Item S1. Risk of Reporting Bias and Bayesian Analyses for Frequent Hemodialysis Network Nocturnal Study

As described in the Methods, the sample size and follow-up period of the Frequent Hemodialysis Network Nocturnal Trial were not sufficient to provide a well-powered comparison of mortality between the nocturnal and conventional dialysis treatment interventions. In addition, we had not hypothesized that the treatment interventions would have persisting effects on mortality following the termination of the treatment phase of the trial. In this situation, the only possible way in which a p-value smaller than 0.05 could be obtained for the mortality comparison is for the observed treatment difference to have been substantially greater than expected during the design of the trial. Thus, the fact that we have provided this detailed report of the long-term treatment effect on mortality was contingent on the occurrence of a highly unexpected result. In this situation, there is a substantial risk that the deviation of the observed treatment effect from the null hypothesis is partly or fully due to random variation rather than a true effect of the treatment.

We have complemented the standard survival analysis presentation comparing mortality between the treatment groups with a set of Bayesian analyses to help with interpretation. The Bayesian approach provides a mathematically rigorous way to determine the implications of the data in the context of an assumed *prior distribution* that reflects a range of treatment effects that would be viewed as plausible in the absence of the data from the present trial, with treatment effects viewed as more likely being given more weight than treatment effects viewed as less likely. Under the Bayesian framework, the study's standard estimated hazard ratio (HR) of 3.88 and 95% confidence interval of 1.27-11.79 reflect a prior distribution in which all HRs between 0 and $+\infty$ are equally likely on the logarithmic scale. Because few treatments evaluated in

clinical trials actually have extreme HRs substantially below or substantially greater than 1, this prior distribution may be unrealistic, and lead to implausible estimates of HRs when random extreme results are observed in the data.

By contrast, the prior distributions labeled as "conservative" or "enthusiastic" displayed in Figure 4 correspond to two different perspectives in which highly extreme HRs are unlikely. These two prior distributions were chosen to reflect the authors' interpretation of a conservative perspective, in which beneficial and harmful effects of the intervention are equally likely, and an enthusiastic perspective, in which a beneficial effect is likely and a substantial adverse effect is highly unlikely. The posterior distributions displayed in the two panels of the figure depict the probabilities that the true HRs fall into different ranges given the observed data in the context of these two prior distributions. As would be expected, the posterior distributions are consistent with HRs considerably closer to 1 than the observed HR of 3.88.