Potentially inappropriate drug use in older people: a nationwide comparison of different explicit criteria for population-based estimates

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Identifying potentially inappropriate medications is of central importance in order to reduce the occurrence of drug-related problems and adverse drug events in older patients.
- Several assessment tools for inappropriate drug use have been developed over the past two decades, both in the US and in Europe.
- Recent reviews have emphasized major differences in the development, structure and content of these tools. However, only a handful of original studies have compared the actual prevalence of potentially inappropriate drug use according to the different existing criteria.

WHAT THIS STUDY ADDS

- For the first time, a nationwide, population-based study used five different sets of criteria developed in five different countries to measure the prevalence of potentially inappropriate drug use among older people.
- Overall, 16% to 24% of all older adults (≥65 years) in Sweden are exposed to medications whose expected benefits are deemed lower than the risks they present.

AIMS

The aim was to investigate the prevalence of potentially inappropriate medication use among older people in Sweden according to five different published sets of explicit criteria from Europe and the US.

METHODS

This was a nationwide cross-sectional, register-based study across the whole of Sweden in 2008. All individuals aged 65 years and older were included ($n = 1\,346\,709$, both community-dwelling and institutionalized persons). We applied all drug-specific criteria included in the 2012 Beers Criteria, the Laroche's list, the PRISCUS list, the NORGEP criteria and the Swedish National Board of Health and Welfare criteria. The main outcome was the potentially inappropriate drug use according to each set of criteria, separately and combined. Multivariate logistic regression models were used to identify individual factors associated with the use of potentially inappropriate drugs.

RESULTS

The prevalence of potentially inappropriate medication use varied between the explicit criteria from 16% (NORGEP criteria) to 24% (2012 Beers criteria). Overall, 38% of the older people were exposed to potentially inappropriate drug use by at least one of the five sets of criteria. While controlling for other possible covariates, female gender, institutionalization and polypharmacy were systematically associated with inappropriate drug use, regardless of the set of explicit criteria we considered.

CONCLUSION

Although explicit criteria for inappropriate drug use among older people have been reported to be quite different in their content, they provide similar measures of the prevalence of potentially inappropriate drug use at the population level.

- The different sets of criteria we compared measure the overall exposure to potentially inappropriate drug use to a very similar extent (in particular the criteria developed in Europe), even though these sets of criteria overlap very little both in content and in the population they cover.
- This study supports the use of these criteria by public health policy makers, stakeholders and researchers to evaluate the quality of drug use at the population level, especially in a cross-national perspective. However, at the clinical level, our results raise important questions regarding the comprehensiveness of each of these tools, and therefore their applicability in daily practice.

Introduction

Background

Ageing is often associated with chronic conditions and multiple morbidities, leading to an increased use of medications. At the same time, age-related pharmacokinetic and pharmacodynamic changes (e.g. denutrition, increase of the ratio body fat: body water and decline of liver and renal function) affect the distribution, metabolism and excretion of drugs [1–3]. As a consequence of this combination, older people are at high risk of drug–drug interactions and adverse drugs reactions [4, 5] that may, in turn, cause adverse health outcomes, including emergency department visits, hospitalizations, functional decline and mortality [6–10]. Drugs are considered to be potentially inappropriate for older people when the risk of harmful effects exceeds their expected benefit for the patient and when a safer, better tolerated or more effective alternative drug is available [5]. Identifying these 'potentially inappropriate medications' is therefore of central importance in order to reduce the occurrence of drug-related problems and adverse drug events in older patients.

Several assessment tools for inappropriate drug use have been developed over the past two decades, based on implicit or explicit approaches [11]. The latter usually consist of a list of medications that have been considered inappropriate for older people through a literature review and expert consensus methods. These lists include either single drug, drug combination or drug–disease criteria. In contrast to implicit tools (i.e. clinician's assessment), explicit criteria are highly reproducible and can easily be applied to large scale studies of patients with a limited cost [5,12].

Such explicit criteria have been developed in the US [13–17], Canada [18, 19], Australia [20], Ireland [21], France [22], Germany [23], Sweden [24, 25], Norway [26],
Italy [27], Austria [28], Thailand [29] and Taiwan [30]. However, recent reviews have outlined major differences in the development, structure and content of the published criteria [11, 31–34]. These discrepancies raise important concerns about their respective ability to detect potentially inappropriate drug use in older people in different care settings [35]. Only a few original studies have compared the prevalence of potentially inappropriate drug use in a single large cohort according to different sets of explicit criteria [35–38]. These studies have also often been restricted in their generalizability, either by their small sample size or by their selective study setting. Yet, as these criteria have become an important tool in geriatric care, comparisons in large, population-based studies are needed to ascertain the performance of the individual criteria in detecting potentially inappropriate drug use and to determine if the prevalence estimates are consistent across criteria.

Therefore, the aim of the present study was to investigate the prevalence of potentially inappropriate medication use among older people in Sweden according to five different published sets of explicit criteria, in order to compare the estimates provided by these criteria. We also examined individual factors associated with use of potentially inappropriate medications based on each of the five sets of criteria, in order to determine if some of these tools were more sensitive to older people's characteristics (i.e. age, gender, living situation, number of drugs) than others.

Methods

Study population

We used the Swedish Prescribed Drugs Register (SPDR) to analyze the prevalence of prescribed and dispensed

drugs to older people aged 65 years and over. This individual-based register was implemented in 2005 and covers all prescribed drugs delivered from pharmacies to the whole Swedish population (9.7 million inhabitants in 2014) [39]. The SPDR includes, among others, the patients' age, gender and place of residence, and detailed information about the drug and dosage.

In Sweden, drugs are prescribed for a maximum duration of 3 months [40]. For this study, we analyzed information related to people aged 65 years and older who were included in the register between 1 July and 30 September 2008. Based on data about the date of prescription, amount of delivered drug and dosage of each medication, a list of current medications for each individual was computed at the arbitrarily chosen date of 30 September 2008. If the same drug was dispensed more than once during the study period, it was counted as one drug [41–43].

In addition, we obtained data on the living arrangements of each individual by linking the SPDR to the Swedish Social Services Register, which contains information about institutional care provided by municipalities to older people at the national level (in Sweden, the municipality system includes almost all elderly care) [44]. The living situation was categorized into 'community-dwelling' and 'institutionalized', according to a procedure described elsewhere [43]. After exclusion of records with missing values on the living situation (n = 855), the study population consisted of 1 346 709 people, accounting for 81.2% of the entire Swedish population aged $\geq$ 65 years in September 2008 [45].

Measurements

We included sets of explicit criteria that were developed in Europe or in Northern America, published in 2005 or later, and containing a major proportion of drug-specific criteria, as the Swedish Prescribed Drugs Register does not include information about the underlying clinical indications and diagnoses. The STOPP-START criteria, which contain a majority of drug–disease items could, for instance, not be computed based on the available data. Therefore, five different sets of explicit criteria were included in the comparison:

• The 2012 update of the Beers criteria, released by the American Geriatrics Society [17]. The first version of the Beers criteria was issued in 1991 to identify potentially inappropriate medication use among nursing home residents [13] and was revised in 1997 and 2003 in order to be applicable also for community-dwelling older people [14, 16]. The fourth revised edition contains 53 individual medications or medication classes (of which 34 are single drug and drug specific criteria) that are considered as inappropriate for people aged 65 years and older in ambulatory and institutional settings.

• The Laroche list was published in 2007 and was designed to detect potentially inappropriate drug use for people aged 75 years and over both in the community and in nursing home facilities in France [22]. Among the 34 statements included in this list, 29 are drug-specific criteria (including 27 single drugs and two drug combinations).

• The Norwegian General Practice (NORGEP) criteria were published in 2009, with a focus on older adults aged $\geq$70 years [26]. This set contains 36 drug-specific criteria (21 single drugs and 15 drug combinations) deemed to be potentially inappropriate in general practice.

• The PRISCUS list was established in Germany in 2010 [23]. In this set, 83 drugs or drug classes are considered potentially inappropriate for all older people aged $\geq$65 years, regardless of their disease or the clinical condition, both in the community and in the institutional setting.

• The updated version of the criteria issued by the Swedish National Board of Health and Welfare ('Socialstyrelsen') in 2010 [25]. Eight of these 34 criteria are drug-specific, including six single drug criteria and two drug combination criteria [24]. These criteria are applicable for the entire population aged 65 years and older, in the community and in nursing home facilities.

All the drug-specific criteria were extracted from each of these five sets. Corresponding Anatomical Therapeutic Chemical (ATC) codes and dosages were applied to measure the prevalence of potentially inappropriate medication use in our study population. Criteria involving the disease or the clinical conditions of the individuals were not considered. For each set of criteria, the overall prevalence of potentially inappropriate drug use was defined as the proportion of individuals exposed to at least one criterion within the study population.

Statistical analysis

We computed descriptive statistics to measure the overall prevalence of potentially inappropriate drug use according to each set of criteria, separately and combined. When applicable, crude proportions were also used to compare the exposure to single drug and drug combinations criteria. In addition, we carried out a series of multivariate logistic regression models to investigate the associations between the characteristics of the individuals (i.e. gender, age, living situation and number of prescribed medications) and the use of at least one potentially inappropriate drug according to each set of criteria separately. We also examined if these associations remained stable after combining the sets of criteria either into an 'alternative' model (i.e. detection by at least one of the five sets of criteria) or into a 'cumulative' model (i.e. detection by each of the five sets of criteria). Adjusted odd ratios (ORs) and 95% confidence intervals (CIs) were estimated. We used the area under the ROC

curve (AUC) as a proxy to assess the goodness-of-fit of each model. Finally, we measured the level of agreement between the different sets of criteria by using both the sensitivity/specificity and the kappa coefficient. All statistical analyses were performed using SAS JMP v.11.0 (SAS Institute, Inc., USA).

The study was approved by the ethics review board in Stockholm (Dnr 2009/477-31/3).

Results

Characteristics of the study population

Table 1 presents the main characteristics of the study population. The mean (± SD) age was 76.2 (7.2) years and about 6.4% of the study population lived in nursing homes. Overall, they received an average (± SD) of 4.6 (3.4) drugs; 42% received five drugs or more and 9.1% received 10 different drugs or more. The mean (± SD) number of prescribed drugs was higher among institutionalized than among community-dwelling elderly (7.3 ± 3.7 vs. 4.4 ± 3.3, respectively, $P < 0.001$).

Overall prevalence of potentially inappropriate drug use

The prevalence of potentially inappropriate medication use varied from 16% (NORGEP criteria) to 24% (2012 Beers criteria) of the study population (Table 2). The application of the criteria from the Swedish National Board of Health and Welfare provided a prevalence of 19%, very similar to the prevalence measured by PRISCUS and

Table 1

Characteristics of the study population (n = 1 346 709), Sweden 2008

	Male (n = 572 150)		Female (n = 774 559)	
	n	%	n	%
Age (years)				
Mean (SD)	75.3 (7.5)	-	77.0 (8.1)	-
Median (IQR)	74 (12)	-	76 (13)	-
65 to 74	291 783	51.0%	334 118	43.1%
75 to 84	202 774	35.4%	281 581	36.4%
85 to 94	74 036	12.9%	145 843	18.8%
95 and over	3557	0.6%	13 017	1.7%
Living situation				
Home	546 467	95.5%	713 930	92.2%
Nursing home	25 683	4.5%	60 629	7.8%
Number of drugs				
Mean (SD)	4.4 (3.3)	-	4.7 (3.5)	-
Median (IQR)	4 (4)	-	4 (5)	-
0	23 737	4.1%	24 441	3.2%
1	89 294	15.6%	109 834	14.2%
2	83 619	14.6%	107 868	13.9%
3	77 006	13.5%	99 901	12.9%
4	69 085	12.1%	90 007	11.6%
5 and more	229 409	40.1%	342 508	44.2%

Table 2

Proportion of older people exposed to potentially inappropriate medications in Sweden, 2008 (n = 1 346 709)

	Single drug criteria		Drug combinations criteria*		Overall exposure	
	n	%	n	%	n	%
NORGEP	126 094	9.4%	120 143	8.9%	215 088	16.0%
PRISCUS	238 387	17.7%	-	-	238 387	17.7%
Laroche	240 573	17.9%	62 162	4.6%	256 167	19.0%
Swedish National Board of Health and Welfare	161 240	12.0%	152 240	11.3%	257 079	19.1%
Beers (2012)	325 256	24.1%	-	-	325 256	24.1%
At least one of the five sets of criteria	447 111	33.2%	232 754	17.3%	506 607	37.6%
All the sets of criteria	50 753	3.8%	26 953	2.0%	70 209	5.2%

*The PRISCUS list and the Beers criteria contain no criteria based on drug combinations

Laroche's criteria (18% and 19%, respectively). For single drug criteria, the prevalence ranged from 9.4% (NORGEP) to 24% (2012 Beers), and for drug combination criteria from 4.6% to 11% (Laroche's and Swedish National Board of Health and Welfare criteria, respectively).

Overall, 38% of the older people were exposed to potentially inappropriate drug use according to at least one of these five sets of criteria. 25% were detected by at least two sets of criteria and 18% by three sets of criteria or more. Exposure to potentially inappropriate medications according to all five criteria was prevalent in 5.2% of the study population (Table 2 and Supplementary material, Appendix 2). Among the individuals exposed to potentially inappropriate drugs according to any of the five sets of criteria, 14% were detected simultaneously by all five sets of criteria, 27% were detected by at least four sets of criteria and 34% were detected by only one of the sets of criteria (Supplementary material, Appendix 3).

The most common potentially inappropriate medications

The most common potentially inappropriate medications detected by at least one of the five sets of criteria were benzodiazepines or benzodiazepine-like drugs with hypnotic or sedative proprieties (zolpidem: 5.4% of all individuals in total, 2.0% receiving >5mg day^{-1}, oxazepam: 4.6%, 0.01% receiving >60mg day^{-1}, zopiclone: 7.3%, 3.9% receiving >3.75mg day^{-1}). Diazepam was the most commonly used drug among those deemed inappropriate by all sets of criteria (1.3%) (Supplementary material, Appendix 1). Overall, drugs with anticholinergic properties were used by 5.5 % (n = 73,917) of the older people.

Factors associated with potentially inappropriate medications

Overall, whatever the set of criteria, women were more often exposed to potentially inappropriate drugs than men (range 18%–27% vs. 13%–21%, respectively). Older people living in institutions also more often received these medications than community-dwelling individuals (range 36–51% vs. 15%–22%) (Table 3). In adjusted multivariate logistic regression analysis (Table 3), older age and higher number of prescribed medications were independently correlated with an increased likelihood of being exposed to potentially inappropriate drug use, regardless of the set of criteria we used to detect this exposure (OR ranges 1.01–1.02 and 1.27–1.67, respectively). Institutionalization was also significantly associated with greater odds of being prescribed potentially inappropriate medications (OR range 1.44–2.29).

We also found that most of these associations remained of similar magnitude when we combined the criteria in either an 'alternative' model (i.e. detection as user of potentially inappropriate drugs by at least one of the six sets of criteria) or a 'cumulative' model (i.e. detection by each of the six sets of criteria). However, in this second model, higher age was associated with slightly decreased odds (OR 0.99, 95% CI 0.98, 0.99) of being detected as a potential user of inappropriate medications (Supplementary material, Appendix 2).

Level of agreement between the different sets of criteria

The overall average sensitivity of the sets of criteria towards each other varied from 48% (NORGEP criteria) to 69% (2012 Beers criteria). The average level of specificity ranged from 85% (2012 Beers criteria) to 92% (PRISCUS criteria). The kappa coefficient varied from 0.37 (Swedish Indicators and 2012 Beers criteria) to 0.75 (Laroche and PRISCUS lists) (Supplementary material, Appendix 4 and 5).

Discussion

In this nationwide study of 1.3 million individuals aged 65 years and older in Sweden, comparing the analyses by five different sets of criteria developed in five different countries, we found that 16% to 24% of all older people were exposed to potentially inappropriate drug use.

In the community setting, potentially inappropriate drugs were used by 15% to 22% of the population. This prevalence is very consistent with the results of a recent systematic review, which reported a median rate of inappropriate medication prescriptions of 20% (IQR 18.1–25.6%) [46]. In contrast, between 36% and 51% of the individuals living in institutions received potentially inappropriate medications, in line with prior studies conducted in Europe [10, 43, 47–50] and in North America [19,51]. As expected, the number of prescribed drugs was

positively associated with an increased likelihood of being exposed to potentially inappropriate medications [40, 47, 52, 53]. Also, similar to most studies investigating gender differences [27, 47, 53, 54], women were at greater risk of being exposed to potentially inappropriate drugs, even after adjusting for the number of medications used.

However, we found a surprisingly small overlap between the populations covered by each of the five sets of explicit criteria we applied in this study. Among people exposed to potentially inappropriate drugs according to any of the five sets of criteria, only 14% were captured simultaneously by all sets of criteria (while for 34% of them we found no overlap at all between the different criteria). In our opinion, this raises important questions about the comprehensiveness of each of these tools. The heterogeneity in the lists of medications included in each of these sets of criteria probably explains most of these discrepancies. As reported in prior original studies [35, 36] and systematic reviews [11, 32, 33], only a few drugs are common to all the lists of potentially inappropriate drugs published over the last decade (e.g. diazepam, clomipramine and amitriptyline). Moreover, the dosage criteria may vary from one list to the other. Hence, although haloperidol is considered as inappropriate at a dosage >2mg day^{-1} in the PRISCUS list, there is no dosage restriction in the Beers criteria. Likewise, although both Laroche's and the PRISCUS lists have deemed zopiclone to be inappropriate in doses >3.75mg day^{-1}, the NORGEP criteria have established the threshold at 7.5mg day^{-1}, while neither the Swedish nor the Beers criteria mention this medication as being potentially inappropriate. These differences can lead to considerable variations, especially in the case of zolpidem (ranging from 5.4% to 1.9%) and oxazepam (ranging from 4.6% to 0.01%). Moreover, several of the commonly prescribed drugs are included in only one of the five sets of criteria we compared, leading to even more variations, e.g. tramadol, propiomazine (Swedish criteria), dextropropoxyphene (NORGEP criteria), spironolactone or risperidone (Beers criteria).

In fact, the most striking finding lies in this apparent paradox. The different sets of criteria we compared measure the overall exposure to potentially inappropriate drug use to a very similar extent (in particular criteria developed in Europe), even though these sets of criteria overlap very little both in content and in the population they cover. In addition, no matter which set of criteria we applied, we found similar associations between older people's socio-demographic characteristics and their use of potentially inappropriate drugs, suggesting that these tools are consistent in capturing not only the overall prevalence of potentially inappropriate drug use but also the differences across subgroups of the population. These findings strongly support the idea that besides their role at the clinical level in identifying inappropriate use of specific drugs among older people, at a population

Table 3

Factors associated with the exposure to potentially inappropriate medications in Sweden, 2008

	NORGEP		PRISCUS		Laroche		Swedish National Board of Health and Welfare		Beers 2012	
	n (%)	Adjusted OR (95% CI)*	n (%)	Adjusted OR (95% CI)*	n (%)	Adjusted OR (95% CI)*	n (%)	Adjusted OR (95% CI)*	n (%)	Adjusted OR (95% CI)*
Gender										
Male	75 010 (13.1%)	1	89 685 (15.7%)	1	94 075 (16.4%)	1	90 752 (15.9%)	1	117 616 (20.6%)	1
Female	140 078 (18.1%)	1.36 (1.35, 1.37)	148 702 (19.2%)	1.15 (1.14, 1.16)	162 092 (20.9%)	1.21 (1.20, 1.22)	166 327 (21.5%)	1.35 (1.34, 1.36)	207,640 (26.8%)	1.31 (1.30, 1.33)
Age group										
65–74 years	79 507 (12.7%)	1	82 896 (13.2%)	1	86 294 (13.8%)	1	92 044 (14.7%)	1	120 998 (19.3%)	1
75–84 years	82 320 (17%)	1.03 (1.02, 1.04)	91 439 (18.9%)	1.20 (1.18, 1.21)	99 496 (20.5%)	1.25 (1.23, 1.26)	100 742 (20.8%)	1.09 (1.08, 1.1)	124 482 (25.7%)	1.12 (1.11, 1.13)
85–94 years	48 753 (22.2%)	1.08 (1.06, 1.09)	58 540 (26.6%)	1.49 (1.47, 1.51)	64 385 (29.3%)	1.56 (1.54, 1.58)	59 473 (27.1%)	1.11 (1.09, 1.12)	73 314 (33.3%)	1.24 (1.23, 1.26)
95 years and over	4508 (27.2%)	1.13 (1.08, 1.17)	5512 (33.3%)	1.72 (1.65, 1.78)	5992 (36.2%)	1.73 (1.67, 1.79)	4820 (29.1%)	0.91 (0.87, 0.94)	6462 (39%)	1.23 (1.19, 1.28)
Living situation										
Home	183 700 (14.6%)	1	204 852 (16.3%)	1	218 091 (17.3%)	1	217 785 (17.3%)	1	281 146 (22.3%)	1
Nursing home	31 388 (36.4%)	1.93 (1.90, 1.96)	33 535 (38.9%)	1.79 (1.77, 1.82)	38 076 (44.1%)	2.01 (1.97, 2.04)	39 294 (45.5%)	2.29 (2.25, 2.33)	44 110 (51.1%)	2.16 (2.12, 2.19)
Number of drugs										
Less than 5	44 319 (5.7%)	1	63 404 (8.2%)	1	63 148 (8.2%)	1	46 185 (6%)	1	94 510 (12.2%)	1
Five or more	170 769 (29.9%)	6.5 (6.42, 6.57)	174 983 (30.6%)	4.42 (4.38, 4.47)	193 019 (33.8%)	5.07 (5.02, 5.12)	210 894 (36.9%)	8.44 (8.34, 8.53)	230 746 (40.4%)	4.41 (4.37, 4.45)

OR odds ratio; CI confidence interval; All outcomes were significant at the 0.001 level.

*Multivariate logistic regression models performed separately, with the use of potentially inappropriate drugs (yes vs. no) as categorical dependent variable. Independent variables included gender, age group, living situation and number of delivered drugs. 1 indicates the reference category.

level these five sets of criteria have the ability to provide robust prevalence measures within a narrow range (stretching from a 'minimal estimate' [NORGEP] to a 'maximal estimate' [Beers]). In addition, our results suggest that the PRISCUS list, the Laroche list and the Swedish criteria provide very consistent 'intermediate' estimates that may prove useful in cross-national comparisons at the European level.

Several limitations should be noticed and should call for caution in the interpretation of our results. First, we used data from 2008 (last available data at the time this study was conducted) and the patterns of drug use in Sweden might have slightly changed since that year, although the overall trend seems to have been relatively stable between 2008 and 2013 [24].

Second, our findings rely on the exposure to potentially inappropriate drugs for a given period of 90 days, based on the assumption that the drugs prescribed and dispensed during that period reflect with accuracy the actual drug consumption. This means that neither the drugs prescribed before that 3 month period and consumed at a slower rate than intended, nor the drugs that were prematurely discontinued during that period would have been taken into account in our analyses. In addition, due to the nature of the Swedish Prescribed Drugs Register, over-the-counter drugs were not included in the prevalence measures. However, in Sweden almost all drugs are available only on prescriptions. It should also be noted that drugs administered during a hospitalization and from drug store rooms in long term care facilities are not included in the register, which might have induced a small underestimation of the use of drugs among institutionalized people [55].

Third, among the drugs detected by applying the different sets of criteria, several were specific to the Swedish market (e.g. propiomazine) or to the Swedish national guidelines (e.g. tramadol). On the other hand, many of the drugs listed in the different sets of criteria were not available in Sweden in 2008 (including temazepam, reserpine, loprazolam, bromazepam and pentobarbital). The difficulty of applying criteria or quality indicators developed in other national settings has been reported in previous studies [35, 56–58] and has led to the development of country-specific assessment tools. Differences in availability of drugs across countries also restrict the generalizability of our results beyond Sweden, especially to non-European countries. However, again, our findings show a very similar overall prevalence of potentially inappropriate drugs use, although the US criteria capture a slightly broader population compared with the four European lists.

Fourth, the lack of information about the clinical conditions associated with the use of potentially inappropriate drugs is another limitation. In fact, this absence of information about the chronic illnesses and co-morbidities of the individuals justifies our choice not to include the STOPP-START criteria [21, 59], which contain many drug–disease criteria that make them very valuable and accurate as a screening tool in the clinical setting [37, 60–62] but more difficult to use in nationwide register-based studies. We strongly believe that future register studies should consider record-linkage methods to match pharmacy claims data with clinically relevant information from inpatient and primary care databases, in order to gain more insight on the disease-specific inappropriate medications [63]. Finally, a more general limitation lies in the fact that register-based studies can only report drug prescription and delivery patterns, and merely assume that these reflect adequately the actual use of drugs by the patients (given that adherence to treatments may vary) [64].

In conclusion, for the first time, a nationwide, population-based study used five different sets of criteria developed in five different countries to examine the prevalence of potentially inappropriate drug use among older people. Overall, 16% to 24% of the elderly population in Sweden is exposed to medications whose expected benefits are deemed lower than the risks they present. Although explicit criteria for inappropriate drug use have been reported to be quite different in their content and outcomes, they give strikingly similar measures of the prevalence of potentially inappropriate drug use.

In our opinion, this study supports the use of these criteria by public health policy makers, stakeholders and researchers to evaluate the quality of drug use at the population level, especially in a cross-national perspective. However, at the clinical level, our results raise important questions regarding the comprehensiveness of each of these tools, and therefore their applicability in the daily practice.

Competing Interests

REFERENCES

1 Shi S, Klotz U. Age-related changes in pharmacokinetics. Curr Drug Metab 2011; 12: 601–10.

2 Mangoni AA, Jackson SHD. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical applications. Br J Clin Pharmacol 2003; 57: 6–14.

3   Merle L, Laroche ML, Dantoine T, Charmes JP. Predicting and preventing adverse drug reactions in the very old. Drugs and Aging 2005; 22: 375–92.

4   Mallet L, Spinewine A, Huang A. The challenge of managing drug interactions in elderly people. Lancet 2007; 370: 185–91.

5   Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, Hanlon JT. Appropriate prescribing in elderly people: how well can it be measured and optimised? Lancet 2007; 370: 173–84.

6   Gurwitz JH, Field TS, Harrold LR, Rothschild J, Debellis K, Seger AC, Cadoret C, Fish LS, Garber L, Kelleher M, Bates DW. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. JAMA 2003; 289: 1107–16.

7   Budnitz DS, Pollock DA, Weidenbach KN, Mendelsohn AB, Schroeder TJ, Annest JL. National surveillance of emergency department visits for outpatient adverse drug events. JAMA 2006; 296: 1858–66.

8   Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. N Engl J Med 2011; 365: 2002–12.

9   Corsonello A, Pedone C, Lattanzio F, Lucchetti M, Garasto S, Di Muzio M, Giunta S, Onder G, Di Iorio A, Volpato S, Corica F, Mussi C, Antonelli Incalzi R. Potentially inappropriate medications and functional decline in elderly hospitalized patients. J Am Geriatr Soc 2009; 57: 1007–14.

10 Ruggiero C, Dell'Aquila G, Gasperini B, Onder G, Lattanzio F, Volpato S, Corsonello A, Maraldi C, Bernabei R, Cherubini A. Potentially inappropriate drug prescriptions and risk of hospitalization among older, Italian, nursing home residents: the ULISSE project. Drugs Aging 2010; 27: 747–58.

11 Kaufmann CP, Tremp R, Hersberger KE, Lampert ML. Inappropriate prescribing: a systematic overview of published assessment tools. Eur J Clin Pharmacol 2013; 70: 1–11.

12 Laroche ML, Charmes JP, Bouthier F, Merle L. Inappropriate medications in the elderly. Clin Pharmacol Ther 2009; 85: 94–7.

13 Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. Arch Intern Med 1991; 151: 1825–32.

14 Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update Arch Intern Med 1997; 157: 1531–6.

15 Zhan C, Sangl J, Bierman A. Potentially inappropriate medication use in the community-dwelling elderly. Findings from the 1996 Medical Expenditure Panel Survey. JAMA 2001; 286: 2823–9.

16 Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med 2003; 163: 2716–24.

17 Campanelli CM. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012; 60: 616–31.

18 McLeod PJ, Huang AR, Tamblyn RM, Gayton DC. Defining inappropriate practices in prescribing for elderly people: a national consensus panel. CMAJ 1997; 156: 385–91.

19 Rancourt C, Moisan J, Baillargeon L, Verreault R, Laurin D, Grégoire J-P. Potentially inappropriate prescriptions for older patients in long-term care. BMC Geriatr 2004; 4: 9.

20 Basger BJ, Chen TF, Moles RJ. Inappropriate medication use and prescribing indicators in elderly Australians: development of a prescribing indicators tool. Drugs Aging 2008; 25: 777–93.

21 Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing 2008; 37: 673–9.

22 Laroche M-L, Charmes J-P, Merle L. Potentially inappropriate medications in the elderly: a French consensus panel list. Eur J Clin Pharmacol 2007; 63: 725–31.

23 Holt S, Schmiedl S, Thürmann PA. Potentially inappropriate medications in the elderly: the PRISCUS list. Dtsch Arztebl Int 2010; 107: 543–51.

24 Hovstadius B, Petersson G, Hellström L, Ericson L. Trends in inappropriate drug therapy prescription in the elderly in sweden from 2006 to 2013: assessment using national indicators. Drugs Aging 2014; 31: 379–86.

25 Indicators of good drug therapy in the elderly. Stockholm: Swedish National Board of Health and Welfare, 2010; 96.

26 Rognstad S, Brekke M, Fetveit A, Spigset O, Wyller TB, Straand J. The Norwegian General Practice (NORGEP) criteria for assessing potentially inappropriate prescriptions to elderly patients. A modified Delphi study. Scand J Prim Health Care 2009; 27: 153–9.

27 Maio V, Del Canale S, Abouzaid S. Using explicit criteria to evaluate the quality of prescribing in elderly Italian outpatients: a cohort study. J Clin Pharm Ther 2010; 35: 219–29.

28 Mann E, Böhmdorfer B, Frühwald T, Roller-Wirnsberger RE, Dovjak P, Dückelmann-Hofer C, Fischer P, Rabady S, Iglseder B. Potentially inappropriate medication in geriatric patients: the Austrian consensus panel list. Wien Klin Wochenschr 2012; 124: 160–9.

29 Winit-Watjana W, Sakulrat P, Kespichayawattana J. Criteria for high-risk medication use in Thai older patients. Arch Gerontol Geriatr 2008; 47: 35–51.

30 Chang C-B, Yang S-Y, Lai H-Y, Wu R-S, Liu H-C, Hsu H-Y, Hwang S-J, Chan D-C. Using published criteria to develop a list of potentially inappropriate medications for elderly patients in Taiwan. Pharmacoepidemiol Drug Saf 2012; 21: 1269–79.

31 Levy HB, Marcus E-L, Christen C. Beyond the Beers criteria: A comparative overview of explicit criteria. Ann Pharmacother 2010; 44: 1968–75.

32 Dimitrow MS, Airaksinen MSA, Kivelä S-L, Lyles A, Leikola SNS. Comparison of prescribing criteria to evaluate the appropriateness of drug treatment in individuals aged 65 and older: a systematic review. J Am Geriatr Soc 2011; 59: 1521–30.

33 Chang C-B, Chan D-C. Comparison of published explicit criteria for potentially inappropriate medications in older adults. Drugs Aging 2010; 27: 947–57.

34 Marriott J, Stehlik P. A critical analysis of the methods used to develop explicit clinical criteria for use in older people. Age Ageing 2012; 41: 441–50.

35 Chang C-B, Chen J-H, Wen C-J, Kuo H-K, Lu I-S, Chiu L-S, Wu S-C, Chan D-CD. Potentially inappropriate medications in geriatric outpatients with polypharmacy: application of six sets of published explicit criteria. Br J Clin Pharmacol 2011; 72: 482–9.

36 Vishwas HN, Harugeri A, Parthasarathi G, Ramesh M. Potentially inappropriate medication use in Indian elderly: comparison of Beers' criteria and Screening Tool of Older Persons' potentially inappropriate Prescriptions. Geriatr Gerontol Int 2012; 12: 506–14.

37 Hudhra K, García-Caballos M, Jucja B, Casado-Fernández E, Espigares-Rodriguez E, Bueno-Cavanillas A. Frequency of potentially inappropriate prescriptions in older people at discharge according to Beers and STOPP criteria. Int J Clin Pharm 2014; 36: 596–603.

38 San-José A, Agustí A, Vidal X, Formiga F, López-Soto A, Fernández-Moyano A, García J, Ramírez-Duque N, Torres OH, Barbé J. Inappropriate prescribing to older patients admitted to hospital: A comparison of different tools of misprescribing and underprescribing. Eur J Intern Med 2014; 25: 6–8.

39 Statistics Sweden. Population statistics, January-June 2014. Stockholm: Statistiska Centralbyråns (SCB), 2014.

40 Johnell K, Fastbom J, Rosén M, Leimanis A. Inappropriate drug use in the elderly: a nationwide register-based study. Ann Pharmacother 2007; 41: 1243–8.

41 Wettermark B, Hammar N, Fored CM, MichaelFored C, Leimanis A, Otterblad Olausson P, Bergman U, Persson I, Sundström A, Westerholm B, Rosén M. The new Swedish Prescribed Drug Register--opportunities for pharmacoepidemiological research and experience from the first six months. Pharmacoepidemiol Drug Saf 2007; 16: 726–35.

42 Johnell K, Fastbom J. Antiepileptic drug use in community-dwelling and institutionalized elderly: a nationwide study of over 1,300,000 older people. Eur J Clin Pharmacol 2011; 67: 1069–75.

43 Haasum Y, Fastbom J, Johnell K. Institutionalization as a risk factor for inappropriate drug use in the elderly: a Swedish nationwide register-based study. Ann Pharmacother 2012; 46: 339–46.

44 Care of older people in Sweden 2008. Stockholm: Swedish National Board of Health and Welfare, 2009.

45 Statistics Sweden. Beskrivning av Sveriges befolkning 2008 [Description of the population in Sweden 2008]. Stockholm: Statistiska Centralbyråns (SCB), 2010.

46 Opondo D, Eslami S, Visscher S, de Rooij SE, Verheij R, Korevaar JC, Abu-Hanna A. Inappropriateness of medication prescriptions to elderly patients in the primary care setting: a systematic review. PLoS One 2012; 7: e43617.

47 Barnett K, McCowan C, Evans JMM, Gillespie ND, Davey PG, Fahey T. Prevalence and outcomes of use of potentially inappropriate medicines in older people: cohort study stratified by residence in nursing home or in the community. BMJ Qual Saf 2011; 20: 275–81.

48 Shah SM, Carey IM, Harris T, DeWilde S, Cook DG. Quality of prescribing in care homes and the community in England and Wales. Br J Gen Pract 2012; 62: e329–36.

49 Ruggiero C, Lattanzio F, Dell'Aquila G, Gasperini B, Cherubini A. Inappropriate drug prescriptions among older nursing home residents: the Italian perspective. Drugs Aging. 2009. 15–30.

50 Hosia-Randell HMV, Muurinen SM, Pitkälä KH. Exposure to potentially inappropriate drugs and drug-drug interactions in elderly nursing home residents in Helsinki, Finland: a cross-sectional study. Drugs Aging 2008; 25: 683–92.

51 Lau DT, Kasper JD, Potter DEB, Lyles A, Bennett RG. Hospitalization and death associated with potentially inappropriate medication prescriptions among elderly nursing home residents. Arch Intern Med 2005; 165: 68–74.

52 Bongue B, Laroche ML, Gutton S, Colvez A, Guéguen R, Moulin JJ, Merle L. Potentially inappropriate drug prescription in the elderly in France: a population-based study from the French National Insurance Healthcare system. Eur J Clin Pharmacol 2011; 67: 1291–9.

53 Schubert I, Küpper-Nybelen J, Ihle P, Thürmann P. Prescribing potentially inappropriate medication (PIM) in Germany ' s elderly as indicated by the PRISCUS list. An analysis based on regional claims data. Pharmacoepidemiol Drug Saf 2013; 22: 719–27.

54 Johnell K, Weitoft GR, Fastbom J. Sex differences in inappropriate drug use: a register-based study of over 600,000 older people. Ann Pharmacother 2009; 43: 1233–8.

55 Läkemedel 2007. En jämförelse baserad på Socialstyrelsens läkemedelsregister. 2008 p. 144.

56 Leikola S, Dimitrow M, Lyles A, Pitkälä K, Airaksinen M. Potentially inappropriate medication use among Finnish non-institutionalized people aged ≥65 years: a register-based, cross-sectional, national study. Drugs Aging 2011; 28: 227–36.

57 Fialová D, Topinková E, Gambassi G, Finne-Soveri H, Jónsson PV, Carpenter I, Schroll M, Onder G, Sørbye LW, Wagner C, Reissigová J, Bernabei R. Potentially InappropriateMedication Use Among Elderly Home Care Patients in Europe. JAMA 2005; 293: 1348–58.

58 Kölzsch M, Kopke K, Fischer T, Hofmann W, Kuhnert R, Bolbrinker J, Kuhlmey A, Dräger D, Kreutz R. Prescribing of inappropriate medication in nursing home residents in Germany according to a French consensus list: a cross-sectional cohort study. Pharmacoepidemiol Drug Saf 2011; 20: 12–9.

59 O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing 2015; 44: 213–8.

60 O'Sullivan DP, O'Mahony D, Parsons C, Hughes C, Murphy K, Patterson S, Byrne S. A prevalence study of potentially inappropriate prescribing in Irish long-term care residents. Drugs Aging 2013; 30: 39–49.

61 Hill-Taylor B, Sketris I, Hayden J, Byrne S, O'Sullivan D, Christie R. Application of the STOPP/START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. J Clin Pharm Ther 2013; 38: 360–72.

62 Grace AR, Briggs R, Kieran RE, Corcoran RM, Romero-Ortuno R, Coughlan TL, O'Neill D, Collins R, Kennelly SP. A Comparison of Beers and STOPP Criteria in Assessing Potentially Inappropriate Medications in Nursing Home Residents Attending the Emergency Department. J Am Med Dir Assoc 2014; 15: 830–4.

63 Cahir C, Fahey T, Teeling M, Teljeur C, Feely J, Bennett K. Potentially inappropriate prescribing and cost outcomes for older people: a national population study. Br J Clin Pharmacol 2010; 69: 543–52.

64 Johnell K, Råstam L, Lithman T, Sundquist J, Merlo J. Low adherence with antihypertensives in actual practice: the association with social participation--a multilevel analysis. BMC Public Health 2005; 5: 17.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix 1
Comparison of the most commonly prescribed potentially inappropriate medications, Sweden 2008

Appendix 2
Combination estimates of inappropriate drug use: prevalence and associated factors, Sweden 2008

Appendix 3
Number of sets of criteria concomitantly capturing the individuals that have been detected as potentially inappropriate drug users by at least one of the sets of criteria, Sweden 2008

Appendix 4
Sensitivity and specificity of the different sets of criteria, Sweden 2008

Appendix 5
Level of agreement between each set of criteria: kappa coefficient, Sweden 2008