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ORIGINAL RESEARCH ARTICLE

The Association Between Potentially Inappropriate Prescribing and Medication-Related Hospital Admissions in Older Patients: A Nested Case Control Study

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Abstract

Introduction Medication-related problems can cause serious adverse drug events (ADEs) that may lead to hospitalization of the patient. There are multiple screening methods to detect and reduce potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs). Whether this will result in less medication-related hospitalizations is unknown. The study objective was to assess the risk of preventable medication-related hospital admissions associated with potentially inappropriate prescribing, using the Beers 2012 and the Screening Tool of Older Person's Prescriptions and the Screening Tool to Alert doctors to Right Treatment (STOPP & START) 2008 criteria.

Design, setting and participants A nested case–control study was conducted with a subset of Dutch participants from the Hospital Admissions Related to Medication (HARM) study. Cases were defined as patients aged ≥65 years with a potentially preventable medication-related hospital admission. For each case, one control was selected, matched for age and sex. The primary determinant was the presence of one or more PIMs according to the Beers 2012 and STOPP 2008 criteria. The secondary determinant was the presence of one or more PIMs and PPOs according to the STOPP & START 2008 criteria. The strength of the association between inappropriate prescribing and medication-related hospital admission was evaluated with multivariate logistic regression and expressed as odds ratios (ORs) with 95 % confidence intervals (CIs).

Results The prevalence of Beers 2012 criteria PIMs in the total cohort was 44.4 %. The prevalence of STOPP &

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Key Points

Potentially inappropriate medications (PIMs) identified with the STOPP 2008 criteria were significantly associated with preventable medication-related hospital admissions, whereas PIMs identified with the Beers 2012 criteria were not.

The STOPP and the START 2008 criteria can be used to identify older people at risk of medication related problems.

Medicines prescribed to older people should be reviewed regularly by a multidisciplinary team, in order to prevent adverse drug events.

START 2008 criteria PIMs and PPOs were, respectively, 34.1 and 57.7 %. STOPP 2008 criteria PIMs were associated with preventable medication-related hospital admissions [OR adjusted for number of drugs and comorbidities (OR_{adj}) 2.30, 95 % CI 1.30–4.07], whereas there was no association with Beers 2012 criteria PIMs (OR_{adj} 1.49, 95 % CI 0.90–2.47). STOPP PIMs and START PPOs together were also associated with preventable medication-related hospital admissions (OR_{adj} 3.47, 95 % CI 1.70–7.09).

Conclusion Our study shows that patients with potentially inappropriate prescribing detected with the STOPP & START 2008 criteria are at risk of preventable medication-related hospital admissions. The STOPP & START 2008 criteria can be used to identify older people at risk of medication-related problems.

1 Introduction

Medication-related problems can cause serious adverse drug events (ADEs) that may lead to hospitalization of the patient. A meta-analysis from Beijer and de Blaey [1] shows that the percentage of patients hospitalized because of adverse drug reactions varied from 0.2 to 41.3 %. The proportion of adverse drug reaction-related hospitalizations in the elderly was 19.6 ± 4.6 % (mean ± confidence interval) [1]. A more recent systematic review shows that the median prevalence of adverse drug reactions leading to hospitalization in elderly was 10.0 % [95 % confidence interval (CI) 7.2–12.8] [2]. The Hospital Admissions Related to Medication (HARM) study showed that 5.6 % of the unplanned hospital admissions in the Netherlands are medication related, and that 46 % of these hospital admissions can be classified as potentially preventable [3]. Medication-related hospital admissions were almost twice as common among patients older than 65 years than among younger patients, with polypharmacy (defined as five or more medicines in long-term use at the time of admission) being found to be the most important medication-related risk factor. The HARM study recommended regular review of the medication use of high-risk patients to detect potential medication-related problems, such as underprescription and overprescription, interactions, and user convenience [3].

Multiple screening methods are available to detect and reduce inappropriate prescribing, such as the Screening Tool of Older Person's Prescriptions and the Screening Tool to Alert doctors to Right Treatment (STOPP & START) criteria, the Beers criteria, the Laroche list, the PRISCUS list, and the NORGEP criteria. The most commonly used criteria in the Netherlands are the Beers and the STOPP & START criteria. The STOPP & START criteria are incorporated in the national (Dutch) guideline "Polypharmacy in the elderly" [4]. A list of potentially inappropriate medications (PIMs) was developed in the USA by Beers and colleagues for nursing home residents in 1991, and was subsequently expanded and revised in 1997 and 2003 to cover all geriatric care settings. The criteria were updated in 2012 [5]. The 2012 Beers criteria categorize PIMs into three groups: (1) medication to avoid in older adults regardless of diseases or conditions, (2) medication considered potentially inappropriate when used in older adults with certain diseases or syndromes, and (3) medication that should be used with caution [5]. Another screening method to identify inappropriate prescribing is the STOPP & START criteria, which were developed in 2008 in Ireland [6, 7]. The STOPP criteria comprise a list of 65 evidence-based indicators of PIMs, including drug–drug interactions, drug–disease interactions, therapeutic duplication, treatment duration, and drugs that increase the risk of cognitive decline or falls. The START criteria consist of 22 evidence-based indicators of potential prescribing omissions (PPOs) in older people with specific medical conditions. Recently, a new version of the STOPP & START criteria was published (STOPP & START 2015) [8]. Previous studies have shown that the STOPP 2008 criteria identify significantly more PIMs than the Beers criteria 2003 and 2012 [9–14], and are therefore considered clinically more relevant [12, 15, 16]. Other studies have shown that inappropriate prescribing, identified with either the Beers 2003 or STOPP & START 2008 criteria, is associated with a clinically relevant endpoint, such as medication-related hospital admissions [17–20]. However, no studies have investigated the association between inappropriate medication use identified with the Beers 2012 criteria and the STOPP & START 2008 criteria and medication-related hospital admissions. We carried out a nested case–control study involving elderly patients of the HARM study to assess the association between potentially inappropriate prescribing according to both the Beers 2012 and STOPP & START 2008 criteria and medication-related hospital admissions.

2 Methods

2.1 Setting

This study involved a subset of patients of the HARM study, in which the frequency and diagnosis of medication-related hospitalizations were determined, and a case–

control design was used to determine risk factors for potentially preventable admissions [3] Data were collected between September 2005 and June 2006 in 21 Dutch hospitals (university, teaching, and general hospitals). The hospitals were selected from all regions to obtain a representative sample. In each hospital, a specially trained researcher screened all unplanned admissions for a potentially medication-related cause for 40 days over 2 consecutive months. Admissions involving patients younger than 18 years, patients admitted for obstetric indications or self-poisoning, and patients admitted to a psychiatric ward were excluded. For all remaining admissions, the documented reason for admission and medication use before admission were assessed by means of a trigger list. This trigger list consisted of 537 combinations of symptoms and medicines that have been mentioned in the literature as reasons for hospitalization [21]. As this list was not validated, any admission that matched this list was discussed with the hospital physician treating the patient. If admission and medication use were deemed possible, the patient was included as a case and was followed up during admission. Hospital physicians were also asked to report potential cases not identified with the trigger list. Two clinical pharmacists independently assessed all the cases with respect to the causal relationship between the suspected medicine and the reason for hospitalization, using an adjusted version of the algorithm of Kramer et al. [22]. In this version, the answers to three questions are used to classify causality as "possible", "probable", or "unlikely"; "unlikely" cases were excluded [3]. The same pharmacists also assessed the preventability of the admissions, according to a modified version of the algorithm of Schumock and Thornton [23]. If the assessments of the pharmacists disagreed, they met to reach consensus (2.5 % of the cases for the causality assessment and 26 % of the cases for the preventability assessment) [3]. For each case, one control was selected from patients admitted for planned surgery in the same hospital, matched by age (by 5-year age group) and sex. In the HARM study, almost 13,000 unplanned admissions were screened, of which 714 (5.6 %) were medication related. Almost half (46.5 %) of these admissions were potentially preventable, resulting in 332 case patients matched with 332 controls. The following data were collected for each patient: sex, age, information from the medical record (medical history, diagnostic procedures, cognitive function and outcomes), medication history and clinical laboratory data up to 1 year before admission, and information about the living situation. All included patients provided a written informed consent to use their medical information for research purposes.

2.2 Study Design and Population

A nested case–control design was used to evaluate the association between the presence of potentially inappropriate prescribing, identified with the Beers 2012 and STOPP & START 2008 criteria, and medication-related hospital admissions. Cases were patients aged ≥65 years with preventable medication-related hospital admissions selected from the HARM study. For each case, the control from the HARM study was used, matched on age (by 5-year age group) and sex.

2.3 Determinants

The primary determinant was the presence of one or more PIMs identified with the Beers 2012 criteria and the Dutch version of the STOPP 2008 criteria. The secondary determinant was the presence of one or more PPOs and one or more PIMs and PPOs together, identified with the Dutch version of the STOPP & START 2008 criteria [24].

Recently, a new version of the STOPP & START criteria was published (STOPP & START 2015) [8]. In this study, we used the STOPP & START 2008 criteria, as the updated version of the STOPP & START was not available when the study was conducted. For each patient, PIMs and PPOs were determined on the basis of medication use at baseline, which was defined as the date of admission to hospital.

The Dutch version of the STOPP & START 2008 criteria differs from the original criteria in that two of the STOPP criteria are considered as START criteria (e.g., the criterion "not using a proton pump inhibitor when using an NSAID" and the criterion "not using a laxative when using opiates"). Since the use of low-dose aspirin is considered to carry the same risk of gastric ulcers or gastric bleeding as the use of NSAIDs, Dutch guidelines on gastric protection consider both drug classes as one risk class. Since in most cases it is not desirable to stop aspirin, a proton pump inhibitor is advised (depending on age and medical history). Furthermore, opiates often cannot easily be stopped. Therefore, while it is often appropriate to continue an opiate or aspirin, it is a prescribing omission if the doctor forgets to prescribe a laxative or proton pump inhibitor. Medication that is not available in the Netherlands was deleted from both screening methods, and all criteria were adjusted to current Dutch guidelines, if necessary. Two hospital pharmacists (AVW and CvdS) identified the PIMs and PPOs. When information was deemed inconclusive, a geriatrician (RvM) also applied the screening methods, after which, decisions were made based on consensus.

In order to investigate whether the risk of medication-related hospital admissions increases with the number of PIMs and/or PPOs, the presence of PIMs and/or PPOs was

further subclassified into three categories: none, one, and two or more PIMs and/or PPOs.

The HARM study also assessed the causal relationship between the suspected medicine and the reason for hospitalization in the cases. In the current study, we assessed whether the suspect medicine from the HARM study was associated with the PIM/PPO identified in individual cases. The assessment was based on clinical judgment.

2.4 Potential Confounding Factors

The following covariates from the HARM study were studied as potential risk factors: living situation [independent or dependent (i.e., in a nursing home, in a care home, or at home with nursing care)], cognition, number of prescribed medicines, kidney function, and number of comorbidities (according to number of diseases in the medical history of the patient). Cognitive function before admission was obtained from the medical record or was discussed with the physician and assessed as "normal" or "impaired" (this is the way cognitive function is assessed in everyday practice in the Netherlands; formal tests, such as the Mini-Mental State Examination, are not routinely used) [3]. On the basis of serum creatinine values nearest to the hospitalization, kidney function before admission was calculated using the Modification of Diet in Renal Disease (MDRD) formula [25].

2.5 Statistical Analysis

For both cases and controls, the prevalence of each covariate was determined at baseline. Student's *t* test was performed to assess the significance of differences in the mean of continuous variables between cases and controls. Differences in categorical variables were evaluated with conditional logistic regression and expressed as odds ratios (ORs) with 95 % CIs. The strength of the association between inappropriate prescribing (identified with the Beers 2012 or STOPP & START 2008 criteria) and preventable medication-related hospital admissions was evaluated with logistic regression and expressed as ORs with 95 % CIs. Patients with no PIM/PPO were used as the reference group in the logistic model. Covariates were included in the logistic regression model if they induced a change in the regression coefficient of at least 10 % [26]. Data were collected in Microsoft Excel 2007. All statistics calculations were carried out with the SPSS statistical package (version 19.0).

3 Results

In total, 169 cases and 169 controls met the inclusion criteria, taken from a cohort of 1428 patients (see Table 1). Patients who did not live independently, who had cognitive impairments, who used four or more drugs, who had three or more comorbidities or who had an MDRD of <30 ml/min had a higher risk of medication-related hospital admission than patients who lived independently, who did not have cognitive impairment, or who used three or fewer drugs, who had none or one comorbidity, or who had an MDRD of >60 ml/min. The prevalence of Beers 2012 criteria PIMs in the total cohort was 44.4 %. The prevalence of STOPP & START 2008 criteria PIMs and PPOs were, respectively, 34.1 and 57.7 %.

Table 2 shows the association between PIMs identified with the Beers 2012 and the STOPP 2008 criteria and potentially preventable medication-related hospital admissions. ORs were adjusted (OR_{adj}) for number of drugs and comorbidities. STOPP 2008 criteria PIMs were associated with preventable medication-related hospital admissions (OR_{adj} 2.30, 95 % CI 1.30–4.07), whereas Beers 2012 criteria PIMs were not (OR_{adj} 1.49, 95 % CI 0.90–2.47). The presence of two or more PIMs identified with the Beers 2012 criteria and the STOPP 2008 criteria was associated with a higher risk of medication-related hospital admission than the detection of no PIMs (Beers 2012 OR_{adj} 4.25, 95 % CI 1.69–10.69; STOPP OR_{adj} 3.08, 95 % CI 1.02–9.31) (Table 2). STOPP 2008 criteria PIMs and START 2008 criteria PPOs together were also associated with preventable medication-related hospital admissions (OR_{adj} 3.47, 95 % CI 1.70–7.09).

In the HARM study, there was a causal relationship between the medication used and the reason for hospitalization within the cases. We found that the PIMs/PPOs identified with the STOPP & START 2008 criteria were associated with the suspect medication in 23 % of the cases; the PIMs identified with the Beers 2012 criteria were associated with the suspect medication in 17 % of the cases.

The STOPP & START criteria most involved in the medication-related hospital admissions were (1) the omission of a proton pump inhibitor when using an NSAID and (2) the use of benzodiazepines in patients with a history of falls and impaired balance. The most involved Beers 2012 PIMs were (1) the use of benzodiazepines and (2) NSAIDs.

4 Discussion

The presence of PIMs identified with the STOPP 2008 criteria was associated with preventable medication-related hospital admissions (OR_{adj} 2.30, 95 % CI 1.30–4.07), whereas there was no association with Beers 2012 criteria PIMs (OR_{adj} 1.49, 95 % CI 0.90–2.47). The presence of two or more PIMs identified with both methods was associated with a higher risk of medication-related hospital admission than the detection of no PIMs. STOPP 2008

Table 1 Baseline characteristics

Risk factor	Cases ($n = 169$)	Controls ($n = 169$)	OR crude (95 % CI)
Mean age (years)	79.4 (range 65–93)	78.5 (range 65–92)	
Sex			
Male	80 (47.3 %)	80 (47.3 %)	
Female	89 (52.7 %)	89 (52.7 %)	
Living situation			
Independent	87 (51.5 %)	118 (69.8 %)	Reference
Dependent	64 (37.9 %)	29 (17.2 %)	4.08 (2.12–7.84)
Unknown	18 (10.7 %)	22 (13.0 %)	1.22 (0.56–2.68)
Cognition			
Normal cognition	90 (53.3 %)	119 (70.4 %)	Reference
Impaired cognition	33 (19.5 %)	5 (3.0 %)	11.52 (3.44–38.61)
Unknown	46 (27.2 %)	45 (26.6 %)	2.05 (0.64–6.57)
No. of drugs			
0–3	23 (13.6 %)	65 (38.5 %)	Reference
4–6	39 (23.1 %)	55 (32.5 %)	2.67 (1.21–5.89)
≥7	107 (63.3 %)	49 (29.0 %)	6.43 (3.18–12.98)
No. of comorbidities			
0–1	25 (14.8 %)	62 (36.7 %)	Reference
2	41 (24.3 %)	50 (29.6 %)	1.85 (0.96–3.55)
≥3	103 (60.9 %)	57 (33.7 %)	4.29 (2.35–7.82)
Renal function			
MDRD >60 ml/min	58 (34.3 %)	57 (33.7 %)	Reference
MDRD ≥30 < 60 ml/min	73 (43.2 %)	44 (26.0 %)	1.51 (0.87–2.61)
MDRD <30 ml/min	28 (16.6 %)	8 (4.7 %)	2.99 (1.16–7.74)
Unknown	10 (5.9 %)	60 (35.5 %)	0.16 (0.06–0.38)

CI confidence interval, *MDRD* Modification of Diet in Renal Disease, *OR* odds ratio

criteria PIMs and START 2008 criteria PPOs together were also associated with preventable medication-related hospital admissions (OR_{adj} 3.47, 95 % CI 1.70–7.09).

Only a few studies have examined the association between PIMs/PPOs and clinical outcomes, but to date, none have assessed the direct association between PIMs identified with the Beers 2012 and STOPP 2008 criteria and the risk of preventable medication-related hospital admission. A systematic review of the use of the STOPP & START 2008 criteria concluded that there was only limited evidence regarding the clinical impact of the criteria [27]. A study of 302 patients (>75 years and positive frailty profile) showed that inappropriate prescribing according to the STOPP & START 2008 criteria contributed to hospital admission in 27 % of the patients [20]. Australian research showed that overall PIM exposure, based on Beers 2003 criteria, was associated with an elevated risk of unplanned hospitalization ($OR_{adj.}$ 1.18, 95 % CI 1.15–1.21) [19]. Gallagher and O'Mahony [16] prospectively evaluated the performance of the STOPP 2008 and Beers 2003 criteria in terms of identifying PIMs with a clear causal association with acute hospital admission. The STOPP 2008 criteria identified a significantly higher proportion of patients requiring hospitalization as a result of PIM-related adverse events than did the Beers 2003 criteria (Mann–Whitney $Z = -15.33$, $P < 0.001$). A limitation of the Gallagher and O'Mahony [16] study was that the causal association of the PIMs with the presenting complaint was assessed on the basis of clinical judgment as opposed to strict causality and avoidability criteria. Another study compared the proportion of patient PIMs according to the Beers 2003 criteria and STOPP 2008 criteria with the proportion of preventable ADEs associated with hospital admission. The likelihood of a serious preventable ADE increased significantly when STOPP 2008 criteria PIMs were prescribed (OR 1.85, 95 % CI 1.51–2.26). Prescription of Beers 2003 criteria PIMs did not significantly increase the ADE risk (OR 1.28, 95 % CI 0.95–1.72) [15]. We also found STOPP 2008 criteria PIMs to be associated with a serious preventable ADE leading to hospitalization. An observational study of 871 patients has directly compared the Beers 2012 and STOPP 2008 criteria with ADEs rather than acute hospitalization as the outcome. This study showed that STOPP 2008 criteria PIMs were significantly associated

Table 2 Risk of medication-related hospital admissions associated with PIMs and PPOs screened with the Beers 2012 and STOPP & START criteria

Risk factor	Cases ($n = 169$)	Controls ($n = 169$)	Crude OR (95 % CI)	Adjusted OR[a] (95 % CI)
Beers 2012				
No PIM	76 (45.0 %)	112 (66.3 %)	Reference	Reference
PIM	93 (55.0 %)	57 (33.7 %)	2.24 (1.45–3.47)	1.49 (0.90–2.47)
Number of PIMs				
No PIM	76 (45.0 %)	112 (66.3 %)	Reference	Reference
1	47 (27.8 %)	44 (26.0 %)	1.46 (0.89–2.39)	1.02 (0.58–1.80)
≥2	46 (27.2 %)	13 (7.7 %)	6.41 (2.82–4.56)	4.25 (1.69–10.69)
STOPP				
No PIM	93 (55.0 %)	130 (76.9 %)	Reference	Reference
PIM	76 (45.0 %)	39 (23.1 %)	2.68 (1.64–4.38)	2.30 (1.30–4.07)
Number of PIMs				
No PIM	93 (55.0 %)	130 (76.9 %)	Reference	Reference
1	48 (28.4 %)	33 (19.5 %)	2.02 (1.19–3.44)	2.13 (1.15–3.94)
≥2	28 (16.6 %)	6 (3.6 %)	6.65 (2.50–17.71)	3.08 (1.02–9.31)
START				
No PPO	54 (32.0 %)	89 (52.7 %)	Reference	Reference
PPO	115 (68.0 %)	80 (47.3 %)	2.59 (1.58–4.24)	1.41 (0.78–2.56)
Number of PPOs				
No PPO	54 (32.0 %)	89 (52.7 %)	Reference	Reference
1	51 (30.2 %)	36 (21.3 %)	2.62 (1.43–4.81)	1.62 (0.80–3.30)
≥2	64 (37.9 %)	44 (26.0 %)	2.57 (1.48–4.47)	1.26 (0.64–2.47)
STOPP & START				
No PIM/PPO	28 (16.6 %)	77 (45.6 %)	Reference	Reference
PIM/PPO	141 (83.4 %)	92 (54.4 %)	5.46 (2.87–10.37)	3.47 (1.70–7.09)
Number of PIMs/PPOs				
No PIM/PPO	28 (16.6 %)	77 (45.6 %)	Reference	Reference
1	45 (26.6 %)	33 (19.5 %)	4.78 (2.27–10.04)	4.61 (1.97–10.78)
≥2	96 (56.8 %)	59 (34.9 %)	5.87 (2.97–11.57)	2.86 (1.32–6.20)

CI confidence interval, *OR* odds ratio, *START* Screening Tool to Alert doctors to Right Treatment, *STOPP* Screening Tool of Older Person's Prescriptions, *PIM* potentially inappropriate medication, *PPO* potential prescribing omission

[a] Adjusted for number of drugs and comorbidities

with ADEs (OR 2.36, 95 % CI 1.10–5.06), whereas, like our findings, Beers criteria PIMs were not [13]. Another direct comparison between the Beers 2012 and STOPP 2008 criteria was made by Cahir et al. [28]. This study showed there was an almost one-third increase in the expected rate of hospital visits (including accident and emergency department visits, inpatient visits, and outpatient visits, for the 6 months prior to the participant's date of consent) for those with two or more PIMs defined by the STOPP criteria 2008, after adjusting for patient and practice level covariates. There was no significant association between the number of hospital visits and the Beers 2012 criteria [28]. Pasina et al. [29] also found inappropriate drug use according to the Beers 2012 criteria not to be significantly associated with health outcomes (adverse clinical events, re-hospitalization, and all-cause mortality) 3 months after discharge. In general, the results of our study are in line with most of these earlier studies as far as they are comparable.

Our findings are also similar to those of other studies with regard to the prevalence of PIMs identified with the Beers 2012 and STOPP 2008 criteria, although it should be remembered that our study population consisted of patients hospitalized because of ADEs. We found that the prevalence of Beers 2012 criteria PIMs in the total cohort was 44.4 %, whereas other studies reported a prevalence of between 22.9 and 58.4 % [13, 14, 29, 30]. We found the prevalence of STOPP & START 2008 criteria PIMs and PPOs to be, respectively, 34.1 and 57.7 %, whereas Castillo-Páramo et al. [31] reported a prevalence of PIMs of 37.5 % in a primary care setting; the prevalence of PPOs was 45.9 %. This difference may have occurred because

we considered two STOPP criteria as START criteria. A multicenter study involving 900 patients in six European hospitals reported an overall PIM prevalence rate of 51.3 % using the STOPP 2008 criteria, varying from 34.7 to 77.3 %. Using the START 2008 criteria, the overall PPO prevalence rate was 59.4 %, ranging from 51.3 to 72.7 % [10]. Other studies, involving hospitalized patients, reported a prevalence of STOPP 2008 criteria PIMs ranging from 35 to 56.2 % [13–16].

In our study, STOPP 2008 criteria PIMs and START 2008 criteria PPOs together were associated with preventable medication-related hospital admissions (OR_{adj} 3.47, 95 % CI 1.70–7.09), whereas the STOPP 2008 criteria alone showed a less strong association with preventable medication-related hospital admissions (OR_{adj} 2.30, 95 % CI 1.30–4.07). This observation shows the advantage of combining PIMs and PPOs in one screening method, as more potential medication-related problems are identified when inappropriate prescribing and prescribing omissions are combined in one method than when only inappropriate prescribing is covered. We found that PIMs/PPOs identified with the STOPP & START 2008 criteria were associated with the suspect medication identified in the HARM study (and hence with hospitalization) in 23 % of the cases, whereas PIMs identified with the Beers 2012 criteria were associated with the suspect medication in 17 % of the cases. Reasons for acute hospital admission when STOPP & START 2008 criteria PIMs/PPOs were not associated with hospitalization were non-adherence to the medication regimen, administration errors, and inadequate monitoring of therapy. This result emphasizes that current screening methods are not designed to identify all inappropriate prescribing and other causes of medication-related hospital admission, but instead give an overview of the most common PIMs and PPOs in older people. Although in 77 % of the cases the PIMs/PPOs found with the STOPP & START 2008 criteria and 83 % of the cases found with the Beers 2012 criteria were not directly related to the reason for hospitalization, these patients had a medication-related hospital admission. The presence of a PIM or PPO could therefore be seen as an indicator of an increased risk of medication-related problems in older individuals and should prompt re-assessment of the patient's medication by a multidisciplinary team in order to prevent ADEs.

This was the first study to investigate the association between PIMs identified with the Beers 2012 or STOPP 2008 criteria and medication-related hospital admissions; however, it had several limitations. First, database information is not always complete; for example, laboratory data may be missing or duration of treatment is not registered. However, this is often the case when patients come to an emergency department with an acute illness and thus reflects clinical practice. Secondly, questions can be raised as to whether a case–control study is the best possible design. Since medication-related hospital admission is a rare, but clinically relevant, outcome, a case–control design is the most efficient way to find these kind of clinical outcomes. Therefore, in the HARM study, a case–control design was chosen. The database only contains information about the cases and controls as described in the protocol. Since we used this database for our study, we had no other option than to choose the same research design. Third, the selected control group (planned surgery admissions in the same hospital, matched for age and sex) may not be ideal, because these patients are less ill than patients with unplanned admissions, since they were able to undergo planned surgery. This may affect the prevalence of PIMs identified in the control group and therefore the association between PIMs and medication-related hospital admission. However, the number of previous admissions was relatively comparable between cases and controls in the HARM study, which suggest that the two groups were at equal risk of unplanned hospitalization. Fourth, the ADEs caused by inappropriate prescribing can lead to different clinical outcomes, such as higher frequency of primary care visits, acute hospital admission, re-hospitalization, and death. In this study, we focused exclusively on the association between PIMs and preventable medication-related hospital admissions, which is only the tip of the iceberg of medication-related problems associated with PIMs. The association would probably have been stronger had we used other clinical outcomes, such as those mentioned above.

5 Conclusion

The presence of PIMs identified with the STOPP 2008 criteria was associated with preventable medication-related hospital admissions, whereas there was no association with Beers 2012 criteria PIMs. The presence of two or more PIMs identified with both methods was associated with a higher risk of medication-related hospital admission than the detection of no PIMs. STOPP 2008 criteria PIMs and START 2008 criteria PPOs together were also associated with preventable medication-related hospital admissions, which shows the advantage of combining PIMs and PPOs into one screening method, as more potential medication-related problems are identified.

Our study shows that patients with a PIM according to the STOPP 2008 criteria are at risk of medication-related problems. However, not all medication-related hospital admissions could be directly related to a PIM or PPO. Therefore, it is important, when reviewing a patient's medication list, to combine explicit screening tools with

critical clinical judgment. In conclusion, this study shows that, in a Dutch population, the STOPP & START 2008 criteria can be used to identify older people at risk of medication-related problems. For the Beers criteria, the clinical relevance should be further investigated.

Compliance with Ethical Standards

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