

Inappropriate drug prescribing in older adults

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Structure

- **What does appropriate prescribing mean?**
- **How should we identify subjects at risk of drug related problems (DRPs) and adverse drug reactions (ADRs)?**
- **How should we review prescribing for an older patient?**
- **Which tools and strategies can help us to reduce inappropriate 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 »

Categories of inappropriate prescribing

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

Is inappropriate prescribing frequent?

Inappropriate prescribing

- 186 patients admitted to an acute geriatric unit
 - Almost 60% of prescriptions: 1 inappropriate rating
 - 30% of patients were taking 1 drug-to-avoid
 - Under-prescribing in 50% of patients

Spinewine A et al. J Am Geriatr Soc 2007; 55:658–665

Over- and mis-prescribing

Table 3. Percentage of Drugs with Inappropriate Ratings on Admission and at Discharge Using the Medication Appropriateness Index (MAI)

MAI Criterion	Control		Intervention	
	Baseline (n = 633)	Discharge (n = 654)	Baseline (n = 728)	Discharge (n = 766)
				%
Indication	9.8	7.5	12.1	2.6
Choice	23.2	18.5	25.4	6.1
Dosage	28.0	25.1	26.5	6.8
Modalities correct	19.3	17.9	17.6	8.1
Modalities practical	15.0	16.8	17.3	3.3
Drug-drug interactions	7.4	6.7	7.3	1.3
Drug-disease interactions	18.8	15.4	18.1	4.6
Duplication	3.0	2.3	5.2	1.0
Duration	16.7	13.8	20.5	6.1
Cost	23.2	25.8	23.1	10.7
Overall*	59.9	64.5	59.8	27.3

* Inappropriate rating in at least 1 of the 10 criteria.

Under-prescribing

Condition

Osteoporosis

AF

IHD

HF

Myocardial
infarction

...

% patients undertreated

72%

40%: anticoag/aspirin

42%: aspirin

42%: ACEI

61%: β -blocker

...

Consequences of inappropriate prescribing

- **Drug related problems (DRPs) and Adverse drug reactions (ADRs)**
- **Drug interactions**
- **Duplication of drug therapy**
- **Decreased quality of life**
- **Medication non-adherence**
- **Unnecessary cost**

Consequences of inappropriate prescribing

- **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;50:1962-1968.

Increased vulnerability to ADRs in older people

Older people are 2-3 times more at risk for adverse drug reactions due to:

Pirmohamed M. BMJ 2004; 329:15-19

- altered pharmacokinetics
- altered pharmacodynamics
- cumulative insults to the body (eg. co-morbidity, polypharmacy)

Barat I. Br J Clin Pharm 2001;51:615-622

- non-compliance
- lack of available data
- medical errors

Tools and strategies to screen for and prevent DRPs/ADRs

- **Medication review**
- **Avoiding use of potentially inappropriate medications (PIM)**
- **Computer-based prescribing systems**
- **Comprehensive geriatric assessment (CGA)**

Petrovic M et al. Drugs Aging 2012; 29: 453-462

Onder G et al. Age Ageing 2013; 42: 284-291

Screening- identification of subjects at risk of ADR

- **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;159:2553-2560
 - An attempt to identify specific patient's characteristics associated with an increased risk: *restrospective study, relied on voluntarily reported ADRs, under reporting*
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: evidence

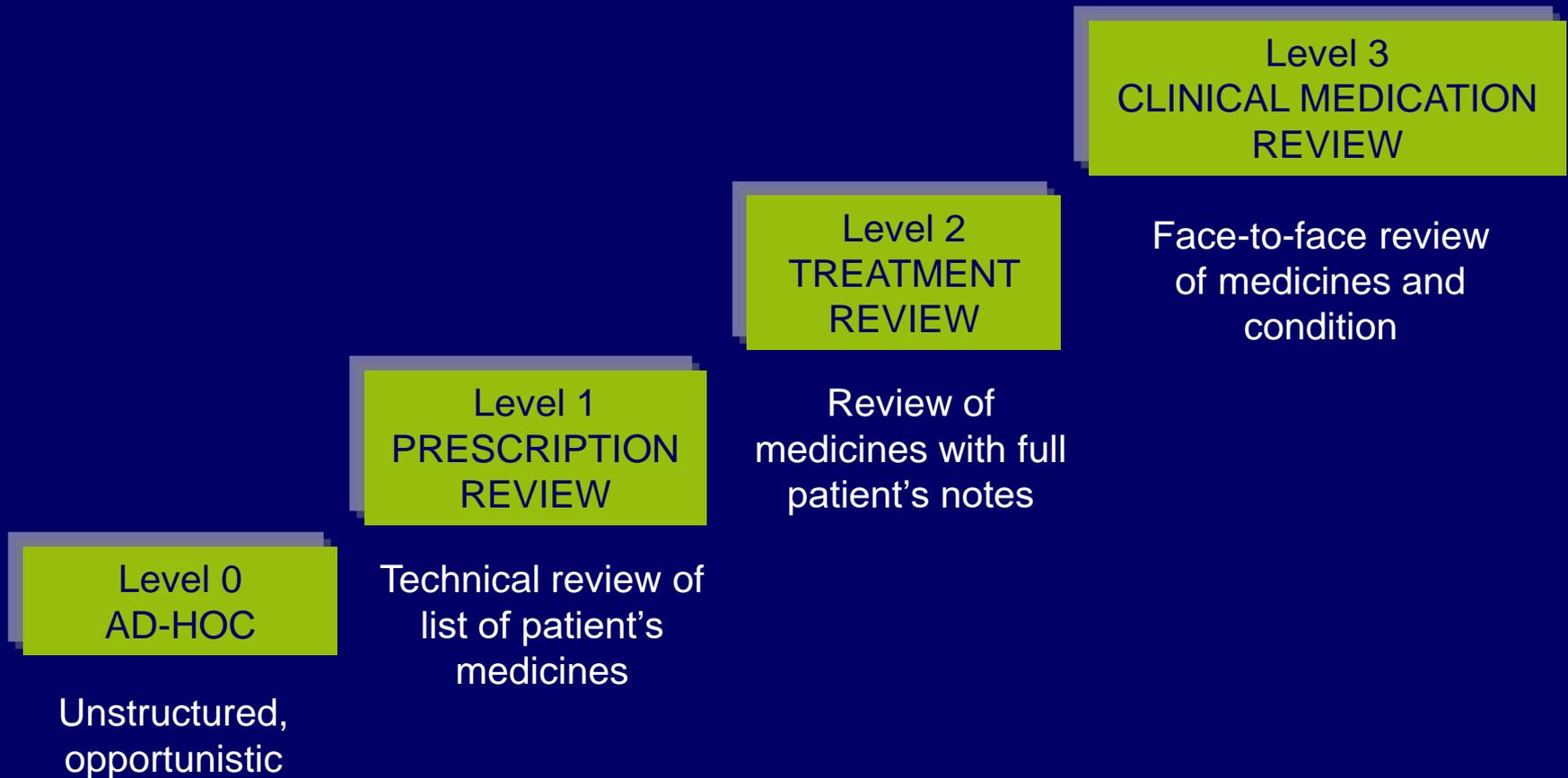
- **The GerontoNET ADR risk score represents the *only tool available so far* to identify patients at risk of ADR, which may be target of interventions aimed at reducing their risk of ADR**
- **However...**
 - *it still should be validated in different settings and studies*
 - *the need for identification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

O'Connor M. et al. Age Ageing 2012;41:771-776.

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



Reporting adverse drug reactions on a geriatric ward: *spontaneous reporting vs. patient interview (by pharmacists)*

	Patients	Patients with ADRs	Number of ADRs
spontaneous reporting	168	12	12
patient interview	56	23	32

Interviewed patients (n = 56)

	Mean	Median	Range
Age (years)	80.1	80.0	62 – 94
Length of stay (days)	18.6	14.0	4 – 61
Number of drugs			
patients with ADR (n=23)	9.3	8.0	6 – 16
patients without ADR (n=33)	8.3	9.0	3 – 14

Reporting adverse drug reactions on a geriatric ward: *spontaneous reporting vs. patient interview (by pharmacists)*

Results of the patient interview

Gender	Male	10	(43%)	
	Female	13	(57%)	
Causality	Probable	23	(72%)	
	Possible	9	(28%)	
Level	1 = no change			13 (41%)
	2 = stopped / dose changed			12 (37%)
	3 = stopped + additional therapy			7 (22%)
Severity	Serious ADR	12	(38%)	
	Non-serious ADR	20	(62%)	
Type	Type A	32	(100%)	
	Type B	0	(0%)	

Impact on appropriateness of prescribing

Geriatric medicine services

Coleman et al ¹⁰⁴	Nine primary care physician practices, USA	Nine intervention practices [cluster]; nine family doctors, 169 patients	Chronic care clinic including visit with geriatrician, nurse, and pharmacist	24 months	P: No significant improvements in the prescription of high-risk medications at 12 months (2.94 high-risk medications per patient in the intervention group vs 3.26 in the control group; $p=0.57$) and 24 months (1.86 vs 2.54, respectively; $p=0.20$) O: No difference in selected geriatric syndromes
Schmader et al ¹⁰⁵	11 Veteran Affairs hospitals and clinics, USA	834 patients	Multidisciplinary geriatric team care (including a geriatrician) for inpatients and outpatients (2x2 factorial design)	12 months	P: Higher improvements in the number of unnecessary drugs in intervention than in control patients (-0.6 vs +0.1, $p<0.0001$), inappropriate prescribing (47% decrease vs 25% increase in MAI score, $p<0.0001$), and number of conditions with underuse (-0.4 vs +0.1; $p<0.001$) in inpatients. Higher improvements in the number of conditions with underuse in intervention than in control outpatients (-0.2 vs +0.1; $p<0.0004$) O: Decreased risk of serious adverse drug reactions in outpatients
Saltvedt et al ¹⁰⁶	Single Hospital, Norway	254 patients	Multidisciplinary geriatric team care (including a geriatrician)	Until hospital discharge	P: Lower prevalence of potential drug-drug interactions in intervention than in control group at discharge ($p=0.009$, 36% decrease from admission to discharge vs 17%, respectively), and of anticholinergic medications ($p=0.03$, 78% vs 10% decrease, respectively); no difference in prescription of Beers' drugs ($p>0.05$, 60% vs 33% decrease, respectively)
Crotty et al ¹⁰⁷	Ten residential care homes, Australia	Ten facilities [cluster]; 154 residents	Two multidisciplinary case conference (including a geriatrician), 6-12 weeks apart	3 months	P: Higher improvements in prescribing appropriateness in intervention than in control group (55% decrease vs 10% decrease in MAI scores, $p=0.004$) O: No differences in resident behaviour
Strandberg et al ¹⁰⁸	Ambulatory care, Finland	400 patients with CVD	Geriatrician-driven treatment review plus nutritional and smoking recommendations	3 years	P: Significant increase in the use of evidence-based drugs in the intervention compared with control group (β blockers $p=0.02$, ACE-I $p=0.0001$, ARA $p=0.007$, statins $p<0.0001$) O: Significant improvements in blood pressure and cholesterol levels, but no difference in major cardiovascular events and total mortality

Impact on appropriateness of prescribing

RCT, 203 patients, one acute geriatric unit, Belgium

Pharmaceutical care from admission to discharge

- ↑ appropriateness of prescribing (MAI, ACOVE)
- 90% acceptance rate

- Trend toward ↓ mortality and ED visits

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

RCT, 400 patients ≥80y, 2 internal medicine wards, Sweden

Pharmaceutical care from admission to discharge(+ after)

- 16% ↓ hospital visits
- 46% ↓ ED visits
- 80% ↓ drug-related readmissions

Gillespie U et al. Arch Intern Med 2009;169:894-900

Medication review: evidence

- Good evidence that collaboration with pharmacists can decrease the risk of drug-related problems
- Mixed / lacking evidence for effect on:
 - Health outcomes
 - HRQoL
 - Cost-effectiveness of care

Chisholm-Burns Med Care. 2010;48:923-933

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

Avoiding use of potentially inappropriate medications (PIM)

Medication Assessment Tools

1) Explicit (criteria based): drugs to avoid

- Beers (1991, updates 1997, 2003, 2012, 2015)
- 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, 2015)

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)

■ Explicit

- criterion-based
- reviews, consensus, experts
- focus on drugs/diseases

■ Process

- prescription accords with accepted standards
- should have causal links to important outcomes

■ Implicit

- judgement-based
- focus on the patient

■ Outcome

- indicators of adverse outcomes

Avoiding use of potentially inappropriate medications (PIM)

■ 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

Beers criteria

- **Developed by expert group in US in 1991, updated in 1997, 2003, 2012, 2015**
- **Drugs with risk > benefit in older patients**
- **2 parts:**
 - non-recommended drugs in older people
 - conditionally non-recommended drugs
- O/M

Examples of non-recommended drugs in older people

Generic name

Propoxyphene
Indometacine
Phenylbutazone
Pentazocine
Oxybutynin
Flurazepam
Amitriptyline
Perphenazine-amitriptyline
Doxepine
Meproamate
Lorazepam > 3 mg daily
Oxazepam > 60 mg daily
Alprazolam > 2 mg daily
Temazepam > 15 mg daily
Zolpidem > 5 mg daily

Generic name

Triazolam > 0,25 mg daily
Diazepam
Digoxine > 0,125 mg daily
Dipyridamole
Methyldopa
Chlorpropamide
Belladonna alkaloids
Chlorpheniramine
Diphenhydramine
Hydroxyzine
Cyproheptadine
Promethazine
Dexchlorpheniramine
Ergot mesyloids
Iron suppelements > 325 mg daily
Ticlopidine

Conditionally non-recommended drugs in older people

Pathology	treatment
Heart failure	sodium containing drugs (sodium carbonate: effervescent tablets)
Gastric ulcer	NSAIDs, aspirin
Arrhythmia	Tricyclic antidepressants
Depression	methyldopa
Obesity	Olanzapine

Beers criteria



- Somme 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)

ACOVE criteria

- **Assessing Care Of the Vulnerable Elders**
 - Literature study + expert opinion
 - 22 pathologies, syndromes, clinical situations
 - 236 indicators (prevention, diagnosis, therapy, monitoring)
 - 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**



Criteria concerning therapy

Indication	Therapy
Diabetes	low dose aspirine
Diabetes with proteinuria	ACE inhibitor
Diabetes, TC > 240 g/dl	lipid lowering agent
Heart failure with LVEF < 40%	ACE inhibitor

Criteria concerning monitoring

Therapy	Monitoring
Digoxine, with symptoms of intoxication	determine plasma level within 24 hours
Anticoagulans	determine INR 3 days after initiation
Anticoagulans (chronic use)	determine INR monthly

Criteria concerning prevention

Therapy 1	Therapy 2
Corticoids during > 1 month	Start Calcium + Vitamine D
NSAID and hystory of peptic ulcer	PPI or misoprostol

ACOVE criteria



- Operationalisability
- No recent update



- Geriatric conditions included
- Encompass Tx, prevention, monitoring, education and documentation
- Applicable to patients with dementia and poor prognosis

STOPP / START criteria

- **Screening tool of older persons' potentially inappropriate prescriptions (STOPP)**
 - 80 criteria, O/M
- **Screening tool to alert doctors to the right treatment (START)**
 - 34 criteria, U

STOPP/START criteria

STOPP

- Aspirin > 150mg/d
- SSRI in case of clinically significant hyponatremia
- PPI for an ulcer in full therapeutic dose > 8 w

START

- Antidepressant in case of major depressive symptoms during at least 3 months

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

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;89:845-854.

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 anticoagulants; 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

Explicit instruments

- Pros of using explicit criteria in your daily practice
 - Relatively easy to remember and to detect
 - Provides support to identify inappropriate prescribing in the elderly

HOWEVER...

Explicit instruments

- **Cons of using explicit criteria in daily practice**
 - This is just one part of the story...
 - The patient's perspective is often not taken into consideration
- *We should not limit our evaluation to the application of such criteria*

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?

MAI



- Time consuming
- Knowledge-dependent

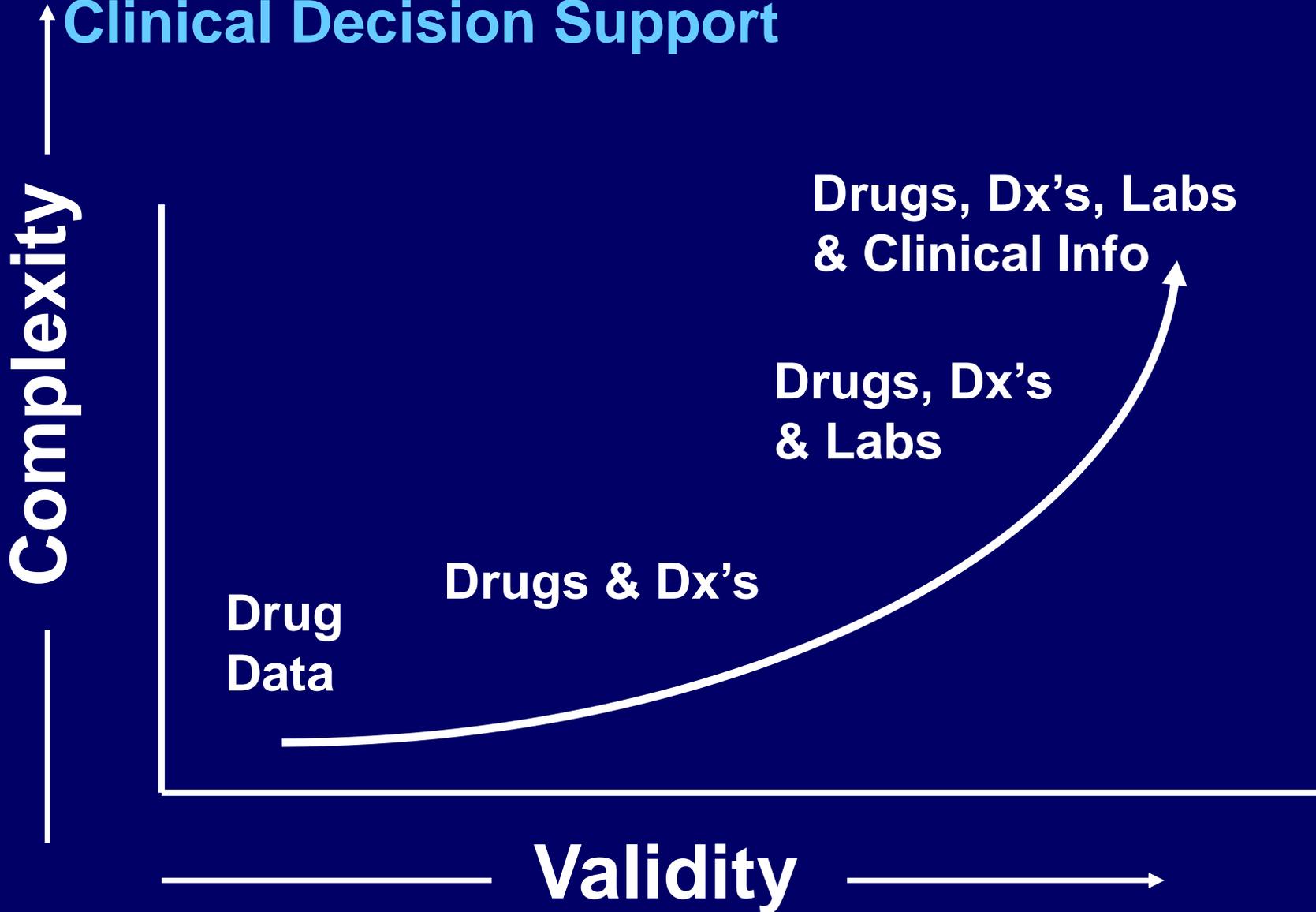


- Comprehensive and systematic
- Includes operational definitions, explicit instructions, and examples
- Excellent as an educational « tool » for students!

Computer-based prescribing systems

- Clinical Decisions Support Systems (CDSS) and Computerized Prescription Support System (CPSS) are interactive softwares, designed
 - As potentially powerful tools to prevent ADRs
 - To support at the time of prescribing
 - All categories of inappropriate prescribing can be addressed, if prescription data are linked to clinical data
- 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.

Translating Quality Measures into Clinical Decision Support



Computer-based prescribing systems

▪ Disadvantages

- Very few studies demonstrated an improvement in patient outcomes
- Challenging to implement
- Existing systems are not geriatric specific
- High volume of alerts: risk of unimportant warnings
- Some prescribers are reluctant to use

Gurwitz J et al. J Am Geriatr Soc 2008; 56: 2225-2233.

Wolfstadt J et al. J Gen Intern Med 2008;23:451-458.

Strom B et al; Arch Intern Med. 2010;170:1578-1583.

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.

Comprehensive geriatric assessment (CGA): evidence

- CGA in association with a 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

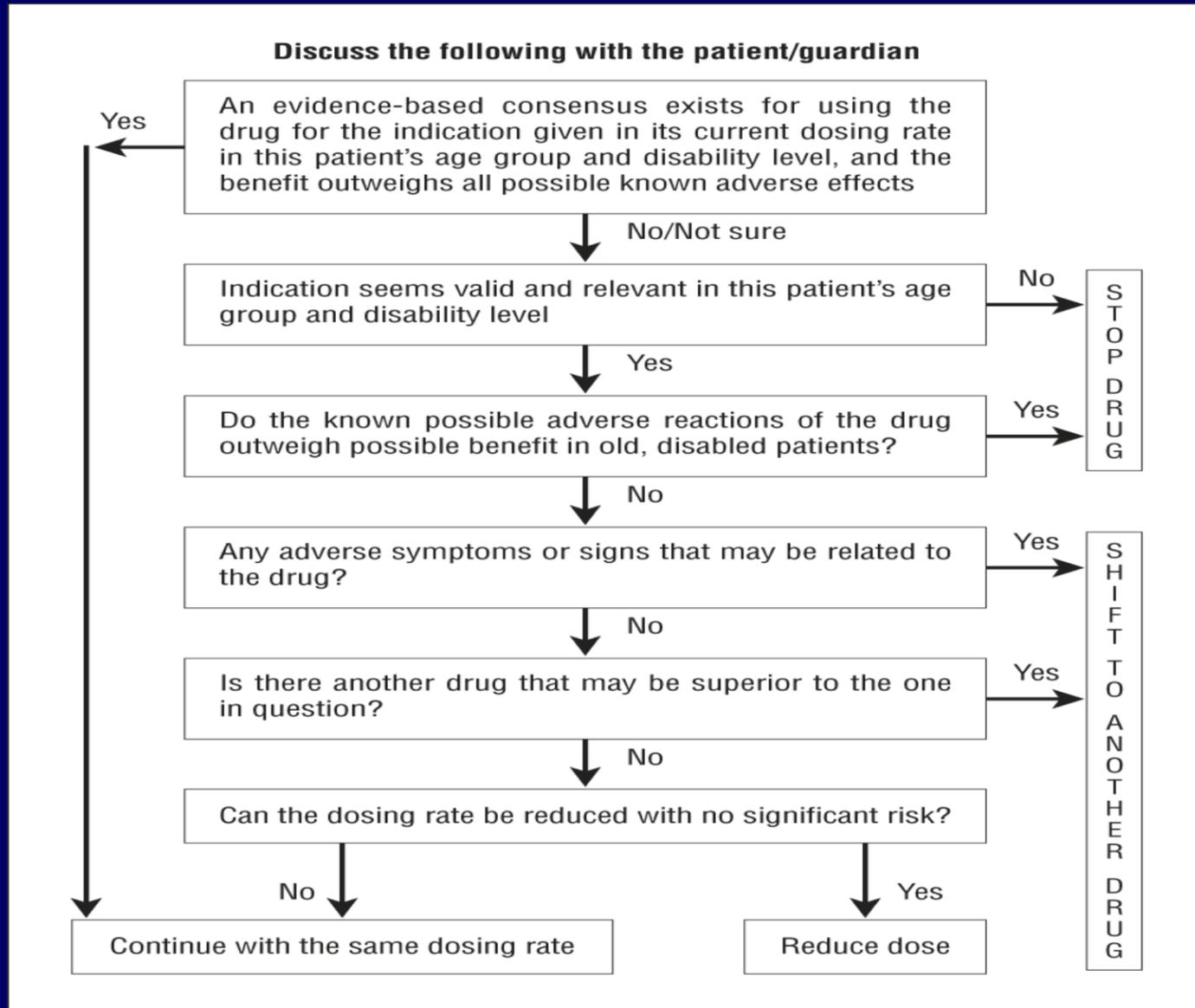
- CGA allows a complete and global assessment and management of the health care problems, *including evaluation of drugs* with the goal of recognizing and preventing potential drug-related problems and improve quality of prescribing.

Onder G et al. Curr Drug Metab 2011;12:647-651.

- 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.

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

Systematic approach for drug cessation in complex older adults



COLLABORATIVE CARE

- Multidisciplinary teams
 - Geriatric medicine services/CGA
 - Collaboration with
 - Clinical pharmacists
 - Nurses
 - Collaboration with the patient
-
- Computerized support
 - Educational approaches

THM: Conclusions

- None of the existing approaches shows 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.**

Development and clinical trials of a new Software ENgine for the Assessment & Optimization of drug and non-drug Therapy in Older peRsons



No	Partner Organization	Scientist
01	University College Cork, Ireland	Denis O'Mahony
02	University of Aberdeen, UK	Roy Soiza
03	Ghent University Hospital, Belgium	Mirko Petrovic
04	Helix Health Ltd, Dublin, Ireland	Noel Stenson
05	Hospital Universitario Ramón y Cajal, Madrid, Spain	Alfonso Cruz-Jentoft
06	Instituto Nazionale di Riposo e Cura per Anziani, Ancona, Italy	Antonio Cherubini
07	Health Economics Consulting, Norwich Medical School, Univ. of East Anglia, UK	Ric Fordham
08	Landspítali University Hospital, Reykjavik, Iceland	Adalsteinn Gudmundsson
09	University of Iceland, Reykjavik, Iceland	Anna Birna Almarsdóttir
10	GABO:mi Gesellschaft für Ablauf-organisation:milliarium mbH & Co. KG, Munich	Otilia Postea
11	ClinInfo S.A., Lyon, France	Patrick Chevarier

IGRIMUP

Invitation to join

- IGRIMUP (International Group for Reducing Inappropriate Medication Use & Polypharmacy), founded during IAGG 2013 in Seoul, Korea is an open group focused on preventing negative effects of drugs by avoiding polypharmacy and Inappropriate Medication Use (IMU).
- Researchers capable of promoting this goal in their country and/or internationally are welcome. Please feel free to forward us names of other leading figures, regardless of country or profession, that are interested in and willing to join the group.
- We hope that you will share your thoughts about the issues prevalent in your country's health care system on reducing inappropriate medication use, and ideas for change.

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