Appendices

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Appendix A: Physical therapy protocol

The exercise program for comprised 16 supervised sessions during 8 weeks

Time (week)	Exercises	repetitions or time
0-8	stationary bicycling for warming up and cooling down or cardiovascular training	gradual increase 7-15 min or longer
0-8	pully, strap around healthy ankle, stay and keep balance on injured side, move healthy leg forward, backward and sideward by standing in all 4 directions	3x12
0-4	calf raises on a leg press	3x12
0-8	standing hip extension in a "multi-hip" trainings device	3x12
0-4	balance on wobble board on both feet	
0-8	stair walking, walking, running, jumping according the patients ICF challenging with throwing a ball	10 min
5-8	calf raises standing on one leg	3x12
1-8	leg press, place the shinbone horizontal and the knee starting at 110˚, unilateral	3x12
5-8	lunges (according the needs of the patient) with < 90˚ knee flexion	3x12
5-8	balance on wobble board on one foot challenging with throwing a ball	3 min
5-8	crosstrainer as cardiovascular and cooling down training	10 min or more

footnote:
By all exercises is it important to keep the patients individual needs and limitations focused by using the ICF.

The uninjured side is also less trained as usual and therefore both sides should be trained. Besides training of the lower extremity, "core stability" training is of importance for good posture positioning and moving.

The active rehabilitation program is designed around cardiovascular (circulation), coordination and balance, and closed chain strength exercises. Shearing forces in the knee are less using closed chain exercises compared to open chained exercises. The closed chain exercises activate both agonists and antagonists around the knee joint resulting in a direct rotatory movement and prevent in shearing forces seen by open chained exercises. (Heijne 2004, 2006 studied the role of open and closed exercises in the rehabilitation after a reconstruction of the anterior cruciate ligament and advised to be careful with open chained exercises in the early start of rehabilitation).

Home exercise program

In addition, a home exercise program was provided to all participants. It consisted of one leg

standing during 60 seconds and a step-down exercise comprising 3, 9, 10 repetitions, twice a week

Appendix B: Differences in pooled mean costs and effects (95% CI), incremental cost-effectiveness ratios, distribution of incremental cost-effect pairs around the quadrants of the cost-effectiveness planes, and percentage of bootstrapped cost-effectiveness pairs located in the non-inferiority region of the cost-effectiveness planes for the unadjusted costs and effects.

Analysis	Sample size		Outcome	ΔC (95%CI)	ΔE (95%CI)	ICER	Distribution CE-plane (%)				
	PT	APM		€	Points	€/point	NE*	SE †	SW‡	NW§	Non-inferiority region
Main analysis - Imputed dataset	161	158	IKDC (Range: 0 – 100)	-2056 (-3326 to -1019)	-3.8 (-8.0 to 0.5)	544	0.0	3.4	96.6	0.0	96.4
	161	158	QALYs (Range: 0 - 1)	-2056 (-3326 to -1019)	-0.024 (-0.071 to 0.023)	85,953	0.0	16.2	83.8	0.0	91.7

APM=Arthroscopic Partial Meniscectomy, C=Costs, CE-plane=Cost-Effectiveness plane, E=Effects, ICER=Incremental Cost Effectiveness Ratio, IKDC=International Knee Documentation Committee, PT=Physical Therapy, QALYs=Quality Adjusted Life Years, SA=Sensitivity Analysis

* Refers to the northeast quadrant of the CE-plane, indicating that PT is more effective and more costly than APM

† Refers to the southeast quadrant of the CE-plane, indicating that PT is more effective and less costly than APM

‡ Refers to the southwest quadrant of the CE-plane, indicating that PT is less effective and less costly than APM

§ Refers to the northwest quadrant of the CE-plane, indicating that PT is less effective and more costly than APM

Appendix C: Deviations from the original trial protocol

The following updates were recorded in the study protocol (and updated in the registries) during the conduct of this trial:

1. Participating centers:

   a. The trial has not started in the VU Medical Center and in the Sint Antonius hospitals.

In both hospitals the staff of the orthopedic surgery department could not agree on participating in this trial.

   b. Several centers have been included during the conduct of this trial:
      i. Noord-West Ziekenhuis groep, Alkmaar (November 2013)
      ii. Jan van Goyen Medical Center, Amsterdam (July 2013)
      iii. Elisabeth Tweesteden Ziekenhuis, Tilburg (June 2014)
      iv. Slotervaart Ziekenhuis, Amsterdam (August 2014)
      v. Tergooi Ziekenhuis, Hilversum (September 2014)
      vi. Medisch Centrum Haglanden, the Hague (April 2015)

2. Follow-up outcomes

   a. The outcome physical examination at 24 months follow-up was removed from the study protocol in 2014 since it was believed that this outcome would have no added value.

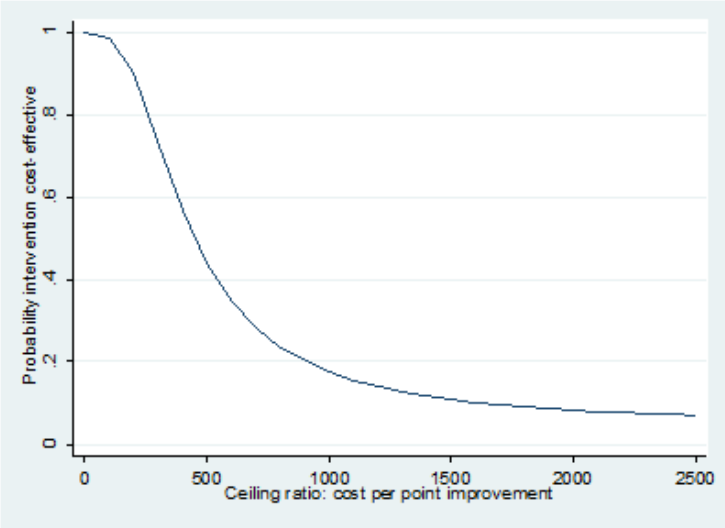
2. Interim analysis sample size by independent committee

   a. In August 2015 we performed an interim analysis to recalculate our sample size. Initially the sample size was based on a power of 90%, an alpha of 0.05, a standard deviation (SD) of 18 points and a non-inferiority threshold of 8 points on the IKDC 'Subjective Knee Form'. We calculated that with 20% loss to follow-up after 24 months and 25% delayed APM in PT group, 201 patients would be needed per group in this equivalence type RCT. This meant a total of 402 patients.
   However, the SD was based on the reported standard deviation by Crawford and colleagues, who found the an SD of 20 points on the International Knee Documentation Committee (IKDC) in a group of postoperative patients. Although we expected the SD to be smaller in our group after longer (24 months) post-enrolment, we used the SD of 20 for our sample size calculation to prevent the risk of being underpowered.
   After 100 inclusions at 12 months post-enrolment, we performed an interim analysis to recalculate our SD and to prevent unnecessary inclusions. We found an SD of 17.5 and recalculated our sample size with an SD of 18 points. We found that we would need 160 patients per group, 320 patients in total.

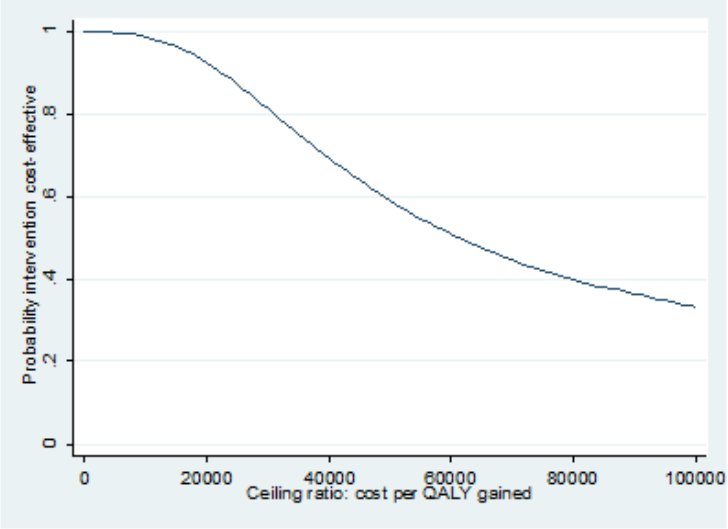
This recalculation was done and approved by an independent committee (August 2015).

Appendix D: Cost-effectiveness acceptability curves indicating the probability of PT being cost-effective in comparison with APM for different values of willingness-to-pay for the IKDC (a) and QALYs (b)

(a)



(b)



APM=Arthroscopic Partial Meniscectomy, IKDC=International Knee Documentation Committee, PT=Physical Therapy, QALYs=Quality Adjusted Life Years