

What's the Evidence? Osteopathy Answers Back

**Osteopathy – Art and Science
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University of North Texas Health Science Center**



■ **Primary Mission**

To conduct basic and clinical research to elucidate the mechanisms of action of osteopathic manipulative treatment (OMT) and to provide an evidence-based foundation for its efficacy

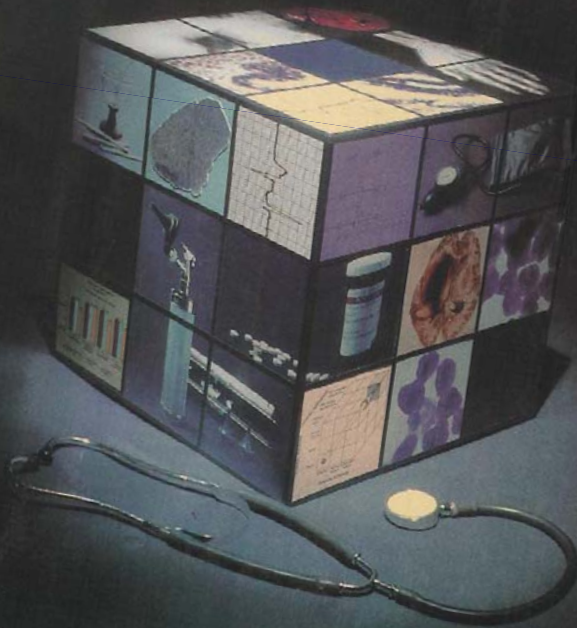
Presentation Objectives

- **Briefly review historical development of evidence-based medicine (EBM)**
- **Present the evidence base for osteopathic manipulative treatment (OMT) of low back pain (LBP) as a prototypical condition**
- **Present the results and recommendations of a comprehensive systematic review of OMT**
- **Present novel EBM approaches relative to diagnosis and therapy in osteopathy**

EBM in North America: The McMaster Group

CLINICAL EPIDEMIOLOGY
A BASIC SCIENCE FOR CLINICAL MEDICINE

DAVID L. SACKETT
R. BRIAN HAYNES
PETER TUGWELL



THIRD EDITION

**EVIDENCE-BASED
MEDICINE**

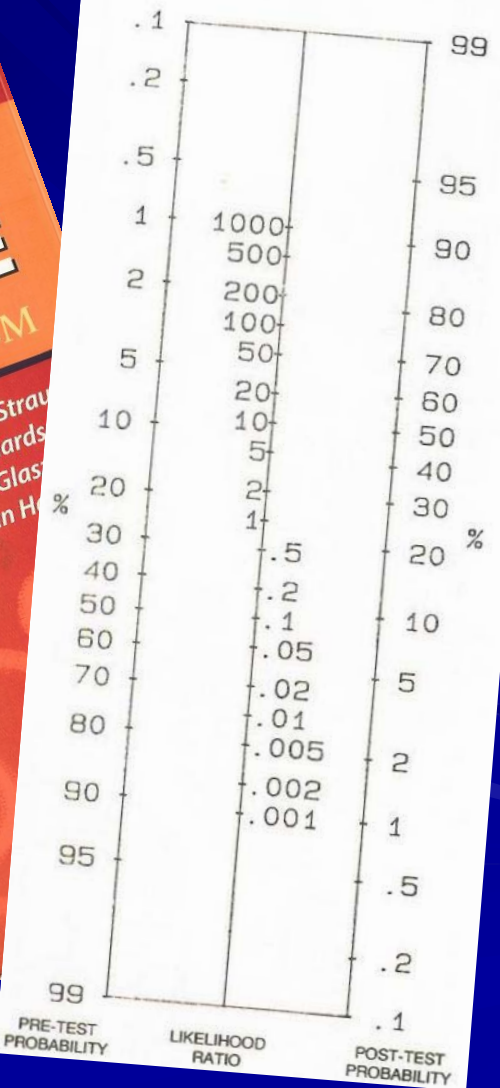


How to Practice and Teach EBM

Sharon E. Straus
W. Scott Richards
Paul Glasziou
R. Brian Haynes



NOMOGRAM* FOR INTERPRETING
DIAGNOSTIC TEST RESULTS



EBM in the United Kingdom: The UK Cochrane Centre

- “...It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or sub-specialty, adapted periodically, of all relevant randomized controlled trials.”

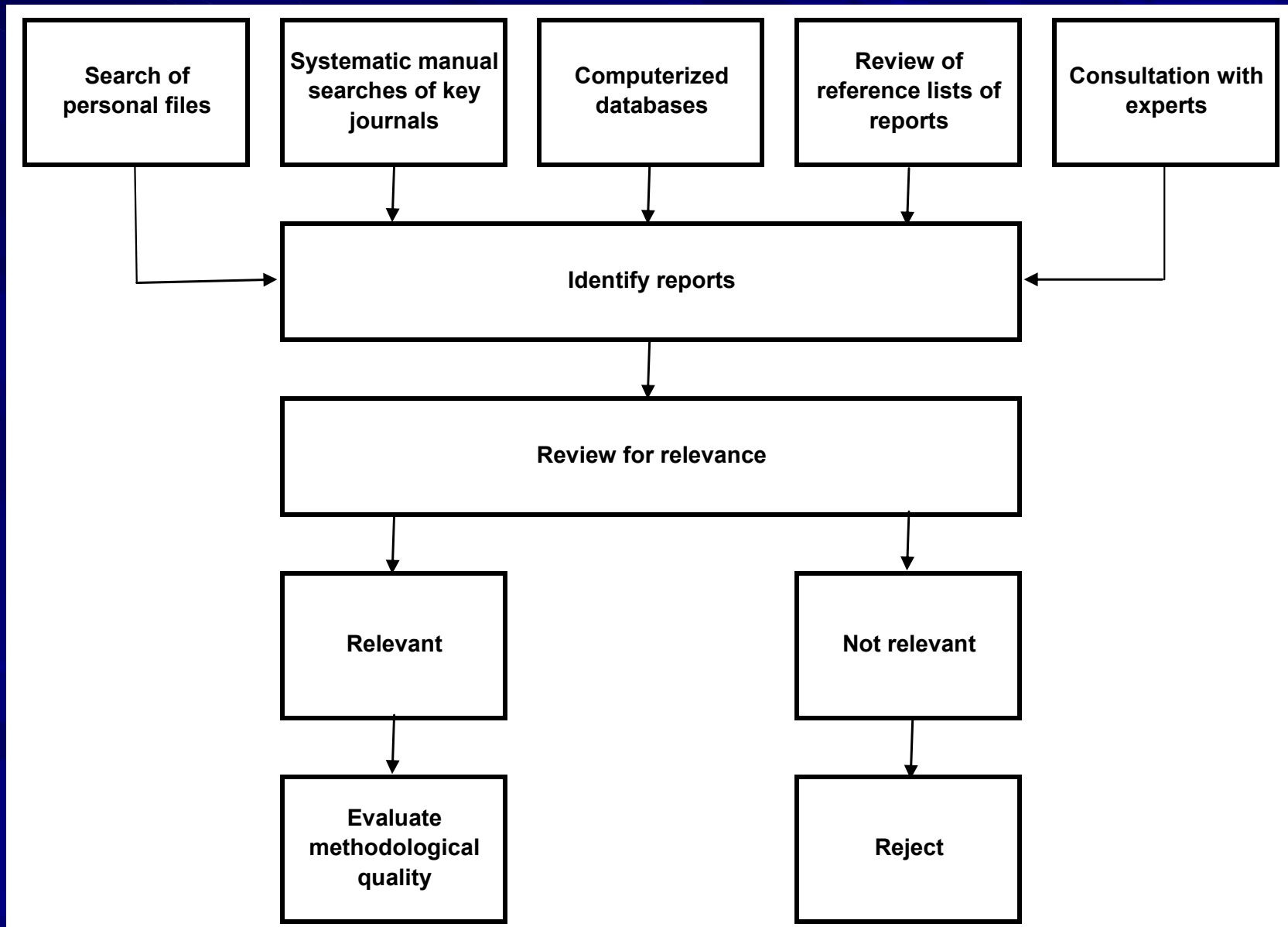
– *Archie Cochrane*

The International Perspective: World Health Organization

- **Consultation on Osteopathy**
 - Milan, Italy Feb. 26-28, 2007
 - Development of WHO Guidelines on Basic Training and Safety in Osteopathy
- **International regulatory and licensing issues (osteopathy vs osteopathic medicine)**
- **Greater emphasis on evidence-based osteopathy at future consultations**
- **Consistent with WHO's shifting priorities from expert opinion to systematic reviews***

*Oxman AD, Lancet 2007; doi:10.1016/S0140-6736(07)60675-8

The Systematic Review Process



OMT for Low Back Pain Where is the Evidence?



The NEW ENGLAND
JOURNAL of MEDICINE

JAMA

THE LANCET

Spine

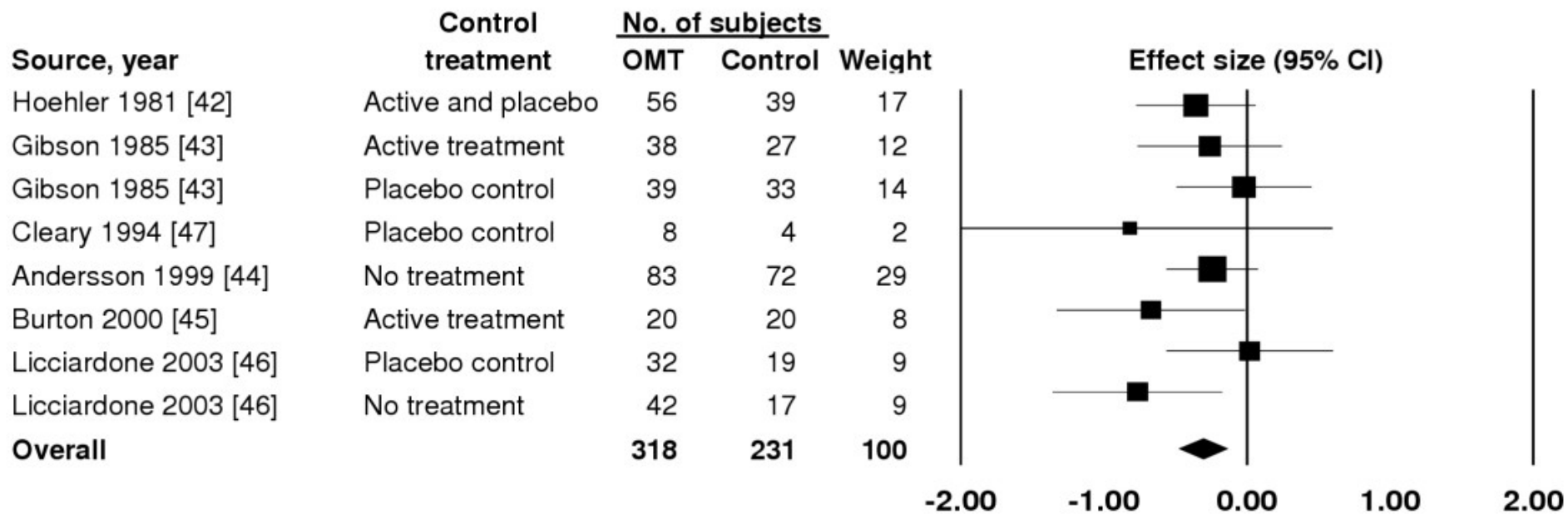
An international journal
for the study of the spine

Research Methodology: The Evidence Pyramid



Adapted from Straus SE et al. Evidence-Based Medicine: How to Practice and Teach EBM, 3rd ed 2005 (RCT denotes randomized controlled trial; SR, systematic review)

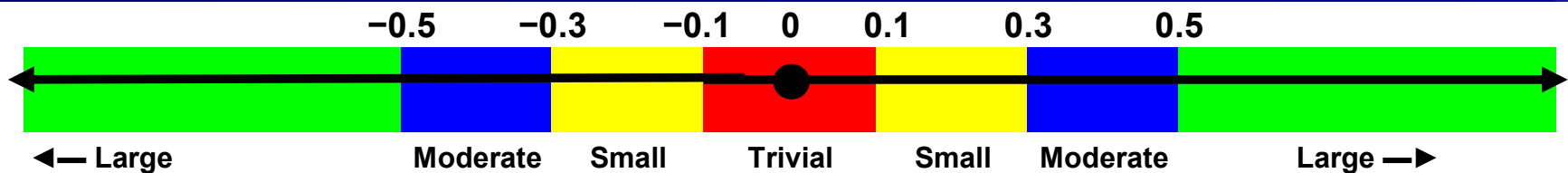
SRMA of OMT for LBP: Overall Analysis



ES = -0.30 (-0.47 - -0.13); P = .001

Favors OMT

Favors Control



OMT for LBP Subgroup Analysis: — by Control Group

Subgroup Analyses According to Control Group

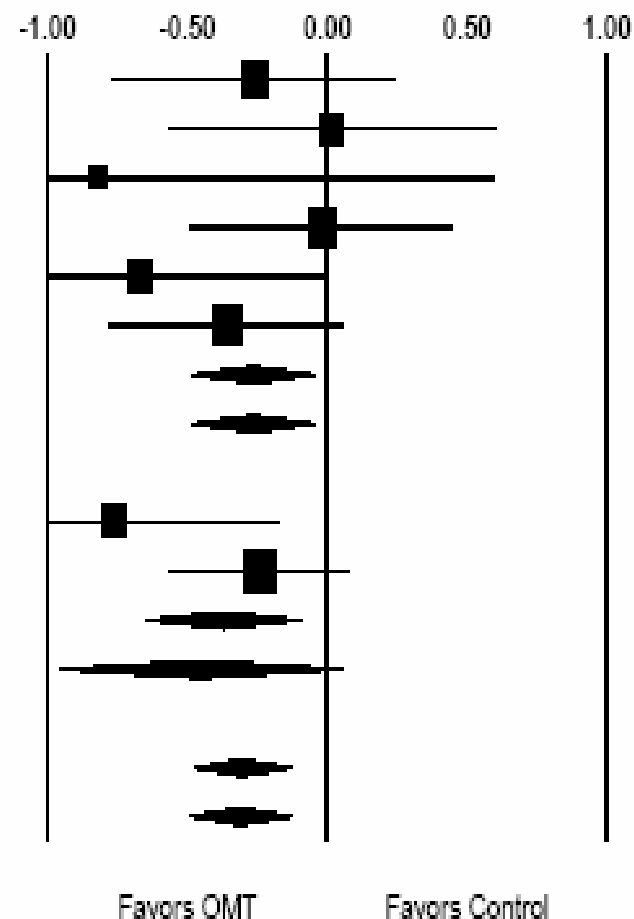
ControlGroup	Country	Citation	Year	TimeEffect	N1	N2
Active or Placebo	UK	Gibson	1985	1-3 Months	38	27
Active or Placebo	US	Liocciardone	2003	3-12 Months	32	19
Active or Placebo	UK	Cleary	1994	3-12 Months	8	4
Active or Placebo	UK	Gibson	1985	0-1 Month	39	33
Active or Placebo	UK	Burton	2000	0-1 Month	20	20
Active or Placebo	US	Hoehler	1981	0-1 Month	56	39

ES = -0.26 (-0.48 - -0.05); P = .02

Usual Treatment	US	Liocciardone	2003	0-1 Month	42	17
Usual Treatment	US	Andersson	1999	1-3 Months	83	72

ES = -0.53 (-0.76 - -0.30); P < .001

Fixed	Combined (8)	318	231
Random	Combined (8)	318	231



OMT for LBP Subgroup Analysis: — by Country of Trial

Subgroup Analyses According to Country

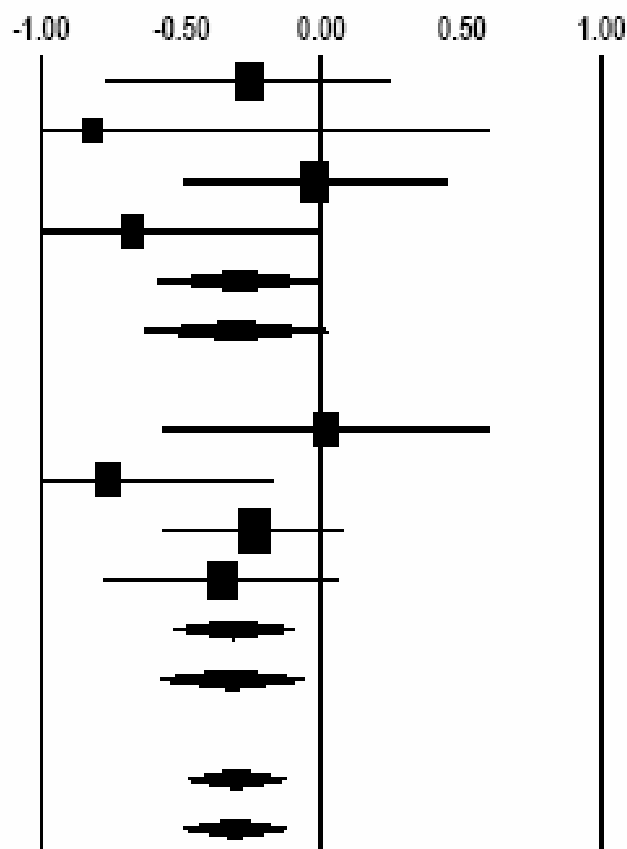
Country	Citation	Year	ControlGroup	TimeEffect	N1	N2
UK	Gibson	1985	Active or Placebo	1-3 Months	38	27
UK	Cleary	1994	Active or Placebo	3-12 Months	8	4
UK	Gibson	1985	Active or Placebo	0-1 Month	39	33
UK	Burton	2000	Active or Placebo	0-1 Month	20	20

ES = -0.29 (-0.58 - -0.00); P = .05

US	Licciardone	2003	Active or Placebo	3-12 Months	32	19
US	Licciardone	2003	Usual Treatment	0-1 Month	42	17
US	Andersson	1999	Usual Treatment	1-3 Months	83	72
US	Hoehler	1981	Active or Placebo	0-1 Month	56	39

ES = -0.31 (-0.52 - -0.10); P = .004

Fixed	Combined (8)	318	231
Random	Combined (8)	318	231



Favors OMT

Favors Control

OMT for LBP Subgroup Analysis: — by Duration of Follow-Up

Subgroup Analyses According to Duration of Follow-Up - All Contrasts

TimeEffect	Country	Citation	Year	ControlGroup	N1	N2
0-1 Month	UK	Burton	2000	Active or Placebo	20	20
0-1 Month	UK	Gibson	1985	Active or Placebo	39	32
0-1 Month	UK	Gibson	1985	Active or Placebo	39	32
0-1 Month	UK	Gibson	1985	Active or Placebo	39	33
0-1 Month	UK	Gibson	1985	Active or Placebo	39	34
0-1 Month	US	Hoehler	1981	Active or Placebo	41	28
0-1 Month	US	Hoehler	1981	Active or Placebo	56	39
0-1 Month	US	Lioccardone	2003	Active or Placebo	42	23
0-1 Month	US	Lioccardone	2003	Usual Treatment	42	17

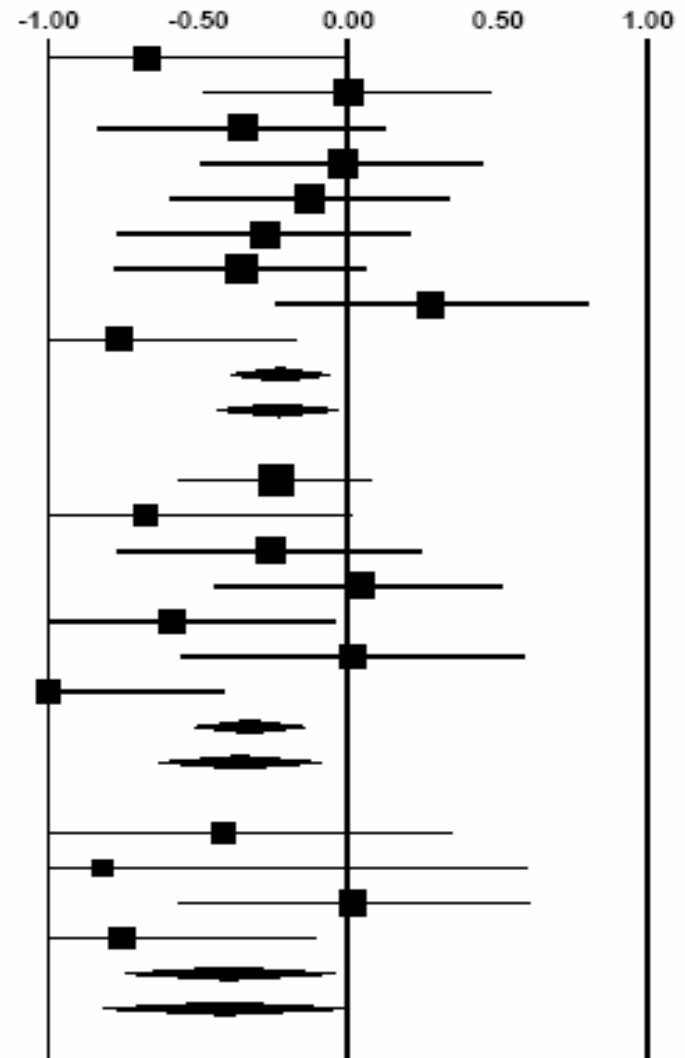
ES = -0.28 (-0.51 - -0.06); P=.02

1-3 Months	US	Andersson	1999	Usual Treatment	83	72
1-3 Months	UK	Burton	2000	Active or Placebo	19	18
1-3 Months	UK	Gibson	1985	Active or Placebo	38	27
1-3 Months	UK	Gibson	1985	Active or Placebo	38	32
1-3 Months	US	Hoehler	1981	Active or Placebo	33	25
1-3 Months	US	Lioccardone	2003	Active or Placebo	36	19
1-3 Months	US	Lioccardone	2003	Usual Treatment	36	16

ES = -0.33 (-0.51 - -0.15); P<.001

3-12 Months	UK	Burton	2000	Active or Placebo	15	15
3-12 Months	UK	Cleary	1994	Active or Placebo	8	4
3-12 Months	US	Lioccardone	2003	Active or Placebo	32	19
3-12 Months	US	Lioccardone	2003	Usual Treatment	32	15

ES = -0.40 (-0.74 - -0.05); P=.03



SRMA Conclusions: OMT Efficacy in LBP

- Pain reduction is statistically greater than expected from placebo effects (twice as great)
- Pain reduction is clinically important; comparable to NSAIDs, including COX-2 inhibitors, and may last longer*†
- Pain reduction persists at least through the first three months of treatment, and possibly as long as the first year

*Bjordal JM et al, *BMJ* 2004;329:1317-doi:10.1136/bmj.38273.626655.63.

†van Tulder MW et al, *Cochrane Database Syst Rev* 2000 CD000396.

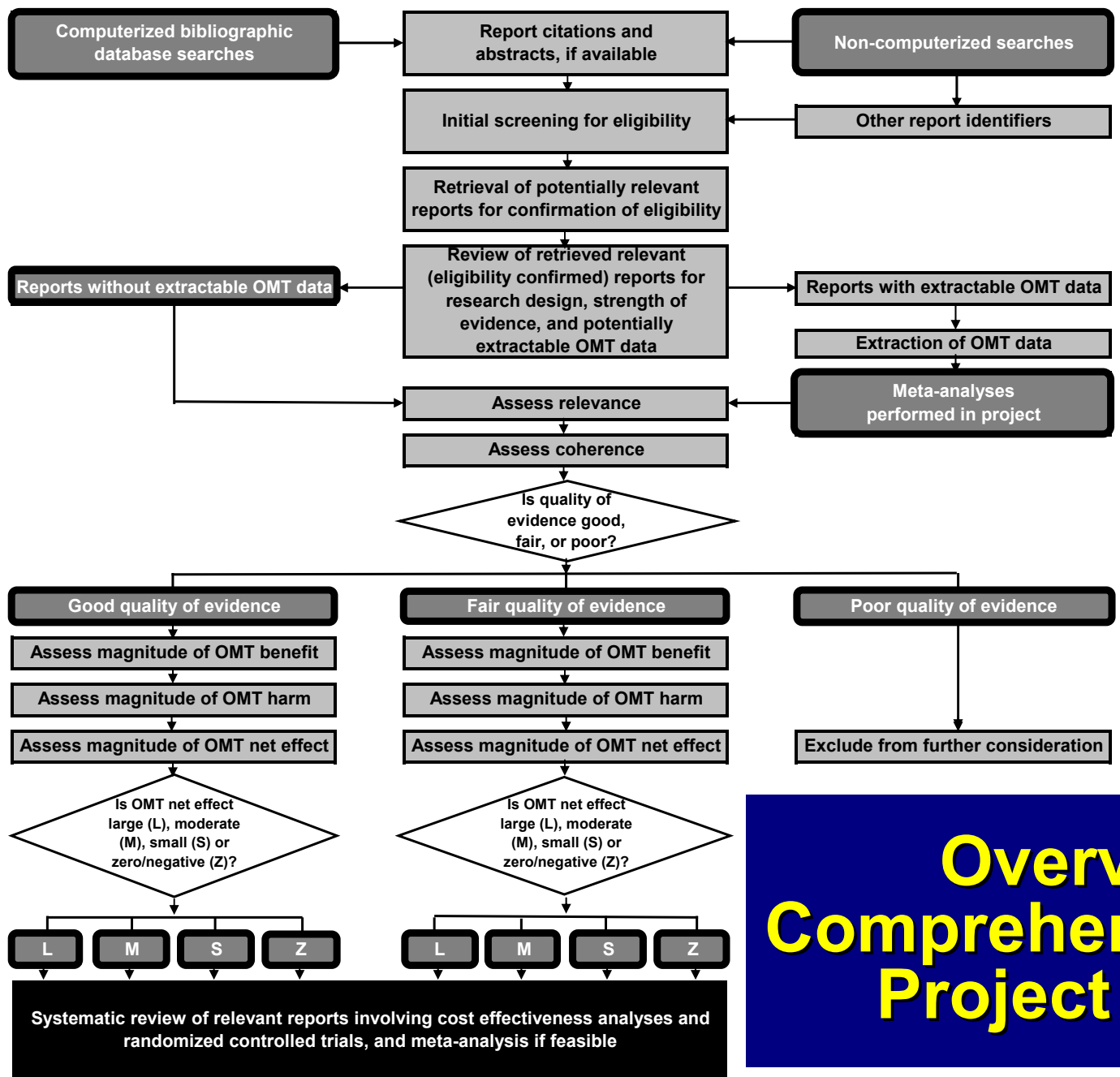
FACT Commentary on SRMA

- “In summary, this paper presents an exercise that has obviously been carried out very skillfully and carefully. It gives clear, although still preliminary, evidence that OMT is much more than placebo.”
- “How much more, however, should be assessed in at least two sufficiently powered trials ... The present paper is a perfect argument in an application for funding.”

The OSTEOPATHIC Trial

- **OSTEOPATHic Health outcomes In Chronic low back pain (Aug 2006 – Oct 2010)**
- **Phase III, placebo controlled RCT (N=488)**
- **2 x 2 Factorial design**
- **Primary outcomes**
 - Visual analogue pain scale
 - Roland-Morris Disability Questionnaire
 - Medical Outcomes Study SF-36 Health Survey
 - Work disability
 - Satisfaction with back care

		Osteopathic Manipulative Treatment	
		Group A	Group B
Ultrasound Physical Therapy	Group A OMT UPT (n=122)	Group B Sham OMT UPT (n=122)	
	Group C OMT Sham UPT (n=122)	Group D Sham OMT Sham UPT (n=122)	



Overview of Comprehensive SRMA Project for AOA

Comprehensive SRMA Project: EBM Recommendations for OMT

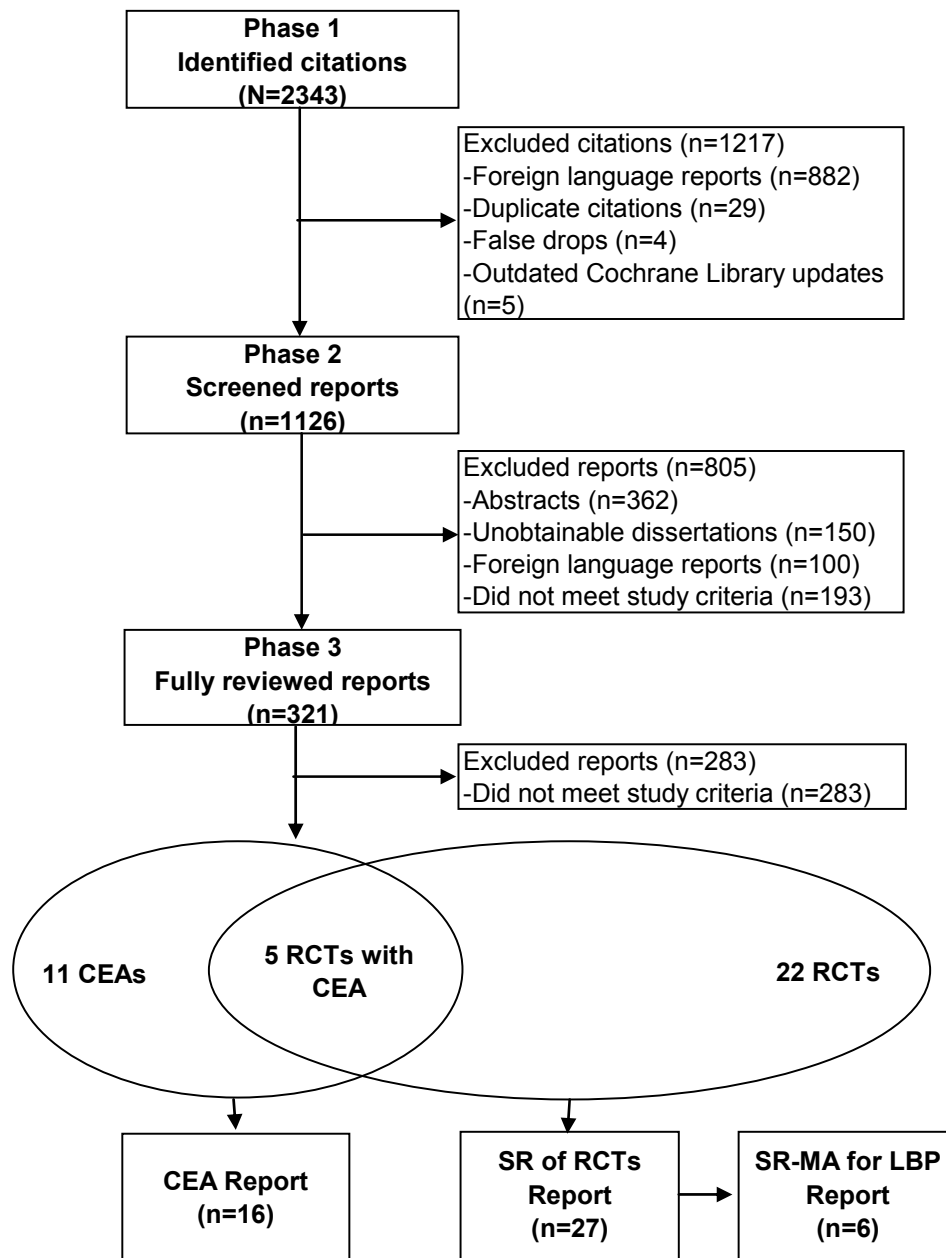
Classification of Recommendations

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 OMT to eligible patients
B	Recommend providing OMT to eligible patients
C	No recommendation for or against providing OMT
D	Recommend against providing OMT
I	Insufficient evidence for or against providing OMT

Licciardone JC, Principal Investigator, funded American Osteopathic Association

Comprehensive SRMA Project Flow Chart



Flow chart of osteopathic literature search results and review of citations and reports. CEA denotes cost effectiveness analysis; LBP, low back pain; MA, meta-analysis; RCT, randomized controlled trial; and SR, systematic review.

SRMA Project Conclusions

- **There is evidence to recommend the use of OMT for low back pain**
- **More research is needed to provide evidence on the efficacy of OMT for other clinical conditions**
- **More research is needed to provide evidence on the cost-effectiveness of OMT**
- **OMT generally appears to be safe based on a comparison of reported adverse events and the volume of treatments provided. However, more research is needed to assess the risk of rare (but potentially serious) complications of cervical HVLA manipulation**

Osteopathic Clinical Trials: ClinicalTrials.gov – Jan 2007

Target Disorder or Condition	ClinicalTrials Identifier	Status	NIH Funded	Phase	N	Start Date	End Date†	Blinding	Control	Design
Chronic low back pain	NCT00315120	Ongoing	Yes	III	488	Aug 2006	Oct 2010	Double	Placebo	Factorial
Pneumonia	NCT00258661	Ongoing	No	NS	360	Mar 2004	Jul 2007	Double	Placebo	Factorial
Carpal tunnel syndrome	NCT00394043	Ongoing	Yes	II	138	Oct 2006	Jan 2010	Double	Placebo	Parallel
Low back pain	NCT00394264	Ongoing	No	II	100	Oct 2006	Dec 2007	Single	Active	Parallel
Muscle tension	NCT00403936	Completed	No	NS	100	Apr 2005	May 2005	Single	Active	Crossover
Pregnancy	NCT00298935	Completed	No	NS	99	Jul 2003	May 2006	Double	Placebo	Parallel
Postoperative N/V	NCT00387361	Ongoing	No	II	60	Oct 2006	Mar 2007	Double	Placebo	Parallel
Low back and hip pain	NCT00410397	Ongoing	No	NS	20	Dec 2006	Feb 2007	Single	Placebo	Parallel
Emphysema	NCT00034112	Completed	Yes	II	NS	Apr 2001	Mar 2002	NS	Placebo	Parallel
Spastic cerebral palsy	NCT00011024	Completed	Yes	II	NS	Sep 1998	Jun 2004	NS	NS	NS
Otitis media	NCT00010465	Completed	Yes	II	NS	NS	NS	Double	Placebo	NS

- 5 additional clinical trials registered during 2007
- 18 clinical trials completed or in progress

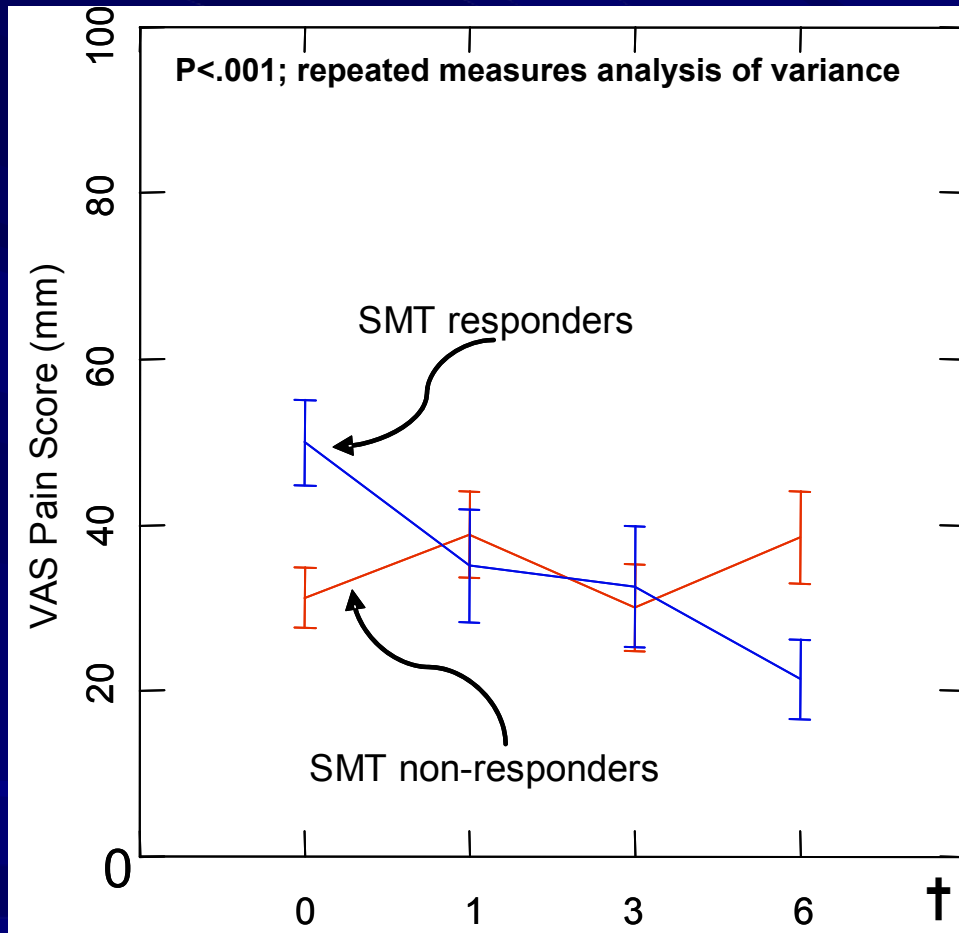
EBM Building Blocks for OMT

- OMT effect size = 0.30
- On 100-mm VAS, standard deviation = 25 mm*
- Thus, OMT reduces LBP by 7.5 mm on a 100-mm VAS
- What is the clinical relevance?
- Need a new paradigm – the “OMT responder”
- Then can compute EBM measures such as:
 - Relative risk reduction (RRR)
 - Absolute risk reduction (ARR)
 - Number needed to treat (NNT)
 - Number needed to harm (NNH)
 - Likelihood of help vs harm (LHH)
- For now, must depend on indirect comparisons
 - OMT effect size vs placebo/active treatment = 0.26
 - NSAIDs (including COX-2 inhibitors) vs placebo = 0.23[†]

*Assendelft WJJ et al, *Ann Intern Med* 2003;138:871-881

†Bjordal JM et al, *BMJ* 2004;329:1317

The OMT Responder



- Percentage of OMT responders based on re-analysis of data from the North Texas Clinical Trial of OMT for chronic low back pain*
 - 41% of completers
 - 27% of entrants

*Licciardone JC et al, Spine 2003;28:1355-1362

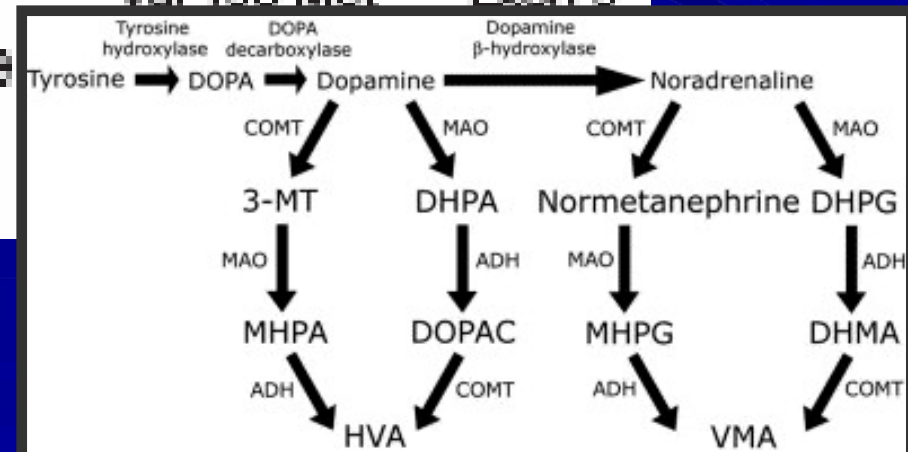
†Licciardone JC, Int J Osteopath Med 2007;10:3-7

EBM Nomogram for Predicting OMT Response in CLBP

- **A modified nested case-control study (N=450)**
 - Establish likelihood ratios for individual predictors of OMT response
 - Establish likelihood ratios for multiple predictors of OMT response

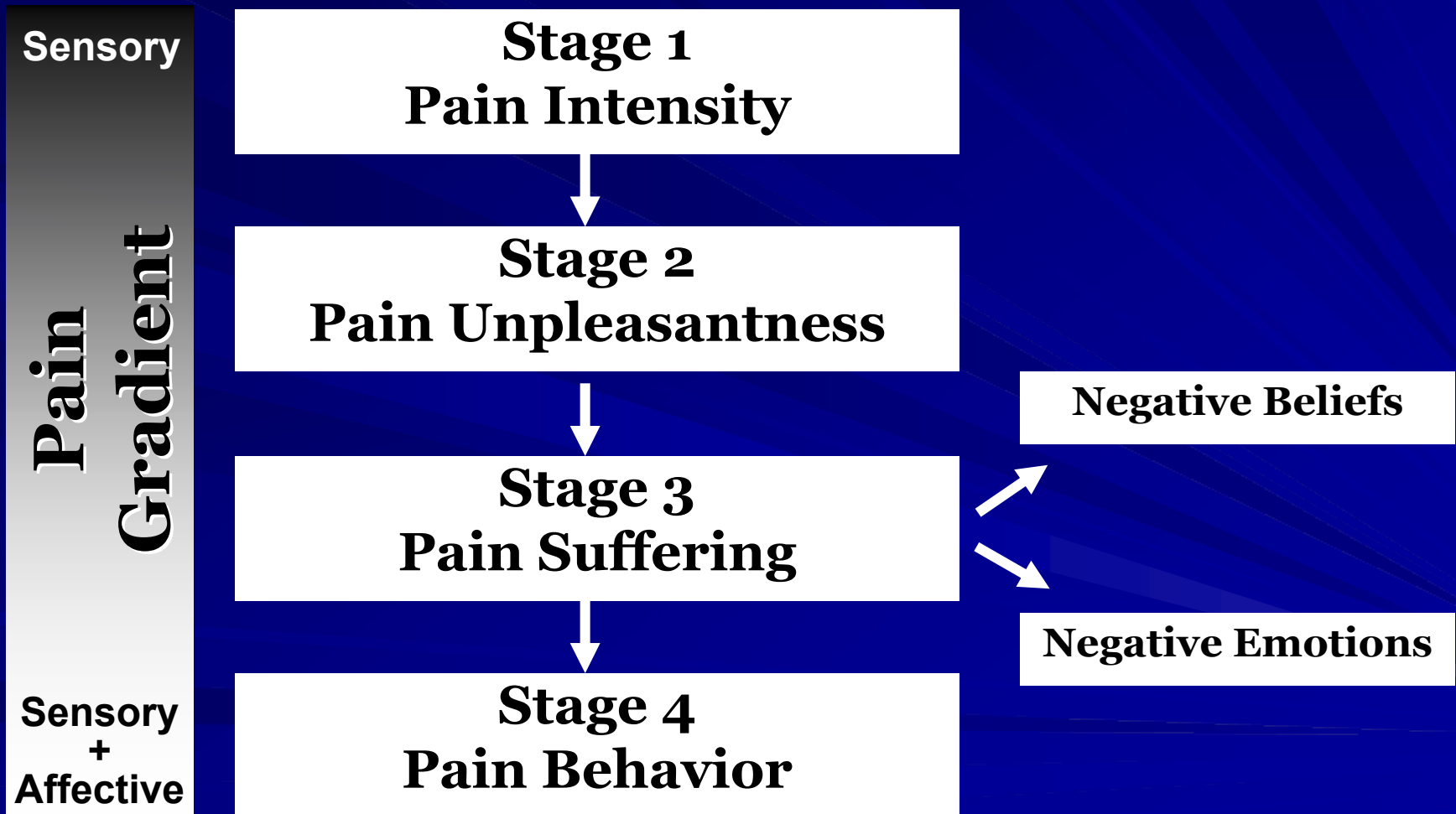
High Priority Candidate Genes for Human Pain

Gene	Molecule	SNP	Location
IL6	Interleukin 6	G 174 C	Promoter
NOS1	Neuronal nitric oxide synthase	AAT VNTR	Intron 20
IL1B	Interleukin 1 β	C 511 T	Promoter
TNF α	Tumor necrosis factor α	G 308 A	Promoter
SLC6A4	Serotonin transporter	5HTTLPR	Promoter
GDNF	Glia-derived nerve factor	(AGG) $_n$	3'-UTR
BDKRB2	Bradykinin receptor 2	C 58 T	Promoter
COMT	Catechol-O-methyltransferase	Val 158 Met	Exon 3
NOS2A	Inducible nitric oxide synthase		
PDYN	Prodynorphin		
OPRM1	μ -Opioid receptor		



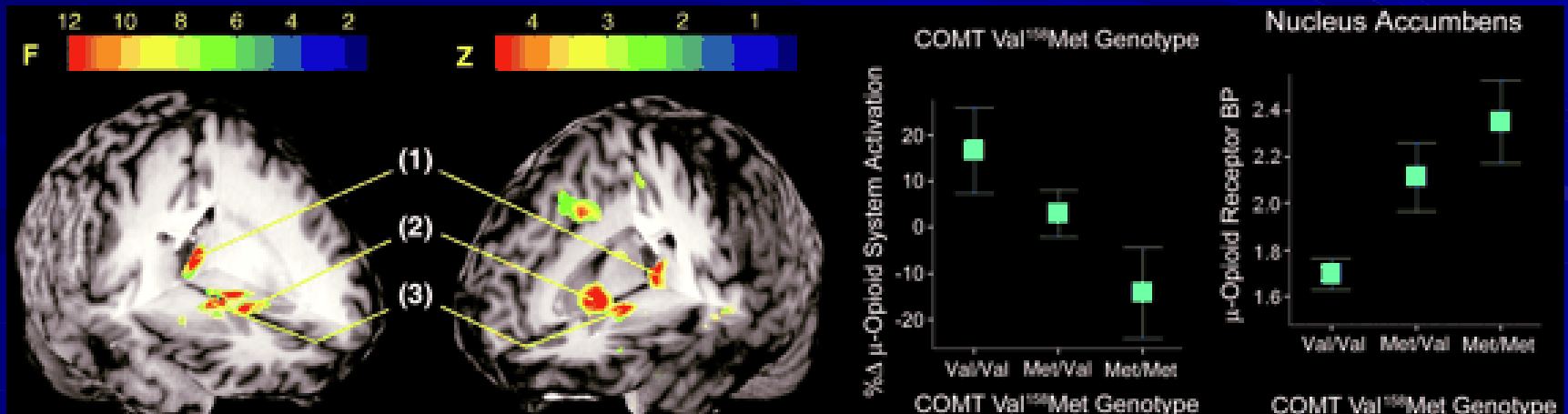
Belfer I et al, *Anesthesiology*
2004;100:1562-72

Stages of Pain Processing Model

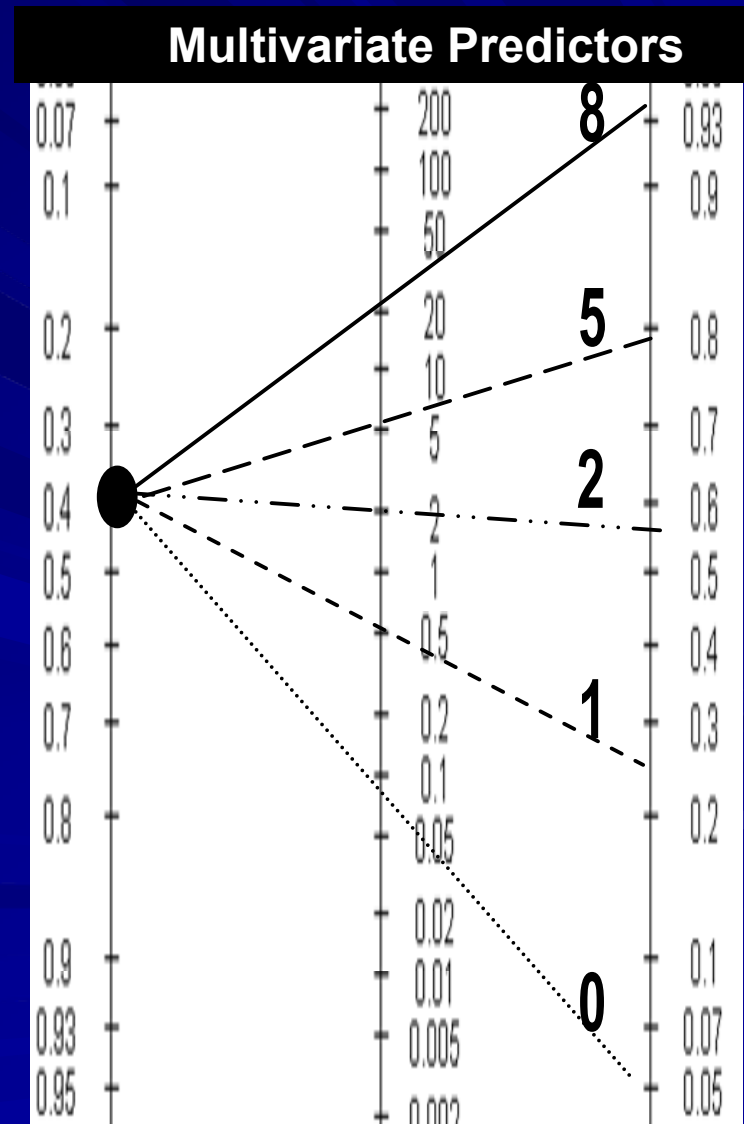
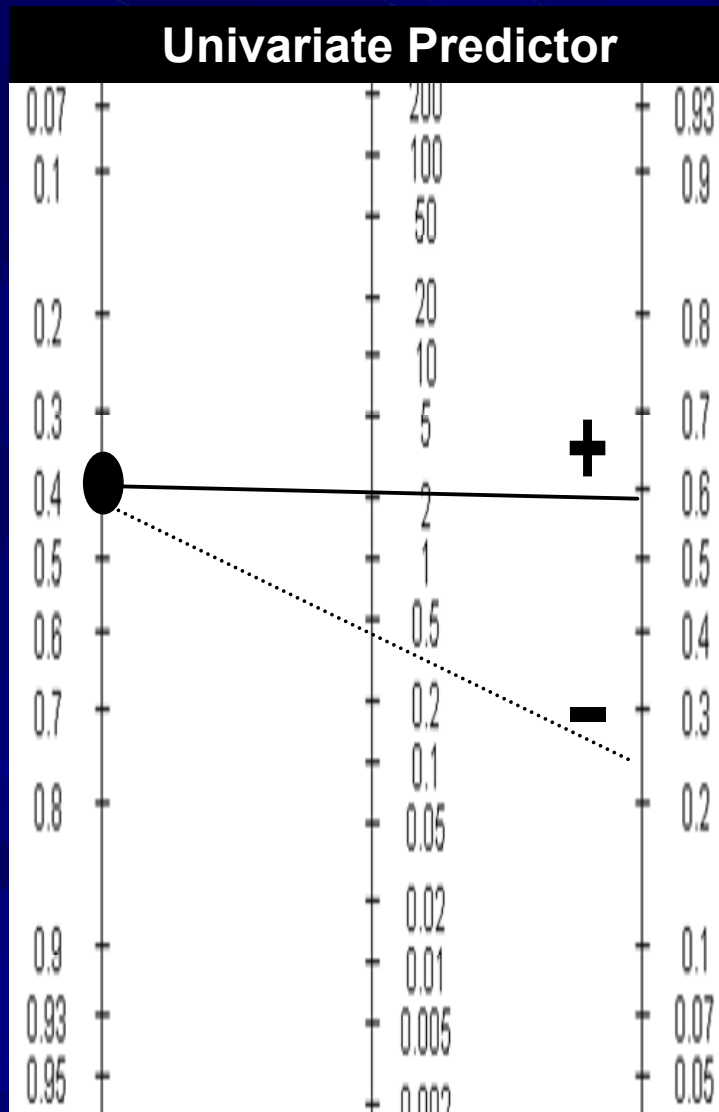


COMT: μ -Opioid Responses and Sensory/Affective Ratings of Pain

- Healthy volunteers (N=29) with sustained pain challenge (5% saline, masseter muscle)
- PET scans, μ -opioid receptor-selective radiotracer
- *met¹⁵⁸met* homozygotes showed decreased μ -opioid system activation in response to pain (and increased μ -opioid receptor binding)
- *met¹⁵⁸met* homozygotes also showed higher sensory and affective ratings of pain and a more negative internal affective state



Pre- and Post-Test Likelihood of Response to OMT in CLBP



OMT for CLBP: A NorTex PBRN Cohort Study



- Cohort study, 2-stage cluster sampling (N=450)
- Primary outcomes
 - Pain, functional status, general health, work disability, satisfaction with care, interpersonal processes of care
- NorTex PBRN affords opportunities for implementation of translational research

Licciardone JC and Cardarelli R, Multiple principal investigators, pending application, National Institutes of Health

Somatic Dysfunction

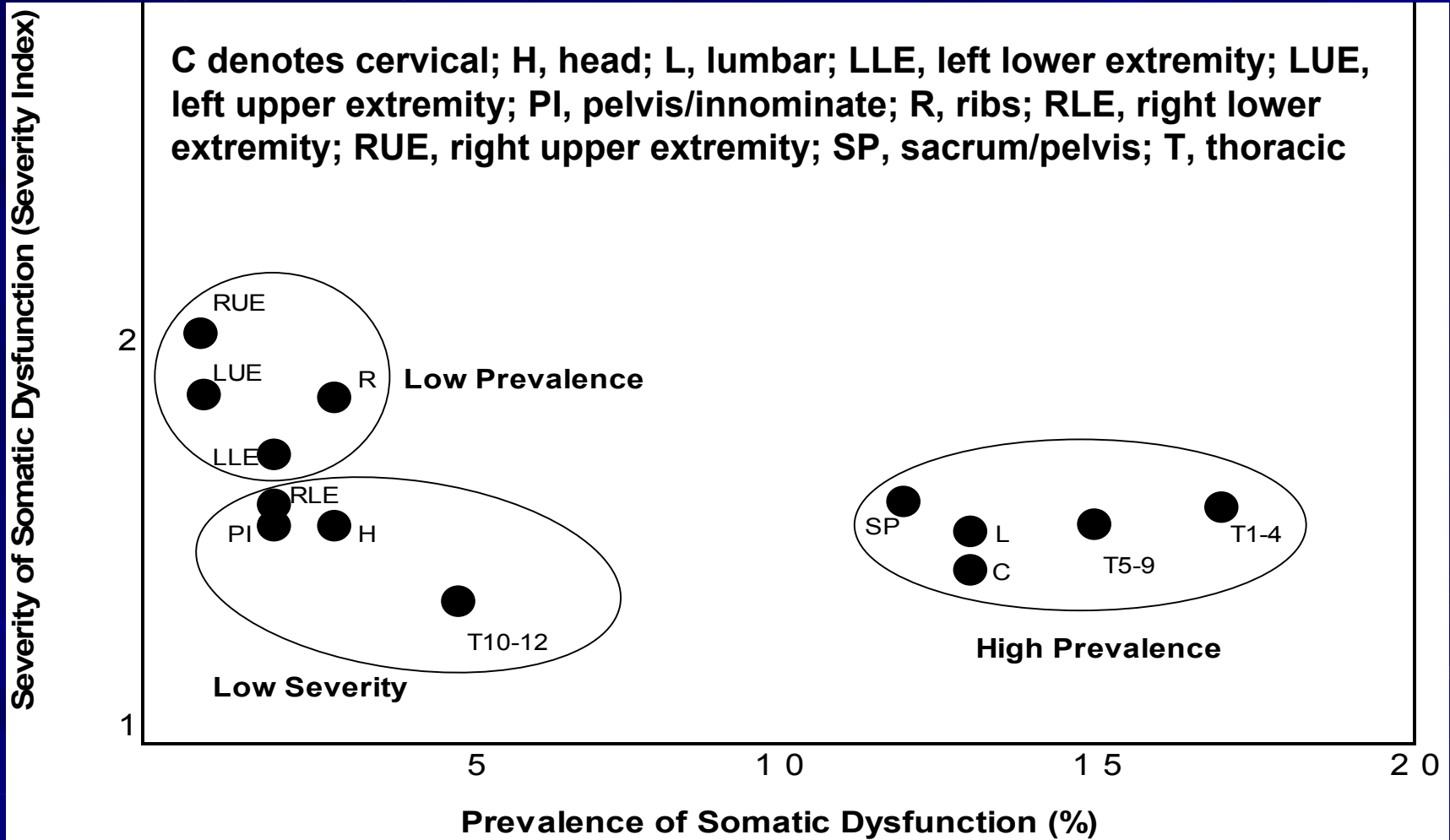
- **Somatic dysfunction*** is defined as “impaired or altered function of related components of the somatic (body framework) system: skeletal, arthrodiar, and myofascial structures, and related vascular, lymphatic, and neural elements”

Relationship of OMT to Somatic Dysfunction and LBP

Low Back Pain

		Present	Absent
<u>Somatic Dysfunction</u>	Present	Clinical LBP: OMT indicated	Subclinical LBP: OMT may provide secondary prevention
	Absent	Clinical LBP: OMT not indicated	Healthy: OMT not indicated

Burden of Somatic Dysfunction in Primary Care



Viscerosomatic Dysfunction in Type 2 Diabetes



	Somatic dysfunction is present	Somatic dysfunction is absent	Total
History of type 2 diabetes	47	12	59
No history of type 2 diabetes	15	17	32
Total	62	29	91

	a	b
	c	d

Sensitivity = $a/(a + c) = 47/62 = 76\%$

Specificity = $d/(b + d) = 17/29 = 59\%$

Positive predictive value = $a/(a + b) = 47/59 = 80\%$

Negative predictive value = $d/(c + d) = 17/32 = 53\%$

LR+ = $\text{sensitivity}/(100\% - \text{specificity}) = 76\%/41\% = 1.85$

LR- = $(100\% - \text{sensitivity})/\text{specificity} = 24\%/59\% = 0.41$

Pre-test likelihood of somatic dysfunction = $173/1199 = 14\%$

Pre-test odds of somatic dysfunction = $\text{pre-test probability}/(100\% - \text{pre-test probability}) = 14\%/86\% = 16\%$

Post-test odds of somatic dysfunction (+ test) = $\text{pre-tests odds} \times \text{LR+} = 16\% \times 1.85 = 30\%$

Post-test odds of somatic dysfunction (- test) = $\text{pre-test odds} \times \text{LR-} = 16\% \times 0.41 = 7\%$

Post-test likelihood of somatic dysfunction (+ test) = $\text{post-test odds}/(\text{post-test odds} + 100\%) = 30\%/130\% = 23\%$

Post-test odds of somatic dysfunction (- test) = $\text{post test odds}/(\text{post-test odds} + 100\%) = 7\%/107\% = 7\%$

Increasing Demands for EBM Relative to OMT

I was hoping you could help me. My DME of our Allopathic family medicine residency wants me to provide Evidence Based Medicine regarding OMT in order to prove to him we are not "quacks"? Please help!

John Licciardone - Re: Mentor program

Dr. Licciardone,

Hello again!

I am presenting one of your articles for journal club this Tuesday. OMT is my topic. My goal is to see if it has benefits in treatment via evidence-based medicine. As an osteopathic, I am personally interested in this but also I desire to be educated to inform the allopathic community. The article I chose was yours on Lower Back Pain, OMT, and meta-analysis.

When presenting the article or the concept of the author (difficulties, The

familiar with it?

I look forward to hearing from you.



Centers for Medicare & Medicaid Services

Osteopathic Medicine and Primary Care




OSTEOPATHIC MEDICINE
AND PRIMARY CARE

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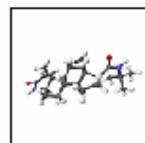
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Advancing Osteopathy

- **“...Two roads diverged in a wood, and I...
I took the one less traveled by, And that
has made all the difference.
– From *The Road Not Taken*, Robert Frost**

Acknowledgments

■ Clinical Research Lab and Collaborators

- Faculty, fellows, and staff of The Osteopathic Research Center
- Graduate students within GSBS and SPH
- Faculty within TCOM, GSBS, and SPH

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- Osteopathic Professional Organizations
 - American Osteopathic Association
 - American Osteopathic Foundation
 - American Association of Colleges of Osteopathic Medicine
- National Institutes of Health
 - National Center for Complementary and Alternative Medicine