
The Atherosclerotic Disease Multiple Intervention Trial (ADMIT) was designed to determine the safety and efficacy of varying combinations of anticoagulant, antioxidant vitamin, and HDL-cholesterol raising therapy in patients with peripheral arterial disease (PAD) (Am Heart J. 140:792, 2000). In ADMIT 468 patients with PAD were sequentially randomized to low-dose warfarin, antioxidant vitamin cocktail (vitamins E, C, and β-carotene), and immediate-release niacin (3 grams per day), or corresponding placebo(s) in a 2X2X2 factorial design. A stated objective of ADMIT was to test the ability to blind subjects and research staff to study interventions. The study design included use of active placebo (intermittent low-dose niacin) and blinded laboratory monitoring (warfarin) to confound identification of drug assignment. At completion of the study participants, study staff, and local investigators completed a questionnaire on perceived study drug assignments. A high percentage (72%) of participants on active niacin correctly identified their drug assignment, however, only 21% of participants receiving niacin placebo correctly identified their drug assignment. Overall, less than half (47%) of participants correctly determined their Niacin drug assignment. Only slightly better than half of participants randomized to active warfarin (57%), and less than half (13%) randomized to warfarin placebo correctly identified their drug assignment. Overall, only 22% of participants randomized to antioxidant vitamins or placebo correctly identified their drug assignment. In every case, study coordinators and investigators were less successful in correctly identifying participant’s drug assignment. Reported symptoms which correlated with correct identification of drug assignment were: bruising (warfarin), skin rash, flushing (niacin)( all P<0.05). There was a borderline (p =0.06) association of carotenemia with identification of antioxidant vitamin drug assignment. Although a high percentage of participants who were randomized to active niacin correctly identified their drug assignment, overall blinding to niacin, warfarin, and antioxidant vitamin or corresponding placebo(s) was effective in the ADMIT study. This reflects the use of active placebo for niacin, blinded laboratory monitoring for warfarin, and lack of biological cues for antioxidant vitamins.