Effectiveness of Multicomponent Nonpharmacological Delirium Interventions
A Meta-analysis

Tammy T. Hshieh, MD; Jirong Yue, MD; Esther Oh, MD; Margaret Puelle; Sarah Dowal, MSW, MPH; Thomas Travison, PhD; Sharon K. Inouye, MD, MPH

**IMPORTANCE** Delirium, an acute disorder with high morbidity and mortality, is often preventable through multicomponent nonpharmacological strategies. The efficacy of these strategies for preventing subsequent adverse outcomes has been limited to small studies to date.

**OBJECTIVE** To evaluate available evidence on multicomponent nonpharmacological delirium interventions in reducing incident delirium and preventing poor outcomes associated with delirium.

**DATA SOURCES** PubMed, Google Scholar, ScienceDirect, and the Cochrane Database of Systematic Reviews from January 1, 1999, to December 31, 2013.

**STUDY SELECTION** Studies examining the following outcomes were included: delirium incidence, falls, length of stay, rate of discharge to a long-term care institution (institutionalization), and change in functional or cognitive status.

**DATA EXTRACTION AND SYNTHESIS** Two experienced physician reviewers independently and blindly abstracted data on outcome measures using a standardized approach. The reviewers conducted quality ratings based on the Cochrane risk-of-bias criteria for each study.

**MAIN OUTCOMES AND MEASURES** We identified 14 interventional studies. The results for outcomes of delirium incidence, falls, length of stay, and institutionalization were pooled for the meta-analysis, but heterogeneity limited our meta-analysis of the results for change in functional or cognitive status. Overall, 11 studies demonstrated significant reductions in delirium incidence (odds ratio [OR], 0.47; 95% CI, 0.38-0.58). Four randomized or matched trials reduced delirium incidence by 44% (OR, 0.56; 95% CI, 0.42-0.76). The rate of falls decreased significantly among intervention patients in 4 studies (OR, 0.38; 95% CI, 0.25-0.60); in 2 randomized or matched trials, the rate of falls was reduced by 64% (OR, 0.36; 95% CI, 0.22-0.61). Length of stay and institutionalization also trended toward decreases in the intervention groups, with a mean difference of −0.16 (95% CI, −0.97 to 0.64) day shorter and the odds of institutionalization 5% lower (OR, 0.95; 95% CI, 0.71-1.26). Among higher-quality randomized or matched trials, length of stay trended −0.33 (95% CI, −1.38 to 0.72) day shorter, and the odds of institutionalization trended 6% lower (OR, 0.94; 95% CI, 0.69-1.30).

**CONCLUSIONS AND RELEVANCE** Multicomponent nonpharmacological delirium prevention interventions are effective in reducing delirium incidence and preventing falls, with a trend toward decreasing length of stay and avoiding institutionalization. Given the current focus on prevention of hospital-based complications and improved cost-effectiveness of care, this meta-analysis supports the use of these interventions to advance acute care for older persons.

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Delirium is an acute confusional state marked by inattention and global cognitive dysfunction. It is multifactorial and develops owing to interactions between risk factors and noxious insults. Common yet underdiagnosed, delirium is particularly prevalent among the hospitalized elderly, occurring in 29% to 64%, and contributes to more than $164 billion in health care costs in the United States annually. Delirium significantly increases risk of falls, functional decline, dementia, prolonged hospital length of stay, and institutionalization. The strong correlation between delirium and hospital-related falls has led to calls for delirium prevention quality metrics to improve hospital care and prevent falls in older persons. Most important, at least 30% to 40% of delirium cases are preventable. Surprisingly, most hospitals do not have delirium prevention programs or their protocols are inconsistently implemented, with variable adherence.

Systematic reviews and clinical guidelines have recommended targeted multicomponent nonpharmacological intervention strategies for prevention of delirium (eTable in the Supplement). The Hospital Elder Life Program (HELP) is the original evidence-based approach targeted to delirium risk factors, which is widely known and disseminated. The HELP uses an interdisciplinary team and trained volunteers to implement practical interventions, including reorientation, early mobilization, therapeutic activities, hydration, nutrition, sleep strategies, and hearing and vision adaptations. The HELP has been cost-effective and successful in preventing delirium and functional decline. Studies have evaluated modified HELP models. New multicomponent nonpharmacological delirium interventions have been developed, targeting perioperative patients or using volunteers, family members, and nurses in the delivery of interventions. However, differing outcomes were examined across studies, and a systematic examination of their effectiveness has not been conducted to our knowledge. Most recently, there have been systematic reviews and guidelines, but these statements underscored the limitations of small samples, heterogeneous outcomes, and variable adherence. A need exists for more definitive review to expedite dissemination in practice and spur further research into areas of uncertain outcomes.

Therefore, the primary aims of our study were (1) to perform a systematic review of all studies related to multicomponent nonpharmacological delirium interventions and (2) to conduct a quantitative meta-analysis evaluating the effect of these interventions on important clinical outcomes. Secondary aims were to evaluate whether the quality of studies with respect to risk of bias influenced effectiveness.

Methods

Literature Search

We conducted a comprehensive systematic literature review to identify all studies related to delirium prevention from January 1, 1999, to December 31, 2013. Databases searched included PubMed, Google Scholar, ScienceDirect, and the Cochrane Database of Systematic Reviews. For search terms, we used a combination of keyword terms and specific phrases representing delirium prevention, targeted multicomponent intervention, multicomponent intervention, nonpharmacological intervention, and Hospital Elder Life Program. Review articles were examined for secondary references, and all bibliographies from retrieved articles were screened for other relevant studies. Studies were included in the review if they met the following inclusion criteria: they were original articles, the median or mean age of participants was 65 years or older, they discussed relevant topics given the search terms, they were published in English, and they included human participants. Studies were excluded after full review for the following reasons: they contained no relevant outcome measures, they were study protocols, they used no control groups, they were a cost-effective analysis, or they were qualitative studies, case series, commentaries, reviews, guidelines, or recommendations. Studies involving patients with terminal illness or insufficient data were also excluded. The remaining articles were evaluated and excluded if they failed the following second-level inclusion criteria: (1) they studied multicomponent nonpharmacological delirium interventions, (2) they assessed delirium incidence and not prevalence, and (3) they used a validated delirium instrument for ascertainment (Figure 1).

Study Selection

The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram and checklist. The initial search yielded 2334 articles published between January 1, 1999, and December 31, 2013 (Figure 1). After exclusion based on screening criteria (relevance, language, age range, and nonhuman study), the number of articles was narrowed to 236. More than half of these articles (n = 119) were not interventional studies. Based on this initial screen and augmented by article reference lists, 46 articles were selected for full review by 2 independent clinical reviewers (T.T.H. and J.Y.). Thirty-two articles did not meet second-level inclusion criteria, which required delirium prevention (not treatment), validated delirium assessment methods, and multicomponent nonpharmacological delirium interventions. Therefore, 14 original articles were selected for inclusion in the meta-analysis, encompassing 12 unique intervention trials. The 2 additional studies included addressed different outcomes in other study subgroups. Bogardus et al examined function and cognition after discharge in a subgroup from a study by Inouye et al. Stenvall et al focused on falls among the participants from a study by Lundström et al.

Outcome Measures

Primary outcomes examined in this study were delirium incidence and falls. Incident delirium, defined as new-onset delirium during hospitalization, was measured with validated delirium instruments. Of 14 articles, 12 used the Confusion Assessment Method, and 2 used the Delirium Observation Screening Scale. Falls were defined as the total number per 1000 patient-days, and presented values were recalcualted to adhere to these units.

The secondary outcomes examined in this study included length of stay, rate of discharge to a long-term care institution (institutionalization), and change in functional cog-
The study followed the approaches outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram and checklist, the Meta-analysis of Observational Studies in Epidemiology (MOOSE) consensus statement, and the Cochrane Handbook for Systematic Reviews of Interventions. In total, 2334 articles were found. Of these, 2098 were excluded based on our screening criteria. A further 32 of these did not meet our second-level inclusion criteria. Yielding 46 articles that met our initial screening criteria. On further review, 42 articles were included.

Quality Assessment
We examined the quality of studies included in the meta-analysis using the 6 domains of the Cochrane Collaboration’s tool for assessing risk of bias. These domains included a random or balanced allocation method, allocation concealment, completeness of outcome data, lack of selective outcome reporting, and absence of other sources of bias, as well as blinding of participants, personnel, and outcome assessors.

Data Collection
A standardized data extraction protocol was developed with input from experts in delirium (J.Y. and S.K.I.), multicomponent interventions (J.Y. and S.K.I.), geriatrics (T.T.H., J.Y., E.O., and S.K.I.), and systematic reviews and meta-analysis (J.Y., E.O., and T.T.). Two reviewers (T.T.H. and J.Y.) independently extracted and cross-checked data from all articles, assessing study quality using standard criteria. Two additional reviewers (E.O. and S.K.I.) conducted spot checks to confirm the accuracy of extracted data and resolve any discrepancies.

The 14 articles were abstracted for the reference (primary author and publication year), study characteristics (design, duration, setting, country of study, and number of patients), and patient characteristics (mean age, sex, and type). For each outcome (delirium incidence, falls, length of stay, institutionalization, and change in functional or cognitive status), the reviewers extracted the means (SDs), number of occurrences or total number in the sample, and odds ratios (ORs) or relative risks (95% CIs), as applicable. Finally, quality ratings were conducted as described above. When essential data were not reported, corresponding authors were contacted up to 3 times.

Statistical Analysis
Following standard procedures, we performed a meta-analysis on 14 articles. Intervention trials that used formal methods for balanced allocation between treatment and control arms through randomization or prospective individual matching designs were combined into the group we refer to as randomized or matched trials (RMTs). We considered these trials separately from other interventional studies (non-RMTs) that did not use such rigorous designs. We made the decision to include randomized clinical trials (RCTs) with matched blinded trials because the few RCTs precluded a meta-analysis separately. We also judged that the robust methods and balanced allocation with prospective matching and blinded outcome assessment made some studies of comparable quality to RCTs and combinable without excessive heterogeneity.

For proportions and rates (eg, delirium incidence, falls, and institutionalization), ORs (95% CIs) were estimated according to intent-to-treat principles. For statistically significant effects, we calculated the number needed to treat (NNT) from the risk difference using the inverse of the pooled absolute risk. For continuous data (eg, length of stay and change in functional or cognitive status), the means (SDs) and mean differences were used for outcomes pooled on the same scale (eg, length of stay and Mini-Mental State Examination score), and standardized mean differences were used for outcomes pooled on different scales (eg, various functional status measures).
The study results considered for inclusion in the meta-analysis were assessed for heterogeneity using \( \chi^2 \) statistic Q, with \( P < .10 \) as the threshold indicator for heterogeneity of effects. In addition, \( I^2 \) was used to estimate the proportion of total variation due to heterogeneity across studies. \( I^2 \) values of less than 25% were regarded as low heterogeneity, and fixed-effects models for the meta-analysis were used. \( I^2 \) values of 25% to 75% represented moderate heterogeneity, and a random-effects model was applied. \( I^2 \) values exceeding 75% represented high heterogeneity, and a meta-analysis was not considered appropriate for the interpretation. All statistical analyses for the meta-analysis were performed using Review Manager software (RevMan, version 5.2; The Cochrane Collaboration).

To assess associations between study quality and effectiveness of interventions, we used linear regression analysis to determine at the study level whether there was an association between the continuous Cochrane Collaboration’s risk of bias score (range, 0–6) and the multiplicative increase in odds (ie, OR) of incident delirium with intervention vs control. In addition, we divided studies into lower-quality and higher-quality subgroups based on a Cochrane Collaboration risk of bias score of less than 3 vs 4 or higher and performed an independent meta-analysis of studies falling into each of these 2 categories.

All statistical tests performed were 2-sided. Statistical significance was indicated by \( P < .05 \) or a 95% CI that excluded the null.

## Results

### Study Characteristics

The analytic sample for the present study included 14 articles. Six studies involved RMTs, and 8 studies involved non-RMTs (Table 1). Two nonrandomized trials had high-quality study designs, with prospective individual matching and rigorously blinded outcome assessment.\(^{5,23}\) Among 8 non-RMTs, 3 used nonmatched concurrent controls, and 5 used historical controls. Overall, approximately 4267 patients at 12 sites (acute medical and surgical wards in academic and community hospitals) were involved; their mean age was 79.7 years. All studies involving non-acute care settings were excluded based on our criteria. Of 14 studies, 9 involved HELP adapta-

### Table 1. Characteristics of Studies

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Design</th>
<th>Study Duration, mo</th>
<th>Patient Type or Setting</th>
<th>Mean Patient Age, y</th>
<th>Quality Measures(^a)</th>
<th>Interventions(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andro et al,(^27) 2012 (France)</td>
<td>Historically controlled (non-RMT)</td>
<td>18</td>
<td>Medical (n = 256)</td>
<td>84.7</td>
<td>1/6 (O)</td>
<td>6/6 (C, E, H, V, W)</td>
</tr>
<tr>
<td>Babine et al,(^14) 2013 (United States)</td>
<td>Historically controlled (non-RMT)</td>
<td>3</td>
<td>Medical (n = 516)</td>
<td>≥70.0</td>
<td>1/6 (O)</td>
<td>6/6 (C, E, H, P, V, W)</td>
</tr>
<tr>
<td>Bo et al,(^28) 2009 (Italy)</td>
<td>Nonrandomized clinical trial (non-RMT)</td>
<td>4</td>
<td>Medical (n = 252)</td>
<td>82.4</td>
<td>3/6 (I, O, X)</td>
<td>4/6 (C, E, P, W)</td>
</tr>
<tr>
<td>Bogardus et al,(^23) 2003 (United States)</td>
<td>Nonrandomized clinical trial, matched/blinded (RMT)</td>
<td>36</td>
<td>Medical/geriatric (n = 705)</td>
<td>80.0</td>
<td>5/6 (B, I, O, S, X)</td>
<td>6/6 (C, E, H, P, V, W)</td>
</tr>
<tr>
<td>Caplan and Harper,(^20) 2007 (Australia)</td>
<td>Historically controlled (non-RMT)</td>
<td>5</td>
<td>Medical/geriatric (n = 37)</td>
<td>84.7</td>
<td>3/6 (I, O, S)</td>
<td>4/6 (C, H, V, W)</td>
</tr>
<tr>
<td>Chen et al,(^16) 2011 (Taiwan)</td>
<td>Historically controlled (non-RMT)</td>
<td>20</td>
<td>Surgical (n = 179)</td>
<td>73.0</td>
<td>3/6 (B, I, O)</td>
<td>2/6 (E, C)</td>
</tr>
<tr>
<td>Holt et al,(^29) 2013 (England)</td>
<td>Historically controlled (non-RMT)</td>
<td>12</td>
<td>Medical/geriatric (n = 362)</td>
<td>85.4</td>
<td>4/6 (B, I, O, X)</td>
<td>5/6 (C, E, H, V, W)</td>
</tr>
<tr>
<td>Inouye et al,(^5) 1999 (United States)</td>
<td>Nonrandomized clinical trial, matched/blinded (RMT)</td>
<td>36</td>
<td>Medical (n = 852)</td>
<td>79.7</td>
<td>5/6 (B, I, O, S, X)</td>
<td>6/6 (C, E, H, P, V, W)</td>
</tr>
<tr>
<td>Jeffs et al,(^30) 2013 (Australia)</td>
<td>Randomized clinical trial (RMT)</td>
<td>30</td>
<td>Medical (n = 648)</td>
<td>79.3</td>
<td>6/6 (A, B, I, O, S, X)</td>
<td>2/6 (C, E)</td>
</tr>
<tr>
<td>Kratz,(^31) 2008 (United States)</td>
<td>Nonrandomized clinical trial (non-RMT)</td>
<td>36</td>
<td>Medical/surgical (n = 137)</td>
<td>≥70.0</td>
<td>1/6 (O)</td>
<td>6/6 (C, E, H, P, V, W)</td>
</tr>
<tr>
<td>Lundström et al,(^17) 2007 (Sweden)</td>
<td>Randomized clinical trial (RMT)</td>
<td>32</td>
<td>Surgical (n = 199)</td>
<td>82.2</td>
<td>5/6 (A, I, O, S, X)</td>
<td>1/6 (E)</td>
</tr>
<tr>
<td>Martinez et al,(^32) 2012 (Chile)</td>
<td>Randomized clinical trial (RMT)</td>
<td>9</td>
<td>Medical (n = 287)</td>
<td>78.2</td>
<td>6/6 (A, B, I, O, S, X)</td>
<td>3/6 (C, E, H, V)</td>
</tr>
<tr>
<td>Stenvall et al,(^18) 2007 (United States)</td>
<td>Randomized clinical trial, single-blind (RMT)</td>
<td>32</td>
<td>Surgical (n = 199)</td>
<td>82.2</td>
<td>5/6 (A, B, I, S, X)</td>
<td>3/6 (E, H, P)</td>
</tr>
<tr>
<td>Vidán et al,(^26) 2009 (Spain)</td>
<td>Nonrandomized clinical (non-RMT)</td>
<td>18</td>
<td>Medical/geriatric (n = 542)</td>
<td>84.0</td>
<td>1/6 (O)</td>
<td>6/6 (C, E, H, P, V, W)</td>
</tr>
</tbody>
</table>

Abbreviation: RMT, randomized or matched trial.

\(^a\) Quality measures include the following: allocation concealment (A); blinding of participants, personnel, and outcome assessors (B); completeness of outcome data (B); selective outcome reporting (O); random-sequence generation or balanced allocation (S); and other sources of bias (X).

\(^b\) Evidence-based nonpharmacological interventions include the following: cognition or orientation (C), early mobilization (E), hearing (H), sleep/wake cycle preservation (P), vision (V), and hydration (W).
tions or included at least 4 of 6 evidence-based interventions from HELP (Table 1).

**Delirium Incidence**

Eleven studies measured delirium incidence (Table 2). Overall, the meta-analysis involving 4267 patients showed that the odds of delirium were 53% lower in the intervention group compared with controls (OR, 0.47; 95% CI, 0.38-0.58) (Figure 2). The NNT in the combined sample was 14.3 (95% CI, 11.1-20.0).

Stratified by study type, multicomponent nonpharmacological delirium interventions lowered the odds of delirium by 44% (relative risk, 0.56; 95% CI, 0.42-0.76) among 977 intervention patients included in 4 RMTs and by 63% (OR, 0.37; 95% CI, 0.27-0.53) among 752 intervention patients included in 7 non-RMTs (Table 2 and Figure 1 in the Supplement). The NNTs were 20.0 (95% CI, 12.5-33.3) among RMTs and 11.1 (95% CI, 8.3-16.7) among non-RMTs. Delirium incidence was also stratified by patient type (eFigure 2 in the Supplement).

**Falls**

Four studies examined the number of falls per patient-days (Table 2). Combined, the meta-analysis involving 1038 patients showed that the odds of falling were 62% lower among intervention patients (OR, 0.38; 95% CI, 0.25-0.60) (Table 2 and Figure 2). This outcome represents the equivalent of 4.26 falls prevented per 1000 patient-days or 2.79 falls per 1000 patient-days among intervention patients compared with 7.05 falls per 1000 patient-days among controls.

Stratified by study type, multicomponent nonpharmacological delirium interventions lowered the odds of falling significantly among 245 intervention patients included in 2 RMT studies (OR, 0.36; 95% CI, 0.22-0.61) (Table 2 and eFigure 3 in the Supplement). This outcome represents 8.53 falls prevented per 1000 patient-days or 4.34 falls per 1000 patient-days among intervention patients compared with 12.87 falls per 1000 patient-days among controls. The odds of falling trended lower among 274 intervention patients included in 2 non-RMT studies (OR, 0.46; 95% CI, 0.19-1.10). This outcome represents the equivalent of 2.34 falls prevented per 1000 patient-days or 1.35 falls per 1000 patient-days among intervention patients compared with 3.69 falls per 1000 patient-days among controls.

**Length of Stay**

Nine studies measured length of stay (Table 2). Overall, the meta-analysis involving 3358 patients showed that the mean difference was −0.16 (95% CI, −0.97 to 0.64) day shorter in the intervention group compared with controls (Table 2 and Figure 3). Stratified by study type, multicomponent nonpharmacological delirium interventions decreased length of stay by −0.33 (95% CI, −1.38 to 0.72) day among 977 intervention patients in-

### Table 2. Meta-analysis of the Effect of Multicomponent Nonpharmacological Delirium Interventions

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention</th>
<th>Control</th>
<th>Odds Ratio or Mean Difference (95% CI)</th>
<th>I² Value, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Delirium Incidence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMTs</td>
<td>NA</td>
<td>977</td>
<td>117</td>
<td>1000</td>
</tr>
<tr>
<td>Non-RMTs</td>
<td>46</td>
<td>752</td>
<td>164</td>
<td>1013</td>
</tr>
<tr>
<td>Combined</td>
<td>129</td>
<td>1729</td>
<td>301</td>
<td>2022</td>
</tr>
<tr>
<td><strong>Falls</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMTs</td>
<td>18</td>
<td>245</td>
<td>64</td>
<td>240</td>
</tr>
<tr>
<td>Non-RMTs</td>
<td>6</td>
<td>274</td>
<td>31</td>
<td>279</td>
</tr>
<tr>
<td>Combined</td>
<td>24</td>
<td>519</td>
<td>95</td>
<td>519</td>
</tr>
<tr>
<td><strong>Institutionalization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMTs</td>
<td>101</td>
<td>389</td>
<td>105</td>
<td>388</td>
</tr>
<tr>
<td>Non-RMTs</td>
<td>19</td>
<td>168</td>
<td>27</td>
<td>231</td>
</tr>
<tr>
<td>Combined</td>
<td>120</td>
<td>557</td>
<td>132</td>
<td>619</td>
</tr>
<tr>
<td><strong>Length of Stay</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMTs</td>
<td>NA</td>
<td>977</td>
<td>NA</td>
<td>1009</td>
</tr>
<tr>
<td>Non-RMTs</td>
<td>NA</td>
<td>561</td>
<td>NA</td>
<td>811</td>
</tr>
<tr>
<td>Combined</td>
<td>NA</td>
<td>1538</td>
<td>NA</td>
<td>1820</td>
</tr>
<tr>
<td><strong>Change in Functional Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMTs</td>
<td>NA</td>
<td>426</td>
<td>NA</td>
<td>426</td>
</tr>
<tr>
<td>Non-RMTs</td>
<td>NA</td>
<td>118</td>
<td>NA</td>
<td>98</td>
</tr>
<tr>
<td>Combined</td>
<td>NA</td>
<td>544</td>
<td>NA</td>
<td>524</td>
</tr>
<tr>
<td><strong>Change in Cognitive Status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMTs</td>
<td>NA</td>
<td>426</td>
<td>NA</td>
<td>426</td>
</tr>
<tr>
<td>Non-RMTs</td>
<td>NA</td>
<td>188</td>
<td>NA</td>
<td>470</td>
</tr>
<tr>
<td>Combined</td>
<td>NA</td>
<td>714</td>
<td>NA</td>
<td>896</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; RMT, randomized or matched trials.
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studies. Combined, the standard mean difference for functional status was 0.01 (95% CI, 0.25-2.51) in favor of targeted interventions, but the results did not achieve statistical significance (Table 2).

Four studies examined institutionalization after hospital discharge (Table 2). Overall, the meta-analysis involving 176 patients showed that the odds of discharge to long-term care were 5% lower (OR, 0.95; 95% CI, 0.71-1.26) in the intervention group, but the results did not achieve statistical significance (Table 2 and Figure 3).

Stratified by study type, the trends are consistent, with an OR for institutionalization among 389 intervention patients in 2 RMTs of 0.94 (95% CI, 0.69-1.30) in favor of multicomponent nonpharmacological delirium interventions, but the results were not statistically significant (Table 2 and eFigure 6 in the Supplement). The OR for institutionalization among 168 patients involved in 2 non-RMTs was 0.79 (95% CI, 0.25-2.51) in favor of targeted interventions, but the results did not achieve statistical significance.

Four studies measured change in functional status, including 1 high-quality RMT and 3 non-RMTs (Table 2). Random-effects models were used owing to high heterogeneity of these studies. Combined, the standard mean difference for functional status was 0.01 (95% CI, 0.25-2.51) in favor of targeted interventions, but the results did not achieve statistical significance (Table 2).

Eleven studies measured delirium incidence. Three randomized or matched trials and 5 non-randomized or matched trials demonstrated significant reductions in delirium incidence. P < .001, and heterogeneity was low at $I^2 = 18%$. Weighting was assigned according to the inverse of the variance. Odds ratios less than 1 indicate decreased delirium incidence. Four studies examined the number of falls per patient-days. Individually, only Stenwall et al24 (a randomized or matched trial) demonstrated significant reduction in the number of falls. $P < .001$, and heterogeneity was low at $I^2 = 0%$. Weighting was assigned according to the inverse of the variance. Odds ratios less than 1 indicate decreased rate of falls. NNT indicates the number needed to treat.

Four studies examined institutionalization after hospital discharge (Table 2). Overall, the meta-analysis involving 176 patients showed that the odds of discharge to long-term care were 5% lower (OR, 0.95; 95% CI, 0.71-1.26) in the intervention group, but the results did not achieve statistical significance (Table 2 and Figure 3).

Stratified by study type, the trends are consistent, with an OR for institutionalization among 389 intervention patients in 2 RMTs of 0.94 (95% CI, 0.69-1.30) in favor of multicomponent nonpharmacological delirium interventions, but the results were not statistically significant (Table 2 and eFigure 6 in the Supplement). The OR for institutionalization among 168 patients involved in 2 non-RMTs was 0.79 (95% CI, 0.25-2.51) in favor of targeted interventions, but the results did not achieve statistical significance.

Four studies measured change in functional status, including 1 high-quality RMT and 3 non-RMTs (Table 2). Random-effects models were used owing to high heterogeneity of these studies. Combined, the standard mean difference for functional status was 0.01 (95% CI, 0.25-2.51) in favor of targeted interventions, but the results did not achieve statistical significance (Table 2 and Figure 3).

Eleven studies measured delirium incidence. Three randomized or matched trials and 5 non-randomized or matched trials demonstrated significant reductions in delirium incidence. P < .001, and heterogeneity was low at $I^2 = 18%$. Weighting was assigned according to the inverse of the variance. Odds ratios less than 1 indicate decreased delirium incidence. Four studies examined the number of falls per patient-days. Individually, only Stenwall et al24 (a randomized or matched trial) demonstrated significant reduction in the number of falls. $P < .001$, and heterogeneity was low at $I^2 = 0%$. Weighting was assigned according to the inverse of the variance. Odds ratios less than 1 indicate decreased rate of falls. NNT indicates the number needed to treat.

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cost savings of approximately $10,000 per case prevented or institutionalized, with greater than 60% odds reduction (OR, 0.38; 95% CI, 0.38-0.58). In 2008, there were 13.2 million hospital discharges of older patients in the United States, with a mean hospital stay of 5.5 days. Based on our results, preventing falls per 1000 patient-days, 326,996 falls can be prevented annually with these interventions. This finding translates into an additional $4.5 billion to $6.7 billion Medicare savings annually from preventable falls. Few intervention strategies have proved effective for fall prevention in the hospital. Most fall interventions have focused on identifying fall risk and implementing various alarms that limit patient mobility. Although minimally effective for preventing falls, these approaches result in unintended consequences of decreased physical and cognitive functioning. Notably, 12 of 14 studies examined in this meta-analysis included exercise interventions designed to enhance mobility. The well-documented effectiveness of these strategies for fall prevention is worthy of special emphasis.

While a trend toward benefit existed, the lack of significant association between delirium interventions and length of stay and institutionalization is not surprising given multiple complex influences on these outcomes, including multimorbidity and psychosocial factors (supports, finances, and caregiver preferences), all of which make the ultimate disposition unpredictable. Furthermore, because sample sizes were small, our meta-analysis may have been underpowered to detect true differences.

The few studies examining functional and cognitive decline, as well as their substantial heterogeneity, limited our ability to examine these outcomes. In addition, the preferred outcome with delirium prevention should be functional and quality studies compared with 0.38 (95% CI, 0.23-0.64) among lower-quality studies ($P = .28). When examining whether higher quality yielded better outcomes for falls, length of stay, and institutionalization, the subgroup differences were also not statistically significant (95% CI, 0.38-0.58). In 2008, there were 13.2 million hospital discharges of older patients in the United States, with a mean hospital stay of 5.5 days. Based on our results, approximately 1 million cases of delirium in the hospital could have been prevented by multicomponent nonpharmacological interventions each year, resulting in Medicare cost savings of approximately $10,000 per case prevented or $10 billion per year.1,2

The effect on fall prevention is a novel and important finding, with greater than 60% odds reduction (OR, 0.38; 95% CI, 0.25-0.60). Because delirium is the leading contributor to hospital falls,1,3 prevention of falls with these interventions is a consistent and compelling result. Furthermore, given their status as Medicare no-pay conditions, fall prevention has become a top priority among US hospitals. If 4.26 falls can be avoided with multicomponent nonpharmacological delirium interventions per 1000 patient-days, 326,996 falls can be prevented annually with these interventions. This finding translates into an additional $4.5 billion to $6.7 billion Medicare savings annually from preventable falls. Few intervention strategies have proved effective for fall prevention in the hospital. Most fall interventions have focused on identifying fall risk and implementing various alarms that limit patient mobility. Although minimally effective for preventing falls, these approaches result in unintended consequences of decreased physical and cognitive functioning. Notably, 12 of 14 studies examined in this meta-analysis included exercise interventions designed to enhance mobility. The well-documented effectiveness of these strategies for fall prevention is worthy of special emphasis.

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The few studies examining functional and cognitive decline, as well as their substantial heterogeneity, limited our ability to examine these outcomes. In addition, the preferred outcome with delirium prevention should be functional and
cognitive stability (ie, maintenance) and not improvement or decline. Only 1 study examined function and cognition at admission and 6 months after discharge. Performing cognitive and functional reassessments at the time of discharge when patients may still be delirious and acutely deconditioned is suboptimal, and waiting until they have returned to a stable condition should be the preferred approach.

Our study has several noteworthy strengths. The meta-analysis allowed us to extend conclusions beyond populations contained in a single study, particularly given the variable and limited number of studies and the small study sizes available for review. We used a comprehensive search strategy and systematic review method. With more than 4200 study participants in the pooled analyses, there was improved power for a meta-analysis of the study results. We limited heterogeneity and rigorously controlled for potential sources of bias by adhering to clear, predetermined selection criteria and evaluating the quality of our selected studies based on the Cochrane risk-of-bias guidelines. Our stratified models for delirium incidence, falls, and institutionalization confirmed that observed outcome associations were robust across study designs. Heterogeneity analysis allowed us to account for study factors that could be influencing our outcomes of interest across multiple trials. The use of quality ratings facilitated our evaluation of the studies; however, quality scores did not correlate significantly with effectiveness.

Several limitations of our study are worthy of comment. The final number of included studies is small, and many of them had limited sample sizes. Less than one-third of the interventions evaluated were RCTs (29% [4 of 14]), the criterion standard for evidence-based practice. Blinding was difficult to achieve in nonpharmacological intervention studies by the unitwide nature of many interventions. Therefore, data available for synthesis may have been limited, restricting the strength of our conclusions. In particular, there were only 4 studies examining the outcome of falls, 2 of which were historically controlled studies with smaller sample sizes. Most important, selective reporting bias in the literature would have decreased our overall effect on falls. Despite similarities in research questions and interventions across studies, there remained a moderate degree of heterogeneity for all studies examining length of stay and change in functional or cognitive status and for non-RMTs examining institutionalization. This heterogeneity, which likely stems from variations in study designs, sample characteristics, sample sizes, and outcome measures used, limits the interpretation of our pooled estimates. Despite these limitations, the findings of this meta-analysis are highly clinically relevant for the hospitalized geriatric population.

A few studies were not included in our meta-analysis despite their being well designed and influential in the field of delirium prevention. These articles were excluded based on our predetermined inclusion criteria. Studies by Marcantonio et al and Milisen et al were excluded because they primarily involved consultation for preventive management of delirium and not multicomponent nonpharmacological delirium interventions. Cole et al, Naughton et al, and Zaubler et al published work on effective multicomponent nonpharmacological interventions but included patients with delirium in their studies. Therefore, these were not considered primary prevention studies because incident delirium rates could not be calculated.

Conclusions

In conclusion, this meta-analysis suggests that multicomponent nonpharmacological interventions are effective in decreasing delirium incidence and preventing falls, potentially saving more than $16 billion annually in the United States alone. Therefore, these strategies hold great promise to influence the most important and prevalent conditions affecting seniors during hospitalization. Our systematic review and meta-analysis demonstrate that these interventions decrease the substantial health care and societal burden of delirium incidence and falls, improving quality of life for these patients and their families.

**REFERENCES**


