Appropriateness of prescribing in older patients

Which tools should be used?

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Appropriate prescribing

- Introduction: what and why?
- HOW?
  - Instruments available
  - Focus on European perspective
  - Predictive validity
- Conclusions
1. Introduction

Appropriateness of prescribing
What is appropriate prescribing?

- A prescription that maximises **efficacy** and **safety**, minimises **costs**, and respects patient’s **choices**. (Barber N. Pharm J 1996;257:289-91)

- « Pharmacological appropriateness »
  - Only 1 dimension

- Other dimensions
  - What the patient wants
  - The « general good »
What is appropriate prescribing?

- More complex than for younger patients
  - Comorbidities and polymedication
  - PK/PD changes
  - Physical/cognitive impairment
  - Limited clinical evidence
  - Goals of treatment might differ
  - ...

Primary care clinicians’ experiences with treatment decision making for older persons with multiple comorbidities

To improve decision making, clinicians need:
- More data
- Alternative guidelines
- Approaches to reconciling their own and their patients’ priorities
- An altered reimbursement system
- The support of their subspecialist colleagues

Categories of inappropriate prescribing

- Prescribing more drugs than are clinically indicated
- Inappropriate with regard to:
  - Choice of medicine
  - Dosage
  - Duration
  - Modalities of administration
  - Drug interactions (/drug or /disease)
  - Cost
- Failure to prescribe drugs that are needed
Instruments and measures: why for?

- Research
  - Descriptive
  - Evaluative
- Education and training
- Clinical practice
- Other uses
  - Accreditation
  - Reimbursement
  - ...
2. Measurement

Existing instruments

Predictive validity
Instruments: main characteristics

- **Explicit**
  - Criterion-based
  - < reviews, consensus, experts
  - Focus on drugs/diseases

- **Process**
  - Prescription accords with accepted standards
  - Should have causal links to important outcomes

- **Implicit**
  - Judgment-based
  - Focus on the patient

- **Outcome**
  - Indicators of adverse outcomes
### Example

<table>
<thead>
<tr>
<th>Process</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Explicit</strong></td>
<td>Admission to hospital for fall and patient taking a LA-BZD</td>
</tr>
<tr>
<td>- LA-BZD</td>
<td></td>
</tr>
<tr>
<td>- LA-BZD in patients with fall</td>
<td></td>
</tr>
<tr>
<td><strong>Implicit</strong></td>
<td>Patient with a fall; evaluation to decide whether a medication contributed</td>
</tr>
<tr>
<td>Patient with LA-BZD for insomnia for 5 years, other risk factors for fall, patient open to attempt progressive discontinuation</td>
<td></td>
</tr>
</tbody>
</table>

**Patient with a fall:**
- Evaluation to decide whether a medication contributed.
Explicit instruments

The Beers’ criteria

- Potentially inappropriate medications in older adults (n=68)
- Drugs to avoid, risks > benefits
- Drugs – drugs in certain diseases
- O/M

## Explicit instruments

### The Beers’ criteria

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Drugs-diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Amitriptyline</td>
<td>- BZD - depression, falls, urinary incontinence, COPD</td>
</tr>
<tr>
<td>- Diazepam, flurazepam, clorazepate,…</td>
<td>- Anticholinergics – urinary retention, chronic constipation, cognitive impairment</td>
</tr>
<tr>
<td>- Propoxyphene</td>
<td>-</td>
</tr>
<tr>
<td>- Ticlopidine, Dipyridamole</td>
<td>-</td>
</tr>
<tr>
<td>- Amiodarone</td>
<td>-</td>
</tr>
<tr>
<td>- Fluoxetine</td>
<td>-</td>
</tr>
<tr>
<td>- Loraz.&gt;3 mg, alpraz.&gt;2mg</td>
<td>-</td>
</tr>
<tr>
<td>- VKA + aspirin / NSAID</td>
<td>-</td>
</tr>
<tr>
<td>- ...</td>
<td>-</td>
</tr>
</tbody>
</table>
Explicit instruments

The Beers’ criteria

- Some drugs controversial
- Many drugs not available in Europe
- Only 2 aspects of inappropriate prescribing
- Easy and rapid to use
- Data available in administrative databases

Cross-sectional study; 2707 patients receiving home care in 8 European countries

Figure 2. Prevalence of Potentially Inappropriate Medication Use by Individual Criteria (Beers 1997, Beers 2003, and McLeod 1997)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>458/2707</td>
<td>106/428</td>
<td>106/412</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>295/2707</td>
<td>67/428</td>
<td>56/412</td>
</tr>
<tr>
<td>Italy</td>
<td>295/2707</td>
<td>136/428</td>
<td>29/412</td>
</tr>
<tr>
<td>Finland</td>
<td>295/2707</td>
<td>136/428</td>
<td>29/412</td>
</tr>
<tr>
<td>Norway</td>
<td>295/2707</td>
<td>136/428</td>
<td>29/412</td>
</tr>
<tr>
<td>Iceland</td>
<td>295/2707</td>
<td>136/428</td>
<td>29/412</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>295/2707</td>
<td>136/428</td>
<td>29/412</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>295/2707</td>
<td>136/428</td>
<td>29/412</td>
</tr>
<tr>
<td>Denmark</td>
<td>295/2707</td>
<td>136/428</td>
<td>29/412</td>
</tr>
</tbody>
</table>

Fialova et al. JAMA 2005;293:1348-58
### Other explicit criteria of inappropriate medications

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Beers</th>
<th>McLeod</th>
<th>Rancourt</th>
<th>Laroche</th>
<th>STOPP</th>
<th>Winit-Watjana</th>
<th>NORGEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>US</td>
<td>Canada</td>
<td>Canada</td>
<td>France</td>
<td>Ireland</td>
<td>Thailand</td>
<td>Norway</td>
</tr>
<tr>
<td>Method</td>
<td>Delphi</td>
<td>Delphi</td>
<td>Delphi</td>
<td>Delphi</td>
<td>Delphi</td>
<td>Delphi</td>
<td>Delphi</td>
</tr>
<tr>
<td>Experts (n)</td>
<td>12</td>
<td>32</td>
<td>4</td>
<td>15</td>
<td>18</td>
<td>17</td>
<td>47</td>
</tr>
<tr>
<td>Delphi rounds</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Applicable age group (y)</td>
<td>≥65</td>
<td>≥65</td>
<td>≥65</td>
<td>≥75</td>
<td>≥65</td>
<td>NA</td>
<td>≥70</td>
</tr>
<tr>
<td>Statements (n)</td>
<td>68</td>
<td>38</td>
<td>111</td>
<td>34</td>
<td>65</td>
<td>77</td>
<td>36</td>
</tr>
<tr>
<td>Drug-disease interactions (n)</td>
<td>20</td>
<td>11</td>
<td>0</td>
<td>5</td>
<td>39</td>
<td>32</td>
<td>0</td>
</tr>
<tr>
<td>Drug-drug interactions (n)</td>
<td>1</td>
<td>11</td>
<td>37</td>
<td>2</td>
<td>5</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Prescription duplications (n)</td>
<td>0</td>
<td>0</td>
<td>10</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Suggestions for alternative drugs provided</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Prevalence (%)a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>community</td>
<td>18.3–41.9</td>
<td>10.4</td>
<td>NA</td>
<td>NA</td>
<td>21.4</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>hospital</td>
<td>14–44.4</td>
<td>12.5</td>
<td>NA</td>
<td>NA</td>
<td>35.0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>long-term care</td>
<td>18–34.9</td>
<td>14.9</td>
<td>54.7</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

a  Prevalence range given for Beers criteria data.

NA = not available; NORGEP = Norwegian General Practice criteria; STOPP = Screening Tool of Older Person's potentially inappropriate Prescriptions criteria.
Additional « European Beers criteria »

- **Germany: Priscus list** (Holt S et al, 2010)
  - 83 potentially inappropriate medications

- **Italy** (Maio V et al., J Clin Pharm Ther 2010)
  - 23 inappropriate medications
  - Prevalence, retrospective cohort of outpatients: 25.8%

- **Portugal** (Soares et al, 2008)
Explicit instruments

- The ACOVE criteria
  - Assessing Care Of the Vulnerable Elder
  - 68 medication-related indicators
  - If… then… (unless…)
  - O/U/M

Wenger and Shekelle Ann Intern Med 2001;135:642-6
ACOVE criteria

Domains of care taken into consideration

- Continuity of care
- Dementia
- Depression
- Diabetes mellitus
- End-of-life care
- Falls and mobility disorders
- Hearing impairment
- Heart failure
- Hospital care
- Hypertension
- Ischaemic heart disease
- Malnutrition
- Medication management
- Osteoarthritis
- Osteoporosis
- Pain management
- Pneumonia and influenza
- Pressure ulcers
- Screening and prevention
- Stroke and atrial fibrillation
- Urinary incontinence
- Vision impairment
ACOVE criteria: examples

- **Prescribing indicated medications**
  - β-blocker for patient with heart failure
  - Daily aspirin therapy for patients with diabetes

- **Avoiding inappropriate medications**
  - Avoid strongly anticholinergics medications if alternative exists

- **Education, continuity and documentation**
  - Drug regimen review at least annually

- **Medication monitoring**
  - Follow-up of response to newly started long-term therapy within 6 months
  - INR checked within 4 days after starting therapy
ACOVE criteria

- Pros and cons
  - Operationalisability
  - Geriatric conditions included
    - Encompass Tx, prevention, monitoring, education and documentation
    - Applicable to patients with dementia and poor prognosis
ACOVE criteria: what about Europe?

- **UK** (Steel et al. QSHC 2004;13:260-4)
- **Netherlands (1)** (van der Ploeg et al., QSHC 2008;17:291-5)
- **Netherlands (2)** (Wierenga et al. Drugs Aging 2011;28:295-304)
  - Development and validation of a set of explicitly phrased QIs, based on the native ACOVE criteria
  - Setting: elderly hospitalized patients in the Netherlands
  - 49 ACOVE-derived criteria + 39 new QIs
  - Inter-rater reliability: excellent
Prescribing indicated medication

ALL diabetic elders with proven cardiovascular disease should be offered daily aspirin (acetylsalicylic acid) therapy (80–100 mg/day) OR ELSE an increased risk for cardiovascular complications exists

IF an elder has hypertension and has renal parenchymal disease with lowered glomerular filtration rate (creatinine >150 μmol/L) or microalbuminuria, THEN therapy with an ACE inhibitor or angiotensin II type I receptor antagonist should be offered

IF an elder had a transient ischaemic attack or non-invalidating stroke and no history of atrial fibrillation, THEN prophylaxis should be offered. The first choice treatment is aspirin 38–100 mg/day in combination with dipyridamole 200 mg twice daily (slow release). Both are to be given life long. If there is a contraindication for aspirin, THEN clopidogrel should be given

Continuity and documentation of care

IF an elder is discharged from a hospital to a home or nursing home, THEN a discharge summary that includes information on medication at admission and discharge should be sent to the outpatient physician or nursing home within 14 days

IF a new drug is prescribed to an elder on an ongoing basis for a chronic medical condition, THEN the prescribed drug should have a clearly defined indication documented in the patient’s record

Avoiding inappropriate medication

IF an elder requires analgesia, THEN meperidone (pethidine) should NOT be used OR ELSE there is risk for severe confusion

IF an elder has dementia, THEN a long half-life benzodiazepine such as diazepam, flurazepam, flunitrazepam, clorazepate or chlordiazepoxide should NOT be used

Monitoring of medication

IF an elder uses a maintenance dose of digoxin, THEN the maximal dosage per day is 0.125 mg UNLESS a lower dosage has previously been insufficiently effective for the patient and therapeutic drug monitoring has shown therapeutic blood levels at this high dosage

IF an elder is started on a new selective serotonin receptor inhibitor antidepressant treatment during the hospital stay, THEN evaluation of sodium levels should be performed by the prescribing physician (minimum once during hospital stay) or should be continued after discharge by a general practitioner (yearly) OR ELSE hyponatraemia could occur
Explicit instruments

- The STOPP / START criteria
  - Screening tool of older persons’ potentially inappropriate prescriptions (STOOPP)
    - 65 criteria, O/M
    - 33 not found in Beers’ criteria
  - Screening tool to alert doctors to the right treatment (START)
    - 22 criteria, U

The STOPP/START criteria: examples

**STOPP**
- Aspirin > 150mg/d
- SSRI with a history of clinically significant hyponatremia
- PPI for peptic ulcer disease at full therapeutic dosage for > 8 wks
- Benzodiazepines in patients with recurrent falls
- Glibenclamide or chlorpropamidewith type 2 diabetes mellitus

**START**
- Antidepressant drug in Mo-Se depressive symptoms lasting ≥ 3 months
- Antihypertensive therapy where SBP consistently>160 mmHg
- Antiplatelet therapy in diabetes if one or more co-existing major cardiovascular risk factor present

STOPP / START criteria

- Reliability
  - Inter-rater (Ryan et al., Ann Pharmacother 2009)
    - Hospital and community pharmacists
    - Good reliability
Explicit criteria: similarities and differences

- **Similarities**
  - LA-BZD and TCAs
  - 1st gen antiH1, digoxin, dipyridamole
  - BZD and falls, antichol and urinary retention,…

- **Differences**
  - Many!
  - Reasons
    - Medication availability and prescribing patterns
    - Differing opinions

Chang and Chan. Drugs Aging 2010;27:947-57
Explicit tools in clinical practice: take home message

There is a role for inappropriate prescribing screening tools in everyday clinical practice.

They should enhance, not replace good clinical judgement.

(Hamilton et al., BMC Geriatrics 2009;9:5)
Can explicit indicators be transferred between countries?

- Yes, to some extent, BUT:
  - Need for going through a process of modification and contextualisation
Implicit instruments

The Medication Appropriateness Index (MAI)

- 10 questions per drug

1. Valid indication?
2. Appropriate choice?
3. Correct dose?
4. Modalities of treatment correct?
5. Modalities of treatment practical?
6. Clin. significant drug-drug interactions?
7. Clin. significant drug-disease interactions?
8. Duplication?
9. Appropriate duration?
10. Cost?

Implicit instruments

- **The MAI**
  - Time consuming
  - Knowledge-dependent
  - Comprehensive and systematic
  - Includes operational definitions, explicit instructions, and examples
  - Valid and reliable
  - Excellent educational « tool » for students

Explicit vs implicit: agreement?

- 256 outpatients, ≥5 medications
- Explicit evaluation: Beers
- Implicit evaluation: physician + pharmacist
- $\kappa=0.10-014 \rightarrow$ Disagreement!
- 61% of Beers’ drugs not problematic

« Although drug-to-avoid criteria are useful as guides for initial prescribing decisions, they are insufficiently accurate to use as stand-alone measures of prescribing quality. »

Steinman et al., Arch Intern Med 2009;169:1326-32
Explicit vs implicit: agreement?

Although drug-to-avoid criteria are useful as guides for initial prescribing decisions, they are insufficiently accurate to use as stand-alone measures of prescribing quality. 

Steinman et al., Arch Intern Med 2009;169:1326-32
2. Measurement

Existing instruments
Predictive validity
Is there a link between process measures and adverse health outcomes?

- Mortality
- Morbidity: hospital (re)admission, adverse drug events,…
- Cost
- Quality-of-life
<table>
<thead>
<tr>
<th>Sample</th>
<th>Criteria*</th>
<th>Results†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gupta et al⁶</td>
<td>19932 Medicaid beneficiaries, USA</td>
<td>Beers 1991 (do not use)</td>
</tr>
<tr>
<td>Fick et al⁷</td>
<td>2335 managed care patients, USA</td>
<td>Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Fu et al⁸</td>
<td>2305 community-dwellers (MEPS), USA</td>
<td>Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Laroche et al⁹</td>
<td>2018 patients admitted to the acute geriatric unit of a teaching hospital, France</td>
<td>Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Franci et al⁶</td>
<td>444 community-dwellers (MEPS), USA</td>
<td>Beers 2003 (do not use)</td>
</tr>
<tr>
<td>Zuckerman et al⁵</td>
<td>487 383 community-dwellers, USA</td>
<td>Beers 2003 (do not use)</td>
</tr>
<tr>
<td>Rask et al⁶</td>
<td>406 Medicare-managed care patients, USA</td>
<td>McLeod and Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Perri et al⁷</td>
<td>1117 residents in 15 Georgia nursing homes, USA</td>
<td>Beers 1997 (do not use, dose)</td>
</tr>
<tr>
<td>Raivio et al⁶</td>
<td>425 patients admitted to seven nursing homes and two hospitals, Finland</td>
<td>Beers 1997 (do not use, dose)</td>
</tr>
<tr>
<td>Onder et al⁶</td>
<td>5152 patients in 81 hospitals, Italy</td>
<td>Beers 2003 (do not use, dose)</td>
</tr>
<tr>
<td>Page et al⁶</td>
<td>389 admitted to two adult internal medicine services</td>
<td>Beers 2003 (do not use, dose)</td>
</tr>
<tr>
<td>Aparasu et al⁶</td>
<td>471 community-dwellers (MEPS) taking a psychotropic drug, USA</td>
<td>Beers psychotropic (do not use, drug-disease interaction)</td>
</tr>
<tr>
<td>Chang et al⁶</td>
<td>882 patients in outpatient clinics, Taiwan</td>
<td>Beers 1997 (do not use, dose, drug-disease interaction)</td>
</tr>
<tr>
<td>Lau et al⁶</td>
<td>3372 nursing home residents (MEPS), USA</td>
<td>Beers 1997 (do not use, dose, drug-disease interaction)</td>
</tr>
<tr>
<td>Hanlon et al⁷</td>
<td>3234 community dwellers (Duke EPESE), USA</td>
<td>(1) DUR criteria and (2) Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Fillenbaum et al⁷</td>
<td>3165 community-dwellers (Duke EPESE), USA</td>
<td>(1) DUR criteria and (2) Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Klarin et al⁷</td>
<td>785 ambulatory and nursing home patients in a rural area, Sweden</td>
<td>Beers 1997 (high severity do not use), McLeod (drug-disease interactions), duplication, drug-drug interactions</td>
</tr>
<tr>
<td>Schmader et al⁸</td>
<td>208 community-dwellers, USA</td>
<td>MAI (summed score)</td>
</tr>
</tbody>
</table>
The evidence is **mixed and contradictory** that inappropriate prescribing, defined by process measures, is associated with adverse patient outcomes. No clear conclusions can be made about predictive validity

**Questions:**
- Do current instruments measure « the wrong things »?
- Is it the design of studies that need to be strengthened?

## Predictive validity: recent evidence

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample</th>
<th>Indicator</th>
<th>Outcome</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albert et al., 2010</td>
<td>7459 retirees, USA</td>
<td>Beers 2003 &amp; NCQA</td>
<td>Hospital admission</td>
<td>+</td>
</tr>
<tr>
<td>Dedhiya et al., 2010</td>
<td>7594 NH residents, USA</td>
<td>Beers 2003</td>
<td>Hospital admission and mortality</td>
<td>+</td>
</tr>
<tr>
<td>Lai et al., 2009</td>
<td>5741 outpatients, Taiwan</td>
<td>Beers 2003</td>
<td>ED visits and hospital adm.</td>
<td>+</td>
</tr>
<tr>
<td>Ruggiero et al., 2010</td>
<td>1716 NH residents, Italy</td>
<td>Beers 2003</td>
<td>Hospital admission</td>
<td>+</td>
</tr>
<tr>
<td>Lund et al., 2010</td>
<td>236 outpatients, USA</td>
<td>Beers 2003 (modified)MAI</td>
<td>ADE</td>
<td>+/−</td>
</tr>
</tbody>
</table>
## Predictive validity: recent evidence

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sample</th>
<th>Indicator</th>
<th>Outcome</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berdot et al., 2009</td>
<td>6343 outpatients, France</td>
<td>Beers 2003 and Laroche</td>
<td>Falls</td>
<td>+</td>
</tr>
<tr>
<td>Chrischilles et al., 2009</td>
<td>626 outpatients, USA</td>
<td>Beers 1997 + dupli and DDI</td>
<td>Self-reported ADE</td>
<td>+</td>
</tr>
<tr>
<td>Shiyanbola and Farris, 2010</td>
<td>874 outpatients, USA</td>
<td>Beers 2003 and ACOVE</td>
<td>Self-reported ADE</td>
<td>-</td>
</tr>
<tr>
<td>Lund et al., 2010</td>
<td>236 outpatients, USA</td>
<td>Beers 2003 (modified)MAI</td>
<td>ADE</td>
<td>+/-</td>
</tr>
</tbody>
</table>
3. Conclusion
Existing measures

- No ideal measure
- Choice should depend on study objectives and available data
- Discourage measures that rely exclusively on drug data
- Encourage the use of instruments addressing several dimensions of appropriateness
Almost 60% of prescriptions: 1 inappropriate rating

30% of patients were taking 1 drug-to-avoid

Under-prescribing in 50% of patients

OR (95%CI) for having ≥1 improvement from admission to discharge in the intervention group compared with the control group

- MAI 9.1 (4.2-21.6)
- Drug-to-avoid 0.6 (0.3-1.1)
- Underuse (ACOVE criteria) 6.1 (2.2-17.0)

Trend toward decreased rates of mortality and visits to the emergency department
Perspectives

- **Predictive validity:**
  - Need more evaluation, especially re:
    - instruments other than the Beers criteria
    - Quality of life and cost

- **Instruments**
  - More European data needed
  - Patient or caregiver’s perspective?
Thank you for your attention
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1- No funds were received in support of this presentation.
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Contact details

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