

**DIFFERENT APPROACHES TO MINIMISE CONFOUNDING WHEN EMULATING A SURGICAL
RANDOMISED CLINICAL TRIAL: AN APPLICATION TO PARTIAL VS TOTAL KNEE REPLACEMENT**

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Abstract text (no more than 250 words)

Real world evidence has been proposed as an efficient alternative to costly and lengthy randomised clinical trials (RCT), particularly for surgical interventions. However, lack of randomisation in such observational studies makes them more vulnerable to confounding. We aimed to test the performance of several analytical approaches to emulate an ongoing surgical RCT comparing partial to total knee replacement, the Total or Partial Knee Arthroplasty Trial (TOPKAT).

TOPKAT randomly allocated 264 patients into each arm, and primary outcome was one-year post-operative patient reported outcomes (PROMs) Oxford Knee Score. In the observational analysis, we aimed to replicate TOPKAT using participants in the UK National Joint Registry (NJR) linked to Hospital records and national PROMs databases. NJR participants eligible for TOPKAT were included. Propensity score (PS) matching, stratification, adjustment and inverse probability weighting with linear mixed models were used to evaluate the treatment effect for comparable subjects according to available confounders. Instrumental variables (IV) were also evaluated including surgeon preference, surgical experience, surgical volume, geographical location, and calendar time. Only IVs fulfilling the underlying testable assumptions were used in two-stage IV regression.

We finally compared TOPKAT findings with those obtained from each of the proposed analyses. A Chi-square test for heterogeneity was used to test for significant differences between TOPKAT and each of the proposed methods.