1. Schuller JL, Varosy PD, Nguyen DT. Wide complex tachycardia and adenosine. *JAMA Intern Med*. 2013;173(17):1644-1646.

2. Lee KL, Tai YT. Adenosine in wide complex tachycardia: potential pitfalls in diagnostic value. *Ann Emerg Med*. 1994;24(4):741-747.

3. Lerman BB, Stein KM, Markowitz SM. Adenosine-sensitive ventricular tachycardia: a conceptual approach. *J Cardiovasc Electrophysiol*. 1996;7(6):559-569.

4. Wilber DJ, Baerman J, Olshansky B, Kall J, Kopp D. Adenosine-sensitive ventricular tachycardia: clinical characteristics and response to catheter ablation. *Circulation*. 1993;87(1):126-134.

5. Neumar RW, Otto CW, Link MS, et al; American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 8: adult advanced cardiovascular life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(18)(suppl 3):S729-S767.

In Reply We are in agreement that adenosine-sensitive ventricular tachycardia (VT) is a possibility. Various idiopathic VTs, including outflow tract and fascicular VTs, can terminate with adenosine administration.[1] Hence, termination of the tachycardia with adenosine alone would not be diagnostic, and other considerations, including the electrocardiogram and clinical situation, should be taken into account to help make the diagnosis. Finally, if an atrial arrhythmia continued without ventricular conduction due to atrioventricular block secondary to adenosine use, this would be confirmation of supraventricular tachycardia.

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1. Badhwar N, Scheinman MM. Idiopathic ventricular tachycardia: diagnosis and management. *Curr Probl Cardiol*. 2007;32(1):7-43.

Angiotensin-Converting Enzyme Inhibitor or Angiotensin Receptor Blocker Use and Renal Outcomes: Prevalent User Designs May Overestimate Benefit

To the Editor The recent study by Hsu et al[1] regarding the renoprotective effect of renin-angiotensin-aldosterone system blockade in patients with predialysis advanced chronic kidney disease, hypertension, and anemia is important but we believe that the findings should be interpreted with caution.

According to the way that angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (ACEI/ARB) users were defined, people who had taken and then ceased ACEI/ARB therapy prior to the first erythropoiesis-stimulating agent (ESA) prescription would have been classified as nonusers. For a proportion of these participants, ACEI/ARB therapy may have been stopped for safety reasons, for example, to attempt to delay dialysis treatment.[2] Indeed, 25% of those defined as nonusers received a prescription for ACEI/ARB in the 90 days prior to the first ESA prescription, and many "nonusers" had clear indications for ACEI/ARB therapy. This study design could create differential misclassification where those defined as ACEI/ARB users were more likely to have better kidney function or slower decline than those defined as nonusers. A "new user" design including all patients who initiate ACEI/ARB therapy rather than prevalent users may have led to less bias and provided a more balanced comparison.[3]

To draw an analogy, in a study of car driving and mortality risk among people 80 years and older, based on the design used by Hsu et al,[1] we would classify people who do not currently drive as nondrivers, even if they had stopped driving in their 70s. Many of the people who had stopped driving in their 70s would have done so because of failing health and increased frailty. This group will, of course, be at high risk of dying. The study will find that driving is associated with marked survival benefits and might lead us to advocate driving as a way of living longer. The reality is that as people approach death they often decide it is time to stop driving. A better design would be to start observing people from when they commenced driving.

Although the authors used a propensity score analysis to try and ensure comparability between the groups, this cannot compensate for unmeasured confounders, such as rate of change of kidney function.[4]

The authors conclude that "withholding ACEI/ARB therapy is unwarranted and may hasten the onset of ESRD [end-stage renal disease]."[1(p353)] We believe that the findings of this study are interesting but should not provide false reassurance about the effectiveness and safety of ACEI/ARB use in advanced chronic kidney disease.

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1. Hsu TW, Liu JS, Hung SC, et al. Renoprotective effect of renin-angiotensin-aldosterone system blockade in patients with predialysis advanced chronic kidney disease, hypertension, and anemia. *JAMA Intern Med*. 2014;174(3):347-354.

2. Ahmed AK, Kamath NS, El Kossi M, El Nahas AM. The impact of stopping inhibitors of the renin-angiotensin system in patients with advanced chronic kidney disease. *Nephrol Dial Transplant*. 2010;25(12):3977-3982.

3. Ray WA. Evaluating medication effects outside of clinical trials: new-user designs. *Am J Epidemiol*. 2003;158(9):915-920.

4. Glynn RJ, Schneeweiss S, Stürmer T. Indications for propensity scores and review of their use in pharmacoepidemiology. *Basic Clin Pharmacol Toxicol*. 2006;98(3):253-259.

In Reply We appreciate the comments of Tomlinson and Smeeth concerning that the differential misclassification would tend to bias our results toward favoring angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (ACEI/ARB) use in patients with predialysis advanced chronic kidney disease, hypertension, and anemia. We performed additional analyses to address the question raised in the letter. However, their speculation is not evidenced by the further analysis from our cohort.

To minimize the possibility of misclassification of those who had taken and then, for safety reasons, ceased ACEI/ARB therapy prior to the first erythropoiesis-stimulating agent (ESA) prescription as nonusers, we redefined the nonusers (the referent group) as those who have not ever been treated with an ACEI/ARB up to 3 months and 6 months before commencing ESA therapy, respectively. Our data showed that the adjusted hazard ratios (95% CIs) of chronic dialysis in ACEI/ARB users were 0.94 (0.91-0.97) and 0.95 (0.92-0.98), respectively, and of dialysis or death, 0.94 (0.91-0.96) and 0.95 (0.92-0.98), respectively. Similar results could also be observed in the multivariable models further adjusted for the propensity score. The serial sensitivity analyses suggest our previously published data[1] that the hazard ratio of long-term dialysis or death for the ACEI or ARB users was 0.94 compared with nonusers was an unbiased estimate.

We acknowledge the "new user" design[2] is a good method for pharmaco-epidemiological research. However, it may not be applicable to our study. In fact, the number of new ACEI or ARB users who had never used an ACEI or ARB at least 6 months prior to the first ESA prescription was only 1159 (8.2% of total ACEI or ARB users[1]) in our cohort. The sample size was too small to secure a sufficient statistical power for the study. Few patients with advanced chronic kidney disease were also recognized to improve their renal function by stopping ACEI or ARB therapy in our study,[1] and it has been mentioned in the small-scale observational study by Ahmed et al.[3] However, our study and the study by Ahmed et al[3] are not comparable and have differences in case number (28 497 vs 52), median follow-up period (7 vs 30 months) and study outcomes (70.7% dialysis and 20.0% death vs 9.6% dialysis and 9.6% death). Obviously, the medical conditions in our cohort were much complex, indicating the beneficial impact of stopping ACEI/ARB therapy observed in the study by Ahmed et al[3] is not generalizable to our study population.

In conclusion, we are confident in the validity of our study, and we also believe the observational study using a representative national database is one of the most feasible study designs for the predialysis hypertensive patients with advanced CKD. The implication of our study is to reassure that the renoprotective effect of ACEI/ARB use still exists in predialysis patients with advanced chronic kidney disease and "withholding ACEI/ARB therapy is unwarranted" for patients with advanced CKD unless indicated by clinical evidence.

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1. Hsu TW, Liu JS, Hung SC, et al. Renoprotective effect of renin-angiotensin-aldosterone system blockade in patients with predialysis advanced chronic kidney disease, hypertension, and anemia. *JAMA Intern Med*. 2014;174(3):347-354.

2. Ray WA. Evaluating medication effects outside of clinical trials: new-user designs. *Am J Epidemiol*. 2003;158(9):915-920.

3. Ahmed AK, Kamath NS, El Kossi M, El Nahas AM. The impact of stopping inhibitors of the renin-angiotensin system in patients with advanced chronic kidney disease. *Nephrol Dial Transplant*. 2010;25(12):3977-3982.

Improving Medication Adherence and Helping Patients Make Lifestyle Changes

To the Editor In the study by Cohen et al,[1] the authors report no improvement in cardiovascular risk factors when dietician or nurse-led education was provided to patients following acute coronary syndrome (ACS) compared with usual care. This study represents an alternative approach to standard educational interventions that could be provided through clinic-based cardiac rehabilitation (CR) following ACS.

Another major factor to consider when modifying CR services is medication adherence, as improvements in this behavior may predict further success with other, more complex lifestyle changes.[2] In general, an adequate focus on medication adherence has only been achieved by more intense CR programs requiring a longer schedule of visits.[2] The study by Cohen et al[1] appeared to have a sufficient level of intensity and patient contact such that a pharmacist could have been included in order to assess and promote medication adherence.

As reported by Cohen et al,[1] it appears that medication adherence in the study was high; however, they did not report the percentage of patients stopping all guideline-recommended medications. Only percentages for individual medications are presented, and this is an unusual and inadequate measurement for reporting medication adherence.[3] Ho et al[4] demonstrated that patients who stop using all medications by 1 month after discharge are 10% more likely to have died during the 12 months following ACS. Given the 12-month time frame of the study by Cohen et al[1] and the multiple visits required in the intervention, we would have been interested to see more emphasis placed on additional measures of medication adherence and interventions seeking to improve it. We are currently conducting a study investigating the impact on medication adherence from pharmacist home visits following ACS to help address this issue.[5]

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Conflict of Interest Disclosures: None reported.

1. Cohen A, Assyag P, Boyer-Chatenet L, et al; Réseau Insuffisance Cardiaque (RESICARD) PREVENTION Investigators. An education program for risk factor management after an acute coronary syndrome: a randomized clinical trial. *JAMA Intern Med*. 2014;174(1):40-48.