Medication safety in vulnerable patient groups
- Elderly patients -

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Conflict of interest: nothing to disclose.
Control questions

1. Should all medicines be started with the same initial dose in a 40-year-old and an 80-year-old?

2. Is creatinine a reliable indicator of glomerular filtration rate in the elderly subject?

3. Use of PIM is rarely appropriate in elderly patients – correct?

Learning Objectives

- parameters, that influence pharmacokinetics and pharmacodynamics in elderly patients
- different classification systems for PIM (Potentially Inappropriate Medication)
- problems with the application of drugs in elderly patients
Global Demographics: 
From pyramid (1980) to bell (2015) to barrel (2050)

The situation in Europe

Source: Calculations by Emi Suzuki based on WDI 2014 and UN World Population Prospects 2012 Revision

Elderly patients are the most important target group of pharmacotherapy.


Multiple co-morbidities ➔ polypharmacy

Beware of:

- drugs that are suboptimal or lacking an indication
- therapeutic duplication
- multiple prescribing doctors
- drug interactions
- vicious cycle of polypharmacy
- complementary medicines
A non-uniform group

„Go-go-patients“ „Slow-go-patient“ „No-go-patient“

Alterations in pharmacokinetics

- reduction in renal clearance
- drug absorption changes little
- altered volume of drug distribution
- loss of first pass metabolism
Alterations in pharmacodynamics

- increased central nervous system sensitivity
- increased sensitivity for anticholinergic effects

Therapy based on guidelines?

- patients > 65 rarely enrolled in clinical trials
- patients on polypharmacy often excluded from clinical trials

→ only a few guidelines adequately address the elderly
Case example

83-year-old woman

fall

PIM = Potentially Inappropriate Medication

- unfavourable balance of risks and benefits
- limited effectiveness in older adults
- carry an increased risk of adverse drug events
- with certain diseases or syndromes
International PIM-lists

<table>
<thead>
<tr>
<th>author</th>
<th>country</th>
<th>year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beers et al.</td>
<td>USA</td>
<td>1991</td>
</tr>
<tr>
<td>McLeod et al.</td>
<td>Canada</td>
<td>1997</td>
</tr>
<tr>
<td>Fick et al.</td>
<td>USA</td>
<td>2003 (update Beers-list)</td>
</tr>
<tr>
<td>Laroche et al.</td>
<td>France</td>
<td>2007</td>
</tr>
<tr>
<td>Gallagher, O’Mahony et al.: STOPP</td>
<td>Ireland</td>
<td>2008</td>
</tr>
<tr>
<td>Rognstad et al.</td>
<td>Norway</td>
<td>2009</td>
</tr>
<tr>
<td>Holt et al.: PRISCUS</td>
<td>Germany</td>
<td>2010</td>
</tr>
<tr>
<td>Wehling et al.: FORTA</td>
<td>Germany</td>
<td>2011 (validation 2014)</td>
</tr>
<tr>
<td>American Geriatrics Society: Beers Criteria 2012</td>
<td>USA</td>
<td>2012 (2nd update Beers-list)</td>
</tr>
<tr>
<td>O’Mahony et al.: STOPP/START</td>
<td>Ireland</td>
<td>2014 (version 2)</td>
</tr>
</tbody>
</table>

2012 AGS Beers Criteria

53 medications or medication classes divided into three categories

1) **PIM**

<table>
<thead>
<tr>
<th>Organ System or Therapeutic Category or Drug</th>
<th>Rationale</th>
<th>Recommendation</th>
<th>Quality of Evidence</th>
<th>Strength of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopinepine, immediate release</td>
<td>Torsade de pointes, with QT prolongation</td>
<td>Avoid</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
</tbody>
</table>

2) **PIM with certain diseases and syndromes**

<table>
<thead>
<tr>
<th>Disease or Syndrome</th>
<th>Drug</th>
<th>Rationale</th>
<th>Recommendation</th>
<th>Quality of Evidence</th>
<th>Strength of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure</td>
<td>NSAIDs and COX-2 inhibitors (主要用于治疗慢性心力衰竭)</td>
<td>Potential to promote fluid retention and exacerbate heart failure</td>
<td>Avoid</td>
<td>NSAIDs: moderate COX-2: moderate Thienodihydropyridines: high Calcium channel blockers: low Dihydropyridines: moderate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cilazapril</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Memantine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Desmopressin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3) **PIM to be used with caution in older adults**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rationale</th>
<th>Recommendation</th>
<th>Quality of Evidence</th>
<th>Strength of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin for primary prevention of cardiovascular events</td>
<td>Lack of evidence of benefit versus risk in individuals aged &gt; 80</td>
<td>Use with caution in adults aged &gt; 80</td>
<td>Low</td>
<td>Weak</td>
</tr>
</tbody>
</table>

STOPP
Screening Tool of Older Persons’ potentially inappropriate Prescriptions

65 clinically significant criteria for potentially inappropriate prescribing

C. Gastrointestinal System

1. Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause (risk of delayed diagnosis, may exacerbate constipation with overflow diarrhoea, may precipitate toxic megacolon in inflammatory bowel disease, may delay recovery in unrecognized gastroenteritis).

2. Diphenoxylate, loperamide or codeine phosphate for treatment of severe infective gastroenteritis i.e. bloody diarrhoea, high fever or severe systemic toxicity (risk of exacerbation or protraction of infection).

3. Prochlorperazine (Stemetil) or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonism).

4. PPI for peptic ulcer disease at full therapeutic dosage for > 8 weeks (earlier discontinuation or dose reduction for maintenance/prophylactic treatment of peptic ulcer disease, oesophagitis or GORD indicated).

5. Anticholinergic antispasmodic drugs with chronic constipation (risk of exacerbation of constipation).


START
Screening Tool to Alert doctors to the Right Treatment

22 evidence-based prescribing indicators for commonly encountered diseases

(iii) Calcium and vitamin D supplement in patients with known osteoporosis (previous fragility fracture, acquired dorsal kyphosis).
**FORTA - Fit for the aged**

4 categories: A – Absolutely, B – Beneficial, C – Careful, D – Don’t

190 items

<table>
<thead>
<tr>
<th>Substance/group</th>
<th>FORTA Class (original FORTA class in parentheses if different from consensus results)</th>
<th>Nr. of raters</th>
<th>Consensus coefficient, Round 1 (cutoff 0.800)</th>
<th>Expert ratings on a numerical scale A=1, B=2, C=3, D=4</th>
<th>Selection of pertinent comments given by participating experts during the consensus procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow-release melatonin (2-4 mg)</td>
<td>C</td>
<td>18</td>
<td>0.813</td>
<td>3.1; 3</td>
<td>Caution: not for long-term use</td>
</tr>
<tr>
<td>Zopiclone (3.75-7.5 mg)</td>
<td>C</td>
<td>18</td>
<td>1.000</td>
<td>3.0; 3</td>
<td>Recommendation: lowest possible dosages recommended</td>
</tr>
<tr>
<td>Tetacyclic antidepressant Mirtazapine (15-30mg)</td>
<td>C</td>
<td>20 (R1) 20 (R2)</td>
<td>0.775</td>
<td>3.0; 3 (R1) 3.0; 3 (R2)</td>
<td>Recommendation: other substances should be favored when symptoms of depression are not present Caution: anticholinergic side effects</td>
</tr>
<tr>
<td>Tricyclic antidepressant Doxepine (25-50mg)</td>
<td>C</td>
<td>18</td>
<td>0.801</td>
<td>3.4; 3</td>
<td>Recommendation: other substances should be favored when symptoms of depression are not present Caution: anticholinergic side effects</td>
</tr>
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</table>

**Beers Criteria versus STOPP**

Beers...

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PIM prevalence

- Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals.

- Prevalence of potentially inappropriate medications and risk of adverse clinical outcome in a cohort of hospitalized elderly patients: results from the REPOSI Study.

- STOPP better than Beers‘ in Europe?
- Is there a European PIM-Tool?

PIM-lists are variable in form and content -
Results from a study conducted at UKE (Germany)
GERAS – The UKE-PIM-Tool

4. Procedure by insomnia
In patients aged > 65 years use of **zopiclone 3.75 mg** is recommended.

Compliance – specific barriers

- polypharmacy
- cognitive impairment
  - forgetfulness
  - lack of understanding
- handling of medicines
  - problems opening packaging due to loss of fine motor skills
  - swallowing problems
  - vision loss
  - …
Sensible prescribing in older patients

- Is it needed?
- Start low, go slow!
- Keep it simple.
- Review regularly.
- Work in teams.

Take home messages

Prescribing of a new drug – if: „Start low, go slow!”

PIM should be avoided in the elderly

Handling of medicines can be a problem in the elderly → non-compliance
Control questions

1. Should all medicines be started with the same initial dose in a 40-year-old and an 80-year-old?

2. Is creatinine a reliable indicator of glomerular filtration rate in the elderly subject?

3. Use of PIM is rarely appropriate in elderly patients – correct?