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Helicobacter pylori eradication and aspirin: a puzzle yet to be solved

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(Article begins on next page)

# ***Helicobacter pylori* eradication and aspirin: a puzzle yet to be solved**

We read with great interest the Article by Chris Hawkey and colleagues<sup>1</sup> on the *Helicobacter* Eradication Aspirin Trial (HEAT). The authors should be commended for performing such a complex trial. Although the trial was conceived to evaluate the role of *Helicobacter pylori* eradication in older patients (aged  $\geq 60$  years) prescribed aspirin, the study was not planned to verify the eradication. A breath retest was randomly performed in only 10% of patients, reporting *H pylori* eradication in 146 (90.7%) of 161 patients receiving active eradication therapy. Such high eradication is usually achieved only with quadruple therapies lasting 10 days or longer, but not with 7-day triple therapies.<sup>2,3</sup> Furthermore, *H pylori* eradication was unexpectedly observed in 41 (24.0%) of 171 patients in the placebo group. Although exposure to clarithromycin, which occurred in 13 (32%) of the 41 control patients with a negative repeat breath test, might theoretically support these results,<sup>4</sup> there is no clear explanation for the remaining cases. These findings suggest that it would have been worthwhile to assess the eradication in a new larger random sample in both groups. During the first 2.5 years of follow-up, prescriptions for aspirin decreased progressively in both study groups, while prescriptions for proton pump inhibitors increased in both groups. Even if analyses were adjusted for time-varying prescribed medications, this trend might have had consequences on the second part of the follow-up with regard to the primary outcome, and a type two error cannot be excluded.

HEAT is an important study showing that *H pylori* eradication confers some benefits in the primary prevention of ulcer bleeding. However, future trials should evaluate *H pylori* eradication in all enrolled patients, and adopt more rigorous criteria on the use of proton pump inhibitors to better clarify the effect of eradication on aspirin-associated ulcer bleeding.

We declare no competing interests.

\*Luigi Gatta, Angelo Zullo, Dino Vaira  
**gattalg@gmail.com**

Gastroenterology Unit, Versilia Hospital, 55041 Lido di Camaiore, Italy (LG); Gastroenterology and Digestive Endoscopy, 'Nuovo Regina Margherita' Hospital, Rome, Italy (AZ); Department of Medical and Surgical Sciences, IRCCS S. Orsola Hospital, University of Bologna, Bologna, Italy (DV)

- 1 Hawkey C, Avery A, Coupland CAC, et al. *Helicobacter pylori* eradication for primary prevention of peptic ulcer bleeding in older patients prescribed aspirin in primary care (HEAT): a randomised, double-blind, placebo-controlled trial. *Lancet* 2022; **400**: 1597–606.
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- 4 Peterson WL, Graham DY, Marshall B, et al. Clarithromycin as monotherapy for eradication of *Helicobacter pylori*: a randomized, double-blind trial. *Am J Gastroenterol* 1993; **88**: 1860–64.