ONTOP: Can Non-Pharmacological Interventions be recommended to prevent or reduce critical outcomes in older subjects?

Antonio Cherubini
IRCCS-INRCA, Ancona (Italy)
CONFLICT OF INTEREST DISCLOSURE

I have no potential conflict of interest to report
Workpackage2 ONTOP

General Information

• Start month 1
• End month 54
• Lead Institution: IRCCS-INRCA

Institutions involved

• IRCCS-INRCA (IstitutoNazionale di Riposo e Cura per Anziani)
• ABDN (University of Aberdeen)
• Hospital Universitario Ramóny Cajal/SERMAS
Non pharmacological therapies, i.e. exercise, physiotherapy, occupational therapy, speech & language therapy, nutritional therapy, psychological therapy can be as or more effective than drug therapy in the treatment of several chronic conditions. Drug therapy and non-drug therapies are complementary in the management of older people with multimorbidity. To date, there is no widely used compendium of non-pharmacological therapies for the common chronic medical conditions of late life and this might represent an important reason why they are underappreciated and underused in clinical practice.
Objectives of the WP2-ONTOP

• To undertake a thorough literature search of systematic reviews concerning non-pharmacological treatments of 15 prevalent medical conditions affecting older people.

• To define in bullet-point format indications and contraindications of non-pharmacological therapies for which there is the strongest evidence base in each of the 15 chronic conditions.
Progress: 15 Conditions of interest

- Delirium
- Falls
- Pressure Sores
- Urinary Incontinence
- Dementia
- Frailty/Sarcopenia
- Heart Failure
- Stroke
- Orthostatic Hypotension
- Malnutrition
- Arthritis
- Vision Impairment
- Hearing Impairment
- COPD
- Diabetes
Evidence of and recommendations for non-pharmacological interventions for common geriatric conditions: the SENATOR-ONTOP systematic review protocol

Abraha I., BMJ Open, 2015

Methods and analysis: The conditions of interest for which the evidence about efficacy of nonpharmacological interventions will be searched include delirium, falls, pressure sores, urinary incontinence, dementia, heart failure, orthostatic hypotension, sarcopaenia and stroke. For each condition, the following steps will be undertaken: (A) prioritising clinical questions; (B) retrieving the evidence (MEDLINE, the Cochrane Library, CINAHL and PsychINFO will be searched to identify systematic reviews); (C) assessing the methodological quality of the evidence (risk of bias according to the Cochrane method will be applied to the primary studies retrieved from the systematic reviews); (D) developing recommendations based on the evidence (Grading of Recommendations Assessment, Development and Evaluation (GRADE) items—risk of bias, imprecision, inconsistency, indirectness and publication bias—will be used to rate the overall evidence and develop recommendations).
Tasks 1-4

• **Task 1**: Formulation and prioritization of the clinical questions:
  → setting up a multidisciplinary panel;
  → to formulate and to prioritize answerable clinical questions (PICO methodology)

• **Task 2**: Compiling evidence
  → perform specific training for research team
  → develop high sensitive search strategy
  → identify and to assess full text of SR
  → identify and to assess full text of primary studies

• **Task 3**: Quality assessment & synthesis of primary studies for recommendation (GRADE approach)

• **Task 4**: Preparation of user friendly summary of indications and contraindications for use in SENATOR RCT
**Systematic review**

- Formulate question
- Select outcomes
- Rate importance
- Outcomes across studies
- Create evidence profile with GRADEpro
- Rate quality of evidence for each outcome

**Guideline development**

- **Formulate recommendations:**
  - For or against (direction)
  - Strong or conditional/weak (strength)

  **By considering:**
  - Quality of evidence
  - Balance benefits/harms
  - Values and preferences

- Revise if necessary by considering:
  - Resource use (cost)

- **Grade overall quality of evidence across outcomes based on lowest quality of critical outcomes**

  - “We recommend using...”
  - “We suggest using...”
  - “We recommend against using...”
  - “We suggest against using...”

**Randomization increases initial quality**

1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias

**Summary of findings & estimate of effect for each outcome**
DELIRIUM
The outcomes that guided recommendation for the PREVENTION of delirium are:

- **Critical outcome:** delirium incidence
- **Important outcomes:**
  - delirium severity,
  - duration of delirium
  - functional decline
  - length of hospital stay
  - quality of life
  - nursing home admission
  - psychotropic drug use
The outcomes that guided recommendation for the TREATMENT of delirium are:

• **Critical outcomes:**
  ▪ worsening of functional status
  ▪ complete remission *(added by the panel)*

• **Important outcomes:**
  ▪ duration of delirium
  ▪ severity of delirium
  ▪ psychotropic drug use
  ▪ death
  ▪ incidence of behavioural
  ▪ worsening of cognitive status
  ▪ length of hospital stay
  ▪ quality of life
  ▪ nursing home admission
  ▪ cost of intervention
Criteria for the SR selection

1. the use of at least one medical literature database;
2. the inclusion of at least one primary study; and
3. the use of at least one non-pharmacological intervention for delirium prevention or treatment for patients of 60+ years of age.
Potentially relevant reviews identified: 3329
Medline (Pubmed): 657
Embase: 2525
The Cochrane Library: 160
DARE: 73
PsycInfo (OVID): 67
CINAHL (EBSCO): 142

Reviews excluded based on title/abstract evaluation: 3249

Reviews identified for full-text evaluation: 80

Reviews excluded with reason: 54

Systematic review/meta-analysis included: 26

Primary studies evaluated for inclusion: 78

Primary studies excluded with reason: 47

Primary studies identified from SR/meta-analysis: 31
Prevention
Identification of non pharmacological interventions

• Single component intervention, e.g. Bright Light therapy, era plugs, staff education, music therapy...

• Multiple component intervention
Clinical questions: delirium prevention
Multicomponent intervention

• Should multicomponent non-pharmacological interventions be used to prevent delirium in older patients receiving urgent surgical treatment?

• Should a multicomponent non-pharmacological intervention performed by families be recommended to prevent delirium in older patients hospitalised in medical departments?

• Should a multicomponent non-pharmacological intervention performed by a trained interdisciplinary team be recommended to prevent delirium in older patients hospitalised in medical departments?
Multicomponent intervention

Surgical setting

2 RCTs (Lundstrom 2007; Marcantonio 2001)

1 CCT (Deschodt 2012)

<table>
<thead>
<tr>
<th>Author</th>
<th>Type of study</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome</th>
<th>Study period</th>
<th>Setting</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lundstrom 2007</td>
<td>Randomized trial</td>
<td>199 patients with femoral neck fracture aged 70+ (mean age 82), 74% women</td>
<td>Staff education (focusing on the assessment, prevention and treatment of delirium and associated complication): application of comprehensive geriatric assessment, management and rehabilitation</td>
<td>Primary: number of days of post-operative delirium. Secondary: complications during hospitalization, length of stay, and in-hospital and one-year mortality.</td>
<td>May 2000 and December 2002</td>
<td>A specialized geriatric ward or a conventional orthopedic ward</td>
<td>Government, not for-profit</td>
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<tr>
<td>Marcantonio 2001</td>
<td>Randomized trial</td>
<td>86 patients 65+ admitted emergently for surgical repair of hip fracture (mean age 79), 79% women</td>
<td>Proactive geriatrics consultation</td>
<td>Primary: delirium incidence (DSI, (MDAS) (CAM) MMSE) Secondary outcomes: delirium severity (MDAS, CAM), cognitive status (MMSE), length of stay, nursing home discharge</td>
<td>not reported</td>
<td>Orthopedic dept.</td>
<td>Private non-profit</td>
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<tr>
<td>Deschodt 2012</td>
<td>Controlled clinical trial</td>
<td>171 people with hip fracture aged 65 and older; female 65%</td>
<td>inpatient geriatric consultation teams</td>
<td>Incidence and duration of delirium (CAM), severity of delirium (Delirium Index), and cognitive status (MMSE)</td>
<td>unclear</td>
<td>Two trauma wards</td>
<td>None</td>
</tr>
<tr>
<td>Björkelund 2010</td>
<td>Before/after study</td>
<td>263 patients with hip fracture, age ≥65 years; female 70%</td>
<td>Multifactorial intervention (supplemental oxygen, hydration, nutrition, monitoring of vital physiological parameters, adequate pain relief, avoid delay in transfer logistics, daily delirium screening using OBS scale, avoid polypharmacy, and perioperative/anesthetic period protocol)</td>
<td>Delirium incidence (SPMSQ; OBS scale)</td>
<td>April 2003 - April 2004</td>
<td>Orthopedic ward</td>
<td>Government</td>
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<tr>
<td>Chen</td>
<td>Before/after study</td>
<td>256 patients (mean age 71, female 46%) undergoing elective abdominal surgery (e.g. gastrectomy).</td>
<td>The intervention (modified Hospital Elder Life Program): daily hospital-based care protocol, which included 3 key protocols, i.e., early mobilization, nutritional assistance, and therapeutic (cognitive) activities 3 times daily.</td>
<td>Primary: functional and nutritional status, cognitive function. Secondary: depressive symptoms, cognitive function, and delirium (CAM)</td>
<td>August 2007 - April 2009</td>
<td>Gastrointestinal ward</td>
<td>Government, not for-profit.</td>
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<td>Milisen 2001</td>
<td>Before/aft er study</td>
<td>120 patients with a traumatic fracture of proximal femur, median age 81, 80% females.</td>
<td>Education of nursing staff, systematic cognitive screening, consultative services, use of a scheduled pain protocol</td>
<td>Delirium incidence (CAM); severity of delirium; cognitive and functional status (MMSE).</td>
<td>Unclear</td>
<td>Emergency room and 2 traumatological units</td>
<td>Private for profit/Go vernment</td>
</tr>
<tr>
<td>Wong 2005</td>
<td>Before/aft er study</td>
<td>99 patients with hip fracture, average age 82 years, female 78%</td>
<td>Ten strategies protocol (oxygen delivery, nutrition and hydration, minimizing medications, regulation of bladder/bowel function, early mobilization, prevention and treatment of major peri- and post-operative complications.</td>
<td>Major outcomes: proportions of subjects with delirium (CAM), discharge destination and length of stay.</td>
<td>15 August and 24 December 2001</td>
<td>Surgical orthopedic setting</td>
<td>Not reported</td>
</tr>
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<tr>
<td>Williams 1985</td>
<td>Before-after study</td>
<td>227 patients, mean age 79 years, female 82%</td>
<td>Preventing approaches related to: strange environment, altered sensory input, loss of control and independence, disruption in life pattern, immobility and pain, and disruption in elimination pattern. Ameliorative approaches related to: mild behaviors suggestive of confusion, sundowning, unsafe behavior, hallucinations or illusions, and fright.</td>
<td>Incidence of delirium or acute confusion identified using a score based on 4 types of behaviors.</td>
<td>unclear</td>
<td>Surgical orthopedic setting</td>
<td>Government, not for-profit.</td>
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</table>
Prevention. Multicomponent intervention (surgery) – incidence of delirium: GRADE

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Non-pharmacological</th>
<th>Usual care</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
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<tr>
<td>Lundstrom 2007</td>
<td>56</td>
<td>102</td>
<td>73</td>
<td>97</td>
</tr>
<tr>
<td>Marcantonio 2001</td>
<td>20</td>
<td>62</td>
<td>32</td>
<td>64</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>76</td>
<td>164</td>
<td>161</td>
<td>100.0%</td>
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</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 1 (P = 0.62); I² = 0%
Test for overall effect: Z = 3.51 (P = 0.0004)

GRADE

- RISK OF BIAS: -1
- INCONSISTENCY: no
- INDIRECTNESS: no
- IMPRECISION: no

→ From High quality (RCT) to MODERATE quality of evidence
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<td></td>
<td>Events</td>
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<tr>
<td><strong>5.9.1 Randomised trials</strong></td>
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<td>Lundstrom 2007</td>
<td>56</td>
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<td>Marcantonio 2001</td>
<td>20</td>
<td>62</td>
<td>32</td>
<td>64</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>164</td>
<td>161</td>
<td>161</td>
<td>75.9%</td>
</tr>
<tr>
<td>Total events</td>
<td>76</td>
<td>105</td>
<td></td>
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<td>Heterogeneity: Tau² = 0.00; Chi² = 0.25, df = 1 (P = 0.62); I² = 0%</td>
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<td>Test for overall effect: Z = 3.51 (P = 0.0004)</td>
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<tr>
<td><strong>5.9.2 Controlled clinical trial</strong></td>
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<tr>
<td>Deschodt 2012</td>
<td>35</td>
<td>94</td>
<td>41</td>
<td>77</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>94</td>
<td>77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>35</td>
<td>41</td>
<td></td>
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<tr>
<td>Heterogeneity: Not applicable</td>
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<tr>
<td>Test for overall effect: Z = 2.09 (P = 0.04)</td>
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<tr>
<td>Total (95% CI)</td>
<td>258</td>
<td>238</td>
<td></td>
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<tr>
<td>Total events</td>
<td>111</td>
<td>146</td>
<td></td>
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<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 2 (P = 0.88); I² = 0%</td>
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<tr>
<td>Test for overall effect: Z = 4.08 (P &lt; 0.0001)</td>
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<tr>
<td>Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0%</td>
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</tbody>
</table>
Recommendation

In patients aged ≥ 65 years, subjected to emergency surgery, a non pharmacological multicomponent interventions to prevent delirium is recommended (strong recommendation/moderate quality of evidence).

Abraha I., PLoS One. 2015
Abraha I., J Nutr Health Aging. 2016
Limitations of the study

I. The arbitrary age cut-off that may limit the applicability of the evidence from the present overview to patients with less than 60 years of age;

II. The studies examined were heterogeneous in terms of intervention, study design, population, outcome and instrument assessment;

III. The lack of assessment of cost-effectiveness.

Abraha I., PLoS One. 2015
Limitations

I. Primary studies were generally of limited sample size; there was substantial variation in the characteristics of the intervention and the authors of primary studies used different conceptual frameworks, and sometimes broad, and quite generic descriptions, of the interventions.

II. The heterogeneity of the types and characteristics of the interventions, even within the same class of non-pharmacological interventions, was the most significant problem.

III. In some studies, the description of the interventions was too vague to allow a complete understanding of what was actually performed. In addition, even in cases in which the intervention is well characterized, the dosage of the intervention, and the means used for its delivery, varied considerably.

IV. The variation in the characteristics of the interventions was particularly pronounced in the trials ascribed to behavioural management techniques.

Abraha I., BMJ Open, 2017
Recommendations for the SENATOR software
Recommendations
Surgery prevention (1)

Target patients: patients aged ≥ 65 years admitted to a surgical ward for an urgent intervention.

→ The non-pharmacological intervention to prevent delirium should be multicomponent and include at least the following components:

Ambulate early
• a) Get the patient out of bed on postoperative day 1 and for several hours each day
• b) Administer physical therapy daily; administer occupational therapy, as needed

Oxygenate
• a) Supplement oxygen to maintain blood oxygen saturation >90%, preferably >95% (with caution in patients with COPD)
• b) Correct systolic blood pressure to a level of >2/3 of baseline or >90 mmHg
Recommendations
Surgery prevention (2)

Hydrate and feed
• a) Restore serum sodium, potassium and glucose to normal levels
• b) Treat dehydration or fluid overload
• c) Ask the patient to use dentures and position him/her properly for meals
• d) If the patient is unable to eat, consider other means of feeding

Control pain
• a) Follow national, local or hospital guidelines for the treatment of pain
• d) Assess the underlying causes of the pain
Recommendations
Surgery prevention (3)

Regulate bladder and bowel function
• a) Check for bowel movement by postoperative day 2 and every 48 hours afterwards
• b) Actively prevent and treat constipation
• c) Remove urinary catheter by postoperative day 2 and screen for retention or incontinence afterwards
• d) Employ a skin care program for patients with established incontinence
Recommendations
Surgery prevention (4)

Prevent, detect early, and treat major postoperative complications

a) For suspected myocardial infarction/ischemia, perform an electrocardiogram and analyze cardiac enzymes
b) For supraventricular arrhythmias/atrial fibrillation, ensure appropriate ventricular rate control, balanced electrolytes, and administer anticoagulants in cases of persistent atrial fibrillation.
c) Prevent pulmonary embolus with appropriate doses of prophylactic anticoagulants
d) For pneumonia/chronic obstructive pulmonary disease, screen and treat as needed
e) Screen for and treat urinary tract infection
f) Transfuse blood if hemoglobin levels are <8 g/dl.
Senator ONTOP Publications


Senator ONTOP Publications


Senator ONTOP Publications


Conclusions

• Non pharmacological interventions can be as effective or more effective than drugs
• The heterogeneity of the methodology and quality of non pharmacological studies is a significant obstacle to their synthesis, dissemination and implementation in clinical practice
• An improvement in the methodological quality of studies is necessary to advance this area
The ONTOP Group members

- Abraha I,
- Rimland JM,
- Dell'Aquila G,
- Trotta F
- Pierini V,
- Carrieri B,
- Cruz-Jentoft AJ
- Soiza R,
- Gudmusson A,
- Petrovic M,
- O'Mahony D,
- Lozano-Montoya I,
- Vélez-Díaz-Pallarés M,
- Montero-Errasquín B,
- Correa-Pérez A,
Acknowledgment

Other Delphi panel members: Hubert Blain, Karen Andersen Ranberg, Regina Roller-Wirnsberger, Fabio Salvi, Andrea Corsonello, Adalsteinn Gudmundsson, Akner Gunnar, Mirko Petrovic.

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