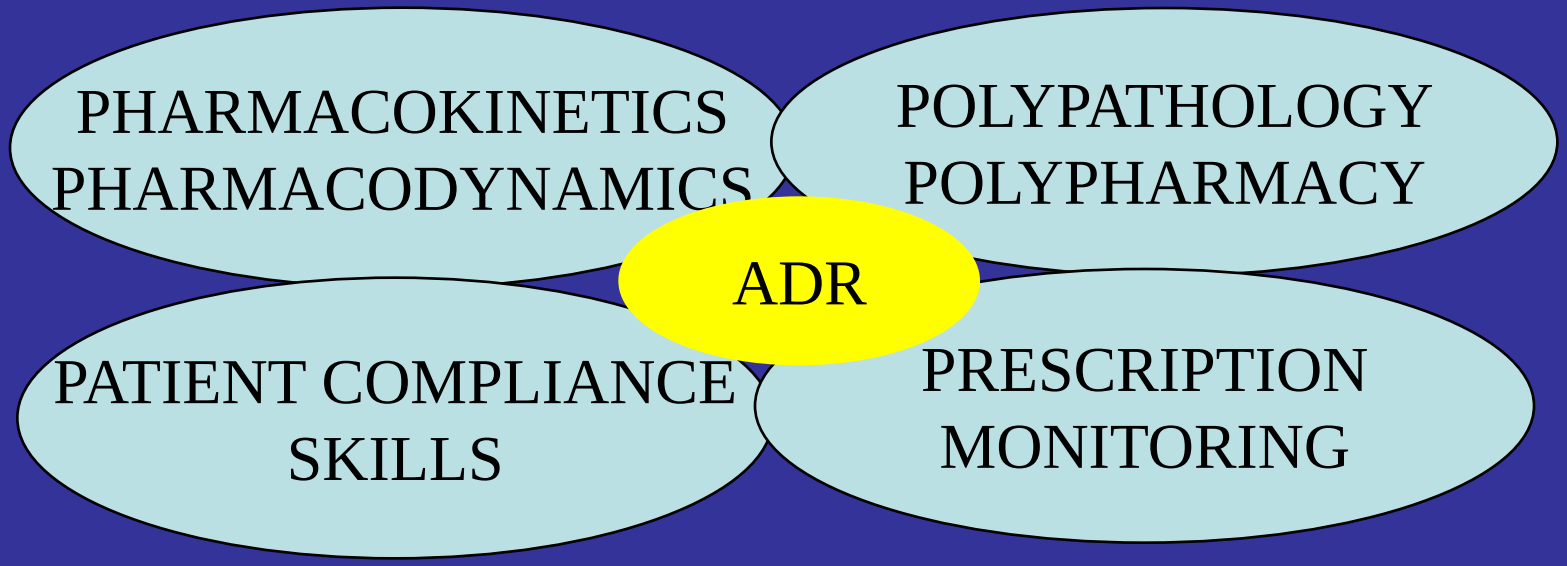
Interdisciplinary detection of potential drug related problems in older people

Prof. dr. Mirko Petrovic

Department of Internal Medicine, Ghent University
Department of Geriatrics, Ghent University Hospital,
Ghent, Belgium

Factors for ADRs in older people



Most important factor for ADRs is the number of prescribed drugs.

J Am Geriatr Soc 1996;44:194-7

Features of polypharmacy

Medication not indicated

Duplicate medications

Concurrent interacting medications

Contraindicated medications

Inappropriate dosage

Drug treatment of adverse drug reaction

Improvement following discontinuance

Structure

- 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 DRPs and ADRs?

Approaches to screen and prevent the occurrence of DRPs and ADRs

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

Case of Mrs. M.

Mrs. M is an 81 years old widow, living alone in her own house. She suffers from diabetes mellitus, hypertension, ischemic heart disease, glaucoma, osteoarthritis and osteoporosis. Her weight is 46 kg and she is 160 cm tall. Because of osteoarthritis she reports slowness and reduced level of physical activity.

She is currently on the following drugs: Atenolol 50 mg/day, Perindopril 5 mg/day, Pantoprazole 20 mg/day, Metformin 1000 mg/day, Hydrochlorothiazide 12.5 mg/day, Timolol eye drops (0.5%, twice daily in both eyes), ASA 100 mg/day, Diazepam 5 mg/day. Her blood pressure is 152/88 mmHg and her last HbA1c was 8.2%.

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 5-7 ≥ 8	 1 1.90 4.07	 1.35 - 2.68 2.93 - 5.65	 0 1 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

Brighton Adverse Drug Reactions Risk (BADRI) Model

	Odds Ratio	95% CI
Hyperlipidemia	3.32	1.81- 6.07
No of drugs ≥ 8	3.30	1.93 - 5.65
Length of stay ≥ 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

Tangiisuran B et al. PLos ONE 2014; 9: e111254

MRS. M
GerontoNet ADR risk score

- *Mrs. M presents with multiple risk factors for ADR, including co-morbidity and polypharmacy.*

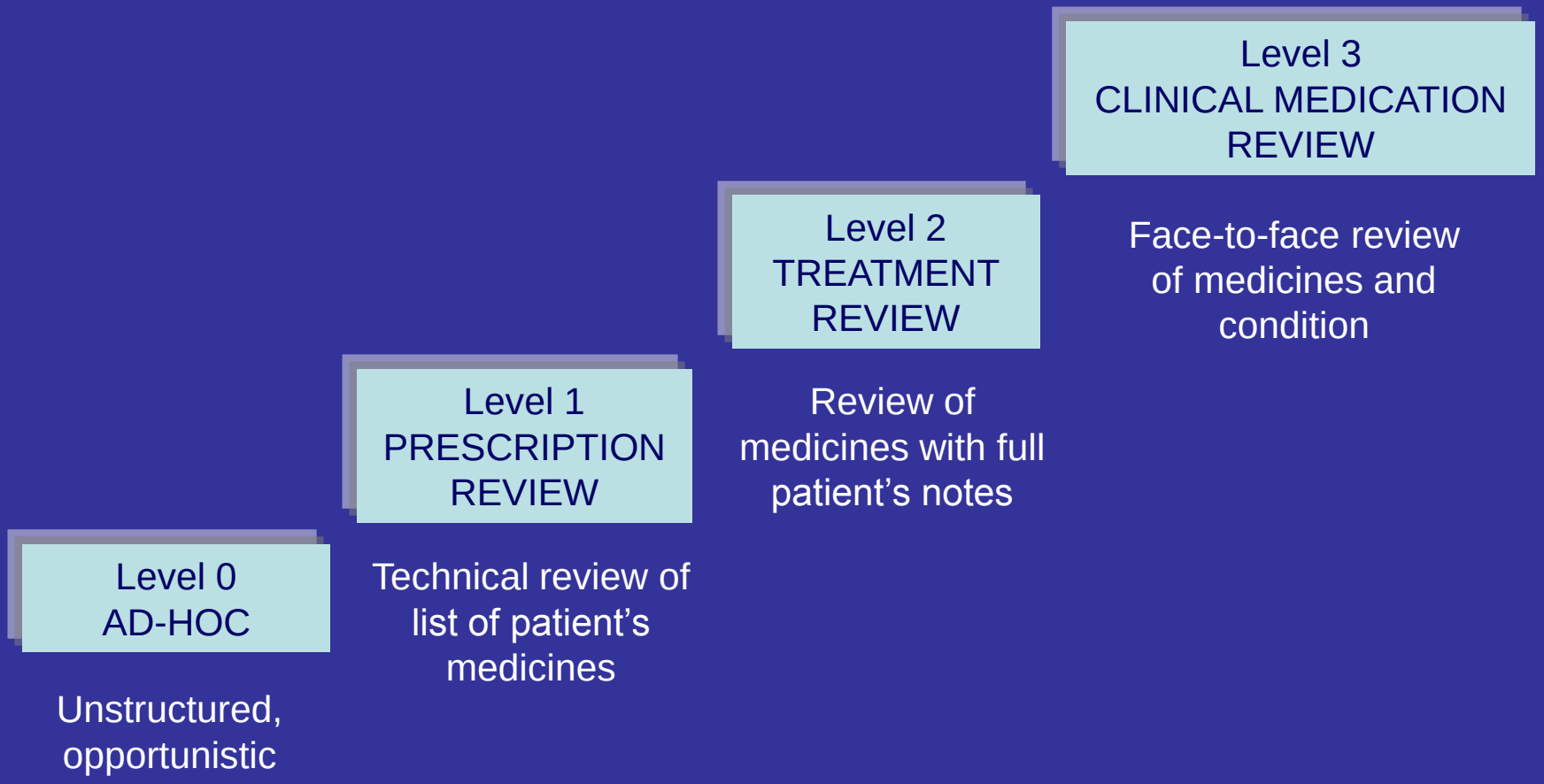
- *She screened positive on the risk of ADR based on the GerontoNet ADR risk score*
  - *(score=5; ≥ 4 co-morbid conditions: 1 point and ≥ 8 drugs: 4 points), suggesting a high risk for ADR and the need for an intervention to prevent the risk of ADR.*

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

	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

Somers A et al. Eur Clin Pharmacol 2003;58:707-14

Reporting adverse drug reactions on a geriatric ward: spontaneous reporting vs. patient interview

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%)

Somers A et al. Eur Clin Pharmacol 2003;58:707-14

Impact on appropriateness of prescribing

RCT, 203 patients, one acute geriatric unit, Belgium	RCT, 400 patients ≥80y, 2 internal medicine wards, Sweden
Pharmaceutical care from admission to discharge	Pharmaceutical care from admission to discharge(+ after)
- ↑ appropriateness of prescribing (MAI, ACOVE) - 90% acceptance rate	- 16% ↓ hospital visits - 46% ↓ ED visits - 80% ↓ drug-related re-admissions
- Trend towards ↓ mortality and ED visits	
Spinewine A et al. J Amer Geriatr Soc 2007; 55:658-65	*Gillespie U et al. Arch Intern Med 2009;169:894-900*

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 (2×2 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

Spinewine et al. Lancet 2007;370:173-84.

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
  - HR QoL
  - Cost-effectiveness of care

Chisholm-Burns Med Care. 2010;48:923-933
Spinewine et al. Drugs Aging. 2012;29:495-510.

Mrs. M
Medication review

1. *Structured pharmaceutical anamnesis: information of the GP and the community pharmacist is gathered. Specific questions on use of drugs easily forgotten (such as sleeping pills, inhaled drugs, over-the-counter drugs and supplements and drugs on an 'as needed' basis) and on time and mode of administration are asked.*

2. *Structured screening for drug related problems (DRPs): drugs are assessed for indication, correct dose, choice of the appropriate treatment, frequency and time of intake. Drug-drug interactions, presence of ADRs and under prescribing are also assessed.*

Mrs. M
Medication review

- *Potential DRPs related to the case of Mrs M are the following:*
  - *Perindopril, hydrochlorothiazide, and metformin: are doses adjusted for renal function?*
  - *Metformine: the HbA1C-level is not satisfactory and attempts should be made to improve glucose control, but with due regard to avoiding hypoglycaemic episodes.*
  - *Diazepam: inappropriate in older adults because of increased risk of falls*
  - *Calcium/vitamin D and bisphosphonate may be necessary given the diagnosis of osteoporosis*
  - *Pantoprazole: no clear indication*
  - *Atenolol: not the best choice for the treatment of hypertension*
  - *Timolol: combined use of timolol and atenolol can increase the risk of symptomatic bradycardia and falls*

3. *This list is then discussed with the treating physician and a plan for implementation and evaluation is created.*

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, update 2015)

2) Implicit (judgement based):

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

STOPP: Screening Tool of Older People's potentially inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥65 years of age.

Cardiovascular System

1. Digoxin at a long-term dose > 125μg/day with impaired renal function*
2. Loop diuretic for dependent ankle oedema only i.e. no clinical signs of heart failure
3. Loop diuretic as first-line monotherapy for hypertension
4. Thiazide diuretic with a history of gout.
5. Non-cardioselective beta-blocker with Chronic Obstructive Pulmonary Disease (COPD).
6. Beta-blocker in combination with verapamil
7. Use of diltiazem or verapamil with NYHA Class III or IV heart failure
8. Calcium channel blockers with chronic constipation
9. Use of aspirin and warfarin in combination without histamine H2 receptor antagonist (except cimetidine because of interaction with warfarin) or PPI
10. Dipyridamole as monotherapy for cardiovascular secondary prevention
11. Aspirin with a past history of peptic ulcer disease without histamine H2 receptor antagonist or proton pump inhibitor
12. Aspirin at dose > 150mg day
13. Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event
14. Aspirin to treat dizziness not clearly attributable to cerebrovascular disease
15. Warfarin for first, uncomplicated deep venous thrombosis for > 6 months
16. Warfarin for first uncomplicated pulmonary embolus for > 12 months
17. Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder

** eGFR <50ml/min.*

Central Nervous System and Psychotropic Drugs

1. Tricyclic antidepressants (TCA's) with dementia
2. TCA's with glaucoma
3. TCA's with cardiac conductive abnormalities
4. TCA's with constipation
5. TCA's with an opiate or calcium channel blocker
6. TCA's with prostatism or prior history of urinary retention
7. Long-term (i.e. > 1 month), long-acting benzodiazepines e.g. chlordiazepoxide, fluazepam, nitrazepam, chlorazepate and benzodiazepines with long-acting metabolites e.g. diazepam
8. Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics
9. Long-term neuroleptics in those with parkinsonism
10. Phenothiazines in patients with epilepsy
11. Anticholinergics to treat extra-pyramidal side-effects of neuroleptic medications
12. Selective serotonin re-uptake inhibitors (SSRI's) with a history of clinically significant hyponatraemia
13. Prolonged use (> 1 week) of first generation antihistamines i.e. diphenydramine, cyclizine, chlorpheniramine, promethazine

Single entry for the 81 STOPP.v2 criteria (Screening Tool of Older Person's Prescriptions, version 2)

	STOPP.v2 : medication	& clinical condition → potentially inappropriate medication : consider deprescribing
ANY	**Drug without clinical indication, beyond recommended duration, or duplicate drug class**	in any circumstances
NEURO PSYCHOTROPICS	**Benzodiazepines**	in any circumstances *a fortiori* if for > 4 weeks [dose to be to decreased progressively] respiratory failure
	Hypnotic Z-drugs	in any circumstances (zopiclone, zolpidem, zaleplon)
	Neuroleptics	in any circumstances *a fortiori* if prostatism/ urinary retention & moderated-marked anticholinergic effects parkinsonism or Lewy Body Disease (except quetiapine or clozapine) behavioural and psychological symptoms of dementia (BPSD) unless severe sleep disorder (unless due to psychosis or dementia) phenothiazine as first-line treatment
	TCA (TriCyclic Antidepressant) [because anticholinergic]	& first-line antidepressant treatment & dementia, narrow angle glaucoma, cardiac conduction abnromalities, or prostatism
	SSRI (Serotonin re-uptake inh.)	& hyponatremia (Na^+ < 130mmol/l) current or recent
	Acetylcholinesterase inhib.	& asthma, bradycardia, heart bloc, or unexplained syncopes
	Levodopa / dopamin agonists	& benign essential tremor
	Opioïd, strong	& first-line therapy for mild pain
HEMOSTASIS	Aspirin [see also next line]	& doses > 160 mg per day, long term & peptic ulcer disease history, without concomittant PPI & oral anticoagulant for chronic atrial fibrillation & clopidogrel for 2d stroke prevention (unless concurrent acute coronary syndrome, coronary stent < 12 months, or high grade symptomatic carotid stenosis)
	Antiplatelet [Aspirin included]	& significant bleeding risk (severe hypertension, bleeding diathesis, recent bleeding) & oral anticoagulant in stable atherosclerotic disease in any circumstances, **ticlopidine**
	Oral anticoagulant	& significant bleeding risk (severe hypertension, bleeding diathesis, recent bleeding) & DVT/PE : > 6 months for first DVT; >12 months for first PE & GFR < 30 ml/min for dabigatran & GFR < 15 ml/min for rivaroXaban, apiXaban
CARDIOVASCULAR	Digoxin	& heart failure with normal systolic ventricular function & eGFR< 30ml/min if dose > 125 µg/day long-term
	Amiodarone	& supraventricular tachyarrhythmias, first-line therapy
	βeta-blocker	& verapamil or diltiazem & bradycardia (< 50/min), type II heart bloc bloc AV & asthma requiring treatment if non-selective βeta-blocker (carvedilol, sotalol, ...) & diabetes mellitus with frequent hypoglycemic episodes
	Diltiazem/verapamil	& class III ou IV heart failure
	ACE inhib. or ARBlockers	& hyperkalaemia
	Aldosterone antagonists	& potassium-conserving drug (ACEI, ARB, amiloride, triamtérène) without K^+ monitoring
	Thiazide diuretic	& ion abnormality (K^+< 3,0 mmol/l; Na^+ < 130mmol/l; corrected Ca^{++} > 2,65mmol/l) ; gout
	Loop diuretic	& first-line therapy for hypertension, or with concurrent unirnary incontinence & dependant ankle oedema (no cardiac, liver, renal failure, nor nephrotic syndrome)
	Centrally-active antihypertensives	& no clear intolerance or inefficacy of other classes of antihypertensives
	Sildenafil/tadalafil/vardenafil	& severe heart failure with hypotension (BP < 90mmHg) or concurrent nitrate therapy
	Vasodilatator drugs	& persistant postural hypotension (anti-calcium channel blocker, nitrates, α_1-blockers
ENDOCR	Metformin	& eGFR < 30 ml/min
	Sulphonylureas long duration	in any circumstances (glibenclamide, chlorpropamide, glimépiride for type 2 diabetes))
	Thiazolidenediones	& heart failure (rosiglitazone, pioglitazone)
	Oestrogens (oral or transcutaneous)	& history of breast cancer or venous thromboembolism & intact uterus, without progestogen
	Androgens	& hypogonadism, primary or secondary
GI	PPI	& full dosage > 8 weeks for uncomplicated peptic œsophagitis or gastric ulcer disease
	Oral elemental iron	& doses > 200 mg/day (fumarate > 600, sulphate > 600, glucomnate > 1800 mg/day)
	Metoclopramide	& parkinsonism
	Drugs causing constipation	& chronic constipation, when non-constipating alternatives are available

	STOPP.v2 : medication	& clinical condition → potentially inappropriate medication : consider deprescribing
MUSCULOSKELETAL	NSAID	& eGFR < 50 ml/min & severe hypertension or severe heart failure & COX-2 selective and high cardiovascular risk & oral anticoagulant ; or antiplatelet agent without IPPI & history of peptic ulcer disease or GI bleeding, without PPI ou H2-antagonist & concurrent corticosteroïds without PPI & osteoarthritis, > 3 months, first-line therapy & gout, > 3 months, with no contraindication to xanthine-oxydase inhibitors (allopurinol, ..)
	Oral biphosphonates	& upper GI disease (oesophagitis, gastritis, peptic ulcer disease, bleeding, ...)
	Colchicine	& eGFR < 10 ml/min & gout, > 3 months, with no contraindication to xanthine-oxydase inhibitors (allopurinol, ..)
	Corticosteroïds	& osteoarthritis (other than periodic intra-articular injections) & rhumatoïd arthritis, monotherapy, > 3 months
RESPI	Corticosteroïds, systemic	& moderate-severe COPD, maintenance therapy (instead of inhaled)
	Theophylline	& monotherapy for COPD
	Anticholinergic bronchodilatator	& narrow angle glaucoma & bladder outflow obstruction
	Antihistamines 1st generation	in any circumstances
	Anticholinergics (bronchodilators, TCA, anti-H1, bladder/GI antispasmodic,...)	& dementia, chronic cognitive impairment, delirium, narrow angle glaucoma, prostatism & extra-pyramidal side-effects of neurolpetics ≥ 2 concomittantly

Single entry for the 34 START.v2 criteria (Screening Tool to Alert to Right Treatment, version 2)

	START.v2 : clinical condition	→ potentially inappropraite omission : consider prescribing
MUSCULO	Falls, ostepopenia, housebound	→ vitamin D (≥ 800 à 1000 IU/day)
	Osteoporosis and/or fragility fracture	→ vitamin D + calcium + bone anti-resorptive/anabolic therapy
	Systemic corticosteroïd (>3 months)	→ vitamin D + calcium + bone anti-resorptive/anabolic therapy
	Rhumatoïd arthritis, active & disabling	→ disease-modifying anti-rheumatic drug (methotrexate, rituximab, etanercept...)
	methotrexate	→ folic acid
	Gout, recurrent episodes	→ xanthine-oxydase inhibitor, long-term
CARDIO	Hypertension (>160/90 mmHg)	→ antihypertensive therapy
	Atrial fibrillation	→ oral anticoagulant (if major contraindictation, aspirin 75 - 160 mg/daily)
	Atherosclerosis, documented coronary	→ antiplatelet agent ; + statin if < 85 years + ACEI
	Ischaemic heart disease	→ βeta-blocker
	Systolic heart failure	→ ACEI + βeta-blocker if stable (bisoprolol, nébivolol, métoprolol, carvedilol)
	Diabetes, blood pressure >140/90 proteinuria	→ antihypertensive therapy → IECA (if intolerant of ACEI : ARB)
NEURO PSY	Anxiety, severe	→ SSRI (if SSRI contraindicated : duloxetine, venlafaxine, prégabaline)
	Depressive symptoms, major	→ antidepressant drug (non-tricyclic) if persistant
	Parkinson disease, disabling	→ L-DOPA ou dopamine agonist
	Alzheimer's dementia, mild-moderate	→ acetylcholinesterase inhibitor (donepézil, rivastigmine, galantamine)
	Lewy Body dementia	→ rivastigmine
	Restless legs syndrome	→ dopamine agonist, after exclusion of iron deficiency and severe renal failure
	Pain, moderate-severe	→ high-potency opioïds, after failure of paracetamol, NSAID, low-potency opioïds
	Pain, break-through	→ short-acting opioïds
	Pain, regular opioïds	→ laxative
	Glaucoma, open angle	→ topical therapy (prostaglandin, prostamide or β-blocker)
RESPI	Asthma or COPD	→ mild to moderate : inhaled bronchodilatator (β2-agonist ou anticholinergic) → moderate to severe : inhaled corticosteroïd
	Hypoxaemia (SaO^2 < 89%), chronic	→ home continuous oxygen
	Infections	→ influenza vaccine annually + anti-pneumococcal vaccine at least once
GI	Gastro-œsophagal reflux, severe	→ PPI
	Colic diverticulosis and constipation	→ Fibers supplements
	Atrophic vaginitis, symptomatic	→ topical oestrogens
	Prostatism, symptomatic	→ if prostatectomy non-considered : α1-blocker; 5α-réductase inhibitor

Courtesy: Prof. B. Boland, Univ. Louvain

Older patients with polypharmacy

1. Systematic Review
2. **Development of GheOP³S-tool**
3. Validation of GheOP³S-tool
4. Observational research in community-dwelling older patients
5. Observational research in nursing home residents

STEP 1

Literature search

STEP 2

Selection of clinical relevant items for primary care

STEP 3

Selection of feasible items for community pharmacy practice

↓↓↓

GheOP³S-tool

Ghent Older People Prescriptions community Pharmacy Screening Tool

83 items / 5 parts

Explicit instruments

- Pros of using explicit criteria in our daily practice
  - Relatively easy to remember and to detect
  - Provide support to identify inappropriate prescribing in older people

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. Clinically significant drug-drug interactions?
7. Clinically significant drug-disease interactions?
8. Duplication?
9. Appropriate duration?
10. Cost?

Hanlon et al. Am J Med 1996;100:428-437

Original MAI index

Question per drug	Weight
1. Indication	3
2. Effectiveness	3
3. Dosage	2
4. Correct directions	2
5. Practical directions	1
6. Drug – drug interactions	2
7. Drug – disease interactions	2
8. Duplication	1
9. Duration	1
10. Expense	1

Adapted MAI index

Question per drug	Weight
1. Indication	3
2. Right choice	3
3. Dosage	2
4. Directions	*1*
5. Drug – drug interactions	2
6. Drug – disease interactions	2
7. Duration	1
8. Adverse drug reactions	*2*

Somers A et al. Am J Geriatr Pharmacother. 2012;10:101-109

Implicit intruments

- Time consuming
- Knowledge-dependent

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

Hanlon et al. Am J Med 1996;100:428-437

Mrs. M
Avoiding use of PIM

Beers and START and STOPP criteria identified the following concerns about Mrs. M treatment:

Beers 2012 criteria

- *Diazepam: increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents*

STOPP

- *Diazepam: risk of prolonged sedation, confusion, impaired balance, falls.*
- *Atenolol: risk of masking hypoglycemic symptoms*
- *Pantoprazole: if full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated)*

START

- *Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, where the patient's functional status remains independent for activities of daily living and life expectancy is greater than 5 years*
- *Calcium and vitamin D supplement in patients with known osteoporosis*

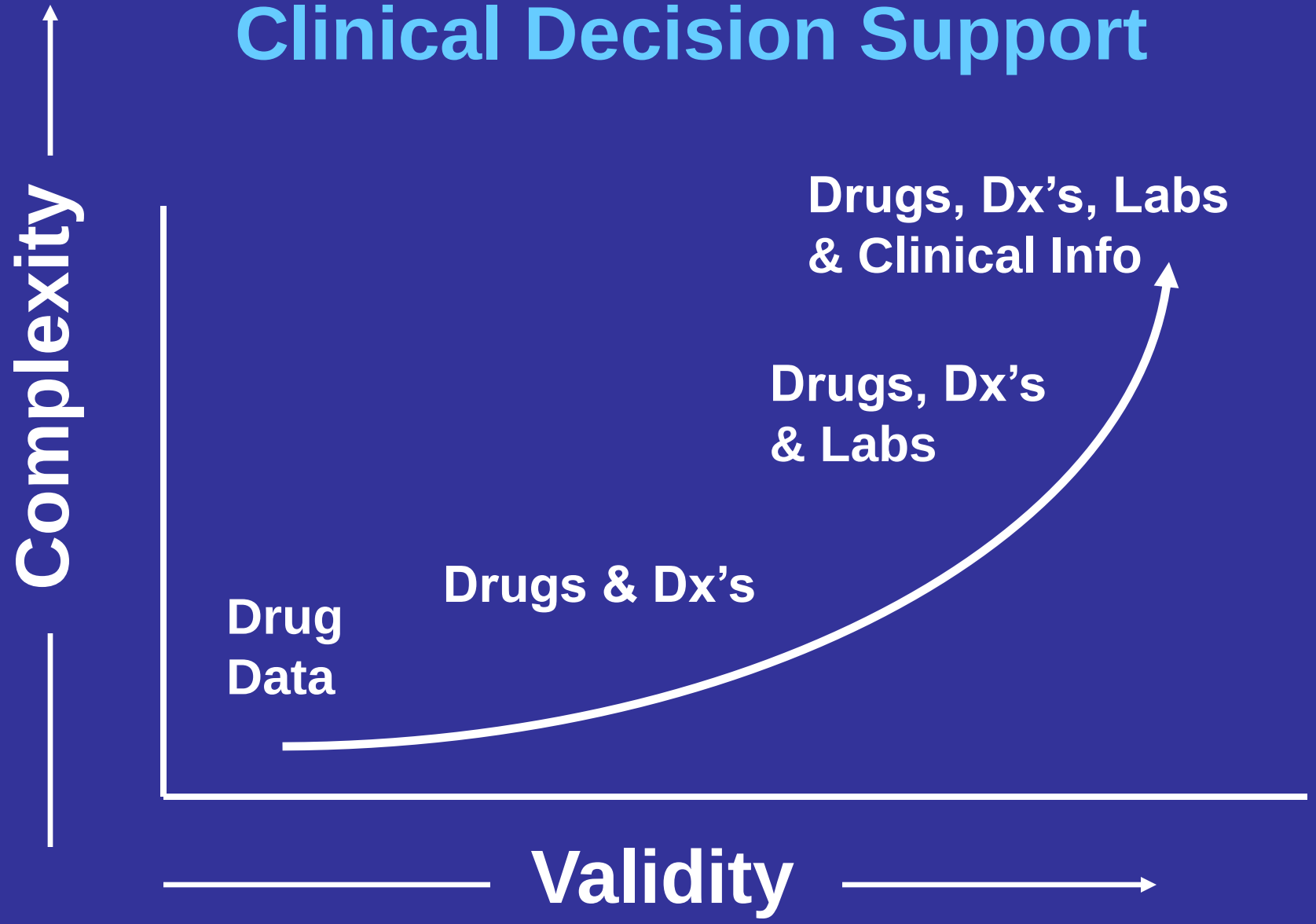
Computer-based prescribing systems

- 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.

Schiff G et al. JAMA 1998; 279: 1024-9.

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 Inten Med 2008;23:451-458.
Strom B et al; Arch Intern Med. 2010;170:1578-1583.

Mrs. M
Computer-based prescribing systems

The following warning messages are taken from the CPSS developed by the Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy

Drug interactions:

1) Pantoprazole- Hydrochlorothiazide (moderate risk): increased risk of hypomagnesaemia in case of prolonged use of PPI

2) Perindopril- Hydrochlorothiazide (moderate risk): increased risk of hypotension at the first dose

3) Metformin- Atenolol (moderate): risk of masking hypoglycemic symptoms

Inappropriate drug use:

- *Diazepam (Beers 2003, Beers 2012, STOPP): risk of prolonged sedation, confusion, impaired balance, falls*
- *Atenolol (STOPP): risk of masking hypoglycemic symptoms*
- *Pantoprazole (STOPP): if full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated)*

Mrs. M
Computer-based prescribing systems

Underuse of drugs:

Statin (START): statin therapy is indicated with a documented history of coronary, cerebral or peripheral vascular disease, where the patient's functional status remains independent for activities of daily living and life expectancy is greater than 5 years

Calcium and vitamin D (START): Calcium and vitamin D supplement in patients with known osteoporosis

Anticholinergic Cognitive Burden (ACB scale):

Atenolol=1; Diazepam=1

Total score = 2 - moderate anticholinergic effect

Mrs. M
Computer-based prescribing systems

Dose:

The following drugs need dose adjustment based on creatinine clearance:

Perindopril, Atenolol, Metformin, Hydrochlorothiazide

GerontoNet

GerontoNet ADR risk score ≥4, suggesting a high risk for ADR.

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 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,
  - not be assumed correctly because of presence of cognitive deficits, disability or social problems or
  - 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 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.

Mrs. M
Comprehensive geriatric assessment

… the CGA identifies several problematic areas of Mrs. M which may limit the use of drugs:

- *Malnutrition –The use of multiple drugs may impair appetite and reduce food intake. In particular metformin may cause anorexia and weight loss. Mrs. M is underweight (BMI < 18 kg/m2) and for this reason treatment with metformin should be reconsidered and opportunity to reduce in the overall number of drugs should be evaluated.*

- *Social problems and frailty – Lack of social support and frailty may suggest potential difficulties in managing complex drug regimens and possible problems in drug adherence. In particular, applying a tight blood pressure and glycaemic control to Mrs. M may be problematic because of potential medication errors and severity and consequences of ADR may be accentuated by these factors.*

Mrs. M
Comprehensive geriatric assessment

- *Falls – Mrs. M presents several risk factors for falls, including polypharmacy, use of benzodiazepines and diuretics and functional limitations (slowness). Therefore the CGA identifies her as a person at high risk for fall. This suggests the need to reduce the number of used drugs and withdrawal from the use of benzodiazepines and diuretics. Vitamin D supplementation may be considered given its positive effects on osteoporosis and falls and its safe profile.*

- *Limited life expectancy – given the presence of the malnutrition, frailty, co-morbidities and advanced age, life expectancy of Mrs. M might not be long enough to get benefit from intensive drug treatment. For example, tight glycaemic control may be unrewarding if life expectancy < 5 years.*

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.

COLLABORATIVE CARE

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

http://www.senator-project.eu

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 Ramõn 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	Landspitali University Hospital, Reykjavik, Iceland	Adalsteinn Gudmundsson
09	University of Iceland, Reykjavik, Iceland	Anna Birna Almarsdottir
10	GABO:mi Gesellschaft für Ablauf-organisation:milliarium mbH & Co. KG, Munich	Otilia Postea
11	ClinInfo S.A., Lyon, France	Patrick Chevarier