1. Mehta RL, Pascual MT, Soroko S, Chertow GM, for the PICARD Study Group. Diuretics, mortality, and nonrecovery of renal function in acute renal failure. *JAMA.* 2002;288:2547-2553.
2. Thadhani R, Pascual M, Bonventre JV. Acute renal failure. *N Engl J Med.* 1996; 334:1448-1460.
3. Shilliday IR, Quinn KJ, Allison ME. Loop diuretics in the management of acute renal failure: a prospective, double-blind, placebo-controlled, randomized study. *Nephrol Dial Transplant.* 1997;12:2592-2596.

To the Editor: Dr Mehta and colleagues[1] failed to adjust for many of the significant differences between patients who did and did not receive diuretics. While the authors use a propensity score designed to adjust for some differences, they did not include acute cardiac failure and physiological indicators of advanced cardiac dysfunction (ie, lower cardiac output and cardiac index, higher pulmonary artery wedge pressure, and higher systemic vascular resistance in the diuretic group) into this model or the multivariate logistic regression; they include only the heart rate (not different between the groups) in the latter. The inclusion of the history of heart failure in the statistical models does not adjust for other or more acute cardiac factors that may have had a significant effect on both diuretic use and mortality.

The authors use 2 different APACHE scoring systems to document that the groups had a similar severity of illness and consequently similar risk of death. This is problematic since these scores are disease-specific and adjustment is necessary for case mix,[2] which was not done in this study.

Patients with a higher pulmonary artery wedge pressure and a lower cardiac index were more likely to receive a diuretic, but may also have been more likely to die, since they included a significant number of patients with cardiogenic pulmonary edema (mean pulmonary artery wedge pressure of 20 mm Hg in association with lower cardiac output and cardiac index, and higher systemic vascular resistance in the diuretic group) and advanced cardiac disease (use of a pulmonary artery catheter and treatment in an intensive care unit). The association between death and decreased response to diuretics suggests that cardiac factors may be responsible, since no amount of diuretic can increase the production of urine by kidneys that are not perfused.

It is possible that the disease itself, not the use of diuretics, was mostly responsible for poor recovery of renal function and death. In fact, a significant lowering of APACHE III scores in the diuretic group suggests the possibility of a decrease in mortality in the subgroup of patients who did respond to such an intervention.

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1. Mehta RL, Pascual MT, Soroko S, Chertow GM, for the PICARD Study Group. Diuretics, mortality, and nonrecovery of renal function in acute renal failure. *JAMA.* 2002;288:2547-2553.
2. Pappachan JV, Millar B, Bennett ED, Smith GB. Comparison of outcome from intensive care admission after adjustment for case mix by the APACHE III prognostic system. *Chest.* 1999;115:802-810.

To the Editor: Dr Mehta and colleagues[1] concluded that the use of diuretics in critically ill patients with ARF is associated with a poor outcome. Even though the authors indicate that observational data prohibit causal inference, they argue that in the absence of compelling contradictory data from clinical trials, the widespread use of diuretics in critically ill patients with ARF should be discouraged. This conclusion, however, may be flawed since the methods used by the authors do not regard the epidemiological theory of causality.

The choice of diuretic use in a critically ill patient is almost invariably a consequence, and not a cause, of the degree of the severity of the clinical picture, such as existence or lack of oligoanuria or electrolyte disarrays. The decision to administer diuretics is guided by the clinical status of the patient and is based on the assessment of a physician who usually has sound knowledge and expertise in the evaluation and prognosis of critically ill patients with ARF. The element of chance does not play any role in this assignment.

Since a poor outcome such as death is also a direct consequence of the degree of severity of clinical status of the patient at the time of presentation, both diuretic use and poor outcome are likely independent consequences of a single underlying cause. The use of multivariate statistics cannot resolve such flaws in the causal model of this observational study. The only conclusion that can be inferred from this study is that patients whose ARF has been assessed by a physician to be so severe to require diuretic use have a poor outcome.

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1. Mehta RL, Pascual MT, Soroko S, Chertow GM, for the PICARD Study Group. Diuretics, mortality, and nonrecovery of renal function in acute renal failure. *JAMA.* 2002;288:2547-2553.

In Reply: Dr Emmett highlights the important point that odds ratios and relative risks are not equivalent, or nearly so, when the outcomes of interest in a cohort study are not rare. Using the equation of Zhang and Yu,[1] the relative risks (diuretic use vs nonuse on the first day of consultation) of in-hospital mortality and death or nonrecovery were 1.25 and 1.36, respectively.

Dr Tedesco is correct that the study sample was limited to those patients in whom nephrology consultation was requested. It is possible (probable, in fact) that consultation was not requested for some patients with rapid recovery of renal function. We stated that the results cannot be extrapolated to other clinical settings (including among individuals with more mild forms of ARF), although ARF prevention studies also suggest no benefit to diuretic therapy.[2]

Dr Unnikrishnan and colleagues are correct that the increase in mortality seen among patients treated with diuretics was restricted to those who were relatively unresponsive to diuretics, as assessed by a furosemide dose equivalent per milliliter of urine output per day of 0.5 or more. Figure 2 demonstrates the composite end point of time to death or provision of dialysis, not just the time to death. It is worth emphasizing that those individuals who responded more briskly to diuret-