



# Effective Health Care

## Comparative Effectiveness of Antipyretic Agents for the Management of Febrile Seizures and Dengue

### Nomination Summary Document

#### Results of Topic Selection Process & Next Steps

- The topic, *Comparative Effectiveness of Antipyretic Agents for the Management of Febrile Seizures*, was found to be addressed by the following systematic reviews and guidelines. Given that the existing systematic reviews and guidelines cover this nomination, no further activity will be undertaken on this topic.

#### Systematic Reviews

- Rosenbloom E, Finkelstein Y, Adams-Webber T, et al. Do antipyretics prevent the recurrence of febrile seizures in children? A systematic review of randomized controlled trials and meta-analysis. *Eur J Paediatr Neurol*. 2013 Nov;17(6):585-8. PMID: 23702315
- Offringa M, Newton R. Prophylactic drug management for febrile seizures in children. *Cochrane Database Syst Rev*. 2012 Apr 18;4:CD003031.
- Graves RC, Oehler K, Tingle LE. Febrile seizures: risks, evaluation, and prognosis. *Am Fam Physician*. 2012 Jan 15;85(2):149-53. PMID: 22335215

#### Guidelines

- CG160. Feverish Illness in Children: Assessment and Initial Management in Children Younger than 5 Years. Issued April 2013. <http://www.nice.org.uk/guidance/cg160/>
  - Medical Services Commission. Febrile seizures. Victoria (BC): British Columbia Medical Services Commission; 2010 Sep 1. 7. <http://www.guideline.gov/content.aspx?id=38901&search=febrile+seizure>
  - American Academy of Pediatrics Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures. Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics*. 2008;121(6):1281–1286.
- The topic, *Comparative Effectiveness of Antipyretic Agents for the Management of Dengue*, is not feasible for a full systematic review due to the limited data available for a review at this time. This topic could potentially be considered for new research in comparative effectiveness.

#### Topic Description

**Nominator(s):** Individual

**Nomination Summary:** The nominator is interested in understanding the comparative effectiveness of antipyretics agents, such as acetaminophen, in the management of dengue and febrile seizures. He is concerned about the side effects associated with the usage of

antipyretics agents. Common side effects associated with acetaminophen, in the case of overdose or in the presence of risk factors, include hepatotoxicity, respiratory failure, metabolic acidosis, and renal failure. The nominator is also concerned that lowering the body temperature with antipyretic agents may undermine a “fundamental host defense mechanism” essential to stopping virus replication in dengue.

#### **Staff-Generated PICO**

**Population(s):** Children under 18 years of age with a febrile illness; Individuals (children and adults) with dengue.

**Intervention(s):** Antipyretic agents such as acetaminophen and ibuprofen.

**Comparator(s):** Placebo, other antipyretic agents.

**Outcome(s):** Prevention or recurrence of febrile seizures, reduction of fever, decrease in liver function, renal failure

#### **Key Questions from Nominator:**

1. What is the comparative effectiveness of antipyretic agents for the management of febrile seizures?
2. What is the comparative effectiveness of antipyretic agents for the management of dengue?

## **Considerations**

- This topic has two main areas: 1. Antipyretics for the management of febrile seizures in children and adolescents; and 2. Antipyretics for the management of dengue in children and adults.

#### **Febrile Seizures**

- Febrile seizures are convulsions brought on by a fever in infants or small children. They are the most common type of seizure in childhood, affecting 2-5% of children between the ages of 6 and 60 months.
- There are no specific laboratory tests indicated for a simple febrile seizure. Instead focus is placed on diagnosing the cause of fever. Other laboratory tests may be indicated depending on the nature of the underlying febrile illness.
- Most parents will give their children fever-lowering drugs such as acetaminophen or ibuprofen when they have a febrile illness.
- The topic area, *Antipyretics for the management of febrile seizures in children and adolescents*, was found to be addressed by the following systematic reviews:
  - A 2013 systematic review and meta-analysis titled, *Do antipyretics prevent the recurrence of febrile seizures in children? A systematic review of randomized controlled trials and meta-analysis*, which concluded that antipyretics were ineffective in reducing the recurrence of febrile seizures. The review examined three randomized controlled trials comparing the efficacy of antipyretic drugs to placebo in reducing the recurrence rate of febrile seizures in children (6-72 months) with previous febrile seizures.
  - A 2012 systematic review titled, *Febrile seizures: risks, evaluation, and prognosis*, by Graves et al., which concluded that continuous or intermittent antiepileptic or antipyretic medication is not recommended for the prevention of recurrent febrile seizures.
  - A 2012 Cochrane systematic review titled, *Prophylactic drug management for febrile seizures in children*, authored by Offringa and Newton, found no clinically important benefits from intermittent

ibuprofen, or for diclofenac versus placebo followed by ibuprofen, acetaminophen or placebo in children with febrile seizures.

- The topic area, *Antipyretics for the management of febrile seizures in children and adolescents*, was also found to be addressed by the following guidelines, all of which recommended against the use of antipyretics to prevent febrile seizures.
  - A 2013 guideline issued by the National Institute for Health and Care Excellence (NICE) titled, *Feverish Illness in Children: Assessment and Initial Management in Children Younger than 5 Years*, stated that antipyretic agents do not prevent febrile convulsions and should not be used specifically for that purpose.
  - A 2010 guideline by the British Columbia Medical Services Commission in Canada titled, *Febrile Seizures*, recommended against using intermittent administration of antipyretics to prevent recurrent febrile seizures.
  - A 2008 guideline from the American Academy of Pediatrics titled, *Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures*, found no studies have demonstrated that antipyretics, in the absence of anticonvulsants, reduce the recurrence risk of simple febrile seizures. It warned that although antipyretics such as acetaminophen and ibuprofen are considered to be safe and effective for children, hepatotoxicity (with acetaminophen) and respiratory failure, metabolic acidosis, renal failure, and coma (with ibuprofen) have been reported in children after overdose or in the presence of risk factors.

## Dengue

- Dengue is a mosquito-borne infection found in tropical and sub-tropical regions around the world. Dengue rarely occurs in the continental US but it is endemic in Puerto Rico. The incidence of dengue has grown dramatically around the world in recent decades. Over 2.5 billion people, or over 40% of the world's population, are now at risk from dengue.
- Occasionally, the condition develops into a potentially lethal complication called severe dengue (also known as dengue hemorrhagic fever [DHF]).
- There is no specific treatment for dengue fever. The Centers for Disease Control and Prevention (CDC) advises patients to stay well-hydrated and to avoid aspirin (acetylsalicylic acid), aspirin-containing drugs, and other nonsteroidal anti-inflammatory drugs because of their anticoagulant properties. Fever should be controlled with acetaminophen and tepid sponge baths. For patients with severe dengue, close observation and frequent monitoring in an intensive care unit setting may be required. Maintenance of the patient's body fluid volume is also critical to severe dengue care.
- Existing guidance and available literature relevant to the management of dengue is too limited at this time to conduct an AHRQ systematic review at this time.