



Further reflections on TOPKAT and Partial vs. Total Knee Replacement—response to authors

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Response to: Carlson SW, Sierra RJ. Unicompartamental knee arthroplasty over total knee arthroplasty: a more cost-effective strategy for treating medial compartment arthritis. *Ann Transl Med* 2020;8:510.

Argenson JNA, Jacquet C, Ollivier M. Medial femorotibial osteoarthritis of the knee: total or partial knee replacement? *Ann Transl Med* 2020;8:721.

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The acknowledgement by Argenson *et al.* (1) about establishing appropriate inclusion criteria for TOPKAT is appreciated and shows substantial insight. The potential for selection bias (particularly, but not exclusively, with cohort and non-randomised data) is ever present when considering comparative efficacy between two types of knee replacement. Even sophisticated post hoc adjustments and analyses can only account for, but never entirely obviate, such a critical and initial selection bias. Thresholds of disease and individual choice characteristics for implant type, by both surgeons and patients, are highly varied in normal practice and equipoise is often difficult to achieve (hence the Expertise design employed for TOPKAT) (2). Thus, the slightest bias, in an area which clearly lacks high effect sizes and enormous differences, will influence interpretation, conclusions (and therefore recommended practice). Using a randomised design in a carefully selected large population (suitable for both TKR and PKR) was a deliberate and key feature of the study and addresses some of the issues from other high quality cohort work (3,4).

The issue of complications and revision rate is one of the more notable aspects of the findings, and again, very sensibly raised by all commentary authors. Admittedly, an RCT of limited sample is not ideal to detect the incidence of low frequency events, but the differences between RCT findings and registry data cannot go unnoticed. The likely

explanation is that, despite the pragmatic design and external validity of multiple sites in TOPKAT, and unlike the surgeon body in any larger cohort or registry, none of the surgeons in the RCT were new to PKR. As such, registries (which will also include the performance of technically inexperienced surgeons) will undoubtedly influence the revision rate of a technically demanding procedure. Add in a likely lower threshold for revision outside the controlled environment of an RCT, and the inconsistency becomes less surprising. The main consequence of this contention is the disquiet surrounding recommendations for best practice. Until improved methodology is found future policy setting for practice must take the findings from both types of study into account. TOPKAT presently tells us that PKR in the hands of experienced surgeons is somewhat better, whereas registry data estimates somewhat higher rates of revision (5), most likely contributed from a less PKR experienced surgeon group and amplified by heterogeneity of revision thresholds in routine practice (although some assumptions are made here as we do not have that granularity of data). The conclusion, as was stated in the paper and in the commentaries, is to recommend PKR, but with a surgeon comfortable and experienced in the procedure (6). Note TOPKAT did not show any real detriment to TKR in comparison, and therefore surgeons who perform a good TKR for anteromedial OA should not be dissuaded from doing so.

We also cannot disagree with Mssrs Argenson, Jacquet, Ollivier over their thoughtful final conclusion sentence and their point about 10 year data. A point reinforced by Carlson and Sierra from the Mayo Clinic (7) in their equally considerate commentary referencing their own quality study comparing PKR (UKA) and TKR in the older patient (8). Five year data is useful but the 10-year picture will be more informative and we are in the process of collecting these longer term data. It will be less complete due to expected mortality but will still offer insight into the most appropriate long term surgical replacement for medial compartment OA. Indeed if there are larger or even different signals at 10 years we may have to revise our current interpretation. But that is exactly what constitutes good evaluation science – uncertainty, controlled bias, open mindedness and a justified conclusion.

However, as a postscript, merely obtaining 10-year data will never *guarantee* inclusion in any “best practice” policy creation. Bias can take many forms and many external factors can affect acceptance and implementation of even the most robust science. For example, TOPKAT, despite its Lancet credentials and being the largest ever, mid-term, level-1 randomised comparison of PKR v TKR was outright rejected for peer reviewed conference and publication on several occasions. The interpretation of such action is much less straightforward...!

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Footnote

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