

**Table 1** Excluded studies

Trial	Reason For exclusion
Banderet 1977 <sup>43</sup>	Results not clearly stated regarding AMS incidence
Bernhard 1998 <sup>44</sup>	Not a placebo-controlled trial
Bradwell 1981 <sup>32</sup>	Diagnostic criteria for AMS not clearly defined
Bradwell 1982 <sup>45</sup>	Prevention of AMS using acetazolamide was not a study outcome
Carlsten 2004 <sup>33</sup>	Results not clearly stated regarding AMS incidence
Ellsworth 1987 <sup>34</sup>	Raw data not clearly stated
Ellsworth 1988 <sup>46</sup>	Results not clearly given regarding AMS incidence
Fischer 2004 <sup>35</sup>	Prevention of AMS using acetazolamide was not a study outcome
Forward 1968 <sup>47</sup>	Diagnostic criteria of AMS not clearly defined
Gray 1971 <sup>48</sup>	Prevention of AMS using acetazolamide was not a primary outcome; Diagnostic criteria of AMS not clearly defined
Greene 1981 <sup>36</sup>	Diagnostic criteria for AMS not clearly defined
Hillenbrand 2006 <sup>37</sup>	Included Nepali porters from local population as participants
Hussain 2001 <sup>10</sup>	Results not clearly stated regarding AMS incidence
Hussain 2003 <sup>49</sup>	Prevention of AMS using acetazolamide was not a study outcome
Jain 1986 <sup>50</sup>	Results not clearly stated regarding AMS incidence
Jensen 1990 <sup>51</sup>	Prevention of AMS using acetazolamide was not a study outcome. Treatment of AMS using acetazolamide was an outcome.
Kayser 2008 <sup>5</sup>	Study had an uncontrolled arm which was not randomised
Kronenberg 1967 <sup>38</sup>	Study did not include acetazolamide as an intervention; Prevention of AMS was not a primary outcome
Lalande 2009 <sup>52</sup>	Prevention of AMS using acetazolamide was not a primary study outcome; Altitude was simulated
McIntosh 1986 <sup>53</sup>	Diagnostic criteria for AMS not clearly defined
Moraga 2007 <sup>4</sup>	Study not adequately blinded
Olzowy 1975 <sup>20</sup>	Not a randomised controlled trial. Unclear outcome criteria.
Ritschel 1998 <sup>54</sup>	Not a randomised controlled trial; Was not placebo controlled
Singh 1986 <sup>55</sup>	Prevention of AMS using acetazolamide was not a primary study outcome; Possible duplicate of the trial Jain 1986[51]
Sutton 1979 <sup>56</sup>	Prevention of AMS using acetazolamide was not a study outcome
Utz 1970 <sup>21</sup>	Results not clearly stated regarding AMS incidence.
Vuyk 2006 <sup>57</sup>	Study not clearly randomised; Not placebo controlled
White 1984 <sup>58</sup>	Results not clearly stated regarding AMS incidence
Wright 1983 <sup>59</sup>	Results not clearly stated regarding AMS incidence
Wright 1995 <sup>60</sup>	Intervention dose not stated; Diagnostic criteria and incidence of AMS not clearly stated
Wright 2004 <sup>61</sup>	Acetazolamide arm was open. Not a randomised trial
Zell 1988 <sup>39</sup>	Results not clearly stated regarding AMS incidence

- 1 Salisbury R, Hawley E. The Himalaya by the numbers: a statistical analysis of mountaineering in the Nepal Himalaya. Vajra, 2011.
- 2 Hunt L. Mount Kilimanjaro: climb and punishment. Telegraph Travel, 2010.
- 3 Imray C, Booth A, Wright A, Bradwell A. Acute altitude illnesses. *BMJ* 2011;343:d4943.
- 4 Moraga FA, Flores A, Serra J, Esnaola C, Barriento C. Ginkgo biloba decreases acute mountain sickness in people ascending to high altitude at Ollague (3696 m) in northern Chile. *Wilderness Environ Med* 2007;18:251-7.
- 5 Basnyat B, Gertsch JH, Johnson EW, Castro-Marin F, Inoue Y, Yeh C. Efficacy of low-dose acetazolamide (125 mg BID) for the prophylaxis of acute mountain sickness: a prospective, double-blind, randomized, placebo-controlled trial. *High Alt Med Biol* 2003;4:45-52.
- 6 Kayser B, Hulsebosch R, Bosch F. Low-dose acetylsalicylic acid analog and acetazolamide for prevention of acute mountain sickness. *High Alt Med Biol* 2008;9:15-23.
- 7 Joint Formulary Committee. British National Formulary. BMA, RPS 2011. (No 61.)
- 8 Bailey DM, Davies B. Acute mountain sickness; prophylactic benefits of antioxidant vitamin supplementation at high altitude. *High Alt Med Biol* 2001;2:21-9.
- 9 Gertsch JH, Seto TB, Mor J, Onopa J. Ginkgo biloba for the prevention of severe acute mountain sickness (AMS) starting one day before rapid ascent. *High Alt Med Biol* 2002;3:29-37.
- 10 Roncin JP, Schwartz F, D'Arbigny P. EGb 761 in control of acute mountain sickness and vascular reactivity to cold exposure. *Aviat Space Environ Med* 1996;67:445-52.
- 11 Hussain MM, Aslam M, Khan Z. Acute mountain sickness score and hypoxemia. *J Pak Med Assoc* 2001;51:173-9.
- 12 Dumont L, Mardirosoff C, Tramer MR. Efficacy and harm of pharmacological prevention of acute mountain sickness: quantitative systematic review. *BMJ* 2000;321:267-72.
- 13 Gertsch JH, Basnyat B, Johnson EW, Onopa J, Holck PS. Randomised, double blind, placebo controlled comparison of ginkgo biloba and acetazolamide for prevention of acute mountain sickness among Himalayan trekkers: the prevention of high altitude illness trial (PHAIT). *BMJ* 2004;328:797.

- 14 Hackett PH, Roach RC. High-altitude illness. *N Engl J Med* 2001;107-14.
- 15 Basnyat B, Gertsch JH, Holck PS, Johnson EW, Luks AM, Donham BP.  
Acetazolamide 125 mg BD is not significantly different from 375 mg BD in the prevention of acute mountain sickness: the prophylactic acetazolamide dosage comparison for efficacy (PACE) trial. *High Alt Med Biol* 2006;7:17-27.
- 16 Roach RC, Bärtsch P, Hackett PH, Oelz O, Committee. LLASC. The Lake Louise acute mountain sickness scoring system. In: Sutton JR, Coates G, Huston CS, eds. Hypoxia and molecular medicine: proceedings of the 8th international hypoxia symposium. *Queens City Printers* 1993;272-4.
- 17 Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Cochrane Collaboration 2011.
- 18 Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539-58.
- 19 Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analysis. *BMJ* 2003;557-60.
- 20 Olzowy M. Prevention of altitude sickness. *Fortschr Med* 1975;93:1415-22.
- 21 Utz G, Schlierf G, Barth P, Linhart P, Wollenweber J. Prevention of acute mountain sickness using acetazolamide. *Munch Med Wochenschr* 1970;112:1122-4.
- 22 Basnyat B, Hargrove J, Holck PS, Srivastav S, Alekh K, Ghimire LV, et al.  
Acetazolamide fails to decrease pulmonary artery pressure at high altitude in partially acclimatized humans. *High Alt Med Biol* 2008;9:209-16.
- 23 Basnyat B, Holck PS, Pun M, Halverson S, Szawarski P, Gertsch J, et al.  
Spironolactone does not prevent acute mountain sickness: a prospective, double-blind, randomized, placebo-controlled trial by SPACE Trial Group (spironolactone and acetazolamide trial in the prevention of acute mountain sickness group). *Wilderness Environ Med* 2011;22:15-22.
- 24 Chow T, Browne V, Heileson HL, Wallace D, Anholm J, Green SM. Ginkgo biloba and acetazolamide prophylaxis for acute mountain sickness: a randomized, placebo-controlled trial. *Arch Intern Med* 2005;165:296-301.
- 25 Gertsch JH, Lipman GS, Holck PS, Merritt A, Mulcahy A, Fisher RS, et al.  
Prospective, double-blind, randomized, placebo-controlled comparison of acetazolamide versus ibuprofen for prophylaxis against high altitude headache: the

Headache Evaluation at Altitude Trial (HEAT). *Wilderness Environ Med* 2010;21:236-43.

- 26 Van Patot MCT, Leadbetter G 3rd, Keyes LE, Maakestad KM, Olson S, Hackett PH. Prophylactic low-dose acetazolamide reduces the incidence and severity of acute mountain sickness. *High Alt Med Biol* 2008;9:289-93.
- 27 Hackett PH, Rennie D, Levine HD. The incidence, importance, and prophylaxis of acute mountain sickness. *Lancet* 1976;2:1149-55.
- 28 Larson EB, Roach RC, Schoene RB, Hornbein TF. Acute mountain sickness and acetazolamide. Clinical efficacy and effect on ventilation. *JAMA* 1982;248:328-32.
- 29 Burki NK, Khan SA, Hameed MA. The effects of acetazolamide on the ventilatory response to high altitude hypoxia. *Chest* 1992;101:736-41.
- 30 Seupaul RA, Welch J, Malka S, Emmett T. Pharmacologic prophylaxis for acute mountain sickness: a systematic shortcut review. *Ann Emerg Med* 2012;59:307-17.
- 31 Kayser B, Dumont L, Lysakowski C, Combescure C, Haller G, Tramer MR. Reappraisal of acetazolamide for the prevention of acute mountain sickness: a systematic review and meta-analysis. *High Alt Med Biol* 2012;13:82-92.
- 32 Bradwell AR, Burnett D, Davies F. Acetazolamide in control of acute mountain sickness. *Lancet* 1981;1:180-3.
- 33 Carlsten C, Swenson ER, Ruoss S. A dose-response study of acetazolamide for acute mountain sickness prophylaxis in vacationing tourists at 12,000 feet (3630 m). *High Alt Med Biol* 2004;5:33-9.
- 34 Ellsworth AJ, Larson EB, Strickland D. A randomized trial of dexamethasone and acetazolamide for acute mountain sickness prophylaxis. *Am J Med* 1987;83:1024-30.
- 35 Fischer R, Lang SM, Leitl M, Thiere M, Steiner U, Huber RM. Theophylline and acetazolamide reduce sleep-disordered breathing at high altitude. *Eur Respir J* 2004;23:47-52.
- 36 Greene MK, Kerr AM, McIntosh IB, Prescott RJ. Acetazolamide in prevention of acute mountain sickness: a double-blind controlled cross-over study. *BMJ* 1981;283:811-3.
- 37 Hillenbrand P, Pahari AK, Soon Y, Subedi D, Bajracharya R, Gurung P, et al. Prevention of acute mountain sickness by acetazolamide in Nepali porters: a double-blind controlled trial. *Wilderness Environ Med* 2006;17:87-93.

- 38 Kronenberg RS, Cain SM. Hastening respiratory acclimatization to altitude with benzolamide (CL 11,366). *Aerospace Med* 1967;39:296-300.
- 39 Zell SC, Goodman PH. Acetazolamide and dexamethasone in the prevention of acute mountain sickness. *West J Med* 1988;148:541-5.
- 40 Ellsworth AJ, Meyer EF, Larson EB. Acetazolamide or dexamethasone use versus placebo to prevent acute mountain sickness on Mount Rainier. *West J Med* 1991;154:289-93.
- 41 Nicholson AN, Smith PA, Stone BM, Bradwell AR, Coote JH. Altitude insomnia: studies during an expedition to the Himalayas. *Sleep* 1988;11:354-61.
- 42 Reinhart WH, Goerre S, Barstch P. Acetazolamide reduces the erythropoietin response to hypoxia at high altitude in humans. *J Wilderness Med* 1994;5:312-7.
- 43 Banderet LE. Self-rated moods of humans at 4300 m pretreated with placebo or acetazolamide plus staging. *Aviation Space Environ Med* 1977;48:19-22.
- 44 Bernhard WN, Schalick LM, Delaney PA, Bernhard TM, Barnas GM. Acetazolamide plus low-dose dexamethasone is better than acetazolamide alone to ameliorate symptoms of acute mountain sickness. *Aviation Space Environ Med* 1998;69:883-6.
- 45 Bradwell AR, Delamere JP. The effect of acetazolamide on the proteinuria of altitude. *Aviation Space Environ Med* 1982;53:40-3.
- 46 Ellsworth AJ, Meyer EF, Larson EB. Acetazolamide or dexamethasone use versus placebo to prevent acute mountain sickness on Mount Rainier. *West J Med* 1988;154:289-93.
- 47 Forward SA, Landowne M, Follansbee JN, Hansen JE. Effect of acetazolamide on acute mountain sickness. *N Engl J Med* 1968;279:839-45.
- 48 Gray GW, Sinclair D, Bryan AC, Houston CS. Carbon dioxide response curves at altitude. *Aerospace Med* 1971;42:1069-73.
- 49 Hussain MM, Aslam M. Hypoxia and pulmonary acclimatisation at 4578 m altitude: the role of acetazolamide and dexamethasone. *J Pak Med Assoc* 2003;53:451-8.
- 50 Jain SC, Singh MV, Sharma VM, Rawal SB, Tyagi AK. Amelioration of acute mountain sickness: comparative study of acetazolamide and spironolactone. *Int J Biometeorol* 1986;30:293-300.
- 51 Jensen JB, Wright AD, Lassen NA, Harvey TC, Winterborn MH, Raichle ME, et al. Cerebral blood flow in acute mountain sickness. *J Appl Physiol* 1990;69:430-3.

- 52 Lalande S, Snyder EM, Olson TP, Hulsebus ML, Orban M, Somers VK, et al. The effects of sildenafil and acetazolamide on breathing efficiency and ventilatory control during hypoxic exercise. *Eur J Appl Physiol* 2009;106:509-15.
- 53 McIntosh IB, Prescott RJ. Acetazolamide in prevention of acute mountain sickness. *J Int Med Res* 1986;14:285-7.
- 54 Ritschel WA, Paulos C, Arancibia A, Agrawal MA, Wetzelsberger KM, Lucke PW. Pharmacokinetics of acetazolamide in healthy volunteers after short- and long-term exposure to high altitude. *J Clin Pharmacol* 1998;38:533-9.
- 55 Singh M. Comparative study of acetazolamide and spironolactone on body fluid compartments on induction to high altitude. *Int J Biometeorol* 1986;30:33-41.
- 56 Sutton JR, Houston CS, Mansell AL, McFadden MD, Hackett PM, Rigg JR, et al. Effect of acetazolamide on hypoxemia during sleep at high altitude. *N Engl J Med* 1979;301:1329-31.
- 57 Vuyk J, Van Den Bos J, Terhell K, De Bos R, Vletter A, Valk P, et al. Acetazolamide improves cerebral oxygenation during exercise at high altitude. *High Alt Med Biol* 2006;7:290-301.
- 58 White AJ. Cognitive impairment of acute mountain sickness and acetazolamide. *Aviat Space Environ Med* 1984;55:598-603.
- 59 Wright AD, Bradwell AR, Fletcher RF. Methazolamide and acetazolamide in acute mountain sickness. *Aviat Space Environ Med* 1983;54:619-21.
- 60 Wright AD, Imray CH, Morrissey MS, Marchbanks RJ, Bradwell AR. Intracranial pressure at high altitude and acute mountain sickness. *Clin Sci* 1995;89:201-4.
- 61 Wright AD, Beazley MF, Bradwell AR, Chesner IM, Clayton RN, Forster PJ, et al. Medroxyprogesterone at high altitude. The effects on blood gases, cerebral regional oxygenation, and acute mountain sickness. *Wilderness Environ Med* 2004;15:25-31.