Polypharmacy Optimization Method

(Drenth et al. Drugs and Aging 2009; 26: 687-701
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1. Ask the patient what she/he really uses (Table 1)
2. Ask for adverse effects (Table 1 and 2)
3. Look at undertreatment (Table 3)
4. Look at (contra)indications (Table 4)
5. Look at interactions (Table 5)
6. Look at the dose and dose frequency (Table 6)

Table 1. Structured History taking of Medication use (SHIM) questionnaire

Questions asked per drug on the medication list, provided by the community pharmacist:
1. Do you use this drug as prescribed (dosage, dose frequency, dosage form)?
2. Do you experience any side effects?
3. What is the reason for deviation (of dosage, dose frequency, or dosage form) or not taking a drug at all?
4. Do you use any other drugs, prescribed by a physician, which are not mentioned on this list? (View medication vials)
5. Do you use non-prescription drugs?
6. Do you use homeopathic drugs or herbal medicines (especially st. Johns wort)?
7. Do you use drugs that belong to somebody else?
8. Are there any drugs that you use 'on demand'?
9. Do you use drugs that are no longer prescribed?
Questions concerning the use of medicines:
10. Do you independently take your medication?
11. Do you make use of a dosage system?
12. Can you have problems with swallowing your medication?
13. In case of inhalation therapy: What kind of inhalation system do you use? Do you experience any problems handling this system?
14. In case of eye drops: Do you experience any difficulties with the use of eye drops?
15. Do you ever forget to take your medication? If so, which medication, how come, and what do you do?
Questions concerning medication knowledge
16. Do you know why you should use this medication?
17. Do you know who prescribed this medication?
Questions concerning beliefs about medicine
18. Do you believe that your medication is health-improving?
19. Will you continue to use your medication?
20. Will you consult your doctor in case of medication-related problems?
21. Would you like to comment on or ask a question about your medication?

Table 2. Common adverse effects

anticonvulsants	drowsiness
anti-parkinsonic drugs	hallucinations, postural hypotension
antipsychotic drugs	drowsiness, extrapyramidal syndrome
cumarins	bleeding
digoxin	nausea, bradycardia
lithium	delirium, nausea, ataxia, drowsiness
opioids	drowsiness, constipation
sulfonylurea anti-diabetics	hypoglycemia
tricyclic antidepressants	drowsiness, postural hypotension
verapamil, diltiazem	bradycardia, hypotension, constipation

Table 3. Common undertreated conditions and advised medication according to guidelines

• Angina pectoris	β-receptor-blocker
• Atrial fibrillation	Cumarins, when contraindicated acetylsalicylic acid
• Cardiovascular disease[1]	Acetylsalicylic acid, in case of over-sensitivity clopidogrel
• Cardiovascular disease + LDL>2.5	Statin
• Cerebral infarction/TIA	Consider antihypertensive treatment, even if blood pressure is normal
• COPD	Inhalational anticholinergics/β2-agonists
• Corticosteroids used >1 month	Medication to prevent osteoporosis
• Depression	Antidepressant
• Diabetes mellitus	Statin
• Diabetes with proteinuria	ACE inhibitor
• Heart failure	ACE inhibitor, if necessary β-receptor-blocker
• Hypertension	Antihypertensive treatment
• Insufficient daylight	Vitamin D
• Myocardial infarction	Acetylsalicylic acid, ACE inhibitor, β-receptor-blocker
• NSAID	Drugs to protect the stomach
• Opioids	Laxatives
• Osteoporosis	Medication to treat osteoporosis
• Pain	Analgesics

[1] Cardiovascular disease: caused by atherothrombotic processes with clinical manifestations such as myocardial infarction, angina pectoris, cerebral infarction, transient ischemic attack (TIA), aortic aneurysm, and peripheral arterial vessel disease.

Table 4. Conditions with possible contraindicated drugs

COPD	long-acting benzodiazepines, non-selective β-receptor-blocking drugs (propranolol, carvedilol, labetalol, sotalol)
Dementia	potent anticholinergic agents[1]
Heart failure	verapamil, diltiazem, short-acting nifedipine, NSAIDs, rosiglitazone
Lower urinary tract syndrome	anticholinergic agents[1]
Gastric ulcer or gastritis	NSAIDs
Narrow angle glaucoma	potent anticholinergic agents[1]
Constipation	verapamil, diltiazem, anticholinergic agents[1]
Postural hypotension	tricyclic antidepressants
Parkinson's disease	metoclopramide, all antipsychotics except clozapine and quetiapine
Hyponatriemia (SIADH)	SSRIs
Falls	psychoactive drugs

1. Potent anticholinergic drugs: spasmolytics, tricyclic antidepressants, anticholinergic antiparkinsonic drugs

Table 5. Clinically relevant interactions

Drug	***Interaction***	***Effect***
ACE inhibitors	NSAIDs, potassium-sparing diuretics	Decreased renal function, hyperkalemia
Antidepressants	Enzyme inducers[1]	Less antidepressant effect
Antihypertensives	Vasodilators, antipsychotic drug, tricyclic antidepressants	Increased antihypertensive effect
	NSAIDs	Decreased antihypertensive effect
β-receptor-blocking drugs	Anti-diabetic drugs	Masks hypoglycemia
	Fluoxetine, paroxetine (especially in combination with metoprolol and propranolol)	Bradycardia
Corticosteroids (oral)	NSAIDs	Gastroenteric ulcers
	enzyme inducers[1]	Decreased corticosteroid effect
Cumarins	NSAIDs, metronidazole, miconazole	Bleeding
	rifampicin	decreased anticoagulative control
Digoxin	NSAIDs, diuretics, kinidine, verapamil, diltiazem, amiodarone	Digoxin intoxication
Lithium	NSAIDs, thiazide diuretics, antipsychotics	Lithium toxicity
Phenytoine	Enzyme inhibitors[2]	Increased toxicity
Sulfonylurea anti-diabetics	SSRIs, chloramphenicol, cumarins, phenylbutazone	Hypoglycemia
SSRIs	Diuretics, NSAIDs	Hyponatremia, gastric bleeding
Tetracycline	Antacids, iron	Decreased availability

1. Important enzyme inducers: carbamazepine, rifampicin, phenobarbital, phenytoin, St. Johns wort

2. Important enzyme inhibitors: verapamil, diltiazem, amiodarone, fluconazole, miconazole, ketoconazole, erythromycin, claritromycin, sulfonamides, cimetidine, ciprofloxacin, and grapefruit juice

Patients should be advised not to drink grapefruit juice or to take St. John's wort if they are using any of the following drugs:

Antiarrhythmic agents: kinidine
Histamine antagonists: astemizole, terfenadine
Benzodiazepines: alprazolam, diazepam, midazolam, triazolam
Calcium channel blockers: diltiazem, felodipine, nifedipine, verapamil, lercanidipine, nitrendipine
HIV medication: indinavir, nelfinavir, ritonavir, saquinavir
Hormones: estradiol, hydrocortisone, progesterone, testosterone
Immune modulators: cyclosporine, tacrolimus
Macrolide antibiotics: claritromycin and erythromycin
Statins: atorvastatine, simvastatin
Other: aripiprazole, buspirone, dexamethason, docetaxel, domperidone, fentanyl, haloperidol, irinotecan, propranolol, risperidone, salmeterol, tamoxifen, taxol, vincristine, zolpidem.

Table 6. Adjustment of dosage in renal insufficiency

Calculate the creatinine clearance or GFR (http://nephron.com/cgi-bin/CGSI.cgi).

	Decreased renal function
ACE INHIBITORS	
benazepril	Clcr 10-30 ml/min: start with 2.5-5 mg once daily. Adjust dosage based on effect.
captopril	Clcr 10-30 ml/min: start with 12.5-25 mg once daily. Adjust dosage based on effect until 75-100 mg/day
cilazapril	Clcr 10-30 ml/min: start with max. 0.5 mg/day. Adjust dosage based on effect until max. 2.5 mg/day
enalapril	Clcr 10-30 ml/min: start with max. 5 mg/day. Adjust dosage based on effect until max. 10 mg/day
lisinopril	Clcr 10-30 ml/min: start with max. 5 mg/day. Adjust dosage based on effect until max. 40 mg/day
perindopril	Clcr 30-50 ml/min: max. 2 mg/day; Clcr 10-30 ml/min: max. 2 mg every two days
quinapril	Clcr 30-50 ml/min: start with 5 mg/day; Clcr 10-30 ml/min: start with 2.5 mg/day. Adjust dosage based on effect.
ramipril	Clcr 20-50- ml/min: start with max. 1.25 mg/day. Adjust dosage based on effect. Clcr 10-20 ml/min: insufficient data for sound advise
trandolapril	Clcr 10-30 ml/min: start with max. 0.5 mg/day. Adjust dosage based on effect until max. 2 mg/day
zofenopril	Clcr 10-50 ml/min: start with max. 7.5 mg/day. Adjust dosage based on effect until max. 15 mg/day
ANTIBIOTICS	
CEFALOSPORINS	
cefalexine	Clcr 10-50 ml/min: prolong interval to once per every 12 hours.
cefalotine	Clcr 50-80 ml/min 2 g every 6 hours; 30-50 ml/min 1.5 g every 6 hours; 10-30 ml/min 1 g every 8 hours.
cefamandol	Clcr 50-80 ml/min 2 g every 6 hours, in case of life-threatening infection 1.5 g every 4 hours; Clcr 30-50 ml/min 2 g every 8 hours, in case of life-threatening infection 1.5 g every 6 hours; Clcr 10-30 ml/min 1.25 g every 6 hours, in case of life-threatening infection 1 g every 6 hours.
cefazoline	Clcr 30-50 ml/min: 500 mg every 12 hours; 10-30 ml/min: 500 mg every 24 hours.
cefradine	Clcr 10-30 ml/min: contra-indicated
ceftazidim	Clcr 30-50 ml/min: 1 g every 12 hours; 10-30 ml min: 1 g every 24 hours.
ceftibuten	Clcr 30-50 ml/min: 200 mg every 24 hours; 10-30 ml/min: 100 mg every 24 hours.
cefuroxim parenteral	Clcr 10-30 ml/min: standard dosage every 12 hours.
CHINOLONES	
ciprofloxacine	Clcr 10-30 ml/min: 50% of normal dosage
levofloxacine; ofloxacine	Clcr 30-50 ml/min: 50% of normal dosage; Clcr 10-30 ml/min: 25% of normal dosage
norfloxacine	Clcr 10-30 ml/min: prolong interval to once every 24 hours
NITROFURANTOIN	
Nitrofurantoin	Clcr 10-50: contra-indicated. Risk of neuropathy and failure of therapy.
MACROLIDE	
claritromycin	Clcr 10-30 ml/min: 50% of normal dosage with normal dose frequency
PENICILLINS	
amoxicillin/clavulanate	Clcr 10-30 ml/min: standard dosage every 12 hours (orally, i.v. of .im.)
benzylpenicillin	Clcr 10-30 ml/min: dosage dependent of indication. Consider intended effect, risks of overdosage and underdosage.

piperacillin	Clcr 30-50 ml/min: max. 12 g per day in 3 or 4 doses; Clcr 10-30 ml/min: max. 8 g per day in 2 doses
piperacillin/tazobactam	Clcr 30-50 ml/min: piperacillin/tazobactam 12 g/1.5 g per day in 3 or 4 doses Clcr 10-30 ml/min: piperacillin 4 g/0.5 g every 12 hours
TETRACYCLINeS	
tetracycline	Clcr 10-30 ml/min: maintenance dosage 250 mg once daily
ANTIDIABETICS	
metformin	Clcr 30-50 ml/min: start with twice daily 500 mg; Clcr 10-30 ml/min: contra-indicated
sulfonylurea (ex. tolbut)	Clcr < 50 ml/min start with half the dosage
ANTIHISTAMINICS	
acrivastin	Clcr 10-50 ml/min: 50% of normal dosage OR prolong interval to 1-2x per day
cetirizin/levocetirizin/hydroxyzin/fexofenadin/terfenadin	Clcr 10-50 ml/min: 50% of normal dosage
ANTIMYCOTICS	
fluconazole	In case of >once daily dosing regimen: Clcr 10-50 ml/min: normal starting dosage, decrease maintenance dosage until 50% of normal dosage
flucytosin	Clcr 30-50 ml/min: prolong interval to once every 12 hours, then based on serum plasma concentration Clcr 10-30 ml/min: prolong interval to once every 24 hours, then based on serum plasma concentration
terbinafin	Clcr 10-50 ml/min: 50% of normal dosage
ANTIPARKINSON MEDICATION	
Pramipexol	Clcr 30-50 ml/min: start with 0.125 mg (=0.088 base) twice daily, then based on effect/adverse events Clcr 10-30 ml/min: start with 0.125 mg (=0.088 base) once daily, then based on effect/adverse events
ANTITHROMBOTICS	
eptifibatide	Clcr 10-50 ml/min: normal starting dosage, then 50% of normal dosage
tirofiban	Clcr 10-30 ml/min: 50% of normal dosage
ANTIVIRAL MEDICATION	
aciclovir orally	Decrease dosage used for herpes zoster treatment: Clcr 10-30 ml/min: 800 mg 3 times a day.
amantadine	Start with 200mg, maintenance dosage: Clcr 50-80 ml/min: 100 mg once daily ; Clcr 30-50 ml/min: 100 mg every 2 dayen; Clcr 10-30 ml/min 100 mg every 3 dayen.
cidofovir	Clcr 10-50 ml/min: preferably do not use
famciclovir	Clcr 30-50 ml/min: normal dosage every 24 hours; 10-30 ml/min: 50% of normal dosage every 24 hours
foscarnet	Clcr 30-80 ml/min: dosage according to schedule manufacturer; 10-30 ml/min: do not use
ganciclovir	INDUCTION: Clcr 50-80 ml/min: 50% of normal dosage every 12 hours; 30-50 ml/min: 50% of normal dosage every 24 hours; 10-30 ml/min: 25% of normal dosage every 24 hours MAINTENANCE: Clcr 50-80 ml/min: 50% of normal dosage every 24 hours; 30-50 ml/min: 25% of normal dosage every 24 hours; 10-30 ml/min: 12.5% of normal dosage every 24 hours.
oseltamivir	Clcr 10-30 ml/min: 50% of normal dosage OR normal dosage but double interval
ribavirine	Clcr 10-50 ml/min: dosage based on hemoglobin concentration
valaciclovir	Clcr 10-80 ml/min: adjust dosage according to schedule manufacturer
valganciclovir	Clcr 30-50 ml/min: 50% of normal dosage plus double interval Clcr 10-30 ml/min: 50% of normal dosage twice a week
β-RECEPTOR-INHIBITING DRUGS	
Acebutolol; atenolol	Clcr 10-30 ml/min: 50% of normal dosage

bisoprolol	Clcr 10-20 ml/min: start with 50% of normal dosage. Then max. 10 mg/day
sotalol	Clcr 30-50 ml/min: max 160 mg/day; Clcr 10-30 ml/min: max. 80 mg/day
CA ANTAG, DIHYDROPYR	
barnidipine	Clcr 10-50 ml/min: contra-indicated
DIGOXIN	
digoxin	Clcr 10-50 ml/min: decrease initial dosage by 50%, then go to 0.125 mg/day. Next adjust dosage based on clinical symptoms.
DMARDs	
anakinra	Clcr < 30 ml/min: contra-indicated
methotrexate	Clcr 40-70 ml/min: 50% of normal dosage. Clcr < 40 ml/min: based on serum plasma concentration
GOUT MEDICATION	
allopurinol	Clcr 50-80 ml/min: 300 mg/day; 30-50 ml/min: 200 mg/day; 10-30 ml/min: 100 mg/day
benzbromarone	Clcr 10-30 ml/min: contra-indicated
colchicin	Clcr 10-50 ml/min: 0.5 mg/day
H2-ANTAGONISTS	
nizatidin; cimetidine; famotidine; ranitidin	Clcr 10-30 ml/min: 50% of normal dosage, once daily
HYP, SED, ANX, ANTIPSYCH	
Chloralhydrate	Clcr 10-50 ml/min: preferably do not use
Meprobamate	Clcr 10-50 ml/min: 50% of normal dosage OR double dosage interval
risperidone	Clcr 10-50 ml/min: 50% of normal dosage, then based on effect and adverse events
ethambutol	Clcr 10-50 ml/min: 50% of normal dosage
MUSCLE RELAXANTS	
Baclofen	Clcr 10-50 ml/min: start with 5 mg once daily, then adjust based on effect and adverse events.
tizanidine	Clcr 10-30 ml/min: start with 2 mg once daily, then increase dosage slowly based on effect and adverse events. End with increasing the dose frequency.
NSAIDs	All NSAID's: Clcr 30 ml/min: consider if chronic use is indicated. Check renal function previously to and 1 week after start
OPIOIDs	
morphine	Clcr 10-50 ml/min: dosage based on effect and adverse events. Be alert to accumulation of M6G
tramadol	Clcr 10-30 ml/min: decrease dose frequency to 2-3 x per day In case of retard tablet max. 200 mg per day
TUBERCULOSTATICS	
VERTIGO MEDICATION	
piracetam	Clcr 30-50 ml/min: 50% of normal dosage; Clcr 10-30 ml/min: 25% of normal dosage
XANTHINE DERIVATES	
pentoxiphylline	Clcr 30-50 ml/miin: 400 mg twice daily; Clcr 10-30 ml/min: 400 mg once daily