Potentially inappropriate prescribing in nursing home residents detected with the community pharmacist specific GheOP³S-tool

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Abstract

Background. The Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S-)tool was recently developed to screen for potentially inappropriate prescribing (PIP).

Objective. We aim (1) to determine PIP prevalence in older nursing home (NH) residents with polypharmacy using the GheOP³S-tool and (2) to identify those PIPs that are most frequently detected.

Method. A cross-sectional study was carried out between February and June 2014 in 10 NHs in Belgium, supplied by a community pharmacy chain. For each NH, 40 residents (≥70 years, using ≥5 chronic drugs) were included. PIP prevalence was determined using the GheOP³S-tool.

Results. 400 NH residents were included [mean age (±SD): 86.2 (±6.3) years; median number of drugs (±IQR): 10 (7-12)]. A total of 1728 PIPs were detected in 387 (97%) participants (Median: 4; IQR: 2-6). The most prevalent items can be assigned to three categories: long-term use of central nervous system drugs (i.e. benzodiazepines, antidepressants and antipsychotics), use of anticholinergic drugs (mutual combinations and with underlying constipation/dementia) and underuse of osteoporosis prophylaxis.

Conclusion. Screening for PIP by means of the GheOP³S-tool revealed a high prevalence of PIP among older NH residents with polypharmacy. This finding urges for initiatives on the patient-level, but also on a broader, institutional level.

IMPACT OF FINDINGS FOR PROFESSIONALS

- The prevalence of potentially inappropriate prescribing in Belgian nursing homes is high.
- The most prevalent PIP-items can be assigned to the following three main categories: long-term use of drugs that influence the central nervous system, use of anticholinergic drugs and underuse of osteoporosis prophylaxis. These issues should therefore be targeted first.
- A GheOP³S-tool screening could be part of a periodic evaluation of nursing home residents' medication or, on the institutionalized level, serve as benchmarking for the quality of prescribing.

INTRODUCTION

Nursing home residents are particularly vulnerable to (potentially) inappropriate prescribing ((P)IP) as they are more fragile, receive therapy from multiple health care workers and are often prescribed a high number of drugs(1). It makes prescribing in this setting a complex and challenging task(2, 3). Additionally, PIP (i.e. overuse, underuse and misuse of drugs) is often associated with increased prevalence of adverse drug events (ADEs) and health care utilization(4). Other health care professionals such as pharmacists and nurses, could assist physicians in the medication management process to ensure the most effective and safe pharmacotherapy for the patient(5).

Screening of medication by pharmacists, preferably as a part of a full medication review with multidisciplinary consultation, is a proposed strategy to improve the appropriateness of prescribing(1, 6, 7) and has been shown to be effective (5). However, significant improvements on hospitalizations or mortality are currently lacking(7). This is probably due to the use of inappropriate outcome measures (i.e. number of drugs, MMSE-improvement etc), a lack of power to detect statistically significant differences or – most importantly – the poor acceptance rate and continuation of recommendations resulting from the reviews(5, 8). Additionally, there exist practical barriers to the systematic performance of a medication review among nursing home residents. This includes the lack of pharmacists with specific training in geriatric pharmacotherapy, the lack of centralized medical records and insufficient computerized support(8).

Recently, we developed the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP^{3}S-) tool, an explicit screening tool to detect PIPs with high clinical relevance for older patients(9). This screening tool provides the community pharmacist with the possibility to initiate a medication review process in a systematic and straightforward way, solely based on medication dispensing data available in the community pharmacy. Ideally, the results of a medication screening with the GheOP^{3}S-tool should be discussed with the prescribing physician to confirm clinical relevance for the specific patient. Based on the outcomes of the pharmacist-physician consultation, suggestions for medication changes are proposed. Lastly, these suggestions are to be discussed with the patient, and a final treatment plan is to be decided on.

AIM OF THE STUDY

The GheOP³S-tool has already been tested in ambulatory patients(10), where it showed to detect all three categories of PIP: overuse, misuse and underuse. In the current observational study, we aim to perform a screening for PIP in nursing home residents using the GheOP³S-tool and to identify those PIPs that are most frequently detected.

ETHICS APPROVAL

Ethics approval was received of the Ethics Committee of the Ghent University Hospital.

METHOD

This manuscript describes a cross-sectional study, carried out between February and June 2014, in 10 nursing homes in Flanders (i.e. the Dutch speaking part of Belgium) supplied by a community pharmacy chain. The pharmacy chain provided the research centre with an anonymized dataset, previously set up to examine problems for robotic unit dose drug dispensing. This database was set up as follows: 10 nursing homes were randomly selected out of a sample of 33 nursing homes which are all supplied by the community pharmacy chain. From each selected nursing home, forty residents meeting the following inclusion criteria were randomly selected: (1) aged 70 years or older and (2) using 5 of more chronic (i.e. according to a set regimen) drugs registered in the Belgian Commented Drugs Repertory(11). The dataset contained the residents' medication records and basic demographics (age & gender). Each drug was assigned a seven-digit code in accordance with the Anatomical Therapeutic Chemical (ATC) Classification System formulated by the World Health Organization Collaborating Centre for Drug Statistics Methodology(12).

We applied the GheOP³S-tool(9) to the patients' chronic medication in the received dataset. The choice to use this screening-tool was deliberate. First, the GheOP³S-tool makes it possible to screen for PIP in settings where clinical data are not available. Second, the GheOP³S-tool is adapted to the European market and addresses all types of PIP. Third, the GheOP³S-tool offers the pharmacists a backbone to get started with the process of a medication review. An elaborate document describing rationale, alternative treatment plans and scientific background information empowers the pharmacists to initiate pharmacist-physician contacts to discuss the considered clinically relevant PIP-items. The GheOP³S-tool consists of 83 items, categorized in 5 different parts *(Part 1: Potentially inappropriate drugs, independent of diagnosis, Part 2: Potentially inappropriate drugs, dependent on diagnosis, Part 3: Potential Prescribing Omissions (PPOs), Part 4: Drug Drug Interactions (DDIs) of specific relevance and Part 5: General care-related items to be addressed in the*

community pharmacy). Part 5 of the GheOP³S-tool was not applied in the current study as this part reflects on pharmacy work processes and is not applicable to the bulk supplying for nursing homes. With regard to the diagnoses in Part 2, drug proxies were used. Only diagnoses that unambiguously could be derived from the patient's medication (e.g. diabetes from insulin, gout from allopurinol, etc) were taken into account. We also identified the GheOP³S-criteria that accounted for the highest proportion of PIP. The PIP screening with the GheOP³S-tool was performed manually by 3 researchers (EP, CVD and KM) and double-checked by the main investigator (ET). The STROBE standardized reporting guidelines for cross-sectional studies were followed to ensure the uniform conduct and reporting of the research(13).

Descriptives were displayed as counts with percentages and means with standard deviations or medians with interquartile ranges as appropriate. The PIP prevalence is represented as the proportion of residents with at least one PIP and the median number of PIPs per resident.

RESULTS

The 400 randomly included residents had a mean age (± SD) of 86.2 (±6.3) years with 63% of residents (250) being older than 85 years. Three quarters (298 residents) of the population was female. The total number of medicines taken was 4079, with an absolute range varying between 5 to 34 drugs per resident and a median of 10 per resident (Interquartile Range (IQR): 7-12).

Considering Part 1 to Part 4 of the GheOP³S-tool, a total of 1728 PIPs were detected in 387 (97%) participants (Median: 4; IQR: 2-6). Figure 1 represents the distribution of number of PIPs detected per patient according to the full GheOP³S-tool, as well as according to each part of the tool. All types of PIP (overuse, underuse and misuse) are detected. The 5 most prevalent items for each part of the GheOP³S-tool are reported in Table 1. The items of Part 2 and Part 3 are displayed in two ways; relative to the total population and relative to the overall drug or disease prevalence. A complete list of the prevalence of all individual GheOP³S-criteria is reported as Online Supplement.

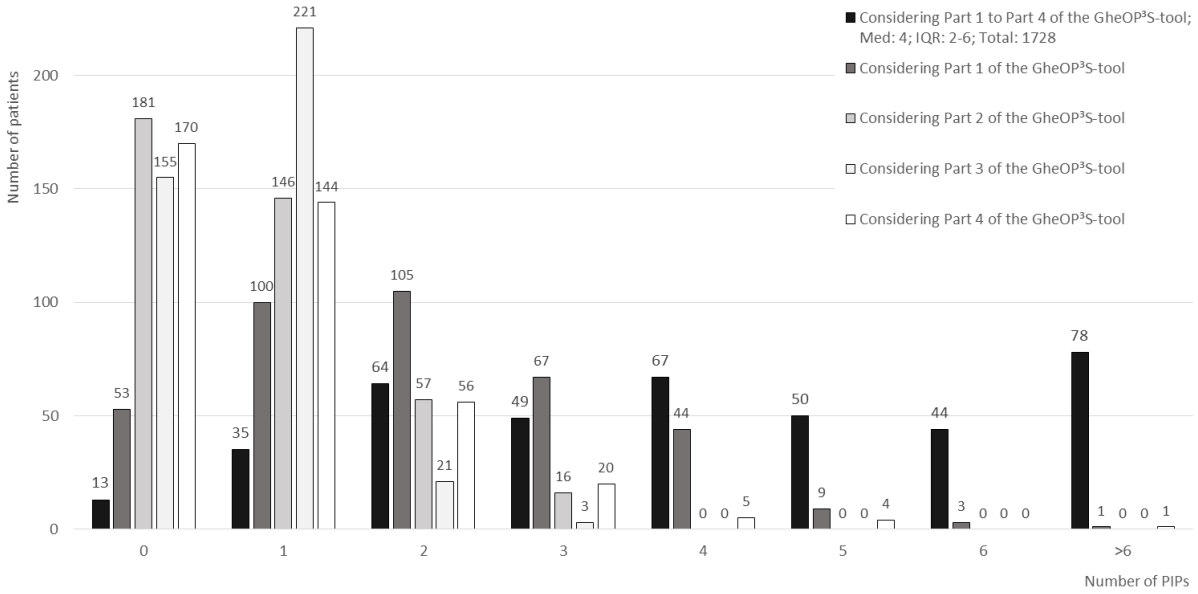

***Figure 1**: Distribution of the number of PIP-items detected per patient, using the GheOP³S-tool (n = 400; Part 1: Potentially inappropriate drugs, independent of diagnosis, Part 2: Potentially inappropriate drugs, dependent on diagnosis, Part 3: Potential prescribing omissions and Part 4: Drug-drug interactions of specific relevance)*

Table 1: Most prevalent GheOP³S-criteria of each part of the GheOP³S-tool, n = 400			
	GheOP³S-criterion	**N, % (relative to total population)**	**N, % (relative to overall drug or disease prevalence)**
Part 1: Potentially inappropriate drugs, independent of diagnosis		**341 (85%)**	
1	Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days OR Any short- or long-acting benzodiazepine	212 (53%)	
	Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days	195 (49%)	
	Any short- or long-acting benzodiazepine	35 (9%)	
	Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days AND Any short- or long-acting benzodiazepine	18 (5%)	
2	Any antidepressant ≥1 year	169 (42%)	
3	Any antipsychotic drug ≥1 month	117 (29%)	
4	Any PPI at full dose ≥8 weeks	73 (18%)	
5	Any oral non-steroidal anti-inflammatory drug	35 (9%)	
Part 2: Potentially inappropriate drugs, dependent on diagnosis		**219 (55%)**	
1	Anticholinergics with constipation	149 (37%)	149/199 (75%)
2	Calcium channel blockers with constipation	43 (11%)	43/197 (22%)
3	Anticholinergics with dementia or cognitive impairment	36 (9%)	36/51 (71%)
4	Oral corticosteroids >1 week with hypertension	19 (5%)	19/221 (9%)
5	Thiazide and loop diuretics with gout	18 (5%)	18/27 (67%)
Part 3: Potential prescribing omissions		**245 (61%)**	
1	The patient has an elevated risk for osteoporosis and is not prescribed Calcium and Vitamin D supplementation.	214 (54%)	214/295 (73%)
2	The patient is taking narcotic analgesics and is not prescribed appropriate preventative bowel regimen.	35 (9%)	35/84 (42%)
3	The patient is taking oral corticosteroids for ≥1 month and is not prescribed a Calcium and Vitamin D supplementation.	15 (4%)	15/25 (60%)
4	The patient is taking an equivalent of 7.5 mg of oral prednisone or more for ≥3 months and is not prescribed calcium/Vitamin D supplementation and bisphosphonates.	7 (2%)	7/11 (64%)
5	The patient is taking methotrexate and is not prescribed folic acid	1 (0%)	1/1 (100%)

	supplementation.		
Part 4: Drug-drug interactions of specific relevance		**230 (58%)**	
1	Any combination of anticholinergic drug	163 (41%)	
2	Oral antidiabetics/insulin and β-blocker	41 (10%)	
	Oral antidiabetics/insulin and non-selective β-blocker	8 (2%)	
	Oral antidiabetics/insulin and selective β-blocker	37 (9%)	
3	Oral non-steroidal anti-inflammatory drug and diuretic	22 (6%)	
4	Bisphosphonate and calcium, magnesium, zinc, iron or aluminium	22 (6%)	
5	RAAS inhibitor and potassium sparing diuretic, potassium supplements or potassium containing drugs	20 (5%)	
***RAAS**: Renin angiontensin aldosteron system*			

DISCUSSION

In this observational study, we detected at least one PIP in 97% of the 400 randomly included nursing home residents, with a median of 4 PIPs per resident. This is in concordance with two other Belgian studies and with studies from other European countries(3, 5, 14, 15). Some studies report lower prevalence rates, however in these cases, the researchers evaluated PIP with a smaller subset of published criteria or only screened for one aspect of PIP (e.g. underuse)(16, 17). On the other hand, compared with a recent systematic review, estimating PIP prevalence in the ambulatory setting(18), the prevalence in nursing homes is markedly higher. Although, one previously performed study with the GheOP³S-tool in the ambulatory setting observed a comparable PIP prevalence (at least one PIP in 97% of patients, median of 3 PIP per patient)(10).

The fact that nearly all patients had at least one PIP shows that there is a large room for improvement on the appropriateness of prescribing. During the development of the GheOP³S-tool, the experts unanimously agreed on the clinical relevance of screening for all included items in older patients in general. Whether the detected problems are also clinically relevant for the individual patient, still needs to be assessed during a pharmacist-physician consultation and agreement. The actual rate of inappropriate prescribing will therefore probably be somewhat lower.

The most prevalent PIP-items identified by the GheOP³s-tool can be assigned to the following three main categories: long-term use of drugs that influence the central nervous system (i.e. hypnosedatives, antidepressants and antipsychotics), use of anticholinergic drugs (mutual combinations and with underlying constipation or dementia) and underuse of osteoporosis prophylaxis. Additionally, the use of systemic NSAIDs and the long-term use of high-dose PPIs is

frequent in this population. All of these items are also mentioned by other European observational studies(2, 8, 19). In the observational study, using the GheOP³S-tool in the ambulatory setting, the same items (except for the use of anticholinergic drugs) significantly added to the number of PIP(10). As the use of drugs that influence the central nervous system and drugs with anticholinergic effects significantly adds to the high number of PIP, with possible significant clinical consequences as a result, the inappropriate use of these drug classes should be targeted first. Multiple trials already addressed these specific issues and showed that deprescribing in nursing homes is possible, improves the quality of prescribing and has a positive effect on the quality of life of the patient.

One example is the study be Bourgeois et al(20), in which 66% of chronic benzodiazepine users were successfully discontinued after 8 months, with an improved self-perceived sleep quality and significantly less midnight awakenings(20). Another example, a randomized controlled trial performed in 22 nursing homes, showed that the anticholinergic burden was significantly reduced by a pharmacist-initiated medication review(21).

Despite the fact that the GheOP³S-tool was developed to detect PIP on the patient level, this study also shows that an overall analysis, applied to all residents of one institution, could expose the most urgent issues on a more general level. This way, the GheOP³S-tool might serve as a benchmarking instrument for the prescribing behaviour in a nursing home. The result of such an overall analysis would be the ideal starting point for interdisciplinary case-conferences or the basis for targeted action plans. Using the GheOP³S-tool, the dispensing pharmacist is able to assist prescribers and the nursing home management to increase the quality of prescribing.

Strengths and limitations

This study shows that the recently developed GheOP³S-tool, a validated community pharmacy specific list where limited clinical data are available, is practical and straightforward in screening for PIPs in nursing home residents. This study has nevertheless some limitations. As the GheOP³S-tool is explicit of nature, it does not take into account all patient factors in evaluating the pharmacotherapy, e.g. diagnoses, patient preferences or earlier attempts to tackle PIP. Also, some relevant items might have been missed. To tackle this, a future study will compare a GheOP³s-screening with a full medication review. This way, the items that are systematically missed will be identified and added to the GheOP³S-tool in a future update. Additionally, there were no pharmacist-prescriber contacts to discuss the clinical relevance of the detected items. E.g. the clinical relevance of the interaction between a selective β-blocker and oral antidiabetics/insulin is minimal if glycemic control is good. Also, it is difficult to estimate generalizability to other countries as prescribing behavior can largely differ between geographical regions. Despite the fact that our results match

findings from other European countries, it would still be interesting to compare our results to a GheOP³S-tool application in other European countries.

CONCLUSION

Screening for PIP by means of the GheOP³S-tool showed a high PIP prevalence in older nursing home residents with polypharmacy. This urges for initiatives on the patient-level, but also on a broader, institutional level. The GheOP³S-tool could be part of such an evaluation process in which it could be the starting point for multidisciplinary interventions, initiated by the pharmacist. Such a process aims to improve the quality of prescribing for nursing home residents with polypharmacy.

CONFLICTS OF INTEREST

All authors completed the ICMJE-form. No competing interests were declared.

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Online Supplement:

Supplement Table: Full list of prevalence of all GheOP³S-criteria				
No.	**GheOP³S-criterion**	**N, % (relative to total population, n=400)**		**N, % (relative to overall drug or disease prevalence)**
Part 1b: Potentially inappropriate drugs, independent of diagnosis – Drug classes				
1	Any antidepressant ≥1year	169	42%	
2	Any antipsychotic drug ≥1 month	117	29%	
3	Any drug for arterial vascular disorders	9	2%	
4	Any intermediate acting benzodiazepine or Z-product at full dose or any dose ≥30 subsequent days	195	49%	
5	Any short or long-acting benzodiazepine	35	9%	
6	Any long-acting sulfonylurea derivative	18	5%	
7	Any nasal vasoconstrictor ≥1 month	3	1%	
8	Any oral NSAID	35	9%	
9	Any PPI at full dose[a] ≥8 weeks	73	18%	
10	Any recently marketed drug (black triangles)	13	3%	
11	Any sedating antihistaminic drug	14	4%	
Part 1b: Potentially inappropriate drugs, independent of diagnosis - Specific molecules				
12	Alizapride	5	1%	
13	Bisacodyl	5	1%	
14	Clonidine	3	1%	
15	Codeine and its derivatives for acute cough	6	2%	
16	Dabigatran	3	1%	
17	Digoxin >0,125mg/day	8	2%	
18	Dipyridamole monotherapy (without ASA)	0	0%	
19	Ginkgo biloba or Panax ginseng	3	1%	
20	Liquid paraffin	1	0%	
21	Methyldopa	0	0%	
22	Metoclopramide	13	3%	
23	Pentazocine	0	0%	

24	Phenobarbital	1	0%	
25	Pseudoephedrine oral	0	0%	
26	Rivaroxaban or Apixaban	10	3%	
27	Senna glycosides	1	0%	
28	Picosulfate	4	1%	
29	Theophylline	10	3%	
30	Ticlopidine, new prescription	0	0%	
31	Tramadol, new prescription	30	8%	
Part 2a: Potentially inappropriate drugs, dependent on diagnosis - Drug classes				
32	Any antipsychotic other than quetiapine and clozapine with Parkinson's disease	13	3%	13/54 (24%)
33	Anticholinergics (e.g. Antihistamines, Antidepressants, Antipsychotics, Antispasmodics…) with dementia or cognitive impairment	36	9%	36/51 (71%)
34	Anticholinergics (e.g. Antihistamines, Antidepressants, Antipsychotics, Antispasmodics…) with constipation	149	37%	149/199 (75%)
35	Anticholinergics (e.g. Antihistamines, Antidepressants, Antipsychotics, Antispasmodics…) with BPH	13	3%	13/21 (62%)
36	Calcium Channel Blockers with constipation	43	11%	43/197 (22%)
37	Non-selective beta-blockers with asthma or COPD	9	2%	9/90 (10%)
38	Oral corticosteroids >1 week with diabetes	8	2%	8/103 (8%)
39	Oral corticosteroids >1 week with hypertension	19	5%	19/221 (9%)
40	Thiazide and loop diuretics with gout	18	5%	18/27 (67%)
Part 2b: Potentially inappropriate drugs, dependent on diagnosis - Specific molecules				
41	Alizapride with Parkinson's disease	0	0%	0/54 (0%)
42	Metoclopramide with Parkinson's disease	0	0%	0/54 (0%)
Part 3: Potential prescribing omissions				
43	The patient is taking ≥ an equivalent of 7.5 mg of oral prednisone for ≥3 months and is not prescribed Ca/VitD supplementation and bisphosphonates.	7	2%	7/11 (64%)
44	The patient is taking narcotic analgesics and is not prescribed appropriate preventative bowel regimen (preferably macrogol or lactulose).	35	8%	35/84 (42%)
45	The patient has an elevated risk for osteoporosis (determined via FRAX-tool(22)) and is not prescribed Calcium/Vitamin D supplementation.	214	54%	214/295 (73%)
46	The patient is taking oral corticosteroids for ≥1 month and is not prescribed Ca/VitD supplementation.	15	4%	15/25 (60%)
47	The patient is not reminded and proposed to undergo yearly influenza vaccination.	0	0%	0%
48	The patient is taking methotrexate and is not prescribed folic acid supplementation.	1	0%	1/1 (100%)

Part 4: Drug-Drug interactions of specific relevance				
49	VKA + oral NSAIDs	2	1%	
50	RAAS-inhibitor + potassium sparing diuretic/potassium supplements/potassium containing drugs[b]	20	5%	
51	VKA + Antiplatelet drugs (esp. ASA), unless prescribed by internist/cardiologist	11	3%	
52	VKA + TMP/SMX	0	0%	
53	Oral NSAID + Oral Corticosteroids	4	1%	
54	Oral NSAID + Diuretic	22	6%	
55	Digoxin + Macrolide antibiotics	1	0%	
56	Digoxin + Verapamil/Diltiazem	0	0%	
57	Lithium + RAAS-inhibitors	0	0%	
58	Lithium + Oral NSAID	0	0%	
59	Lithium + Diuretics	0	0%	
60	Theophylline + Quinolones/Macrolides	2	1%	
61	RAAS-inhibitor + Oral NSAID	8	2%	
62	Oral NSAID + SSRI/SNRI	9	2%	
63	RAAS-inhibitor + TMP/SMX	2	1%	
64	Oral antidiabetics/insulin + non-selective beta-blocker	8	2%	
65	Oral antidiabetics/insulin + cardioselective beta-blocker	37	9%	
66	Alprazolam/Midazolam/Triazolam/Zolpidem/Zopiclone + Strong CYP3A4 inhibitor	3	1%	
67	CCB + Strong CYP3A4 inhibitor	0	0%	
68	Oral NSAID + Antipletelet drugs	16	4%	
69	Phenytoin + TMP/SMX	0	0%	
70	First dose RAAS-inhibitor at full dosage + pre-treatment with diuretic	5	1%	
71	Tamoxifen + strong CYP2D6 inhibitors	0	0%	
72	Calcium + Quinolones/Tetracyclines	13	3%	
73	Calcium + Stontium ranelate	5	1%	
74	Calcium + Levothyroxine	10	3%	
75	Bisphosphonate + Calcium, Magnesium, Zinc, Iron or Aluminium	22	6%	
76	VKA + Vitamin K containing drugs/supplements[c]	1	0%	
77	Any combination of anticholinergic drug	163	41%	

ASA**: Acetylsalicylic acid; **BPH**: Benign prostatic hyperplasia; **CCB**: Calcium Channel Blocker; **COPD**: Chronic Obstructive Pulmonary Disease; **CV-

***risk**: Cardiovascular risk; **GI-risk**: Gastro-intestinal risk; **GP**: General Practitioner; **NSAID**: Non Steroidal Anti-Inflammatory Drug; **INR**: International Normalized Ratio; **PPI**: Proton Pump Inhibitor; **RAAS-inhibitor**: Renin-Angiotensin-Aldosteron System Inhibitors; **SNRI**: Serotonin and Noradrenalin Reuptake Inhibitor; **SSRI**: Selective Serotonin Reuptake Inhibitor; **TMP/SMX**: Trimetoprim/Sulfamethoxazol; **VKA**: Vitamin K Antagonist.*

[a] Full dose defined as: >20 mg (es)omeprazole, >20mg pantoprazole, >30mg lansoprazole, >20mg rabeprazole

[b] Some drugs contain considerable potassium amounts: Glucosamine in potassium salt (up to 300mg/tablet), oral nutritional supplements (up to 200mg/unit).... (Recommended Daily Dose: 3000mg/day for ≥60 year old patients)

[c] Some supplements such as oral nutritional supplements contain considerable Vitamin K amounts (up to 13µg/unit). (Recommended Daily Dose: 50-70µg/day for ≥60 year old patients)