



**GHENT
UNIVERSITY**

POLYPHARMACY AND PREVENTION OF DRUG RELATED PROBLEMS

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POLYPHARMACY IN OLDER PATIENTS

POLYPHARMACY

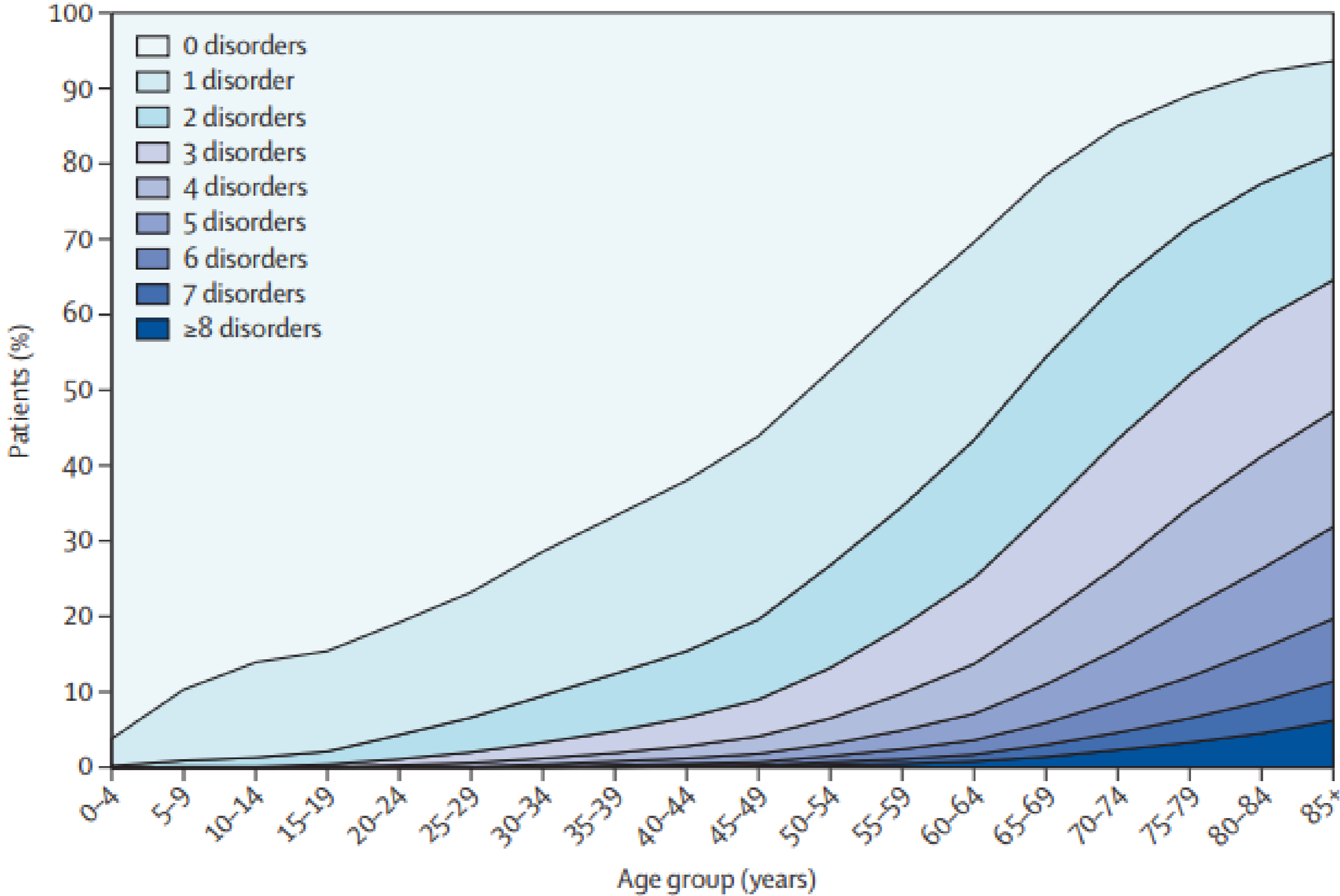
- ≥ 5 medicines
- Prevalence is high, especially in the older population
- Associated with adverse outcomes
 - Mortality
 - Falls
 - Adverse drug events
 - Increased length of stay in hospital
 - Readmission to hospital soon after discharge



FREQUENT PATHOLOGIES & MEDICINES IN OLDER PATIENTS

- Pathologies
 - Heart failure
 - Hypertension
 - Arthrosis
 - Depression
 - Sleep disorders
 - Psychosis
 - Amnesia, dementia
 - Stomach & intestinal problems
 - Diabetes type II
 - Parkinson's disease
 - ...
- Medicines
 - ACE/ARB, diuretics, beta blockers...
 - Antihypertensive drugs
 - Analgesics & NSAIDs
 - Antidepressants
 - Hypnotics
 - Neuroleptics
 - Neuroleptics, anti-Alzheimer's medication
 - Acid inhibitors, anti-diarrheal, laxatives
 - Antidiabetics
 - Anti-parkinson drugs
 - ...

FREQUENT PATHOLOGIES & MEDICINES IN OLDER PATIENTS



WHAT IS THE GOAL

NOT: reducing polypharmacy

BUT: increasing appropriateness of therapy

DRUG RELATED PROBLEMS IN OLDER PATIENTS

DRUG RELATED PROBLEMS (DRP)

- A Drug Related Problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes
- 3 types
 - Overuse (no indication)
 - Misuse (wrong use, but there is an indication)
 - Underuse (no treatment, but there is an indication)

DRUG RELATED PROBLEMS (DRP)

- Causes
 - Inappropriate prescribing (physician, pharmacist)
 - Inappropriate information (physician, pharmacist, nurse)
 - Inappropriate medication adherence (physician, pharmacist, nurse)
 - Inappropriate follow-up/monitoring (physician, pharmacist)

AGE-RELATED CHANGES IN MEDICATION METABOLISM

- Pharmacodynamic changes: from concentration to effect
 - Larger or longer-lasting decrease in blood pressure when using antihypertensive drugs
 - Increased risk of orthostatic hypotension with antihypertensive drugs, α -blockers or CNS agents
 - Hypovolemia due to insufficient fluid intake, use of diuretics or acute illness

AGE-RELATED CHANGES IN MEDICATION METABOLISM

- Pharmacokinetic changes: from dosage to concentration
- Decrease of renal function

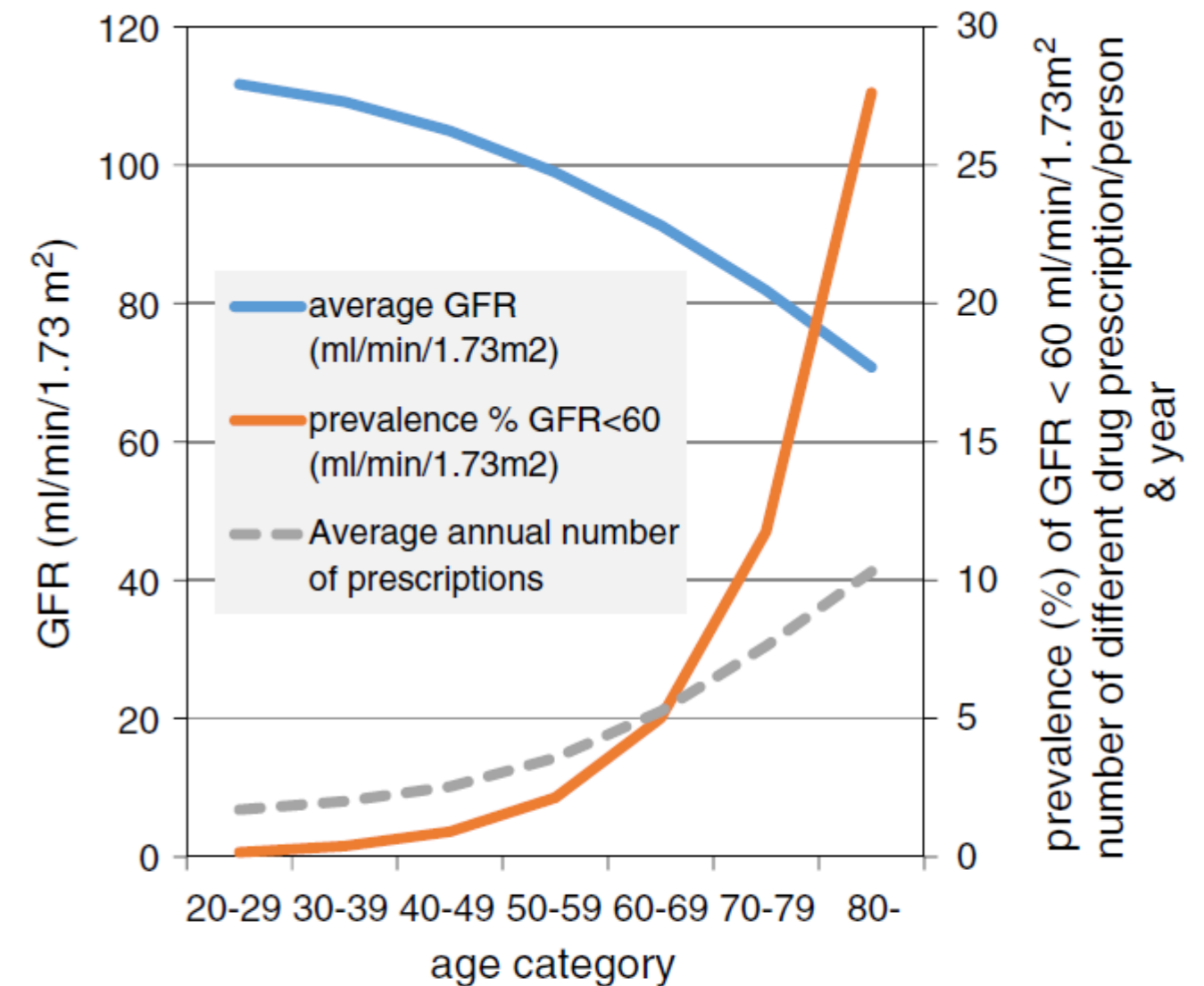


Fig. 1 The average GFR (mL/min/1.73 m²) (left y axis in the figure), the prevalence of lowered renal function (<60 mL/min/1.73 m²) (right y axis in the figure), and the average number of annual prescriptions in different age categories in Sweden 2011 (right y axis). Data regarding median GFR and the prevalence of lowered eGFR are adopted and modified from [22, 23]. *GFR* glomerular filtration rate

AGE-RELATED CHANGES IN MEDICATION METABOLISM

- Dose adjustments of drugs based on renal function
 - Antidiabetics
 - ACE/ARB
 - Diuretics
 - DOACs/LMWHs
 - Allopurinol, colchicine
 - Antibiotics (aminoglycosides, amoxyclav, chinolones...)
 - ...



ADVERSE DRUG EVENTS (ADE) IN OLDER PATIENTS

- Falls (CNS agents, antihypertensive drugs, antidepressants, hypnotics, beta-blockers)
- Electrolyte disorders due to antihypertensive drugs
 - Hypo Na & hypo K by diuretics, hyper K by ACE/ARB, spironolactone
- Confusion, sedation by (combination of) psychotropic drugs, antidepressants, neuroleptics, hypnotics
- Hypoglycemia due to antidiabetics
- Bleeding due to anticoagulants, NSAIDs
- Kidney failure by NSAIDs

HOSPITAL ADMISSION DUE TO DRP

Author	Reference	DRPs	Incidence
Beijer	Pharm World Sci 2002;24:46-54	ADR	17%
Mannesse	Age Ageing 2000;29:35-39	ADR	12%
Nelson	Pharmacother 1996;16:701-07	ADR + DTF	16%
Cunningham	Age Ageing 1997;26:375-82	ADR + DTF	5%
Chan	Intern Med J 2001;31:199-205	ADR + DTF	30%
Courtman	Can J Hosp Pharm 1995;48:161-66	ADR + DTF	31%
Pirmohamed	BMJ 2004;329:15-19	ADR	5,4%
Onder	J Am Geriatr Soc 2002;50:1962-68	ADR	3,2%
van der Hooft	Drug Saf 2006;29:161-68	ADR	3,4%
Somers	J Nutr Health Aging 2010;14:477-82	ADR + DTF	20,9%
Marcum ZA	J Am Geriatr Soc 2012;60(1):34-41	ADR	10,0%

HOW TO PREVENT DRP IN POLYMEDICATED PATIENTS

CLINICAL PHARMACY ACTIVITIES IN THE HOSPITAL



1. Medication reconciliation

Creating the most accurate list possible of all medications

2. Pharmacotherapeutic analysis

Screening of the medication list for DRPs (underuse, misuse, overuse)

3. Pharmacotherapeutic discussion

Possible solutions are proposed and discussed (physician + patient)

4. Pharmacotherapeutic plan

Explanation, implementation & follow-up

MEDICATION RECONCILIATION

= creating the best possible list of all medications a patient is taking

- Use at least 2 sources of information
- Use a structured approach for medication reconciliation
- Record for each drug as much information as possible (starting date, dose, frequency, route of administration...)
- Ask additional questions such as
 - Medications (recently) stopped because of ADRs
 - Drug allergies
 - Use of drugs that are regularly forgotten
- Pay attention for the expectations, experiences and problems of patients regarding their medications



VRAGENLIJST GMA
GESTRUCTUREERDE MEDICATIE ANAMNESE

APOTHEEK

Herkomst: Thuis: _____
 RVT: _____
 Ander ziekenhuis: _____
 Andere: _____

(adrema/ naam)

Gewicht: _____ kg

Bronnen:

- | | |
|---|--|
| <input type="checkbox"/> Patiënt (zelf?)
<input type="checkbox"/> Huisarts (brief/tel)
<input type="checkbox"/> Brief verwijzend ZH
<input type="checkbox"/> Meegebrachte medicatie/ Lijst | <input type="checkbox"/> Familie (tel)
<input type="checkbox"/> RVT (brief/tel)
<input type="checkbox"/> Info vorige opname/consult (datum)
<input type="checkbox"/> Apotheek (brief/tel) |
|---|--|

1. BEVRAGING:

Geneesmiddel	Dosis	O 8u	M 12u	A 18u	N 22u	Frequentie	Route (*)	Laatste inname

2. BIJKOMENDE BEVRAGING:

- Bloedverdunners: Asaflow/ Cardio-aspirine
Plavix/ Ticlid/ Persantine/ Aggrenox
Marcoumar/ Marevan/ Sintrom
Pradaxa/Eliquis/Xarelto/Lixiana

- Inspuitingen: Clexane/Fraxiparine/Fraxodi/Arixtra/Innohep
Insulines
Methotrexaat
Diprophos, ... (ontstekingen)

- Recent (< 2 weken) antibiotica-gebruik
- GM tegen maagklachten
- Pijnstillers
- Puffers (+ medrol)
- Hormonale preparaten (m/v)
- Vitamines/supplementen/homeopathie
(st janskruid-hypericum, calcium)
- Vaccins (griep, pneumococcon >5j?, tetanus >10j?)
- Slaapmedicatie
- Pleisters
- Collyria
- Zalven
- GM 1x/week, 1x/maand, 1x/jaar

3. BIJWERKINGEN MEDICATIE *(welke klachten, welke medicatie, hoe lang)*

4. ALLERGIEËN *(welk geneesmiddel, welke reactie, hoeveel maal, hoelang geleden)*

- Registratie in EPD:
- patiënt meldt geen allergie
 - patiënt meldt allergie
 - patiënt niet bevraagd

Naam:

Datum:

'MEMORY AID'

Record for each drug:

- ✓ Starting date (HM or specific date if recently started)
- ✓ Drug name (written out)
- ✓ Dose
- ✓ Quantity per administration time
- ✓ Stopping date if just before admission (a.o. important for anticoagulants)
- ✓ Route of administration
- ✓ Time(s) of administration (hours)

Caution with drugs that are not taken every day (1x/week, 1x/month...):

e.g. methotrexate, biphosphonates, erythropoetin...

Anticoagulants – antiaggregants:

- Vitamine K antagonists
- LMWH
- Aspirin, clopidogel, prasugrel,...

Ask specifically for:

- ✓ Anticoagulants
- ✓ Inhalators
- ✓ Plasters
- ✓ Eye, ear and nose drops
- ✓ Ointments
- ✓ Vitamines
- ✓ Painkillers (chronic / if needed)
- ✓ Insulin
- ✓ Sleeping pills

Drug information sources:

1. www.bcfi.be
2. Intranet: drug information provided by the hospital pharmacy
3. Drug information sources via Intranet (Farmacotherapeutisch Kompas, UpToDate)

CLINICAL PHARMACY ACTIVITIES IN THE HOSPITAL



MEDICATION REVIEW

Definition:

Medication review is a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug related problems and recommending interventions.

(Pharmaceutical Care Network Europe, 2016)

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DETECTION OF DRP

- No indication (unnecessary drug use)
- Contra-indication (drug – disease interaction)
- Inappropriate choice of drug
- Inappropriate dose (over-, underdose)
- Inappropriate frequency (dayfrequency, weekfrequency)
- Inappropriate time(s) of administration
- Inappropriate route, mode of administration (crushing tablets, IV admin)
- Side effects (adverse drug reactions)
- Drug-drug interactions (drug-drug / drug-food)
- Inappropriate monitoring
- Non adherence
- Inappropriate duration of therapy
- Untreated indication

TOOLS FOR DETECTION AND PREVENTION OF DRP

- Medication assessment tools
 1. EXPLICIT (criteria based)
 - Beers (1991, updates 1997, 2003, 2012, 2015, 2019)
 - McLeod (1997)
 - ACOVE: Assessing Care of Vulnerable Elders (2001)
 - IPET: Improved Prescribing in the Elderly Tool (2002)
 - STOPP/START: Screening Tool of Older Person's Prescriptions & Screening Tool to Alert Doctors to Right Prescriptions) (2008, 2014)
 - GheOP³S: Ghent Older People's Prescriptions community Pharmacy Screening (2016)
 2. IMPLICIT (judgement based)
 - MAI: Medication Appropriateness Index (1992)
 - GMA: Geriatric Medication Algorithm (1994)
 - Lipton's criteria (1993)
 - STRIP: Systematic Tool to Reduce Inappropriate Prescribing (2012)



COMBINATION OF TOOLS FOR MEDICATION REVIEW

- **Explicit** tools << PIMs: Potentially Inappropriate Medicines
 - Drugs to avoid in certain circumstances
 - Drugs to use with caution in older patients
 - Drugs to start in certain circumstances
 - Appropriate use of drugs (education, continuity, monitoring ...)
- **Implicit** tools << judgement of appropriateness of therapy
 - Standardized list of questions per drug
 - Individual judgement: ratings

➔ Explicit approach: PIMs

Woman, 82 years

Reason for admission: dizziness, falls, pain feet

Medical history:

2013: aortic valve stenosis

2013: osteoarthritis

2009: atrial fibrillation – recovered with sotalol

2008: arterial hypertension

2002: Menière – treated with clonazepam

Restless legs syndrome

List of drugs:

- Perindopril 5 mg q24h (8h)
- Fenofibrate 145 mg q24h (20h)
- Clonazepam 0,6 mg q24h (20h)
- Sotalol 80 mg q12h (8h – 20h)
- Paracetamol 325 mg q24h (8h)
- Tramadol 37,5 mg q24h (8h)

Lab values:

BP: 140/80 mmHg

LDL 144 mg/dl, TC 207 mg/dl

K⁺ 5,6 mmol/l, Na⁺ 138 mmol/l

eGFR 40 ml/min/1,73m² (MDRD), ureum 72mg/dl

EXAMPLE: RASP LIST CARDIOVASCULAR AGENTS

1. Cardiovascular system

- 1.1. Antiarrhythmic drugs (Vaughan-Williams classification I, III) in patients with chronic (permanent) atrial fibrillation/flutter
- 1.2. Digoxin in patients with chronic systolic heart failure without optimization of β -blocker therapy (unless contraindications)
- 1.3. Thiazide or loop diuretics in patients with severe or symptomatic electrolyte disturbances
- 1.4. Digoxin in suboptimal trough concentrations (optimal range: 0.5–1.0 ng/mL) in patients with systolic heart failure in sinus rhythm
- 1.5. Loop diuretics as first-line monotherapy for hypertension
- 1.6. Loop diuretics in patients with peripheral edema without any signs of heart failure
- 1.7. Non-cardioselective β -blocker in patients with Chronic Obstructive Pulmonary Disease (COPD)
- 1.8. Spironolactone as first-line therapy without prior use of an angiotensin converting enzyme inhibitor (ACE-I) or an angiotensin receptor blocker (ARB) (exceptions: hypokalemia or ascites)
- 1.9. Other β -blocker than bisoprolol, carvedilol, metoprolol succinate and nebivolol in patients with systolic heart failure
- 1.10. Other angiotensin receptor blocker (ARB) than candesartan or valsartan in patients with systolic heart failure
- 1.11. Nondihydropyridine calcium channel blockers (diltiazem or verapamil) in patients with systolic heart failure (NYHA class III or IV)
- 1.12. Dipyridamole unless in an extended-release formulation with acetylsalicylic acid for secondary prevention of CVA/TIA
- 1.13. Aspirin combined with clopidogrel, without any compelling indication
- 1.14. Vitamin K antagonists for uncomplicated deep venous thrombosis (DVT) for ≥ 3 months ago
- 1.15. Vitamin K antagonists for uncomplicated pulmonary embolism (PE) for ≥ 6 months
- 1.16. Acetylcholinesterase inhibitors in patients with clinical and electrocardiographical signs of significant bradyarrhythmias
- 1.17. Moxonidine in patients with systolic heart failure (NYHA class III or IV)
- 1.18. Acetylsalicylic acid for primary prevention of cardiac events in persons older than 80 years
- 1.19. Statins in primary prevention in persons older than 80 years with a significant decrease of life expectancy
- 1.20. Prolonged use of nitrates/nitrate derivatives if no signs of angina pectoris were present in the last six months

➔ Implicit approach: Appropriateness of therapy

			Indication	Contra-indication	Right choice	Dose	Correct modalities	Inter-actions	Duration	Adverse reactions		
Drug list			3	2	3	2	1	2	1	2	Tot	Recommendation
1	Perindopril 5mg q24h	HF, AHT	0	0	0	2	0	0	0	1	3	Decrease dose to 2,5 mg
2	Fenofibrate 145 mg q24h	?	0	0	3	2	0	0	0	0	5	Switch to simvastatin 20 mg
3	Clonazepam 0,6mg q 24h	Menière	1,5	0	3	0	0	0	1	1	6,5	Decrease, stop
4	Sotalol 80 mg q12h	AF	0	0	1,5	1	0	0	0	0	2,5	Switch to bisoprolol?
5	Paracetamol 375 mg q24h	OA	0	0	0	2	1	0	0	0	3	Increase dose e.g. 3x500mg
6	Tramadol 37,5mg q24h	OA	0	0	1,5	1	0	0	0,5	0	3	Stop
Totale score											23	
<i>Underuse?</i>												Start calcium/vitD Start antico

MEDICATION REVIEW

- Try to link every drug to the patients' co-morbidities
 - Are there comorbidities who are not treated? (underuse)
 - Are there comorbidities who are not treated effectively? (misuse)
 - Are there drugs wherefore there is not an indication (anymore)? (overuse) → 'deprescribing'
- Screen for possible DRPs (using tools) per drug the patient is taking
- Maximum efficacy, minimum risk, minimum costs and with respect for patient preferences

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PHARMACOTHERAPEUTIC DISCUSSION

- After the screening for DRP, discuss the identified problems with
 - the different healthcare providers
 - the (family of the) patient: pay attention for patients characteristics and preferences
- and develop, based on that, a pharmacotherapeutic plan that fits the patient.

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PHARMACOTHERAPEUTIC PLAN

- Explanation, communication and implementation = medication counseling
- What?
 - Education of the patient to improve drug knowledge
 - Assessment and improvement of drug adherence
 - Detection and follow-up of adverse drug reactions
 - Improving the management of drugs



PHARMACOTHERAPEUTIC PLAN

- Explanation, communication and implementation = medication counseling
- Why?
 - Sustainable interventions & therapy adherence
 - Medication changes could cause other DRPs
 - Older people are more likely to experience problems understanding their medication changes
 - Multiple illnesses
 - Multiple medications
 - More often hospitalized



PHARMACOTHERAPEUTIC PLAN

- Explanation, communication and implementation = medication counseling
- How?
 - Creating and maintaining a correct medication scheme
 - What is new?
 - What is stopped?
 - What has changed?
 - Ask for feedback



TAKE HOME MESSAGES

- Polypharmacy and DRPs are highly prevalent in older (hospitalized) patients
- We recommend:
 - A structured approach for medication review, using explicit and implicit criteria
 - A structured approach for medication reconciliation, formally recognized as an essential step at admission / discharge and preferably electronic
- Pay attention for practical issues and medication adherence
- Reevaluate

Thank you for your attention!

Questions?



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