

Supplementary Online Content

Hunter BR, Wang AZ, Bucca AW, et al. Efficacy of benzodiazepines or antihistamines for patients with acute vertigo: a systematic review and meta-analysis. *JAMA Neurol*. Published online July 18, 2022. doi:10.1001/jamaneurol.2022.1858

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This supplementary material has been provided by the authors to give readers additional information about their work.

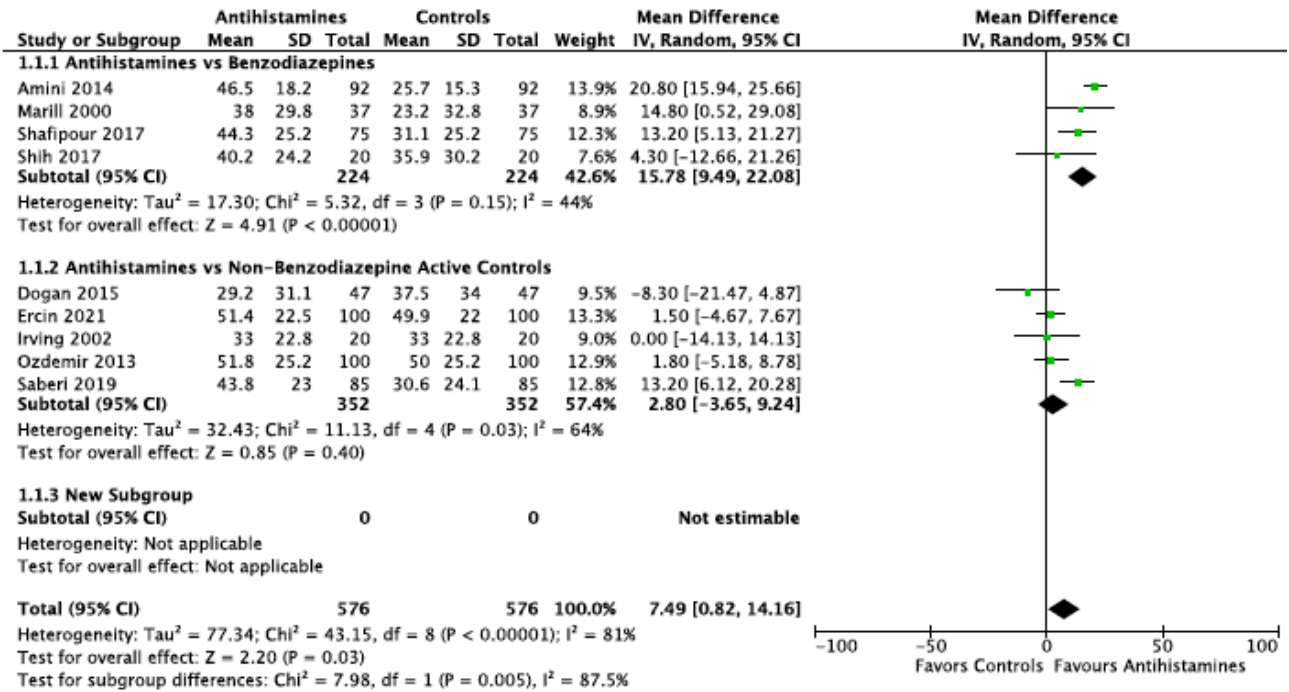
eAppendix. PubMed Search

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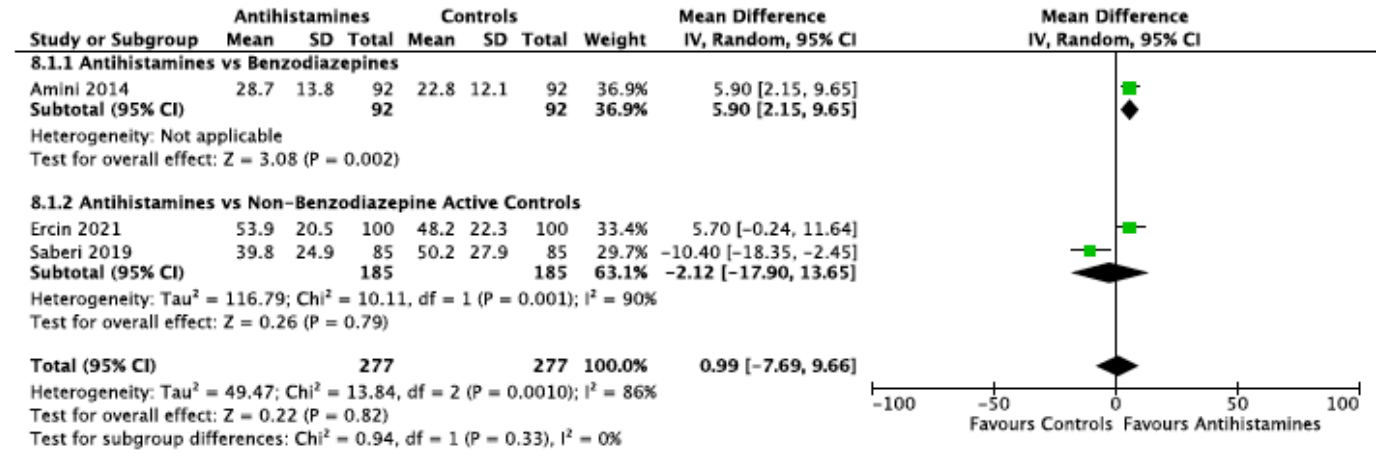
eFigure 1. Sensitivity Analysis for Primary Outcomes of 2 Additional Studies Reporting Visual Analog Score Changes at 2 Hours But Lacking SDs



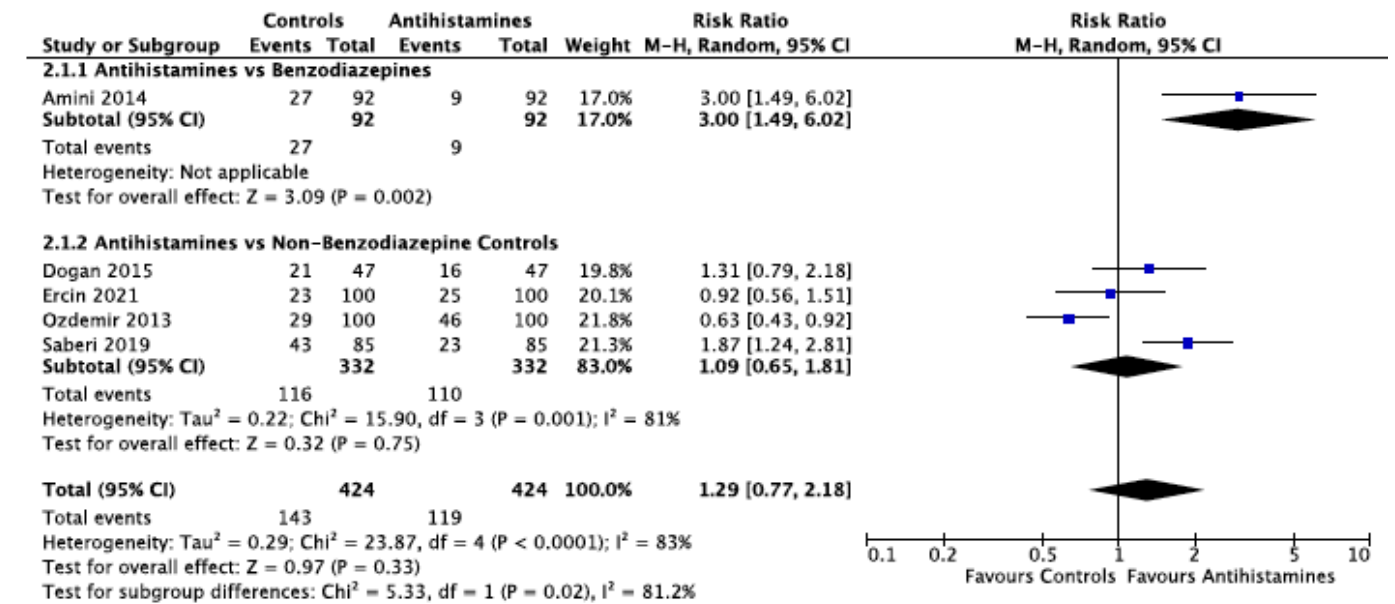
Additional data are from Shafipour et al¹ and Ozdemir et al.²

eFigure 2. Two-Hour Secondary End Points

Change in Nausea VAS

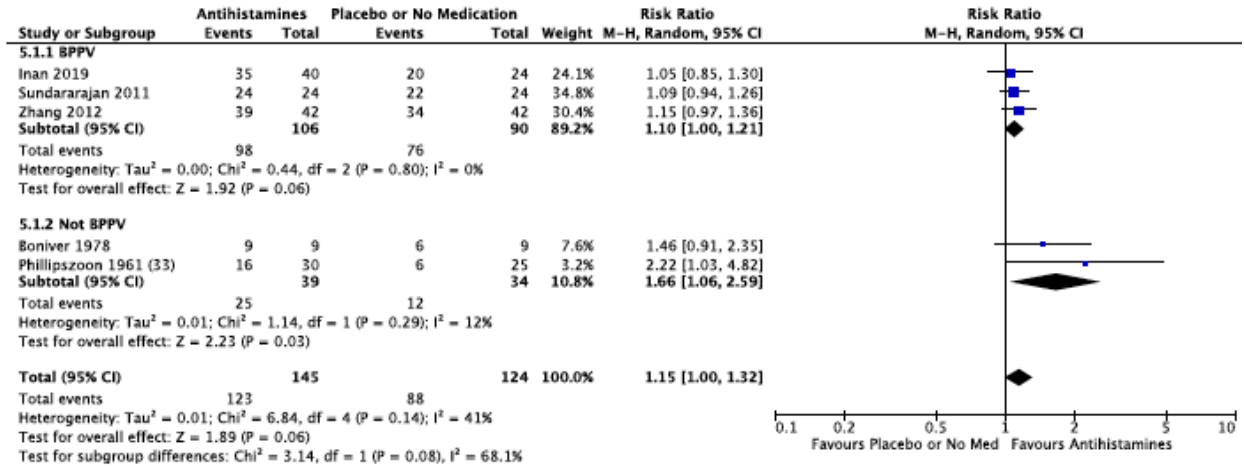


Need for Rescue Medication

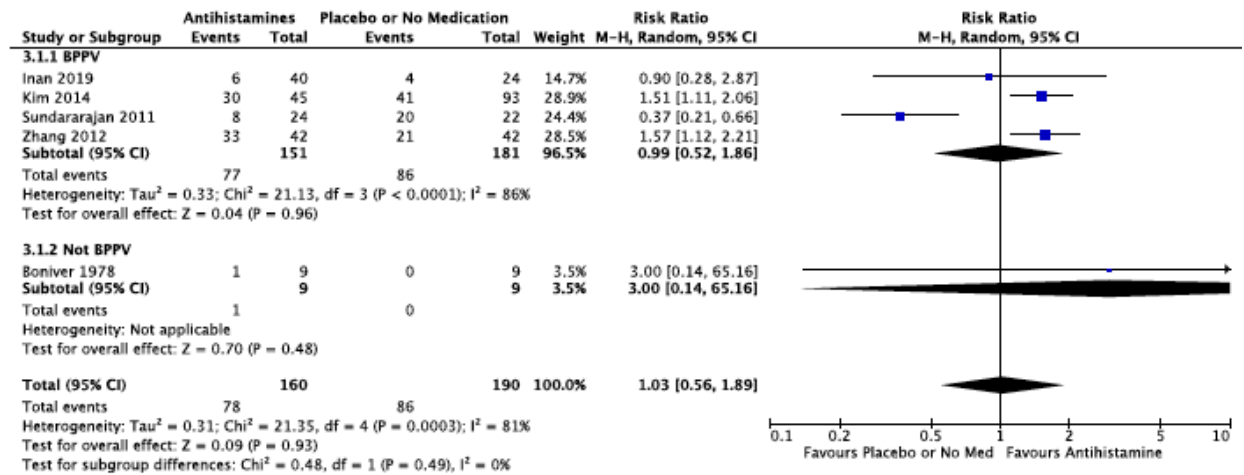


eFigure 3. Antihistamines vs Placebo or No Treatment at 1 Week and 1 Month

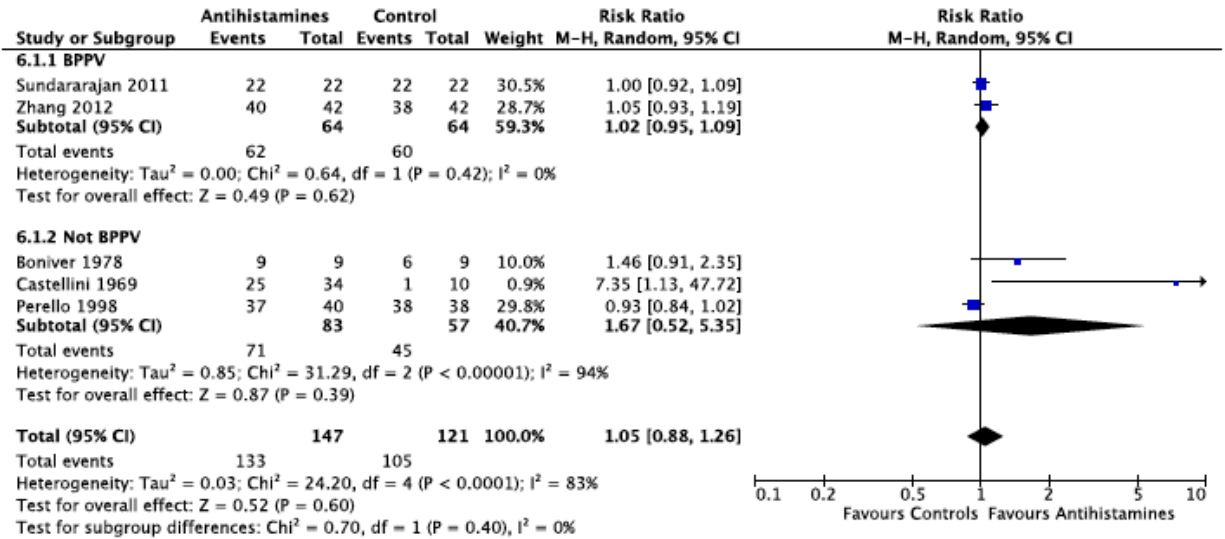
Improvement at 1 week



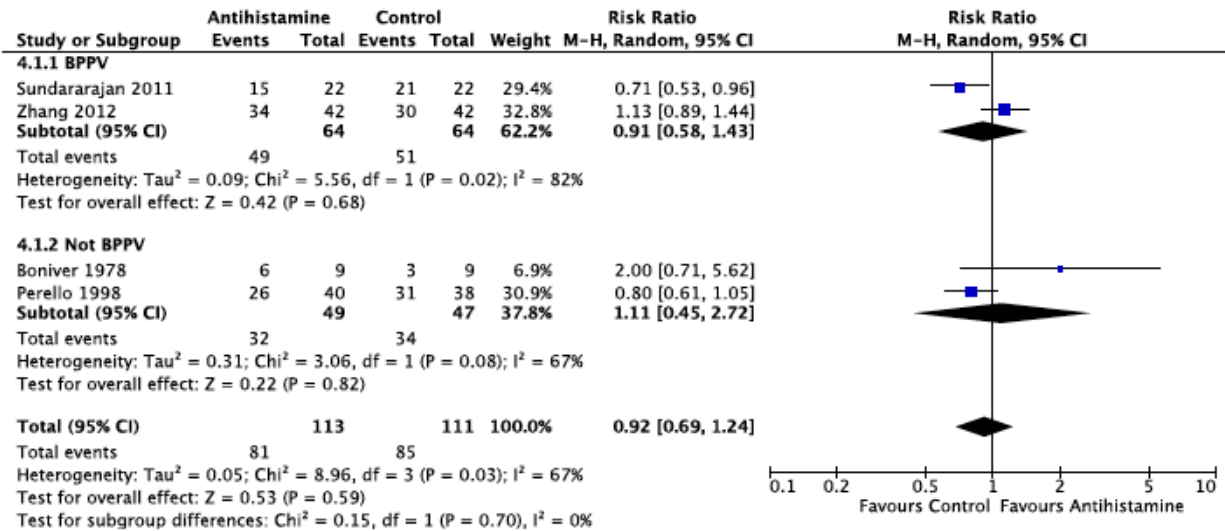
Resolution at 1 week



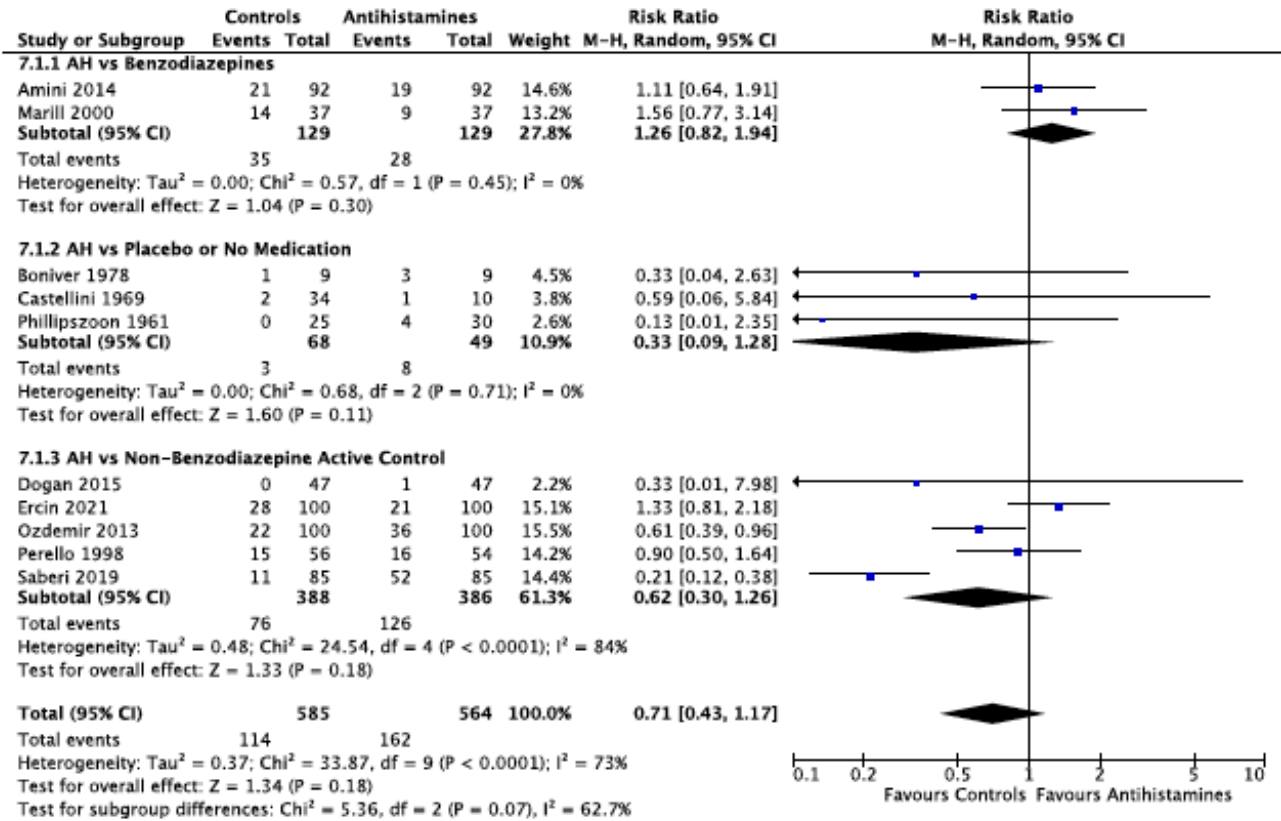
Improvement at 1 month



Resolution at 1 month



eFigure 4. Adverse Events



eTable. Nystagmography Studies

Author, Year	N	Comparators	Type of Vertigo	Nystagmometry Results
Boniver, ³ 1978	18	Flunarizine vs placebo for 3 months	Central or “vascular”	Compared to placebo, flunarizine treatment resulted in significantly more improvement in duration and speed of nystagmus in rotation and caloric stimulation at 1 week through 3 months
Castellini, ⁴ 1969	44	Cinnarizine vs placebo for up to 2 months	Mixed, including Meniere’s, traumatic, “labyrinthopathy” and unknown causes	Nystagmus “Improved” in 27 of 31 treated with cinnarizine, and 0 of 9 treated with placebo
McClure, ⁵ 1980	20	Lorazepam vs diazepam vs placebo for 1 month	Benign positional vertigo	Nystagmus, as rated by an examiner on a 10 point scale, decreased by 3.17 placebo, 3.57 diazepam, and 3.00 lorazepam at 1 month, no significant differences
Mulch, ⁶ 1976*	50	Dimenhydrinate vs diazepam vs high dose sulphiride vs low dose sulphiride vs placebo, single intramuscular dose	37 “peripheral,” 12 “central,” 1 undetermined	Dimenhydrinate and high dose sulphiride significantly decreased nystagmus intensity compared to placebo at 48 minutes; low dose sulphiride and diazepam did not
Perello, ⁷ 1998	110	Cinnarizine vs dotarizine for 45 days	Sudden onset “vertiginous syndromes”	No differences for either group in oculomotor or postural vestibular tests with respect to baseline
Philipszoon, ⁸ 1961	55	Cinnarizine vs placebo for 1 week	Not specified	“Cinnarizine exerted a significant effect compared to placebo” on nystagmometry in patients with vestibular vertigo

*Mulch 1976 is not included in quantitative meta-analysis because no clinical or symptom-based outcomes were reported

eReferences

1. Shafipour LKI, Shafipour V, Ahidashti HA, Charati JY. Intravenous promethazine versus diazepam for treatment of peripheral vertigo in emergency department. *J Mazandaran Univ Med Sci.* 2017;27(149):88-98.
2. Ozdemir H, Akinci E, Coskun F. Comparison of the effectiveness of intravenous piracetam and intravenous dimenhydrinate in the treatment of acute peripheral vertigo in the emergency department. *Singapore Med J.* 2013;54(11):649-652.
3. Boniver R. Vertigo, particularly of vascular origin, treated with flunarizine (R 14 950). *Arzneimittelforschung.* 1978;28(10):1800-1804.
4. Castellini V. [Clinical and electronystagmographic experience with a new drug containing cinnarizine in the treatment of vertigo]. *Boll Mal Orecch Gola Naso.* 1969;87(2):107-131.
5. McClure JA, Willett JM. Lorazepam and diazepam in the treatment of benign paroxysmal vertigo. *J Otolaryngol.* 1980;9(6):472-477.
6. Mulch G. Comparison of the effectiveness of antivertiginous drugs by double blind procedure. The effect of diazepam, dimenhydrinate and sulpirid on the human vestibular spontaneous nystagmus. *Laryngol Rhinol Otol (Stuttg).* 1976;55(5):392-399.
7. Perelló E, Esteller E, Colls A, et al. [Efficacy and safety of dotarizine vs. cinnarizine in the symptomatic treatment of acute balance disorders (common vertigo)]. *An Otorrinolaringol Ibero Am.* 1998;25(3):291-310.
8. Philipszoon AJ. [The effect of cinnarizine on vertigo; an electronystagmographic examination in 55 patients]. *Ned Tijdschr Geneeskd.* 1961;105:657-660.