



**TITLE:** Acetaminophen for Pain or Fever: Clinical Effectiveness and Safety

**DATE:** 09 September 2016

## RESEARCH QUESTIONS

1. What is the clinical effectiveness and safety of different individual doses of acetaminophen for patients with pain or fever?
2. What is the clinical effectiveness and safety of doses in excess of the recommended daily maximum dose (4 g) for patients with pain or fever?
3. What is the safety of chronic use of acetaminophen?

## KEY FINDINGS

Thirty-three systematic reviews and meta-analyses were identified regarding the effectiveness and safety of acetaminophen.

## METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, and meta-analyses. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 1990 and September 1, 2016. Internet links were provided, where available.

## SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

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**Table 1: Selection Criteria**

<b>Population</b>	Patients with pain or fever
<b>Intervention</b>	Oral acetaminophen/paracetamol
<b>Comparator</b>	Different individual or maximum daily doses; Placebo; No comparator (safety)
<b>Outcomes</b>	Clinical effectiveness (e.g. pain or fever reduction); Safety (e.g. adverse events, liver toxicity)
<b>Study Designs</b>	Health technology assessments, systematic reviews, meta-analyses

## RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first.

Thirty-three systematic reviews and meta-analyses were identified regarding the effectiveness and safety of acetaminophen. No relevant health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-analyses

1. Acheampong P, Thomas SH. Determinants of hepatotoxicity after repeated supratherapeutic paracetamol ingestion: systematic review of reported cases. *Br J Clin Pharmacol.* 2016 Jun 4.  
[PubMed: PM27261770](#)
2. da Costa BR, Reichenbach S, Keller N, Nartey L, Wandel S, Juni P, et al. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. *Lancet.* 2016 May 21;387(10033):2093-105.  
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5. Non-invasive treatments for low back pain [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 Feb. [cited 2016 Sep 8]. (Comparative effectiveness review no. 169). Available from:

<https://www.effectivehealthcare.ahrq.gov/ehc/products/553/2178/back-pain-treatment-report-160229.pdf>

See: *Acetaminophen*, page ES-16

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[PubMed: PM27091010](#)
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[PubMed: PM25732175](#)
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[PubMed: PM25429049](#)
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18. Neill AS, Nagle CM, Protani MM, Obermair A, Spurdle AB, Webb PM, et al. Aspirin, nonsteroidal anti-inflammatory drugs, paracetamol and risk of endometrial cancer: a case-control study, systematic review and meta-analysis. *Int J Cancer.* 2013 Mar 1;132(5):1146-55.  
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[PubMed: PM10796810](#)

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**APPENDIX – FURTHER INFORMATION:**

**Previous CADTH Reports**

34. 1000 mg versus 650 mg acetaminophen for pain or fever: a review of the clinical efficacy [Internet]. Ottawa: CADTH; 2016 Jun 17. (Rapid response report: summary with critical appraisal). [2016 Sep 9]. Available from: <https://www.cadth.ca/1000mg-versus-650-mg-acetaminophen-pain-or-fever-review-clinical-efficacy>
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**Systematic Reviews**

*Various Doses Not Specified*

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*Restricting Paracetamol*

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[PubMed: PM15590709](#)

**Review Articles**

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39. Wong A, Graudins A, Kerr F, Greene SL. Paracetamol toxicity: what would be the implications of a change in Australian treatment guidelines? *Emerg Med Australas*. 2014 Apr;26(2):183-7.  
[PubMed: PM24708009](#)
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[PubMed: PM12856055](#)
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[PubMed: PM11847957](#)
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[PubMed: PM8669423](#)

#### **Additional References**

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[PubMed: PM19735211](#)