

# Use of potentially inappropriate medication and polypharmacy in elderly: a repeated cross-sectional study

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## Abstract

Background Potential inappropriate medications (PIM) have an increased risk for adverse drug reactions (ADR) in an elderly population. With increasing age, multimorbidity is growing along with the use of medications. For several years, polypharmacy has been found to increase in western societies. Polypharmacy is associated with an increased risk of ADR. In this study, we analysed the prevalence of PIM in an elderly population and in different strata of the variables age, gender, number of chronic conditions and polypharmacy and how that prevalence changed over time. Methods This is a registry based repeated cross-sectional study including two cohorts included. Individuals aged 75 or older listed at a primary care center in Blekinge on the 31 of March 2011 (cohort 1) or on the 31 of December 2013 (cohort 2) were included in the respective cohorts. Using a chi2 test, the two cohorts were compared on the variables age, gender, number of chronic conditions and polypharmacy. Use of five or more medications at the same time was the definition for polypharmacy. Results Use of PIM decreased from 10.60% to 7.04% (p-value <0.001) between 2011 and 2013, while prevalence of five to seven chronic conditions increased from 20.55% to 23.66% (p-value <0.001). Use of PIM decreased in all strata of the variables age, gender number of chronic conditions and polypharmacy. Except for age 80 to  $\leq$  85 and males, where it increased, prevalence of polypharmacy was stable in all strata of the variables. Conclusions Use of potentially inappropriate medications had decreased in all variables between 2011 and 2013. Polypharmacy does not increase significantly compared to the rest of the population.

## Introduction

One of the most common treatments, especially in elderly patients ( $\geq$ 75 years), are drug therapies. The goal of drug therapy is to prevent, treat or cure disease or symptoms of disease. For elderly people with multimorbidity and polypharmacy, the effect may, however, be the contrary. Advances in drug development in recent decades have resulted in that the health care system today can prevent, treat and cure more symptoms and diseases than ever before. The developments in medical practice and drug development have significantly contributed to the increase in life expectancy that is seen today [ 1].

With longer life expectancy and higher multimorbidity, the risk of polypharmacy increases. Polypharmacy, most commonly defined as the use of five or more medications at the same time, increases the risk of interactions or side effects from drug therapy [ 2, 3]. Adverse drug reactions (ADR) from interactions or side effects can be misinterpreted as new symptoms or diagnoses and generate prescriptions for new medications. This negative spiral of prescribing to treat side effects or interactions is also known as the prescribing cascade and increases the risk of polypharmacy. Except for drug-drug interactions that can increase the risk of the prescribing cascade, drug-diagnose interaction or contraindication can lead to an increased risk [ 4, 5]. With use of multiple medications and the presence of multiple chronic conditions in a patient, the risk of medications that are contraindicated for one of the chronic conditions increases. Side-effects, drug-drug and drug-diagnose interactions all increase the risk of adverse drug events (ADE) [ 6]

The risk of side effects and ADR also increases with physiological age, which is related to changes that occur in the body as we age, for example, altered body fat/water ratio and decreased kidney function. As a result of these changes, the pharmacokinetic and pharmacodynamic properties of medications can be changed. The elderly population therefore has a higher risk of side effects and adverse reactions from e.g. medications that are lipophilic or have a high renal elimination compared to a younger and middle-aged population [ 1, 6]. These medications with a higher risk for side effects are commonly referred to by the term potentially inappropriate medications (PIM) for elderly. The definition of PIM for elderly varies between different quality criteria mainly because they are developed in different countries with different treatment regimens [ 7]. The two frequently used quality criteria are Beers and the Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) criteria [ 8, 9]. In Sweden, the Swedish National Board of Health and Welfare has published a Swedish version in the report; 'Quality indicators for good drug therapy in elderly'. The indicators cover a range of different quality indicators for drug treatment in elderly [ 10]. The purpose of the indicators is to facilitate the follow-up of medical treatment in an elderly population. Use of potentially inappropriate medication (PIM) in the elderly has been found to

lead to increased morbidity and mortality [ 10, 11]. From 2010 to 2014, there was a national campaign to improve care of elderly in Sweden [ 12]. Among many strategies, there was a focus on reducing use of PIM in elderly 75 years and older.

The aim of this descriptive study was to analyse the prevalence of PIM in an elderly population and in different strata of the variables age, gender, number of chronic conditions and polypharmacy and how that prevalence changed over time.

## Methods

### Setting and study populations

Blekinge is located in the southeastern corner of Sweden and is one of the smallest counties with approximately 153 000 inhabitants in 2011 and 2013. Almost all inhabitants are registered to a primary care center in Sweden. The majority of funding for primary health care comes from a specific county council tax, both public (operated by the county council) and private care centers. Both public and private primary care centers were included in the study. We included two cohorts for comparison in this registry based repeated cross-sectional study. For the cohorts, we included individuals aged 75 or older listed at a primary care center in Blekinge on the 31 of March 2011 for the first cohort and, for the second cohort, individuals listed on the 31 of December 2013.

### Data source and measurements

Data on chronic conditions, age and gender in the study were based on anonymized registry information obtained from the County Council of Blekinge from both primary- and secondary care.

Use of medications was identified from the county council's register of dispensed medicines for all inhabitants in Blekinge. Data in this register were received by the County Council from the Swedish eHealth Agency. It contains the same patient level data on prescribed medicines as the national Prescribed Drug Register at Swedish National Board of Health and Welfare, but the coverage is restricted to the residents in the county [ 13, 14].

In Sweden, prescribed medicines are prescribed for use at most three months within the high cost threshold for medicines. Therefore a three month period was used to construct a medicine list on both regularly used and as-needed medicines [ 15]. If the same drug was dispensed more than once it was still counted only once. Since the county council's register of dispensed medicines does not contain exact dose, we used Defined Daily Doses (DDD) to calculate the duration of the drug exposure. We assumed 0.9 DDDs for regularly used medicines based on calculations for regularly used medicines in an elderly population [ 15]. Medicines were classified according to the anatomical therapeutic and chemical (ATC) system [ 16]. A constructed medication list was determined for each individual in the cohorts; 31/3 2011 for cohort 1 and 31/12 2013 for cohort 2. From this constructed medication list, polypharmacy and use of PIM were identified, according to specified definitions.

We used indicator 1.1, 'Medicines that should be avoided unless there are special reasons' from the Swedish National Board of Health and Welfare report 'Quality indicators for good drug therapy in elderly' as the definition of PIM [ 10]. As the title 'Medicines that should be avoided unless there are special reasons' states, it is medicines that should be avoided in patients, 75 years and older, unless there are special reasons because of the higher risk of side effects. If prescribed, the prescriber should have a well-founded indication and the treatment should be evaluated at regular and frequent intervals. This indicator has been used in recent years in both national and local quality indicators in Sweden for evaluating the quality of drug treatment in elderly [ 10]. The following drug groups and substances are included: long acting benzodiazepines, tramadol, propiomazine and medicines with anticholinergic effect.

Multimorbidity was defined as number of chronic conditions. It was determined by using a validated assessment tool that captures chronic conditions grouped in 60 different diagnose categories [ 17]. All information about diagnoses for a two-year period prior to 31/3- 2011 (cohort 1) and 31/12- 2013 (cohort 2) were included.

## Data analyses

All variables were used as categories in the analyses. Gender was categorised as male or female and use of PIM; use or no use of PIM. Age was categorised into four groups: 75-<80, 80-<85, 85-<90 and  $\geq 90$  and number of chronic conditions was divided into five groups or strata: none, one, two to four, five to seven and eight or more, chronic conditions. For the descriptive analysis of the cohorts, use of medications were divided into three strata; no-medication, use of 1 to 4 and use of five or more. A first descriptive analysis of the two cohorts in the different strata of the variables age, gender, use of PIM, number of chronic conditions and polypharmacy was performed. The differences were analysed using chi-square test. A significance level ( $\alpha$ ) of 0.05 and 0.001 was used. Polypharmacy is known to increase the risk of ADR and therefore we wanted to analyse polypharmacy in the different strata [3]. For analysis of polypharmacy in different strata, use of medication was divided into two categories; no use to use of four medications (<5, no-polypharmacy) and use of five or more ( $\geq 5$ , polypharmacy).

We then described the cohorts from use of PIM in different strata of the variables age, gender, number of chronic conditions and polypharmacy and analysed the changes between the 2011 and 2013 cohorts. The cohorts were compared using chi-square test.

The cohorts were then described and analysed from use of polypharmacy in different strata of the variables age, gender and number of chronic conditions. The cohorts were compared using chi-square test. A significance level ( $\alpha$ ) of 0.05 (\*) and 0.001 (\*\*) were used.

Logistic regression was used to analyse how the different strata of the variables from 2011 were associated to the use of PIM 2013. Here only individuals present in both cohorts were included. We created five models; model A adjusted for use of PIM, model B adjusted for PIM and age, model C adjusted for PIM, age and gender, model D adjusted for PIM, age, gender and number of chronic conditions, model E adjusted for PIM, age, gender, number of chronic conditions and polypharmacy. A significance level ( $\alpha$ ) of 0.05 (\*) and 0.001 (\*\*) was used.

We used STATA version 14.0 (Stata Corporation, Texas, USA) for statistical analyses.

## Results

The number of individuals in the 2011 cohort was 15 361 and for 2013 it was 15 945 individuals. Of these, 11 973 (78%) individuals were present in both cohorts. The mean age in both cohorts was 82 years. However, the 2013 cohort had a higher prevalence of individuals 75 to <80 and  $\geq 90$  compared to 2011. Prevalence of PIM decreased from 10.60% to 7.04% (p-value, <0.001). The prevalence of chronic conditions increased over time. Five to seven chronic conditions increased from 20.82% to 23.66% and eight or more chronic conditions increased from 7.72% to 9.48% (p-value, <0.001).

Nonusers of medications decreased from 20.82% to 19.19%, the use of 1-4 medications increased from 46.57% to 47.39% and the prevalence of polypharmacy from 32.62% to 33.41% (p-value <0.001) (Table 1).

Use of PIM decreased in all strata of the variables. Among patients with chronic conditions, the greatest decrease was seen in two to four chronic conditions from 4.28% to 2.75% (p-value, <0.001) (Table 2). Use of PIM decreased among patients with no-polypharmacy from 3.24% to 2.13% (p-value <0.001) and polypharmacy from 7.36% to 4.91% (p-value <0.001).

When analysing changes in prevalence of polypharmacy vs no-polypharmacy, the prevalence of polypharmacy increased in patients aged 80- <85 years from 10.27% to 10.50 % (p-value <0.05) and males from 12.34% to 13.47% (p-value <0.05) (table 3). In patients with one chronic condition, the prevalence decreased from 2.68 to 1.99 (p-value <0.05).

In the univariate analyses, PIM, women, number of chronic conditions and polypharmacy had an increased OR for having PIM 2013. The odds ratio for having PIM 2013 were increased with each strata of number of chronic conditions from OR 1.37 (CI 95% 1.02-1.85, p-value <0.05) for one chronic condition to OR 3.09 (CI 95% 2.24-4.25, p-value <0.001) for eight or more chronic conditions. Polypharmacy increased the odds ratio of having PIM 2013 with 2.63 (CI 95% 2.29-3.02, p-value <0.001) (Table 4).

In the full model those having PIM 2011 had the highest odds of having PIM 2013 (OR 15.10 (CI 95% 12.91-17.91, p-value <0.001)) (table 5). The number of chronic conditions was the only other variable that had significantly increased odds of having PIM 2013 in the full model. From two to four chronic conditions (OR 1.36 (CI 95% 1.03-1.78) to eight and more (OR 1.80 CI 95% 1.25-2.58) the OR of having PIM 2013 increased slightly in each stratum of chronic conditions. Polypharmacy (OR 1.18 CI 95% 0.99-1.40) did, however, not increase the odds of having PIM compared to no-polypharmacy in the full model.

Model A adjusted for use of PIM; Model B adjusted for PIM and age; Model C adjusted for PIM, age and gender; Model D adjusted for PIM, age, gender and number of chronic conditions; Model E adjusted for PIM, age, gender, number of chronic conditions and polypharmacy.

## Discussion

Use of PIM decreased in all the variables, age, gender, number of chronic conditions and polypharmacy, but the decrease was more evident in women, patients with polypharmacy and patients with two to four chronic conditions.

The positive trend of the reduced prevalence of PIM users found in this study corresponds with results from other reports in Sweden during the same time period [ 18-20]. In 2005 the prevalence of PIM was found to be 17% in a Swedish elderly population and a national comparison showed that use of PIM had decreased by 44% between 2005 to 2014 [ 21, 22]. Use of PIM is associated with increased risk for ADRs and hospitalisation [ 23, 24]. Therefore, quality indicators that aim to decrease the use of PIM can lead to an improvement of quality in drug treatment in elderly.

In our study, the prevalence of multimorbidity increased but the prevalence of polypharmacy stayed relatively stable. That polypharmacy stabilises while the number of chronic conditions increases is an interesting finding. One could think that if multimorbidity is increasing that polypharmacy would hence follow. However, the use of medication did increase; just not polypharmacy in comparison with the rest of the population.

As a result of medical developments in recent decades, more morbidities are treatable which has led to increased use of number of medications [ 1]. Number of drugs, as polypharmacy, are frequently used and also found to be an independent risk factor for ADRs while very few studies include a morbidity measurement when evaluating quality of drug treatment [ 25, 26]. Polypharmacy increases the risk of drug-drug interaction considerably [ 4]. Use of medication has been found to increase with age even after adjustment of level of multimorbidity [ 27]. One could argue that the severity of the morbidity is increasing with age and therefore the number of medications increases. Nonetheless, polypharmacy is not wrong, per se, as long as the complete medication list is reviewed, and the risk benefit ratio is considered for the individual patient; this is called appropriate polypharmacy [ 1, 28]. When evaluating quality of drug treatment in elderly and the risk of ADE, it is sometimes difficult to include and to evaluate contraindications for drug use, drug-diagnose interactions that lead to ADEs. This increases the risk of underestimating the risk of ADEs when evaluating risk of drug use in studies.

Our result shows that even if the use of PIM decreases, the prevalence of polypharmacy is stable while the number of chronic conditions increases. The most common drug classes in patients 75 years and older with polypharmacy are not PIM (according to our definition) but cardiovascular drugs (including antithrombotic agents), analgesics and psychotropic drugs [ 29]. These are also the most commonly used drugs in drug-related events such as bleeding or bruising, which are associated with antithrombotic agents and dizziness or unsteadiness due to psychotropic medicines [ 6]. Different methods have been tested to improve drug treatment in elderly. Implementing the STOPP criteria in a hospital setting reduced the number of ADR in a study from Cork University Hospital [ 30]. The STOPP criteria are wider in its definition for PIM than in this study. However, it still demonstrates that improvement of quality of care can be achieved through implementing different systematic methods for optimisation of drug treatment in elderly. There are several studies that show that using a systematic method, such as medication reviews, in multi professional teams reduces the use of PIM and medication cost. It is a method developed not to focus on specific risk medication but a systematic approach to optimise a patient's medical treatment as a whole; diagnoses, medicines and patient's physical conditions, e.g. kidney function [ 31-33].

## Strengths and Limitations

Our definition from the Swedish National Board of Health and Welfare is stricter in its definition and includes fewer drugs and drug classes than other definitions [ 7, 10]. For example, we do not include nonsteroidal anti-inflammatory drug (NSAID) or cardiovascular drugs except for disopyramide. Our definition of PIM is commonly used in Sweden as an indicator for quality of drug treatment in elderly, both nationally and by county councils, and is therefore relevant in this setting. This means that our results cannot be directly translated to other settings where the definition of PIM is broader.

The information of medicines in the study was register data from the county council's register that includes prescribed and pharmacy dispensed medicines for all inhabitants in Blekinge. We were not able to assess use of illegal drugs or over the counter drugs in this study. Data from the Medical Products Agency indicates that 11% of the Swedish population bought prescription drugs from non-approved pharmacies during 2011 [ 34]. By constructing a medicine list on collected prescribed drugs from the index date of hospitalisation and three months back for each risk set, it allowed us to determine, as closely as possible, as to what the patient was using. On the other hand, there is a possibility that we are missing medications used as needed because they are dispensed more rarely than every three months. We were also unable to take compliance into consideration when determining use of PIM.

Multimorbidity in the study population was measured as the number of chronic conditions and is dependent on the quality of registration of diagnoses [ 17]. The recording of diagnoses in this study has not been validated. However, we used registered diagnoses from a two-year period from both primary- and secondary care to get as close to total coverage as possible. Another Swedish study has found that 75% of the total population in Blekinge county had at least one diagnosis registered during a three year period in primary care [ 35]. Other multimorbidity estimates are constructed by giving different diagnoses a weight to how much the diagnosis contributed to need of care or cost [ 36]. In our definition of multi morbidity, all chronic conditions contribute equally to the morbidity estimate and is an expression of the complexity of a patient's need of care.

Blekinge County is a small county in Sweden, both in terms of population and area, and has a relatively simple organisation of health care service, which makes it easy to include data from primary care centers, both public and private, and from secondary care. Our results are applicable to elderly populations in similar settings.

## Conclusion

Our results show that it is possible to decrease the use of PIM in elderly and thereby to improve quality of drug use. The results also show that the complexity of elderly patient's medical care is increasing. The elderly population is growing together with the number of chronic conditions. However, while the use of medications in the elderly population increased the prevalence of polypharmacy remained stable.

With clear and simple quality indicators it is possible to improve quality of drug treatment in elderly. The challenge is to create indicators that measure quality of drug treatment in a population that has clinical value in an individual patient. More focus and effort needs to be directed to methods for optimisation of drug treatment in the individual. Quality indicators for evaluating drug treatment in a population need to continue to be developed. Future studies need to focus on methods of optimising and evaluating the complexity of drug treatment including the context of multimorbidity and polypharmacy.

## Abbreviations

PIM: Potentially inappropriate medications; OR: Odds ratio ADR: Adverse drug reaction ADE: Adverse drug events

## Declarations

## Ethics approval and consent to participate

This study was approved by the Regional Ethical Review Board in Lund (Dnr 2015/712). Due to the requirement of anonymized data, each individual could not be asked for consent to participate; active refusal of participation was instead applied. This was done by publishing information about the planned study in the Swedish local newspapers "Sydöstran" and "Blekinge Läns Tidning". The advertisement presented the study and contained information on how to contact the data extractor in Blekinge county council by phone, email or mail in order to opt out of the study. The data extractor was then responsible for that those who opted out were excluded before any data were delivered to the research manager, Kristine Thorell.

## Consent for publication

Not applicable

## Availability of data and material

The datasets generated and/or analysed during the current study are not publicly available due to individual privacy being compromised.

## Competing interests

The authors declare that they have no competing interests

## Funding

This work was funded by Blekinge county council's research council.

## Authors' contributions

In accordance with the Vancouver Protocol, KT, AH, PM and JF all have contributed to the design of this study. KT, AH and JF researched data and conducted the statistics. KT, AH and PM wrote the manuscript.

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## Tables

Table 1. Descriptive analysis of the two cohorts from 2011 and 2013

Variables		2011 (n)	%	2013 (n)	%	p-value
Total		15 361		15945		
Age	<b>75- &lt;80</b>	6027	39.24	6472	40.59	
	<b>80- &lt;85</b>	4751	30.93	4733	29.68	
	<b>85- &lt;90</b>	3029	19.72	3021	18.95	
	<b>≥90</b>	1554	10.12	1719	10.78	<0.05
Gender	<b>Women</b>	8907	57.98	9167	57.49	
	<b>Man</b>	6454	42.02	6778	42.51	ns
Use of PIM	<b>No</b>	13733	89.40	14823	92.96	
	<b>Yes</b>	1628	10.60	1122	7.04	<0.001
Number of chronic conditions	<b>0</b>	2117	13.78	1762	11.05	
	<b>1</b>	2342	15.25	2076	13.02	
	<b>2-4</b>	6559	42.70	6822	42.78	
	<b>5-7</b>	3157	20.55	3773	23.66	
	<b>≥8</b>	1186	7.72	1512	9.48	<0.001
	<b>No-medication</b>	3198	20.82	3060	19.19	
Polypharmacy	<b>1-4</b>	7153	46.57	7557	47.39	
	<b>≥5</b>	5010	32.62	5328	33.41	<0.001

Table 2 Use of potentially inappropriate medication in 2011 and 2013

Variables	Categories	Use of PIM 2011		Use of PIM 2013		p-value
		No (%)	Yes (%)	No (%)	Yes %	
Age	<b>75- &lt;80</b>	5442 (35.43)	585 (3.81)	6049 (37.94)	423 (2.65)	<0.001
	<b>80- &lt;85</b>	4278 (27.85)	473 (3.08)	4383 (27.49)	350 (2.20)	<0.001
	<b>85- &lt;90</b>	2665 (17.35)	364 (2.37)	2815 (17.65)	206 (1.29)	<0.001
	<b>≥90</b>	1348 (8.78)	206 (1.34)	1576 (9.88)	143 (0.90)	<0.001
Gender	<b>Women</b>	7815 (50.88)	1092 (7.11)	8427 (52.85)	740 (4.64)	<0.001
	<b>Man</b>	5918 (38.53)	536 (3.49)	6396 (40.11)	382 (2.40)	<0.001
Number of chronic conditions	<b>0</b>	1970 (12.82)	147 (0.96)	1689 (10.59)	73 (0.46)	<0.001
	<b>1</b>	2144 (13.96)	198 (1.29)	1982 (12.43)	94 (0.59)	<0.001
	<b>2-4</b>	5901 (38.42)	658 (4.28)	6384 (40.04)	438 (2.75)	<0.001
	<b>5-7</b>	2728 (17.76)	429 (2.79)	3433 (21.53)	340 (2.13)	<0.001
	<b>≥8</b>	990 (6.44)	196 (1.28)	1335 (8.37)	177 (1.11)	<0.001
Polypharmacy	<b>&lt;5</b>	9854 (64.15)	497 (3.24)	10278 (64.46)	339 (2.13)	<0.001
	<b>≥5</b>	3879 (25.25)	1131 (7.36)	4545 (28.50)	783 (4.91)	<0.001

Table 3. Use of polypharmacy in 2011 and 2013.

Variables	Categories	Number of medications 2011		Number of medications 2013		p-value
		<5 (%)	≥5 (%)	<5 (%)	≥5 (%)	
Age	<b>75- &lt;80</b>	4303 (28.01)	1724 (11.22)	4662 (29.24)	1810 (11.35)	ns
	<b>80- &lt;85</b>	3173 (20.66)	1578 (10.27)	3058 (19.18)	1675 (10.50)	<0.05
	<b>85- &lt;90</b>	1925 (12.53)	1104 (7.19)	1850 (11.60)	1171 (7.34)	ns
	<b>≥90</b>	950 (6.18)	604 (3.93)	1047 (6.57)	672 (4.21)	ns
Gender	<b>Women</b>	5793 (37.71)	3114 (20.27)	5987 (37.55)	3180 (19.94)	ns
	<b>Man</b>	4558 (29.67)	1896 (12.34)	4630 (29.04)	2148 (13.47)	<0.05
Number of chronic conditions	<b>0</b>	1846 (12.02)	271 (1.76)	1554 (9.75)	208 (1.30)	ns
	<b>1</b>	1931 (12.57)	411 (2.68)	1759 (11.03)	317 (1.99)	<0.05
	<b>2-4</b>	4571 (29.76)	1988 (12.94)	4849 (30.41)	1973 (12.37)	ns
	<b>5-7</b>	1592 (10.36)	1565 (10.19)	1941 (12.17)	1832 (11.49)	ns
	<b>≥8</b>	411 (2.68)	775 (5.05)	514 (3.22)	998 (6.26)	ns

Table 4. Univariate analysis of the odds ratio to have potentially inappropriate medication 2013 in patients that were present in both cohorts (11973 individuals).

Variables	Categories	Univariate analyses
		OR CI 95%
PIM 2011	<b>No</b>	1
	<b>Yes</b>	16.81 (14.43-19.58)**
Gender 2011	<b>Women</b>	1
	<b>Man</b>	0.74 (0.64-0.85)**
Age 2011	<b>75- &lt;80</b>	1
	<b>80- &lt;85</b>	1.01 (0.86-1.19)
	<b>85- &lt;90</b>	0.96 (0.79-1.18)
	<b>≥90</b>	1.34 (1.03-1.75)*
Number of chronic conditions 2011	<b>0</b>	1
	<b>1</b>	1.37 (1.02-1.85)*
	<b>2-4</b>	1.67 (1.29-2.15)**
	<b>5-7</b>	2.20 (1.68-2.89)**
	<b>≥8</b>	3.09 (2.24-4.25)**
Polypharmacy 2011	<b>&lt;5</b>	1
	<b>≥5</b>	2.63 (2.29-3.02)**

\* p-value<0.05, \*\* p-value<0.001

Tabell 5. The odds ratio to have potentially inappropriate medication 2013 in patients that were present in both cohorts (11973 individuals).

Variables	Categories	Model A	Model B	Model C	Model D	Model E
		OR (CI 95%)				
PIM 2011	No	1	1	1	1	1
	Yes	16.81 (14.43-19.58)**	16.64 (14.28-19.40)**	16.70 (14.31-19.47)**	16.01 (13.71-18.70)**	15.10 (12.91-17.91)**
Gender 2011	Women		1	1	1	1
	Man		0.91 (0.78-1.06)	0.90 (0.77-1.06)	0.90 (0.77-1.06)	0.91 (0.77-1.07)
Age 2011	75- <80			1	1	1
	80- <85			0.97 (0.82-1.16)	0.96 (0.81-1.15)	0.96 (0.80-1.15)
	85- <90			0.84 (0.68-1.05)	0.83 (0.66-1.03)	0.82 (0.66-1.03)
	≥90			1.01 (0.75-1.36)	1.01 (0.75-1.36)	1.00 (0.74-1.35)
Number of chronic conditions 2011	0				1	1
	1				1.24 (0.90-1.70)	1.23 (0.89-1.69)
	2-4				1.40 (1.07-1.83)*	1.36 (1.03-1.78)*
	5-7				1.52 (1.13-2.04)*	1.43 (1.06-1.93)*
	≥8				1.96 (1.38-2.78)**	1.80 (1.25-2.58)*
Polypharmacy 2011	<5					1
	≥5					1.18 (0.99-1.40)

\* p-value<0.05, \*\* p-value<0.001

Model A adjusted for use of PIM; Model B adjusted for PIM and age; Model C adjusted for PIM, age and gender; Model D adjusted for PIM, age, gender and number of chronic conditions; Model E adjusted for PIM, age, gender, number of chronic conditions and polypharmacy.