events, kidney impairment, gastrointestinal bleeding, hepatotoxicity, severe soft tissue infection, empyema, and asthma and/or wheeze. **Results** Overall, 19 studies (11 randomized; 8 nonrandomized) of 241 138 participants from 7 countries and various health care settings (hospital-based and community-based) were included. Compared with acetaminophen, ibuprofen resulted in reduced temperature at less than 4 hours (4 studies with 435 participants; standardized mean difference [SMD], 0.38; 95% CI, 0.08-0.67;  $P = .01$ ;  $I^2 = 49%$ ; moderate quality evidence) and at 4 to 24 hours (5 studies with 879 participants; SMD, 0.24; 95% CI, 0.03-0.45;  $P = .03$ ;  $I^2 = 57%$ ; moderate-quality evidence) and less pain at 4 to 24 hours (2 studies with 535 participants; SMD, 0.20; 95% CI, 0.03-0.37;  $P = .02$ ;  $I^2 = 25%$ ; moderate-quality evidence). Adverse events were uncommon. Acetaminophen and ibuprofen appeared to have similar serious adverse event profiles (7 studies with 27 932 participants; ibuprofen vs acetaminophen: odds ratio, 1.08; 95% CI, 0.87-1.33;  $P = .50$ ,  $I^2 = 0%$ ; moderate-quality evidence). **Conclusions and Relevance** In this study, use of ibuprofen vs acetaminophen for the treatment of fever or pain in children younger than 2 years was associated with reduced temperature and less pain within the first 24 hours of treatment, with equivalent safety.

### 2) **Efficacy and safety of acetaminophen vs ibuprofen for treating children's pain or fever: a meta-analysis**

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/485730>

Perrott DA, Piira T, Goodenough B, Champion GD. Efficacy and safety of acetaminophen vs ibuprofen for treating children's pain or fever: a meta-analysis. Arch Pediatr Adolesc Med. 2004 Jun;158(6):521-6. doi: 10.1001/archpedi.158.6.521. PMID: 15184213.

**Abstract-Objective:** To summarize studies testing the efficacy and safety of single-dose acetaminophen and ibuprofen for treating children's pain or fever. **Data sources:** Reports were gathered by searching computerized databases (from their inception through May 2002) and registries, relevant journals, and bibliographies of key articles. **Study selection:** Seventeen blinded, randomized controlled trials with children (<18 years) receiving either drug to treat fever or moderate to severe pain. **Data extraction:** Under a fixed-effects model, outcome measures for an initial single dose of ibuprofen vs acetaminophen were the risk ratio for achieving more than 50% of maximum pain relief, effect size for febrile temperature reduction, and risk ratio for minor and major harm. **Data synthesis:** Ibuprofen (4-10 mg/kg) and acetaminophen (7-15 mg/kg) showed comparable efficacy (3 pain relief trials; 186 children). The risk ratio point estimates was 1.14 (95% confidence interval [CI], 0.82-1.58) at 2 hours after receiving the dose, and 1.11 (95% CI, 0.89-1.38) at 4 hours. Ibuprofen (5-10 mg/kg) reduced temperature more than acetaminophen (10-15 mg/kg) at 2, 4, and 6 hours after treatment (respective weighted-effect sizes: 0.19 [95% CI, 0.05-0.33], 0.31 [95% CI, 0.19-0.44], and 0.33 [95% CI, 0.19-0.47]) (9 fever trials; 1078 children). For ibuprofen 10 mg/kg (acetaminophen, 10-15 mg/kg), corresponding effect sizes were 0.34 (95% CI, 0.12-0.56), 0.81 (95% CI, 0.56-1.03), and 0.66 (95% CI, 0.44-0.87). There was no evidence the drugs differed from each other (or placebo) in incidence of minor or major harm (17 safety trials; 1820 children). **Conclusions:** In children, single doses of ibuprofen (4-10 mg/kg) and acetaminophen (7-15 mg/kg) have similar efficacy for relieving moderate to severe pain, and similar safety as analgesics or antipyretics. Ibuprofen (5-10 mg/kg) was a more effective antipyretic than acetaminophen (10-15 mg/kg) at 2, 4, and 6 hours posttreatment.

**3) Effectiveness of paracetamol versus ibuprofen administration in febrile children: A systematic literature review <https://onlinelibrary.wiley.com/doi/abs/10.1111/jpc.13507>**

Narayan K, Cooper S, Morphet J, Innes K. Effectiveness of paracetamol versus ibuprofen administration in febrile children: A systematic literature review. J Paediatr Child Health. 2017 Aug;53(8):800-807. doi: 10.1111/jpc.13507. Epub 2017 Apr 24. PMID: 28437025.

**Abstract:** Aim: The use of antipyretics to manage the febrile child is becoming increasingly popular. Paracetamol and ibuprofen are the most commonly used interventions to manage fever in children; however, there have been no comparative analyses. The aim of the study is to evaluate the evidence comparing paracetamol to ibuprofen in the treatment of fever in children. Methods: A systematic review of randomised controlled trials investigating the administration of oral paracetamol and ibuprofen to reduce fever in children. Children aged 1 month to 12 years with a temperature between 37.5 and 41°C were included. A total of 3023 papers were identified. After removal of duplications, application of inclusion criteria and screening, eight papers were subjected to critical appraisal and included in this study. **Results:** Six of the studies identified that ibuprofen was slightly, but not significantly, better at reducing fever in children than paracetamol. Dosage variances and route of temperature measurement ranged between studies, limiting the comparability of studies. While ibuprofen was reported to be marginally more effective at reducing fever and fever associated discomfort in children, there is insufficient data to conclude that ibuprofen is superior to paracetamol. **Conclusion:** There is little evidence supporting the superior efficacy of paracetamol or ibuprofen in the treatment of fever in children with indications that both drugs are equally effective.

**4) Prescribing Controversies: An Updated Review and Meta-Analysis on Combined/Alternating Use of Ibuprofen and Paracetamol in Febrile Children**

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6560148/>

Trippella, Giulia, et al. "Prescribing controversies: an updated review and meta-analysis on combined/alternating use of ibuprofen and paracetamol in febrile children." *Frontiers in pediatrics* 7 (2019): 217.

**Abstract:Background:** Ibuprofen and paracetamol are the only antipyretics recommended in febrile children. According to international guidelines the choice of the drug should rely on the child's individual characteristics, while a controversial issue regards the combined or alternate use of the two drugs. **Objective:** To compare the efficacy and safety of combined or alternating use of ibuprofen and paracetamol in children. **Methods:** A systematic review of literature was performed on Medline and Embase databases. The included studies were randomized controlled trials analyzing the efficacy of combined or alternating therapy with antipyretics in febrile children vs. monotherapy. A meta-analysis was performed to measure the effect of treatment on child's temperature and discomfort. Adverse effects were analyzed as secondary outcome. **Results:** Nine studies were included, involving 2,026 children. Mean temperature was lower in the combined therapy group at 1 h (mean difference: -0.29°C; 95%CI: -0.45 to -0.13) after the initial administration of therapy. No statistical difference was found in mean temperature at 4 and 6 h from baseline. A significant difference was found in the proportion of children reaching apyrexia at 4 and 6 h with the combined treatment (RR: 0.18, 95%CI: 0.06 to 0.53, and 0.10, 95%CI: 0.01-0.71, respectively) and at 6 h with alternating treatment (RR: 0.30, 95% CI: 0.15-0.57), compared to children treated with monotherapy. The child's discomfort score was slightly lower with alternating therapy vs. monotherapy. The pooled mean difference in the number of medication doses per child used during the first 24 h was not significantly different among groups. **Discussion:** Combined or alternating therapy resulted 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 modest as well. According to our findings, evidences are 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

**Summary of the Evidence:**

Author (Date)	Level of Evidence	Sample/Setting (# of subjects/ studies, cohort definition etc. )	Outcome(s) studied	Key Findings	Limitations and Biases

<p>1) Eunicia Tan, M BChB<sup>1,2</sup>; Irene Braithwaite, PhD<sup>3</sup>; Christopher J. D. McKinlay, PhD<sup>4,5</sup>; et al, 10/30/2020</p>	<p>Systematic Review and Meta-analysis</p>	<ul style="list-style-type: none"> <li>- 19 studies (11 randomized, 8 non-randomized) with 241138 participants under 2 years from 7 countries and both hospital based and community based healthcare settings</li> <li>- the following databases were searched: MEDLINE, Embase, CINAHL, Cochrane Central Register of Controlled Trials and the trial registers ClinicalTrials.gov, and the Australian New Zealand Clinical Trials Registry, through March 2019</li> </ul>	<p>Comparison of acetaminophen vs ibuprofen for short term treatment of pain and fever in children under 2 years</p>	<ul style="list-style-type: none"> <li>- Moderate-quality evidence from 4 studies showed ibuprofen was associated with greater reduction in temperature at 4 hours compared to acetaminophen</li> <li>- Low- evidence non-randomized trials showed similar efficacy in fever reduction between the two at 4 hours, 1-3 days, and &gt; 3 days</li> <li>- Children treated with ibuprofen were twice as likely to be afebrile within 4 hours, and at 4-24 hrs, but no difference between 1-3 days</li> <li>- Ibuprofen was associated with less pain compared to acetaminophen at 4-24 hours</li> <li>- Low rates of adverse effects across all studies for both, similar likelihood of kidney impairment, liver toxicity, and asthma/wheezing between the 2 medications</li> </ul>	<ul style="list-style-type: none"> <li>- Lack of data about analgesic outcomes within 4 hours</li> <li>- Limited data on younger infants</li> <li>- Limited data on long term adverse effects</li> <li>- Evidence regarding risk of serious bacterial infection is inconclusive</li> <li>- Need further studies on infants younger than 6 months old and long term follow up and monitoring for AE</li> </ul>
<p>2) David A Perrott<sup>1</sup>, Tiina Piira, Belinda Goodenough, G David Champion6/2004</p>	<p>Systematic Review and Meta- Analysis</p>	<ul style="list-style-type: none"> <li>-17 blinded, randomized control studies including 1820 participants under 18 years old</li> <li>- the following electronic databases were utilized: MEDLINE, EMBASE, Cochrane Library, Biological Abstracts, Biological Abstracts/RRM, CINAHL, Dissertation Abstracts International, EBM Reviews-Best Evidence, EBM Reviews-Database of Abstracts of Reviews of Effectiveness, ERIC, Expanded Academic ASAP, General Science Abstracts, Health Reference Center Academic, Health Source Plus, HealthStar, Oxford Pain Relief Database, PsychInfo, and Web of Science, through May 2002</li> </ul>	<p>Comparison of efficacy and safety of single dose of ibuprofen and acetaminophen in treating children's pain and fever</p>	<ul style="list-style-type: none"> <li>- Found drugs were generally equally effective in achieving 50% pain relief, with slightly higher results for ibuprofen</li> <li>- Ibuprofen was more effective at reducing fever than acetaminophen (most pronounced at 4 and 6 hours after treatment- 15% more children were likely to have fever)</li> <li>- When the same dose of ibuprofen and Tylenol were given, the point-estimates favoring ibuprofen for fever relief were twice as large</li> <li>- safety profiles were similar for both drugs- they appear to be equally as safe as each other and as placebo</li> </ul>	<ul style="list-style-type: none"> <li>- only searched published studies, so could have been publication bias</li> <li>- outcome measures were not always explained in detail- sometimes number of AE in total were reported as opposed to number of people experiencing specific AE</li> <li>- more research is needed with multidose regimens lasting more than a few hours, and with net therapeutic benefits of repeated doses of medications for longer term pain and fever</li> <li>- lack of data comparing effects greater than 6 hours</li> </ul>
<p>3) Kaajal Narayan, Simon Cooper, Julia Morphet , and</p>	<p>Systematic Review and Meta-analysis</p>	<ul style="list-style-type: none"> <li>- 8 randomized control studies including 1632 children between 1 month and 12 years</li> </ul>	<p>Comparison of efficacy of ibuprofen vs paracetamol</p>	<ul style="list-style-type: none"> <li>- Results from 6 studies showed ibuprofen was slightly better at reducing fever than acetaminophen, but not significantly</li> </ul>	<ul style="list-style-type: none"> <li>- the study incorporated a variety of age ranges, drug doses, routes of measuring temperature,</li> </ul>

<p>Kelli Innes, 4/24/2017</p>		<p>old with fever between 37.5-41 deg C</p> <ul style="list-style-type: none"> <li>- searched the following electronic databases: CINAHL Plus, Cochrane Library, Web of Science, EBM Reviews, Ovid MEDLINE, Scopus, The Joanna Briggs Institute and Google Scholar</li> </ul>	<p>(acetaminophen) in treating fever and fever-related discomfort in children</p>	<ul style="list-style-type: none"> <li>- Also looked at fever-related discomfort- no statistically significant difference, but ibuprofen group had less discomfort at 24 and 48 hours (at 24 hours, 69% of children given ibuprofen reported no discomfort compared to 44% of children given acetaminophen)</li> <li>- Ibuprofen had a faster onset in reducing fever than acetaminophen (41 min vs 72 min)</li> <li>- Ibuprofen had slightly greater reduction in temperature reduction than acetaminophen</li> <li>- although ibuprofen is slightly better at reducing fever, the results are not significant and thus ibuprofen and acetaminophen can be considered equally effective in reducing childhood fever</li> </ul>	<p>and additional drugs, so the results may not be standardized or generalizable</p> <ul style="list-style-type: none"> <li>- further studies are needed with larger sample sizes and more standardized doses, with more specific age groups</li> <li>- this study only slightly looked at fever-related discomfort, and did not study the effects on general pain-relief between the 2 drugs.</li> <li>- Study did not look at adverse effects between the 2 drugs</li> </ul>
<p>4) Giulia Trippella, Martina Ciarcià, Maurizio de Martino, and Elena Chiappini, 6/5/2019</p>	<p>Systematic review and Meta-analysis</p>	<ul style="list-style-type: none"> <li>- 9 randomized controlled trials including 2,026 children aged 6 months to 14 years, presenting with fever &gt; 37.8 deg C</li> <li>- Databases used: Medline, Embase, and Google Scholar</li> </ul>	<p>Evaluation of efficacy and safety of combining or alternating ibuprofen and acetaminophen for fever relief in children</p>	<ul style="list-style-type: none"> <li>- No statistically significant difference in mean temperature at 4 and 6 hours from baseline</li> <li>- Combined vs single: % of children remaining febrile was lower in combined medication group at 4 and 6 hours from baseline, mean temperature was lower after 1 hour, however very wide confidence interval</li> <li>- Alternating vs single: no difference at 4 hours, lower % of febrile children in alternating group after 6 hours</li> <li>- Slightly lower discomfort levels in children receiving alternating therapy</li> <li>- No difference in adverse effects, though some studies showed warning signs that combined therapy could cause renal issues, and risk of administration errors increases with alternative or combined therapy</li> <li>- Concluded that benefit of combined/ alternative therapy is slight and not so clinically relevant, so it is better to stick with only one therapy</li> </ul>	<ul style="list-style-type: none"> <li>- Study was limited by poor quality evidence, as well as large heterogeneity between studies- population samples (including age, comorbidities, and etiology of fever), doses of medications, frequency of administration, and methods of measuring body temperatures</li> <li>- There was a small number of trials, so the impact of the variations could not adequately be assessed, and there is a risk of population bias</li> <li>- This study also didn't study children younger than 6 months</li> </ul>

### Conclusion(s):

- Briefly summarize the conclusions of each article Then provide an overarching conclusion.

#### Summary of Conclusions of each article:

- 1) Ibuprofen was associated with greater fever reduction and pain relief within the first 24 hours than acetaminophen, with similar safety between the 2 drugs.
- 2) Ibuprofen is a more effective antipyretic than acetaminophen at 2, 4, and 6 hours, and is equally effective at pain relief. The 2 drugs have similar safety profiles.
- 3) This study found a slight benefit in ibuprofen over acetaminophen at reducing fever and fever-related discomfort. However, it concluded that the results are not significant and ibuprofen and acetaminophen can be considered equally effective in reducing fever in children.
- 4) When comparing combined and alternating therapies (alternating between acetaminophen and ibuprofen) to taking either acetaminophen or ibuprofen alone, there is no statistically significant benefit of combined or alternating therapy in reducing fever or pain/ discomfort. The adverse effects also seem to be equal and not serious according to this study, however there is some concern that combined therapy could cause renal issues, and there is increased risk of administration and dosage errors with alternating/ combined therapies. Thus, it is better to use only one therapy.

#### Overall Conclusion:

According to all of the articles, ibuprofen is a better choice than acetaminophen in order to reduce fever- both more quickly and overall, and to reduce pain/ discomfort more significantly. Furthermore, as seen in the last article, ibuprofen alone is better than alternating or combining with acetaminophen. Although one article states that the benefits of ibuprofen are only slightly and not significantly greater than acetaminophen, all articles agree that neither have significant adverse effects and adverse effects do not differ between the 2 medications. Thus, the benefits of ibuprofen appear to be greater without any significantly greater harms.

### Clinical Bottom Line:

#### Weight of the Evidence:

All 4 of my studies were systematic reviews and meta-analyses, so overall, they had the highest level of evidence possible, and the sample sizes of each were fairly large, also contributing to weight of evidence.

- 1) Although this paper aimed to study the effects on children under 2 years of age, most of the articles they used included children up to 18 years of age. In terms of my search question, this actually makes the weight of evidence even stronger, since I am looking at the effects for children in general, not just infants. Some weaknesses, as previously mentioned, were that they had limited information on infants less than 6 months old, did not calculate the effects on pain relief within 4 hours, and did not follow up long term to look at risks of adverse effects. They also used some non-randomized control trials, which have lower levels of evidence. Yet, the higher quality evidence showed ibuprofen to be better than acetaminophen, while low quality evidence showed the 2 medications to be equally effective, which gives further support for the fact that ibuprofen is more effective. Some other strengths of this paper were that when they excluded 2 articles that were at high risk of bias, they still got the same results, and they also analyzed subgroups of lower and higher doses of ibuprofen vs acetaminophen, and the results were still consistent with all of these subgroups. Overall, I do believe that this article can strongly conclude that ibuprofen is more effective than acetaminophen for children, with equal safety profiles.
- 2) The greatest weakness of this paper is that it is older. However, it most directly relates to my question, and based on my research, is the first and main studied which directly looked at this question and came up with this conclusion. I also wanted to include it to demonstrate that this information and data pointing to the superiority of ibuprofen over acetaminophen is not so new, even though still today, many parents think acetaminophen is better and are reluctant to give ibuprofen to their children.. Furthermore, while it was able to strongly conclude that ibuprofen and acetaminophen are both safe and do not cause major harm events, there is not enough detailed research on minor harm events between the 2. Some strengths of this study include that it involved many trials with a large number of participants, and they were all randomized control trials, it included data from 2, 4, and 6 hours after giving the medication, and it compared different doses of ibuprofen. With doses of ibuprofen closer to the dose of Tylenol given, the benefits with ibuprofen in reducing fever were twice as much! I believe overall that this article has strong evidence pointing to the benefit of ibuprofen over acetaminophen.
- 3) The weaknesses of this article are that it did not discuss adverse events related to either of the drugs, it was not so standardized or specific, and incorporated a variety of ages, dosage strengths, frequencies of drug administration and routes of measuring temperature, as well as multiple doses vs one dose vs alternating vs combined. However, it did a good job at organizing and comparing only those that were equal to each other, such as comparing rectal to rectal and tympanic to tympanic temperatures. Another strength is that it tried to equate them as much as possible and point out when they were not equated. For example, it quoted an article that showed ibuprofen to be more effective than acetaminophen, but then pointed out that in this study, the maximum dosage of ibuprofen was given but not the maximum dosage of acetaminophen. Finally, a strength is that all studies were randomized control trials. Although the end point of this study was that ibuprofen is not significantly greater than Tylenol at reducing fever and pain, it still concludes that it is slightly better, so it could be clinically relevant.
- 4) The weaknesses of this study are similar to the previous studies- large heterogeneity between the studies- in population samples (including age, comorbidities, and etiology of fever), doses of medications, frequency of administration, and methods of measuring body temperatures. Some strengths were that it checked the temperature at 1, 4, and 6 hours, as well as followed up on day 2 and 3, it looked at the number of doses of antipyretics given after day 1 in both groups, and it discussed adverse events as well as reporting specific adverse events that occurred.

**Magnitude of Effects:** The magnitude of the effects overall was not so large- although all articles were on the same page and agreed that ibuprofen is more effective than acetaminophen, the third article did not even show statistically significant effects, but the first 2 articles did show a greater difference. The greatest difference seen was in the first and second article, which stated that children treated with ibuprofen were **twice** as likely to be afebrile within 4 hours and at 4-24 hours than those treated with acetaminophen. However, overall, acetaminophen is still effective at

reducing fever in a majority of cases, though ibuprofen has clearly been proven to be better than either acetaminophen alone or combined/alternative therapy. The benefits for pain were even of smaller magnitude- 2 of the articles stated no difference, while the others did state that there was a difference.

**Clinical Significance** I believe that these results are definitely clinically significant. As one of the articles mentioned, parents are generally more quick to give their children acetaminophen when they have a fever due to a preconceived notion that it is “better” and has less adverse effects. However, according to this research, that is clearly not true. The main thing I like to look at when assessing for clinical significance is harms vs benefits- if something is beneficial but could also cause some sort of harm, the risks may outweigh the benefits. Yet, according to all studies, ibuprofen and acetaminophen have similar safety profiles and one does not have greater adverse effects than the other. Thus, even if ibuprofen is only slightly better at reducing fever than acetaminophen which was at least the conclusion reached by all articles, it is worthwhile to use it as the first-line treatment for fever in children. Furthermore, at least some studies stated that ibuprofen is also a better pain reliever than acetaminophen, so that is an added bonus.

**Other Considerations** I think it would be worthwhile to do studies with more standardized data, such as comparing more specific ages, specific doses and using the same types of thermometers. I also think it would be beneficial to do more studies on infants and younger children, since the data in that area seems to be lacking, and parents are usually most concerned about fevers and how to treat them when they are dealing with younger children.