

Appropriateness of prescribing in older patients

Which tools should be used?

Anne Spinewine

MPharm, MSc, PhD

Université catholique de Louvain, Belgium

Louvain Drug Research Institute and CHU Mont-Godinne

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
 - ...

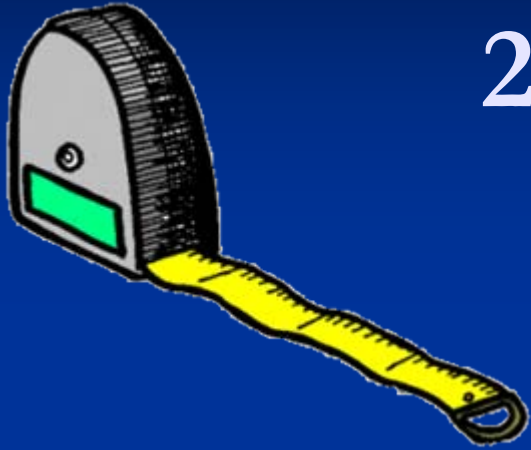
- Primary care clinicians' experiences with treatment decision making for older persons with multiple comorbidities
 - To improve decision making, clinicians need:
 - More data
 - Alternative guidelines
 - Approches to reconciling their own and their patients' priorities
 - An altered reimbursement system
 - The support of their subspecialist colleagues

Categories of inappropriate prescribing

- Prescribing more drugs than are clinically indicated | *OVER-*
- Inappropriate with regard to:
 - Choice of medicine
 - Dosage
 - Duration
 - Modalities of administration
 - Drug interactions (/drug or /disease)
 - Cost | *MIS-*
- Failure to prescribe drugs that are needed | *UNDER-*

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

■ Implicit

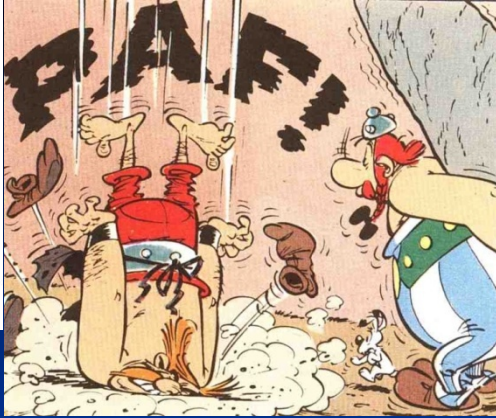
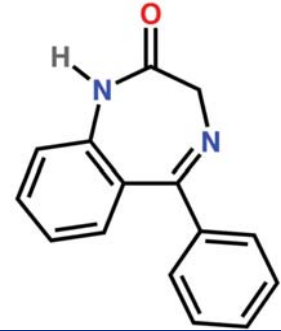
- Judgment-based
- Focus on the patient

■ Process

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

■ Outcome

- Indicators of adverse outcomes



Example

■ Process

■ Outcome

■ Explicit

- LA-BZD
- LA-BZD in patients with fall

Admission to hospital for fall and patient taking a LA-BZD

■ Implicit

Patient with LA-BZD for insomnia for 5 years, other risk factors for fall, patient open to attempt progressive discontinuation

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

Drugs

- Amitriptyline
- Diazepam, flurazepam, clorazepate,...
- Propoxyphene
- Ticlopidine, Dipyridamole
- Amiodarone
- Fluoxetine
- Loraz.>3 mg, alpraz.>2mg
- VKA + aspirin / NSAID
- ...

Drugs-diseases

- BZD - depression, falls, urinary incontinence, COPD
- Anticholinergics – urinary retention, chronic constipation, cognitive impairment
- ...

Explicit instruments

■ The Beers' criteria



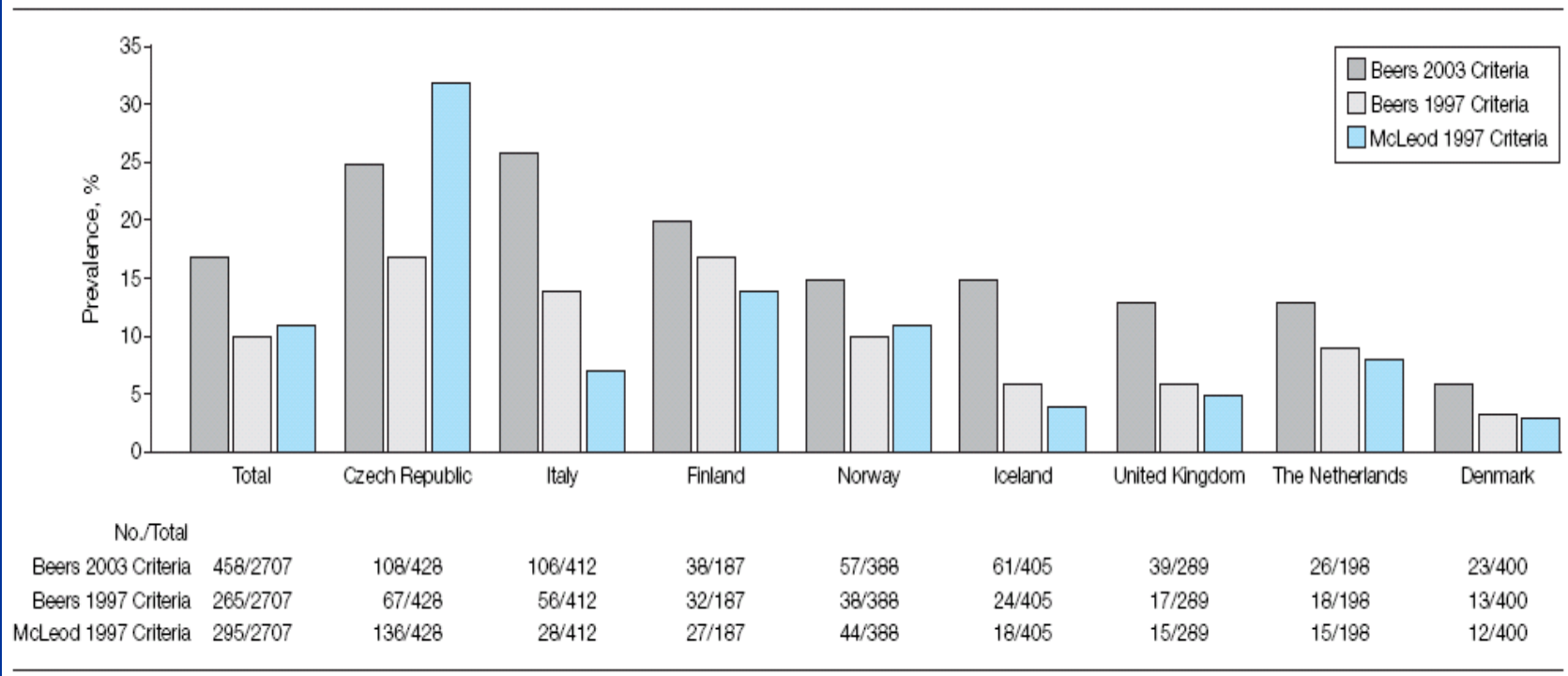
- Some drugs controversial
- Many drugs not available in Europe
- Only 2 aspects of inappropriate prescribing



- 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 1997,¹⁵ Beers 2003,¹⁷ and McLeod 1997¹⁶)



Other explicit criteria of inappropriate medications

Table I. Basic characteristics of the seven sets of explicit criteria of potentially inappropriate medications evaluated

Characteristics	Beers	McLeod	Rancourt	Laroche	STOPP	Winit-Watjana	NORGE P
Year	2003	1997	2004	2007	2008	2008	2009
Country	US	Canada	Canada	France	Ireland	Thailand	Norway
Authors	Fick et al. ^[13]	McLeod et al. ^[21]	Rancourt et al. ^[23]	Laroche et al. ^[24]	Gallagher et al. ^[25]	Winit-Watjana et al. ^[15]	Rognstad et al. ^[26]
Method	Delphi	Delphi	Delphi	Delphi	Delphi	Delphi	Delphi
Experts (n)	12	32	4	15	18	17	47
Delphi rounds	2	2	2	2	2	3	3
Applicable age group (y)	≥65	≥65	≥65	≥75	≥65	NA	≥70
Statements (n)	68	38	111	34	65	77	36
Drug-disease interactions (n)	20	11	0	5	39	32	0
Drug-drug interactions (n)	1	11	37	2	5	12	15
Prescription duplications (n)	0	0	10	2	2	0	1
Suggestions for alternative drugs provided	No	Yes	No	Yes	No	No	No
Prevalence (%) ^a							
community	18.3–41.9	10.4	NA	NA	21.4	NA	NA
hospital	14–44.4	12.5	NA	NA	35.0	NA	NA
long-term care	18–34.9	14.9	54.7	NA	NA	NA	NA

a Prevalence range given for Beers criteria data.

NA = not available; NORGE P = 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

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

Avoiding inappropriate medication

IF an elder requires analgesia, THEN meperidine (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

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

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 (STOPP)
 - 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 chlorpropamide with 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

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
- $\kappa=0.10-0.14 \rightarrow$ Disagreement!

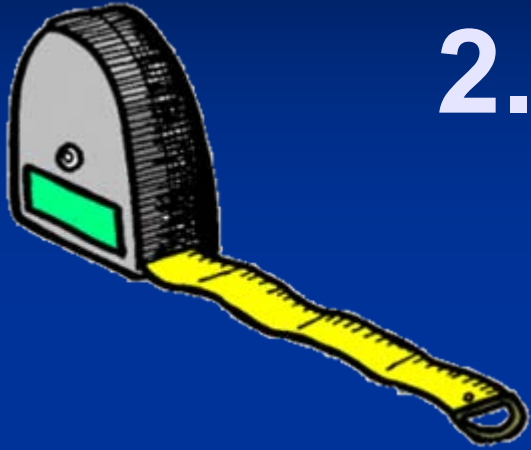
« Although drug-to-avoid criteria are useful as guides for initial prescribing decisions, they are insufficiently accurate to use as stand-alone measures of prescribing quality. »

Explicit vs implicit : agreement?

Table 2. Most Common Drugs Identified by the Beers and Zhan Criteria and Expert Assessment of Those Drugs^a

Type of Drug	Beers Criteria (214 Drugs Flagged)		Zhan Criteria (91 Drugs Flagged)	
	Drugs Meeting Criteria, No.	Drugs That Met Criteria and Were Deemed Problematic by Expert Team, No. (%)	Drugs Meeting Criteria, No.	Drugs That Met Criteria and Were Deemed Problematic by Expert Team, No. (%)
Antihistamines	42	21 (50)	42	21 (50)
Tricyclic antidepressants	18	15 (83)	15	14 (93)
Benzodiazepines	15	5 (33)	2	1 (50)

« 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. »



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

	Sample	Criteria*	Results†
Gupta et al ⁷²	19932 Medicaid beneficiaries, USA	Beers 1991 (do not use)	No significant difference in mortality (p=0.31)
Fick et al ⁷³	2336 managed care patients, USA	Beers 1997 (do not use)	Higher cost and use of health care (p=0.0001)
Fu et al ⁷⁴	2305 community-dwellers (MEPS), USA	Beers 1997 (do not use)	Poor self-rated health (p=0.006)
Laroche et al ⁷⁵	2018 patients admitted to the acute geriatric unit of a teaching hospital, France	Beers 1997 (do not use)	No significant increased risk of adverse drug reactions (OR 1.0, 95% CI 0.8-1.3)
Franic et al ⁷⁶	444 community-dwellers (MEPS), USA	Beers 2003 (do not use)	No significant difference in HRQOL (results not provided)
Zuckerman et al ⁷⁷	487 383 community-dwellers, USA	Beers 2003 (do not use)	Increased risk of nursing home admission over the next 2 years (RR 1.31; 99% CI 1.26-1.36)
Rask et al ⁷⁸	406 Medicare-managed care patients, USA	McLeod and Beers 1997 (do not use)	No significant difference of self-reported adverse drug events (OR 1.42, 95% CI 0.90-2.25)
Perri et al ⁷⁹	1117 residents in 15 Georgia nursing homes, USA	Beers 1997 (do not use, dose)	Higher risk of death/admission/emergency visit (OR 2.34, 95% CI 1.61-3.40)
Raivio et al ⁸⁰	425 patients admitted to seven nursing homes and two hospitals, Finland	Beers 1997 (do not use, dose)	No significant difference in mortality (HR 1.02, 95% CI 0.7-1.37) and admissions (OR 1.40, 95% CI 0.93-2.11)
Onder et al ⁸¹	5152 patients in 81 hospitals, Italy	Beers 2003 (do not use, dose)	No significant difference in mortality (OR 1.05, 95% CI 0.75-1.48), length of stay (OR 1.09, 95% CI 0.95-1.25), and adverse drug reaction (OR 1.20, 95% CI 0.89-1.61)
Page et al ⁸²	389 admitted to two adult internal medicine services	Beers 2003 (do not use, dose)	No significant difference in adverse drug event (OR 1.51, 95% CI 0.98-2.35), length of stay (1.03, 0.64-1.63), discharge to higher levels of care (1.39, 0.82-2.34), and in-hospital mortality (1.49, 0.77-2.92)
Aparasu et al ⁸³	471 community-dwellers (MEPS) taking a psychotropic drug, USA	Beers psychotropic (do not use, drug-disease interaction)	No significant difference in health care use, and activities of daily living (p>0.05)
Chang et al ⁸⁴	882 patients in outpatient clinics, Taiwan	Beers 1997 (do not use, dose, drug-disease, interaction)	Higher rate of adverse drug reactions (RR 15.3, 95% CI 4.0-58.8)
Lau et al ⁸⁵	3372 nursing home residents (MEPS), USA	Beers 1997 (do not use, dose, drug-disease interaction)	Higher risk of death (OR 1.21, 95% CI 1.00-1.46) and admission (1.28, 1.10-1.50)
Hanlon et al ⁸⁶	3234 community dwellers (Duke EPESE), USA	(1) DUR criteria and (2) Beers 1997 (do not use)	(1) No significant difference in mortality (OR 0.85, 95% CI 0.69-1.24) and higher risk of decline in functional status (2.04, 1.32-3.16) for interactions and basic-self care (2) No significant difference in mortality (1.02, 0.85-1.23), decline in functional status
Fillenbaum et al ⁸⁷	3165 community-dwellers (Duke EPESE), USA	(1) DUR criteria and (2) Beers 1997 (do not use)	(1) Increased outpatient visits ($\beta=0.82$, 95% CI 0.27-1.37), but no increased time to admission (HR 1.06, 95% CI 0.90-1.25), or time to nursing home entry (HR 1.06, 95% CI 0.76-1.47) (2) Increased time to admission (HR 1.20, 95% CI 1.04-1.39), but no increased outpatient visits ($\beta=0.48$, -0.01 to 0.97, or time to nursing home entry (HR 0.93, 95% CI 0.69-1.08)
Klarin et al ⁸⁸	785 ambulatory and nursing home patients in a rural area, Sweden	Beers 1997 (high severity do not use), McLeod (drug-disease interactions), duplication, drug-drug interactions	Higher admission (OR 2.00, 95% CI 1.33-3.00) No significant difference in mortality (HR 0.93, 95% CI 0.67-1.29)
Schmader et al ⁸⁵	208 community-dwellers, USA	MAI (summed score)	Higher hospital admission (p=0.07) and unscheduled visit (p=0.05); better blood pressure control (p=0.02)


Predictive validity

*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

Reference	Sample	Indicator	Outcome	Association
Albert et al., 2010	7459 retirees, USA	Beers 2003 & NCQA	Hospital admission	+
Dedhiya et al., 2010	7594 NH residents, USA	Beers 2003	Hospital admission and mortality	+
Lai et al., 2009	5741 outpatients, Taiwan	Beers 2003	ED visits and hospital adm.	+
Ruggiero et al., 2010 	1716 NH residents, Italy	Beers 2003	Hospital admission	+
Lund et al., 2010	236 outpatients, USA	Beers 2003 (modified)MAI	ADE	+/-

Predictive validity: recent evidence

Reference	Sample	Indicator	Outcome	Assoc-iation
Berdot et al., 2009 	6343 outpatients, France	Beers 2003 and Laroche	Falls	+
Chrischilles et al., 2009	626 outpatients, USA	Beers 1997 + dupli and DDI	Self-reported ADE	+
Shiyanbola and Farris, 2010	874 outpatients, USA	Beers 2003 and ACOVE	Self-reported ADE	-
Lund et al., 2010	236 outpatients, USA	Beers 2003 (modified)MAI	ADE	+/-

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

Effect of a Collaborative Approach on the Quality of Prescribing for Geriatric Inpatients: A Randomized, Controlled Trial

Anne Spinewine, PhD,* Christian Swine, MD,*[§] Soraya Dhillon, PhD,^{||} Philippe Lambert, PhD,[¶]
Jean B. Nachega, MD, MPH, DTM&H,^{***} Léon Wilmotte, MPharm,^{*†} and
Paul M. Tulkens, MD, PhD^{*‡}

JAGS 2007;55:658-65

- 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**



Contact details

- Anne Spinewine
- Université catholique de Louvain, Belgium
 - Louvain Drug Research Institute, Clinical Pharmacy Research Group
 - CHU Mont-Godinne
- Email: anne.spinewine@uclouvain.be

Disclosure of interest

- 1- No funds were received in support of this presentation.
- 2- No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this presentation.