

Inappropriate drug prescribing in older adults *and how to reduce it*

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Introduction

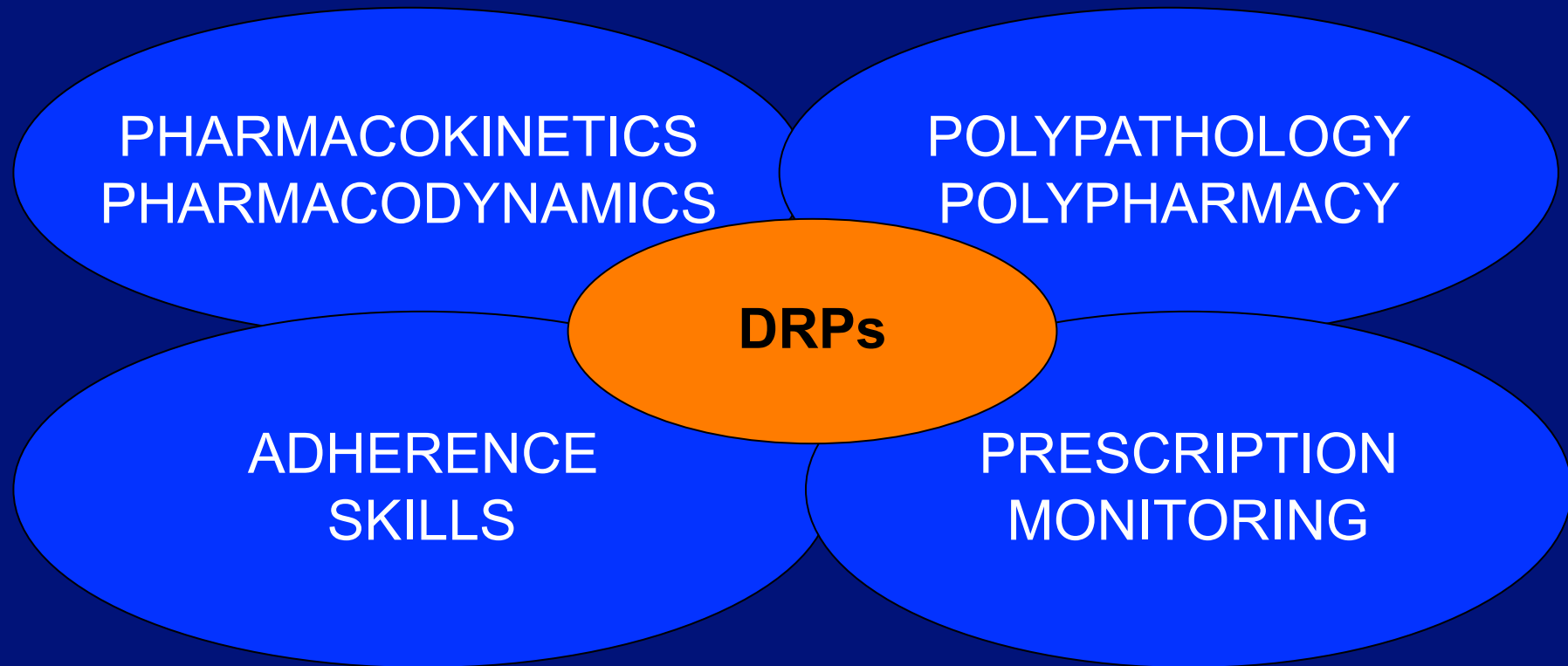
- Drug related problems (DRPs) and adverse drug reactions (ADR) represent a major burden on health care.
- In Western countries ADRs cause 10-20% of all hospital admissions, and are responsible for about 5-10% of in-hospital costs.

Lazarou J et al. JAMA. 1998;279:1200-1205.

Onder G et al. J Am Geriatr Soc. 2002;50:1962-8.

Introduction

Factors contributing to DRPs in older people



Introduction

- DRPs and ADRs in older people are frequently preventable
 - Screening and prevention programs aimed at reducing the rate of iatrogenic illness are necessary

Hakkarainen K et al. PLoS One 2012;7(3):e33236.

Approaches to screen and prevent the occurrence of DRPs and ADRs

- Screening- identification of subjects at risk of ADR
- Medication review
- Avoiding use of potentially inappropriate medications (PIM)
- Computer-based prescribing systems
- Comprehensive geriatric assessment (CGA)

Strategies to reduce the risk of iatrogenic illness in complex older adults

Onder G, van der Cammen T, Petrovic M, Somers A, Rajkumar C.

Age Ageing 2013; 42: 284-291

Screening- identification of subjects at risk of ADR: evidence

- Few data exist that allow stratification of patients according to likelihood of an ADR
 - An attempt to develop a risk stratification model: *not enough statistical power power to develop a risk score*

Bates D et al. Arch Intern Med. 1999;159:2553-60
 - An attempt to identify specific patient's characteristics associated with an increased risk: *restrospective study, relied on voluntarily reported ADRs*

Johnston P et al. Am J Health Syst Pharm. 2006; 63:2218-2227

**Development and Validation of a Score to
Assess Risk of Adverse Drug Reactions
Among In-Hospital Patients 65 Years or
Older:
the GerontoNet ADR risk score**

*Onder G, Petrovic M, Tangiisuran B, Meinardi M, Markito-Notenboom W,
Somers A, Rajkumar C, Bernabei R, van der Cammen T.*

Arch Intern Med 2010, 170: 1142-1148

Variables of the GerontoNet ADR risk score

	Odds Ratio	95% CI	Points
≥ 4 co-morbid conditions	1.31	1.04 - 1.64	1
Heart failure	1.79	1.39 - 2.30	1
Liver disease*	1.36	1.06 - 1.74	1
No of drugs, < 5	1		0
5-7	1.90	1.35 - 2.68	1
≥ 8	4.07	2.93 - 5.65	4
Previous ADR	2.41	1.79 - 3.23	2
Renal failure**	1.21	0.96 - 1.51	1

*transaminases > 2 x upper normal limit; ** GFR < 60 ml/min

Screening- identification of subjects at risk of ADR

- The GerontoNET ADR risk score represents a tool to identify patients at risk of ADR, which may be target of interventions aimed at reducing their risk of ADR
- However...
 - *it still should be validated in different settings and studies*
 - *the need for identification of new risk factors to be added to the score*

O'Connor M. et al. Age Ageing 2012;41:771-6.

**Development and Validation of a Risk
Model for Predicting Adverse Drug
Reactions in Older People
during Hospital Stay:
Brighton Adverse Drug Reactions Risk
(BADRI) Model**

*Tangiisuran B, Scutt G, Stevenson J, Wright Onder G,
Petrovic M, van der Cammen T, Rajkumar C, Davis G
PLoS ONE 2014; 9(10): e111254*

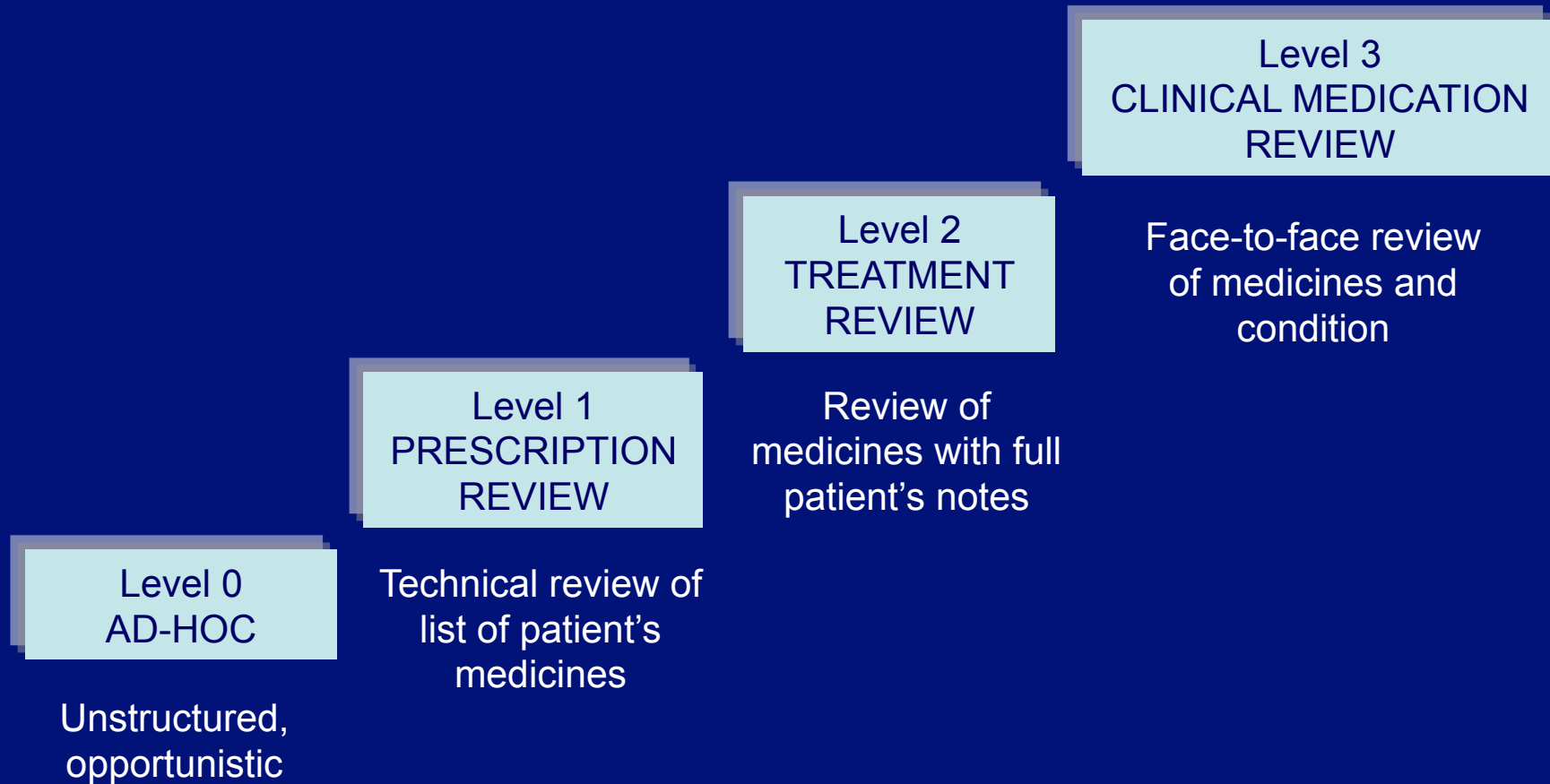
Brighton Adverse Drug Reactions Risk (BADRI) Model

	Odds Ratio	95% CI
Hyperlipidemia	3.32	1.81- 6.07
No of drugs \geq 8	3.30	1.93 - 5.65
Length of stay \geq 12 days	2.27	1.35 - 3.83
Use of anti-diabetic agents	1.91	1.04 - 3.49
High WCC on admission	1.55	0.94 - 2.55

Medication review

- An individualized assessment provided by a clinical pharmacist: during which the medication list is analyzed in a structured manner, with full access to the medical file, in order to identify drug related problems.
- *First step: identification* of all the medications that the patient is taking.
- *Second step: the medication list is screened* for drug related problems i.e. any misuse, underuse or overuse of drugs.
- *Third step: possible solutions* to the drug related problems (DRPs) are then discussed with the treating physician and, if possible, with the patient.

Medication review



Medication review: evidence

- *Better results have been reported when pharmacists are skilled and work in the context of a multidisciplinary team.*

Spinewine et al. J Am Geriatr Soc 2007;55:658-65

- *A team-based care including pharmacists results in an important reduction of adverse drug events.*

Chisholm-Burns Med Care. 2010;48:923-33

- Pharmacotherapy for older patients is improved, but the evidence of the impact on health outcomes, quality of life or cost-effectiveness of care is mixed and not conclusive.

Spinewine et al. Drugs Aging. 2012;29:495-510.

Clinical studies assessing the effect on ADR of clinical pharmacists' intervention in the context of a multidisciplinary team

Author	Population	Design	Intervention	Results
Klopotoska (2010)	115 patients in ICU (mean age 63 years)	RCT	Hospital pharmacist reviewed medication orders for patients admitted to the ICU and discussed those during patient review meetings with the attending ICU physicians.	Preventable adverse drug events were reduced from 4.0 per 1,000 monitored patient-days during the baseline period to 1.0 per 1,000 monitored patient-days during the intervention period (P = 0.25).
Schnipper (2009)	322 in-hospital patients (62% age > 60 years)	Cluster-RCT	Computerized medication reconciliation tool and process redesign involving physicians, nurses, and pharmacists	Adverse drug events rate was 1.44 per patient among control patients and 1.05 per patient among intervention patients (adjusted relative risk, 0.72; 95% CI 0.52-0.99).
Kucukarslan (2003)	165 in-hospital patients (mean age 55 years)	RCT	Rounding team including a pharmacist	Rate of preventable adverse drug events was reduced by 78%, from 26.5 per 1000 hospital days to 5.7 per 1000 hospital days
Leple (1999)	75 patients in ICU	RCT	A senior pharmacist made rounds with the ICU team and remained in the ICU for consultation in the morning, and was available on call throughout the day	The rate of preventable ordering adverse drug events decreased by 66% from 10.4 per 1000 patient-days (95% confidence interval [CI], 7-14) before the intervention to 3.5 (95% CI, 1-5; P<.001) after the intervention. In the control unit, the rate was essentially unchanged during the same time periods: 10.9 (95% CI, 6-16) and 12.4 (95% CI, 8-17) per 1000 patient-days.

Avoiding use of potentially inappropriate medications (PIM)

- **Medication Assessment Tools**

- 1) Explicit (criteria based): drugs to avoid**

- Beers (1991, updates 1997, 2003, 2012)
 - McLeod (1997)
 - ACOVE: Assessing Care of Vulnerable Elders (2001)
 - IPET: Improved Prescribing in the Elderly Tool (2002)
 - STOPP: Screening Tool of Older Person's Prescriptions/ START: Screening Tool to Alert doctors to Right Treatment) (2008)

- 2) Implicit (judgement based):**

- MAI: Medication Appropriateness Index (1992)
 - GMA: Geriatric Medication Algorithm (1994)
 - Lipton's criteria (1993)

Avoiding use of potentially inappropriate medications (PIM)

	■ Process	■ Outcome
■ Explicit	<ul style="list-style-type: none">- 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	

Beers criteria

- Drugs to avoid, risks > benefits
- Drugs to avoid in certain diseases/
conditions
 - O/M

Beers criteria



- Some drugs controversial
- Many drugs not available in Europe
 - Better situation with the 2012 version
- Only 2 aspects of inappropriate prescribing



- Easy and rapid to use

Beers criteria

Table 1. Applicability of the 2003 and 2012 Beers Criteria to Belgium

Level of Analysis	n/N (%)	
	2003	2012
Medications or medication classes ^a	38/48 (79.2)	49/53 (92.5)
Molecules listed ^b	60/100 (60.0)	100/177 (56.5)
Individual criteria ^c	47/66 (71.2)	84/99 (84.8)

STOPP/ START criteria

- Screening tool of older persons' potentially inappropriate prescriptions (STOPP)
 - 80 criteria
 - 33 not found in Beers criteria
- Screening tool to alert doctors to the right treatment (START)
 - 34 criteria

Gallagher et al. Int J Clin Pharmacol Ther 2008;46:72-83

O'Maahony D et al. Age Ageing, advance access, October 16, 2014

Avoiding use of PIM: evidence

- Use of STOPP/START criteria leads to significant and sustained improvements in the appropriateness of prescribing at discharge and for up to 6 months after discharge
 - suggesting that this tool represents a simple and easily applied method of optimizing prescribing appropriateness in older hospitalized patients.

Gallagher P et al. J Clin Pharm Ther. 2007; 32:113-21.

- STOPP criteria seem significantly associated with avoidable adverse drug events that cause or contribute to urgent hospitalization.

Gallagher P et al. Clin Pharmacol Ther 2011;89:845-54.

Beers vs STOPP START

- Similarities
 - Criteria: BZD & falls; CCB & constipation; long-acting sulfonylurea;...
- Differences
 - ~ 75% of Beers criteria do NOT overlap with STOPP
 - ~ 55% of the STOPP criteria are not part of Beers
 - Beers: more focus on anticholinergics; delirium; dementia
 - STOPP: more focus on anticoag; opiates; PPIs

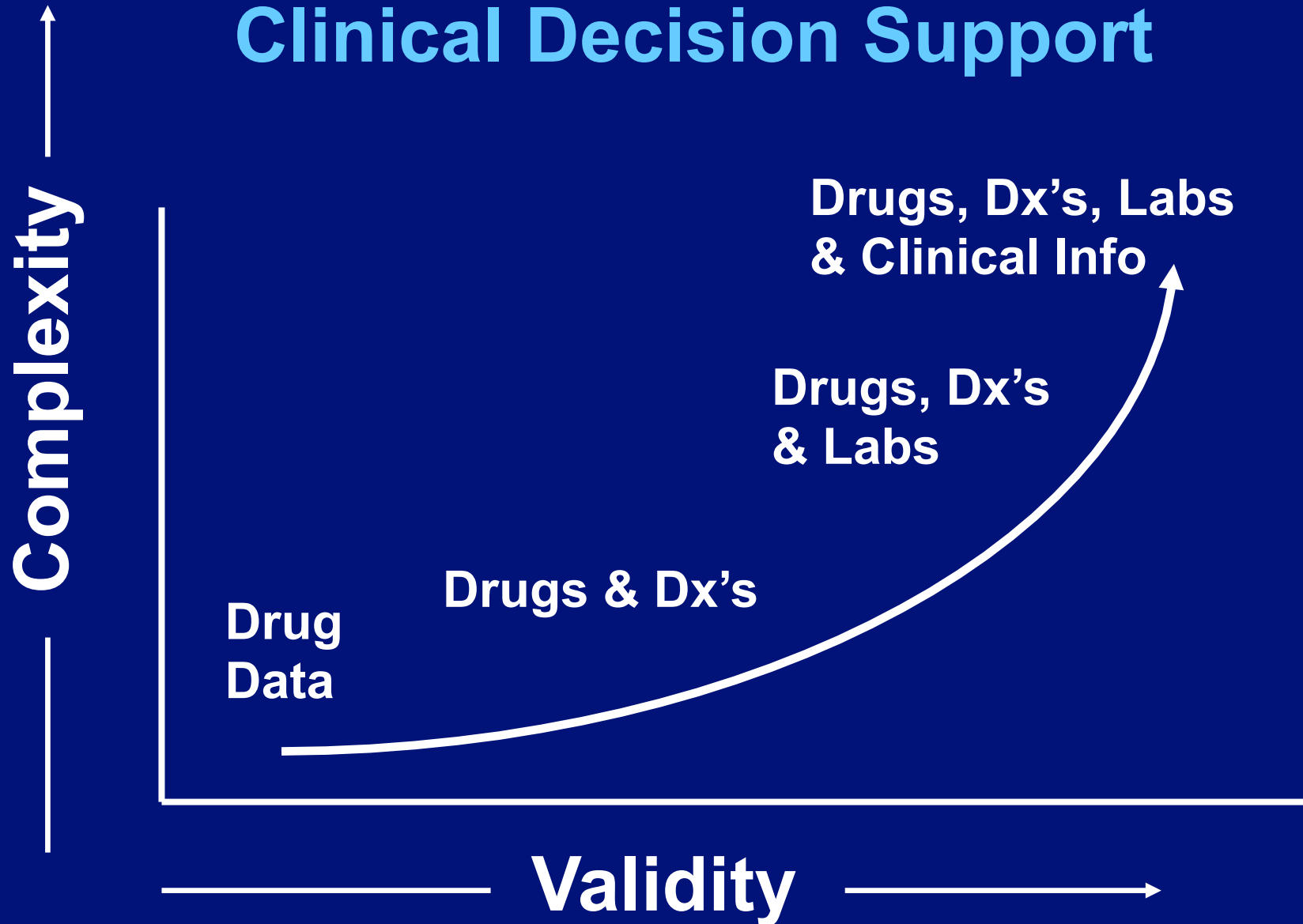
Beers vs STOPP START

In conclusion, we believe that the 2012 Beers criteria have greater relevance for European countries. Because the majority of criteria for inappropriate prescribing do not overlap in Beers and STOPP, both lists will continue to coexist. Furthermore, the addition to Beers of criteria

Computer-based prescribing systems

- Clinical Decisions Support Systems (CDSS) and Computerized Prescription Support System (CPSS) are interactive softwares, designed
 - to correct prescription,
 - with the aim of reducing prescribing errors,
 - improving prescribing appropriateness and ultimately lead to a reduction of iatrogenic illness.
 - provide support at the time of prescription by implementing different algorithms and tools to identify potentially inappropriate prescribing, drug interactions, risk of iatrogenic illness, appropriate drug dosage and contraindicated treatments.
- Computerized Provider Order Entry Systems (CPOE), which are based on these softwares, enable providers to enter medical orders into a computer system that is located within an inpatient or ambulatory setting. CPOE introduces automation at the time of ordering, and can occur instantly, accurately, reliably, and more legibly than handwritten orders.

Translating Quality Measures into Clinical Decision Support



Computer-based prescribing systems: evidence

- Very few studies demonstrated an improvement in patient outcomes. A systematic review evaluating the effects of CPOE based on CDSS on the development of adverse drug events showed that only 5 out of 10 eligible studies reported a statistically significant reduction in the number of adverse drug events.

Wolfstadt J et al. J Gen Intern Med 2008;23:451-8.

- In an RCT conducted in 2 academic centres in the US, CDSS intervention was shown to be effective in reducing the prescribing of an undesired drug-drug combination, but it caused clinically important treatment delays in patients who needed immediate drug therapy.

Strom B et al; Arch Intern Med. 2010;170:1578-83.

Computer-based prescribing systems: evidence

- Limitations:
 - not standardized, with different types of tool or algorithms implemented depending on study or population considered.
 - often do not assess the complexity of older adults related to comorbidity, geriatric syndromes and impairments in multiple systems (i.e. cognitive and functional impairments), being mainly focused on pharmacological issues.
- Clear evidence suggesting an effect of computer-based prescribing systems is lacking.
- Efforts are required to further integrate additional clinical and laboratory information into these systems, including specific symptoms, geriatric conditions and functional status to the use of specific medications.

Comprehensive geriatric assessment (CGA)

- Medical complexity plays an important role in the onset of ADR and should always be considered before prescribing a pharmacological treatment in older people.
- Drugs that have proven in clinical trials clear beneficial effects to treat a chronic conditions and which use is indicated in clinical guidelines should be used carefully in complex older adults
 - since they may interact with co-existing diseases or geriatric syndromes, may not be assumed correctly because of presence of cognitive deficits, disability or social problems or may be useless because the health expectancy of the patient is too short to determine a beneficial effect of the drug.

Tinetti M et al. N Engl J Med 2004; 351: 2870–74.

Comprehensive geriatric assessment (CGA): evidence

- CGA in association with an integrated team of geriatricians, nurses, clinical pharmacists and other professionals (=multidisciplinary team) assessing and managing the health care problems identified by the CGA, and developing individualized care plans, results in more detailed evaluation, improved care planning, and overall better quality of care.

Ellis G et al. BMJ. 2011;343:d6553.

- Limitation: heterogeneity in terms of structural components and care processes.

Comprehensive geriatric assessment (CGA): evidence

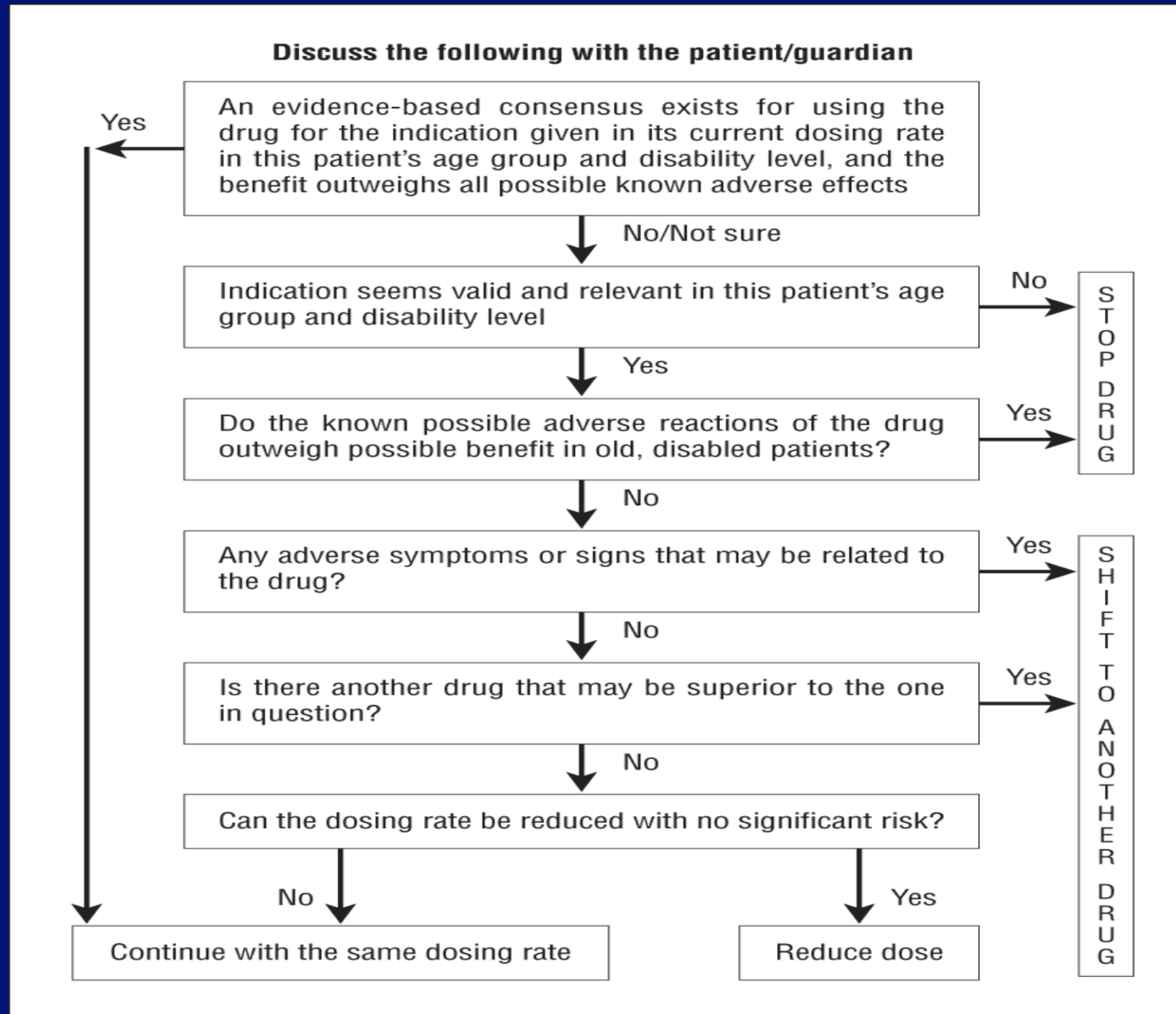
- CGA allows a complete and global assessment and management of the health care problems, including evaluation of drugs with the goal of recognizing and preventing potential drug-related problems and improve quality of prescribing.

Onder G et al. 2011;12:647-51.

- CGA associated with a multidisciplinary team approach, as compared with usual care in frail older adults shows a 35% reduction in the risk of a serious ADRs and a substantial reduction in unnecessary and inappropriate drug use, in the number of conditions with omitted drugs significantly associated with the intervention.

Schmader K et al. Am J Med. 2004;116:394-401.

Systematic approach for drug cessation in complex older adults



Drug cessation in complex older adults: time for action

van der Cammen T, Rajkumar , Onder G, Sterke C, Petrovic M.

Age Ageing 2014; 43(1): 20-5.

Systematic approach for drug cessation in complex older adults

- From a clinical viewpoint, drug cessation seems most warranted in the following situations:
 - falls, delirium, and cognitive impairment,
 - articles selected: 7 for falls, none for delirium and 2 for cognition

Systematic approach for drug cessation in complex older adults

- **Summary on the effectiveness of drug cessation on falls**
 - Withdrawal of psychotropics is effective in reducing rate of falls.
 - A prescribing modification programme for primary care physicians significantly reduced risk of falling.
- **Summary on the effectiveness of drug cessation on delirium and cognitive impairment**
 - No studies available on drug cessation in delirium.
 - Withdrawal of psychotropics is associated with improved cognition.
 - Systematic reduction of polypharmacy in community-dwelling older adults can result in an improvement of cognitive function.

THM: Conclusions

- None of the existing approaches did show a clear beneficial effect on patients' health outcomes: available evidence on the impact of medication review, avoidance of PIM, computer-based prescribing systems and CGA is mixed and controversial.
- A main limitation of all the described approaches is the lack of standardization.
 - Large differences are described in the delivery of the pharmacist-led medication review.
 - Criteria to assess quality of prescribing vary across countries and no widely accepted gold standard exists, yet.
 - Computer-based prescribing systems are often home-grown and they implement different types of information, tools and algorithms.
 - Geriatric assessment and management programs are heterogeneous in terms of structural components and care processes.

THM: Conclusions (cont.)

- Most of the available research is focused on a *single* intervention targeting either clinical or pharmacological factors causing ADR.
- When these approaches were combined, as for studies assessing the efficacy of an intervention based on experienced pharmacists performing medication review in the context of a multidisciplinary team, positive effects on patients' health outcomes were shown.
- Safe drug use goes along with global assessment of patients clinical and functional parameters and that integration of skills from different health care professionals is needed to address medical complexity of older adults.
- The challenge for future research is to *integrate* valuable information obtained by existing instruments and methodologies in a complete and global approach targeting all potential factors involved in the onset of ADR.

COLLABORATIVE CARE

Multidisciplinary teams

Geriatric expertise/CGA

Collaboration with

General practitioners

Clinical pharmacists

Nurses

Involvement of the patient

Computerized support

Educational approaches