Approach to Osteopathic Research: The ORC Experience in Studying OMT for Low Back Pain

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Presentation Objectives

- Provide a historical perspective of The Osteopathic Research Center's establishment of a research niche in studying OMT for low back pain
- Describe methodological aspects and present main results of the OSTEOPATHIC Trial of OMT for chronic low back pain
- Present secondary results of the OSTEOPATHIC Trial that address the mechanisms underlying osteopathic medicine's manual diagnostic and therapeutic modalities
- Present national health services data that further corroborate and extend the OSTEOPATHIC Trial findings

HISTORICAL PERSPECTIVE

Timeline of Selected Events Relating to ORC Research on Low Back Pain

1981 Hoehler et al publication in JAMA (negative study)
1995 Osteopathic Medicine: Past, Present, and Future: a conference sponsored by the Josiah Macy, Jr. Foundation
1996 Establish research collaboration with TCOM - Department of Osteopathic Manipulative Medicine (OMM)
1997 Acquire 1-year AOA grant to conduct clinical outcomes study of OMT in OMM department clinic ($26,710)
1999 Acquire 2-year AOA grant to conduct randomized controlled trial (RCT) of OMT for chronic low back pain (LBP) ($69,388)
1999 Andersson et al publication in NEJM (negative study)
2002 The ORC is formally established at UNTHSC in Fort Worth, TX
2003 Licciardone et al publication in Spine (equivocal study)
2005 Licciardone et al publication in BMC Musculoskeletal Disorders (systematic review and meta-analysis [SRMA] is first study to definitively show significant improvement in LBP with OMT)
2005 Acquire 5-year NIH grant to conduct the OSTEOPATHIC Trial ($778,231 + OHF matching funds)
2006 Acquire 1-year grant to conduct comprehensive update of SRMA project ($99,998)
2009 AOA establishes first and only clinical practice guideline based primarily on 2005 SRMA results
2010 AOA Clinical Guideline Subcommittee publication of clinical practice guideline for OMT in patients with LBP in JAOA
2010 OSTEOPATHIC Trial grant acquires 1-year extension from NIH
2010 AOA guideline for OMT in patients with LBP is accepted by AHRQ National Guideline Clearinghouse
2010 ORC establishes the CONCORD-PBRN to study OMT and osteopathic medicine in the primary are setting
2011 OSTEOPATHIC Trial patient follow-up and data collection is completed
2011 ORC's CONCORD-PBRN is certified as a primary care research network by AHRQ
2011 ORC begins trainings 14 Patient-Centered Research fellows nationwide to conduct OMT and osteopathic research (162 contact hours)
2012 OSTEOPATHIC Trial receives AOF - Purdue Partners Against Pain Award
2013 Licciardone et al publication in Ann Fam Med (first RCT to show significant and clinically relevant results with OMT)
2013 Licciardone et al authors receive AOA George W Northup, DO, Medical Writing Award
2013 ORC invited by NIH-NCCAM to coordinate development of a research concept to conduct a national multisite study of manual therapy for LBP ($10-15 million)
2013 ORC seeking osteopathic profession funding to conduct the OSTEOPATHIC II Trial ($3 million)
2014 ~15 OSTEOPATHIC Trial manuscripts in various stages of publication

BACKGROUND ON OMT FOR LOW BACK PAIN

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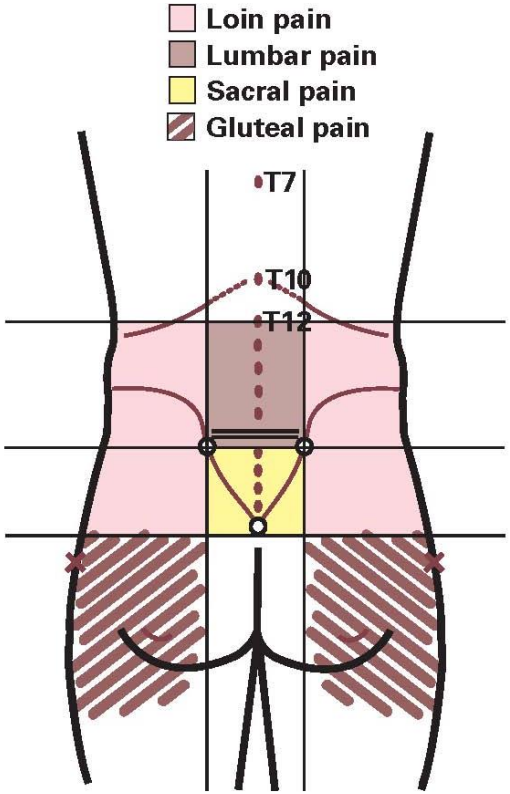
Low Back Pain
Societal Impact

- LBP is **common** worldwide
- Global Burden of Disease Study 2010*
  - 632 million persons worldwide
  - Leading cause of years lived with disability
- Vast majority of LBP, such as that attributed to lumbar strain and sprain, is considered **"non-specific"**
- The costs to society for LBP are enormous – exceeding **$100 billion** annually in the United States†
- Medical care for nonspecific low back pain in the United States has been described as **"overspecialized, overinvasive, and overexpensive"**‡

***Vos T. Lancet 2013;380:2163-2196**
†Katz JN. J Bone Joint Surg Am 2006;88 Suppl 2:21-24
‡Waddell G. Spine 1996;21:2820-2825

Low Back Pain
Classification

- **LBP Definition**
  - Pain, muscle tension, or stiffness
  - Localized below the costal margin and above the inferior gluteal folds
  - With or without leg pain (sciatica)
- **LBP Chronicity**
  - **Acute**: 4-6 weeks since onset
  - **Subacute**: 4-6 weeks to 3 months since onset
  - **Chronic**: Greater than 3 months since onset



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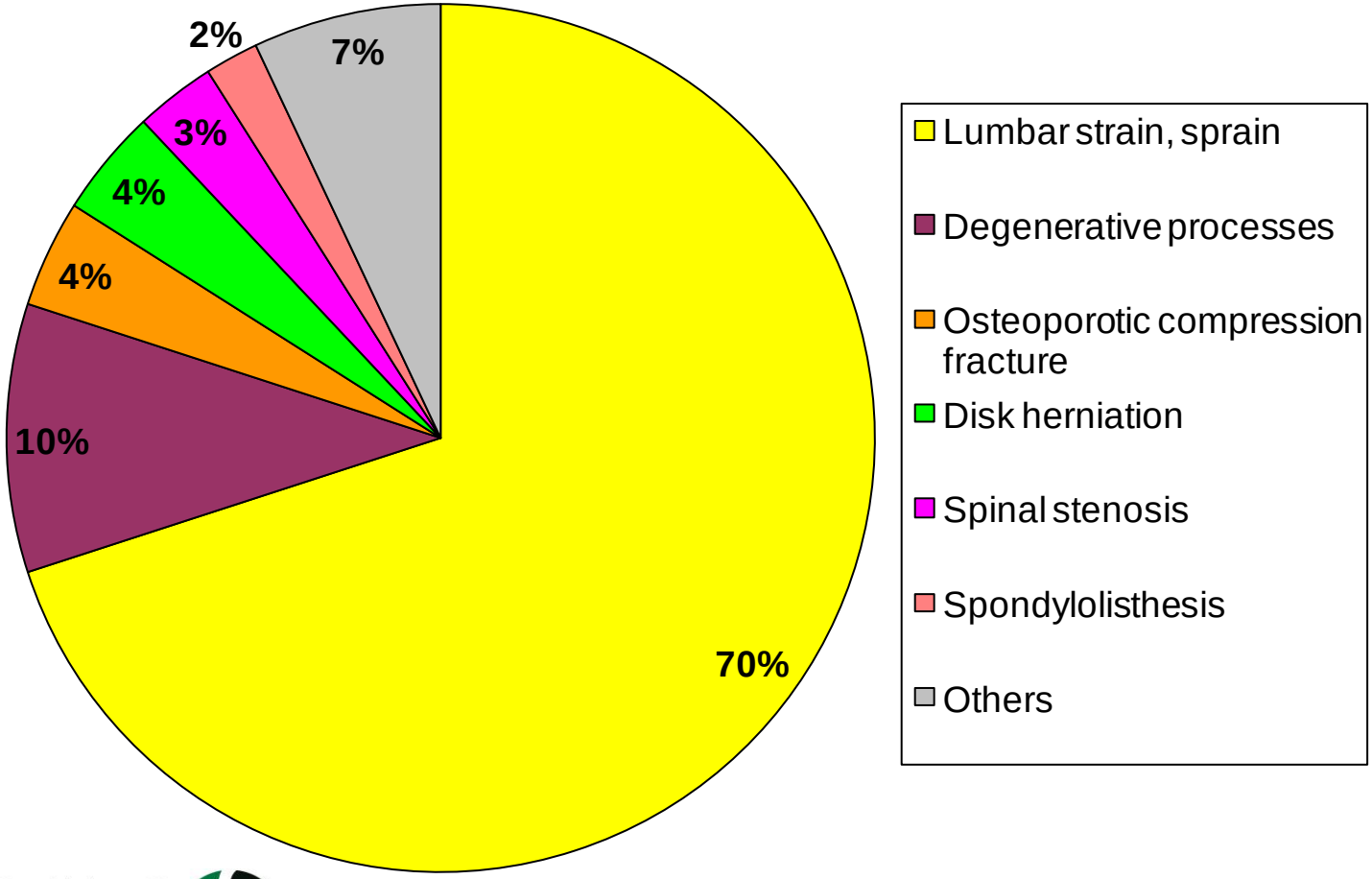
Jensen S. Aust Fam Physician 2004;33:393-401.

Low Back Pain
Etiology



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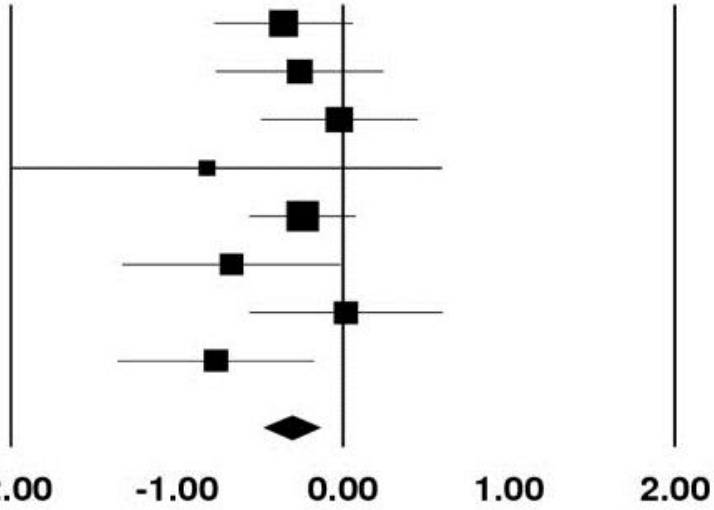
*Deyo RA and Weinstein JN. New Engl J Med 2001;344:363-370.

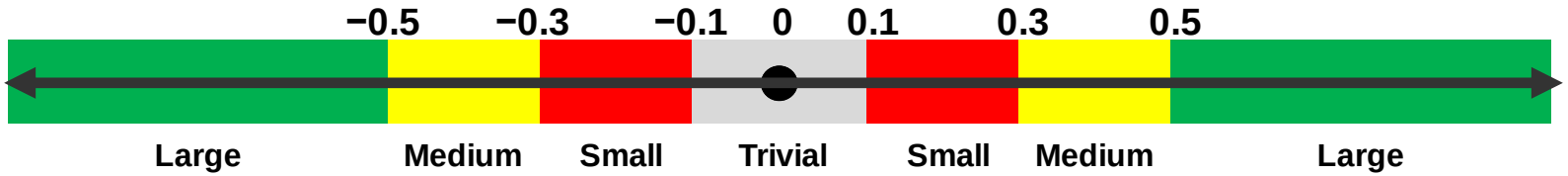
Systematic Review of OMT*

Low Back Pain

Source, year	Control treatment	No. of subjects OMT	Control	Weight
Hoehler 1981 [42]	Active and placebo	56	39	17
Gibson 1985 [43]	Active treatment	38	27	12
Gibson 1985 [43]	Placebo control	39	33	14
Cleary 1994 [47]	Placebo control	8	4	2
Andersson 1999 [44]	No treatment	83	72	29
Burton 2000 [45]	Active treatment	20	20	8
Licciardone 2003 [46]	Placebo control	32	19	9
Licciardone 2003 [46]	No treatment	42	17	9
Overall		**318**	**231**	**100**



ES = –0.30 (–0.47 - –0.13); P = .001



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*Licciardone JC. BMC Musculoskel Disorders 2005;6:43

EBM Recommendations (2005)

Classification of Recommendations

Quality of Evidence	Net Benefits: Substantial	Moderate	Small	Zero/Negative
Good	A	B	C	D
Fair	B	B	C	D
Poor	I	I	I	

A	Strongly recommend providing intervention to eligible patients
B	Recommend providing intervention to eligible patients
C	No recommendation for or against providing intervention
D	Recommend against providing intervention
I	Insufficient evidence for or against providing intervention

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OMT Clinical Practice Guideline
AOA 2010

- Publication of **first and only guideline** for osteopathic medicine (OMT) in patients with low back pain*
  - The AOA recommends that osteopathic physicians use osteopathic manipulative treatment (OMT) in the care of patients with low back pain. Evidence from systematic reviews and meta-analyses of randomized clinical trials **(Evidence Level 1a)** supports this recommendation.
  - Potentially important **implications for reimbursement schedules** by Medicare, Medicaid, and third-party insurance carriers

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***Clinical Guideline Subcommittee on Low Back Pain. J Am Osteopath Assoc 2010;110:653-666**

OSTEOPATHIC TRIAL METHODS

The OSTEOPATHIC Trial*

Research Design

- **OSTEOPAT**hic **H**ealth outcomes **I**n **C**hronic low back pain (**Aug 2006 – Jan 2011**)
- **Phase III, sham controlled RCT (N=455)**
- **2x2 factorial design** (ClinicalTrials.gov: NCT00315120)
  - 2nd factor was ultrasound therapy (UST)
- **6 treatment sessions** over 8 weeks, with final outcomes assessment at week 12
- **Outcome measures**
  - **Visual analogue pain scale**
  - Roland-Morris Disability Questionnaire
  - Medical Outcomes Study SF-36 Health Survey (general health)
  - Work disability
  - Satisfaction with back care

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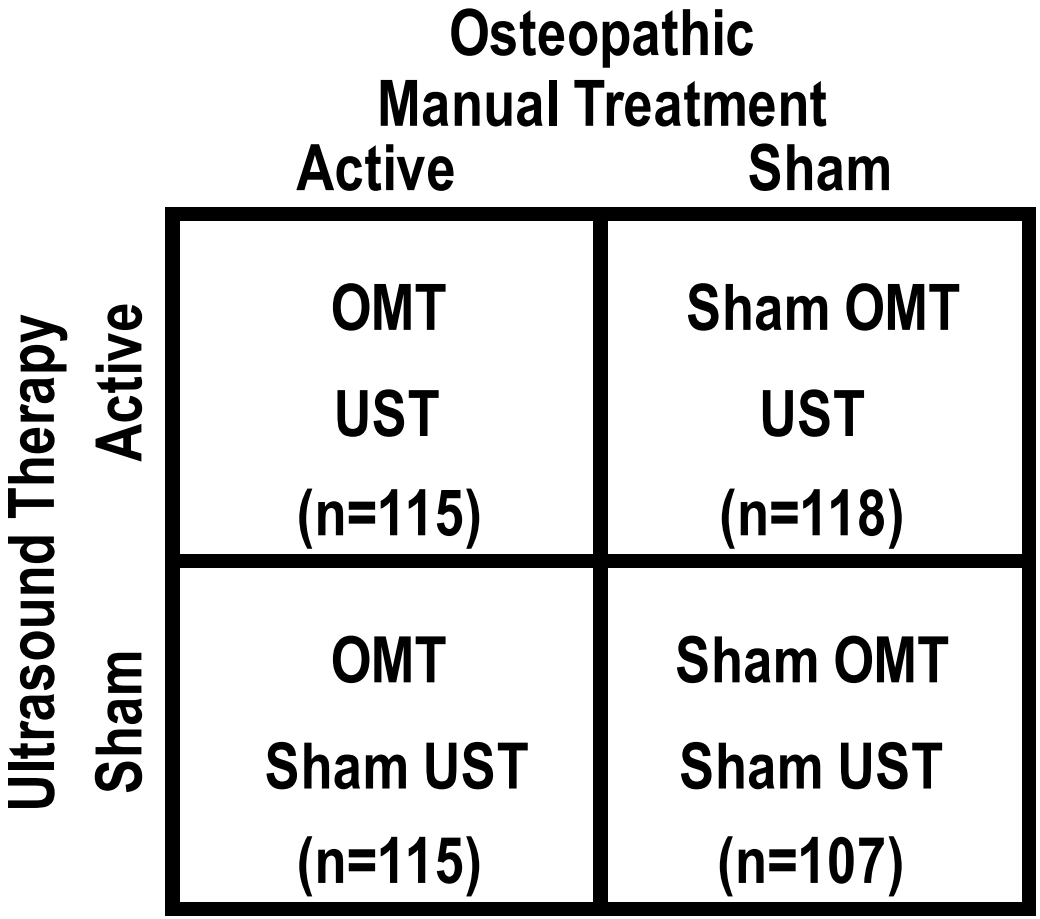
*Licciardone JC, et al. Osteopath Med Prim Care 2008;2:5

The OSTEOPATHIC Trial

The OMT "Megatrial" (N=455)



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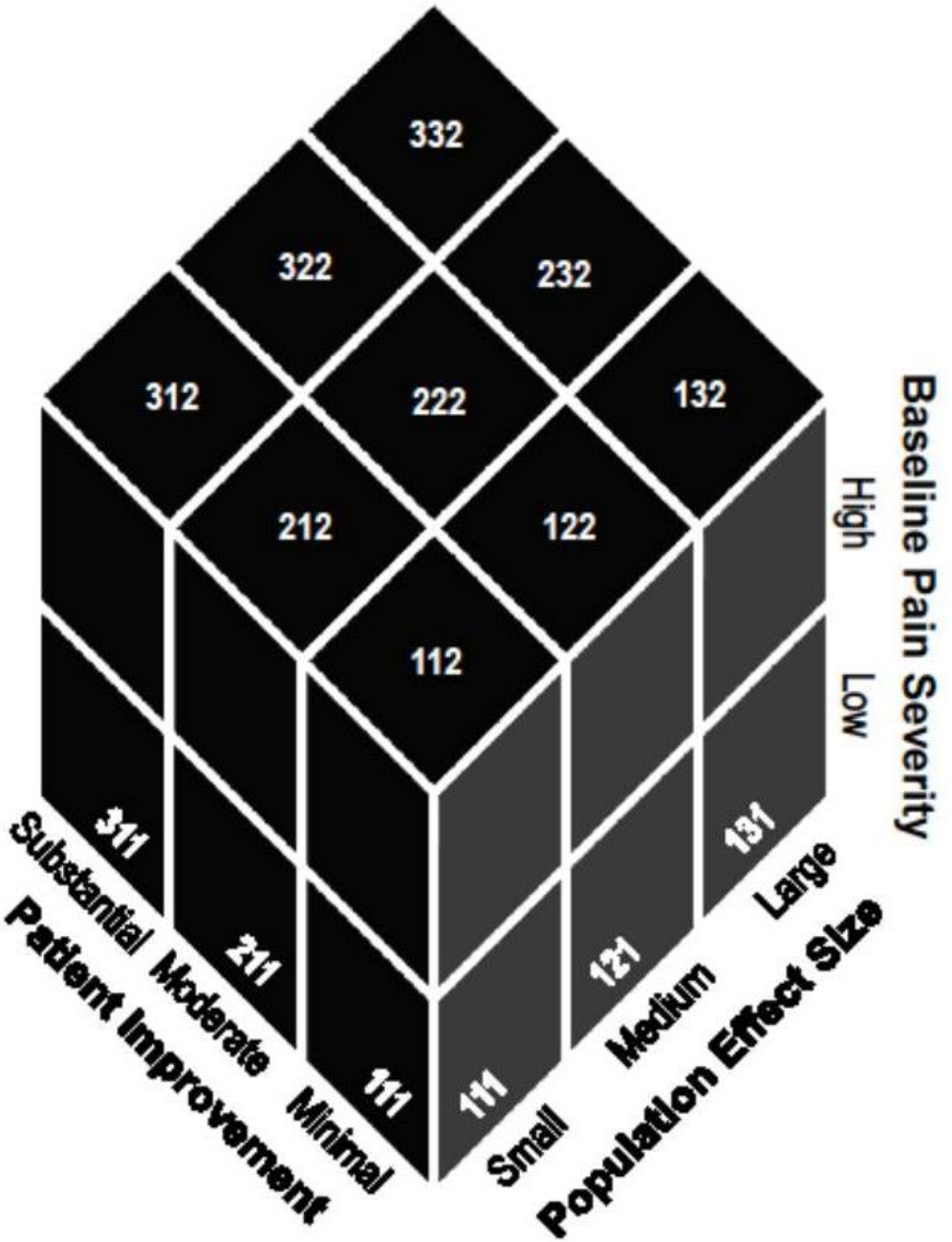
OMT Protocol

- **Algorithmic** approach
- Diagnostic examination for somatic dysfunction at each treatment visit
- 10 minutes for standard techniques (targeted lumbosacral, iliac, and pubic regions)
  - HVLA
  - Muscle energy
  - Myofascial release
  - Articulatory
  - Soft tissue
  - Tender point treatment (counterstrain)
- 5 minutes for optional techniques

Multi-Dimensional Assessment

- Classify pain improvement (reduction) in individual patients
- Measure the OMT effect across all patients
- Explore the OMT effect in patient subgroups



*Licciardone JC, et al. Man Ther 2013;18:533-540

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Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials

IMMPACT Benchmarks for Patient Changes*

Improvement	Pain Reduction Threshold (100-mm VAS)	
	Relative	Absolute
Moderate	30%	20 mm
Substantial	50%	40 mm

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*Dworkin RH. J Pain 2008;9:105-121

Cochrane Back Review Group

Criteria for Clinical Relevance*

Response Ratio (RR)

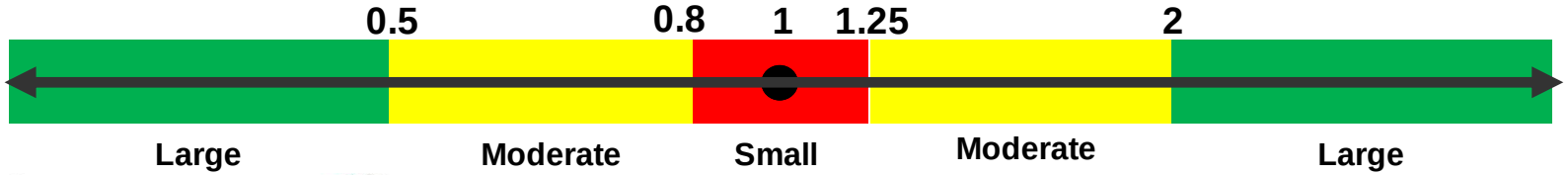
$$= \frac{A/(A+B)}{C/(C+D)}$$

Determined for both moderate and substantial improvement

Intervention	Response	Non-Response	Total
Active	A	B	A+B
Sham	C	D	C+D

Effect Sizes

- Small: RR < 1.25
- Medium: 1.25 ≤ RR ≤ 2
- Large: RR > 2



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*Furlan AD. Spine 2009;34:1929-1941

RESULTS

CONSORT Flow Diagram

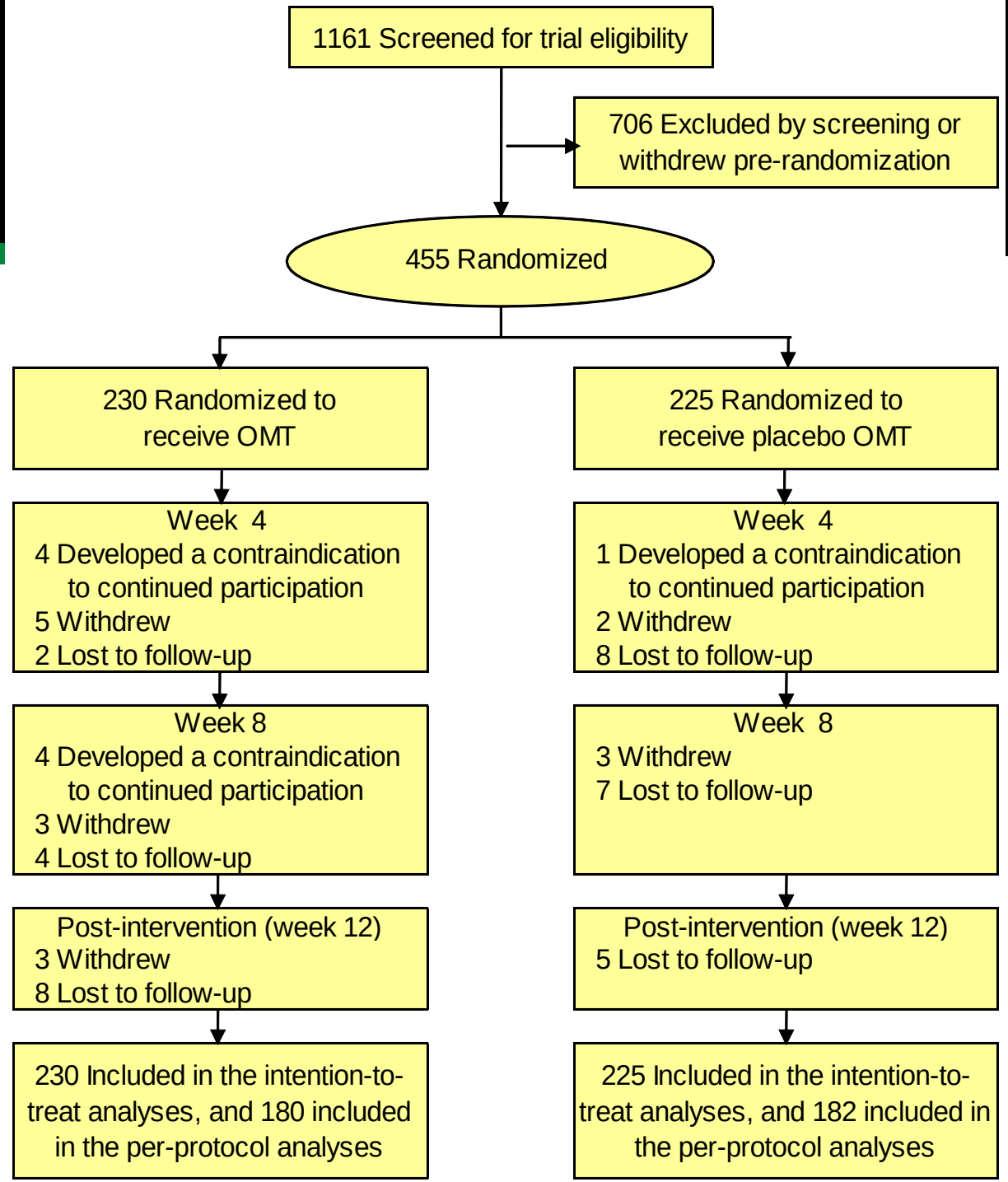
Adherence
382 (84%) received all treatments
396 (87%) attended week 12 visit

Care Providers
2058 (80%) treatments were delivered by faculty physicians

Safety Profile
27 (6%) reported adverse event
9 (2%) were classified as SAE
No SAE was adjudicated as definitely or probably related to treatment

No significant differences between OMT and sham OMT on any of the above

Contraindications to Trial Continuance
8 in OMT group vs. 1 in sham OMT group (P = 0.04). However, only 1 contraindication (recurrent back spasticity following treatment) was adjudicated as "possibly" related to OMT



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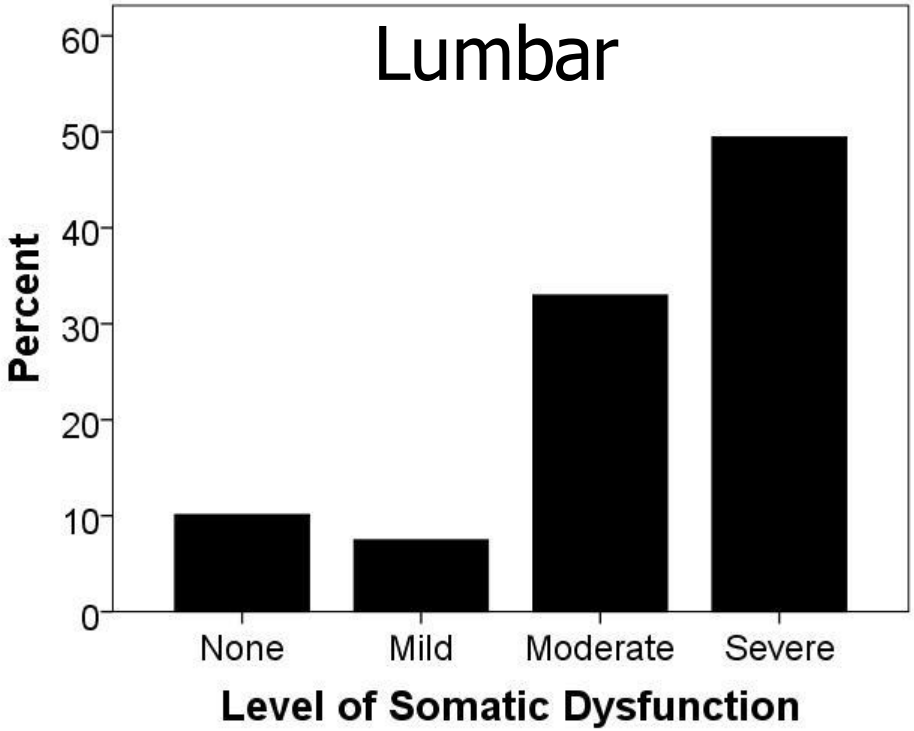
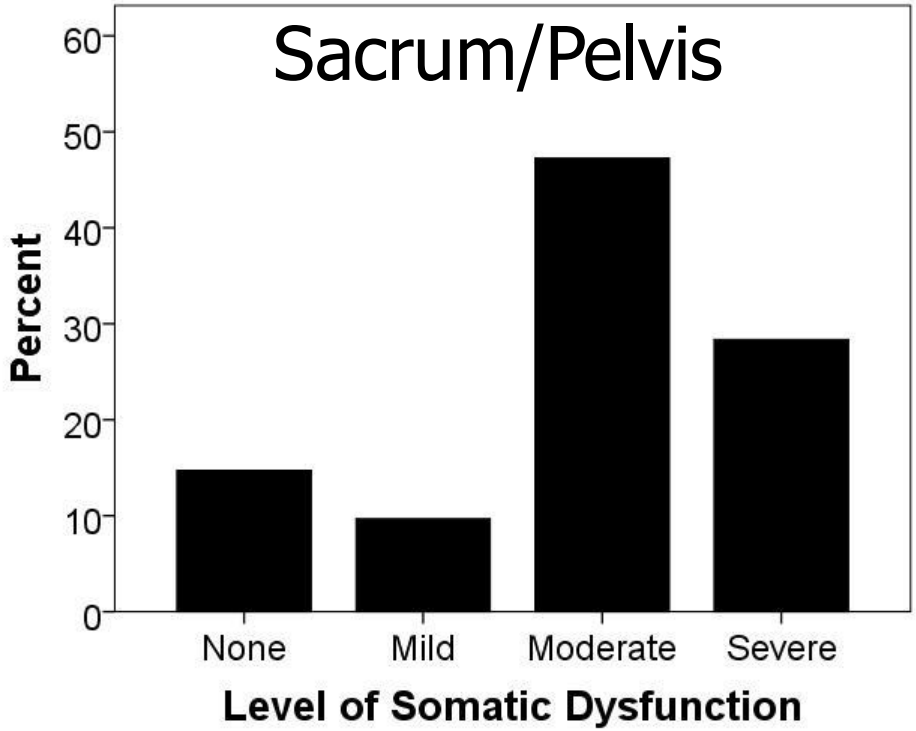
Baseline Somatic Dysfunction*
Lumbar and Sacrum/Pelvis†





Somatic dysfunction – "impaired or altered function of related components of the somatic (body framework) system: skeletal, arthrodial, and myofascial structures, and related vascular, lymphatic, and neural elements" (based on TART criteria)

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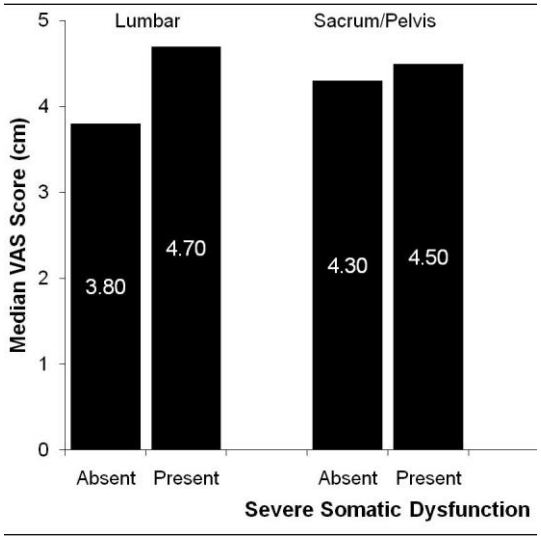
*AACOM. Glossary of Osteopathic Terminology; 2009

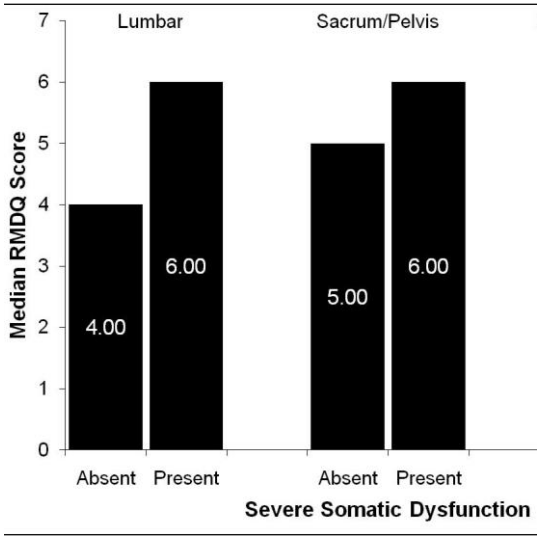
†Licciardone JC, et al. J Am Osteopath Assoc 2012; 112:420-428

Association of Somatic Dysfunction with LBP and Back-Specific Disability* At Baseline

P=0.003



P=0.01 P=0.02



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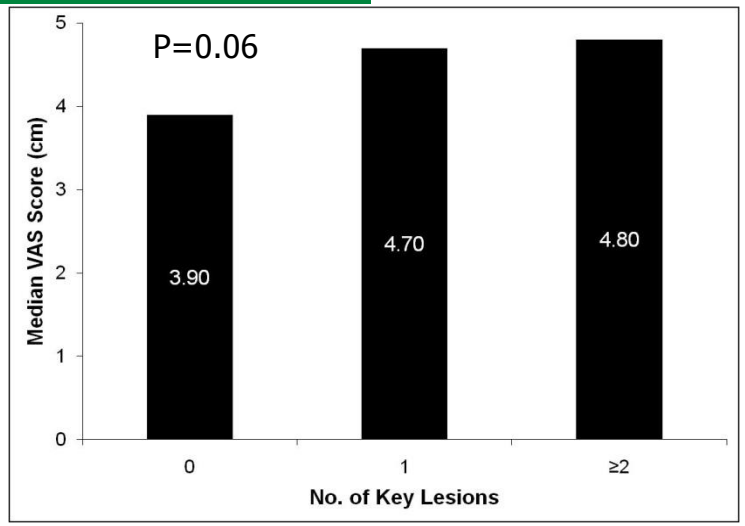

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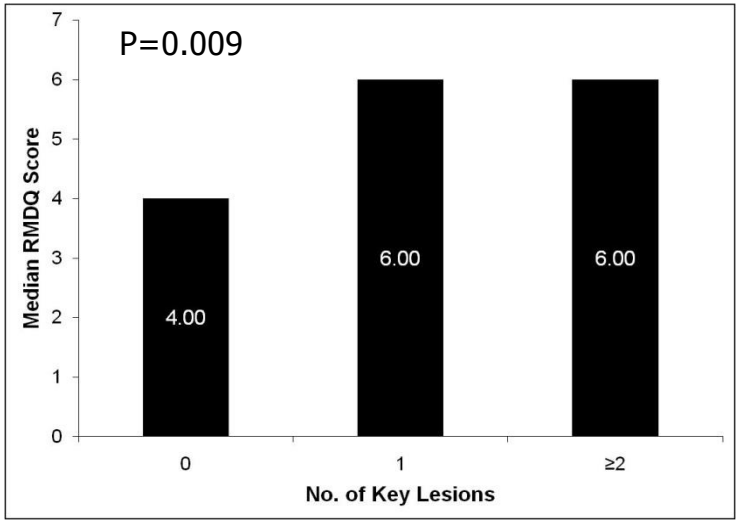

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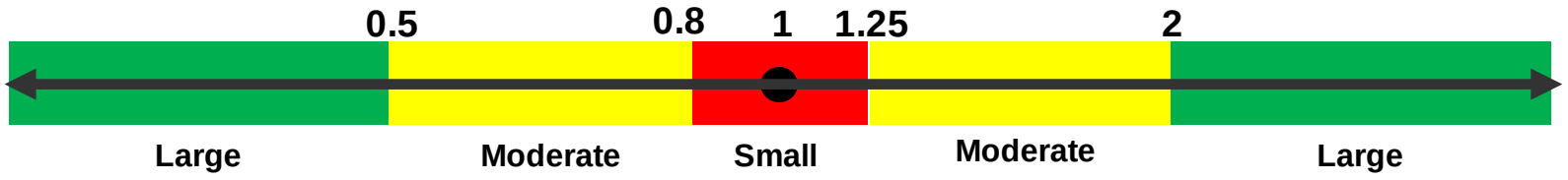
*Licciardone JC, et al. J Am Osteopath Assoc 2012; 112:420-428

Response Ratios (RRs)*
Intention-to-Treat Analysis

LBP Reduction Threshold†	OMT RR	OMT 95% CI	OMT P	UST RR	UST 95% CI	UST P
			Intention-to-Treat Analysis (n=455)			
≥30% (moderate)	1.4	(1.2 to 1.6)	<0.001	1.0	(0.9 to 1.2)	0.85
≥50% (substantial)	1.4	(1.1 to 1.8)	0.002	1.1	(0.9 to 1.4)	0.43
≥20 mm (moderate)	1.5	(1.2 to 1.9)	<0.001	1.0	(0.8 to 1.3)	0.96
≥40 mm (substantial)	2.0	(1.2 to 3.2)	0.007	1.1	(0.7 to 1.8)	0.72



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*Licciardone JC. Ann Fam Med 2013;11:122-129

Overall Secondary Outcomes*
Intention-to-Treat Analysis

Secondary Outcome	OMT vs. Placebo OMT Main Effects Groups: OMT (n=230)	Placebo OMT (n=225)	P
Median (IQR) RMDQ score			
Week 4	4 (2 to 8)	5 (2 to 9)	0.32
Week 8	3 (1 to 7)	3 (2 to 8)	0.14
Week 12	2 (1 to 6)	3 (1 to 7)	0.07
Median (IQR) SF-36 GH score			
Week 4	71 (55 to 82)	72 (52 to 86)	0.39
Week 8	72 (57 to 85)	72 (52 to 85)	0.61
Week 12	72 (52 to 87)	72 (57 to 87)	0.87
Percent (95% CI) lost one or more work days in past 4 weeks because of LBP			
Week 4	10 (4 to 16)	14 (7 to 21)	0.41
Week 8	6 (2 to 11)	19 (12 to 27)	0.005
Week 12	11 (5 to 17)	8 (3 to 13)	0.41
Percent (95% CI) very satisfied with back care			
Week 4	52 (46 to 59)	34 (28 to 41)	<0.001
Week 8	61 (54 to 67)	39 (33 to 46)	<0.001
Week 12	66 (60 to 73)	43 (36 to 50)	<0.001

*Licciardone JC, et al. Ann Fam Med 2013;11:122-129

Usual Care*
Co-Treatments for LBP†

Percent (95% CI) ever used as a LBP co-treatment during study	OMT	Sham OMT	P
Exercise programs	19 (14 to 24)	20 (14 to 25)	0.82
Lumbar supports	1 (0 to 3)	1 (0 to 2)	>0.99
Non-prescription drugs	46 (39 to 52)	45 (39 to 52)	0.95
Prescription drugs	13 (9 to 18)	20 (15 to 26)	0.048
CAM therapies	15 (11 to 20)	17 (12 to 22)	0.63
Physical therapy	11 (7 to 15)	8 (4 to 11)	0.17
Hospitalization	0 (0 to 0)	0 (0 to 1)	0.49
Surgery	0 (0 to 1)	0 (0 to 0)	>0.99

***Significant difference in prescription drug use persisted after controlling for simultaneous use of all other co-treatments.**

†Licciardone JC, et al. Ann Fam Med 2013;11:122-129

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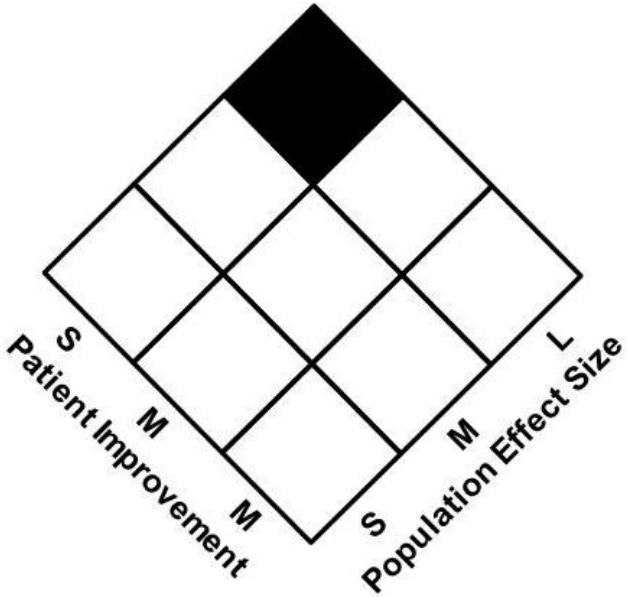
Subgroup Analysis
According to Baseline Pain Severity

Outcomes of osteopathic manual treatment at week 12 according to baseline pain severity.[a]

Outcomes	LBPS (<50 mm) RR	(95% CI)	P	HBPS (>= 50 mm) RR	(95% CI)	P	P for heterogeneity
Primary outcome							
Substantial LBP improvement (>=50% reduction in VAS score)	1.15	(0.88 to 1.50)	0.30	2.04	(1.36 to 3.05)	<0.001	0.02
Secondary outcomes							
Back-specific functioning							
Clinically important change (>=5 point reduction in RMDQ score)	0.77	(0.46 to 1.30)	0.33	1.80	(1.08 to 3.01)	0.02	0.02

Classification of OMT efficacy in achieving primary outcome among patients with high baseline pain severity



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[a]Licciardone JC, et al. Man Ther 2013; 18:533-540

Mechanism of Action*
Reduction in TNF-α

	Reduction in TNF-α Concentration, no. (%)				
	OMT	Placebo OMT	RR	95% CI	P
Overall Analysis	22/28 (79)	14/27 (52)	1.52	(1.00 to 2.29)	0.04
Subgroup Analyses According to Clinical Response Status					
Moderate improvement in LBP					
Responders	17/20 (85)	6/15 (40)	2.13	(1.11 to 4.06)	0.006
Non-responders	5/8 (62)	8/12 (67)	0.94	(0.48 to 1.83)	>0.99
Substantial improvement in LBP					
Responders	16/18 (89)	5/12 (42)	2.13	(1.07 to 4.25)	0.01
Non-responders	6/10 (60)	9/15 (60)	1.00	(0.52 to 1.92)	>0.99

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*Licciardone JC, et al. J Am Osteopath Assoc 2012; 112:596-605

Mechanism of Action*
Remission of Psoas Syndrome

- Changes in biomechanical dysfunctions with OMT
  - Non-neutral lumbar dysfunction
  - Pubic shear
  - Innominate shear
  - Restricted sacral nutation
  - Psoas syndrome

	Responders	Non responders	Unadjusted		Fully adjusted	
	No. (%)	No. (%)	OR	95% CI	OR	95% CI
Psoas syndrome						
Progression	14 (10)	18 (21)	1.00	… …	1.00	… …
Stable	88 (61)	54 (64)	2.10	0.96 - 4.55	2.45	0.88 - 6.83
Remission	43 (30)	13 (15)	4.25	1.67 - 10.82	5.11	1.54 - 16.96

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***Licciardone JC, et al. Manual Therapy (under review)**

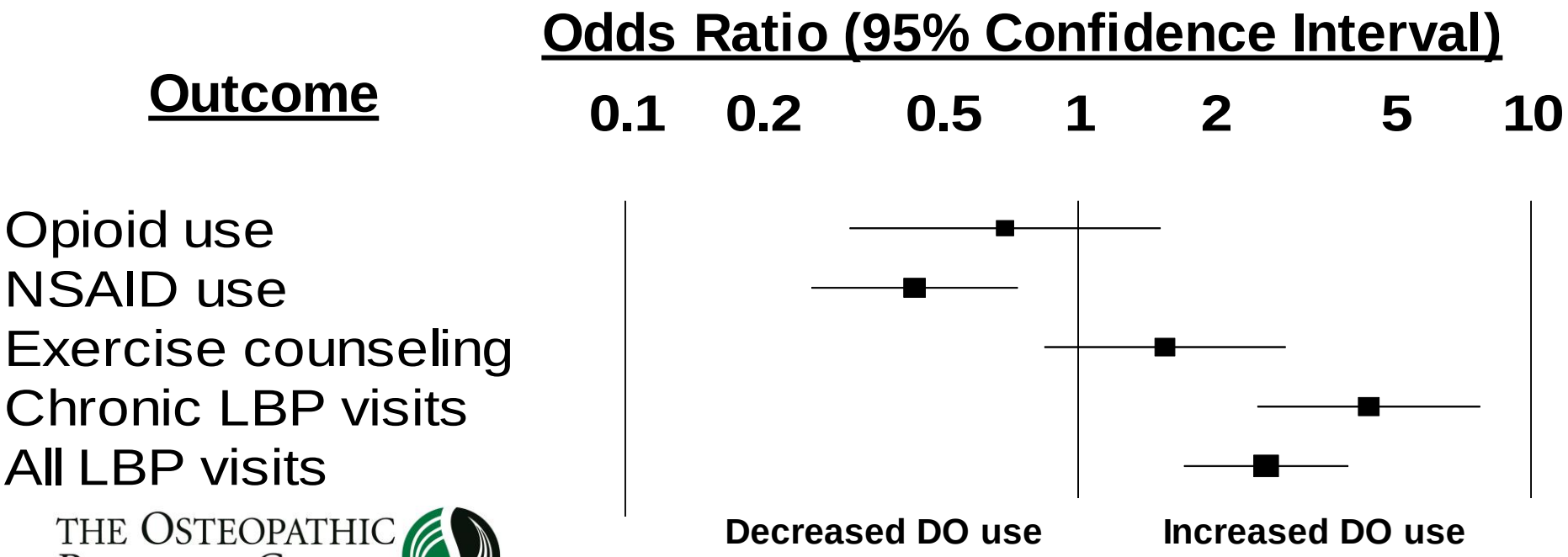
COMMENTS

Conclusions

- OMT provides **moderate-substantial LBP improvement**, that meets/exceeds the CBRG criterion for medium effect size
- OMT patients **less often used prescription drugs** for LBP
- OMT was **safe, parsimonious, and well accepted** by patients as based on high levels of treatment adherence
- OMT patients were **very satisfied** with their back care
- **Additional research is needed** to assess long-term efficacy of OMT in relieving CLBP, including its cost-effectiveness and its impact on secondary outcomes

National Ambulatory Medical Care Survey, 2003-2004

- Multiple logistic regression analysis of patient visits for low back pain
  - 1,042 (42 million wherein LBP was chief complaint)
  - Compared DO and MD visits for LBP while controlling for patient factors (age, sex, race, ethnicity, geographic region, MSA status), visit context (injury etiology), and physician factors (PCP, specialty, shared care)



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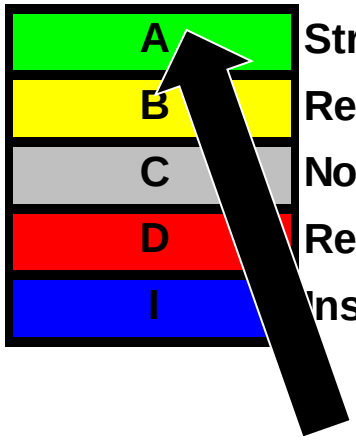
Licciardone JC, Osteopath Med Prim Care 2008;2:11

EBM Recommendations (2013)

Classification of Recommendations

Quality of Evidence	Net Benefits: Substantial	Moderate	Small	Zero/Negative
Good	A	B	C	D
Fair	B	B	C	D
Poor	I	I	I	I



- **A** Strongly recommend providing intervention to eligible patients
- **B** Recommend providing intervention to eligible patients
- **C** No recommendation for or against providing intervention
- **D** Recommend against providing intervention
- **I** Insufficient evidence for or against providing intervention

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OSTEOPATHIC Trial

Acknowledgments

- **Funding of overall study**
  - National Institutes of Health – National Center for Complementary and Alternative Medicine (K24-AT002422)
  - Osteopathic Heritage Foundation (Columbus, Ohio)
- **Safety officers**
  - Richard Virgilio, DO, MS; Bernard Rubin, DO, MPH
- **Data Safety and Monitoring Board**
  - Sejong Bae, PhD (chair) and members
- **Review and comments on manuscript**
  - Michael Bergamini, PhD; Brian Gladue, PhD
- **Treatment providers**
  - 15 faculty physicians, fellows, and residents
- **Research staff**
  - 22 faculty, research, and laboratory personnel

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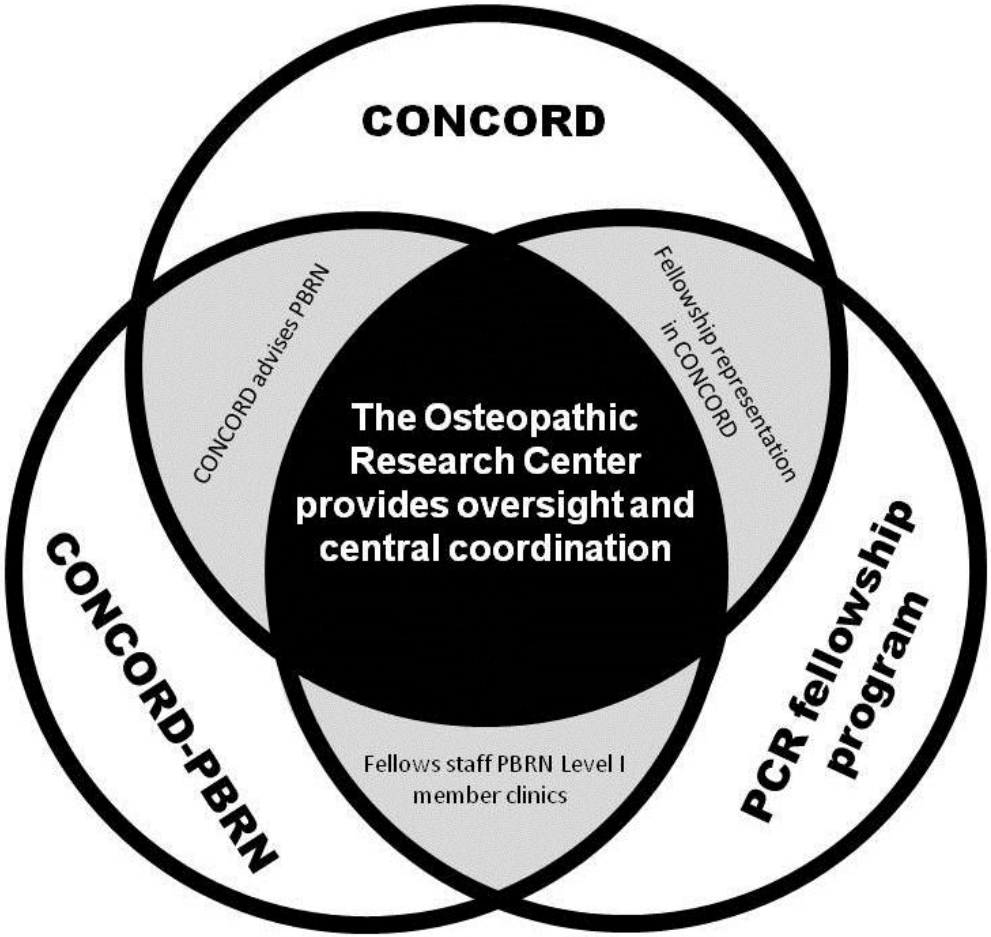
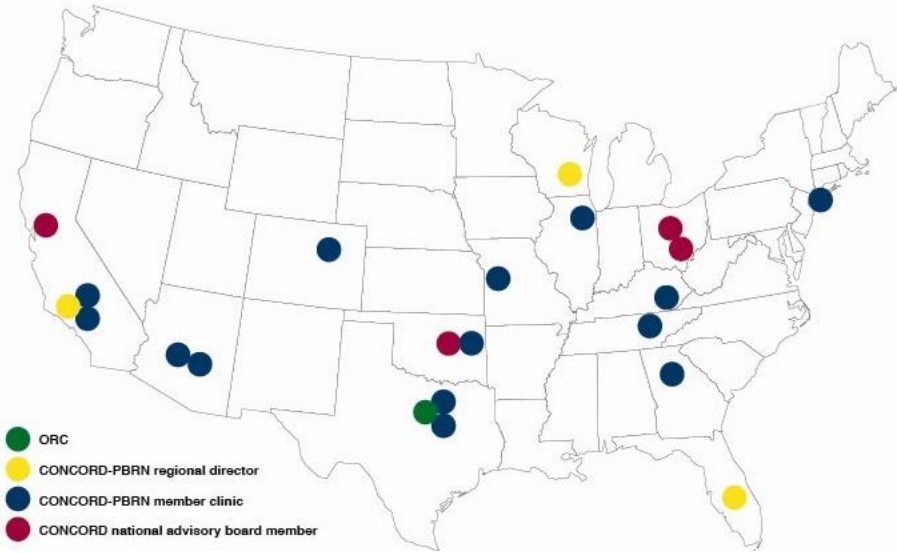
New ORC Research Paradigm*





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*Licciardone JC. J Am Osteopath Assoc 2012;112:447-456

CONCORD-PBRN
Card Study – Front

□ Male □ Female Age: __ __ __ yrs. If <1 yr.__ __ months or, if < 1 month, __ __ days

PRIMARY ICD-9 CODE: __ __ __

SECONDARY ICD-9 CODE: __ __ __

TERTIARY ICD-9 CODE: __ __ __

□ **Structural Examination Not Performed**

If performed, circle any clinically relevant TART Findings corresponding to the regions below:

	H	C	T	L	S	P	LE	UE	R	A/O
Tenderness:	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N
Asymmetry:	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N
Restricted Motion:	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N
Tissue Texture Changes:	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N	Y|N
Region Not Examined	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9

If you circle a wrong letter or code number, then draw a single diagonal line through the circled letter or number (e.g., 

) and then circle the correct letter or 739.x code number

739.x code numbers: .0 Head, .1 Cervical, .2 Thoracic, .3 Lumbar, .4 Sacrum, .5 Pelvis, .6 Lower Extr,7 Upper Extr, .8 Rib cage, .9 Abdomen/Other

PLEASE FILL OUT OTHER SIDE!

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TECHNIQUES: CIRCLE all 739.x codes used in this encounter PLEASE FILL OUT OTHER SIDE!

(if you circle a wrong number, then correct it as follows: ⊘4)

☐ **No OMT was Provided during this Encounter**

	H	C	T	L	S	P	LE	UE	R	A/O
Articulatory:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
BLT / LAS:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Chapman's:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Counterstrain:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Cranial:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
FPR:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
HVLA:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Lymphatics:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Muscle Energy:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Myofascial Release:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Percussor:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Soft Tissue:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Still's Technique:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Visceral:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9
Circle if no OMT of Region:	.0	.1	.2	.3	.4	.5	.6	.7	.8	.9

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