
- Objectives:
  - analyze the efficacy, safety, and comparative effectiveness of drugs for **clinically important patient-centered outcomes**, including continence and quality of life;
  - analyze **long-term adherence** to drug treatments;
  - analyze **which characteristics** of women, including demographic characteristics, comorbid conditions, and type and severity of UI, **can modify treatment**
Only urgency UI in community-dwelling women

“Clinically important” outcomes:
- 50% reduction in UI frequency
- Clinically important threshold change in QOL on validated scales
- All self-reported adverse effects irrespective of authors conclusions about causality
- Broad definition of adverse effects and harms

AMSTAR 11
• 94 RCTs included
• 80% women, most with daily urgency incontinence
• ~34,000 patients
• Drugs always compared to placebo or another drug, not to non-surgical management options (ie pelvic floor exercises, biofeedback, etc.)
Figure 1. Continence with drugs for urgency urinary incontinence (pooled with random effects from randomized, controlled trials).

<table>
<thead>
<tr>
<th>Drug (Randomized Trials/Participants, N/n)</th>
<th>Attributable Events per 1000 Treated (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td></td>
</tr>
<tr>
<td>Fesoterodine (2/2465)</td>
<td>130.00 (58.00 to 202.00)</td>
</tr>
<tr>
<td>Oxybutynin (4/992)</td>
<td>114.00 (64.00 to 163.00)</td>
</tr>
<tr>
<td>Solifenacin (5/6304)</td>
<td>107.00 (58.00 to 156.00)</td>
</tr>
<tr>
<td>Tolterodine (4/3404)</td>
<td>85.00 (40.00 to 129.00)</td>
</tr>
<tr>
<td>Trospium (4/2677)</td>
<td>114.00 (83.00 to 144.00)</td>
</tr>
<tr>
<td>Comparative effectiveness</td>
<td></td>
</tr>
<tr>
<td>Fesoterodine vs. tolterodine (2/3312)</td>
<td>55.00 (21.00 to 88.00)</td>
</tr>
</tbody>
</table>
Figure 2. Treatment discontinuation due to adverse effects from drugs for urgency urinary incontinence (pooled results from randomized, controlled trials by using rate arcsine transformation).

<table>
<thead>
<tr>
<th>Drug (Randomized Trials/Participants, N/n)</th>
<th>Attributable Events per 1000 Treated (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety</td>
<td></td>
</tr>
<tr>
<td>Darifenacin (7/3138)</td>
<td>4.00 (−12.00 to 23.00)</td>
</tr>
<tr>
<td>Fesoterodine (4/4433)</td>
<td>31.00 (10.00 to 56.00)</td>
</tr>
<tr>
<td>Oxybutynin (5/1483)</td>
<td>63.00 (12.00 to 127.00)</td>
</tr>
<tr>
<td>Solifenacin (7/9080)</td>
<td>13.00 (1.00 to 26.00)</td>
</tr>
<tr>
<td>Tolterodine (10/4466)</td>
<td>5.00 (−11.00 to 26.00)</td>
</tr>
<tr>
<td>Trospium (6/3936)</td>
<td>18.00 (4.00 to 33.00)</td>
</tr>
<tr>
<td>Comparative safety</td>
<td></td>
</tr>
<tr>
<td>Fesoterodine vs. tolterodine (4/4440)</td>
<td>17.00 (5.00 to 31.00)</td>
</tr>
<tr>
<td>Oxybutynin vs. tolterodine (6/2323)</td>
<td>72.00 (7.00 to 154.00)</td>
</tr>
<tr>
<td>Solifenacin vs. tolterodine (3/2755)</td>
<td>12.00 (−1.00 to 28.00)</td>
</tr>
<tr>
<td>Trospium vs. oxybutynin (2/2015)</td>
<td>1.00 (−32.00 to 48.00)</td>
</tr>
</tbody>
</table>

Favors Active Treatment: −50 |
Favors Control Treatment: 150
See “Table 2 – Conclusions about Pharmacologic Management of UI in Women”

• **Issues:**
  – Trials all very short (2-3 months)
  – Very few include older women, or focus on elder (6)
  – Adverse effects more common in patients taking 7 or more medications
Bottom Line:

• Community-dwelling patients with urgency UI
• All drugs for UI have similar small effect size (less than 200 continent patients per 1000 treated) on clinically important outcomes compared to placebo

BUT

• Adherence rates are low, discontinuation common and adverse effects higher in persons taking 7 or more medications. Long term safety not known.

- Meta-analysis to:
  
  *examine the long-term efficacy and safety of the new oral anticoagulants compared to warfarin in preventing stroke and systemic embolism in patients with atrial fibrillation (AF)*
• n=3 RCTs included (apixaban, rivaroxaban and dabigatran)
• 44,563 patients
• Mean age 70-73 +/- 8 years
• CHADS scores equally distributed in 2 studies, third had almost 90% of patients CHDS 3-6
• Follow-up averaged ~ 2 years
• AMSTAR 10
Figure 2. Forest plot for (A) all-cause stroke and systemic embolism, (B) ischemic and unspecified stroke, and (C) hemorrhagic stroke, new oral anticoagulants (NOA) versus warfarin in patients with AF.
Figure 3. Forest plot for (A) major bleeding, (B) intracranial bleeding, and (C) gastrointestinal bleeding, new oral anticoagulants (NOA) versus warfarin in patients with AF.
Bottom Line:

• In patients with atrial fibrillation, new oral anticoagulants reduced the risk for any stroke or systemic embolism compared to warfarin, and showed a trend towards better secondary outcomes including ischemic stroke, hemorrhagic stroke.

• Inconclusive with respect to major or GI bleeding, but showed lower risk of intracranial bleeding.

• Supports the use of new oral anticoagulants as an alternative to warfarin as long term anticoagulation in AF.

“Does the relationship between elevated BP and mortality vary by objectively measured walking speed among a nationally representative sample of elderly adults?”. 
• Data subset from NHANES study, 1999-2000 and 2001-2002
• 2438 elders age 65 and older who completed a questionnaire and exam
• 3-4 BP measurements and 6 m walk test (if they could walk independently)
• Slow walkers = <0.8 m/sec
Figure 2. Sensitivity analyses of the association of elevated systolic blood pressure (SBP) (≥140 mm Hg) and mortality, stratified by walking speed, in National Health and Nutrition Examination Survey participants 65 years and older (1999-2002), followed up until December 31, 2006.
Bottom Line:

• Higher SBP (>140 mm Hg) associated with increased risk of mortality amongst older adults with medium to fast walk speed

• No association between SBP or DBP (>90 mm Hg) and mortality amongst slower walking adults

• Amongst those who could not complete the walk test, increased SBP and DBP was strongly and independently associated with lower risk of dying

• Gait speed as a vital sign in the elderly?
Martinez FT, et al. **Preventing delirium in an acute hospital using a non-pharmacological intervention.** Age and Ageing 2012; 41: 629–634

“Whether a non-pharmacological intervention delivered by family members could reduce the incidence of delirium, as compared with standard management of elderly inpatients at intermediate or high risk of developing this condition during the course of hospitalization”
• Single-blind RCT
• Included all adults admitted to general medicine ward in hospital over a 10 month period who were at risk of delirium:
  – >70 years
  – Hx of cognitive impairment with MMSE <24 at baseline
  – Alcoholism
  – “metabolic disturbances” on admission
• Excluded those with delirium on admission, no family, not on GIM, in a room with >2 patients
• Intervention:
  – 10 minute education of family members plus pamphlet covering features and prognosis of acute confusion
  – Clock and calendar in room
  – Avoidance of sensory deprivation
  – Presence of familiar objects in room (photos, cushions, radio)
  – Reorientation of patients by family members (date, time recent events)
  – Extended family visiting (5 h per day)

• Outcome: CAM positive or negative
• 1285 potential patients, 287 randomized
Results:
- Mean age 78 +/- 6 years
- 60% male

### Table 2. Study outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control group (n = 143)</th>
<th>Intervention group (n = 144)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident delirium, no. (%)</td>
<td>19 (13.3)</td>
<td>8 (5.6)</td>
<td>0.027</td>
</tr>
<tr>
<td>Mixed delirium, no. (%)</td>
<td>9 (6.3)</td>
<td>2 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Hypoactive delirium no. (%)</td>
<td>8 (5.6)</td>
<td>2 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Hyperactive delirium, no. (%)</td>
<td>2 (1.4)</td>
<td>4 (2.8)</td>
<td></td>
</tr>
<tr>
<td>Median delirium duration (days) (IQR)</td>
<td>3 (1–5)</td>
<td>2 (1–2)</td>
<td>0.37</td>
</tr>
<tr>
<td>Falls, no. (%)</td>
<td>4 (2.8)</td>
<td>0 (0)</td>
<td>0.06</td>
</tr>
<tr>
<td>Median hospital stay (days) (IQR)</td>
<td>9 (5–12)</td>
<td>9 (6–13)</td>
<td>0.36</td>
</tr>
</tbody>
</table>
Figure 2. Time-to-event curves of the studied patients.
• Limitations:
  – Contamination of control group as randomization occurred within same unit
  – Non-blinded outcome assessors
  – 1 or 2 patients per room – is this realistic?
  – Family cooperation and involvement essential
Bottom Line:

• In older adults at risk for delirium admitted to a general medicine unit, a multi-component intervention delivered by family members was effective at reducing the incidence of delirium compared to usual care.

• Low cost, low risk intervention, therefore we should have low threshold for implementation.