Longitudinal effects of depression on cognitive function in haemodialysis patients

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INTRODUCTION AND AIMS
Patients with depression are often excluded from intervention studies to reduce cognitive functional decline, with significant implications for clinical trials in haemodialysis (HD) patients where depression is highly prevalent. The longitudinal relationship and associated causal inference between depression and cognitive impairment in HD patients is poorly characterised.

METHODS
587 Prevalent HD patients from 12 centres completed a range of assessments 6 monthly for 18 months as part of the SHAREHD stepped-wedge evaluation. These included demographics, meta-cognition score (memory and concentration, range 0-36), symptom burden including depression (POS-S Renal), health-related quality of life (EQ-5D-5L) and health literacy. The influence of depression on meta-cognition was modelled by linear mixed-effects regression adjusted for time-varying covariates to account for correlated observations within-subjects inherent to longitudinal repeated measures. A minimum clinically important difference in cognition was defined as 0.5 SD of the meta-cognition score at baseline.

RESULTS
From 587 patients, 509 (87%) had complete data, with median age 65 years, dialysis vintage 2.8 years and 16% non-Caucasian. At baseline, 245 patients (48%) reported depression [mild, 130 (25.5%); moderate, 70 (13.8%); severe, 45 (8.8%)]. Depression (mild or worse) was more common in the cognitively impaired (68% vs 38%, P<0.001). Age, health literacy, symptom burden and the mobility, pain and self-care domains of the EQ-5D-5L were strongly associated with worse cognition and depression scores suggesting confounding. Unadjusted models noted that a worsening of depression by 1 unit was associated with a decline in cognitive function of 1.40 points (95 CI 1.27-1.54), reducing to 0.57 (95% CI 0.40-0.74) after adjusting for the time-varying co-variates of pain, anxiety, weakness, drowsiness, self-care, educational level and health literacy. Worsening depression correlated with worsening cognition, however cognition in patients whose depression improved progressed similarly to those whose depression had not altered (figure). Excluding patients whose depression improved increased the adjusted effect of a unit change in depression on cognition to 0.67 (95% CI 0.48-0.86).

CONCLUSIONS
In HD patients there is a statistically significant longitudinal association between worsening depression and cognitive functional decline, however, even if a patient's depression went from none to the most severe category over 18 months, the associated cognitive decline (2.3 points) is comfortably below the clinically meaningful difference (3.1 points). Interventional studies on cognition should not exclude HD patients with depression.