component required for proof. Although the formal statistical boundary was conservative and evaluated only after accrual of ample data, the board elected to continue the trial for an additional 6 months after the boundary was crossed. Data that were accrued thereafter independently confirmed both the magnitude and statistical significance of the apparent benefit. We thus respectfully disagree with Pierard and Davis. The board appropriately protected the interests of society and the trial participants and provided a valid estimate of the treatment effect.[4]

The evaluation by Koller et al. ignores the significant reduction in death from any cause that we observed. If death from any cause is added to our primary composite outcome (a standard approach to account for competing risks), then the absolute risk difference increases and the number needed to treat declines.

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Obesity and Risk of Death

TO THE EDITOR: A challenging issue with the study reported on by Pischon et al. (Nov. 13 issue)[1] is where to measure the waist. The accepted standard for measuring the waist circumference put forth by the third National Health and Nutrition Examination Surveys (NHANES III) protocol,[2] as noted by Mahley in the *Williams Textbook of Endocrinology*,[3] is: "to measure waist circumference, locate the top of the right iliac crest. Place a measuring tape in a horizontal plane around the abdomen at the level of the iliac crest. Before reading the tape measure, ensure that the tape is snug but does not compress the skin and is parallel to the floor. Measurement is made at the end of a normal expiration." However, Pischon et al. report that in their study, "waist circumference was measured either at the narrowest circumference of the torso or at the midpoint between the lower ribs and the iliac crest." International acceptance of measurement tools is paramount.

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TO THE EDITOR: Pischon et al. support the use of waist circumference or waist-to-hip ratio in addition to body-mass index (BMI) in assessing the risk of death. Engeland et al. found that height is inversely associated with mortality among men and to some degree among women.[1] My recent study[2] and a meta-analysis,[3] both of which used cross-sectional data, provide support for the superiority of measures of central obesity — especially waist-to-height ratio — over BMI for discriminating the presence or absence of cardiologic and metabolic risk factors. Pischon et al. appropriately adjusted for height when calculating the mortality risk associated with anthropometric indexes. It would be helpful if the authors would determine the relative risk of death according to waist-to-height ratio and its comparison with other anthropometric data. For a fair comparison, height should not be adjusted for other studied anthropometric indexes.

Pischon et al. indicated that they observed no significant association between hip circumference and mortality risk. Larger hip circumference was shown to be an independent predictor of a lower mortality rate in a Swedish female cohort.[4] Did Pischon et al. confirm that?

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TO THE EDITOR: Pischon et al. show that assessment of abdominal obesity adds important information to BMI. However, the question as to how abdominal obesity should be measured still remains unanswered. We have previously shown that waist circumference and waist-to-height ratio are better indicators of prevalent conditions associated with cardiovascular risk than other variables.[1,2] To analyze the predictive value of these variables, we assessed mortality in pooled data from two cohort studies, Diabetes Cardiovascular Risk-Evaluation: Targets and Essential Data for Commitment of Treatment (DETECT)[2] and the Study of Health in Pomerania (SHIP),[3] which involved a total of 10,652 subjects, 55.9% of whom were women. The mean age (±SD) was 54.8±15.6 years, and the mean follow-up was 6.4±3.3 years. After multiple adjustments for confounders, comparing the fifth with the third quintile, only a high waist-to-height ratio was significantly associated with mortality in both men and women.

Even though our two studies were far smaller than the study conducted by Pischon et al., our results indicate that it is too early to generally recommend the use of waist circumference. Waist-to-height ratio is as easy to assess as waist circumference and might add more information. Moreover, if a general cutoff point is used, unlike waist-to-height ratio, waist circumference might underestimate the relative amount of abdominal fat in short subjects and overestimate it in tall subjects.

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THE AUTHORS REPLY: In the European Prospective Investigation into Cancer and Nutrition (EPIC), most centers followed the guidelines established by World Health Organization (WHO)[1] for measuring waist circumference (i.e., midway between the inferior margin of the last rib and the crest of the ilium, in a horizontal plane), while a few centers chose to measure waist circumference as the narrowest torso circumference. A recent systematic review[2] revealed that 30% of published studies on the association of waist circumference with health outcomes adopted the WHO recommendations and 27% adopted the method of measuring the narrowest torso circumference, whereas only 4% adopted the method described in the NHANES III protocol cited by Gaglione. In addition, the review indicated that the type of protocol adopted in these studies had no substantial influence on the association of waist circumference with health outcomes.[2]

As indicated by Can and by Schneider and colleagues, the waist-to-height ratio was proposed as a measure of abdominal adiposity that takes height directly into account.[3] We used BMI and waist circumference (or waist-to-hip ratio) to assess the degree of general and abdominal adiposity, respectively, and we adjusted our analysis for height. Within our study, waist-to-height ratio was correlated with BMI to a similar extent to that which we reported for waist circumference (Pearson partial-correlation coefficients, adjusted for age and study center, were 0.87 among men and 0.85 among women). Also, the overall results for the association with risk of death were similar to those derived from our calculation with the use of waist circumference. For example, the relative risk in the highest as compared with the lowest quintile of the waist-to-height ratio in the multivariable-adjusted model (including BMI) was 2.22 (95% confidence interval [CI], 1.94 to 2.55; P<0.001 for trend) among men and 2.03 (95% CI, 1.76 to 2.34; P<0.001 for trend) among women.

As Can indicated, hip circumference was associated with mortality in some studies; howev-

er, this association may depend on adjustments for other anthropometric variables. As we mentioned in our article, hip circumference was not significantly related to risk of death in the multivariable-adjusted model that also included BMI. The relative risk in the highest as compared with the lowest quintile was 1.02 (95% CI, 0.91 to 1.14; P=0.48 for trend) among men and 0.92 (95% CI, 0.80 to 1.06; P=0.53 for trend) among women.

We feel that our data support the use of waist circumference or waist-to-hip ratio as the most established anthropometric measures of abdominal adiposity in addition to BMI for the assessment of the risk of death in middle-aged and older persons.

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Pulmonary Complications of Sickle Cell Disease

TO THE EDITOR: In their review, Gladwin and Vichinsky (Nov. 20 issue)[1] list events that can precipitate acute pulmonary complications of sickle cell disease, but the inflammatory response after surgical procedures was not discussed. The very high incidence of postoperative complications in sickle cell disease has been assumed to be due to increased sickling.[2] However, limited data from humans exposed to severe acute and chronic hypoxia suggest that increased sickling does not invariably trigger vaso-occlusion.[3,4] No dose effect of the dilution or removal of sickle erythrocytes by means of aggressive transfusion was detected in one large study.[2] In the postoperative setting, chronic vascular inflammation may play a more prominent role than sickling.[3,4] Management with hyperoxygenation, aggressive hydration, and blood transfusion should therefore be reexamined.

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THE AUTHORS AND A COLLEAGUE REPLY: In response to Firth: we agree with the need for prospective, randomized trials involving patients with sickle cell disease who have undergone surgery. The Preoperative Transfusion Sickle Cell Study Group is the only prospective, randomized trial of a standardized perioperative protocol in sickle cell disease. The 1127 enrollees included 179 patients who had not received a transfusion and were followed in a registry. Since cholecystectomy was the most common surgery, it was used to compare the effects of transfusion with no transfusion on complication rates.[1] A total of 38% of the group of patients who had not received a transfusion had an acute sickle cell complication as compared with 12% of the aggressive-transfusion group and 18% of the conservative-transfusion group. Acute chest syndrome was twice as common in the patients who had not received a transfusion. The mortality in this group was 5% as compared with 0% in the transfusion groups. Our more recent prospective trials using preoperative transfusion protocols continue to provide support for its further use.[2] At present, the data support preoperative transfusion in patients with sickle cell disease who are undergoing major surgery, de-