persons with diabetes.[2] We therefore do not recommend CACS screening for patients with diabetes.

We agree with Dr Pletcher and colleagues that the results of our study address only the circumstances of individuals at intermediate risk, and that larger studies of individuals at lower risk are needed to assess potential benefit in such individuals. We also agree that the use of a relatively expensive test such as CAC screening is unlikely to be cost beneficial in individuals at low risk. Pletcher et al suggest that we include ethnicity as a covariate in our analyses. We conducted these analyses, and both ROC areas and Cox regression results remained the same. They also recommend that we normalize the distribution of CACS by using log CAC scores in the model. The predicted event rates using log CAC scores, displayed in the figure, give similar but more striking results. In particular, the CACS significantly improved risk prediction in all categories of the FRS greater than or equal to 10%, but now also in the category less than 10%. Log transformation does not change the rank order of the calcium scores, and thus the ROC areas remain identical, showing better discrimination for the model including CACS. This further supports our conclusion that calcium score can be used effectively to provide valuable prognostic information in individuals at intermediate risk.

We also agree with Pletcher et al that both the FRS and the CACS performed relatively poorly in our cohort. We suggested in our article that this might have been partly due to the relatively narrow age range (>47 years) and the exclusion of individuals with diabetes.

We disagree with a number of the statements of Dr Budoff and colleagues. First, their remark that our cohort "was largely (89%) a population of elderly white men" is incorrect. Only 38% of our cohort were elderly (ie, older than 65 years) white men. Furthermore, the median FRS in our cohort falls within the intermediate range of FRS as defined by the National Cholesterol Education Program.[3] Cohorts in most of the studies that Budoff et al cite were at considerably lower risk and therefore of much less clinical interest. Budoff et al further incorrectly state that we used a minimum lesion size of 8 mm^3 to define loci of calcification. In fact, we indicated that the scoring method used was "identical to that used for the Multi-Ethnic Study of Atherosclerosis (MESA)." In both our study and the MESA study, the minimum lesion size is 5 mm^3. Furthermore, this minimum lesion size and the minimum lesion size in the reports that Budoff et al cite are larger than that originally reported by Agatston.

Budoff et al suggest that our use of 6-mm–thick image slices was responsible for our finding of subsequent CHD events in participants without coronary calcium. We have published a report comparing our 6-mm slice protocol with that used by Budoff et al for commercial scanning.[4] This study involved a subset of our cohort who were scanned with both the 6-mm and 3-mm image slices and followed up for 7.5 years. We found the same hazard ratios, the same ROC areas, and the same prevalence of CHD events in those with zero scores using both 6-mm and 3-mm scans.

We also point out that risk factors in all individuals in the cohort were measured. In contrast, all other reported studies of CACS and "risk factors" are based on self-reported risk factors. Variability and imprecision arising from self-reported risk factors is undoubtedly much greater than that which might have resulted from the use of 6-mm slices.[5] We believe that the most reasonable interpretation is that previous reports have overestimated the predictive value of CACS compared with "risk factors," and that the value of risk factors for prediction in those studies is highly underestimated due to misclassification.

Finally, regarding the insistence on use of electron beam tomography rather than simply CT, the purpose of the "Methods" section is to provide sufficient detail to allow others to replicate our study, and we have done so. Use of the term "computed tomography" or "CT" is entirely accurate. Comparison of various brands of CT scanner is a marketing issue that is not germane to our investigation and its conclusions.

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Inflammation, Cholesterol Levels, and Risk of Mortality Among Patients Receiving Dialysis

To the Editor: Dr Liu and colleagues[1] reported that among patients receiving dialysis, cholesterol levels and mortality were inversely associated among patients with chronic inflammation but were positively associated in those without inflammation. The authors concluded that inverse relationships between cholesterol and mortality in previous studies of this

population are due to the cholesterol-lowering effect of malnutrition and systemic inflammation, rather than to a protective effect of high cholesterol levels. However, there is considerable epidemiologic, clinical, and laboratory evidence that high cholesterol levels protect against infections, while low cholesterol levels predispose to infections.[2]

For instance, in a 15-year follow-up study of more than 100 000 healthy individuals, cholesterol levels were inversely associated with the risk of being admitted to the hospital with a diagnosis of infectious disease.[3] Evidently, low cholesterol levels analyzed at baseline could not have been caused by a disease these individuals had not yet acquired. Children with Smith-Lemli-Opitz syndrome have extremely low cholesterol levels and experience frequent and severe infections, which can be prevented with supplementary dietary cholesterol.[4]

Numerous experimental studies have demonstrated an important role of low-density lipoprotein cholesterol (LDL-C) as an effective inhibitor of bacterial toxins. For instance, the survival of rats with experimental hypolipidemia challenged with lipopolysaccharide or gram-negative bacteria is much lower, and the survival of mice with familial hypercholesterolemia challenged similarly is much higher than normal.[5]

Finally, in at least 7 studies of people aged 60 and older, total mortality was inversely associated with cholesterol levels, or high cholesterol levels were associated with longevity.[2]

Therefore, if statin treatment should be used in dialysis patients, it may be wise to use the lowest possible dose, if any at all.

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To the Editor: We are concerned that the sample of Dr Liu and colleagues[1] may not be representative of US patients who receive dialysis. The median age of patients receiving incident dialysis in the United States is 64.5 years,[2] whereas in the study by Liu et al it was 57.2 years for all patients and 53.7 years for those without malnutrition-inflammation complex syndrome (MICS). The renal transplant rate in the US dialysis population is approximately 5.5 per 100 patient-years.[2] One would thus expect 103 in the cohort of Liu et al, but this is substantially fewer than the 153 the authors reported. Hence, the younger age and the higher transplant rate in this study indicate a dialysis population that is substantially healthier than average.

The authors stated that their findings support aggressive treatment of hypercholesterolemia in patients receiving dialysis. We disagree with this conclusion, as the authors' own analyses in the subgroup of patients with MICS, who comprise 75% of all patients of the study, indicate either inverse or no association between total serum cholesterol levels and outcome, even after adjustments for MICS. These findings indicate a strong association between elements of malnutrition-inflammation and prospective mortality in patients undergoing dialysis. Hence, the treatment of MICS may have a higher priority than treatment of hypercholesterolemia or other conventional cardiovascular risk factors in patients receiving dialysis.[3]

Moreover, it is possible that decreasing serum cholesterol levels in these patients is harmful, since the lipoprotein pool may serve as an effective scavenger to bind with and neutralize the circulating lipopolysaccharides (ie, bacterial endotoxin) in patients with heart failure and fluid overload,[4] a common condition in patients receiving dialysis. Low levels of serum lipoproteins, including cholesterol, may be associated with increased levels of unbound circulating lipopolysaccharides and a higher prevalence of inflammation and cachexia.[4,5] To our knowledge, there are few published studies suggesting that high cholesterol levels and obesity are related to impaired survival among patients with chronic illness. Therefore we caution against the authors' use of the term "spurious" for the paradoxically inverse associations that have been consistently observed between such conventional risk factors as hypercholesterolemia and obesity and improved survival in patients receiving maintenance dialysis.

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In Reply: Dr Ravnskov and Drs Kalantar-Zadeh and Anker argue that high cholesterol levels may confer protection against infection and circulating lipopolysaccharides (ie, bacterial endotoxin) and that hypercholesterolemia should not be treated among patients receiving dialysis. Ravnskov cites the protective effects of dietary cholesterol supplementation in children with Smith-Lemli-Opitz syndrome, in whom cholesterol levels are extremely low (approximately 8-62 mg/dL [0.21-1.61 mmol/L]), as well as epidemiologic findings that low total cho-