Centralization and directional preference: an updated systematic review with synthesis of previous evidence

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Table 1. Description of studies into centralization and directional preference (N = 43)

First author and date	Study design / Purpose	Population from which participants were recruited	Participants after inclusion / exclusion criteria	Intervention: MDT / DP & control OR classification	Follow-up: weeks (w), months (m), year (y)	Outcomes - clinical or MDT-related	Results - only SD between groups reported
Albert & Manniche 2012	Randomised controlled trial (RCT)	477 with sciatica referred to back centre	181 randomized (acute-chronic)	Symptom-guided exercises (DP) + stabilization exercises .V. sham exercises	2m, 1y (93-95%)	Global RMDQ Leg pain NR signs EQ-5D Sick leave	DP: Global (<0.008); NR some SD
Albert 2012	Prospective cohort: 2ndary RCT / types of disc lesions related to pain responses	See above	181: 165 (91%) back & referred pain	MDT Ax	3m, 1y	Cent. Decrease NB Peripheralization ISQ MRI	Cent. 25.5% 44% 16% Non-Cent. 7% 8% Types disc lesions not associated with Cent. / non-Cent.
Al-Obaidi 2013	Prospective cohort / Cent. v partial Cent.	297: 193 eligible	105 CLBP: 62 Cent. / 43 partial Cent.	MDT	5w, 10w	Pain Fear-avoidance	Cent. pain with activities (<0.001); NS

			(PC)			Disability Physical performance	overall pain
Apeldoorn 2016	Prospective cohort / test-retest changes spinal control after Ax	LBP ± leg pain	114 acute-chronic LBP	MDT Ax	Ax only	DP with Cent. DP no Cent. No DP	51 (45%) 23 (20%) 40 (35%) DP with Cent. better spinal control (<0.02)
Bonnet 2011	RCT	LBP	54 LBP	MDT Guideline-based group	1w	Cent. Disability Pain	62% v 17% (0.008)
Desai 2012	Case studies / effect of ESI on DP	NP with cervical radiculopathy	3 acute-chronic	MDT Ax after ESI	2w	DP only after ESI	Full resolution of symptoms
Edmond 2014	Retrospective cohort /	Convenience sample with FOTO data classified as Cent. / non-Cent.	328 NP acute-chronic	Classified as: Cent. + DP, Non-Cent + DP, Non-Cent + non-DP	Discharge	Function Pain	Cent. 40% DP 70% Cent. or DP: function (≤0.01); pain (NS)
Elenburg 2016	Case study / MDT despite spine fractures	Not given	1 LBP with lumbar fractures	MDT Ax & treatment	1m	Function Pain	Almost full resolution

Flavell 2016	Prospective cross-sectional / classification systems	316: 197 (62%)	150 CLBP (76%)	MDT Ax	Ax only	Cent. / Periph Dysfunction Other Postural	32% 36% 31% 1%
Franz 2017	Pragmatic controlled study	47 consenting consecutive LBP	44 military LBP	MDT (DP) (22) Usual care (22)	3m	Pain Disability PGE HC Stability DP	DP: pain, PGE, disability 3m (<0.05)
Garcia 2013	RCT	182 CLBP	148 CLBP (81%)	MDT (DP) Back school (BS)	1m, 3m, 6m (99-100%)	Pain Disability QoL	MDT: disability 1m (0.004); all other (NS)
Garcia 2016	Prospective cohort: 2ndary RCT / better responders DP		140 / 148 (95%) DP	Baseline characteristics	1m	Pain Disability DP	Older age (0.01). Cent. leg pain high pain (NS)
Gregg 2014	Retrospective cohort / factors associated with outcomes	Consecutive	1076 LBP	Hall classification* and treatment. 12 prognostic variables (age, gender, pain, disability,	6m	Pain Function RTW	pain factors (<0.01); DP, surgery (<0.09). age, shorter pain (<0.001). job (<0.001), female, pain,

				surgery, DP)			DP (<0.07).
Hagovska 2014	Pragmatic controlled study / effect Cent.	Not given	31 LBP discopathy 24 no-LBP controls	MDT Healthy controls	3m	Pain Disability Cent. EMG	NS between groups. Cent. 100% 1m
Halliday 2016	RCT	133 consented	70 (53%) CLBP with DP	MDT MCE	8w	Pain GPE Function Muscle	MDT: GPE (0.03)
Heintz & Hegedus 2008	Case study / use of TBC	Not given	1 NP	TBC	6w	Pain Disability ROM	Cent. with mobilisation
Hosseinifar 2013	RCT	75:41 (55%)	37 (90%)	MDT MCE	Discharge	Pain Disability Muscle	MCE (<0.05)
Lopez-Diaz 2015	RCT	Not given	30 LBP	Mobilization Modalities	Discharge	Pain ROM Cent.	Mobilization: Cent. (<0.001)
Mazzone 2016	Cross-sectional / kinematics during extension	Not given	18 LBP and 17 no LBP	Spine kinematics in LBP subgroups	Ax only	MSI CPR subgroups: manipulation stabilisation Cent. DP	100% 35% 24% 18% 47%
Moncelon 2015	RCT	Not given	14 CLBP with DP	MDT Usual care	Six sessions	Function Pain	

Murphy 2011[1]	Prospective cohort / DBCDG classification	Consecutive LBP in one year	264 acute-chronic LBP	According to classification	Not recorded	Red flags Cent. Pain provocation NR Myofascial	3% 41% 50% 24% 10%
Murphy 2011[2]	Prospective cohort / DBCDG classification	Consecutive NP in one year	95 acute-chronic NP	According to classification	Not recorded	Red flags Cent. Pain provocation NR Myofascial	1% 27% 69% 19% 22%
Ojha 2013	Case study / 2 categories TBC	Not given	1 CLBP	TBC = DP + manipulation	7w	Disability ROM	
Otero 2014	Prospective cohort / MDT syndromes, Cent. DP	Consecutive	349 patients with LBP	MDT	Discharge	Classification Cent. DP Stability MDT	92% Der. 71% / 76% at discharge 73% 90%
Otero 2016	Prospective cohort / MDT syndromes, Cent. DP	Consecutive	297 patients with NP	MDT	Discharge	Classification Cent. DP Stability MDT	92% Der. 75% / 82% at discharge 86% 92%-
Padmana-	Case study	Not given	1 CLBP with	DP + treadmill	3w	Pain	

bhan 2011			spinal stenosis			Disability ROM	
Petersen 2011	RCT	1619: 350 (27%)	350 CLBP Cent. or Peripheral-ization	MDT Manipulation	2m, 1y (93%)	Disability Pain GPE QoL Satisfaction Further HC	MDT: 2m, 1y Disability (0.02, 0.03). Cent./Periph. (NS)
Petersen 2015	2ndary RCT / factors related to positive outcome in RCT above	Not given	350 LBP effect modifiers	as above		Age Duration Pain variables NR	MDT: NR + Periph. (RR 10.5)
Robinson 2016	Case study with DP	Not given	1 sub-acute LBP	DP	4w	Pain Disability ROM MRI	
Rose 2016	Retrospective cohort / Cent. v non-Cent.	Not given	11 NP	Cent. (6) Non-Cent (5)	Discharge	Disability Cent.	Cent: Disability: (0.005)
Stanton 2011	Cross-sectional study / Prevalence & reliability TBC	545 LBP > 90 days	250 acute or subacute LBP	Testing out algorithm criteria for 4 sub-groups	Ax only	Manipulation Stabilization DP Traction: + 1 subgroup	42% 17.5% 31% 9.5% 25%

						Kappa	0.52
Surkitt 2016	2ndary RCT (Ford et al., 2016) / discogenic* sub-group	2038 CLBP ± leg pain DP + Discogenic*	78 met criteria	DP v Guideline-based advice	5w, 10w, 26w, 52w	Pain Function Psychosocial General health	DP: back pain 10w (0.003)
Takasaki 2010	Case study / effect on disc	Not given	1 LBP with MRI	MDT	1m	Pain Disability MRI	Cent. & disc displacement resolved
Takasaki 2016	Case study / effect on CCFT	NP	1 NP	MDT	Discharge	CCFT	CCFT negative after Cent.
van Helvoirt 2014	Prospective cohort / effect of TESI	132 referred for HLDS	69 non-Cent HLDS candidates	Transforaminal epidural steroid injection (TESI)	2w, 1y	Resolved Cent. Non-Cent / B Surgery	16% 46% 16% 22%
van Helvoirt 2016	Prospective cohort / 2ndary above different outcomes	132 referred for HLDS	77 non-Cent. HLDS candidates	TESI	1y	Leg pain* Disability* GPE Back pain^ HADS^	Surgery v non-surgery * (0.001); Cent. v non-Cent *^ (<0.05)
Werneke 2011	Prospective cohort / effect of Cent. on outcomes	Selected from FOTO database	692 acute-chronic LBP ± leg pain	MDT	1m	Pain Functional status Psychological distress	Non-Cent. v Cent. worse outcomes (<0.001)

Werneke 2014	Reliability study at levels MDT training	PT different levels of MDT training	47 PTs 1662 patients	2 independent MDT assessments	Ax only	Agreement: (MDT, DP, Cent.) Level training	Kappa 0.11 to 0.44
Werneke 2016	Retrospective cohort / MDT, Cent. DP as prognostic factors	2066 LBP selected from FOTO database	723 for who complete data	MDT	1m	Pain Functional status Psychological distress	Cent. and DP added little to predicting outcomes
Werneke 2018	Prospective cohort / DP & STarT	LBP high STarT risk from FOTO	138 LBP	DP v non-DP Other variables (pain, function, MDT training)	Discharge	Disability Psychological distress	DP (65%) disability (0.03)
Williams 2011	Case study with lateral component	Not given	1 discogenic LBP	MDT	2m	Disability	Resolution with Cent.
Wu 2018	Case studies DP with LUTS	Not given	3 CLBP with LUTS	MDT	<2m	Prostate Symptom Index	Complete resolution
Yarnbowicz 2018	Prospective cohort / Cent. DP prevalence, & outcome	1006 LBP consecutive patients	940 initial 639 full data	DP Cent. No DP no-Cent. Not classifiable (NC)	Discharge	Pain Function Prognosis	Cent. 20% Non-Cent. 39% NC 23% DP Cent. pain & function (<0.001)

2ndary = secondary analysis of previous study; Ax = assessment; CLBP = chronic low back pain; CCFT = Cranio-cervical flexion test; CPR = clinical prediction rules; DBCDG = diagnosis-based clinical decision guide; Der. = Derangement; EMG = electromyography of erector spinae muscle activity; ESI = epidural steroid injection; FOTO = Focus on Therapeutic Outcomes; GPE = Global Perceived Effect; HADS = Hospital Anxiety Depression Scale; HC = healthcare; HLDS = herniated lumbar disc surgery; HE = healthcare; LUTS = lower urinary tract symptoms; MCE = motor control exercises; MDT = Mechanical Diagnosis and Therapy or the McKenzie Method; MSI = movement system impairment; NR = nerve root; NS = no significant difference; PT = physical therapists; QoL = Quality of Life; RCT = randomized controlled trial; ROM = range of movement; RR = relative risk; STarT = subgroups for targeted treatment back screening tool; TBC = treatment based classification system.

*Discogenic = at least 4 of: Back $\pm$leg pain; sitting limited to 60 minutes; forward bending somewhat difficult; lifting somewhat difficult; sit to stand somewhat difficult; coughing or sneezing somewhat difficult; symptoms worse the next day; working on manual job; onset associated with flexion / rotation and/or compression loading.

*Hall classification = four sub-groups based on site of symptoms and DP; and fifth sub-group with heightened pain behaviours (Gregg et al. 2014)

Table 2. Prevalence - Centralization and directional preference

Summary of previous studies - Centralization (N = 31) (May and Aina, 2012)

	Duration	Symptoms	N	(%)
	Acute	**LBP + NP**	**236 / 317**	**77%**
	Sub-acute	**LBP**	**62 / 123**	**50%**
	Chronic	**LBP**	**227 / 567**	**40%**
	Mixed	**LBP**	**1584 / 3738**	**42%**
		Neck pain	**62 / 168**	**37%**
TOTAL			**2109 / 4745**	**44%**

Summary of previous studies - directional preference (N = 5), (May and Aina, 2012)

TOTAL			**1661 / 2368**	**70%**

Studies from the present review (N = 21)

	Duration	Symptoms	N	Cent.	DP	No DP
Albert (2012)[N2]	Mixed	Sciatica	165	25%	59%	15%
Al-Obaidi (2013)	Chronic	LBP	105	59%	41%	
Apeldoorn (2016)	Mixed	LBP +/-	114	45%	20%	35%

Edmond (2014)	Mixed	NP	328	40%	30%	30%	(Ext. 80%, Flex. 10%, Lat. 10%)
Flavell (2016)	Chronic	LBP	150	32%		68%	
Garcia (2016)	Chronic	LBP +/-	148		95%	5%	(Ext. 50%, Flex. 5%, Lat. 40%)
Hagovska (2014)	Chronic	Sciatica	31	100%			
Halliday (2016)	Chronic	LBP	133	73%	27%		(Ext. 86%, Flex. 5.5%, Lat. 8.5%)
Mazzone (2016)	Chronic	LBP	17	47%		53%	
Murphy (2011)[1]	Chronic	LBP +/-	264	41%			
Murphy (2011)[2]	Chronic	NP +/-	95	27%			
Otero (2014)	Mixed	LBP	349	76%	16%	8%	(Ext. 80%, Flex. 4%, Lat. 13%)
Otero (2016)	Mixed	NP	297	82%	10%	8%	(Ext. 84%, Flex. 3%, Lat. 14%)
Petersen (2011)	Chronic	LBP +/-	350	53%		47%	
Stanton (2011)	(Sub)-Acute	LBP +/-	250		31%	69%	
Surkitt (2016)[N38]	Chronic	LBP +/-	78	51%			
van Helvoirt (2014)[N11]	Chronic	Sciatica post-TESI	69	46%	16%	22%	
Werneke (2011)	Mixed	LBP +/-	692	36/45%		64/55%*	
Werneke (2016)	Mixed	LBP +/-	723	39%	29%	32%	
Werneke (2018)	Mixed	LBP	138		65%	35%	

Yarnbowicz (2018)[N19]	Mixed	LBP	639	20%	64%	13%	

* = depended on outcome: pain/function; Ext. = extension; Flex. = flexion; Lat. = Lateral

[N44] = missing numbers; the superscript number is the discrepancy between total and accounted for

	Duration	Symptoms	N	Cent.	DP	No DP	UC
TOTAL	**Mixed**	**LBP**	**2655**	**975**	**788**	**873**	**19**
		Sciatica	**265**	**104**	**108**	**40**	**13**
	Sub-acute	**LBP**	**250**		**77**	**173**	
	Chronic	**LBP**	**1245**	**548**	**220**	**439**	**38**
	Mixed	**Neck pain**	**720**	**401**	**128**	**191**	
TOTAL			**5135**	**2028**	**1321**	**1716**	**70**
%			**100%**	**39.5%**	**26%**	**33.5%**	**1%**

Cent. = centralisation; DP = directional preference; no-DP = neither response; UC = uncounted

Table 3. PEDro quality scale for randomised controlled trials (N = 10) (3 / 88 disagreements) 97% agreement

First author and date	1	2	3	4	5	6	7	8	9	10	11	Total out of 10	Overall quality
Albert 2012	√	√	X	√	X	X	√	√	√	√	√	7	Moderate
Bonnet 2011	√	√	X	√	X	X	X	√	X	√	X	4	Low
Franz 2017	X	X	X	√	X	X	X	√	X	√	√	5	Low
Garcia 2013	√	√	√	√	X	X	√	√	√	√	√	8	High
Hagovska 2014	X	X	X	X	X	X	X	√	X	√	√	3	Low
Halliday 2016	√	√	√	√	X	X	√	√	√	√	√	8	High
Hosseinifar 2013	√	√	X	√	X	X	√	X	X	√	√	5	Moderate
Lopez-Diez 2015	√	√	√	√	√	√	√	√	X	√	√	9	High
Moncelon 2015	√	X	X	X	X	X	√	√	X	√	√	4	Low
Petersen 2011	√	√	√	√	X	X	√	X	√	√	√	7	Moderate

PEDro scores: 1. Eligibility criteria were satisfied; 2. Subjects randomly allocated to groups; 3. Allocation was concealed; 4. Groups similar at baseline regarding most important prognostic indicators; 5. Blinding of subjects; 6. Blinding of all therapists; 7. Blinding of all assessors; 8. Measures of jey outcomes were obtained from more than 85% of those initially allocated to groups; 9. All subjects for who outcome measures were available received the treatment or the control as allocate, or where this was not the case, data were analysed by "intention to treat"; 10. Reports of between-group statistical comparison were reported for at least one key outcome; 11. Study provided both point measures and measures of variability for at least one outcome measure. Score is out of ten item is not included.

Table 4. Prognostic study scores (N = 12) **Disagreements 24 / 150** **Agreement = 84%**

Author	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Total (15)	Quality
Albert 2012	√	√	√	√	√*	√*	√*	√	√	√	√	√*	√	√	√	15	High
Al-Obaidi 2013	√	√	√	X	X	√	X	√	√	√	√	√	√	X	√	11	High
Edmond 2014	X	X	√	X	X	X	√	√	√	√	√	X	√	√	X	8	Moderate
Garcia 2016	√	√	√	√*	√	√	√	X	X	√	√	√	√	√	√	13	High
Gregg 2014	√	X	√	X	X	X	X	√	X	√	√	X	X	√	X	6	Low
Petersen 2015	√	√	√	X	X	√	√	√	X	√	√	√	√	√	√	12	High
Rose 2016	X	X	X	X	√	√	√	X	X	√	√	X	X	X	√	6	Low
Surkitt 2016	√	√	X	√	√	√	√	X	X	√	√	√	√	X	√	12	High
van Helvoirt 2014	√	√	√	√	√	√	X	X	X	√	√	X	X	X	X	8	Low
Werneke 2011	X	X	√	X	X	X	X	X	X	√	√	X	√	√	√	6	Low
Werneke 2016	X	X	√	X	X	X	X	√	√	√	√	X	√	√	√	8	Low
Werneke 2018	X	X	√	X	X	X	X	X	X	√	√	X	√	√	√	6	Low

* with information from the accompanying study (Albert & Manniche 2012; Garcia et al. 2014; Petersen et al. 2011)

Quality items (from Hartvigsen et al. 2015): 1. Study population clearly defined; 2. Study population described; inclusion / exclusion criteria / chronicity; 3. Study population represent population of interest**; 4. Completeness of follow-up described for each point of follow-up to one year**; 5. Completeness of follow-up adequate - 85%**; 6. Reasons for loss to follow-up adequately described; 7. No important differences (characteristics and outcomes) between completers and non-completers; 8. Prognostic tests defined enough to be replicated; 9. Performance of prognostic tests are standardised; 10. Outcomes are defined; 11. Outcomes well established; 12. Method, setting, timing outcomes same for all participants; 13. Data presented sufficiently to assess adequacy of analysis; 14. Statistical analysis sufficiently described and appropriate to account for other prognostic factors, such as multivariate analysis**; 15. No selective reporting of results.

** these items were slightly amended from the original as described in the text.