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# Reverse epidemiology of blood pressure in dialysis patients

**To the Editor:** Agarwal implies that the paradoxical associations found between higher blood pressure (BP) values and better survival are limited to prevalent dialysis patients [1]. We recently studied a 15-month cohort of 40,933 hemodialysis patients and found that high predialysis systolic BP conferred survival advantages even after adjustment for dialysis vintage categories, among others [2]. Shoji *et al* showed that intradialysis hypotension and orthostatic hypotension after hemodialysis are significant and independent factors affecting mortality in hemodialysis patients [3]. A recent study by Lopez-Gomez *et al* showed that a high predialysis BP was frequently observed in those hemodialysis patients who had the highest interdialytic weight gain, increased food intake, better nutritional status, and improved clinical outcome, including better survival [4]. Hence, we caution against categorical dismissal of the reverse epidemiology of BP, only because they appear counterintuitive based on observations from the general population. Indeed, the reverse epidemiology is not restricted to BP, but has also been observed with regard to obesity, hypercholesterolemia, and hyperhomocysteinemia, among others [5].

Moreover, the reverse epidemiology is not restricted to dialysis patients but may also exist in over 20 million Americans, including patients with heart failure, advanced age, malignancies, AIDS, and several other chronic disease states [5]. Therefore, we believe that the reverse epidemiology phenomenon deserves a more global and inclusive point of view. Further studies are needed to explore mechanisms behind such paradoxical associations, and to assess what BP range is the best for dialysis patients. Examining methods to improve nutritional status and inflammation in dialysis and other similar patient populations may be a crucial step to that direction.

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## Reply from the Authors

Many of the answers that explain the paradoxical association between low blood pressure (BP) and high mortality lie within the studies that Kalantar-Zadeh *et al* cite. First, the large study they have performed has only a two-year follow-up, which may be insufficient to reveal hypertension as a risk factor for cardiovascular disease [1]. Correction for the dialysis vintage does not remove the bias that exists in a prevalent cohort study; antihypertensive drug use or cardiovascular disease, especially heart failure, have not been considered when studying the impact of BP on total mortality. For example, patients with heart failure may have a greater mortality despite a lower BP compared to patients without heart failure on hemodialysis [2]. A relationship between good nutrition and hypertension suggests that favorable clinical characteristics are associated with a higher BP, but does not suggest that lowering BP or limiting sodium intake in those with hypertension is associated with worse outcomes [3]. Shoji *et al* relate intradialytic—not interdialytic—hypotension as a risk factor for mortality [4]. Epidemiology helps us understand the nature and scope of the problem. Causality cannot be deduced from paradoxically relating low BP to increased mortality. The correlation of lower BP with short-term mortality may simply be a reflection of a higher level of sickness. Controlling hypertension is protective in long-term cohort studies [5], and in studies that examine the influence of systolic hypertension on cardiovascular events rather than total mortality [6]. Hence, lowering BP through nonpharmacologic and pharmacologic means should be a key element of management of