APPENDIX A: Prehabilitation for TKA—Table of Evidence

Prepared by: Ellie Rubin, SPT	**Topic:** Randomized Controlled Trials on the Effect of Prehabilitation prior to Inpatient Primary Total Knee Arthroplasty (TKA) **Databases searched:** PubMed, CINAHL, Web of Science **Inclusion criteria:** RCTs comparing prehab+post-op PT intervention with post-op PT only; PEDro score ≥ 6/10; level 1b evidence			
Author/ Year/ PEDro Score	**Subjects/ Intervention**	**Prehab Exercise Protocol and Progression**	**Outcomes/Results** (All results based on p-value of <0.05 for significance)	**Conclusions/Limitations**
Alghadir et al (2016)[1] PEDro 7/10	Subjects: n = 50 Experimental Group (EG) (n = 25) received pre- and post-op PT for: 1. Improving LE strength and mobility; 2. Transfer and gait training with AD; 3. Prescription of HEP. Control Group (CG) (n = 25) received only post-op PT.	Frequency/Duration: 3-4x per day (1 session supervised by PT and additional 2-3 sessions completed individually) for the final 5 days pre-operatively. 30-min long sessions composed of: - Strength training: active assisted knee flex/ext and hip abd/add/ext; number of reps or sets was not specified in article. - Step training: ascending/descending stairs; number of steps and height of step not specified. - Short-distance amb with AD (cane or walker); distance not specified.	EG compliance w/ prehab was not specified. Outcomes were measured at baseline (pre-operatively) and at 3-weeks and 6-weeks post-op. Visual analogue scale (VAS) for pain assessment: Both groups had significant reduction in pain intensity from baseline to 3-weeks post-op, baseline to 6-weeks post op, and between 3-weeks and 6-weeks post-op. Tx effect was in favor of EG; however, this difference did not achieve statistical significance. Lower extremity functional scale (LEFS): EG had significant improvement b/t baseline and post-op week 6; CG had significant improvement from baseline to post-op week 3, baseline to post-op week 6, and between post-op weeks 3 and 6. Despite non-significant improvement in EG LEFS score from baseline to post-op week 3, between-group difference at post-op week 3 was also non-significant (mean difference in favor of CG: 1.6 points; 95 CI -5.12, 8.32). LEFS scores at 6-weeks post-op were also not significantly different b/t groups.	Significant improvements in physical function and pain symptoms were reported in both groups; however, there were no differences in observed tx effect between the two groups. While both groups were statistically similar at baseline, mean baseline LEFS score for the CG was 3 points less than that of the EG, which may explain how the CG change in score from baseline to 3-weeks post-op met the threshold for statistical significance, while the difference in LEFS score at 3 weeks b/t the groups remained insignificant. Due to the variability and lack of clarity in prehab intervention methods, dosing, and subject compliance, the ability to make conclusions regarding treatment efficacy is limited. Additionally, it is highly unlikely that such a short duration of tx would have provided enough exposure to prehab to produce clinically meaningful change in the outcomes.[2]
Beaupre et al (2004)[3] PEDro 7/10	Subjects: n = 131 EG (n = 65) pre- and post-op PT for: 1. Improving knee strength and mobility; 2. Education on ADLs, functional mobility, use of ADs, and post-op ROM routine. CG (n = 66) received post-op PT only.	Frequency/Duration: 3x per week for 4 weeks (12 sessions total). 1-hr long sessions composed of: - Warm-up: hot pack to affected knee (15-20 min). - Stationary bike at low intensity (5 min. in Wk 1; progressed to 10 min. in Wk 2). - Strength training (30 min) 5 exercises: quad sets, SLR to 45°, short arc quads, isotonic knee ext. in sitting from 90°-0°, seated knee flex w/ resistance band. Wks 1-2: 3 sets of 10 reps; Wks 3-4: 3 sets of 15. - Cool down w/ ice pack to affected knee (15-20 min).	Compliance: 64/65 EG subjects completed all 12 tx sessions. Hospital length of stay (LOS): 1 day less on avg. for EG compared to CG; however, this difference did not attain statistical significance. 31/66 CG subjects were transferred to subacute rehab following surgery (47%), compared to 23/65 EG subjects (35%). Post-op complications: DVT: 3 subjects in EG and 6 subjects in CG, 2 in each group also had PE; Superficial surgical site infection: 2 subjects in EG and 3 in CG; Hospital readmissions in 1st post-op year for related complications: 5 in EG (included 1 manipulation for poor ROM and 1 revision due to deep prosthetic infection) and 6 in CG group (2 manipulations for poor ROM). Subjective and physical performance outcomes (WOMAC, knee flexion ROM, hamstring strength, quad strength, and quality of life (QoL) as reported using SF-36) were assessed at baseline, after the 4 weeks of intervention (preoperatively), and at 3-mo, 6-mo, and 1-year post-op. No significant differences were found across time or between groups.	There was no tx effect as a result of prehab on knee ROM, strength, pain, function, or QoL. Nonsignificant trend was found in favor of the EG for shorter hospital LOS. This prehab intervention focused primarily on strength training, and thus may not have provided enough variety of training to impact outcomes. While strength training alone can improve pain and function in individuals with knee OA, in order to maximize intervention effectiveness for this population, patients should participate in a more complete exercise program that also includes ROM, stretching, functional balance, and aerobic exercises.[4] Despite the lack of significance for LOS, the EG's reduced LOS by 1 day is certainly clinically relevant; difference in percentage of home-discharges is also clinically meaningful, although it does not appear to have impacted risk of adverse effects or functional recovery.[5] Additionally, as the initial post-op assessment did not occur until 3 months after surgery, any differences that occurred in the early postoperative period may have been missed.

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Calatayud et al (2017)[6]
 	
PEDro 7/10
	Subjects: n = 50
	
	EG (n = 25) received pre-op PT intervention for LE strengthening and balance training, in addition to standard post-op PT.
	
	CG (n = 25) received standard post-op PT only.
		Frequency/Duration: 3x per week for 8 weeks (24 sessions total).
		
		1-hr long sessions composed of:
		- Dynamic warm-up (2 sets of 20): calf raises and step-ups; step height not specified.
		- Low intensity biking (10 min).
		- Strength training (4 exercises): seated leg press, knee ext., hamstring curl, and standing hip abd.
		  - 5 sets of 10 reps w/ 60 sec. rest b/t sets; resistance based on 10 rep max.
		  - A single warm-up set of 10 active reps was completed prior to beginning each exercise.
		- Balance training on Bosu Ball: 4 sets of 30 sec. in DLS; 4 sets of 15 sec. in SLS, starting with non-affected leg.
		- Cool down w/ static stretching: hip abd's, hamstrings, quads, ankle PFs.
			Following prehab intervention, 2 subjects in EG cancelled TKA surgery due to level of functional gains made during treatment.
			
			Hospital LOS: 1.95 days less for EG compared to CG.
			Post-op complications: No subjects in EG subjects had any post-op complications compared with 3 subjects in CG participants.
			
			Subjective and physical performance outcomes were measured at baseline, after the 8 wks of intervention (preoperatively), and at 1-mo and 3-mo post-op. At all measurements times after baseline, between-group differences were significantly different in favor of the EG for WOMAC score, SF-36 physical functioning scale, VAS, AROM knee flexion/extension, hamstring strength, hip abd strength, TUG, and stair-climbing test.
			
			Compared to the CG, the EG also demonstrated significantly greater quad strength after 8 wks of prehab and at 3-months post-op; no difference in quad strength was found between groups at 1-mo post-op.
				Unlike previous studies, the prehab protocol in this study used higher volume and intensity of training, resulting in short- and longer-term significant improvement in strength, ROM, and functional measures, as well as reduced pain and hospital LOS compared with control subjects. The increased volume and intensity of resistance training used in this protocol was designed with the goal of maximizing neuromuscular activation of the targeted muscle fibers in order to promote muscular hypertrophy and strength gains over a short period of time.[2]
				
				Even so, the 8-week duration of this prehab intervention is longer than many of the other published studies on prehab. A training period of at least 6-8 weeks has been recommended to achieve significant gains in strength due to hypertrophy of muscle tissue.[7] With shorter training periods, gains in the tension-generating capacity of muscle may still be the result of neural adaptation, as opposed to structural change in the actual muscle tissue.[8]
				
				These normal training-induced physiologic adaptations to resistance exercise could provide additional explanation as to why previous studies with lower intensity and shorter duration of prehab did not observe differences in treatment effect.

Matassi et al (2014)[9] PEDro 6/10	Subjects: n = 122 EG (n = 61) received a prehab HEP for improving knee mobility, in addition to standard post-op PT. CG (n = 61) received only standard post-op PT.	Subjects were instructed to complete HEP at a frequency/duration of 5x per week for 6 weeks. HEP was performed 1x w/ researcher at baseline assessment. Subjects received a handout with written description and images of required exercises: - Static stretching of quads and hamstrings: 4 x 30 sec. hold B/L w/ 10 sec. rest b/t stretches. - Strength training (4 exercises): quad sets x 5 sec. hold, hamstring curls, long arc quads w/ 5-sec hold in mid-flexion; step-ups/downs (step height not specified). - 1 set, working up to a 20-rep max. Subjects were given a log book w/ daily check marks to indicate compliance with HEP.	Compliance: Based on review of logbooks, EG subjects completed HEP 79.4% of the time (±23). From the EG group, 2 subjects were unable to complete intervention due to increased knee pain and development of ipsilateral adductor tendinitis, respectively. Hospital LOS: non-significant reduction of LOS by 1 day for EG. Post-operative complications: Over the initial year post-op, 5/61 subjects (8.2%) in the EG had post-op knee stiffness requiring manipulation under anesthesia, compared with only 3/61 subjects (4.9%) in the CG. Knee mobility (AROM/PROM) was measured at baseline, after the 6 wks of prehab (preoperatively), and at 3-mo, 6-mo, and 1-year post-op. Following 6 wks of prehab intervention, EG group had significant improvement in PROM and AROM w/ knee flex and knee ext.; prehab adherence was significantly related to change in knee flex PROM. Immediately post-op, b/t group significant difference in favor of the EG for duration to achieve 90° of AROM knee flex: 5.8 days (±2.1) for EG compared to the 6.9 days (±1.9) for CG ($p = 0.0016$). No differences in PROM or AROM knee flexion were found b/t groups at 3-mo, 6-mo, and 1-year post-op.	Prehabilitation may have provided immediate post-op benefit by reducing hospital LOS and time to achieve 90 degrees AROM knee flex by approx. 1 day. As hospital d/c is based, in large part, on swift recovery of relevant functional activities (sit-to-stand transfers, amb, stair-climbing), it makes sense that regaining knee ROM more quickly would contribute to faster achievement of these goals, and thus shorter inpatient hospital time.[5] However, it does not appear that the addition of this prehab HEP maintained its effect following hospital discharge, nor does it appear to have reduced the risk of post-op knee joint stiffness. Reliability of these results is limited by the methods of intervention and data collection; in addition to lack of supervision with exercises, there was also no follow-up with EG subjects to ensure understanding and proper completion of exercises. This variability in subject compliance and activity performance limits the ability to draw conclusions about clinical relevance. Additionally, as the next post-op assessment did not occur until 3 months after surgery, any differences that occurred in the early postoperative period may have been missed.

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Topp et al (2009)[10] PEDro 6/10	Subjects: n= 54 EG (n= 26) received pre- and post-op PT for: 1. LE strengthening and flexibility; 2. Prescription of HEP. CG (n = 28) received post-op PT only.	Frequency: 3x per week (1 session was PT-supervised, with remaining 2 completed individually at home). Duration: Varied based on individual subject's date of surgery. 1-hr sessions were composed of: - Warm-up: walking (5 min). - Strength training w/ theraband (9 exercises): squats, hip flex/ext., hip abd/add, ankle PF/DF, and knee flex/ext.; number of sets/reps not specified. - Step training: forward step-ups to 8-inch step; lateral step-ups to 8-inch step; number of sets/reps not specified. - Static stretching: gluteus, hip, hamstring, calf, trunk, upper back, lower back, and triceps. - Cool-down: walking (5 min). Subjects documented compliance with HEP using an exercise log.	Compliance: Avg. of 13.04 sessions, ranging from 4 to 23. Outcomes were measured at baseline (at least 4 wks before surgery), 1-wk pre-op, 1-mo post-op, and 3-mo post-op. 1-week pre-op: Significant tx effect in favor of EG on 30-sec chair rise test; nonsignificant tx effect in favor of EG on 6-min walk test, speed w/ ascending/descending stairs, quad strength, and decreased strength asymmetry b/t LEs. CG had significantly greater pain compared to EG; CG had nonsignificant decline in performance of all functional tasks, injured leg quad strength, and increased in LE strength asymmetry. 1-mo post-op: Significant within-group and b/t group difference in favor of EG on 30-sec chair rise. CG had significant decrease in performance on 6-min walk test and surgical leg quad strength, whereas EG had no change with other functional tasks or quad strength. CG reported less knee pain with activity but had significant increase in quad strength asymmetry from baseline. 3-mo post-op: EG had significant reduction in pain intensity and significant increase in speed w/ ascending/descending stairs and B/L quad strength. While both groups had significant improvement on 30-sec chair rise test from baseline, b/t group comparison showed tx effect significantly in favor of EG (mean difference: 1.62 reps; 95 CI, 1.19, 2.05). CG significantly improved distance on 6-min walk test, but also had significant increase in asymmetry of quad strength from baseline.	Prehab was effective at improving both short- and long-term post-op outcomes related to knee pain, physical function, mobility, and quad strength. In particular, prehab appears to have moderated the typical post-op increase in quad strength asymmetry. This tx effect has significant clinical benefit, as post-operative quad strength asymmetry has been associated with weight-bearing asymmetry, worse long-term functional mobility,[11] and increased risk for other orthopedic problems.[12] Although duration of prehab was not standardized, the average session compliance rate suggests an average treatment duration of approx. 4.5 weeks. While this training duration is shorter than the recommended 6-8 weeks for true strength gain, this prehab protocol did employ a higher volume of exercises compared with other trials, which could have contributed to the success of treatment. Results from this study suggest that prescribing patients with a prehab HEP, with ongoing PT-supervised tx sessions, can be successful in improving post-TKA outcomes.
Villadsen et al (2014)[13] PEDro 7/10	Subjects: n = 165 (indicated for TKA or THA; results stratified by joint). EG (n = 41 TKA) PT-led group prehab for: 1. Postural control and stability; 2. 3-hr in-clinic edu. session on post-op ROM routine. CG (n = 40 TKA) received the same 3-hr edu session and a pamphlet w/ various knee strengthening exercises.	Frequency/Duration: 2x per week for 8 weeks (16 sessions total). 1-hr long group sessions composed of: - Warm-up on stationary bike at low to mod intensity (10 min). - Postural control and functional strengthening (2-3 sets of 10-15 reps): bridges and sit-ups w/ Swiss ball, forward/backward lunge, lateral lunge, standing hip abd, seated knee flex/ext, sit-to-stands w/ DLS, step-ups/downs (initial step height not specified). Increased resistance, step height, and/or level of challenge when subject demonstrated good control and quality of movement w/ min exertion. - Cool down: walking.	Compliance: 62/84 (74%) of EG attended pre-specified goal of 12 or more group exercise sessions; median number of session = 13, with an avg. of 7-8 subjects at each session. All subjects from both groups attended the 3-hr in-clinic educational session. Post-op complications: 1 of the TKA subjects in the CG developed a deep peri-prosthetic infection, requiring surgical revision. From baseline to 6-wks post-op: Significant between-group difference in favor of EG for KOOS ADL and pain scores and general health as reported in the EQ-5D. No observed tx effect on quad strength. From baseline to 3-mo post-op: No between-group differences in treatment effects were found. No observed tx effect on quad strength.	Prehab was associated with improved pain and function at 6-weeks post-op; however, tx effect was not maintained at 3-months post-op. Nonetheless, short-term improvement in pain and function is certainly of great benefit to patients during the initial TKA recovery phase. Based on the median number of 13 attended prehab sessions, duration of intervention could be approximated at 6.5 weeks. However, this prehab intervention does not appear to have had substantial effect on quadriceps muscle strength. Improving post-op quad strength is a primary outcome of interest with a prehab protocol, as greatest post-op strength loss of up to 85% occurs in quads of the surgical leg[14] and is associated with increased knee instability,[15] reduced physical function, and increased disability.[14,16]

Fernandes et al (2017)[17] PEDro 6/10	The purpose of this study was to analyze the cost-utility and 12-month clinical effect of the prehab intervention provided in the RCT by Villadsen et al (2014).[13] See **Subjects/Interventions** and **Prehab Exercise Protocol and Progression** from study by Villadsen et al (2014) (above).[13]		When stratifying measurements by affected joint, no difference in prehab effect was found b/t TKA and THA subjects; thus, results included all subjects, regardless of joint replacement procedure. Hospital LOS: While differences in total length of hospital stay were not statistically significant, the EG did have an avg. reduction in LOS by 2.4 days in comparison to CG (EG = 4.8 days; CG = 7.2 days). From baseline to 12-mo post-op: Significant between-group difference in favor of EG for HOOS/KOOS QoL domain; no between-group differences for HOOS/KOOS ADL or pain scores. Cost-utility analysis of health care services (cost of intervention, health care utilization, and patient expenses) was measured using Quality Adjusted Life Years (QALYs) as calculated by the EQ-5D-3L. Conventional threshold value of 40,000 euros was used to indicate a “willingness-to-pay a good value of money” for a QALY gain. No differences were found between groups for all primary or secondary health care costs associated with the surgical episode. A significant between-group gain in QALY was found in favor of the EG, with a moderate effect size of 0.59. Cost-utility: 84% probability of the cost-effectiveness of prehab intervention, based on the threshold for willingness to pay for a QALY gained. Sensitivity analysis confirmed robustness of result.	While the difference between groups in hospital LOS did not meet the threshold for statistical significance, a reduced stay by 2.4 days is clinically meaningful to the patient, as well as to the hospital. While prehab intervention did not result in one-year post-op clinical effects on function or pain, it was associated with improved quality of life. Results from the cost-utility analysis suggest that up to 8 weeks of prehab intervention could be implemented as standard care prior to joint replacement, without additional associated costs. However, these results did not provide evidence that prehab serves to reduce overall patient costs. Nonetheless, there appears to be a high probability that patients would consider prehab to be a cost-effective service.
Huber et al (2015)[18] PEDro 8/10	Subjects: n = 55 EG (n = 22) received prehab for: 1. PT-supervised neuromuscular exercise training; 2. PT-provided education intervention. CG (n = 23) received only the pre-op PT education.	Frequency/Duration: 2x per week for 4-12 weeks, depending on date of surgery. For specific exercises, see protocol from RCT by **Villadsen et al (2014)**[13] (above). Individual exercises were progressed by varying number of reps, direction of motion, and velocity of movement when subject could perform 3 sets of 15 reps w/ good quality of motion and min. exertion. Education intervention (3 sessions over the last 4 weeks pre-operatively): - Knee joint anatomy. - Recommendations on post-op pain management. - Details on post-op rehab phases.	Median number of attended sessions was 10 (IQR: 8, 14); 76.2% attended pre-defined goal of 8+ sessions; 1 EG subject withdrew after 1st training session. Outcomes measured at baseline, 1-week pre-op, and 6-weeks, 3-mo, and 12-mo post op. For the primary outcome (30 second chair rise) there were no within-group or between-group tx effects at any of the measured time points. Secondary subjective measures: From baseline to 6-weeks post-op, both groups had significant improvements in KOOS ADL; only the CG had significant improvement in KOOS pain score. From baseline to 3-mo post-op, both groups had significant improvement in KOOS ADL and pain scores and the physical function dimension of the SF-36. No additional improvement was observed at 12-mo post-op.	This trial used the same prehab exercise protocol as the Villadsen et al (2014)[13] and Fernandes et al (2017)[17] studies. Unlike results from Villadsen et al., this study did not find a significant effect of prehab on pain and function outcomes at 6-weeks post-op. Similarly, no additional benefits of prehab were measured at 3-mo post-op. There are a few factors that may have affected this difference in results. The median number of 10 prehab sessions in this study is on the lower end in terms of adequate dosage to elicit clinical benefit.[19] Indeed, the median number of prehab sessions completed in this study was 3 less than in the Villadsen et al study. Based on the median number of 10 attended prehab sessions, duration of intervention could be approximated at 5 weeks. This too could be considered on the low end of adequate prehab dosage.

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References

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