Multicenter Osteopathic Pneumonia Study in the Elderly (MOPSE)

The Primary Outcomes
BACKGROUND
MOPSE
(Multicenter Osteopathic Pneumonia Study in the Elderly)

- A registered study at www.clinicaltrials.gov
- Conducted between March 2004 and April 2007
- Protocol Paper: www.jaoa.edu
- Main Outcomes Paper: www.om-pc.com
Funded by a Consortium of Osteopathic Foundations

- Brentwood Foundation (Ohio)
- Colorado Springs Osteopathic Foundation (Colorado)
- Foundation for Osteopathic Health Services (Maryland)
- Muskegon General Osteopathic Foundation (Michigan)
- Northwest Oklahoma Osteopathic Foundation (Oklahoma)
- Osteopathic Founders Foundation (Oklahoma)
- Osteopathic Institute of the South (Georgia)
- Osteopathic Heritage Foundation (Ohio)
- Quad City Osteopathic Foundation (Iowa)
Multicenter study structure

Osteopathic Foundations

Ohio – Doctors Hospital

Michigan – Mount Clemens

Missouri – NERMC

New Jersey – Kennedy Stratford

Texas – OMCT, Plaza & John Peter Smith

Osteopathic Research Center in Fort Worth, Texas

AT Still Research Institute in Kirksville, Missouri
Study Methods
Primary Hypothesis

• Osteopathic Manipulative Treatment will:
  – Reduce length of stay (LOS)
  – Reduce time to clinical stability
  – Improve the symptomatic and functional recovery score
Length of stay (LOS)

- A traditional measure
- Taken from the time and date the order was written for;
  - Admission
  - Discharge
  - Or the closest approximation found in the chart
- At midnight, a new day starts
Time to Clinical Stability

- Measured DAILY – The # of days it takes for all SEVEN clinical measures to be “stable”
  - Lowest Systolic BP ≥ 90 mmHg
  - Highest Heart Rate ≤ 100 beats / minute
  - Highest Respiratory Rate ≤ 24 breaths / minute
  - Highest Temperature 38 degrees Centigrade
  - Lowest Oxygen Saturation ≥ 90%
  - Ability to eat by mouth or feeding tube
  - Mental status grossly back to baseline

Symptomatic and Functional Recovery Score (SFRS)

- Calculated from a pneumonia-specific validated questionnaire
  - Cough, Dyspnea, Sputum production, Pleuritic chest pain, and Fatigue
- Higher SFRS, the worse the symptoms
- Measured on
  - Admission (Day 1), Day 14, Day 30 and Day 60

1. Randomized Controlled Clinical Trial
   - Efficacy study, not a mechanistic study
2. Seamless Design
   - Not to interfere with usual care
3. Blinded Study
   - For the decision makers
4. Three arm study design
   - OMT group
   - Light touch “sham” group
   - Conventional care only group
5. OMT is an adjunctive treatment modality
   • Does not replace conventional care
6. Balances uniformity with individualization
   • 15 minutes standard, 5 minutes specific
7. Best effect design over pragmatic design
   • Build upon the previous studies
8. 24 hour window
   • From admission to first treatment
Inclusion Criteria

• Age ≥ 50 years
• NEW pulmonary infiltrate on x-ray
• Two of the following
  – New, increased cough
  – Fever ≥ 38 degrees Centigrade
  – Pleuritic chest pain
  – New findings on physical exam
  – Respiratory rate ≥ 25 bpm
  – Mental status change
  – WBC ≥ 12,000 cells/mm³
Exclusion Criteria

- Nosocomial Pneumonia
- Lung Abscess
- Advancing Pulmonary Fibrosis
- Bronchiectasis
- Pulmonary Tuberculosis
- Lung Cancer
- Metastatic Cancer
- Acute Rib or Vertebral Fracture
- Previous Participation
Eight Standardized Techniques

1. Thoracolumbar soft tissue
2. Rib raising
3. Doming of the diaphragm myofascial release
4. Cervical soft tissue
5. Suboccipital decompression
6. Thoracic inlet myofascial release
7. Thoracic lymphatic pump
8. Pedal lymphatic pump
Primary Outcomes:
1) Length of Hospital Stay
2) Time to Clinical Stability
3) Rate of Symptomatic and Functional Recovery

Secondary Outcomes:
- Duration of IV and oral antibiotic treatment
- Treatment Endpoints: Death, Respiratory Failure and Discharge
- 60-day Re-admission
- Success in Blinding
Two Kinds of Statistical Analysis

• Intention to treat analysis
  – Everyone who randomized into the study
    • Excludes for change in diagnosis
    • Excludes for first treatment beyond 30 hours

• Per protocol analysis
  – Everyone who got the protocol as designed
    • Excludes for first treatment beyond 24 hours
    • Excludes for treatment contrary to protocol
    • Excludes subjects who dropped out of the study
    • Excludes for missing a treatment session
RESULTS
Subject Recruitment
(from seven community hospitals)

3,426 Screened

543 Eligible

406 Randomized

2,883 Not Eligible

137 Declined
Demographics

- Antibiotic Selection
  - 84% agreement with practice guidelines
- Demographics
  - No differences, except
    - Aspiration risk (LT > CCO) by ITT analysis
    - Current Alcohol Use (OMT < LT, CCO) by PP analysis
- Pneumonia Severity Index
  - no between group differences
Randomization and Numbers

406 Randomized

OMT
135 Assigned
130 ITT
96 PP

LT
136 Assigned
124 ITT
95 PP

CCO
135 Assigned
133 ITT
127 PP

ITT = Intention to treat statistical analysis
PP = Per protocol statistical analysis
### Mean LOS

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<thead>
<tr>
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<tbody>
<tr>
<td><strong>Intention to treat analysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>130</td>
<td>124</td>
<td>133</td>
</tr>
<tr>
<td><strong>Mean LOS (SD)</strong></td>
<td>4.5 days (SD 2.7)</td>
<td>4.9 days (SD 2.7)</td>
<td>4.5 days (SD 2.6)</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td>0.53</td>
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<tbody>
<tr>
<td><strong>Per protocol analysis</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>n</strong></td>
<td>96</td>
<td>95</td>
<td>127</td>
</tr>
<tr>
<td><strong>Mean LOS (SD)</strong></td>
<td>4.0 days (SD 2.0)</td>
<td>4.4 days (SD 2.4)</td>
<td>4.5 days (SD 2.6)</td>
</tr>
<tr>
<td><strong>p</strong></td>
<td>0.01</td>
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(OMT < CCO)
## Time to Clinical Stability

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<tr>
<td><strong>Intention to treat analysis</strong></td>
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</tr>
<tr>
<td>n = 121</td>
<td>n = 118</td>
<td>n = 130</td>
<td></td>
</tr>
<tr>
<td>2.5 days (SD 1.6)</td>
<td>2.5 days (SD 1.4)</td>
<td>2.6 days (SD 1.6)</td>
<td>p = 0.97</td>
</tr>
<tr>
<td><strong>Per protocol analysis</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>n = 90</td>
<td>n = 90</td>
<td>n = 124</td>
<td></td>
</tr>
<tr>
<td>2.3 days (SD 1.4)</td>
<td>2.5 days (SD 1.5)</td>
<td>2.6 days (SD 1.6)</td>
<td>p = 0.47</td>
</tr>
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Symptomatic and Functional Recovery Score (no statistical difference)

OMT (n=99)
LT (n=102)
CCO (n=99)

Group x Time P=0.24
Group P=0.47

Mean SFRS (SD)

Admission 14-day 30-day 60-day

Measurement Point
## Treatment End Point Data:

**Intent to treat analysis**

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<tbody>
<tr>
<td>n = 124</td>
<td>n = 124</td>
<td>n = 132</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>2%</td>
<td>3%</td>
<td>6%</td>
</tr>
<tr>
<td>Respiratory Failure</td>
<td>3%</td>
<td>3%</td>
<td>8%</td>
</tr>
<tr>
<td>Discharged Alive</td>
<td>95%</td>
<td>94%</td>
<td>86%</td>
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*p = 0.08*
## Treatment End Point Data: By per protocol analysis

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<tr>
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<td>96</td>
<td>95</td>
<td>132</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>0%</td>
<td>3%</td>
<td>6%</td>
</tr>
<tr>
<td><strong>Respiratory Failure</strong></td>
<td>1%</td>
<td>2%</td>
<td>7%</td>
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</table>
| **Discharged Alive** | 99% | 95% | 87% | \(p = 0.006\)
Treatment Endpoint

Intention-to-Treat Analysis

Per-Protocol Analysis

P = 0.006

P = 0.08

OMT (n=124) blue LT (n=124) green CCO (n=132) red

OMT (n=96) blue LT (n=95) green CCO (n=127) red
### 60-Day Readmission Rate

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<td><strong>By intention to treat analysis</strong></td>
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<tr>
<td>n</td>
<td>93</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>17%</td>
<td>20%</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>0.64</td>
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<tbody>
<tr>
<td><strong>By per protocol analysis</strong></td>
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<tr>
<td>N</td>
<td>80</td>
<td>79</td>
<td>92</td>
</tr>
<tr>
<td>11%</td>
<td>20%</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>0.16</td>
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Blinding: Percent Correctly Identifying their Group

Intention to treat analysis

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<tr>
<td>53 %</td>
<td>44 %</td>
<td>49 %</td>
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Per protocol analysis produced similar numbers.
Conclusions and Discussion
Conclusions

• By ITT analysis
  – outcomes not improved

• By PP analysis
  – OMT decreased LOS, duration IV antibiotics, and Mortality
    • Relative to the CCO group

• LT groups
  – outcomes tended to fall between the OMT and CCO outcomes
Changing Mean Length of Stay for Pneumonia in the Elderly

- **1992-93 Pilot**: 14 days
- **1996-98 Texas Study**: 7.5 days
- **2004-07 MOPSE**: 4.5 days
Points for Discussion

• Does the shortened hospital LOS make OMT obsolete?
  – Where might OMT find a therapeutic role?
• How significant are the positive outcomes?
  – ITT analysis verses PP analysis
• Is LT more like OMT or CCO?
  – How should the three group outcomes be interpreted?
Stay tuned for the panel discussion