



**HAL**  
open science

## To what extent does the indicator “concurrent use of three or more psychotropic drugs” capture use of potentially inappropriate psychotropics among the elderly?

Eva Lesén, Max Petzold, Karolina Andersson, Anders Carlsten

### ► To cite this version:

Eva Lesén, Max Petzold, Karolina Andersson, Anders Carlsten. To what extent does the indicator “concurrent use of three or more psychotropic drugs” capture use of potentially inappropriate psychotropics among the elderly?. *European Journal of Clinical Pharmacology*, 2009, 65 (6), pp.635-642. 10.1007/s00228-009-0623-x . hal-00534946

**HAL Id: hal-00534946**

**<https://hal.science/hal-00534946>**

Submitted on 11 Nov 2010

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# To what extent does the indicator “concurrent use of three or more psychotropic drugs” capture use of potentially inappropriate psychotropics among the elderly?

Eva Lesén · Max Petzold · Karolina Andersson · Anders Carlsten

Received: 3 November 2008 / Accepted: 13 January 2009 / Published online: 12 February 2009  
© Springer-Verlag 2009

## Abstract

**Purpose** The indicator “concurrent use of three or more psychotropic drugs” has been used as a measure of quality in drug use among the elderly. The aim of our study was to assess to what extent the indicator captures the use of specific psychotropics associated with an increased risk of adverse events among the elderly, i.e., potentially inappropriate psychotropic drugs (PIP).

**Methods** All individuals aged 75 years and older in Sweden purchasing prescribed psychotropic drugs in 2006 constituted the study population ( $n=384,904$ ). Data on purchased psychotropic drugs from the Swedish Prescribed Drug Register were used. The overlap between individuals with the indicator and individuals using PIP was assessed with sensitivity, specificity, positive and negative predictive values and likelihood ratio as outcome measures.

**Results** Among the psychotropic drug users, 15% had the indicator and 39% used PIP. The proportion of individuals with the indicator among all individuals using PIP was 27% (sensitivity). The proportion of individuals without the indicator among all individuals not using PIP was 93% (specificity). The positive predictive value was 72%, and the negative predictive value was 67%. Differences in outcome measures were observed between different categories of PIP.

**Conclusions** The indicator “concurrent use of three or more psychotropics” can be technically easy to use, but PIP is more specific. Three quarters of all individuals who used PIP in this study were not captured by the indicator.

However, two thirds of all individuals with the indicator used PIP. When selecting instruments to assess appropriateness in drug therapy in the elderly, clinical relevance should be balanced against convenience of use.

**Keywords** Elderly · Inappropriate drugs · Polypharmacy · Psychotropic drugs · Quality indicators · Registries

## Introduction

Drug prescribing for the elderly presents challenges due to age-related changes in body composition and drug elimination, that affect the body's sensitivity to drugs [1]. Consequently, the selection of appropriate drug therapy is complex. Appropriate care should take aspects of risk-benefit assessments, available healthcare resources and patient individuality into account [2]. When this concept is applied to data on drug use only, there is a need to transform and simplify this definition into suitable criteria. Such explicit criteria often focus on pharmacological appropriateness, i.e. choice of drug, dose, drug interactions, duplications and duration of drug therapy, and omit aspects of patients' preferences, comorbidities and underprescribing [3]. These criteria are considered to measure the use of *potentially* inappropriate drugs.

The development of explicit criteria for measuring the use of potentially inappropriate drugs among the elderly, such as Beers' criteria, has primarily occurred in North America [4–7], but also in other countries [8–10]. The usefulness of such criteria depends on the availability of drugs and prescribing patterns, and they are therefore not easily transferable between countries. A study involving eight European countries found that approximately half of the drugs listed in the criteria originating from North America were not approved for sales in the European countries under study [11]. Further, there were large variations between the European countries.

E. Lesén (✉) · M. Petzold · K. Andersson · A. Carlsten  
Nordic School of Public Health,  
P.O. Box 12133, 402 42 Gothenburg, Sweden  
e-mail: eva.lesen@nhv.se

A. Carlsten  
Department of Research and Development,  
The National Corporation of Swedish Pharmacies (Apoteket AB),  
Gothenburg, Sweden

Quality indicators can be used for assessing the level of quality in healthcare. Measures used as quality indicators should fulfil certain characteristics, such as being measurable, established, relevant, interpretable and subject to being influenced. An indicator should also fulfil basic requirements regarding reliability and validity, including having causal links to relevant health outcomes, such as morbidity or quality of life. The ideal indicator should detect all cases of suboptimal utilization and not classify optimal utilization as suboptimal, i.e. it should have high sensitivity, specificity and predictive values [12–14]. Indicators should be developed based on the scientific literature or consensus techniques [15].

Concurrent use of multiple psychotropic drugs, such as a benzodiazepine, a tricyclic antidepressant and a low-dose antipsychotic, has been proposed as an indicator of the inappropriate use of drugs among the elderly [16]. The related indicator “concurrent use of three or more psychotropic drugs” [irrespective of the Anatomical Therapeutic Chemical (ATC) classification system therapeutic subgroup] is included in a proposal of quality indicators and explicit criteria for measuring quality in drug use among the elderly in Sweden [17]. The proposal is based on Swedish recommendations, internationally published explicit criteria and expert opinions. This indicator has been used in several research studies [9, 18–23] as well as in recent national assessments of quality and efficiency in the Swedish healthcare system [24]. The indicator is considered to be a proxy for polypharmacy (concurrent use of multiple drugs) and to signal poor quality in the treatment of psychiatric disorders. It is also considered to signal an increased risk of adverse outcomes and drug–drug interactions [17]. However, as there are situations when the use of multiple psychotropic drugs is considered appropriate [25], there is a risk that the indicator may classify appropriate use as poor quality. It is not specified which psychotropics should be included in the combinations for the indicator to measure inappropriate care. An indicator measuring the number of psychotropic drugs used concurrently is thus less informative with respect to the associated risks than measures on specific inappropriate psychotropics. Therefore, the aim of our study was to assess to what extent the indicator “concurrent use of three or more psychotropic drugs” captures the use of specific psychotropics associated with an increased risk of adverse events among the elderly, i.e. potentially inappropriate psychotropic drugs (PIP). A list of such PIP is included in the proposal mentioned earlier (Table 1) [17].

## Methods

### Study population

The study population included all individuals aged 75 years and older on 1 January 2006 in Sweden who had purchased

at least one prescribed psychotropic drug (ATC codes N05 and N06 [26]) in a Swedish pharmacy during 2006. The age cut-off of 75 years was chosen since this was the limit used in the national assessment of quality and efficiency in the Swedish healthcare year 2006. The analyses included all prescribed psychotropic drugs purchased by individuals in the study population during the study period.

### Data description

Data from the Swedish Prescribed Drug Register were used [27]. The register includes prescribed drugs purchased at all Swedish pharmacies and thereby excludes drugs used in hospitals or purchased over the counter. Information about the patient and the purchased drug (type and amount) is included in the register. Information on prescribers' dosage instructions was available only as a free text section, which is not statistically processable. This dosage information was missing for all prescriptions dispensed as multi-dose packages (ApoDos).

### Assessment of prescribed daily doses

The defined daily dose (DDD [26]) is a technical unit and often lacks clinical relevance when measuring how drugs are used among the elderly. Therefore, a review of prescribed daily doses (PDDs) was conducted in the register. Dosage instructions for a random sample of dispensed prescriptions of all psychotropic substances were performed in the data set. A wide distribution of the patients' sex, age, geographical residence and date of purchase was sought. A PDD was estimated for each reviewed prescription based on drug strength and dosage instruction. Thereafter, a substance-specific population average PDD was estimated. For each substance, values from additional dosage instructions were added until there were no substantial changes in the calculated population average PDD, as judged by the first author. The median number of reviewed instructions per substance was 160 (range 27–295). Midazolam was excluded from the review since the majority of dosage instructions were “according to given instructions”. Substances used by fewer than 100 individuals were also excluded from the review ( $n=18$ ; mean number of users per substance was 32), since the estimations of substance-specific PDDs for these very rare substances would be uncertain and correspond to a negligible impact on results. A theoretical consumption rate of 0.5 DDD/day was assumed for these substances. Substances without assigned DDDs were excluded from the study, since their treatment periods could not be calculated ( $n=8$ ; each used by fewer than 300 individuals). None of the excluded substances were classified as PIPS.

A similar review for commonly dispensed psychotropic substances was performed for multi-dose users to investigate

**Table 1** Definition of potentially inappropriate combinations of psychotropics and potentially inappropriate psychotropic substances, and prevalence among psychotropic drug users aged 75 years and older in Sweden in 2006 ( $n=384,904$ )

Classification	ATC code	Prevalence	
		<i>n</i>	Percentage
<b>PICP</b>			
Two or more benzodiazepines	N05BA+N05CD	10,733	2.8
Two or more psychotropics in the same class	N05A+N05A, N05B+N05B, N05C+N05C, N06A+N06A	41,546	10.8
Two or more antipsychotics	N05A+N05A	2,850	0.7
Two or more anxiolytics	N05B+N05B	7,648	2.0
Two or more hypnotics	N05C+N05C	22,034	5.7
Two or more antidepressants	N06A+N06A	13,256	3.4
Two or more psychotropics with anticholinergic effects	See list of PIPS below	1,006	0.3
<b>PIPS</b>			
Long-acting benzodiazepines		64,707	16.8
Diazepam	N05BA01	29,213	7.6
Nitrazepam	N05CD02	13,024	3.4
Flunitrazepam	N05CD03	22,470	5.8
Psychotropics with anticholinergic effects		50,258	7.0
Chlorpromazine	N05AA01	291	0.1
Levomepromazine	N05AA02	3,917	1.0
Prochlorperazine	N05AB04	2,211	0.3
Chlorprothixene	N05AF03	219	0.1
Hydroxizine	N05BB01	25,309	6.6
Clomipramine	N06AA04	2,594	0.7
Trimipramine	N06AA06	398	0.1
Amitriptyline	N06AA09	14,231	3.7
Nortriptyline	N06AA10	576	0.1
Maprotiline	N06AA21	512	0.1
Miscellaneous		45,789	11.9
Propiomazine	N05CM06	44,178	11.5
Triazolam	N05CD05	1,611	0.4

PICP, Potentially inappropriate combinations of psychotropics; PIPS, potentially inappropriate psychotropic substances; ATC, Anatomical Therapeutic Chemical classification system

whether there were substantial differences in PDDs between regular and multi-dose users. This was assessed by the first author. The review was performed in a database at Dosapoteket in Gothenburg, a pharmacy producing multi-dose packages. The database includes information on the prescribed drug, patients' age and sex and dosage instructions.

#### Definitions of measures

The following definition of concurrent use of three or more psychotropic drugs was used as the standard. At least three different psychotropic drug substances should be concurrently used for at least 40 days, not necessarily consecutive, during the study period. The substances used concurrently were not necessarily the same for all 40 days. The treatment period was assumed to start on the day of purchase, and the theoretical daily drug consumption rate was based on the estimated PDD for

each substance according to the review of dosage instructions. The lower limit for number of days of concurrent use was set to be clinically relevant and to exceed temporary short-term treatments, including start packages ( $\leq 30$  days of treatment).

PIP was defined as the use of potentially inappropriate combinations of psychotropics (PICP) or potentially inappropriate psychotropic substances (PIPS), according to a proposal from the Swedish National Board of Health and Welfare [17] (Table 1). The definition of PICP was based on concurrent use of at least two different substances in the specified categories for at least 40 days (not necessarily consecutive or the same substances all 40 days) during the study period. The use of PIPS was defined as at least one purchase during the study period. Alimemazine (ATC R06AD01) and promethazine (ATC R06AD02) are used as hypnotics in clinical practice. These were excluded from the analyses since these are not classified as psychotropics

according to the ATC system and would therefore not be identified by the indicator.

#### Assessment of the indicator

The use of PIP was classified as the reference against which the indicator “concurrent use of three or more psychotropics” was compared. In subanalyses, the indicator was assessed against PICP and PIPS separately. PICP and PIPS were then classified as the references. Sensitivity, specificity, positive and negative predictive values and the likelihood ratio of the indicator were calculated. The sensitivity measures the proportion of individuals with the indicator among all individuals using PIP. The specificity measures the proportion of individuals without the indicator among all individuals not using PIP. The positive predictive value measures the proportion of individuals using PIP among all individuals with the indicator. The negative predictive value measures the proportion of individuals not using PIP among all individuals without the indicator. The likelihood ratio indicates how much more likely the indicator is to be found among individuals using PIP, compared to individuals not using PIP. Data management and the identification of individuals using the indicator and PIP were performed using SAS ver. 9.1 for Windows (SAS Institute, Cary, NC).

#### Analyses of stability

The theoretical drug consumption rate was altered as follows, using the same rate for all substances: 0.5 DDD/day, 0.75 DDD/day, 1 DDD/day, 1.5 DDD/day, 2 DDD/day. The following required minimum numbers of days of concurrent use were applied: 1, 7, 14, 75 and 120 days. These alterations

were compared to the previously defined standard. Limits for days of concurrent use were set to avoid obvious collisions with commonly dispensed amounts.

Since the total target population was included, confidence intervals or *p* values were not calculated around prevalence measures or mean values. The project was approved by the regional ethics board in Gothenburg, Sweden (no. 263-07).

## Results

### Characteristics of the study population

Among all individuals aged 75 years and older in Sweden in 2006, 384,904 individuals (48%) had purchased at least one psychotropic drug, and were thereby enrolled in the study population. Compared to the whole Swedish population aged 75 years and older, the population of psychotropic drug users were represented by a larger proportion of women (68.7 vs. 60.8%) and a larger proportion of individuals aged 85 years and older (38.9 vs. 29.6%) [28]. The majority of individuals had regularly dispensed drugs only (69.6 vs. 25.7% via multi-dose only). Some individuals (4.7%) shifted during the study period, primarily from regular to multi-dose use. The method used in this study was independent of dispensing type.

Among the different categories of PICP, the use of two or more psychotropics in the same class was most common in the study population of psychotropic drug users (Table 1). Of all purchased prescriptions during the study period, 16.9% were classified as PIPS. Propiomazine was the most common single PIPS, used by 11.5% of all individuals, while long-acting benzodiazepines as a group were used by 16.8%. The indicator “concurrent use of three or more

**Table 2** Prevalence of concurrent use of three or more psychotropics and of potentially inappropriate psychotropics among psychotropic drug users aged 75 years and older in Sweden in 2006 ( $n=384,904$ )

Categories of psychotropic drug users	Concurrent use of three or more psychotropics		Potentially inappropriate psychotropics (PICP or PIPS)		Potentially inappropriate combinations of psychotropics (PICP)		Potentially inappropriate psychotropic substances (PIPS)	
	<i>n</i>	Percentage	<i>n</i>	Percentage	<i>n</i>	Percentage	<i>n</i>	Percentage
Total ( $n=384,904$ )	56,518	14.7	150,686	39.1	46,742	12.1	138,538	36.0
Men ( $n=120,513$ )	15,882	13.2	48,026	39.9	14,673	12.2	44,209	36.7
Women ( $n=264,391$ )	40,636	15.4	102,660	38.8	32,069	12.1	94,329	35.7
Subjects 75–84 years ( $n=235,006$ )	32,728	13.9	92,470	39.3	28,176	12.0	85,075	36.2
Subjects 85 years and older ( $n=149,898$ )	23,790	15.9	58,216	38.8	18,566	12.4	53,463	35.7
Individuals with regularly dispensed drugs only ( $n=267,905$ )	23,828	8.9	102,899	38.4	25,644	9.6	97,102	36.2
Individuals with multi-dose dispensed drugs only ( $n=98,960$ )	27,333	27.6	39,896	40.3	17,325	17.5	34,624	35.0

psychotropics” and use of PICP were more common among individuals with multi-dose dispensed drugs only than among those with regularly dispensed drugs only (Table 2).

#### Assessment of prescribed daily doses

The PDDs estimated for individuals with regularly and multi-dose dispensed drugs were similar. The mean PDD for psychotropic drugs in total was 0.54 DDDs (range 0.1–1.2). The mean theoretical consumption rate, based on PDD, differed between the major psychotropic drug groups as follows: antipsychotics, 0.25 (0.1–0.6); anxiolytics, 0.42 (0.1–0.7); hypnotics, 0.64 (0.3–1.0) and antidepressants, 0.76 (0.3–1.2) DDD/day. Estimated PDDs for all substances are available from the authors by request.

#### Assessment of the indicator

Figure 1 shows the relation between the indicator and use of PIP, PICP and PIPS in the study population. Among the psychotropic drug users, the sensitivity of the indicator versus PIP was 27%, and the specificity was 93% (Table 3). The positive predictive value was 72%, and the negative predictive value was 67%. Individuals using PIP were fourfold more likely to have the indicator compared to individuals not using PIP (likelihood ratio). The sensitivity was higher and the specificity was lower among those with multi-dose dispensed drugs than in those with regularly dispensed drugs. The sensitivity for PICP only as a reference against the indicator was markedly higher than for PIPS only (66 vs. 23%), while the specificity was only slightly higher (92 vs. 90%). Outcome measures varied between the subcategories of PIP.

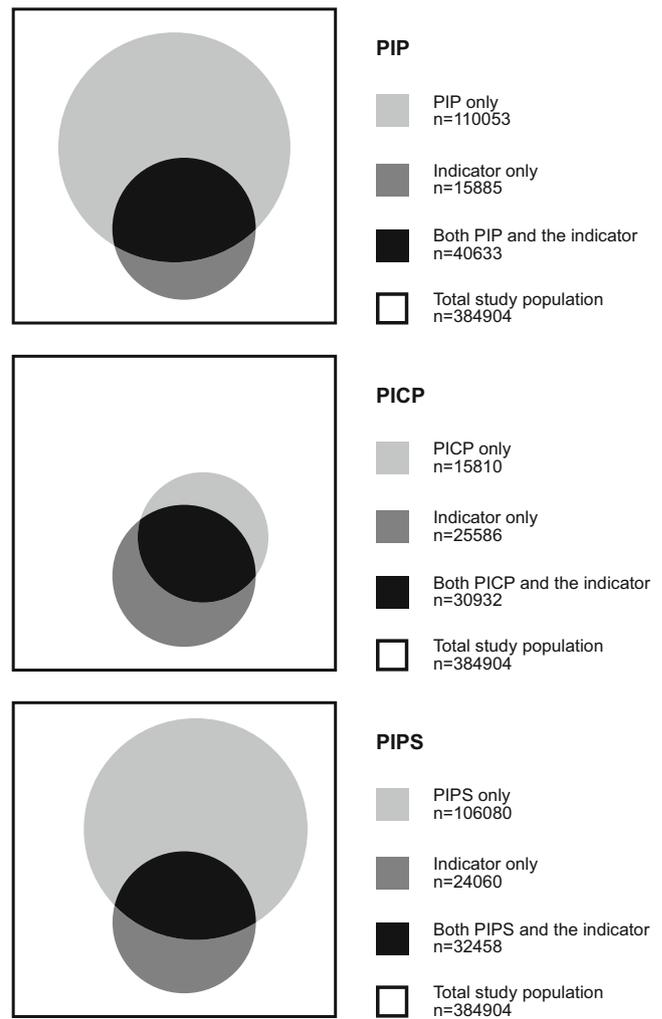
#### Analyses of stability

The sensitivity of the indicator decreased with increasing theoretical drug consumption rates and increasing required number of days of concurrent use (Fig. 2). Although less pronounced, the specificity showed a reversed pattern. Sensitivity and specificity were similar for 1, 7, and 14 days of concurrent use, and the trends became more distinct after the limit of 14 days was passed.

## Discussion

The indicator “concurrent use of three or more psychotropics” missed three quarters of the individuals using PIP. Among those individuals with the indicator, two thirds used PIP. Outcome measures varied markedly between the categories of PIP.

The indicator captured the use of PICP to a higher extent than the use of PIPS. This may partly be explained by the



**Fig. 1** Illustration of the relation between prevalence of any potentially inappropriate psychotropics (*PIP*,  $n=150,686$ ), potentially inappropriate combinations of psychotropics (*PICP*,  $n=46,742$ ) and potentially inappropriate psychotropic substances (*PIPS*,  $n=138,538$ ), respectively, and the indicator “concurrent use of three or more psychotropics” among psychotropic drug users aged 75 years and older in Sweden, in 2006 ( $n=384,904$ )

similar definitions used for the indicator and for PICP. PICP is a measure of combinations of specified psychotropic substances, while the indicator measures any combinations of psychotropic drugs. Furthermore, PICP measures combinations of two or more substances instead of three or more, as measured by the indicator. However, as large differences in results were observed between different categories of PICP, the similarities in definitions would not explain the results as a whole.

The study population only included individuals purchasing psychotropic drugs during the study period; this is in contrast to other studies that used all individuals aged 75 years and older as the study population [23, 24]. The prevalence and specificity of the indicator are affected by whether the study

**Table 3** Outcome measures for the use of any potentially inappropriate psychotropics and categories of PICP and PIPS against the indicator “concurrent use of three or more psychotropic drugs” among psychotropic drug users aged 75 years and older in Sweden, in 2006 ( $n=384,904$ ). Any potentially inappropriate psychotropic, PICP and PIPS, respectively, was classified as the reference in the assessments

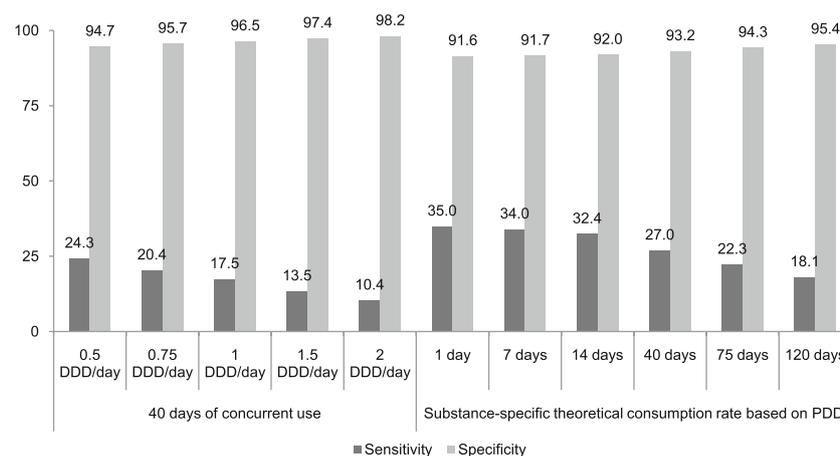
	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Likelihood ratio
Any potentially inappropriate psychotropic (PICP or PIPS)	27.0	93.2	71.9	66.5	4.0
Individuals with regularly dispensed drugs only	17.7	96.6	76.5	65.3	5.2
Individuals with multi-dose dispensed drugs only	46.7	85.3	68.2	70.3	3.2
PICP	66.2	92.4	54.7	95.2	8.7
Two or more benzodiazepines	67.3	86.8	12.8	98.9	5.1
Two or more antipsychotics	78.7	85.8	4.0	99.8	5.5
Two or more anxiolytics	82.2	86.7	11.1	99.6	6.2
Two or more hypnotics	63.0	88.3	24.6	97.5	5.4
Two or more antidepressants	79.7	87.6	18.7	99.2	6.4
Two or more psychotropics with anticholinergic effects	76.5	85.5	1.4	99.9	5.3
PIPS	23.4	90.2	57.4	67.7	2.4

population includes psychotropic drug users only or all individuals irrespective of psychotropic drug use. Our study therefore gives a higher prevalence and a lower specificity.

Outcome measures were affected by how the treatment periods were defined. Higher theoretical drug consumption rates and higher limits for number of days of concurrent use yielded lower sensitivities. The changes in specificity were reversed and less pronounced. Both the prevalence of the indicator and of PICP are expected to decrease when the treatment periods are shortened. As PIPS is defined independently of treatment periods, its prevalence is not affected by such changes in definitions, thereby demonstrating the importance of choosing clinically and methodologically relevant definitions when measuring concurrent use of drugs.

Users of multi-dose are a selected population with special needs. Previous studies have found that multi-dose users may be more exposed to potentially inappropriate drug use compared to those using regularly dispensed drugs [29]. Similar findings were observed in the study reported here. The prevalence of the indicator was markedly higher and the use of PIP was slightly more common among those with multi-dose dispensed drugs than among those with regularly dispensed drugs. There were differences in how the indicator captured the use of PIP between the two populations. It is thus important to consider these populations separately.

The indicator is relatively easy to apply in quality assessments as opposed to PIP, which would argue for its use if it is considered an appropriate measure of quality.



**Fig. 2** Sensitivity and specificity of the indicator “concurrent use of three or more psychotropic drugs” against the use of any potentially inappropriate psychotropics among psychotropic drug users aged 75 years and older in Sweden, in 2006 ( $n=384,904$ ). *Left* Minimum number of 40 days of concurrent use was constant, and the theoretical

drug consumption rate was altered. *Right* Theoretical drug consumption rate was constant based on substance-specific theoretical drug consumption rates [prescribed daily dose (PDD) for each substance] and the minimum number of days of concurrent use was altered. DDD Defined daily dose

However, a high number of psychotropic drugs does not automatically imply a high risk of adverse events for the individual patient, as there are situations when the use of multiple psychotropic drugs is considered appropriate [25]. Thus, the relevance of the indicator would increase if it captured the use of specific inappropriate combinations or substances. Drugs with an unfavourable risk–benefit ratio are classified as potentially inappropriate when safer or equally effective alternatives are available. Such explicit criteria have been used extensively in research on the quality in drug use among the elderly. The scientific documentation is substantial regarding the use of such criteria [30, 31]. However, in some cases, it is possible that drugs classified as potentially inappropriate may have been appropriately prescribed. For instance, tricyclic antidepressants, such as amitriptyline, are sometimes used for neuropathic pain, at doses that are in general lower than those when used as an antidepressant. Antidepressant substances with a more favourable risk–benefit profile, such as selective serotonin reuptake inhibitors, are available [32], but for neuropathic pain, alternative treatment options are scarce. Nonetheless, drugs are classified as PIP regardless of indication or dosage. The classification of PIP is more informative on the associated risks, while the indicator can be relatively easy to use.

#### Strengths and limitations

One of the main strengths of our study design was the review of the PDDs conducted before the treatment periods were estimated. As illustrated, there were considerable differences between substances in the ratio between the PDD and the DDD. Thus, a theoretical consumption rate based on one rate for all substances would likely classify treatment periods with less certainty.

The concurrent use of drugs can be classified in numerous ways. In order to make the definition of concurrent use manageable in the data analyses, some limitations have to be introduced. The definition did not take into consideration whether or not the days of concurrent use were consecutive, nor did it discriminate between which specific substances were used during the days of concurrent use over the study period. This constraint may have reduced the clinical relevance of the definition.

#### Conclusion

The indicator “concurrent use of three or more psychotropics” can be technically easy to use, but PIP is more specific. Of all the individuals who used PIP in this study, three quarters were not captured by the indicator. However, two thirds of all individuals with the indicator used PIP. When selecting instruments to assess appropriateness in

drug therapy in the elderly, clinical relevance should be balanced against convenience of use.

**Acknowledgements** This study is part of a larger project on quality indicators that has received funding from the county council in Region Västra Götaland. The project was designed by the researchers at the Nordic School of Public Health. The authors would like to thank the responsible persons at Dosapoteket in Gothenburg for providing access to the database.

#### References

1. Shi S, Morike K, Klotz U (2008) The clinical implications of ageing for rational drug therapy. *Eur J Clin Pharmacol* 64:183–199
2. Report of a working group prepared for the Director of Research and Development of the NHS Management Executive (1993) What do we mean by appropriate health care? *Qual Health Care* 2:117–123
3. Spinewine A, Schmader KE, Barber N et al (2007) Appropriate prescribing in elderly people: how well can it be measured and optimised? *Lancet* 370:173–184
4. Beers MH (1997) Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. *Arch Intern Med* 157:1531–1536
5. Fick DM, Cooper JW, Wade WE et al (2003) Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med* 163:2716–2724
6. McLeod PJ, Huang AR, Tamblyn RM et al (1997) Defining inappropriate practices in prescribing for elderly people: a national consensus panel. *Can Med Assoc J* 156:385–391
7. Naugler CT, Brymer C, Stolee P et al (2000) Development and validation of an improving prescribing in the elderly tool. *Can J Clin Pharmacol* 7:103–107
8. Laroche ML, Charmes JP, Merle L (2007) Potentially inappropriate medications in the elderly: a French consensus panel list. *Eur J Clin Pharmacol* 63:725–731
9. Brekke M, Rognstad S, Straand J et al (2008) Pharmacologically inappropriate prescriptions for elderly patients in general practice: How common? Baseline data from The Prescription Peer Academic Detailing (Rx-PAD) study. *Scand J Prim Health Care* 26:80–85
10. Basger BJ, Chen TF, Moles RJ (2008) Inappropriate medication use and prescribing indicators in elderly Australians: development of a prescribing indicators tool. *Drugs Aging* 25:777–793
11. Fialova D, Topinkova E, Gambassi G et al (2005) Potentially inappropriate medication use among elderly home care patients in Europe. *JAMA* 293:1348–1358
12. Hoven JL, Haaijer-Ruskamp FM, Vander Stichele RH (2005) Indicators of prescribing quality in drug utilisation research: report of a European meeting (DURQUIM). *Eur J Clin Pharmacol* 60:831–834
13. Andersen M (2006) Is it possible to measure prescribing quality using only prescription data? *Basic Clin Pharmacol Toxicol* 98:314–319
14. Wettermark B, Tomson G, Bergman U (2006) Quality indicators for drug utilization—new European recommendations (in Swedish). *Lakartidningen* 103:3469–3472
15. Campbell SM, Braspenning J, Hutchinson A et al (2003) Research methods used in developing and applying quality indicators in primary care. *Br Med J* 326:816–819
16. Robertson HA, MacKinnon NJ (2002) Development of a list of consensus-approved clinical indicators of preventable drug-related morbidity in older adults. *Clin Ther* 24:1595

17. National Board of Health and Welfare (2003) Indicators for evaluation of the quality in drug use among the elderly: proposal from the National Board of Health and Welfare (in Swedish). Report number 2003-110-20. National Board of Health and Welfare, Stockholm
18. Ruths S (2008) Evaluation of prescribing quality in nursing homes based on drug-specific indicators: The Bergen district nursing home (BEDNURS) study. *Nor J Epidemiol* 18:173–178
19. Linden M, Bar T, Helmchen H (2004) Prevalence and appropriateness of psychotropic drug use in old age: results from the Berlin Aging Study (BASE). In: *Psychogeriatr* 16:461–480
20. Draper B, Brodaty H, Low LF et al (2001) Use of psychotropics in Sydney nursing homes: associations with depression, psychosis, and behavioral disturbances. *Int Psychogeriatr* 13:107–120
21. Giron MS, Forsell Y, Bernsten C et al (2001) Psychotropic drug use in elderly people with and without dementia. *Int J Geriatr Psychiatry* 16:900–906
22. Klarin I, Wimo A, Fastbom J (2005) The association of inappropriate drug use with hospitalisation and mortality - a population-based study of the very old. *Drugs Aging* 22:69–82
23. Johnell K, Fastbom J, Rosen M et al (2007) Inappropriate drug use in the elderly: a nationwide register-based study. *Ann Pharmacother* 41:1243–1248
24. Association of Local Authorities and Regions and The National Board of Health and Welfare (2008) Quality and efficiency in Swedish health care—regional comparisons 2007. Stockholm, Sweden.
25. National Association of State Mental Health Report Program Directors (2001) Technical report on psychiatric polypharmacy. Medical Directors Council and State Medicaid Directors, Alexandria
26. World Health Organization (WHO) Collaborating Centre for Drug Statistics. Methodology ATC index with DDDs. WHOCC, Oslo. Available at: [www.whooc.no](http://www.whooc.no)
27. Wettermark B, Hammar N, Forel CM et al (2007) The new Swedish Prescribed Drug Register—opportunities for pharmacoepidemiological research and experience from the first six months. *Pharmacoepidemiol Drug Saf* 16:726–735
28. Statistics Sweden (2008) The statistical database (Statistikdatabasen). Available at: <http://www.ssd.scb.se/>. Accessed 17 June 2008
29. Johnell K, Fastbom J (2008) Multi-dose drug dispensing and inappropriate drug use: a nationwide register-based study of over 700,000 elderly. *Scand. J Prim Health Care* 26:86–91
30. Jano E, Aparasu RR (2007) Healthcare outcomes associated with Beers' criteria: a systematic review. *Ann Pharmacother* 41:438–447
31. Chutka DS, Takahashi PY, Hoel RW (2004) Inappropriate medications for elderly patients. *Mayo Clin Proc* 79:122–139
32. Wilson K, Mottram P (2004) A comparison of side effects of selective serotonin reuptake inhibitors and tricyclic antidepressants in older depressed patients: a meta-analysis. *Int J Geriatr Psychiatry* 19:754–762