Detecting potentially inappropriate prescribing in patients with unplanned hospitalisation:

what is (to be) changed when patients travel across the interfaces within the health system.

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DETECTING POTENTIALLY INAPPROPRIATE PRESCRIBING IN PATIENTS WITH UNPLANNED HOSPITALISATION: WHAT IS (TO BE) CHANGED WHEN PATIENTS TRAVEL ACROSS THE INTERFACES WITHIN THE HEALTH SYSTEM.

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ABSTRACT

BACKGROUND

Polypharmacy and multimorbidity lead to inappropriate prescribing which is linked to adverse outcomes. Explicit screening criteria identify *potentially* inappropriate prescriptions (PIP). Medication review is proposed as a strategy to reduce these prescriptions. Older patients with high levels of polypharmacy who undergo unplanned hospitalization may benefit more from interventions aimed at reducing IP.

AIM

To (1)determine prevalence and distribution of PIP and (2) evaluate the feasibility of screening for PIP in primary care, focusing on hospitalized patients over 65 years with polypharmacy.

DESIGN AND SETTING

This primary-care based observational study consists of a medication review identifying PIP in patients with unplanned hospitalisation followed by an interview with their GPs.

METHOD

We used the explicit STOPP START screening tool in older patients using ≥ 5 chronic medications undergoing unplanned hospitalisation to identify PIP at the time of admission, at discharge and four weeks later.The primary outcomes were number of medications, number of total PIPs and number of STOPP/START PIP per patient. The secondary outcomes were distribution of PIP per type and reason for medication changes during hospitalization and afterwards.

RESULTS

The mean amount of medications at baseline was 9.6 (range 5-14). All patients had at least one case of PIP with a mean of 4.3 PIP (1-8). The most prevalent types of START PIP were musculoskeletal (44.4%), cardiovascular (27.8%) and analgesic (11.1%) medications. The most common STOPP PIP were the fall-associated (29,1%), neurological drugs (18,2%), and the 'General' group of PIPs.
The number of medications prescribed increased significantly during hospitalization (+1.56, p=0,002). The number of PIP decreased significantly 1 month after hospitalization (-0.5, p=0,008), as did the number of STOPP PIP (-0,33, p =0,01). This trend was observed for START PIP but there was no statistical significance (-0,11, p=0,163).

CONCLUSION

Despite an increase in prescribed medications during hospitalization, inappropriate prescribing decreased after hospital discharge. Our findings suggest that focusing on medication management in the primary care setting following unplanned hospital admission can potentially increase appropriateness of prescribing.

KEYWORDS

Primary health care, inappropriate prescribing, hospital admission, medication review

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

1. Multimorbidity and polypharmacy are associated with inappropriate prescribing (IP) and adverse outcomes.
2. Explicit criteria only identify potential cases of IP. They require complete clinical information. Implicit methods are time consuming, but offer a more nuanced evaluation.
3. There is an increase in attention towards IP in Primary Care.

WHAT THIS STUDY ADDS

1. Elderly patients with polypharmacy that undergo unplanned hospital admission have high prevalence of PIP.
2. PIP may decrease following hospitalisation and this effect persists after one month.
3. Screening for PIP using explicit criteria is feasible in primary care and the General Practitioner may have an important role in this process.

MAIN TEXT

INTRODUCTION

As our population ages, chronic conditions become more prevalent. Multimorbidity, the co-existence of two or more chronic health conditions, and polypharmacy, the use of multiple medications, increase as a result. The prevalence of polypharmacy varies between 39% and 50% in elderly patients. It increases with age and comorbidities (1) and is present in up to 50% of nursing home residents in Europe.(2) In the US it is present in 39% of patients over 65 years.(3,4)
In Belgium, almost 19% of people ≥ 65 years used more than 5 medications daily over the course of at least one year. This number increases to nearly 23% in people over 75 years.(5) Wauters et al. found that polypharmacy was even more prevalent (57.7%) in the oldest old (>80 years) in Belgium. (6)
Both multimorbidity and polypharmacy negatively influence well-being: the resulting complexity of care hinders adherence and facilitates medication interactions. (7,8)
The effects include lower quality of life (QOL), self-rated health, psychological well-being and functional ability.(9,10) Aditionally risk of mortality (11), hospitalisation and health care use increase (6), causing higher costs for patients and the health system (10,11)
The risk of interactions increases with number of medications prescribed.(10,12) Hospitalisation due to adverse drug events (ADE) or medication related problems (MRP) is very common in elderly patients, with rates up to 50%. (13,14)

However, polypharmacy is not always inappropriate or avoidable.(15) Medication review interventions are suggested to improve prescribing and prevent MRP. An important step is to identify prescribed medications that are actually inappropriate.

Potentially inappropriate prescribing (PIP) is often defined as prescription of drugs that are potentially harmful (potentially inappropriate medications, PIM) or the omission of potentially beneficial medication (potential prescribing omissions, PPO). Harmful drugs are those with a negative risk-benefit balance (12,16,17) or usage for a longer period or higher dosage than needed (18) Some

authors use the term misprescribing if a medication significantly increases risk of ADE and overprescribing if no clear clinical indication exists (19–21)

PIP is associated with mortality and hospitalisation and underuse may be even more impactful than overuse. (17,22,23) However overuse is associated with clinically relevant ADEs, poorer QOL and more frequent emergency department visits and hospitalisation due to MRP (12,24,25) There is an increasing focus on PIP as a way to assess or improve quality of care.(25)(26-30) It could be essential to target specific patients when developing interventions.

During hospitalisation, medication changes are frequent and monitoring of patients after discharge can be problematic.(26–28) A lack of continuity of care and transparent communication can negatively impact health and well-being. (26,29) PIP is also more common in patients undergoing hospitalisation, and can lead to readmission(18,23,25,30) Therefore we propose to study PIP specifically in case of unplanned hospitalisation.

There is emerging evidence demonstrating the effect of IP on mortality in Primary Care (PC). Recent studies suggest a higher risk of hospitalisations, ADE and lower QOL.(22,31) Primary Care provides continuity of care and supports information flow between care providers. Primary Care Physicians (PCP) coordinate care and evaluate medication lists. They recognize the challenges associated with polypharmacy and comorbidity, multiple prescribers and lack of communication. (32) An important advantage of Primary Care is accessability, long term care and the ability to counsel patients before referral and treatment.(29)

Recently there has been more research in the primary care setting, as tackling PIP in this setting could be more (cost-)effective.(21) Another important advantage is the vital role of the primary care physician in the management of chronic conditions, including as a prescriber. This level of care may be suited to continuously assess the patient's burden of morbidity, preferences and previous treatment approaches.(19)

The aim of our study is to evaluate the prevalence of PIP in patients over 65 years with polypharmacy using both the START and STOPP-criteria. By performing a medication review around hospitalisation and after one month, we describe changes in (inappropriate) prescribing and the primary care physicians view on PIP. Our study is set in the Primary Care practice, where the necessary medical information such as demographic factors, diagnoses, clinical and technical examinations and previous treatments are available.

METHODS

Study design, setting and participants

We included patients from the population of two primary care practices. The first was a rural practice located in Zottegem, the second was an urban practice located in Ghent. Both practices consisted of two fully trained primary care physicians and one primary care physician in training.

Patients were included starting from 01 June 2019 until 30 November 2019, by screening all incoming hospitalisation and discharge letters using the practices' electronic health records. Any non-elective hospitalisation was considered for inclusion.
Patients who were over 65 years at time of hospitalisation and had more than 5 chronic medications were included. Exclusion criteria were palliative care setting and moderate to severe dementia (defined as an MMSE of 20 or lower) or otherwise unable to consent to inclusion.
All patients were required to provide written informed consent.
The protocol of this study was approved by the Medical Ethics Committee of the University of Ghent (B670201940352)

Data collection

Upon hospitalisation (T0) the researchers gathered the clinical information and laboratory result necessary to identify all relevant comorbidities, diagnoses and previous treatments from the electronic health record. At this time the current chronic medication list was recorded and where possible checked using pharmacy or nursing residence records.
Demographic and patient related factors were gathered, including age, sex, living situation, reason for admission and date of admission.
The medicaton list was re-evaluated at discharge (T1) and one month later (T2). New diagnoses, test results or changes to previous conditions, such as changes in kidney function, were also noted.

Patients who were readmitted during the one month follow-up period were included in baseline analysis (T0) and analysis at discharge (T1) but excluded from analysis after 1 month (T2).

The primary outcomes were number of medications, number of total PIPs and number of STOPP/START PIP per patient.
The secondary outcomes were frequency of PIP per class, frequency of medication groups associated with PIP and reason for medication change during hospitalisation and afterwards.

Medication review

All medications were classified using the ATC system. Changes to medication lists between evaluation moments (T0-T1 and T1-T2) were divided by type (addition, discontinuation or adjustment) and reason for change. All medication lists were reviewed using the updated Dutch version of the STOPP and START-criteria by the researchers. These are relevant to the European setting and successfully identify under-, mis- and overuse.(33–35) All identified PIP were classified by type (STOPP meaning overuse or misuse, START meaning underuse) and subdivided by anatomical group.
Each identified medication was counted as one case of PIP, despite some medications corresponding to multiple criteria (e.g. STOPP D10 and STOPP K2 identify antipsychotics for different reasons)

Statistical analysis

For the primary outcomes, normality checks were carried out using the Shapiro-Wilk test. Normally distributed data were analyzed using the repeated measures ANOVA test. Where sphericity was not met, a Greenhouse-Geisser correction was performed. A p value <0,05 was considered statistically significant.
We chose to exclude patients and perform a complete case analysis if data for the primary outcomes was missing due to readmission (before T2). One participant was readmitted within the first month and was excluded from the analysis.

RESULTS

Baseline characteristics

Patient characteristics are shown in table 1. There were significantly more female patients included (n= 17; 89.5%) than males (n= 2; 10.5%) and the mean age was 84.4 years (73-92 years). The majority (n= 17; 89.5%) lived at home. The mean amount of medications at baseline was 9.6 (5-14) and the median was 9. The reason for hospitalisation is also shown in table 1. The most frequent reason for admission were fall or trauma (n= 5; 26,3%) and pain or functional decline (n= 5; 26,3%).

Distribution of PIP

All patients had at least one case of PIP (range 1-8) with a mean of 4.3 PIP per patient (see table 1).

The baseline distribution of all detected PIP per anatomical group is shown in figures 1 (for START PIPs) and 2 (for STOPP PIPs). The most prevalent types of START PIP were musculoskeletal (44.4%), cardiovascular (27.8%) and analgesic (11.1%) medications. The most common STOPP PIP were the fall-associated (29,1%), neurological drugs (18,2%), and the 'General' group of PIPs, which include any medication without clear evidence based benefit, duplications and medications prescribed past their recommended duration.

Medication changes

The medication changes during hospitalisation (T0-T1) and in the month post-discharge (T1-T2) are presented in tables 2, 3a, 4a and 5a (total, additions, discontinuations and adjustments respectively). The changes are further subdivided by reason for change, including whether or not the medications were linked to PIP. Additionally, we reported the specific START or STOPP-criteria (see tables 3b, 4b and 5b) linked to the medication change if this was the case.

Medication changes were more frequent during hospitalization than in the month post-discharge. Between hospital admission (T0) and discharge (T1) the number of changes was 99 consisting of 55 additions (55.6%), 25 discontinuations (25.3%) and 19 adjustments (19.2%). The most frequent reason for initiation of a drug was a new indication (n= 37, 67.3%) followed by correction of a START PIP (n=9, 16.4%) or an existing untreated condition for which no START criterium exists (n= 9, 16.4%). Discontinuations were most frequently the result of ending indication (n= 8, 32.0%) followed by a STOPP PIP (n=6, 24.0%). Adjustments were most commonly made to adjust therapy to clinical

situation (n= 11, 57.9%) followed by switches to more suitable molecules (n= 3, 15.8%) and as a result of PIP (n= 3, 15.8%).

From discharge (T1) to one month later (T2) there were 39 changes consisting of 10 additions (25.6%), 18 discontinuations (46.2%) and 11 adjustments (28.2%). The most frequent reasons for initiation of a drug was a new indication (n= 4, 40.0%) or an existing untreated condition for which no START criterium exists (n= 4, 40.0%), followed by correction of a START PIP (n=2, 20.0%).
Discontinuations were predominantly the result of ending indication (n= 10, 55,6%) and STOPP PIP (n= 6, 33,3%).
Adjustments were most commonly made to adjust therapy to clinical situation (n= 9, 81.8%) and only one case as a result of PIP (n=1, 9,1%).

Comparison of outcomes (Figures 3, 4a-c)

The number of medications prescribed per patient significantly increased during hospitalisation from 9.33 at T0 to 10.89 at T1 (p=0.002) and then decreased afterwards although not statistically significant to 10.44 at T2 (p= 0.088).
The total number of PIP per patient decreased by 5% from 4.39 at T0 to 4.17 at T1 although this was not statically significant (p= 0.480). STOPP PIP specifically decreased by 2% from 2.56 at T0 to 2.5 at T1 during hospitalisation although this was not significant either (p=0.770).
During the first month post discharge total PIP significantly decreased by 12% from 4.17 at T1 to 3.67 at T2 (p=0.008) and after discharge STOPP PIP specifically decreased significantly as well by 13% from 2.50 at T1 to 2.17 at T2 (p=0.010).
The number of START PIP did not significantly differ at any time (p=0.310), despite appearing to decline from 1.83 at T0 to 1.67 at T1 and 1.56 at T2.

DISCUSSION

Summary

Our results show that potentially inappropriate prescribing was prevalent in elderly patients with polypharmacy that underwent unplanned hospitalisation. All included patients had at least one case of PIP. STOPP PIPs (over- and misuse), most commonly neurologic and fall-associated drugs, were more prevalent than START PIP (underuse), which included mostly preventive musculoskeletal and cardiovascular drugs. The overall number of medications was high upon hospital admission and increased as a result of the hospitalisation. The most common prescription change was addition of new medications during hospitalization and discontinuation of previous medications during the post-discharge period. The most important reason for these changes was the clinical situation of the patient (end of a certain problem or a new diagnosis) however changes linked to specific START or STOPP PIP were frequent as well. We found that some medication changes were also performed to adjust existing under- or overuse that was not described in the START or STOPP criteria.
Medication changes occurred more frequently during hospitalisation than afterwards. Although the number of medications increased during hospitalisation, the frequency of PIP as identified by these criteria decreased. This effect was most observed mostly during the month after hospitalisation,

when recommendations in the discharge letter or adjustments by the primary care physician are usually carried out. These findings imply that medication lists undergo significant changes as a result of unplanned hospitalisation.

Comparison to existing literature

Previous studies have focused on the application of explicit screening tools to retrospective data, including administrative databases.
These cross-sectional studies may have underestimated the quantity of PIPs as a result of missing information. (17,30,36) The prevalence of PIP in our cohort was higher than in the general elderly population and more specifically in Belgium. (21,30) Throughout Europe, the prevalence according to one meta-analysis was 22,6%.(21) However, this number varies between 3-38% depending on the definition and screening/detection method of PIP as well as study population (18,19,36,37) with prevalence exceeding 50% in elderly patients. (23,30) The BELFRAIL cohort shows that in the oldest old underuse was detected in 59% and overuse in 41% of patients.(30)

According to our results PIM (over- or misuse) were more common than PPO (underuse), which was not the case in the BELFRAIL-cohort and other observational studies (18,30,36).
There is evidence that older age and polypharmacy are risk factors for inappropriate prescribing (IP) (23,36), although the correlation is much stronger for overprescribing than underprescribing. (10,18) The relatively old age and high number of prescriptions in our cohort may explain this discrepancy. Our findings do confirm the frequent involvement of cardiovascular and neurologic drugs in PIP, as well as the potential underuse of Calcium, vitamin D and statins i.e. preventive treatment.(17,18)

Furthermore we confirmed that medication changes are common during hospitalisation and overall prescribing increases during this period.(26,27) Recent studies showed that in the months after discharge changes are frequent and depend on the number of medications at discharge.(26) Our results also seem to support that prescribing decreases again following discharge.(27)In contrast to these and other findings, we found that PIP actually decreased after hospital admission and discharge. This means that this timeframe is an opportunity for GPs to review a patient's health status and medication list.

There is a lack of evidence to guide physicians in identifying high risk patients with multimorbidity. The existing literature suggests focusing on patients with a higher number of comorbidities, extreme polypharmacy or 'clusters' of conditions.(12) Previous reviews have concluded that carefully selecting patients at risk for death or hospitalisation may increase the effectiveness of medication review in preventing these events.(38) Our study design is therefore supported by a recent large scale study (23) that showed hospital admission, higher age, greater number of prescription items, and multimorbidity were all associated with a higher rate of PIP.

Strengths

Since we prospectively gathered information and had access to electronic records, discharge letters and medication lists we were able to fully apply all START and STOPP-criteria without any missing data. The study design therefore is representative of daily practice.

Additionally our inclusion criteria resulted in the selection of very old patients with a high number of chronic medications. There was a high rate of PIP, demonstrating the accurate identification of patients with complex care regimens at high risk of MRP.

We therefore conclude that identifying high risk patients and performing complete medication reviews repeatedly is feasible in primary care.

The primary researchers also avoided informing treating physicians of a patient's inclusion before the data collection was finished. Additionally, although data collection started at time of admission, the medication review process itself started after the one month follow-up period, which decreased the likelihood of bias.

Limitations

Although we tried to minimize bias, the Hawthorne effect cannot fully be excluded. All participating physicians were aware of the study design and were exposed to the START and STOPP-criteria as a result, which may have influenced prescribing decisions.

Secondly, while the study design facilitated fast collection of data, the process of medication review was still time consuming. Complete and up to date electronic health records and experience with the START and STOPP-criteria proves to be essential.
Despite our efforts to account for over the counter medications, it is possible that certain drugs were missed during analysis. NSAIDs for example are widely available through pharmacies or family members and commonly initiated for joint pains without consulting a physician. It is possible that patients have these drugs at home and use them more frequently or longer than initially prescribed.

Thirdly, this study has a relatively small sample size. This was due to the short inclusion period (June 2019 until November 2019) during which hospitalisations were less frequent. The exclusion of palliative patients and numeric cut-off of polypharmacy may have led to the exclusion of patients without complex farmacotherapeutical regimens, but who are at risk of MRP.
There is growing evidence that the number of medications – or even the number of PIP – may not necessarily predict the quality of care. Although polypharmacy is linked to worse health outcomes, using the number of medications as an indicator for quality is inadequate.(11,20) More medications – even those that are justified – as well as underuse may both be hazardous. The appropriateness of all prescribing decisions should be assessed in a holistic manner instead.(11,17,30)

Finally our use of explicit criteria means we focused only on pharmacological potential appropriateness. These explicit criteria are usually developed through literature review, expert opinion and consensus.(19,39) As they describe specific instances of IP and are drug- or disease-oriented, they are easier to apply with limited clinical judgment.(14,15) They enable identification of

PIP patterns, but not which PIP are actually inappropriate, avoidable or clinically relevant. The implicit approach to the cases described here was the focus of the second phase of this study, which is described elsewhere.

Research implications

Primary care physicians are willing to continuously review medication prescriptions, but they recognize that this is complex and time consuming.(32) Furthermore evidence concerning the effectiveness of medication review is mixed. Ideally, increasing medication appropriateness should improve both clinical outcomes and patient QOL.
To achieve this goal redefining the concept of polypharmacy, moving away from a numerical cut-off and assessing prescriptions based on indication, efficacy and potential for harm will be necessary (11,17). Spinewine e.a. suggest redefining appropriateness as a continuous scale of prescribing quality instead of a categorical label based on a measurable lower limit (e.g. explicit criteria). An implicit approach is needed to address the burden of co-morbidity, patient preference or previously unsuccesful approaches.(19,20) This is especially relevant for elderly patients.
Implicit screening tools address a wider range of aspects determining appropriateness, but are more time-consuming. We suggest the development of well-designed clinical trials that focus on a well-defined small subgroup of patients. Based on our results we suggest targeting elderly patients with an unplanned hospital admission, who may benefit more from medication optimization.(23,26,40)
The choice of screening methods - either implicit or explicit- depends on the aim of the study. The START and STOPP-criteria are validated and predict ADE and hospitalisations.(33,34)
The second phase of this study consisted of semi-structured interviews with the treating physicians. The results, which are described elsewhere, illustrate that not all PIP is actually inappropriate or avoidable. These interviews expand upon the medication review we performed. It is the first step in the development of studies targeting medication appropriateness by involving physicians, patients and other caregivers. Pharmacists and nurses could be involved in future studies, especially if medication adherence, administration or OTC medication are a focus point.

Studies are being conducted examining complex interventions which include medication review and deprescribing.(12) Our results show that a complete and repeated medical review is feasible, but rigorous research should evaluate the acceptability for both patients and physicians and use valid, reliable and easily applied outcome measures. The European Optimizing thERapy to prevent Avoidable hospital admissions in the Multimorbid elderly (OPERAM) project is currently evaluating the effectiveness The Systematic Tool to Reduce Inappropriate Prescribing (STRIP). This tool combines the START an STOPP criteria with an implicit approach to target patient needs and wishes, aiming to prevent hospital readmissions.(41) The DREAMeR study(40) is an example of an intervention integrating medication review in a broader, goal oriented strategy. We suggest expanding upon these interventions and including clinical outcomes such as ADE, hospitalisations and mortality.

TABLES

Table 1

Baseline characteristics		**n = 19**
Age (years)	*Mean (range)*	84,4 (73-92)
	Std. Deviation	5,673
Sex	*n° male*	2 (10,5%)
	n° female	17 (89,5%)
Practice	*n° Zottegem*	4 (21,1%)
	n° Ghent	15 (78,9%)
Living situation	*n° at home*	10 (52,6%)
	n° at home, with support	7 (36,8%)
	n° assisted living facility	2 (10,5%)
Reason for admission	*Fall or trauma*	5 (26,3%)
	Bleeding	2 (10,5%)
	Infection	4 (21,1%)
	Decompensation of existing condition	3 (15,8%)
	Pain or functional decline	5 (26,3%)
Number of medications at baseline	*Mean (range)*	9,6 (5-14)
	Std. Deviation	2,567
Number of PIP	*Mean (range)*	4,3 (1-8)
	Std. Deviation	2,162
Number of STOPP PIP	*Mean (range)*	2,6 (0-5)
	Std. Deviation	1,539
Number of START PIP	*Mean (range)*	1,7 (0-3)
	Std. Deviation	0,933

Reason for admission	*Fall or trauma*	5 (26,3%)
	Bleeding	2 (10,5%)
	Infection	4 (21,1%)
	Decompensation of existing condition	3 (15,8%)
	Pain or functional decline	5 (26,3%)
Number of medications at baseline	*Mean (range)*	9,6 (5-14)
	Std. Deviation	2,567
Number of PIP	*Mean (range)*	4,3 (1-8)
	Std. Deviation	2,162
Number of STOPP PIP	*Mean (range)*	2,6 (0-5)
	Std. Deviation	1,539
Number of START PIP	*Mean (range)*	1,7 (0-3)
	Std. Deviation	0,933

Table 2

Overview of medication changes

Time of evaluation		Frequency	Percent
During hospitalization	Addition	55	55,6
	Discontinuation	25	25,3
	Switch	19	19,2
	Total	99	100,0
One month post-discharge	Addition	10	25,6
	Discontinuation	18	46,2
	Switch	11	28,2
	Total	39	100,0

Table 3a

Overview of medication additions

Time of evaluation		Frequency	Percent
During hospitalization	new indication[a]	37	67,3
	START PIP (underuse)[b]	9	16,4
	existing indication[c]	9	16,4
	Total	55	100,0
One month post-discharge	new indication[a]	4	40,0
	START PIP (underuse)[b]	2	20,0
	existing indication[c]	4	40,0
	Total	10	100,0

a. new indication arose during study period e.g. new diagnosis

b. adrug that was previously indicated was added (underuse), corresponding with a START criterium

c. a drug that was previously indicated was added (underuse) but there was no corresponding START criterium

Table 3b

Frequency of START criteria leading to start of treatment

Time of evaluation		drugs added	Percent
During hospitalization	START A3	1	11,1
	START CV4	2	22,2
	START GI2a	1	11,1
	START GI3	1	11,1
	START MS5	4	44,4
	Total	9	100,0
One month post-discharge	START A3	1	50,0
	START MS5	1	50,0
	Total	2	100,0

Table 4a

Overview of medication discontinuation

Time of evaluation		Frequency	Percent
During hospitalization	end of indication[a]	8	32,0
	no indication[b]	4	16,0
	previous contra-indication[c]	1	4,0
	new contra-indication[d]	2	8,0
	STOPP PIP (mis-/overuse)[e]	6	24,0
	mistake/unclear	4	16,0
	Total	25	100,0
One month post-discharge	end of indication[a]	10	55,6
	no indication[b]	1	5,6
	new contra-indication[d]	1	5,6
	STOPP PIP (mis-/overuse)[e]	6	33,3
	Total	18	100,0

a. discontinuation of medication where there previously was a valid indication e.g. end of a treatment regimen or resolution of a condition

b. discontinuation of medication that never had a valid indication (overuse) but no STOPP criterium exists

c. discontinuation of medication that was prescribed despite previous contra-indication (misuse) but no STOPP criterium exists

d. discontinuation because of a new contra-indication e.g. deterioration of kidney function or a new condition

e. discontinuation because of over- or misuse, corresponding with a STOPP criterium

Table 4b

STOPP criteria leading to discontinuation of treatment

Time of evaluation		drugs discontinued	Percent
During hospitalization	STOPP A2	1	16,7
	STOPP C2	1	16,7
	STOPP D5/K1	1	16,7
	STOPP F4	1	16,7
	STOPP K3	2	33,3
	Total	6	100,0
One month post-discharge	STOPP A1	1	16,7
	STOPP A2	2	33,3
	STOPP A3	2	33,3
	STOPP B1	1	16,7
	Total	6	100,0

Table 5a

Overview of medication switches

Time of evaluation		Frequency	Percent
During hospitalization	alternate dosage[a]	11	57,9
	different molecule[b]	3	15,8
	alternate administration or frequency[c]	2	10,5
	PIP adjustment[d]	3	15,8
	Total	19	100,0
One month post-discharge	alternate dosage[a]	9	81,8
	alternate administration or frequency[c]	1	9,1
	PIP adjustment[d]	1	9,1
	Total	11	100,0

a. same drug was prescribed, but dosage was adjusted

b. drug was replaced by a drug from the same therapeutic class

c. same drug was prescribed, but mode of administration (e.g. patch instead of tablet) or frequency (e.g. weekly instead of daily) was changed

d. drug was changed or adjusted to increase appropriateness (e.g. a more appropriate class or molecule)

Table 5b

START/STOPP criteria leading to adjustments of existing treatment

Time of evaluation		Frequency	Percent	Valid Percent	Cumulative Percent
During hospitalization	STOPP A3/D5/K1	1	33,3	33,3	33,3
	STOPP D5/K1	1	33,3	33,3	66,7
	STOPP F2	1	33,3	33,3	100,0
	Total	3	100,0	100,0	
One month post-discharge	STOPP C1	1	100,0	100,0	100,0

FIGURES

Figure 1

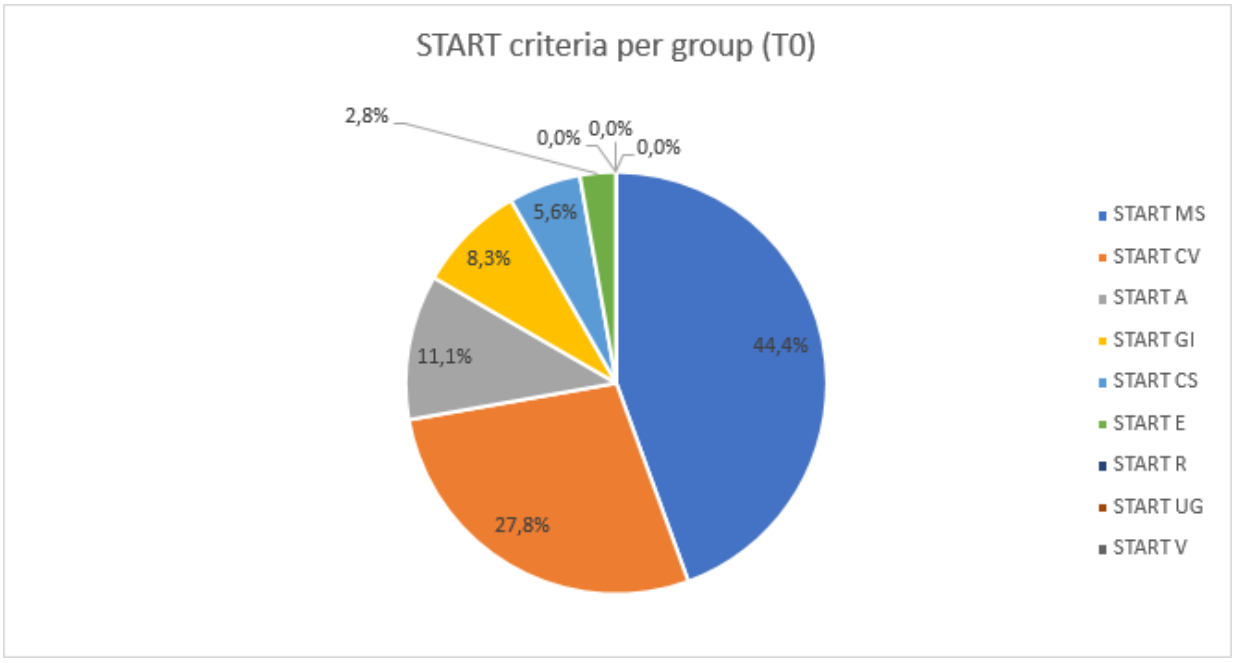
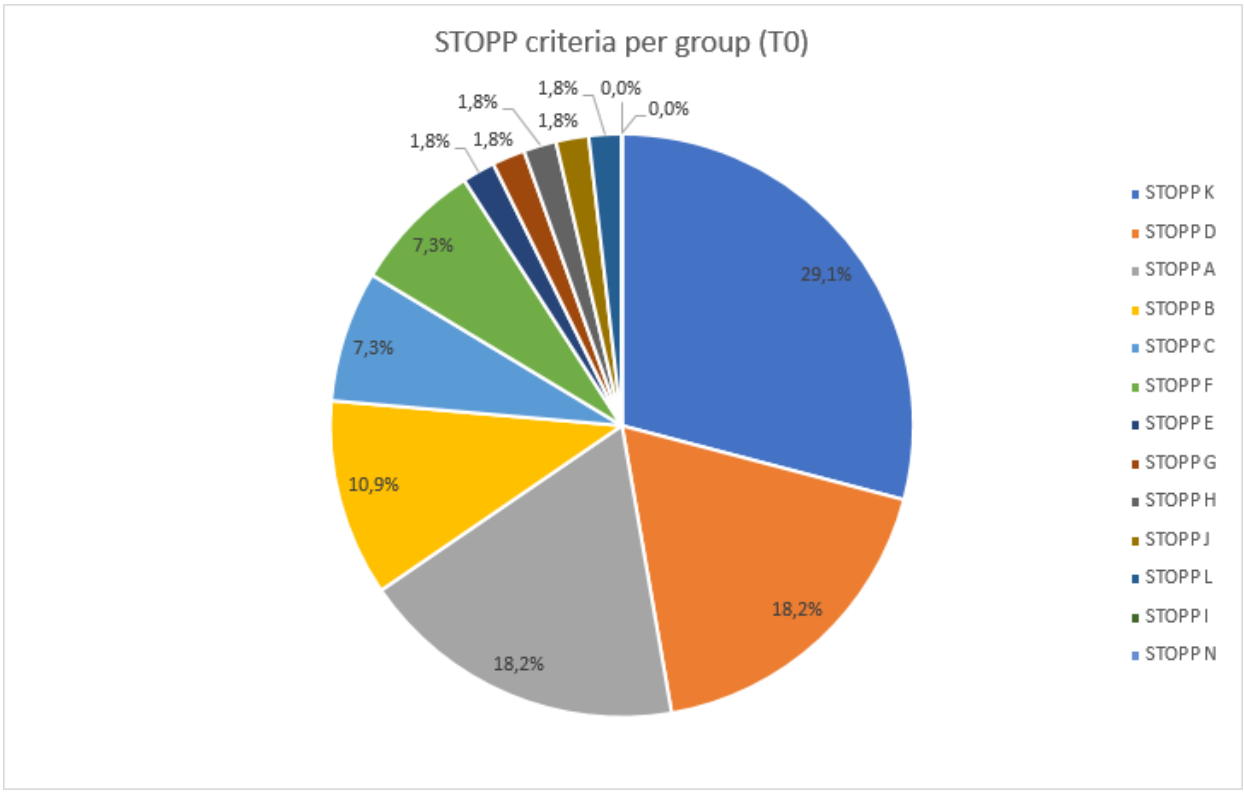


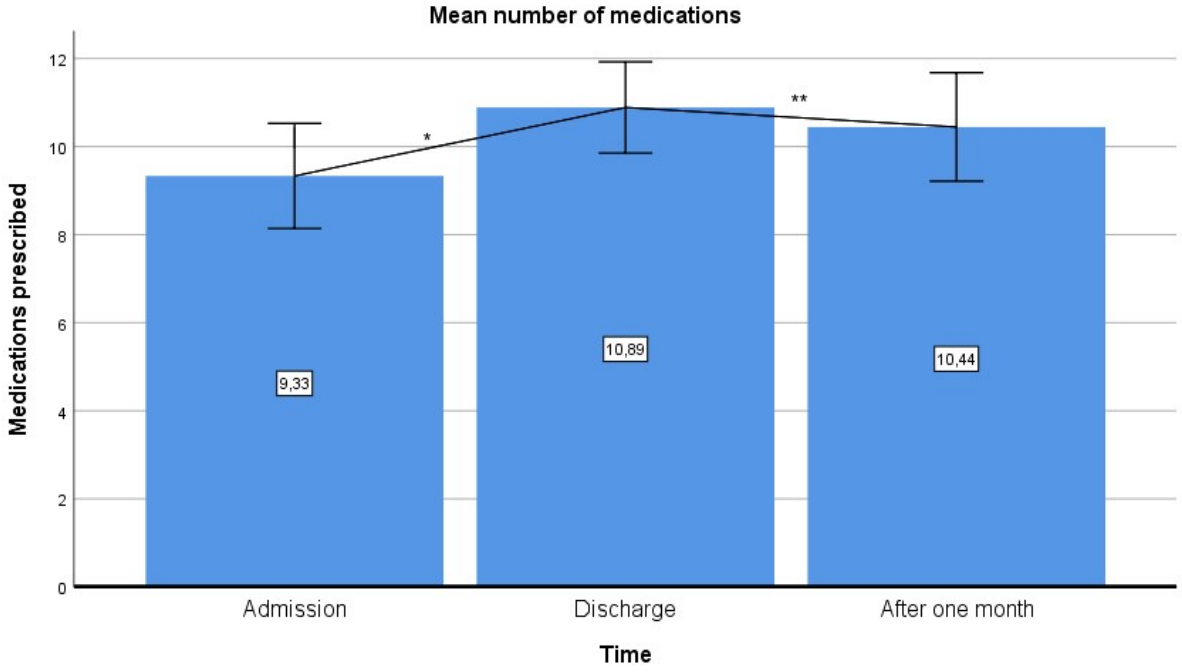
Figure 2



Legend

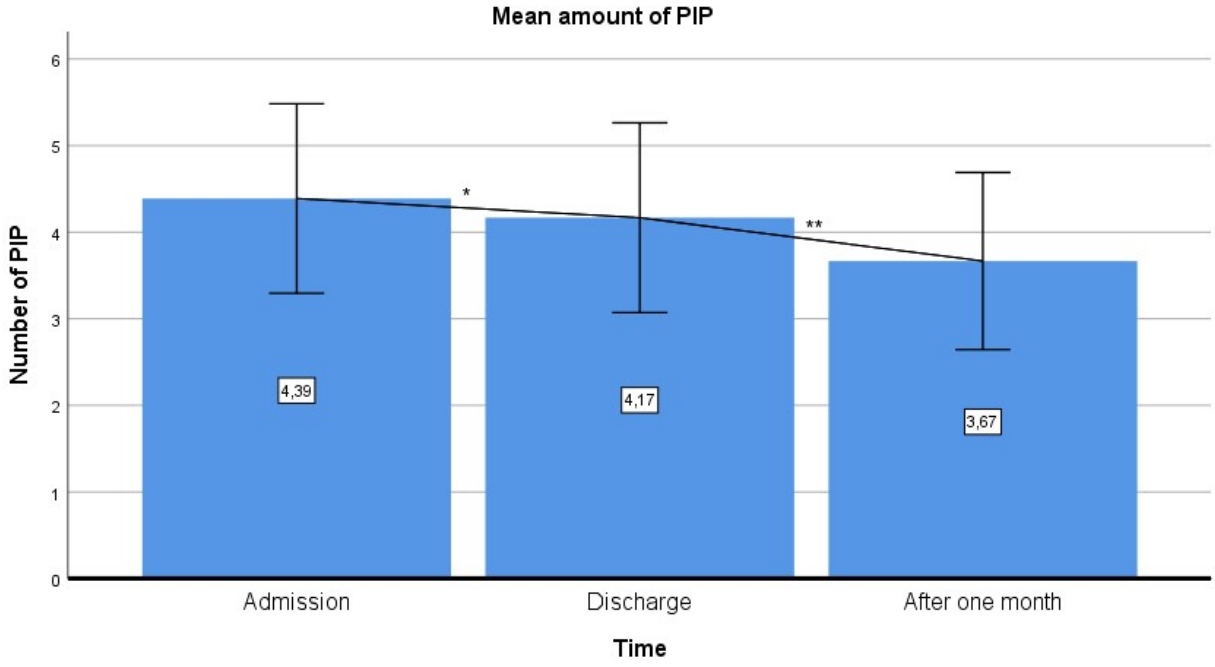
STOPP group code	Corresponding Section
STOPP K	Section Drugs that adversely affect those prone to falls
STOPP D	Section Central Nervous System and Psychotropic Drugs
STOPP A	General section
STOPP B	Section Cardiovascular System
STOPP C	Section Antiplatelet or Antithrombotic agents
STOPP F	Section Gastrointestinal System
STOPP E	Section Impaired Kidney Function
STOPP G	Section Respiratory System
STOPP H	Section Musculoskeletal System
STOPP J	Section Endocrine System
STOPP L	Section Analgesics
STOPP I	Section Urogenital System
STOPP N	Section Anticholinergic Burden
START group code	
START MS	Section Musculuskeletal System
START CV	Section Cardiovascular System
START A	Section Analgesics
START GI	Section Gastrointestinal System
START CS	Section Central Nervous System & Eyes
START E	Section Endocrine System
START R	Section Respiratory System
START UG	Section Urogenital System
START V	Section Vaccines
For the START criteria we decided to recode the sections to avoid confusion with similarly named STOPP criteria. We explain the abbreviations for the subgroups of the criteria here, for the specific criteria we refer to the original publication concerning the STOPP/START criteria.(33)	

Figure 3



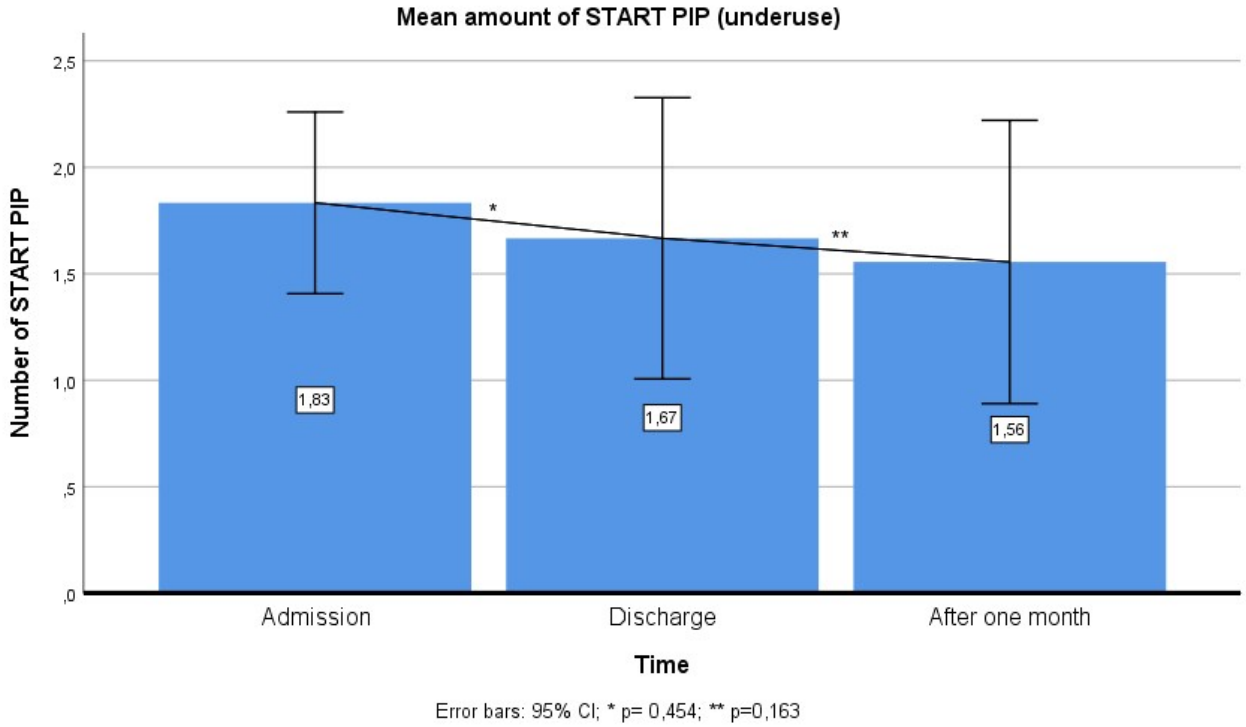
Error bars: 95% CI; * p = 0,002; ** p= 0,088

Figure 4a



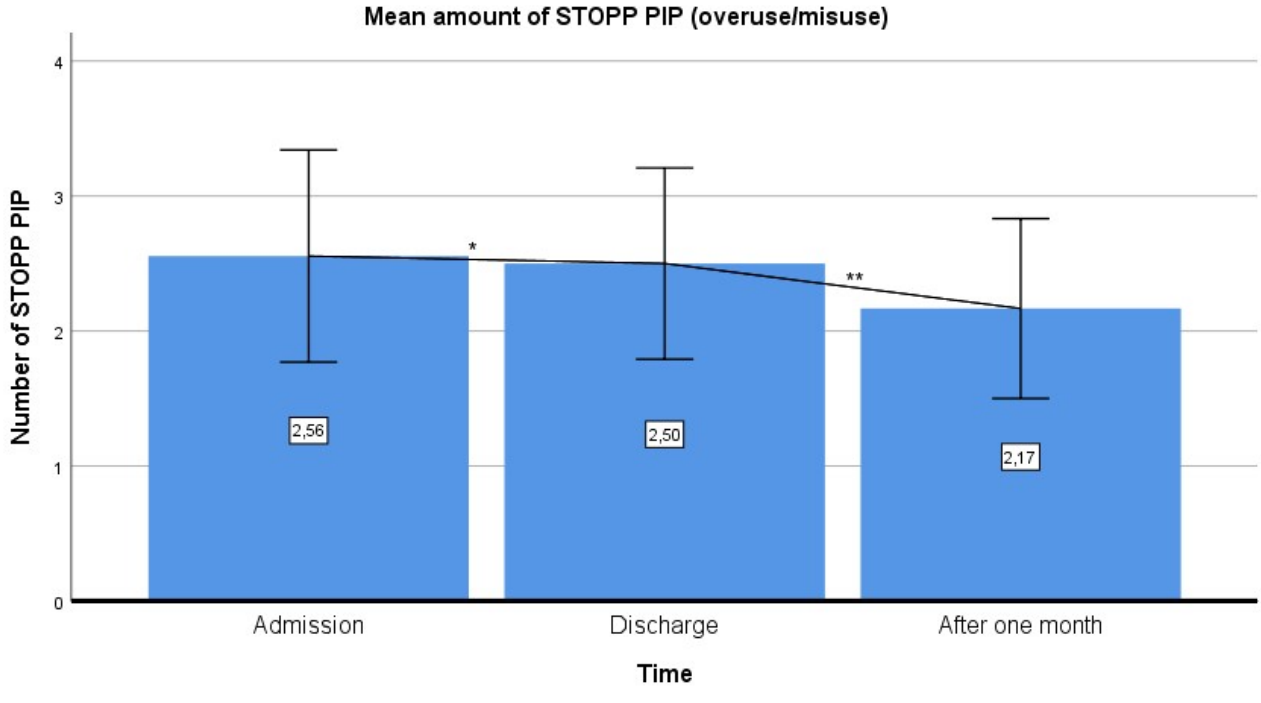
Error bars: 95% CI; * p= 0,481; ** p= 0,008

Figure 4b



Error bars: 95% CI; * p= 0,454; ** p=0,163

Figure 4c



Error bars: 95% CI; * p= 0,772; ** p= 0,01

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