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Letter to the Editor

LETTER TO THE EDITOR

Self-reported antidepressant use in haemodialysis patients is associated with increased mortality independent of concurrent depression severity

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We have recently argued the case for empirical studies evaluating the selective withdrawal of antidepressants in patients with advanced kidney disease [1]. This was in response to a large retrospective analysis that found that haemodialysis patients 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 [HR] 1.18 [95% confidence interval (CI) 1.05–1.31]} compared with patients who initiated SSRIs with lower QT-prolonging potential (fluoxetine, fluvoxamine, paroxetine and sertraline) [2]. Furthermore, we highlighted three randomized placebo-controlled trials of SSRIs in individuals with kidney disease [3–5] that failed to show evidence of efficacy but indicated increased risks of adverse events. We concluded an existent possibility that in some kidney patients, antidepressants may be doing more harm than good, therefore consideration of withdrawing antidepressants in suitable patients may be appropriate. A recent review of the evidence base for antidepressants in the general population reports minimal benefit to the average patient with major depressive disorder and concludes 'Antidepressants should not be used for adults with major depressive disorder before valid evidence has shown that the potential beneficial effects outweigh the harmful effects' [6].

Evidence regarding the association between depression symptoms and survival in dialysis patients is unequivocal [7–9]. However, what is less clear is the role antidepressants have on survival and whether any effect is independent of depression severity. Assimon *et al.*'s [2] analysis, while compelling, does not provide the mortality risk of being on an antidepressant versus not. We therefore went back to reanalyse survival data published previously [7] in order to explore the association between antidepressant use and survival from a large sample of haemodialysis patients ($n = 707$) in which there were 148 deaths. Our original analyses demonstrated that depression severity predicted all-cause mortality after controlling for a variety of covariates [Beck Depression Inventory-II, HR 1.03 (95% CI 1.01–1.04); Patient Health Questionnaire-9 (PHQ-9), HR 1.04 (95% CI 1.01–1.06)]. Using the same analytical methodology and model adjustments, we reran the analyses including antidepressant use within 3 months prior to the study assessment. Seventy-six patients reported being on at least one antidepressant (six missing cases). Of those on antidepressants, 36% died during the study follow-up compared with 19% of patients not on an antidepressant. In adjusted analysis that also controlled for depression severity (PHQ-9), antidepressant use was significantly associated with mortality, increasing the hazard of death 2-fold [adjusted HR 2.0 (95% CI 1.28–3.26); $P = 0.003$; see Figure 1 for survival plot]. Our previously reported findings from the original analysis remained the same, including the significance and effect size of depression severity on mortality. This suggests that the association between antidepressant use and mortality in haemodialysis patients may well be independent of concurrent depression severity. The estimated absolute risk increase of death for those on an antidepressant was 18%, with a numbers needed to harm of ~5.

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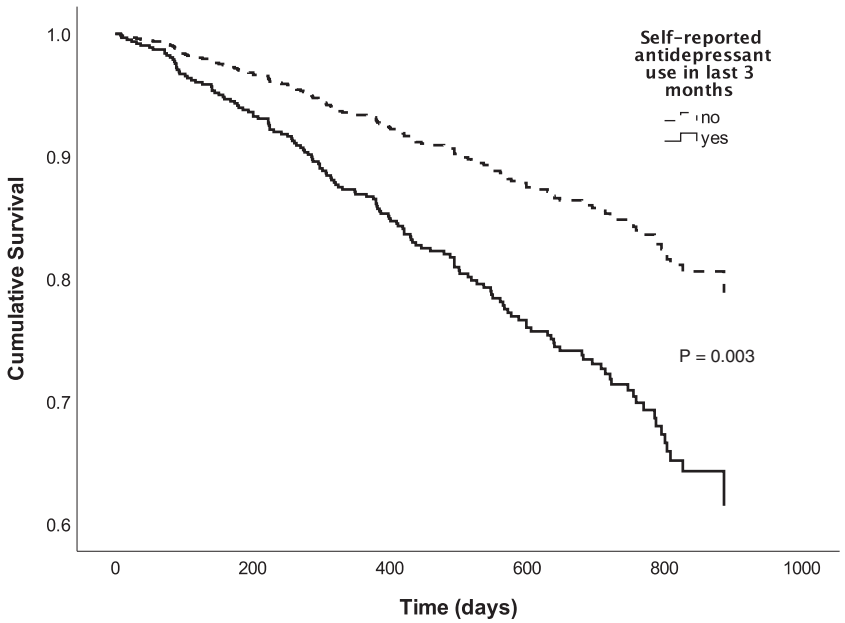

FIGURE 1: Adjusted survival plot comparing patients using an antidepressant in the previous 3 months prior to study assessment versus nouse.

This exploratory reanalysis is limited by patient self-reported antidepressant use. We did not have data on medication type or regimen, dose or treatment vintage. Accordingly, more robust studies are needed to ascertain more reliable estimates from which to establish the absolute mortality risk increase of antidepressants in this setting. Nevertheless, we feel it is important to report this exploratory observation, which in our opinion further supports the call for empirical studies investigating the selective withdrawal of antidepressants in patients with advanced kidney disease.

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CONFLICT OF INTEREST STATEMENT

None declared.

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