

## ORIGINAL ARTICLE

# Acetaminophen for Fever in Critically Ill Patients with Suspected Infection

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**ABSTRACT**


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**BACKGROUND**

Acetaminophen is a common therapy for fever in patients in the intensive care unit (ICU) who have probable infection, but its effects are unknown.

**METHODS**

We randomly assigned 700 ICU patients with fever (body temperature,  $\geq 38^{\circ}\text{C}$ ) and known or suspected infection to receive either 1 g of intravenous acetaminophen or placebo every 6 hours until ICU discharge, resolution of fever, cessation of antimicrobial therapy, or death. The primary outcome was ICU-free days (days alive and free from the need for intensive care) from randomization to day 28.

**RESULTS**

The number of ICU-free days to day 28 did not differ significantly between the acetaminophen group and the placebo group: 23 days (interquartile range, 13 to 25) among patients assigned to acetaminophen and 22 days (interquartile range, 12 to 25) among patients assigned to placebo (Hodges-Lehmann estimate of absolute difference, 0 days; 96.2% confidence interval [CI], 0 to 1;  $P=0.07$ ). A total of 55 of 345 patients in the acetaminophen group (15.9%) and 57 of 344 patients in the placebo group (16.6%) had died by day 90 (relative risk, 0.96; 95% CI, 0.66 to 1.39;  $P=0.84$ ).

**CONCLUSIONS**

Early administration of acetaminophen to treat fever due to probable infection did not affect the number of ICU-free days. (Funded by the Health Research Council of New Zealand and others; HEAT Australian New Zealand Clinical Trials Registry number, ACTRN12612000513819.)

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\*A complete list of investigators in the Permissive Hyperthermia through Avoidance of Acetaminophen in Known or Suspected Infection in the Intensive Care Unit (HEAT) trial is provided in the Supplementary Appendix, available at NEJM.org.

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