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Objectives

- Discuss factors relating to clinical decision making for patients with neck pain, including indications and contraindications for the use of joint manipulation.
- Summarize the evidence for the effectiveness of cervical spine joint and soft tissue mobilization.
- Discuss in general terms the application, development, and validation of clinical prediction rules for establishing treatment effectiveness.
- Summarize the current status of clinical prediction rules as evidence for the effectiveness of thoracic manipulation for neck pain.
- Discuss recent studies on the effectiveness of cervical spine manipulation by physical therapists in the clinical setting.

Clinical Case

- Subjective presentation
- Objective findings
- Assessment
- Decision making re: treatment
  - Red or yellow flags
  - Contraindications, precautions for manual therapy (or save for later?)

Evidence for Manual Therapy for Treatment of Neck Pain
Recent Systematic Reviews:


- Evidence for manual therapy for neck pain: Series of systematic reviews by the same authors:

Systematic Review Methods

- Exhaustive search including MEDLINE, EMBASE, Cochrane Library, Manual Alternative and Natural Therapy, CINAHL, and Index to Chiropractic Literature (ICL)

- Inclusion criteria
  - Randomized controlled trials only
  - Acute, subacute, or chronic patients with diagnosis of mechanical neck pain, with or without cervical headaches, radiculopathy
  - Outcome of pain, function/disability, satisfaction, and/or global change

- Independent review by 2 authors

- Quality of methods were assessed using established Cochrane review criteria

Systematic Reviews: Quality (Strength) of Evidence

[Diagram showing the quality of evidence using GRADE with domains such as study design, within study risk of bias, and consistency of results.]

- High (60%)
- Moderate (50%)
- Low (40%)
- Very Low (20%)

[Legend: Large magnitude of effect, confounding reduces a demonstrated effect, and high dose-response gradient.]

Systematic Reviews: Forest Plots

- Display of multiple study comparisons in one graph

- Shows point estimate (rectangle) and 95% CI for difference between treatments (exp. vs. control)

- Meta-analysis (when possible) gives overall weighted average shown by diamond with width of diamond indicating 95% CI

[Forest plot diagram with impact of treatment on mortality.]

Vertical line in middle of graph = no difference
Evidence for Massage/Soft Tissue Mobilization (Ezzo 2007)

- 19 controlled trials found; all were relatively small, 12 were judged low quality
- Only 6 studies examined massage alone vs. a control; all 6 covered different types of massage
  - 2 studies included only one treatment
  - 1 study utilized self-administered massage
- Conclusion: Limited evidence of no benefit
- Limitations:
  - Many studies lacked details re: massage method and qualifications of practitioner
  - Disability outcomes rarely reported

Manipulation vs. Mobilization

<table>
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<tr>
<th>Study</th>
<th>Manipulation</th>
<th>Mobilization</th>
<th>N1</th>
<th>N2</th>
<th>N1</th>
<th>N2</th>
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<th>N2</th>
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</table>

Focus on effect of manual therapy alone vs. control or other comparison treatment
- Included 27 studies, 9 with low risk of bias
- Moderate evidence: No difference between mobilization and manipulation
- Low quality evidence
  - Manipulation more effective than control for short term pain relief for acute or chronic neck pain
  - Thoracic manipulation better than placebo for short term pain relief of chronic neck pain

Gross et al: Summary

- Relatively few high quality trials, low sample sizes
- Mostly short and intermediate term results; no difference in long term results
- No indications of optimal dose
- Lack of quality evidence for whiplash associated disorders
- Benign, short term side effects (8 studies)
Focused on manual therapy (manipulation or mobilization) combined with exercise

Included 17 studies, 5 with low risk of bias

Miller et al: MT/Ex Effect on Pain*

- Manual therapy + exercise was more effective for:
  - Long term relief of chronic pain vs. placebo or no treatment control (low)
  - Short term relief of pain vs. exercise alone (high)
  - Long term relief of pain vs. manual therapy alone (moderate)
  - Short term relief of pain for acute whiplash vs. traditional care (moderate)
  - Short and long term relief of pain vs. advice (low)
- No long term difference vs. traditional care for subacute and chronic mechanical neck pain (high)

*Strength of evidence in parentheses

Miller et al: MT/Ex Effect on Function*

- Manual therapy + exercise was more effective for:
  - Long term functional improvement vs. placebo or no treatment control (low)
  - Long term functional improvement vs. manual therapy alone (low)
  - Long term functional improvement vs. exercise advice (very low)
- No short or long term difference versus:
  - Exercise only for subacute and chronic mechanical neck pain (high)
  - Traditional care for acute whiplash or for subacute and chronic mechanical neck pain (low)

*Strength of evidence in parentheses
MT + Exercise for Function


- No significant differences for health related quality of life (5 studies)
- Significant differences in global ratings of change vs. waitlist (1 study) or traditional care (2 studies) but not vs. exercise only (3 studies)
- Moderate evidence shows reduced cost of care for MT+Ex (4 studies)

Miller J, et al. Further Research Needed:
- What is the best manual therapy technique?
- What is the best exercise approach?
- What is the optimal dose of manual therapy and exercise?
- Are there patient subgroups that would benefit more than others?

Systematic review
Manual therapy with or without physical medicine modalities for neck pain: a systematic review
Jonathan D'Apice 5, Jordan Miller 6, Anita Gross 6, Stephen J. Buskell 8, Charles H. Goldsmith 5, Nadine Graham 5, Ted Haines 5, Gert Brandt 8, Ian L. Having 8, for the Cervical Overview Group

- Manipulation, mobilization plus various physical medicine modalities were not more effective than various control group comparisons including modality alone, placebo, exercise, and education (low quality evidence)
- Mobilization, massage, heat, E stim and meds are more effective than meds alone for chronic neck pain (very low quality evidence)
- Manual therapy may be less costly than various alternative treatments (moderate quality evidence)
**Challenges with Traditional Research on Manual Therapy for Spine Pain**

- Spontaneous recovery: Some patients get better no matter what treatment
- Lack of examination/diagnostic tests with proven validity
- Wide array of manual therapy approaches; Different practitioners would not agree on:
  - Examination techniques
  - Findings or "diagnosis"
  - Manual therapy techniques
- No way to agree on diagnostic categories or treatment approach

**Result: Clinicians (and Researchers) Can’t Agree on Pathology or Treatment**

- Patients with “nonspecific neck pain” of various causes are all randomized to manual therapy vs. other interventions, with no indication that manual therapy is even appropriate for the patient
- No 2 studies use the same manual therapy approach
- If choice of technique is left up to the therapist (“eclectic approach”), then no 2 patients in a study receive the same technique!
Nonspecific Pain Diagnoses
(IAM Data 2004-06)

Example: Hoving et al, Ann Int Med 2002
- RCT: 183 patients with nonspecific neck pain
  - GP care – education, NSAIDs
  - PT: Physical Therapy” – exercise, modalities
  - MT: Manual Therapy – PTs, DOs, DCs using own approach

- Outcomes
  - Pain
  - Neck Disability Index (NDI)
  - Global rating of perceived recovery – “completely recovered” or “much improved”


Hoving et al, 7 week outcomes
- Pain: Manual therapy was significantly better on pain VAS than PT or GP by 0.9, 1.5 on VAS
- Disability: Manual therapy was better, but differences not statistically significant
- Perceived recovery
  - MT = 68.3% NNT
  - PT = 50.8% - MT vs GP = 3
  - GP = 35.9% - MT vs PT = 7

Hoving et al, Results

Figure 2. Results of primary outcome measures during the 7-week follow-up.
Cost Analysis

- Manual Therapy: $402
- Standard PT: $1167
- GP: $1241

Ingeborg BMJ 2003: F/U on Hoving Study

Comments on Hoving et al
- Sample was “nonspecific neck pain whose clinical presentation did not warrant further diagnostic screening”
- All groups tended to get better over 7 weeks
- Manual therapy group did significantly better at less cost, but differences in pain, disability were not as great as we would hope
  - Are there subgroups that benefit more?
  - Can we identify them?
- If you wanted to incorporate these results into your practice, what would you do?
  - PT, chiropractic, and osteopathic methods used
  - No details on manual therapy techniques

Alternative to Diagnosis on Pathology: Classification Approach

- Classification – an alternative to “Diagnosis” (which nobody can agree on anyway!)
  - Diagnosis – a process to determine the underlying cause (i.e., “tissue at fault”) of a patient’s illness or discomfort
  - Classification – a process of categorizing patients according to treatments for which they have been shown to respond favorably

Diagnosis vs. Classification

- Diagnosis categories (traditional, biomechanical)
  - C6-7 herniated disc
  - Right C5-C6 facet
  - FRS left
- Treatment based classification categories*
  - (Decreased) Mobility
  - Centralization
  - Conditioning and Exercise Tolerance
  - Pain
  - Headaches (Cervicogenic)

Clinical Prediction Rule
- Method developed for diagnostic tests
- Administer a variety of history and objective diagnostic tests, followed by the gold standard
- Determine which of the exam findings are the best predictors for that diagnosis
- Examples:

Types of CPRs
- Diagnostic: probability that a patient has a particular condition
- Prognostic: likely outcome of patients with a specific condition
- Interventions: which patients are likely to respond to a type or set of intervention(s)

Procedure to Develop a CPR*

Step 1: Derivation of a CPR for Treatment Based Classification
- Clinicians and researchers brainstorm potential and standardize a set of predictor variables
  - May be from history or examination
  - Ideally need 10-15 patients per predictor
- Enroll patients; blinded examiner administers standardized history and examination
- Apply the reference criterion
  - In diagnostic studies, the gold standard for diagnosis, such as an MRI
  - In treatment studies, it is a pre-defined favorable response to a standardized intervention, such as spinal manipulation

Step 1: Derivation of a CPR for Treatment Based Classification

- Establish standardized predictor variables
- Enroll patients eligible for treatment
- Determine best set of predictors for a successful outcome
- Standardized intervention
- Standardized History and examination

Step 1 for CPR: Data Analysis

- Analyze which predictor “diagnosed” which patients were most likely to benefit from treatment
- For each predictor, calculate:
  - Sensitivity and specificity (want close to 1)
  - Likelihood ratios
    - Positive – predicts + response to treatment (higher above 1, the better)
    - Negative – predicts unfavorable response to treatment (farther below 1, the better)
- Use multivariate regression analysis to “identify the most parsimonious set of predictor variables” (Childs and Cleland)

Step 2 for CPR: Validation

- Must be done before clinical implementation!
  - When you do an analysis with many predictors, some may be significant just by chance
  - This is unlikely to happen again when the study is repeated (i.e., validated)
  - Validation is also necessary to use the CPR in a different patient population and/or to show that it can be applied by various clinicians
- For diagnosis CPR, can repeat step 1 in a different sample to see if the same predictors emerge
- For treatment CPR, step 2 and 3 may be combined

Step 3: Conduct Impact Analysis

- Assess impact of using CPR in clinic
- 3 Methods
  - Compare outcomes pre/post implementation
  - Randomized controlled designs (better)
    - Randomize each patient to CPR or non-CPR
    - Randomize different clinics to follow CPR or non-CPR approach
  - Patients positive on the rule should have:
    - Better response to treatment than those not selected when given the experimental treatment
    - Worse response to treatment when given the control treatment
Levels of Evidence for CPRs (Childs and Cleland)

Table 4. Levels of Evidence for Clinical Prediction Rules

<table>
<thead>
<tr>
<th>Level</th>
<th>Requirements</th>
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<tbody>
<tr>
<td>I</td>
<td>At least one prospective validation in a different population plus one impact analysis demonstrating change in clinician behavior with beneficial consequences</td>
</tr>
<tr>
<td>II</td>
<td>Validation in one large prospective study, including a broad spectrum of patients and clinicians, or in several similar settings that differ in geographical location and experience levels of clinicians</td>
</tr>
<tr>
<td>III</td>
<td>Validated in only one narrow prospective sample</td>
</tr>
<tr>
<td>IV</td>
<td>Derived but not validated, or validated only in split samples or large retrospective databases or by statistical techniques</td>
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Evidence for Effectiveness of Thoracic Spine Manipulation for Neck Pain

Development of CPR for Neck Pain

- Subjects: Ages 18-60, primary c/o neck pain, Neck Disability Index ≥ 10%
- Standardized history and examination
- Standardized treatment
  - 3 Thoracic thrust manipulations (2 visits)
  - Cervical ROM exercise
  - Maintain usual activity

CPR for Neck Pain (cont.)

- Success = “a great deal better” per global measure within 2 visits
- 42/78 (54%) success rate by this criteria
CPR for Neck Pain (cont.)

- Factors predicting success:
  - Neck pain < 30 days
  - No sxns distal to shoulder
  - Looking up does not aggravate
  - FABQPA < 12
  - Decreased upper thoracic kyphosis
  - Cervical Extension < 30 deg
- 86% success if 3/6 are present


- Some patients in any cohort with neck pain will get better spontaneously
- Significant predictors (baseline findings) may be:
  - Simply predicting those with natural recovery
  - Chance findings
- Need a follow-up study to validate the clinical prediction rule

Validation of CPR for Spinal Manip

- Cleland J, et al. Physical Therapy. 2010;90(9):1239-1250
- 40 subjects with neck pain enrolled at 5 sites across US
- Standardized baseline history and examination
- Categorized according to original CPR (Cleland et al)
  - 3 or more positive = (+) CPR
  - 2 or less positive = (-) CPR
- Patients randomly assigned to exercise or manip/exercise:

Validation of CPR?

- No significant differences in pain or Neck Disability Index scores between those positive vs. negative on the rule
  - CPR not validated
Pain Scale Results (Regardless of CPR Category)
- Manip + exercise better at 1 week but no difference at 4 weeks or 6 months.

![Pain Scale Results Graph](image1)

Neck Disability Index Results (Regardless of CPR Category)
- Manip + exercise better at 4 weeks but no difference at 4 weeks or 6 months, regardless of CPR category

![Neck Disability Index Results Graph](image2)

Global Rating of Change Results

![Global Rating of Change Results Graph](image3)

Conclusions: Cleland et al, 2010
- CPR not validated
- Thoracic manipulation plus exercise more effective than exercise alone for the treatment of neck pain.
More Evidence for T-Manip for Acute Neck Pain

  - Patients (n=45): Mechanical neck pain < 1 mo. Duration
  - Treatment:
    - 5 visits heat/electrotherapy vs. 5 visits heat/electrotherapy (3 with T-manip)
  - Results: Manip significantly more effective for pain, disability, and ROM at 4 weeks

More Evidence for T-Manip for Chronic Neck Pain

  - N = 120 patients with neck pain > 3 mos.
  - Randomized to thoracic manip vs. infrared heat + education
  - Outcomes at end of treatment, 3 and 6 mos: Pain, disability, posture, ROM
  - Results: Pain, disability, ROM, posture all significantly better for manipulation group at 3 and 6 mos.

Systematic Review on Thoracic Manipulation for Neck Pain*

- 6 RCTs included; PEDro scores 6-7 out of 10
- Subjects primarily had acute or subacute pain
- Results: Significant, large effect sizes in favor of manipulation (vs. various control) for pain, ROM, and functional measures.
- Conclusion: “Thoracic spine thrust manipulation may provide short-term improvement in patients with acute or subacute mechanical neck pain. However, the body of literature is weak, and these results may not be generalizable.”


Critical Appraisal of Clinical Prediction
Rules That Aim to Optimize
Treatment Selection for
Musculoskeletal Conditions

- Reviewed 18 articles related to 15 different CPRs published through April 2009
- Only one CPR (lumbosacral manipulation) had been validated, and those results were not confirmed by other authors
- CPRs do not provide strong evidence at this point in time

What About Cervical Spine High Velocity Low Amplitude (“Thrust”) Manipulation?

T Spine Thrust Vs. C Spine Thrust in Patients With Acute Neck Pain: An RCT*

- RCT enrolling subjects who met the CPR for thoracic manipulation
- Subjects randomized to receive 2 sessions consisting of:
  - 3 T-spine manipulations + exercise, or
  - 1 mid cervical spine manipulation + exercise


Adverse Effects

- Thoracic Spine Treatment Group
  - 1st Tx 70% reported transient side effects
  - 2nd Tx 80% reported transient side effects

- Cervical Spine Treatment Group
  - 1st Tx 7% (1 person) report side effect
  - 2nd Tx none reported

- No catastrophic events reported resulting in further medical attention.
Recent RCT: Cervical Manip More Effective than Cervical Mobilization*

- Multicenter RCT enrolling patients with neck pain
- Randomized to receive one visit for:
  - Bilat. thrust manip to C1-C2 and T1-T2, or:
  - Bilat. grade IV mobilization to C1-C2 and T1-T2
- Results: Thrust manipulation showed significantly greater improvement in pain, NDI
- Caution: Only 48 hour follow-up
- No adverse events reported

*Running JR, et al. JOSPT, in press

Risk for Cervical Manipulation

- Transient side effects from cervical manipulation (Cagnie B. Man Ther. 2004:9(3):151-156.)
  - Survey of 465 patients following PT, DO, or DC manipulation
  - 61% had at least one side effect (neck pain, radiating pain, HA, dizziness, blurred vision)
- Most lasted 4-24 hours

Risk for Thoracic Spine Manipulation

- Transient in nature, not catastrophic.
- Recent literature demonstrates that there is greater likelihood for transient side effects.
- Thoracic manipulation causes greater risk of side effects but does not carry the catastrophic risk?

Risk of Serious Injury

- Thrust manipulation risk estimates
  - Risk of serious complications estimated at 6 in 10 million (Hurwitz, Spine, 1996)
  - Risk of death at 3 in 10 million
- Haldeman (Spine, 1999) documented 115 cases of vertebral artery occlusion leading to CVAs after chiropractic manipulation leading to ischemia and CVA
**Risks in Perspective**

<table>
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<tr>
<th>Procedure</th>
<th>Risk / 10,000</th>
<th>Complication</th>
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<tbody>
<tr>
<td>LS Manip</td>
<td>0.001</td>
<td>Cauda Equina</td>
</tr>
<tr>
<td>Cervical Manip</td>
<td>0.006</td>
<td>Death or stroke</td>
</tr>
<tr>
<td>Exercise</td>
<td>0.007</td>
<td>Death</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>100-300</td>
<td>GI Bleed</td>
</tr>
<tr>
<td>C Spine Surgery</td>
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</tr>
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<td>1.6-1.7</td>
<td>Vascular perforation</td>
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<tr>
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<tr>
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<td>1700</td>
<td>Various</td>
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<tr>
<td>Lumbar surgery</td>
<td>20-30</td>
<td>Death</td>
</tr>
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</table>

**Clinical Opinion**

- Even though overall risks are small, the potential for spinal cord or vertebral artery injury is there
- Cervical spine manipulation has not been shown to be more effective than more gentle mobilization techniques (Gross A, et al. Manipulation or mobilisation for neck pain: A Cochrane Review. Man Ther 2010;15(5): 315-33)
- For this reason, mobilization techniques are often preferred and are recommended DPT faculty and other experienced clinicians
- If manipulation is performed, avoid extremes of ROM

**RELATIVE – potential for adverse reactions**

- Adverse reaction to previous manual therapy.
- Pregnancy
- Inflammatory arthritis
- Osteoporosis
- HNP or prolapse
- Advanced DJD
- Inflammatory arthritides
- Spondylolisthesis
- Long term steroids
- Vertigo
- Dependence on HVLA


- Pathology that has lead to bone weakening, i.e. tumor, infection
- Cervical Myelopathy
- Cord Compression
- Nerve root compression with significant worsening
- VBI dx.
- Lack of patient consent
- Patient positioning can not be achieved due to pain or resistance.

Conclusions

- Thoracic spine manipulation may be a reasonable alternative to cervical spine manipulation for the treatment of neck pain.
- No currently validated clinical prediction rule to identify a subset of subjects with better prognosis for manipulation.

Take Home

- CPR approach does not require complex biomechanical examination and analyses to decide on treatment approach.
- These studies suggest that thoracic manipulation is more effective for neck pain than exercise or modalities alone, but no subgroup has been identified that would respond more favorably.
- Mechanism for improvement is unknown:
  - Just because we don’t know why it works, doesn’t mean we can’t use it!
  - There are a lot of “recovering biomechanists” in the PT world!

Stay tuned: Future Research

- Limited, early evidence suggests that C-spine manipulation may be more effective than mobs or T-spine manipulation in the short term.
- Will C-spine manipulation prove to be effective in the long term to reduce chronic pain and disability?