will be flawed. We do not believe that nonparticipation in trials necessarily ensures unbiased conclusions.

Drew Provan, M.D.
Adrian C. Newland, F.R.C.P., F.R.C.Path.
Barts and the London School of Medicine and Dentistry
London, United Kingdom
a.c.newland@qmul.ac.uk
for the Consensus Group

Drs. Provan and Newland report receiving speaking fees from and serving on advisory boards for Amgen, GlaxoSmithKline, and Baxter, and receving institutional research support from Amgen and GlaxoSmithKline. Dr. Newland also reports receiving research support from Bayer, Bio Products Laboratory, Shionogi, and Genentech. No other potential conflict of interest relevant to this letter was reported.

1. George JN. Management of immune thrombocytopenia — something old, something new. N Engl J Med 2010;363:1959-61.
2. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood 2010;115:168-86.
3. George JN, Woolf SH, Raskob GE, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood 1996; 88:3-40.
4. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. Br J Haematol 2003;120:574-96.

THE EDITORIALIST REPLIES: Provan and Newland address the critical issues of financial and intellectual conflicts of interest related to clinical practice guidelines. Although full disclosure of financial conflicts is sufficient for research publications,[1] practice guidelines are different. Disclosing conflicts is not sufficient, since evidence may be open to interpretation. Although experts rarely allow conflicts to consciously influence recommendations, an important association between disclosed conflicts and voting patterns in medical advisory panels has been documented.[2] Therefore, the Institute of Medicine has recommended "an end to direct industry funding of clinical practice guidelines" and "to exclude or substantially limit the participation of individuals with conflicts of interest on panels that develop clinical practice guidelines."[3] Intellectual conflicts of interest, defined as a potential bias of experts who may have strong opinions about specific practices,[4] are avoided by the use of guideline panels composed of clinicians and scientists whose skills are to objectively critique relevant studies.[4,5] Topic experts may participate by providing critical reviews.[4,5] Since guidelines are influential for public policy as well as clinical practice, freedom from financial and intellectual conflicts is essential.

James N. George, M.D.
University of Oklahoma Health Sciences Center
Oklahoma City, OK

Since publication of his article, the author reports no further potential conflict of interest.

1. Drazen JM, De Leeuw PW, Laine C, et al. Toward more uniform conflict disclosures — the updated ICMJE conflict of interest reporting form. N Engl J Med 2010;363:188-9.
2. Lurie P, Almeida CM, Stine N, Stine AR, Wolfe SM. Financial conflict of interest disclosure and voting patterns at Food and Drug Administration Drug Advisory Committee meetings. JAMA 2006;295:1921-8.
3. Lo B, Field MJ, eds. Conflict of interest in medical research, education, and practice. Washington, DC: National Academies Press, 2009.
4. Guyatt G, Akl EA, Hirsh J, et al. The vexing problem of guidelines and conflict of interest: a potential solution. Ann Intern Med 2010;152:738-41.
5. Woolf SH. The 2009 breast cancer screening recommendations of the US Preventive Services Task Force. JAMA 2010;303: 162-3.

Ranibizumab for Age-Related Macular Degeneration

TO THE EDITOR: In their Clinical Therapeutics article on the use of ranibizumab for neovascular age-related macular degeneration (AMD), Folk and Stone (Oct. 21 issue)[1] do not mention the significant risk of death from cardiovascular disease among such patients. In the Age-Related Eye Disease Study (ClinicalTrials.gov number, NCT00000145), during a median follow-up of 6.5 years, 534 of 4753 participants (11.2%) died.[2] Furthermore, development of disease in the other eye is common. In the Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular Age-Related Macular Degeneration (NCT00056836) and Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in Age-Related Macular Degeneration (NCT00061594) trials, in the entire treatment group, the same destructive wet type of AMD developed in the other eye on average within 1 year in 22% of the

patients and within 2 years in 33% of the patients.[3] The risk factors associated with AMD and cardiovascular disease are the same.[4,5] Treatment to control those risk factors should start early, when drusen are first detected. The goals of treatment should be the following: first, to decrease the rate of death from cardiovascular disease; second, to prevent the disease from affecting the good eye; and, finally, to treat the eye involved with advanced disease. Giving repeated intraocular injections to control the disease when it is far advanced is only part of the treatment.

Clement Trempe, M.D.

New England Eye Institute
Boston, MA
clement_trempe@hms.harvard.edu

No potential conflict of interest relevant to this letter was reported.

1. Folk JC, Stone EM. Ranibizumab therapy for neovascular age-related macular degeneration. N Engl J Med 2010;363:1648-55. [Erratum, N Engl J Med 2010;363:2474.]
2. Clemons TE, Kurinij N. Associations of mortality with ocular disorders and an intervention of high-dose antioxidents and zinc in the Age-Related Eye Disease Study: AREDS report no. 13. Arch Ophthalmol 2004;122:716-26.
3. Barbazetto IA, Saroj N, Shapiro H, Wong P, Ho AC, Freund KB. Incidence of new choroidal neovascularization in fellow eyes of patients treated in the MARINA and ANCHOR trials. Am J Ophthalmol 2010;149:939-46.
4. Baird PN, Robman LD, Richardson AJ, et al. Gene-environment interaction in progression of AMD: the CFH gene, smoking and exposure to chronic infection. Hum Mol Genet 2008;17:1299-305.
5. Vine AK, Stader J, Branham K, Musch DC, Swaroo PA. Biomarkers of cardiovascular disease as risk factors for age-related macular degeneration. Ophthalmology 2005;112:2076-80.

TO THE EDITOR: Folk and Stone note that bevacizumab, although considered off-label therapy, is commonly used as an alternative to ranibizumab.[1] In recently reported results from a small, randomized trial, there was no significant difference in efficacy between bevacizumab and ranibizumab for neovascular AMD.[2] However, the total number of injections given over the treatment period in the bevacizumab group was significantly higher than in the ranibizumab group; these increased injections might increase the risk of endophthalmitis. The intravitreal injection of bevacizumab also can induce sterile endophthalmitis. The incidence was reported to be 14.3% in one study from Japan.[3] Hoffmann–La Roche reported 32 cases of endophthalmitis after the off-label intravitreal use of bevacizumab in Canada between November 4 and 20, 2008. Recently (on September 7 and 8, 2010), acute postoperative endophthalmitis developed in 55 of 116 patients after intravitreal injection of bevacizumab in Shanghai, China. Therefore, it will be important to clarify the relative safety of bevacizumab and ranibizumab in studies such as the Comparison of AMD Treatments Trial (NCT00593450).

Jin-Wei Cheng, M.D.
Rui-Li Wei, M.D.

Second Military Medical University
Shanghai, China
ruiliwei@gmail.com

No potential conflict of interest relevant to this letter was reported.

1. Tufail A, Patel PJ, Egan C, et al. Bevacizumab for neovascular age related macular degeneration (ABC Trial): multicentre randomised double masked study. BMJ 2010;340:c2459.
2. Subramanian ML, Abedi G, Ness S, et al. Bevacizumab vs ranibizumab for age-related macular degeneration: 1-year outcomes of a prospective, double-masked randomised clinical trial. Eye (Lond) 2010;24:1708-15.
3. Sato T, Emi K, Ikeda T, et al. Severe intraocular inflammation after intravitreal injection of bevacizumab. Ophthalmology 2010;117:512-6.

Bisphosphonates for Osteoporosis

TO THE EDITOR: In the clinical vignette in the article by Favus (Nov. 18 issue),[1] there is a clear indication for treatment with a bisphosphonate because of the low bone-mineral-density T scores (–2.8 at the femoral neck and –3.1 at the lumbar spine) and a vertebral fracture in a 67-year-old woman. However, we were surprised that the patient was not treated for osteoporosis after the diagnostic evaluation the year before. According to the guidelines of the National Osteoporosis Foundation, treatment is indicated in all postmenopausal women with a T score below –2.5.[2] In addition, there was loss of height and back pain that could indicate an incident vertebral fracture, which is an additional important risk for future fractures.[3]

Because this is a clinical vignette, we would like to emphasize that this patient already had an indication for treatment 1 year before the start of actual treatment. This point is clinically