out" and the potential impact on the primary end point (mostly due to changing guidelines and study design changes). While Gazi and Mikhailidis correctly state that there was a high incidence of dropouts, we should clarify that all subjects (including those who withdrew) were included in the final analysis. The authors ask if the substantial differential LDL cholesterol decrease of 29% between active and placebo groups could reflect active subjects taking a second statin. Of the 15% of atorvastatin-treated subjects taking concomitant lipid-lowering medications, the vast majority took an additional statin. However, considered on its own, this would not explain the 29% reduction in LDL cholesterol compared with placebo. Of the 26.9% of subjects in the placebo group who were taking concomitant lipid-lowering medications (mostly statins), 19.7% took them for ≥30 days. It is likely more important that 42% of subjects with cardiovascular events in the atorvastatin group had stopped their randomized medication >1 year before their event.

We agree that lower blood pressure, as well as lower baseline LDL cholesterol, younger age, lower smoking rates, and a smaller proportion of men combined to place primary prevention subjects in the ASPEN at lower CVD risk than those in the Collaborative Atorvastatin Diabetes Study (3). Despite this apparent lower risk, a greater incidence of cardiovascular events was observed in placebo-treated primary prevention subjects in ASPEN (10.8%) than in CARDS (9.0%), indicating inclusion of "softer" end points, such as hospitalization for angina pectoris and interventions. Nonetheless, trends in CVD event reduction with atorvastatin were at the expected rates for the fatal and nonfatal myocardial infarction end point and in the secondary prevention cohort (2).

The subjects in the secondary prevention group entered the study before the primary prevention group. Secondary prevention subjects would have remained in the study longer were it not for the Safety and Data Monitoring Board recommendation late in the study to stop the study drug in the secondary prevention cohort and begin active treatment. As a result, the durations of follow-up were similar: 4.50 and 4.38 years for secondary versus primary prevention subjects taking atorvastatin and 4.38 and 4.46 years, respectively, for those taking placebo.

The nonsignificance of the ASPEN results has many possible explanations. Nonetheless, the ASPEN study reminds us that the many risk factors for heart disease in diabetes require individualized management for a complete treatment approach.

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R.H.K. has served on an advisory board for, has received honoraria from, and has received grant/research support from Pfizer.

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Prediction of Diabetic Foot Ulcer Occurrence Using Commonly Available Clinical Information

Response to Boyko et al.

In their article, Boyko et al. (1) describe a foot ulcer prediction tool that will be useful in practice, as it is based on simple clinical criteria. The tool is well validated but limited by the patients examined, who were predominantly male (98%), mainly with type 2 diabetes, and were recruited from a hospital diabetes clinic. We have already addressed these problems in a previous publication (2) using a similar, clinically focused foot ulcer prediction tool (3) that included many of the criteria recommended by the International Working Group on the Diabetic Foot (4). Our grading scheme categorized 3,526 patients into low, moderate, or high risk of ulceration. High-risk patients "were 83 times more likely to ulcerate than low risk" patients, and the chance of "low-risk" patients remaining ulcer-free after 2.4 years was 99.7% (2). This tool was valid for type 1 and type 2 diabetic male and female subjects in a population-based cohort. Such foot ulcer prediction tools are thus useful for "all-comers" in a general community setting, as well as in specialized hospital clinics.

Boyko et al. also raised the issue that patients at high risk of ulceration may be at increased risk of death. We demonstrated that the crude mortality rate for high-risk patients was 19.1% compared with 3.4% for low-risk patients (2). Thus, high risk of ulceration is associated with increased death rate as suspected by Boyko et al., which may result in an underestimation of the predictive value of these clinical tools, as patients may die before they develop foot ulcers.

These two studies complement each other by demonstrating that the overall foot ulcer risk assessment is greater than any individual criteria (1) and that the tool is valid in routine clinical practice for all patients in the community (2) and specialized centers (1,2). Foot ulcer prediction tools may be useful in directing educational initiatives and scarce health care resources to those at greatest need.

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Prediction of Diabetic Foot Ulcer Occurrence Using Commonly Available Clinical Information

Response to Leese and Morris

We appreciate the interest of Leese and Morris (1) in our article and enjoyed reading their publication (2), which was published 1 month before our own and hence was not cited by us (3). We wish to point out that their characterization of our population as having been "recruited from a hospital diabetes clinic" is not correct, as we clearly describe that our subjects were recruited from a general internal medicine clinic (3). With regard to the generalizability of our findings, they should be applicable to the ~25 million U.S. veterans and other males with similar clinical and demographic characteristics enrolled in a primary care setting. Although Leese and Morris write that they have "already addressed" foot ulcer prediction in their publication, they do not cite our publication from 1999, which presented a prediction model for diabetic foot ulcer and anticipated several of the findings of our recent article (4).

Leese and Morris describe their findings as useful for "all-comers" in a general community setting and in specialized clinics; they also suggest that their findings are valid for male and female subjects and for both types of diabetes (1). However, their data and analysis do not provide strong support for these statements for several reasons. First, although they used a population-sampling strategy that targeted 8,923 subjects with diabetes, only 3,526 (40%) underwent a clinical foot risk assessment. Thus, most subjects in the sampling frame were not included in the analysis, which certainly raises concerns regarding the validity of findings and limits the degree of confidence with which one can recommend these results for "all-comers." Second, although both sexes and diabetes types were included in their study, the appropriate analysis of interaction to determine whether the results apply similarly in these subgroups of interest was not performed.

Leese and Morris bring up the issue of competing risks, in that individuals at higher risk for diabetic foot ulcer are also at higher risk for death. They refer to our "suspicion" that the death rate in people at high risk for ulcer is increased, but this would not be our preferred wording, as we feel certain about this association, having published data reporting this finding in 1996 (5). Comparison of cumulative risks, as in their report, may thus lead to biased results due to differential follow-up times by degree of risk. Fortunately, analytic methods that compare failure times and employ censoring, which we used in our recent publication, can address this problem.

Hopefully these recent efforts to develop foot ulcer prediction models and others will lead to more accurate identification of individuals at higher risk of foot ulcer and stimulate the development of better preventive strategies to reduce morbidity and mortality from these complications.

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Standards of Medical Care in Diabetes–2006

Response to the American Diabetes Association

I recently encountered a discrepancy in the American Diabetes Association's (ADA's) recommendations regarding conventional versus SI units for HDL cholesterol (1). The article states "raise HDL cholesterol to >40 mg/dl (1.15 mmol/l)." Simple calculation shows that 40 mg/dl = 40 × 0.02586 mmol/l = 1.03 mmol/l, rather than 1.15 mmol/l. The same error is also noted in the 2005 version.

Furthermore, in regard to the ADA's recommendation to use statin therapy for diabetic patients without overt cardiovascular disease (CVD), the recommendation to treat "regardless of baseline LDL" might have extended beyond the evidence quoted. I find the recommendation's evidence rather weak, despite a similar recommendation elsewhere (2). For evidence on diabetic patients without overt cardiovascular problems, two studies are listed (3,4). Here is an abbreviated synopsis:

The Heart Protection Study (3) showed cardiovascular benefit of statin therapy for LDL >3.0 mmol/l similar to