

See related Letters to the Editor, "Confounding of Race/Ethnicity and Age in the Survival among Veterans Obtaining Dialysis in VA and Non-VA Settings," on page 1337.

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## The Case for Selective Withdrawal of Antidepressants in Patients with Advanced Kidney Disease

We read with interest "Comparative cardiac safety of selective serotonin reuptake inhibitors among individuals receiving maintenance hemodialysis" by Assimon *et al.*<sup>1</sup> This large retrospective analysis found that patients on hemodialysis who initiated selective serotonin reuptake inhibitors (SSRIs) with higher QT-prolonging potential (citalopram and escitalopram) had a significantly increased risk of sudden cardiac death (adjusted hazard ratio, 1.18; 95% confidence interval, 1.05 to 1.31) compared with patients who initiated SSRIs with lower QT-prolonging potential (fluoxetine, fluvoxamine, paroxetine, and sertraline). Given the lack of evidence regarding the efficacy of SSRIs for major depressive disorder in patients with advanced kidney disease and the prevalence of premature cardiovascular mortality in this setting, the findings of Assimon *et al.*<sup>1</sup> raise important questions about the use of these agents in this context.

Depression is a common comorbidity among patients with advanced kidney disease,<sup>2</sup> although diagnosis is complicated by the overlap of clinical features of these two conditions. Notwithstanding this, depression in this setting is associated

with adverse clinical outcomes, including increased mortality risk.<sup>3</sup> It is far from clear, however, whether the association is independent of antidepressant use. Three randomized, placebo-controlled trials of SSRIs in individuals with kidney disease<sup>4–6</sup> have failed to provide evidence of benefit while signposting increased risks of adverse events (reviewed in ref. 7). A recent randomized trial comparing sertraline with cognitive behavioral therapy in patients on dialysis showed a modest difference in favor of sertraline,<sup>8</sup> although there was no control group.

We appreciate that additional randomized, controlled trials are needed in this area and that the study of Assimon *et al.*<sup>1</sup> is not able to provide evidence for the absolute mortality risk associated with antidepressant use. However, we feel that there is a real possibility that, in some patients at least, these agents may be doing more harm than good. Hence, it may be appropriate to consider whether withdrawing antidepressants in suitable patients may be the appropriate strategy. Withdrawal could mean withdrawing one agent and switching to another, withdrawing and switching to a psychological treatment, or stopping all together. Antidepressant withdrawal requires careful risk assessment, patient education and counseling, and a considered tapering regimen to mitigate symptoms of withdrawal.<sup>9</sup> We believe that there is a strong case for empirical studies of antidepressant withdrawal in suitable patients with advanced kidney disease.

### DISCLOSURES

None.

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See related Letters to the Editor, "Authors' Reply," on page 1340.

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## Authors' Reply

We thank Chilcot and Farrington<sup>1</sup> for their interest in our paper<sup>2</sup> and thoughtful comments surrounding the treatment of depression in hemodialysis patients. We agree with the letter writers that our observational study was not designed to evaluate the effect of antidepressant pharmacotherapy (versus no treatment) on mortality among individuals with hemodialysis-dependent ESRD. Under our active comparator new-user design, we could only conclude that the initiation of a higher (citalopram and escitalopram) versus lower (fluoxetine, fluvoxamine, paroxetine, and sertraline) QT-prolonging potential selective serotonin reuptake inhibitor (SSRI) was associated with a higher risk of sudden cardiac death.<sup>2</sup> Our study was designed to reflect a clinician's decision to prescribe an SSRI with higher versus lower QT-prolonging potential to a hemodialysis patient (*i.e.*, a treatment choice encountered in real-world practice).<sup>2–4</sup> The study provides population-specific safety information that clinicians can consider when prescribing SSRI therapy to hemodialysis patients.

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