

Supplemental material for:

Sit R, Wu R, Rabago D, et al. Efficacy of intra-articular hypertonic dextrose (prolotherapy) for knee osteoarthritis: a randomized controlled trial. *Ann Fam Med.* 2020;18:235-242.

Supplemental Appendix 1. Change in secondary outcomes from baseline to 52 weeks follow up

Figure 1a. Change in observed WOMAC stiffness score

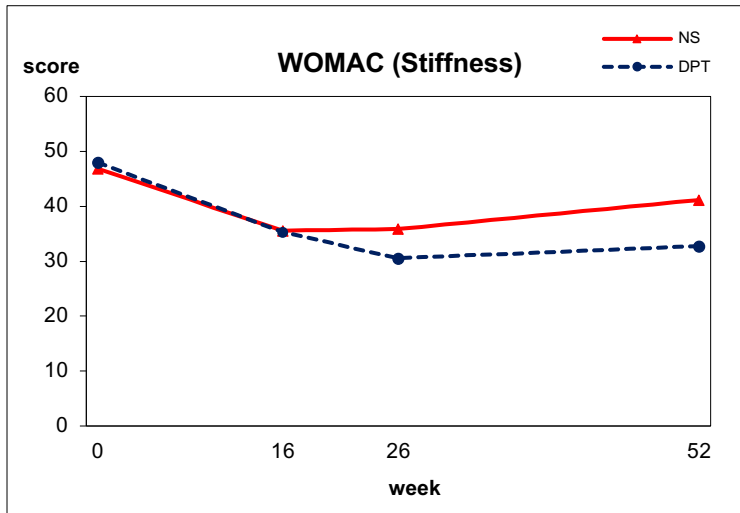


Figure 1b. Change in observed WOMAC function score

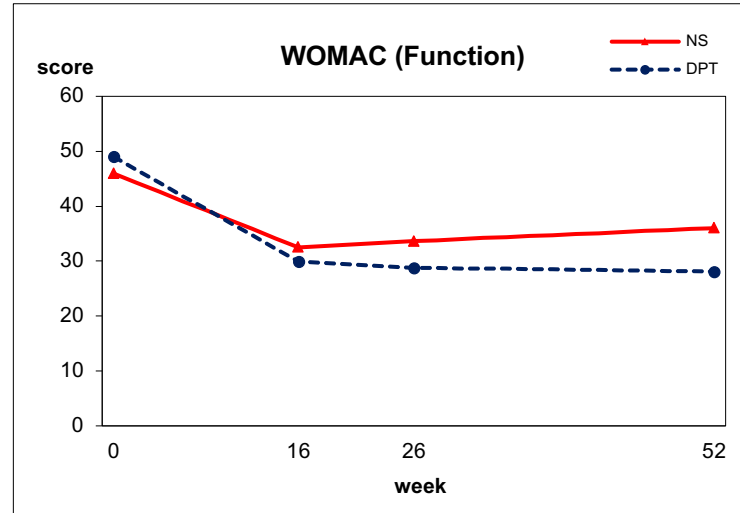


Figure 1c. Change in observed WOMAC composite score

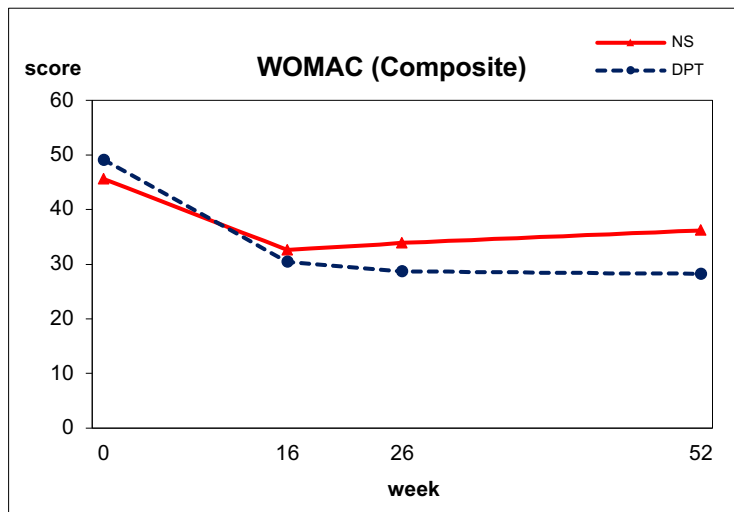


Figure 1d. Change in observed values of Pain intensity (VAS)

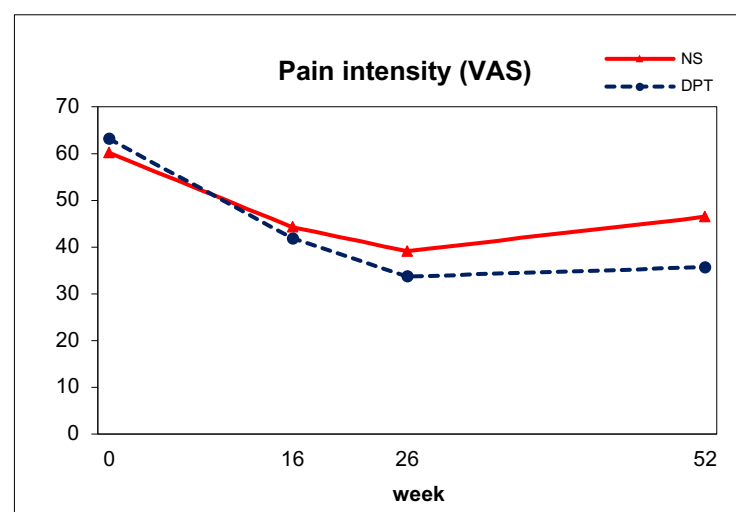


Figure 1e. Change in observed values of Timed up and go

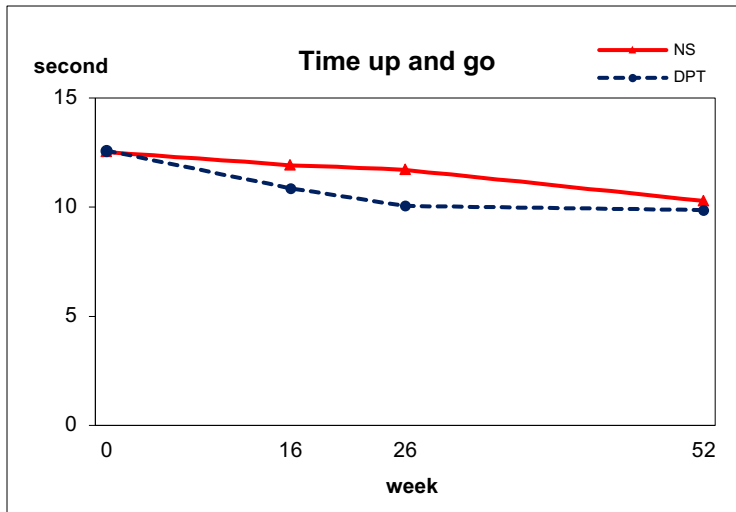


Figure 1f. Change in observed values of 30-second chair stand

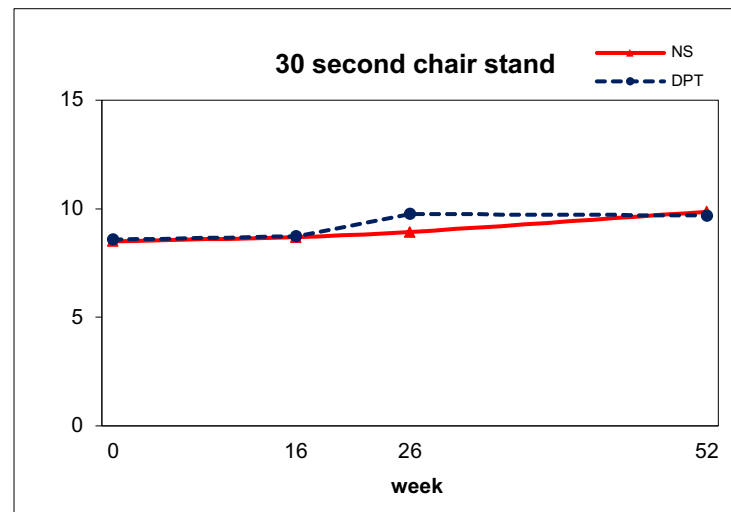


Figure 1g. Change in observed values of 40-m fast-paced walk

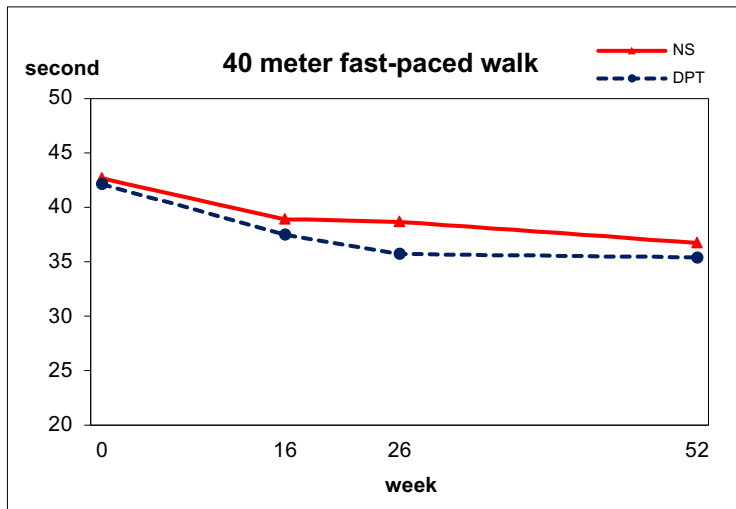


Figure 1h. Change in observed values of EQ-5D VAS

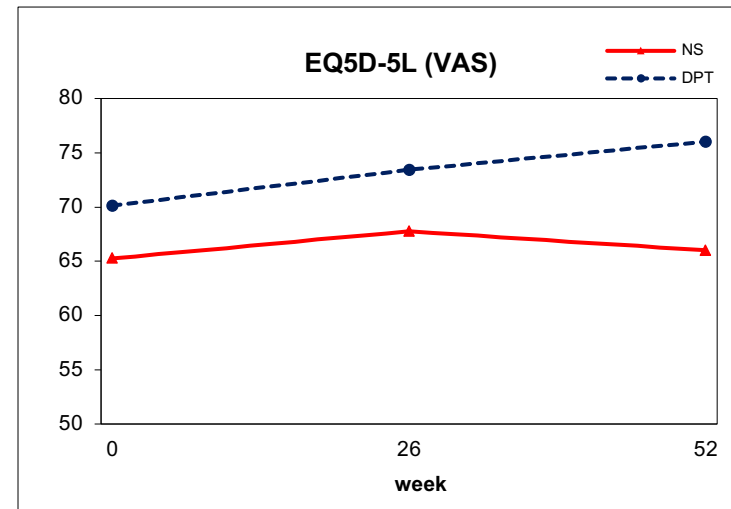
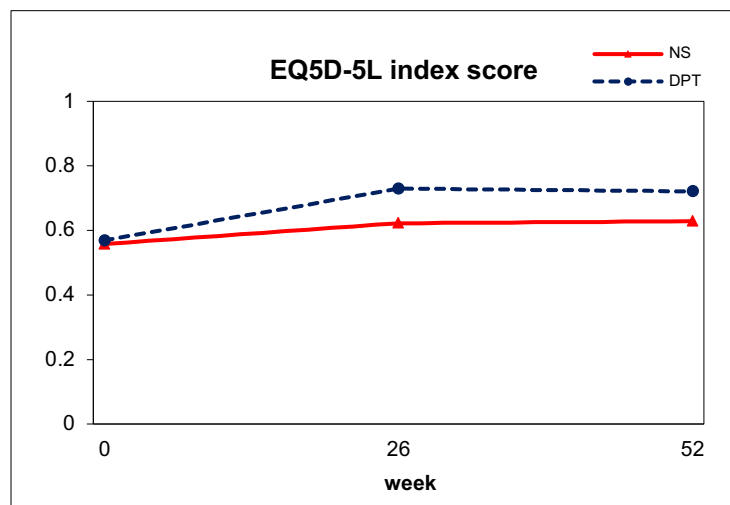


Figure 1i. Change in observed EQ-5D index score



**Supplemental Appendix 2. Results of group effect on WOMAC pain, stiffness, function, composite, VAS, physical function and EQ-5D using linear mixed models**

	16 weeks	p	26 weeks	p	52 weeks	p	Overall trend #	p
Primary outcome								
WOMAC (pain)	-4.81 (-13.47, 3.85)	0.275	-9.73 (-18.39, -1.07)	0.028	-10.34 (-19.20, -1.49)	0.022	-8.26 (-14.83, -1.69)	0.014
Secondary outcomes								
WOMAC (stiffness)	-0.74 (-11.06, 9.58)	0.887	-5.79 (-16.11, 4.53)	0.270	-8.01 (-18.56, 2.54)	0.136	-4.73 (-12.61, 3.15)	0.238
WOMAC (function)	-4.50 (-12.49, 3.49)	0.269	-6.71 (-14.70, 1.28)	0.100	-9.55 (-17.72, -1.39)	0.022	-6.84 (-12.99, -0.69)	0.029
WOMAC (composite)	-4.33 (-12.27, 3.62)	0.285	-7.34 (-15.28, 0.61)	0.070	-9.65 (-17.77, -1.53)	0.020	-7.03 (-13.14, -0.92)	0.024
Pain intensity (VAS)	-3.70 (-13.83, 6.43)	0.473	-6.73 (-16.86, 3.40)	0.192	-10.98 (-21.36, -0.61)	0.038	-7.02 (-14.50, 0.46)	0.066
Timed up and go	-1.13 (-2.74, 0.49)	0.170	-1.73 (-3.34, -0.12)	0.036	-0.73 (-2.38, 0.92)	0.385	-1.22 (-2.46, 0.02)	0.054
30-second chair stand	0.02 (-0.96, 0.99)	0.974	0.81 (-0.17, 1.78)	0.105	0.03 (-0.96, 1.03)	0.952	0.30 (-0.48, 1.08)	0.451
40-m fast-paced walk	-1.07 (-4.29, 2.16)	0.515	-2.62 (-5.84, 0.61)	0.111	-1.78 (-5.07, 1.51)	0.287	-1.84 (-4.40, 0.71)	0.157
EQ-5D VAS	-		4.26 (-2.83, 11.36)	0.238	8.64 (1.36, 15.92)	0.020	6.36 (0.74, 11.98)	0.027
EQ-5D index score	-		0.10 (-0.004, 0.21)	0.058	0.08 (-0.02, 0.19)	0.126	0.09 (0.01, 0.18)	0.037

The data are shown as interaction term between treatment variable and time (95 % confidence interval);

# Overall treatment effect is examined with time indicator 0 for baseline while 1 for follow up visits

\* p = p-value

NS group as the reference group; WOMAC = Western Ontario McMaster University Osteoarthritis Index, VAS= Visual Analogue Score, EQ5D = EuroQol-5D

**Supplemental Appendix 3. Patients requiring analgesics according to a seven-day recall diary presented as the number (percentage)**

	DPT	NS	p-value*
Baseline	7 (18.4%)	8 (21.1%)	0.350
Week 16	8 (21.6%)	7 (18.4%)	0.300
Week 24	10 (27.0)	14 (36.8%)	0.851
Week 52	4 (11.1%)	12 (34.3%)	0.072

\*p-value of group difference using logistic regression with adjustment for baseline values of duration of knee pain and number of chronic diseases, further adjust for analgesics use at baseline for follow up visits.

**Supplemental Appendix 4: Assessment of patient blinding at 52 weeks**

Guess before unmasking	Actual group status		p-value <sup>†</sup>
	DPT	NS	
NS (Placebo)	20 (52.6%)	20 (55.6%)	0.801
DPT	18 (47.4%)	16 (44.4%)	

<sup>†</sup>Chi-squared test. DPT = dextrose prolotherapy, NS = normal saline

### Supplemental Appendix 5: Moderation analysis of BMI and change of WOMAC pain score

