Use of potentially inappropriate medication and polypharmacy in older adults: 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 older adult 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 older adult 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. Individuals aged 75 or older listed at a primary care centre in Blekinge on the 31st March 2011 (cohort 1) or on the 31st 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 0.000) between 2011 and 2013, while prevalence of five to seven chronic conditions increased from 20.55% to 23.66% (p-value 0.000). Use of PIM decreased in all strata of the variables age, gender number of chronic conditions and polypharmacy. Except for age 80 to ≤ 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 older adults (≥75 years), are drug therapies. The goal of drug therapy is to prevent, treat or cure disease or symptoms of disease. For older adults with multimorbidity and polypharmacy, the effect may, however, be to the contrary. Advances in drug development in recent decades have resulted 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 and adverse drug events (ADE) from drug therapy [2, 3]. Adverse drug events increases the risk of hospitalisations [4]. Use of medication increases with age even after adjustment of level of multimorbidity and polypharmacy increases the risk of drug-drug interaction considerably [5, 6]. One could argue that the severity of the morbidity is increasing with age and therefore the number of medications increases. However, polypharmacy has been found to be an independent risk factor for ADEs while very few studies include a morbidity measurement when evaluating quality of drug treatment [7, 8]. 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, 9]. Adverse drug events from interactions or contraindications 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. The risk of prescribing cascade increases with both interactions (drug-drug) and contraindications (drug-disease) [5, 10]. 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. Interaction and contraindications can both also increase the risk of ADE [11]

The risk of ADE 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 and lead to harmful effects from the medical treatment. The population of older adults therefore has a higher risk of ADE for example from medications that are lipophilic or have a high renal elimination compared to a younger and middle-aged population [1, 11]. These medications with a higher risk for ADEs are commonly referred to by the term potentially inappropriate medications (PIM) for older adults. Use of PIM in older adults has been found to lead to increased morbidity and mortality [12, 13]. The definition of PIM for older adults varies between different quality criteria mainly because they are developed in different countries with different treatment regimens [14]. The two frequently used quality criteria are Beers and the Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) criteria [15, 16]. 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 the elderly'. The indicators cover a range of different quality indicators for drug treatment in older adults.

There are diagnose related indicators and medication related indicators [12]. The purpose of the indicators is to facilitate the follow-up of medical treatment in a population of older adults and to evaluate the quality of the treatment. The first medication indicator in the report, 'Medicines that should be avoided unless there are special reasons', define medications that should be avoided in patients, 75 years and older. This is unless there are special reasons because of the higher risk of ADEs. They are called PIM in Sweden and include long acting benzodiazepines, tramadol, propiomazine and medicines with anticholinergic effect [12].

From 2010 to 2014, there was a national information campaign to improve care of older adults in Sweden [17]. Among many strategies, there was a focus on increasing the knowledge about the risk with use of PIM in older adults 75 years and older. The information campaign´s aim was to raise awareness around the risk associated with use of PIM older adults. The campaign was evaluated by measuring use of PIM by defined daily doses (DDD) in aggregated data [17]. In this study, set up as a natural experiment, the effects of information campaign were analysed in individual based data. The aim was to analyse the prevalence of PIM in an older adult population in different strata of variables of importance for medications use. Which are age, gender, number of chronic conditions and number of medications [6, 18]. The study also analysed how that prevalence changed over time during the information campaign.

Methods

Setting and study populations

Blekinge is located in the south eastern 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 centre 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 centres. Both public and private primary care centres 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 centre in Blekinge on the 31st March 2011 for the first cohort and, for the second cohort, individuals listed on the 31st December 2013. The information campaign to improve care of the population of older adults was active between 2010 and 2014. However due to possibility of access to data of medication data the cohorts were chosen for a slightly shorter period. This is because the 31st March 2011 was the earliest date that we had access to a three-month period of medication data within the local register described below. And due to changes in how medication data was encrypted in 2014 the 31st December 2013 was chosen to ensure quality of data for the second cohort.

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 was 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 [19, 20].

In Sweden, prescribed medicines are prescribed for use at most three months within the high cost threshold for medicines [21]. Therefore a three month period was used to construct a medicine list on both regularly used and as-needed medicines [22]. 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 older adult population [22, 23]. Medicines were classified according to the anatomical therapeutic and chemical (ATC) system [24]. 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 [12]. 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 definition of PIM was used in the national information campaign to follow-up the effects of the campaign and therefore it was used in this study also [12]. The following drug groups and substances are included in this definition of PIM: long acting benzodiazepines, tramadol, propiomazine and medicines with anticholinergic effect. The use of PIM was identified from the constructed medication list by the medications ATC-codes.

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 diagnoses categories [25]. 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 ≥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 number of medications was performed. The differences were analysed using chi-square test. A significance level (α) of 0.05 and 0.001 was used. Since polypharmacy is a known risk factor for ADEs we wanted to analyse the prevalence of polypharmacy in the different strata [3]. Therefore, number of medications was divided into two strata for the rest of the analyses; no use to use of four medications (<5, no-polypharmacy) and use of five or more (≥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 (α) of 0.05 (*) and 0.001 (**) were used.

Logistic regression was then 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. To analyse how the different strata of the variables from 2011 were associated with decreased use of PIM 2013 a logistic regression was performed. We created five models; model A adjusted for age, model B adjusted for age and gender, model C adjusted for age, gender and number of chronic conditions, model D adjusted for age, gender, number of chronic conditions and polypharmacy. A significance level (α) 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 ≥90 compared to 2011. Prevalence of PIM decreased from 10.60% to 7.04% (p-value, 0.000). The prevalence of chronic conditions increased over time. Five to seven chronic conditions increased from 20.55% to 23.66% and eight or more chronic conditions increased from 7.72% to 9.48% (p-value, 0.000).

Non users 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 0.000) (Table 1).

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

Variables		2011 (n)	%	2013 (n)	%	p-value
Total		15 361		15945		
Age	**75- <80**	6027	39.24	6472	40.59	
	80- <85	4751	30.93	4733	29.68	
	85- <90	3029	19.72	3021	18.95	
	≥90	1554	10.12	1719	10.78	0.004
Gender	**Women**	8907	57.98	9167	57.49	
	Man	6454	42.02	6778	42.51	0.377
Use of PIM	**No**	13733	89.40	14823	92.96	0.000
	Yes	1628	10.60	1122	7.04	0.000
Number of chronic conditions	**0**	2117	13.78	1762	11.05	
	1	2342	15.25	2076	13.02	
	2-4	6559	42.70	6822	42.78	
	5-7	3157	20.55	3773	23.66	
	≥8	1186	7.72	1512	9.48	0.000
	No-medications	3198	20.82	3060	19.19	
Polypharmacy	**1-4**	7153	46.57	7557	47.39	
	≥5	5010	32.62	5328	33.41	0.000

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, 0.000) (Table 2). Use of PIM decreased among patients with no-polypharmacy from 3.24% to 2.13% (p-value 0.000) and polypharmacy from 7.36% to 4.91% (p-value 0.000).

Table 2 Use of potentially inappropriate medication in 2011 and 2013

Variables	Categories	Use of PIM 2011		Use of PIM 2013		
		No (%)	Yes (%)	No (%)	Yes %	p-value
Age	**75- <80**	5442 (35.43)	585 (3.81)	6049 (37.94)	423 (2.65)	0.000
	80- <85	4278 (27.85)	473 (3.08)	4383 (27.49)	350 (2.20)	0.000
	85- <90	2665 (17.35)	364 (2.37)	2815 (17.65)	206 (1.29)	0.000
	≥90	1348 (8.78)	206 (1.34)	1576 (9.88)	143 (0.90)	0.000
Gender	**Women**	7815 (50.88)	1092 (7.11)	8427 (52.85)	740 (4.64)	0.000
	Man	5918 (38.53)	536 (3.49)	6396 (40.11)	382 (2.40)	0.000
Number of chronic conditions	**0**	1970 (12.82)	147 (0.96)	1689 (10.59)	73 (0.46)	0.000
	1	2144 (13.96)	198 (1.29)	1982 (12.43)	94 (0.59)	0.000
	2-4	5901 (38.42)	658 (4.28)	6384 (40.04)	438 (2.75)	0.000
	5-7	2728 (17.76)	429 (2.79)	3433 (21.53)	340 (2.13)	0.000
	≥8	990 (6.44)	196 (1.28)	1335 (8.37)	177 (1.11)	0.000
Polypharmacy	**<5**	9854 (64.15)	497 (3.24)	10278 (64.46)	339 (2.13)	0.000
	≥5	3879 (25.25)	1131 (7.36)	4545 (28.50)	783 (4.91)	0.000

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 0.03) and males from 12.34% to 13.47% (p-value 0.004) (table 3). In patients with one chronic condition, the prevalence decreased from 2.68 to 1.99 (p-value 0.04).

Table 3. Use of polypharmacy in 2011 and 2013.

Variables	Categories	Number of medications 2011		Number of medications 2013		
		<5 (%)	**≥5 (%)**	**<5 (%)**	**≥5 (%)**	p-value
Age	**75- <80**	4303 (28.01)	1724 (11.22)	4662 (29.24)	1810 (11.35)	0.429
	80- <85	3173 (20.66)	1578 (10.27)	3058 (19.18)	1675 (10.50)	0.026*
	85- <90	1925 (12.53)	1104 (7.19)	1850 (11.60)	1171 (7.34)	0.063
	≥90	950 (6.18)	604 (3.93)	1047 (6.57)	672 (4.21)	0.895
Gender	**Women**	5793 (37.71)	3114 (20.27)	5987 (37.55)	3180 (19.94)	0.702
	Man	4558 (29.67)	1896 (12.34)	4630 (29.04)	2148 (13.47)	0.004*
Number of chronic conditions	**0**	1846 (12.02)	271 (1.76)	1554 (9.75)	208 (1.30)	0.348
	1	1931 (12.57)	411 (2.68)	1759 (11.03)	317 (1.99)	0.042*
	2-4	4571 (29.76)	1988 (12.94)	4849 (30.41)	1973 (12.37)	0.079
	5-7	1592 (10.36)	1565 (10.19)	1941 (12.17)	1832 (11.49)	0.399
	≥8	411 (2.68)	775 (5.05)	514 (3.22)	998 (6.26)	0.720

Significant 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 (Cl 95% 1.02-1.85, p-value <0.05) for one chronic condition to OR 3.09 (Cl 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 (Cl 95% 2.29-3.02, p-value <0.001) (Table 4).

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

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

In the full model those having PIM 2011 had the highest odds of having PIM 2013 (OR 15.10 (Cl 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 (Cl 95% 1.03-1.78) to eight and more (OR 1.80 Cl 95% 1.25-2.58) the OR of having PIM 2013 increased slightly in each stratum of chronic conditions. Polypharmacy (OR 1.18 Cl 95% 0.99-1.40) did, however, not increase the odds of having PIM compared to no-polypharmacy in the full model. When analysing the association of the variables from 2011 individuals with polypharmacy had the highest probability of deprescribing PIM (OR 4.64 (3.96-5.44) in model D. Number of chronic conditions associations with deprescribing PIM where highest in individuals with 5 to 7 (OR 2.82 (2.10-3.80) and 8 or more (OR 2.78 (1.94-3.99) number of chronic conditions in model C. However, the effect was reduced in the full model (OR 1.42 Cl95% 1.04-1.94) (model E) while polypharmacy still had the highest probability to decreased use of PIM (OR 4.40 (3.72-5.22) (table 6).

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

ıles	Categories	Model A	Model B	Model C	Model D	Model E
		OR (Cl 95%)	OR (Cl 95%)	OR (Cl 95%)	OR (Cl 95%)	OR (Cl 95%)
011	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)**
ɐr 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)
011	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)
er of chronic	0				1	1
ıions 2011	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)*
ıarmacy 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.

Table 6. Odds ratio to have deprescribed PIM 2011- 2013 in the strata of the variables

Variables	Categories	Model A	Model B	Model C	Model D	Model E
		OR (Cl 95%)	OR (Cl 95%)	OR (Cl 95%)	OR (Cl 95%)	OR (Cl 95%)
Gender 2011	Women	1	1	1	1	1
	Man	0.64 (0.55-0.75)**	0.66 (0.56-0.78)**	0.66 (0.56-0.77)**	0.71 (0.61-0.84)	0.71 (0.60-0.83)**
Age 2011	75- <80		1	1	1	1
	80- <85		1.07 (0.89-1.28)	1.03 (0.86-1.23)	1.00 (0.83-1.19)	0.99 (0.83-1.19)
	85- <90		1.26 (1.03-1.55)*	1.19 (0.97-1.47)	1.14 (0.93-1.41)	1.16 (0.87-1.56)
	≥90		1.62 (1.23-2.14)**	1.57 (1.19-2.08)*	1.39 (1.05-1.85)*	1.39 (1.05-1.85)*
Number of chronic conditions 2011	0			1		1
	1			1.29 (0.92-1.81)		1.14 (0.81-1.62)
	2-4			1.68 (1.26-2.24)*		1.16 (0.87-1.56)
	5-7			2.82 (2.10-3.80)*		1.42 (1.04-1.94)*
	≥8			2.78 (1.94-3.99)**		1.11 (0.76-1.62)
Polypharmacy 2011	<5				1	1
	≥5				4.64 (3.96-5.44)**	4.40 (3.72-5.22)**

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

Model A adjusted for age; Model B adjusted for age; and gender Model C adjusted for age and gender and number of chronic conditions; Model D adjusted for age, gender and polypharmacy; Model E adjusted for 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 group that had the highest probability to deprescribe PIM during the study period was patients with polypharmacy and high number of 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 [26-28]. To our knowledge this study is the first where the prevalence of PIM has been analysed in relation to of number of chronic conditions and number of medications and the change over time in individual data.

In 2005 the prevalence of PIM was found to be 17% in a Swedish older adult population and a national comparison showed that use of PIM had decreased by 44% between 2005 to 2014 [29, 30]. Use of PIM and polypharmacy is associated with increased risk for ADEs and hospitalisation [4, 31].

In our study, the prevalence of polypharmacy stayed relatively stable, but number of chronic conditions increased. The fact that polypharmacy did not increased significantly while the number of chronic conditions increased, is an interesting finding. One could think that if multi-morbidity 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.

The decrease in PIM in this study was not parallel to a decrease in polypharmacy. 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 [32]. These are also the most commonly used drugs in adverse drug events, such as

bleeding or bruising, which are associated with antithrombotic agents, or dizziness and unsteadiness due to psychotropic medicines [11].

It can be stated that based on this single quality indicator, the use of PIM has improved and thereby the quality of medication treatment in older adults. However, it does not affect the total quality of medications use. The information campaign was a success with regard to that it reduced the use of PIM, especially in patients with high number of chronic conditions and polypharmacy. However, it did not reduce polypharmacy, which is also an important factor for quality in medication use in older adults [18, 33-35].

The results in this study show that the use of a clear and simple quality indicator as decreased use of PIM, can improve the quality of medication treatment in older adults. However, to affect other factors of importance for the quality of medication treatment a combination of quality indicators may be better to use. For example, the STOPP criteria, a collection of quality indicators, reduced the number of ADEs when implemented in a hospital setting in a study from Cork University Hospital [36]. The complete collection of quality criteria in "Quality indicators for good drug therapy in elderly" from Swedish National Board of Health and Welfare can be used in the same way [12]. The effect is more complex to evaluate on a population level, but the clinical effect in the individual is greater.

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 [12, 14]. 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 older adults, 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 [37]. By constructing a medicine list on collected prescribed drugs from the inclusion date for the cohorts and three months back, 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 and therefore underestimating the use of some medications. We were also unable to take compliance into consideration when determining use of PIM. However this method is validated and the time period of three moths have been found to be the most optimal [23]. And considering the Swedish system with high cost threshold there are limited risk of hording medications [21].

Multimorbidity in the study population was measured as the number of chronic conditions and is dependent on the quality of registration of diagnoses [25]. 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 [38]. Other multimorbidity estimates are constructed by giving different diagnoses a weight as to how much the diagnosis contributed to need of care or cost [39]. 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 centres, both public and private, and from secondary care. Our results are applicable to populations with older adults in similar settings.

Conclusion

Our results show that the use of PIM in older adults decreased in all strata of number of chronic conditions and in patients with polypharmacy. The results also show that the complexity of older adult patient's medical care is increasing. The older adult

population is growing together with the number of chronic conditions. However, while the use of medications in the older adult population increased the prevalence of polypharmacy remained stable.

With clear and simple quality indicators it is possible to improve quality of drug treatment in the older adult population. The challenge is to create and evaluate indicators that measure quality of drug treatment in a population that has clinical value in an individual patient. More focus and effort need 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 and implemented. Future studies need to focus on methods for optimising and evaluating the quality of drug treatment when including multi-morbidity and polypharmacy in the context.

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 those that opted out, and they were excluded before any data was delivered to the research manager, Kristine Thorell.

Consent to publish

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. Due to ethical restrictions and the sensitive nature of the data, data is only available after ethical approval according to Swedish regulation: http://www.epn.se.

Competing interests

The authors declare that they have no competing interests

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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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References

1. Shi S, Morike K, Klotz U: **The clinical implications of ageing for rational drug therapy**. *Eur J Clin Pharmacol* 2008, **64**(2):183-199.
2. van den Akker M, Vaes B, Goderis G, Van Pottelbergh G, De Burghgraeve T, Henrard S: **Trends in multimorbidity and polypharmacy in the Flemish-Belgian population between 2000 and 2015**. *PLoS One* 2019, **14**(2):e0212046.
3. Viktil KK, Blix HS, Moger TA, Reikvam A: **Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems**. *Brit J Clin Pharmaco* 2007, **63**(2):187-195.
4. Varga S, Alcusky M, Keith SW, Hegarty SE, Del Canale S, Lombardi M, Maio V: **Hospitalization rates during potentially inappropriate medication use in a large population-based cohort of older adults**. *Br J Clin Pharmacol* 2017, **83**(11):2572-2580.
5. Brath H, Mehta N, Savage RD, Gill SS, Wu W, Bronskill SE, Zhu L, Gurwitz JH, Rochon PA: **What Is Known About Preventing, Detecting, and Reversing Prescribing Cascades: A Scoping Review**. *J Am Geriatr Soc* 2018, **66**(11):2079-2085.
6. Thorell K, Skoog J, Zielinski A, Borgquist L, Halling A: **Licit prescription drug use in a Swedish population according to age, gender and socioeconomic status after adjusting for level of multi-morbidity**. *BMC public health* 2012, **12**:575.
7. Saedder EA, Lisby M, Nielsen LP, Bonnerup DK, Brock B: **Number of drugs most frequently found to be independent risk factors for serious adverse reactions: a systematic literature review**. *Br J Clin Pharmacol* 2015, **80**(4):808-817.
8. Wastesson JW, Morin L, Tan ECK, Johnell K: **An update on the clinical consequences of polypharmacy in older adults: a narrative review**. *Expert opinion on drug safety* 2018, **17**(12):1185-1196.
9. Johnell K: **The controversies surrounding polypharmacy in old age - where are we?** *Expert review of clinical pharmacology* 2018, **11**(9):825-827.
10. Rochon PA, Gurwitz JH: **Optimising drug treatment for elderly people: the prescribing cascade**. *BMJ (Clinical research ed)* 1997, **315**(7115):1096-1099.
11. Davies EA, O'Mahony MS: **Adverse drug reactions in special populations - the elderly**. *Brit J Clin Pharmaco* 2015, **80**(4):796-807.
12. Swedish National Board of Health and Welfare: **Indikatorer för god läkemedelsterapi hos äldre**. In.; 2010: 33.
13. Galli TB, Reis WC, Andrzejevski VM: **Potentially inappropriate prescribing andthe risk of adverse drug reactions in critically ill older adults**. *Pharm Pract (Granada)* 2016, **14**(4):818.
14. Morin L, Fastbom J, Laroche ML, Johnell K: **Potentially inappropriate drug use in older people: a nationwide comparison of different explicit criteria for population-based estimates**. *Br J Clin Pharmacol* 2015, **80**(2):315-324.
15. Hamilton H, Gallagher P, Ryan C, Byrne S, O'Mahony D: **Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients**. *Arch Intern Med* 2011, **171**(11):1013-1019.
16. Campanelli CM: **American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults**. *J Am Geriatr Soc* 2012, **60**(4):616-631.
17. **'Bättre liv för sjuka äldre'** [https://skl.se/integrationsocialomsorg/socialomsorg/aldre/sammanhallenvardomsorgaldre/battrelivforsjukaaldre.1689.html]
18. Belfrage B, Koldestam A, Sjoberg C, Wallerstedt SM: **Number of drugs in the medication list as an indicator of prescribing quality: a validation study of polypharmacy indicators in older hip fracture patients**. *Eur J Clin Pharmacol* 2015, **71**(3):363-368.
19. Wettermark B, Hammar N, Fored CM, Leimanis A, Otterblad Olausson P, Bergman U, Persson I, Sundstrom A, Westerholm B, Rosen M: **The new Swedish Prescribed Drug Register--opportunities for pharmacoepidemiological research and experience from the first six months**. *Pharmacoepidemiol Drug Saf* 2007, **16**(7):726-735.
20. Frisk P, Sporrong SK, Ljunggren G, Wettermark B, von Euler M: **Utilisation of prescription and over-the-counter triptans: a cross-sectional study in Stockholm, Sweden**. *Eur J Clin Pharmacol* 2016, **72**(6):747-754.
21. **What is the high cost threshold?** [http://www.tlv.se/in-english-old/medicines-new/the-swedish-high-cost-threshold/]
22. Johnell K, Fastbom J: **The use of benzodiazpines and related drugs amongst older people in Sweden: associated factors and concomitant use of other psychotropics**. *Int J Geriatr Psychiatry* 2009, **24**(7):731-738.
23. Lau HS, de Boer A, Beuning KS, Porsius A: **Validation of pharmacy records in drug exposure assessment**. *Journal of clinical epidemiology* 1997, **50**(5):619-625.
24. **WHO collaborating Center for Drug Statistics Methodology** [https://www.whocc.no/]

25. Calderon-Larranaga A, Vetrano DL, Onder G, Gimeno-Feliu LA, Coscollar-Santaliestra C, Carfi A, Pisciotta MS, Angleman S, Melis RJF, Santoni G *et al*: **Assessing and Measuring Chronic Multimorbidity in the Older Population: A Proposal for Its Operationalization**. *J Gerontol A Biol Sci Med Sci* 2017, **72**(10):1417-1423.
26. Hovstadius B, Petersson G, Hellstrom 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**(5):379-386.
27. Swedish National Board of Health and Welfare: **'Öppna jämförelser 2014 Läkemedelsbehandlingar'**. https://www.socialstyrelsen.se/publikationer2014/2014-11-1; 2014.
28. Gustafsson M, Sandman PO, Karlsson S, Isaksson U, Schneede J, Sjolander M, Lovheim H: **Reduction in the use of potentially inappropriate drugs among old people living in geriatric care units between 2007 and 2013**. *Eur J Clin Pharmacol* 2015, **71**(4):507-515.
29. Swedish association of Local Authorities and Regions: **Open comparisons Drug Use**. In. Stockholm: Swedish National Board of Health and Welfare,; 2015.
30. Johnell K, Fastbom J, Rosen M, Leimanis A: **Inappropriate drug use in the elderly: a nationwide register-based study**. *Ann Pharmacother* 2007, **41**(7):1243-1248.
31. Endres HG, Kaufmann-Kolle P, Steeb V, Bauer E, Bottner C, Thurmann P: **Association between Potentially Inappropriate Medication (PIM) Use and Risk of Hospitalization in Older Adults: An Observational Study Based on Routine Data Comparing PIM Use with Use of PIM Alternatives**. *PloS one* 2016, **11**(2):e0146811.
32. Wastesson JW, Cedazo Minguez A, Fastbom J, Maioli S, Johnell K: **The composition of polypharmacy: A register-based study of Swedes aged 75 years and older**. *PLoS One* 2018, **13**(3):e0194892.
33. Hedna K, Hakkarainen KM, Gyllensten H, Jonsson AK, Petzold M, Hagg S: **Potentially inappropriate prescribing and adverse drug reactions in the elderly: a population-based study**. *Eur J Clin Pharmacol* 2015, **71**(12):1525-1533.
34. Kovacevic SV, Miljkovic B, Culafic M, Kovacevic M, Golubovic B, Jovanovic M, Vucicevic K, de Gier JJ: **Evaluation of drug-related problems in older polypharmacy primary care patients**. *Journal of evaluation in clinical practice* 2017, **23**(4):860-865.
35. Lai SW, Liao KF, Liao CC, Muo CH, Liu CS, Sung FC: **Polypharmacy correlates with increased risk for hip fracture in the elderly: a population-based study**. *Medicine* 2010, **89**(5):295-299.
36. O'Connor MN, O'Sullivan D, Gallagher PF, Eustace J, Byrne S, O'Mahony D: **Prevention of Hospital-Acquired Adverse Drug Reactions in Older People Using Screening Tool of Older Persons' Prescriptions and Screening Tool to Alert to Right Treatment Criteria: A Cluster Randomized Controlled Trial**. *J Am Geriatr Soc* 2016, **64**(8):1558-1566.
37. Medical Products Agency: **Läkemedelsverkets arbete för att motverka olagliga läkemedel**. In., vol. 1. www.lakemedelsverket.se; 2011.
38. Carlsson L, Strender LE, Fridh G, Nilsson GH: **Clinical categories of patients and encounter rates in primary health care - a three-year study in defined populations**. *BMC public health* 2006, **6**:35.
39. Starfield B, Weiner J, Mumford L, Steinwachs D: **Ambulatory care groups: a categorization of diagnoses for research and management**. *Health services research* 1991, **26**(1):53-74.