

Comparing active lifestyle intervention using renal dietician-led behaviour change techniques versus standard of care after kidney transplantation (CAVIAR): a randomised controlled trial.

Miss Kulli Kuningas¹, Mrs Joanne Driscoll¹, Miss Reena Mair¹, Mrs Helen Smith², Mrs Mary Dutton¹, Mr Edward Day³, Mr Adnan Sharif^{1,2}

¹University Hospitals Birmingham, Birmingham, United Kingdom, ²University of Birmingham, Birmingham, United Kingdom, ³King's College London, London, United Kingdom

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INTRODUCTION. Post-transplantation diabetes (PTDM) affects over a third of patients within the first-year post-transplantation and is linked to long-term cardiovascular events and all-cause mortality. It also ranks as a leading concern for kidney transplant recipients themselves. Both generic and PTDM-specific international guidelines advocate lifestyle intervention to minimise the risk of PTDM but acknowledge the lack of any strong evidence-base to support this guidance. Previous work has shown the potential benefit of renal dietitian intervention to attenuate progression of abnormal glucose metabolism but no randomised-controlled trial has ever been conducted and that was the aim of the CAVIAR study.

METHODS. CAVIAR was a single-centre, randomised, controlled trial recruiting stable kidney transplant recipients without diabetes between 3-24 months' post-transplantation. Participants were randomly assigned to active (personalised renal dietetic-led sessions using evidence-based Behaviour Change Techniques [BCTs]) versus passive lifestyle intervention (current standard of care). Randomisation was stratified by age, body mass index and ethnicity in random permuted blocks. The primary outcome was six-month change in surrogate measures of glucose metabolism (insulin secretion, insulin sensitivity, disposition index) on an intention-to-treat basis. Pre-defined secondary endpoints included patient-reported and cardio-metabolic clinical outcomes. We aimed to recruit 130 patients (65 per randomised arm) for 95% power (assuming a 5% significance level and a two-sided test) to detect a 20% difference in the primary outcome (assuming a 20% drop out). The trial was registered on clinicaltrials.org (identifier: NCT02233491).

RESULTS. Between August 17th 2015 and December 18th 2017, 130 individuals were recruited of whom 103 completed the study (drop-out rate 20.8%). Active versus passive intervention was not associated with any change in glucose metabolism; insulin secretion (mean difference -446 [-3184 to 2292], $p=0.748$), insulin sensitivity (mean difference -0.45 [-1.34 to 0.44], $p=0.319$) or disposition index (mean difference -940 [-5655 to 3775], $p=0.693$). Clinically, active versus passive lifestyle intervention resulted in reduced incidence of post-transplantation diabetes (7.6% versus 15.6% respectively, $p=0.123$) and significant improvement in weight (mean difference -2.47kg [-.401 to -0.92], $p=0.002$). No serious adverse events were noted.

DISCUSSION. This study demonstrates kidney transplant recipients can be encouraged to undertake lifestyle modification under the supervision of a renal dietician with pro-active intervention, underpinned by defined BCTs, which may potentially improve their cardio-metabolic risk profile. The immediate interpretation of our 'negative' primary outcome suggests one of two conclusions; 1) the active lifestyle intervention was ineffective, or; 2) the chosen primary outcome for analysis was invalid. A critical appraisal of our analysis supports the latter conclusion. This study is one of the first lifestyle intervention trials designed to improve health and wellbeing after kidney transplantation, and introduces the concept of incorporating evidence-

based BCTs into post-transplant care. However, further research investigation is warranted to determine beneficial effects on clinical outcomes.