

## Accuracy of Financial Disclosures Reported by Physicians

**TO THE EDITOR:** Okike et al. (Oct. 8 issue)<sup>1</sup> found that the rate of conflict-of-interest disclosure reported by physicians who participated in the 2008 annual meeting of the American Academy of Orthopaedic Surgeons (AAOS) was 79% for directly related payments and 50% for indirectly related payments. I am writing to provide an update on the critical steps the AAOS has taken since the time this study was performed.

The AAOS has worked diligently for years and will continue to perfect, modify, and simplify the disclosure process that physicians use to identify their consulting and other arrangements with companies. Specifically, since 2008, we have made our mandatory disclosure process electronic; required disclosure of all potential conflicts and relationships, regardless of their relevance to the presentation; provided numerous educational programs and materials for our members that emphasize the importance of full disclosure and teach them how to fulfill this requirement; and formed a board project team to review our policies and recommend enhancements.

We believe that mandatory, complete disclosure and the appropriate management of conflicts of interest are essential. Our ongoing efforts to streamline the process and educate our members enable the physicians to focus on their real work — improving the quality of life for our patients with musculoskeletal conditions.

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Dr. Zuckerman reports receiving royalties from Exactech for design of a shoulder-replacement system. No other potential conflict of interest relevant to this letter was reported.

1. Okike K, Kocher MS, Wei EX, Mehlman CT, Bhandari M. Accuracy of conflict-of-interest disclosures reported by physicians. *N Engl J Med* 2009;361:1466-74.

**THE AUTHORS REPLY:** We thank Zuckerman for his response to our article. We agree that the AAOS has taken several important steps to improve the process for disclosing conflicts of interest since the time our study was conducted.

In addition to the steps taken by the AAOS, several recent changes regarding conflict of interest and its disclosure have been made by medical journals,<sup>1</sup> healthcare organizations,<sup>2</sup> universities,<sup>3</sup> pharmaceutical companies,<sup>4</sup> and state governments.<sup>5</sup>

We are optimistic that these changes will serve to promote full disclosure of conflicts of interest by all investigators; such disclosure is a minimum requirement for managing financial conflicts of interest in biomedical research.

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Since publication of their article, the authors report no further potential conflict of interest.

1. Drazen JM, Van der Weyden MB, Sahni P, et al. Uniform format for disclosure of competing interests in ICMJE journals. *N Engl J Med* 2009;361:1896-7.

2. Partners HealthCare to implement new industry interaction recommendations. Press release of Partners HealthCare, Boston, April 10, 2009. (Accessed January 14, 2010, at [http://www.partners.org/documents/CommissionPressRelease\\_PartnersHealthCare2009.pdf](http://www.partners.org/documents/CommissionPressRelease_PartnersHealthCare2009.pdf).)

3. New Johns Hopkins Medicine policies tighten rules on industry interactions. Press release of Johns Hopkins Medicine, Baltimore, April 8, 2009. (Accessed January 14, 2010, at [http://www.hopkinsmedicine.org/Press\\_releases/2009/04\\_07\\_09.html](http://www.hopkinsmedicine.org/Press_releases/2009/04_07_09.html).)

4. Lilly set to become first pharmaceutical research company to disclose physician payments. Press release of Eli Lilly and Company, Indianapolis, September 24, 2008. (Accessed January 14, 2010, at <http://newsroom.lilly.com/releasedetail.cfm?ReleaseID=336444>.)

5. Kowalczyk L. State bans drug firm gifts to doctors: disclosure of fees for consulting mandated. *Boston Globe*. March 12, 2009.

## Ankle–Brachial Index and Peripheral Arterial Disease

**TO THE EDITOR:** Grenon et al. (Nov. 5 issue) have presented a validated method of calculating the ankle–brachial index that is currently used in the evaluation of patients with peripheral arterial

disease.<sup>1,2</sup> The highest systolic pressure in the dorsalis pedis or posterior tibial artery divided by the highest arm pressure determines the validated ankle–brachial index calculation.<sup>1,3</sup> However,

we would suggest that the decision to use this formula may depend on whether a physician wants to screen a patient for peripheral artery disease or wants to pursue follow-up for patients in whom the disease has already been diagnosed. Indeed, Espinola-Klein et al. found that when screening patients for the disease, using the highest artery pressure in the leg to calculate the index caused a group of patients at high risk for cardiovascular events to be overlooked (10.8% of 831 patients).<sup>4</sup> The authors suggest the use of a modified method for calculating the ankle-brachial index in which the lowest pressure in the leg artery is used instead of the highest. Using this modified method, they found that rates of cardiovascular events were comparable for patients with a validated ankle-brachial index of less than 0.90 and those with a modified ankle-brachial index of less than 0.90 (28.4% vs. 25.0%).<sup>4</sup> In conclusion, for follow-up of patients with peripheral arterial disease, taking the highest leg artery pressure seems best, whereas the lowest leg artery pressure might be recommended when screening patients for peripheral arterial disease.

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

1. Grenon SM, Gagnon J, Hsiang Y. Ankle-brachial index for assessment of peripheral arterial disease. *N Engl J Med* 2009; 361(19):e40. (Available at NEJM.org.)
2. White C. Intermittent claudication. *N Engl J Med* 2007; 356:1241-50.
3. Hirsch AT, Haskal ZJ, Hertzner NR, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease); endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation* 2006;113(11):e463-e654.
4. Espinola-Klein C, Rupprecht HJ, Bickel C, et al. Different calculations of ankle-brachial index and their impact on cardiovascular risk prediction. *Circulation* 2008;118:961-7.

**TO THE EDITOR:** Grenon et al. emphasized the importance of calculating the ankle-brachial index in patients with peripheral arterial disease. The measurement method that they describe, which makes use of a Doppler probe and sphygmomanometer, is recommended as the reference method. However, the authors failed to mention the main limitation of this technique, which is its variability within and between observers.<sup>1,2</sup> We recently reported that this variability leads to marked center effects in multicenter studies, despite extensive staff training.<sup>3</sup> The center effect represented about 20% of the whole variability when the ankle-brachial index was considered as a continuous end point and about 10% of the whole variability when it was considered as a binary end point, whereas no center effect was observed for other clinical variables. Therefore, the statement by Grenon et al. that measurement of the ankle-brachial index with the use of Doppler probe and sphygmomanometer “can be used with versatility in the physician’s office” is probably too optimistic, since the variability we describe is reason to limit its routine use. An alternative that could be put forward to standardize measurement of the ankle-brachial index in primary care is the use of a semiautomated device, which would require little observer training and seems subject to less variability.<sup>3</sup>

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1. Nicolai SP, Kruidenier LM, Rouwet EV, Bartelink ML, Prins MH, Tejjink JA. Ankle brachial index measurement in primary care: are we doing it right? *Br J Gen Pract* 2009;59:422-7.
2. Richart T, Kuznetsova T, Wizner B, Struijker-Boudier HA, Staessen JA. Validation of automated oscillometric versus manual measurement of the ankle-brachial index. *Hypertens Res* 2009; 32:884-8.
3. Vierron E, Halimi JM, Tichet J, et al. Center effect on ankle-brachial index measurement when using the reference method (Doppler and manometer): results from a large cohort study. *Am J Hypertens* 2009;22:718-22.

**THE AUTHORS REPLY:** The standard method of reporting ankle-brachial indexes has always been to compare the highest systolic pressures from

the ankle and the arm.<sup>1</sup> Previous reports aimed at assessing the prognosis for patients with reduced ankle-brachial indexes have described different methods of calculation. One method takes the higher of the pressures for the dorsalis pedis and posterior tibial arteries in each leg, calculates the ankle-brachial index with the use of each measure, then uses the lowest of the two indexes calculated to predict prognosis.<sup>2</sup> Another method uses the mean of the pressures in the dorsalis pedis and posterior tibial arteries in each leg,<sup>3</sup> and still others suggest that for situations in which the pressures in the two pedal arteries are different, the lower value may be of benefit as well.<sup>4,5</sup> We agree with these observations.

However, the purpose of the video is to show the average practitioner a simple way of calculating the ankle-brachial index. The calculation used in the video is inaccurate about 10% of the time, which reflects the operator-dependent nature of even this simple procedure. With this in mind, if an average practitioner finds a difference in ankle-brachial indexes because of pressure differences in the two pedal arteries, it is more likely that

the lower result is a false positive, as there may be some difficulty in relocating the Doppler signal when flow is restored. Hence, the higher ankle-brachial index would still be the more accurate and useful result.

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1. Greenland P, Abrams J, Aurigemma GP, et al. Prevention Conference V: Beyond secondary prevention: identifying the high-risk patient for primary prevention: noninvasive tests of atherosclerotic burden: Writing Group III. *Circulation* 2000;101:E16-E22.
2. McKenna M, Wolfson S, Kuller L. The ratio of ankle and arm arterial pressure as an independent predictor of mortality. *Atherosclerosis* 1991;87:119-28.
3. McDermott MM, Tian L, Liu K, et al. Prognostic value of functional performance for mortality in patients with peripheral artery disease. *J Am Coll Cardiol* 2008;51:1482-9.
4. Schröder F, Diehm N, Kareem S, et al. A modified calculation of ankle-brachial pressure index is far more sensitive in the detection of peripheral arterial disease. *J Vasc Surg* 2006;44:531-6.
5. Espinola-Klein C, Rupprecht HJ, Bickel C, et al. Different calculations of ankle-brachial index and their impact on cardiovascular risk prediction. *Circulation* 2008;118:961-7.

## Transfusion of RhD-Positive Blood in “Asia Type” DEL Recipients

**TO THE EDITOR:** The RhD status of transfusion recipients and donors is routinely matched for red-cell transfusion. This worldwide practice is due to the potent immunogenicity of RhD. In East Asians, the frequency of RhD-negative status is only about 0.3%, which sharply limits the supply of RhD-negative blood. However, approximately 30% of RhD-negative persons carry an RhD variant, termed “Asia type” DEL.<sup>1</sup>

Beginning in 2008, my colleagues and I organized a collaborative group of 10 laboratories, located in 10 cities in northern, central, and southern China. This group retrospectively evaluated 104 RhD-negative pregnant women with anti-D alloantibodies from 2005 through 2007. We also tracked 199 consecutive RhD-negative pregnant women with a history of gestations or parturitions in 2008. Women who delivered an RhD-negative infant or received Rh immune globulin were excluded from the study. We distinguished Asia type

DEL through Rh C, c, E, and e phenotypes and DNA-based polymerase-chain-reaction assays or *RHD* sequencing.<sup>2,3</sup> In our retrospective study, we expected a DEL frequency of 0.30 among 104 pregnant women with documented anti-D alloimmunization. However, none of the 104 women expressed the DEL variant. In the second group, of the 199 RhD-negative women who were prospectively investigated for anti-D alloimmunization, 44 (22.1%) expressed the DEL variant. None of the carriers of this variant had anti-D antibodies, whereas such antibodies were detected in 38 of 155 truly RhD-negative women (24.5%) (relative risk of anti-D alloimmunization, 29.3).

The Asian type DEL displays the complete repertoire of RhD antigen epitopes.<sup>4</sup> Our study supports the biochemical observations that the DEL variants express normal RhD and pose virtually no risk of forming anti-RhD antibodies. We suggest that persons in East Asian populations who