Nonpharmacologic Delirium Prevention

- Effectiveness and cost-effectiveness well-demonstrated
- Multiple clinical trials and systematic reviews
- Strong recommendation in multiple delirium guidelines
  - AGS-ACS in U.S.- 2015
  - NICE in U.K. - 2010 (updated 2014)
Delirium Prevention Trials

Systematic review and meta-analysis of delirium prevention trials to evaluate effect on adverse outcomes

T Hshieh, JAMA Intern Med. 2015; 175: 512-52

Methods

• Data Sources: PubMed, Google Scholar, ScienceDirect, Cochrane Database of Systematic Reviews
  – January 1, 1999 – December 31, 2013
• Study selection: Studies of targeted multi-component delirium interventions that reported on any of the following outcomes:
  – Delirium incidence
  – Falls
  – Length of stay
  – Rate of discharge to long-term care institutions
  – Change in functional or cognitive status
Data Extraction

• Two experienced physician reviewers independently and blindly abstracted data
  – Study population
  – Outcome measures
  – Intervention strategy

• Reviewers also determined:
  – Quality ratings (Cochrane Risk of Bias)
  – Number of evidence-based HELP-type interventions

• Abstractions were compared
  – Any disagreements in ratings resolved through consensus conferences with third reviewer
### Results: Delirium Incidence

<table>
<thead>
<tr>
<th>Delirium Incidence</th>
<th>Odds Ratio (95% CI)</th>
<th>Decreased delirium incidence favors intervention</th>
<th>Increased delirium incidence favors control</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andro et al, 2011</td>
<td>0.35 (0.13-0.89)</td>
<td></td>
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<td>Bo et al, 2009</td>
<td>0.39 (0.17-0.93)</td>
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<td>7.3</td>
</tr>
<tr>
<td>Caplan and Harper, 2007</td>
<td>0.11 (0.01-0.99)</td>
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<td>2.6</td>
</tr>
<tr>
<td>Chen et al, 2011</td>
<td>0.03 (0.00-0.44)</td>
<td></td>
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<td>5.7</td>
</tr>
<tr>
<td>Holt et al, 2013</td>
<td>0.31 (0.13-0.74)</td>
<td></td>
<td></td>
<td>9.1</td>
</tr>
<tr>
<td>Inouye et al, 1999</td>
<td>0.62 (0.41-0.94)</td>
<td></td>
<td></td>
<td>21.4</td>
</tr>
<tr>
<td>Jeffs et al, 2013</td>
<td>0.79 (0.40-1.57)</td>
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<td>7.6</td>
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<tr>
<td>Kratz, 2008</td>
<td>0.35 (0.09-1.39)</td>
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<td>3.1</td>
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<tr>
<td>Lundström et al, 2007</td>
<td>0.42 (0.21-0.88)</td>
<td></td>
<td></td>
<td>11.3</td>
</tr>
<tr>
<td>Martinez et al, 2012</td>
<td>0.38 (0.16-0.91)</td>
<td></td>
<td></td>
<td>7.3</td>
</tr>
<tr>
<td>Vidan et al, 2009</td>
<td>0.59 (0.34-1.00)</td>
<td></td>
<td></td>
<td>15.5</td>
</tr>
<tr>
<td>Fixed-effect model: P = .001</td>
<td>0.47 (0.38-0.58)</td>
<td></td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Heterogeneity: $I^2 = 18%$, $P = .27$</td>
<td>NNT = 14.3 (95% CI, 11.1-20.0)</td>
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</tr>
</tbody>
</table>

### Results: Falls

<table>
<thead>
<tr>
<th>Falls</th>
<th>Odds Ratio (95% CI)</th>
<th>Decreased falls, favors intervention</th>
<th>Increased falls, favors control</th>
<th>Weight, %</th>
</tr>
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<tbody>
<tr>
<td>Rabino et al, 2013</td>
<td>0.49 (0.19-1.27)</td>
<td></td>
<td></td>
<td>10.9</td>
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<tr>
<td>Caplan and Harper, 2007</td>
<td>0.33 (0.04-2.93)</td>
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<td>2.5</td>
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<tr>
<td>Martinez et al, 2012</td>
<td>0.11 (0.01-2.05)</td>
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<tr>
<td>Stenwall et al, 2007</td>
<td>0.38 (0.23-0.65)</td>
<td></td>
<td></td>
<td>38.2</td>
</tr>
<tr>
<td>Fixed-effect model: P = .001</td>
<td>0.38 (0.25-0.60)</td>
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<td></td>
<td>100</td>
</tr>
<tr>
<td>Heterogeneity: $I^2 = 0%$, $P = .78$</td>
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</tbody>
</table>
Results: Length of Stay

<table>
<thead>
<tr>
<th>Length of Stay</th>
<th>Mean Difference (95% CI)</th>
<th>Decreased length of stay favors intervention</th>
<th>Increased length of stay favors control</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bo et al., 2009</td>
<td>-0.79 (-1.40 to -0.09)</td>
<td></td>
<td></td>
<td>21.3</td>
</tr>
<tr>
<td>Caplan and Harper, 2007</td>
<td>-4.30 (-13.25 to 4.65)</td>
<td></td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td>Chen et al., 2011</td>
<td>-2.00 (-6.10 to 2.10)</td>
<td></td>
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<td>3.4</td>
</tr>
<tr>
<td>Holt et al., 2013</td>
<td>1.46 (-7.73 to 5.65)</td>
<td></td>
<td></td>
<td>1.2</td>
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<tr>
<td>Inoue et al., 2016</td>
<td>0.40 (0.44 to 1.24)</td>
<td></td>
<td></td>
<td>19.9</td>
</tr>
<tr>
<td>Jeffs et al., 2013</td>
<td>-0.10 (-0.74 to 0.54)</td>
<td></td>
<td></td>
<td>22.0</td>
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<td>Martinez et al., 2007</td>
<td>-1.35 (-2.98 to 0.28)</td>
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<td>12.4</td>
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<tr>
<td>Lunden et al., 2007</td>
<td>-10.00 (-18.79 to -1.31)</td>
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<td>0.8</td>
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<tr>
<td>Vidan et al., 2009</td>
<td>1.55 (0.34 to 2.76)</td>
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<td></td>
<td>16.2</td>
</tr>
<tr>
<td>Random-effect model</td>
<td>P = .69</td>
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<td>100</td>
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<tr>
<td></td>
<td>-0.10 (-0.97 to 0.64)</td>
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<tr>
<td>Heterogeneity: I²  = 62%, P = .006</td>
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</table>

Results: Institutionalization

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<thead>
<tr>
<th>Institutionalization</th>
<th>Odds Ratio (95% CI)</th>
<th>Decreased institutionalization favors intervention</th>
<th>Increased institutionalization favors control</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bogardus et al., 2003</td>
<td>1.00 (0.71 to 1.42)</td>
<td></td>
<td></td>
<td>65.2</td>
</tr>
<tr>
<td>Caplan and Harper, 2007</td>
<td>0.37 (0.09 to 1.52)</td>
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<td>6.7</td>
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<td>Holt et al., 2013</td>
<td>1.24 (0.60 to 2.57)</td>
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<td>Lundstrom et al., 2007</td>
<td>0.69 (0.31 to 1.52)</td>
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<td>14.9</td>
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<tr>
<td>Fixed-effect model, P = .69</td>
<td>0.95 (0.71 to 1.26)</td>
<td></td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Heterogeneity: I²  = 0%, P = .39</td>
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Study Conclusions

• Provides evidence that multicomponent, non-pharmacologic delirium prevention interventions are effective:
  – Reducing incidence of delirium
  – Preventing falls
  – Trend towards avoiding institutionalization
  – Trend towards decreasing length of stay

• One million cases of delirium in the hospital could be prevented → cost savings of $10,000 per case - $10 billion Medicare dollars per year

• Based on preventable falls, $5-7 billion additional Medicare dollars saved per year

HELP-based Interventions

• Of the 14 studies, 12 were based on HELP
• Effectiveness noted if at least 2 of the 6 HELP-based interventions were included in the study
Hospital Elder Life Program (HELP)

• Effective and cost-effective
• Why did it work?
  – Appropriate study population
  – Targeted risk factor intervention
  – Intervention potency tested and assured
  – Standardized protocols
  – Multifactorial approach but individually tailored
  – Trained multidisciplinary staff
  – Built-in quality assurance strategies

Limitations of HELP

• Complex, requires system-wide changes
• Time-intensive behavioral interventions
• Nonpharmacologic—not just a pill
• Not effective for treatment
Design a delirium treatment trial

• Approaches based on pathophysiology: would be ideal
• Lacking this, target to address important areas we know about:
  – Address most common causes
  – Prevent known complications
  – Bolster reserve

Designing the Ideal Intervention

What would it look like?

– Highly potent
– No adverse effects
– Straightforward, standardizable
– Acceptable to patients and staff
New Challenges for Secondary Prevention

• More complex, since treating delirium is more difficult once it occurs
• Many different etiologies need to be addressed
• Multi-pronged approach will be required for potency
• Select factors which are amenable to intervention

What approaches are likely to be effective?

Multi-pronged approach
1. Remove or treat underlying cause(s)
2. Manage delirium behaviors
3. Prevent or remediate complications
4. Restore cognitive and physical function

Caveat: not feasible to address all— prioritize to realistic number
#1. Remove or treat underlying cause(s)

- **Primary approach:**
  - Identify 5-10 most common etiologies
  - Standardized assessments/interventions for these
- **Some individualization:**
  - Stepped approach to further assessments and interventions for potency
  - Must be able to standardize and monitor adherence

Common causes to consider

- Medications
- Infections (UTI, respiratory)
- Dehydration
- Electrolyte imbalance
- Impaired oxygenation
- Severe pain
- Sleep deprivation
#2 Manage delirium behaviors

- Agitation and inappropriate behaviors
- Nonpharmacologic strategies 1st: behavioral interventions, family participation
- Pharmacologic approaches reserved for severe agitation: beware of vicious cycles of medications and worsening delirium
- Low-dose pharmacologic approach

#3 Prevent or remediate complications

- Oversedation/medication adverse effects
- Immobility, functional decline, falls
- Poor oral intake, dehydration/malnutrition
- Aspiration risk
- Sleep disturbance
- Urinary incontinence
- Pressure ulcers
- DVT/pulmonary embolism
#4 Restore cognitive and physical function

- Rehabilitative approaches, targeted to maximizing functioning and independence.
- Consider more intensive PT/OT options
- Cognitive retraining
- Family education and participation
- Coordinated transitional care

Principles of Implementation

- Target at-risk patients
- Pilot test all protocols for feasibility, acceptability, and potency
- Design approach to assure that all interventions are received
- Build in procedures to track and maximize adherence
Implementation Issues

• Multidisciplinary team likely needed for effectiveness:
  – Physician: proactive consultation for causes
  – Nursing: interventions
  – Pharmacist: medications
  – Rehabilitation therapists
  – Trained volunteers
• Develop standardized interventions
• Prioritize: avoid unfeasible number of interventions per patient
• Ongoing monitoring and standardization of team

Assuring Adherence

• Monitoring and assuring adherence may be complex, and will require systematic approaches
• Building in quality assurance will be critical to assure success of this complex intervention
• HELP has developed a number of strategies that can assist
**Issues in Evaluation**

- Randomized controlled trial preferred
- Careful selection of appropriate controls
- Minimize or account for contamination
- Blinded outcome assessment
- Skilled, standardized assessors
- Adequate power
- Minimal drop-outs
- Intention to treat analysis

**How to define “effectiveness”?**

- Choose your endpoints carefully
- Delirium: [do not overweight agitation]
  - Shortening duration and/or severity
  - Decrease delirium recurrence
- Not delirium alone:
  - Reduce adverse clinical outcomes (both short- and long-term): LOS, costs, readmission, NH placement, death
  - Return to functional independence
- NB: Large sample size may be needed