Potentially inappropriate drug use among hospitalised older adults: results from the CRIME study

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Abstract

Background: Beers criteria and screening tool of older person’s prescriptions (STOPP) criteria are widely used to assess potentially inappropriate drug use (PIDU).

Objective: the aims of the present study are (i) to assess the prevalence of PIDU based on 2012 Beers criteria and STOPP criteria and (ii) to determine the impact of PIDU, as defined by these criteria, on health outcomes among older in-hospital patients.

Design: prospective observational study.

Setting and subjects: a total of 871 in-hospital patients participating to the CRImteria to Assess Appropriate Medication Use among Elderly Complex Patients project.

Methods: outcome measures were (i) adverse drug reactions (ADR); (ii) decline in functional status; (iii) combined outcome (ADR or declined in functional status).

Results: the prevalence of PIDU was 58.4% applying Beers criteria, 50.4% applying STOPP criteria and 75.0% combining both sets of criteria. PIDU defined based on STOPP criteria was significantly associated with ADR [odds ratio (OR) 2.36; 95% confidence interval (CI) 1.10–5.06], and decline in physical function (OR: 2.00; 95% CI: 1.10–3.64), while, despite a positive trend, no significant association was observed for Beers criteria or the combination of both criteria. The combined outcome was significantly associated with PIDU defined based on Beers (OR: 1.74; 95% CI: 1.06–2.85), STOPP criteria (OR: 2.14; 95% CI: 1.32–3.47) or both (OR 2.02; 95% CI: 1.06–3.84).

Conclusions: PIDU is common in hospitalised older adults and the combination of Beers and STOPP criteria might lead to the identification of a larger number of cases of PIDU than the application of a single set of criteria. STOPP criteria significantly predict all in-hospital outcomes considered, while Beers criteria were significantly associated with the combined outcome only.

Keywords: inappropriate drug use, older adults, disability, adverse drug reactions, in-hospital, older people

Introduction

In Western countries, adverse drug reactions (ADR) are an important medical problem, resulting in 3–5% of all hospital admissions, accounting for 5–10% of in-hospital costs and being associated with a substantial increase in morbidity and mortality [1–4]. The use of inappropriate drugs, defined as drugs in which the risk outweighs the benefit, is a major factor influencing the likelihood of ADR and negative health outcomes, potentially leading to an increased rate of functional impairment and mortality among the elderly [5–7]. Such negative effects associated with inappropriate drug use...
might be particularly relevant among hospitalised older adults, who are usually ‘frail’ and present with acute diseases, which may increase their susceptibility to adverse medication effects and raise the severity of drug related illnesses [8, 9]. Since 1991 Beers et al. have developed a comprehensive set of explicit criteria to identify potentially inappropriate drug use (PIDU), with the intent of providing a useful tool for assessing the quality of prescribing in older persons, which cannot however represent substitutes for careful clinical consideration by physicians. These criteria were recently updated by the work of an interdisciplinary panel of experts in geriatric care and pharmacotherapy supported by the American Geriatrics Society [10]. An important criticism of the Beers criteria is their restricted applicability to Europe, since several drugs in the Beers list were not approved in most European countries [11, 12]. For this reason, more recently, the screening tool of older person’s prescriptions (STOPP) criteria was developed [13]. These criteria are being increasingly used in Europe and are to some extent considered to be the ‘European Beers criteria’[12].

So far, few studies have evaluated the prevalence and the risk of negative health outcomes associated with PIDU as assessed by these two sets of criteria in hospitalised older adults. Therefore, the aims of the present study are (i) to assess the prevalence of PIDU based on Beers and STOPP criteria and (ii) to determine the impact of PIDU, as defined by these two sets of criteria, on health outcomes of older adults admitted to acute care hospitals.

Methods

Sample and study setting

Data are from the CRIteria to Assess Appropriate Medication Use among Elderly Complex Patients (CRIME) project, an observational study performed in geriatric and internal medicine acute care wards of seven Italian hospitals. Methodology of the CRIME project has been described in detail elsewhere [14, 15]. In brief, the study was funded by the Italian Ministry of Labour, Health and Social Policy to (i) assess quality of prescribing in older adults hospitalised in Italy and (ii) produce recommendations for pharmacological prescribing in older complex patients with complex clinical conditions. All the patients consecutively admitted to participating wards, between June 2010 and May 2011, were enrolled in the study. Exclusion criteria were age <65 years and unwillingness to take part to the study.

Data collection

Participants’ data were collected through a dedicated questionnaire, which was filled in at admission and updated daily by study researchers and it included a variety of information. Cognitive status was assessed using the 30-items Mini-Mental State Examination (MMSE) [16]. Diagnoses were gathered from the patient, attending physicians and by a careful review of medical charts.

Drug assessment

Study researchers recorded, on a specific section of the questionnaire, all the drugs taken by the participants in the 7 days before and during hospitalisation. Particularly they recorded brand name, formulation, daily dose and compliance. Drugs were coded according to the anatomical therapeutic and chemical codes [17].

PIDU

To identify PIDU two sets of criteria were adopted (i) Beers criteria, published by the American Geriatrics Society in 2012 [10] and (ii) STOPP criteria [13].

Regarding Beers criteria both drugs judged as potentially inappropriate due to drug–disease and drug–syndrome interactions that may exacerbate the disease or syndrome and those independent of coexisting diagnoses or syndromes were analysed. Eight STOPP criteria, evaluating appropriateness based on time of exposure to specific drugs (i.e. PPI for peptic ulcer disease at a full-therapeutic dosage for >8 weeks), were not analysed in the present study because assessment of drugs used before hospitalisation was limited at the 7 days before admission. Criteria on long-term use of long-acting benzodiazepines and long-term use neuroleptics in patients with parkinsonism were deemed present if patient was using the drug in the 7 days before admission (instead 1 month as indicated in the original publication) and during hospital stay. Therefore, only 57/65 STOPP criteria were included in the present study.

Outcomes

According to the World Health Organization definition, an ADR was defined as any noxious, unintended and undesired effect of a drug, excluding therapeutic failures, intentional and accidental poisoning and abuse [18]. For each suspected ADR, a study physician coded clinical description, severity and outcome of the ADR, and collected detailed information about the drug(s) potentially involved. The causality between drug use and ADR was assessed using the Naranjo algorithm [19] and only definite or probable ADR caused by drugs used during hospital stay were considered in the present study. If >1 ADR was observed in the same patient, only the first ADR was taken into account.

Functional status was evaluated both at hospital admission and at discharge assessing the participant’s dependency in the following six activities of the daily living (ADL): bathing, locomotion, dressing, eating, bowel and bladder continence and personal hygiene [20]. A score combining number of ADL in which the patients was dependent was calculated both at hospital admission and at discharge (range 0–6) with higher values indicating higher level of dependency. Change in the ADL score was calculated and decline in functional status was defined as an increment of ≥1 point in the score between admission and discharge.

To perform these analyses, 252 participants with the ADL score of 6 (meaning dependent in performing all ADL)
at hospital admission were excluded from the study. This selection led to a final sample of 871 participants.

Finally, an outcome measure combining ADR and decline in functional status was created. Participants reached the combined endpoint if they experienced an ADR or presented a decline in physical function during hospital stay.

**Statistical analysis**

To compare outcomes prevalence in participants according to PIDU, the Chi-square test was used. Logistic regression models were used to estimate the effect of PIDU on study outcomes. Variables considered for adjustment were age, gender, number of diseases, number of drugs used during hospital stay and the ADL score at hospital admission. In former studies these variables were shown to be associated with ADR or functional decline in hospitalised older adults. Additional logistic regression models were performed to assess the impact of number of potentially inappropriate drugs on study outcomes. All analyses were performed using SPSS for Windows version 18.0.

**Results**

**Sample characteristics**

The mean age of 871 participants entering the study was 80.2 [standard deviation (SD) = 7.0] years, 463 (53.2%) were women and they received a mean number of 10.6 (SD 5.6) drugs during hospital stay. Less than half of the patients were hospitalised through emergency department (45.6%) and the mean length of hospital stay was 11.1 (SD 6.6) days. Detailed characteristics of study sample are reported in Table 1.

**Prevalence of PIDU**

During hospital stay 509 (58.4%) patients received one or more potentially inappropriate drugs based on Beers criteria. More specifically, 283 patients (32.5%) used one and 226 (25.9%) two or more potentially inappropriate drugs; drugs defined as potentially inappropriate due to drug–disease and drug–syndrome interactions that may exacerbate a disease or syndrome were used by 302 (34.7%) patients, while those potentially inappropriate independent of coexisting diagnoses or syndromes were used by and 356 (40.9%) patients. As shown in Supplementary data available in Age and Ageing Appendix Table S1, drugs inappropriate in a history of falls or fractures (n = 227; 26.1%) were the most commonly used potentially inappropriate drugs based on Beers criteria, followed by benzodiazepines (n = 108; 12.4%) and drugs inappropriate in dementia and cognitive impairment (n = 85; 9.8%).

During hospital stay 438 (50.4%) patients received one or more inappropriate drugs based on STOPP criteria. More specifically, 282 patients (32.4%) used one and 156 (17.9%) two or more potentially inappropriate drugs. As shown in Supplementary data available in Age and Ageing Appendix Table S1, aspirin in patients with no history of cardiovascular events (n = 150; 17.2%) was the most commonly used potentially inappropriate drugs based on STOPP criteria, followed by neuroleptic drugs in patients with a history of falls (n = 85; 9.8%) and use of opiates in chronic constipation without concurrent use of laxatives (n = 65; 7.5%).

As shown in Figure 1, combination of the two sets of criteria led to identify 653 patients (75.0%) as receiving inappropriate drugs. Overall 294 patients (33.8% of study sample) were identified as receiving potentially inappropriate drugs by both criteria, whereas 215 (24.7%) were identified by Beers criteria only and 144 (16.5%) by STOPP criteria only.

**PIDU and study outcomes**

A total of 37 (4.2% of study sample) definite or probable ADR were recorded during hospital stay. As shown in Table 2, independently from the set of criteria used, the prevalence of ADR was higher among patients using potentially inappropriate drugs when compared with those not receiving inappropriate drugs. After adjusting for potential confounders, PIDU defined based on STOPP criteria was significantly associated with ADR [odds ratio (OR) 2.36;...

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**Table 1. Sample characteristics**

<table>
<thead>
<tr>
<th></th>
<th>All (n = 871)</th>
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<tbody>
<tr>
<td>Age</td>
<td>80.2 ± 7.0</td>
</tr>
<tr>
<td>Female gender</td>
<td>463 (53.2%)</td>
</tr>
<tr>
<td>Admission from emergency department</td>
<td>397 (45.6%)</td>
</tr>
<tr>
<td>≥1 hospital admission in the 12 months</td>
<td>340 (40.3%)</td>
</tr>
<tr>
<td>No. of impaired ADL at admission (mean ± SD)</td>
<td>1.4 ± 1.8</td>
</tr>
<tr>
<td>Unable to complete MMSE</td>
<td>73 (8.4%)</td>
</tr>
<tr>
<td>MMSE score (mean ± SD)</td>
<td>22.5 ± 6.5</td>
</tr>
<tr>
<td>Number of disease (mean ± SD)</td>
<td>4.7 ± 2.5</td>
</tr>
<tr>
<td>No. drugs during stay</td>
<td>10.6 ± 5.6</td>
</tr>
<tr>
<td>Length of stay (mean ± SD)</td>
<td>11.1 ± 6.6</td>
</tr>
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</table>

**Figure 1.** Prevalence of inappropriate drug use based on Beers and STOPP criteria (whole sample = 871).
Table 2. Potentially inappropriate drug use and in-hospital outcomes. Analyses are adjusted for age, gender, number of diseases, number of drugs and number of impaired ADL at hospital admission

<table>
<thead>
<tr>
<th></th>
<th>ADR</th>
<th>Decline in functional status</th>
<th>Combined outcome (ADR or decline in functional status)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rate n (%)</td>
<td>Adjusted OR (95% CI)</td>
<td>Rate n (%)</td>
</tr>
<tr>
<td><strong>Beers criteria</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No Inappropriate drugs (n = 362)</td>
<td>10 (2.8%)</td>
<td>1</td>
<td>16 (4.4%)</td>
</tr>
<tr>
<td>Any inappropriate drugs (n = 509)</td>
<td>27 (5.3%)</td>
<td>1.80 (0.84–3.87)</td>
<td>41 (8.1%)</td>
</tr>
<tr>
<td>No inappropriate drugs (n = 362)</td>
<td>10 (2.8%)</td>
<td>1</td>
<td>16 (4.4%)</td>
</tr>
<tr>
<td>1 inappropriate drugs (n = 283)</td>
<td>13 (4.6%)</td>
<td>1.56 (0.67–3.68)</td>
<td>19 (6.7%)</td>
</tr>
<tr>
<td>≥2 inappropriate drugs (n = 226)</td>
<td>14 (6.2%)</td>
<td>2.15 (0.90–5.14)</td>
<td>22 (9.7%)</td>
</tr>
<tr>
<td><strong>STOPP criteria</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No Inappropriate drugs (n = 433)</td>
<td>10 (2.3%)</td>
<td>1</td>
<td>18 (4.2%)</td>
</tr>
<tr>
<td>Any inappropriate drugs (n = 438)</td>
<td>27 (6.2%)</td>
<td>2.36 (1.10–5.06)</td>
<td>39 (8.9%)</td>
</tr>
<tr>
<td>No inappropriate drugs (n = 433)</td>
<td>10 (2.3%)</td>
<td>1</td>
<td>18 (4.2%)</td>
</tr>
<tr>
<td>1 inappropriate drugs (n = 282)</td>
<td>15 (5.3%)</td>
<td>2.04 (0.88–4.69)</td>
<td>16 (5.7%)</td>
</tr>
<tr>
<td>≥2 inappropriate drugs (n = 156)</td>
<td>12 (7.7%)</td>
<td>3.01 (1.23–7.38)</td>
<td>23 (14.7%)</td>
</tr>
<tr>
<td><strong>Beers + STOPP criteria</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Inappropriate drugs (n = 218)</td>
<td>5 (2.3%)</td>
<td>1</td>
<td>7 (3.2%)</td>
</tr>
<tr>
<td>Any inappropriate drugs (n = 653)</td>
<td>32 (4.9%)</td>
<td>1.90 (0.71–5.06)</td>
<td>50 (7.7%)</td>
</tr>
<tr>
<td>No inappropriate drugs (n = 218)</td>
<td>5 (2.3%)</td>
<td>1</td>
<td>7 (3.2%)</td>
</tr>
<tr>
<td>1 criterion only (n = 359)</td>
<td>10 (2.8%)</td>
<td>1.17 (0.39–3.54)</td>
<td>20 (5.6%)</td>
</tr>
<tr>
<td>Both criteria (n = 294)</td>
<td>22 (7.5%)</td>
<td>2.94 (1.04–8.31)</td>
<td>30 (10.2%)</td>
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OR, Odds Ratio; CI, Confidence Interval; ADR, Adverse Drug Reaction.
In the two sets of criteria: only 25 of the 99 Beers criteria are of two or more potentially inappropriate drugs for all sets of criteria. Differences described may also reflect heterogeneity in the two sets of criteria: only 25 of the 99 Beers criteria are common or very similar to the STOPP criteria, meaning that three-quarters of the Beers criteria do not overlap with STOPP criteria. Similarly, 36 of the 65 STOPP criteria (55%) are not part of the Beers criteria [12].

Our data suggest that the STOPP criteria significantly predict all outcomes considered (ADR, decline in functional status and the combination of these outcomes) [23–25]. Indeed, STOPP criteria are to some extent considered to be the ‘European Beers criteria’ because they were created to overcome limitations of Beers criteria which were developed to be applied to older adults living in the USA and did not account for differences in drug policy and pharmaceutical marketing in other countries [26]. In addition, STOPP criteria deal with drugs that are currently in widespread use in Europe and they place special emphasis on potential adverse drug–drug interactions and duplicate drug class prescription, whereas Beers criteria do not. These differences might explain the fact that STOPP criteria had a slightly better ability to predict adverse health outcomes in hospitalised older adults in our sample when compared with the Beers criteria. However, we cannot exclude that the effect of PIDU defined based on Beers criteria on outcomes examined in this study is smaller that we can detect. We calculated that this study had 80% power to detect a 2.5-fold increased risk of ADR and 2.1-fold increase of decline in physical function related to Beers inappropriate drugs, considering a 0.05 level of Type I error.

An important limitation of this study relates to generalisability of the results. Our findings, which are based on an hospitalised sample cannot be extrapolated to subjects living in the community. In addition, assessment of ADR was based on evaluation performed by a single study physician without independent validation and this may have led to an over identification of potential ADR. Finally, despite the fact that we used a database specifically designed to assess drug use among in-hospital patients, assessment of criteria of PIDU was not the specific focus of the study. For this reason, time of exposure to specific drugs before hospitalisation was not assessed and therefore it was not possible to estimate prevalence of all STOPP criteria.

This is one of the first studies to assess prevalence of PIDU defined based on the 2012 version Beers criteria and to compare prevalence and outcomes related to two sets of criteria widely used to assess PIDU. Former researches adopting both sets of criteria were based on smaller sample sizes and in few case assessed both prevalence and clinical outcomes [23, 24]. Another strength of the present study relates to the use of a database specifically design to assess drug use and its effects in older people. Such a database allowed for the assessment of relevant universal health outcomes directly related to drug use which are not routinely evaluated in larger studies using administrative data [27, 28].

In conclusion, the present study suggests that PIDU is common in older adults hospitalised in Italy and that the combination of Beers and STOPP criteria might lead to the identification of a larger number of cases of PIDU than the application of a single set of criteria. However, STOPP criteria significantly predict all in-hospital outcomes.

Discussion

The present study shows that PIDU is common in hospitalised older adults and that the combination of Beers and STOPP criteria could identify a larger group of patients receiving inappropriate drugs than a single set of criteria. In addition, PIDU is associated with an increased risk of negative health outcomes, but STOPP criteria significantly predict all in-hospital outcomes considered, whereas Beers criteria were significantly associated with the combined outcome only.

The prevalence of PIDU defined by STOPP criteria is slightly lower when compared with the one observed for Beers criteria, but it is in line with former studies assessing this issue in a European sample of in-hospital older adults [21, 22]. However, 8 of 65 (12.3%) of the STOPP criteria were not applied in the present study, including those with the highest prevalence in former studies (i.e. proton pump inhibitors at full-therapeutic dosage for >8 weeks). Therefore, the prevalence of these criteria is probably underestimated in the present sample.

Interesting, the combination of both sets of criteria leads to the identification of a larger number of cases of PIDU: only 33.8% of patients are identified as receiving inappropriate drugs by both sets of criteria, whereas 24.7% are identified only by Beers criteria and 16.5% only by STOPP criteria. Differences described may also reflect heterogeneity in the two sets of criteria: only 25 of the 99 Beers criteria are common or very similar to the STOPP criteria, meaning that...
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considered, while Beers criteria were significantly associated with the combined outcome only.

Key points

- Beers and STOPP criteria were developed to identify patterns of drug use that unnecessarily place older persons at risk of ADR.
- PIDU is common in hospitalised older adults and that the combination of Beers and STOPP criteria could identify a larger group of patients receiving potentially inappropriate drugs than a single set of criteria.
- Use of potentially inappropriate drugs is associated with an increased risk of negative health outcomes, but STOPP criteria seem to better predict these outcomes.

Conflicts of interest

None declared.

Funding

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Supplementary data

Supplementary data mentioned in the text is available to subscribers in Age and Ageing online.

References

Specifying ICD9, ICPC and ATC codes for the STOPP/START criteria: a multidisciplinary consensus panel

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Abstract

Background: the STOPP/START criteria are a promising framework to increase appropriate prescribing in the elderly in clinical practice. However, the current definitions of the STOPP/START criteria are rather non-specific, allowing undesirable variations in interpretation and thus application. The aim of this study was to design specifications of the STOPP/START criteria into international disease and medication codes to facilitate computerised extraction from medical records and databases.

Methods: a three round consensus procedure with a multidisciplinary expert panel was organised to prepare, judge and agree on the design of the STOPP/START criteria specifications in corresponding international disease codes (ICD9 and ICPC) and medication codes (ATC).

Results: after two rounds consensus was reached for 74% of the STOPP criteria and for 73% of the START criteria. After three rounds full consensus was reached resulting in a specification of 61 out of 62 STOPP criteria and 26 START criteria with their corresponding codes. One criterion could not be specified and for some criteria corresponding disease codes were lacking or imperfect.

Conclusion: this study showed the necessity of a consensus procedure as even experts frequently differed on how to specify the STOPP/START criteria. This specification enables next steps such as prognostic validation of these criteria on adverse outcomes and studying the impact of improving appropriate prescribing in the elderly.

Keywords: STOPP/START criteria, inappropriate prescribing, specification, computerised extraction, older people