Title: Long-term treatment outcome on symptomatic osteoarthritis in patients with a meniscal tear: Statistical analysis plan for the 5-year follow-up of the ESCAPE trial

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This statistical analysis plan was developed and published online a priori of the 5 year data analyses. With this document we aim to provide insight and transparency for our statistical analyses and reporting of our results.

Statistical analysis plan of the 5 year follow up

We will analyze the 5-year follow up data following the intention-to-treat principle. To test for robustness of the results, we will also perform an as-treated analysis. In the intention-to-treat analysis, participants will be analyzed in two groups, according to their allocated treatment.

For the as-treated analysis, participants will be divided into three groups: 1) patients allocated to partial meniscectomy who indeed underwent surgery; 2) patients allocated to physical therapy who indeed completed 16 (or more) physical therapy sessions; and 3) patients allocated to physical therapy who underwent surgery during the study period. Participants who did not undergo their allocated treatment (either APM or completion of physical therapy) will be discarded from the as-treated analysis. Their 5 year outcomes will be reported descriptively.

We will analyze binary outcomes with generalized estimating equation (GEE) with exchangeable structure. We will perform GEE analyses to evaluate symptomatic knee OA from baseline to 5 year follow up. Interaction effects of treatment (APM vs physical therapy) and time (baseline, 2 years and 5 years follow-up) will be calculated to test between-group differences in changes over time. The adjusted between-group difference will be assessed by adding potential confounders to the models. These potential confounders are BMI, age, baseline KL score, baseline pain during activities and frequency of pain.

Continuous outcome measures will be analyzed using linear mixed model analysis with random intercept. We will define the overall crude intervention effects by a model with only treatment group and the baseline value of the outcome as independent variables. We will add time and time-by-treatment interaction terms to specify crude intervention effects for each follow-up time point. Adjusted intervention effects will be calculated using similar models, expanded with the following potential confounders as independent variables: level of OA at baseline using the Kellgren and Lawrence

classification[7], baseline pain during weight bearing, BMI at baseline (three categories: <25, 25-30, or 30-35 kg/m2) and gender. In all models, physical therapy will be defined as the reference treatment. All analyses will be performed using IBM SPSS version 27 (IBM, Armonk, NY), and statistical significance will be assessed at the 0.05 level.