Interventions to improve medication use in elderly primary care patients

Lenander, Cecilia

2017

Document Version:
Publisher's PDF, also known as Version of record

Interventions to improve medication use in elderly primary care patients

CECILIA LENANDER
DEPARTMENT OF CLINICAL SCIENCES, MALMÖ | LUND UNIVERSITY 2017

Interventions to improve medication use in elderly primary care patients

Interventions to improve medication use in elderly primary care patients

Cecilia Lenander

LUND
UNIVERSITY

DOCTORAL DISSERTATION
by due permission of the Faculty of Medicine, Lund University, Sweden.
To be defended May 5th 2017 at 9.00 am.

Faculty opponent
Anders Grimsmo

Organization LUND UNIVERSITY	Document name: Interventions to improve medication use in elderly primary care patients
	Date of issue 2017-05-05
Author(s) Cecilia Lenander	Sponsoring organization

Title: Interventions to improve medication use in elderly primary care patients

Introduction: The elderly population is increasing and with age comes a higher risk for contracting diseases and receiving polypharmacy. This can lead to drug-related problems (DRP) and increased health care utilization. Several ways to overcome these problems have been tried.

Objectives: To evaluate two different interventions for improving medication use in elderly primary care patients.

Methods: The SÄKLÄK project was a multi-professional intervention in primary care consisting of self-assessment, peer review, feedback and written agreements for change. Five Swedish primary care centers participated in the intervention and five served as comparison group. The qualitative study in paper I is based on semi-structured interviews with 17 participants of the SÄKLÄK project. Qualitative content analysis was used to explore the participants' perceptions. For paper II, data were collected from the Swedish Prescribed Drug Register on six potentially inappropriate medications (PIMs) prescribed to patients 65 years or older. For paper III-IV, data were collected from medication reviews performed in Skåne according to the LIMM (Lund Integrated Medicines Management) model adopted to primary care. In paper III an analysis of common drug-related problems and suggestions to solve these was performed. In paper IV, the focus was on the use of antipsychotics including how common this use is, indications for prescriptions, and if medication reviews are a method to address possible problems in the use of antipsychotics.

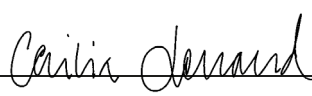
Results: The qualitative analysis in paper I yielded six categories: *multi-professional cooperation, a focus on areas of improvement, the joy of sharing knowledge, disappointment with the focus of the feedback, spend time to save time* and *impact on work*. In paper II a decrease in the prescription of PIMs was seen in both groups, intervention -22.2% and comparison -8.8%. All groups of PIMs decreased, except for antipsychotics in the comparison group. A significant decrease in mean dose/patient was seen in the intervention group after intervention, but not in the comparison group. In paper III the mean age was 87.5 years, 61% used at least 10 medications and 84% of them had a least one DRP. The most common DRP was unnecessary drug therapy (39%) and the most common result was drug withdrawal. Performing medication reviews helped decrease the proportion of patients with at least one PIM ($p<0.001$) and the use of ≥ 3 psychotropics ($p<0.001$). Paper IV showed that the medication reviews reduced the use of antipsychotics by 23%. Of the patients using antipsychotics, 43% had an approved indication while for 15% the indication was not given. Antipsychotic drug use was more common with increasing number of drugs ($p=0.001$).

Conclusions: Methods to improve the medication treatment of elderly patients are needed. Unnecessary treatment is a common drug-related problem in nursing home residents. It is not uncommon for these patients to use 10 or more medications regularly and one way to improve the situation is multi-professional medication reviews. Antipsychotic drug use without an approved indication is also common in this group, despite the risks involved, and medication reviews can correct this. Another problem for elderly patients is the lack of co-operation and information sharing between different levels of care. A method involving self-assessment, peer review, feedback and written agreements for change may promote this.

Key words Elderly, Primary health care, Multi-professional collaboration, Medication reviews, Potentially inappropriate medications, Drug-related problems, Self-assessment, Peer review, Clinical pharmacist

Classification system and/or index terms (if any)

Supplementary bibliographical information		Language English
ISSN and key title 1652-8220		ISBN 978-91-7619-434-8
Recipient's notes	Number of pages 68	Price
	Security classification	

Signature  Date 2017-03-29

Interventions to improve medication use in elderly primary care patients

Cecilia Lenander

LUND
UNIVERSITY

Cover photo private

Faculty of Medicine, Department of Clinical Sciences in Malmö
Lund University, Sweden

ISBN 978-91-7619-434-8
ISSN 1652-8220

Printed in Sweden by Media-Tryck, Lund University
Lund 2017

To Julius and Gustav

Contents

Abstract

Introduction: The elderly population is increasing and with age comes a higher risk for contracting diseases and receiving polypharmacy. This can lead to drug-related problems (DRP) and increased health care utilization. Several ways to overcome these problems have been tried.

Objectives: To evaluate two different interventions for improving medication use in elderly primary care patients.

Methods: The SÄKLÄK project was a multi-professional intervention in primary care consisting of self-assessment, peer review, feedback and written agreements for change. Five Swedish primary care centers participated in the intervention and five served as comparison group. The qualitative study in paper I is based on semi-structured interviews with 17 participants of the SÄKLÄK project. Qualitative content analysis was used to explore the participants' perceptions. For paper II, data were collected from the Swedish Prescribed Drug Register on six potentially inappropriate medications (PIMs) prescribed to patients 65 years or older. For paper III-IV, data were collected from medication reviews performed in Skåne according to the LIMM (Lund Integrated Medicines Management) model adopted to primary care. In paper III an analysis of common drug-related problems and suggestions to solve these was performed. In paper IV, the focus was on the use of antipsychotics including how common this use is, indications for prescriptions, and if medication reviews are a method to address possible problems in the use of antipsychotics.

Results: The qualitative analysis in paper I yielded six categories: *multi-professional cooperation, a focus on areas of improvement, the joy of sharing knowledge, disappointment with the focus of the feedback, spend time to save time* and *impact on work.* In paper II a decrease in the prescription of PIMs was seen in both groups, intervention -22.2% and comparison -8.8%. All groups of PIMs decreased, except for antipsychotics in the comparison group. A significant decrease in mean dose/patient was seen in the intervention group after intervention, but not in the comparison group. In paper III the mean age was 87.5 years, 61% used at least 10 medications and 84% of them had a least one DRP. The most common DRP was unnecessary drug therapy (39%) and the most common result was drug withdrawal. Performing medication reviews helped decrease the proportion of patients with at least one PIM ($p<0.001$) and the use of ≥ 3 psychotropics ($p<0.001$). Paper IV showed that the medication reviews reduced the use of antipsychotics by 23%. Of

the patients using antipsychotics, 43% had an approved indication while for 15% the indication was not given. Antipsychotic drug use was more common with increasing number of drugs (p=0.001).

Conclusions: Methods to improve the medication treatment of elderly patients are needed. Unnecessary treatment is a common drug-related problem in nursing home residents. It is not uncommon for these patients to use 10 or more medications regularly and one way to improve the situation is multi-professional medication reviews. Antipsychotic drug use without an approved indication is also common in this group, despite the risks involved, and medication reviews can correct this. Another problem for elderly patients is the lack of co-operation and information sharing between different levels of care. A method involving self-assessment, peer review, feedback and written agreements for change may promote this.

Abbreviations

ADE – Adverse Drug Event

ADL – Activities of Daily Living

ATC – Anatomical Therapeutic Chemical classification system

BPSD – Behavioral and Psychological Symptoms in Dementia

DDD – Defined Daily Dose

DRP – Drug Related Problems

GP – General Practitioner

FDA – US Food and Drug Administration

LIMM – Lund Integrated Medicines Management

MAI – Medication Appropriateness Index

NSAID – Non-Steroidal Anti-Inflammatory Drugs

OTC – Over the counter

PHASE-20 – Pharmacotherapeutical Symptom Evaluation, 20 questions

PIM – Potentially Inappropriate Medication

SÄKLÄK – Säker läkemedelsanvändning i primärvård (Safe use of medications in primary care)

Original papers

This thesis is based on the following papers, referred to in the text by their Roman numerals:

I. **Lenander C**, Bondesson Å, Midlöv P, Viberg N. Healthcare system intervention for safer use of medicines in elderly patients in primary care – a qualitative study of the participants' perceptions of self-assessment, peer review, feedback and agreement for change. *BMC Family Practice* 2015, 16:117.

II. **Lenander C**, Bondesson Å, Viberg N, Jakobsson U, Beckman A, Midlöv P. Effects of an intervention (SÄKLÄK) on prescription of potentially inappropriate medication in elderly patients. *Fam Pract* 2016, doi: 10.1093/fampra/cmw121

III. **Lenander C**, Bondesson Å, Viberg N, Beckman A, Midlöv P. "Effects of medication reviews on drug-related problems in elderly patients; a cross-sectional study in primary care" Submitted after revision.

IV. **Lenander C**, Midlöv P, Viberg N, Chalmers J, Rogers K, Bondesson Å. "Use of antipsychotic drugs by elderly primary care patients and the effects of medication reviews" Submitted.

Introduction

Demography and related health problems

The elderly population is increasing worldwide and demographic data estimates that 22% of the global population will be older than 65 by the year 2050 [1]. In Sweden, 19.8% of the population was aged 65 years or older in 2015 and the proportion is estimated to increase to 23% by the year 2050 [2].

Aging is known to be associated with an increased prevalence of multiple chronic diseases and, as a result of this, use of more medications. Prescribing is generally based on single-disease evidence/trials, which often do not take into account multimorbidity; something that is now common in those over 65 years of age [3]. Elderly patients are more vulnerable to experience potentially negative effects of medications. With age comes, for example, reduction in kidney function and changes in distribution volumes, affecting the pharmacokinetics for some drugs, resulting in an increased risk of drug-related problems (DRP). A drug-related problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes [4]. DRPs, as for example adverse drug events (ADEs), account for a substantial amount of hospital admissions [5-9] and a majority of these are preventable [5, 10, 11].

Polypharmacy

Polypharmacy can be defined as the use of multiple drugs, or more than are medically necessary, and is a growing concern for older adults [12, 13]. So far, there is no standard cut-off point with regard to the number of medications that is agreed upon for the definition of polypharmacy. Concurrent use of five or more medications, or even 10 or more, has been suggested. There is also some discussion among researchers regarding appropriate and inappropriate polypharmacy; arguing that in some cases the polypharmacy is needed [14]. However, it is known that the use of many medications is increasing the risk of DRPs. In Sweden, 10.7% of patients aged 75 years or above use 10 drugs or more [15].

Potentially inappropriate medications (PIMs)

A group of drugs which could cause many DRPs in elderly are PIMs (potentially inappropriate medications). For drugs in this group, the risk of harm is increased in elderly people and often outweighs the benefits [16]. However, this is on a group level, and for some individuals the benefits are greater than the risk of harm. Guidelines concerning potentially inappropriate medications have been developed in many countries, with Beers criteria [17, 18] being the most well-known. However, in Europe, many of the drugs listed in Beers criteria are unavailable, and criteria corresponding to European drug formularies have been developed. These include, for example, the Swedish quality indicators developed by the Swedish National Board of Health and Welfare [16], the STOPP/START criteria [19], the NORGEP criteria [20] and the EU(7)-PIM list [21]. These lists point out troublesome medications on a population basis, but there still might be individuals that need them.

Medication Appropriateness Index (MAI) [22] is another way of identifying inappropriate medications. MAI is an instrument that determines a drug's suitability to an individual and has been validated for evaluating drug use in the elderly [23]. However, the instrument is time-consuming and therefore less convenient to use in everyday care.

In this thesis the following groups of PIMs, according to the Swedish quality indicators [16], were selected:

Long-acting benzodiazepines

This group includes, for example, diazepam, nitrazepam and flunitrazepam. With these drugs there is a risk for hangover, cognitive impairment, muscle weakness, balance problems and falls [16].

Anticholinergic drugs

The most common anticholinergic drugs among Swedish seniors are: drugs for incontinence, hydroxyzine, tricyclic antidepressants and some antipsychotics (for example levomepromazine) [16]. These drugs can cause cognitive impairment, ranging from mild memory problems to confusion. Elderly patients with Alzheimer dementia are particularly vulnerable, but the risk increases even with normal aging.

Tramadol

In elderly patients, tramadol increases the risk of nausea and confusion. Tramadol should not be combined with other drugs acting on serotonin (for example SSRI), due to an increased risk of serotonergic syndrome [16].

Propiomazine

Propiomazine may cause daytime sedation and extrapyramidal symptoms, like restless legs [16].

NSAID

Treatment of elderly patients with NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) may lead to gastric ulcer and hemorrhage, fluid retention, heart decompensation and decreased renal function [16]. However, these drugs can be bought without prescription and thereby the use of them might be unknown to the doctor.

Antipsychotic drugs

Antipsychotic drugs are indicated to treat psychosis, including delusions, hallucinations, paranoia or distorted thoughts. According to the Swedish quality indicators [16], antipsychotics are a group of medications which should be used with caution in elderly due to the high risk of adverse events. These include extra-pyramidal symptoms, cognitive impairment, sedation and orthostatic hypotension as well as increased risk of stroke and premature death in patients with dementia [24, 25]. Despite this, the use of antipsychotics to treat behavioral and psychological symptoms in dementia (BPSD) is still high [26-28]. The evidence for the efficacy of antipsychotics for treating BPSD is, at best, modest for aggression, and very weak for other symptoms [29].

Multiple prescribers

Many elderly patients have several health care contacts and several different prescribers, both in primary care and in specialized care. With different systems for documentation there is a risk for problems regarding medications, especially in the

transition of care for elderly patients [30, 31]. In Sweden, the main responsibility for the care of elderly often lays with the general practitioner (GP). It is therefore of great importance that the GPs get sufficient training in, and time to, handle these elderly patients. Equally important is the need for correct information about the patient's current medications. However, this is not always the case.

In Sweden, there has been a discussion about a digital solution, where all the patient's medications are listed for health care personnel to see, to solve the problem with knowledge about patients' current medications. Unfortunately, so far there has only been discussions and no decisions.

Pharmacists in Swedish health care

In Swedish health care, pharmacists are more common at the hospitals than in primary care. However, in the last years, more pharmacists have been employed in primary care. Education of staff, medication reviews and optimizing drug supplies are among the tasks performed by pharmacists.

Methods to improve medication use

The Swedish Council on Technology Assessment in Health Care (SBU) concluded in a report in 2009 that no single measure, e.g. medication reviews, can solve today's problem with elderly patients use of medications [32]. Some of the things that need improvement are transfer of information and co-operation between different professions and levels of care [33]. According to a recent review [34], increased interdisciplinary collaboration could enhance medication safety in nursing homes.

Different methods to improve the medication use in the elderly have been tried, e.g. deprescribing, different types of medication reviews, education of health professionals and patients, and projects such as SÄKLÄK.

Deprescribing

Deprescribing is the process of tapering or stopping drugs, aimed at minimizing polypharmacy and improving patient outcomes [35]. MedStopper is a database tool to facilitate deprescribing by matching drugs with indication and thereby ranking the drugs from potentially most stoppable to potentially least stoppable, including information on the rationale for their ranking [36].

Medication reviews

A medication review is a method to analyze, review and follow-up an individual's drug therapy. The review is done in a structured and systematic way, according to local guidelines and routines [37]. Medication reviews at hospitals have been shown to improve drug use [38, 39] and to reduce hospital readmissions [40]. In primary care, medication reviews can reduce total number of drugs, reduce falls and maintain self-rated health [41, 42] as well as save money for the society [43]. There is also evidence that, when doing medication reviews, direct communication between pharmacists and physicians is more efficient than written communication [44]. However, due to significant heterogeneity in set-up and measurements in trials, more studies are needed.

In Sweden, a medication review by their GP is recommended for all patients 75 years or older if they use five or more medications or who has been hospitalized, and for nursing home residents [45]. In Skåne County, medication reviews are performed according to the LIMM (Lund Integrated Medicines Management) model (see method section).

SÄKLÄK

The SÄKLÄK (Säker läkemedelsanvändning i primärvård (Safe use of medications in primary care)) project was initiated by the Swedish Association of Local Authorities and Regions (SALAR) and The Patient Insurance LÖF. The steering committee of the project consisted of one delegate each from six professional organizations (The Swedish College of General Practice, The Swedish Pharmaceutical Society, Geriatric Medicine in Sweden, Riksföreningen för Medicinskt Ansvariga Sjuksköterskor (a Swedish association of authorized nurses), Sweden's National Organization of District Nurses and The Swedish Society of Clinical Pharmacology and Therapeutics). The intervention model was originally developed for, and successfully implemented in hospital care to prevent birth injuries [46]. The model was then tested in orthopedic surgery (PRISS) [47] and also in ongoing projects to improve abdominal surgery and trauma care. The SÄKLÄK project was a pilot study to determine whether this intervention model could be used in primary care to enhance medication safety in elderly patients. The model is based on multi-professional cooperation and consists of self-assessment, peer review, feedback and written agreements for change.

The intervention started with a self-assessment questionnaire, with questions on how patient safety is secured during prescribing of medication, medication use and follow-up, at the primary care center and also in cooperation with pharmacies/hospitals/municipally provided home care. The focus of the questions

was on frail elderly people, on how conditions are to be provided for different measures of importance and how it is ensured that these measures are being followed. A group of selected doctors, nurses and pharmacists, which were experienced in elderly care, served as reviewers in the second step of the intervention. The reviewers analyzed the self-assessment forms, visited the primary care units and had opportunities to ask questions and provided feedback. Finally, the reviewers made an agreement for change with the management of the primary care center.

Types of housing

Independent living

The majority of the 1.9 million elderly people (65 years and above) in Sweden live in their own home with no help from the society [2].

In own home with care at home

For persons in need of help with activities of daily living (ADL) there is a possibility for home help service. Personnel from the local municipality will aid with anything from grocery shopping and cleaning to personal hygiene for a subsidized fee. For patients with health care needs, who cannot access primary care, the care can be provided at home. This way, nurses, physiotherapists and occupational therapists from the municipality will help the patient at home, with assistance from a primary care physician.

Instead of moving to a nursing home, many patients can stay at home with home care. About 223,000 persons received health care at home during 2015 [48]. There has been a shift in Sweden towards more home care and less nursing home care [49].

Nursing homes

A nursing home is a place for people who do not need hospital facilities but cannot be cared for at home. There are differences between countries in quality and quantity in nursing homes, and also concerning nurse and physician contributions [50, 51]. In Sweden, there are around 82,000 nursing home beds and a little over 103,000 persons, over 65 years, that lived in a nursing home sometime during 2015 [48]. This equates to about 5% of the Swedish 65+ population and is the proportion of the

elderly with the highest need of care. The difference between the number of beds available and beds used (over the period measured), additionally illustrates the high mortality for this group.

In Sweden the local municipalities are responsible for nursing, social care and rehabilitation at the nursing homes, while the county councils (usually through local primary care centers) are responsible for medical care. The nurses and other nursing staff at the nursing home are employed by the municipality. The GP, who is employed by the county, usually does weekly visits. The coordination of services is thus a great challenge in the Swedish system.

The municipalities decide, after application, if a person is eligible for a nursing home. The Swedish Social Services Act [52] regulates the general requirements, but it is up to the municipalities to decide on the details. The nursing homes can be run by the municipalities or by private entrepreneurs, but the financing and supervision stay with the municipalities. Sweden has a national taxation system which ensures almost equal financial resources in relation to needs regardless of local tax base [49].

The use of PIMs is higher in nursing home residents compared to elderly people living in their own homes and they also use more medications (26% vs 10.7% using ≥10 medications) [53].

Society and health care are facing a big challenge, to meet the need to care for elderly with multiple illnesses; a group which is expected to increase in coming years. Polypharmacy is common in this group and so is health care utilization, and this is why this is an important issue to address.

Aims of the thesis

The general aim of my thesis was to evaluate methods to improve the drug use in elderly patients in primary care.

Specific aims:

1. The aim of the first paper was to elucidate how the participants perceived a multi-professional intervention consisting of self-assessment, peer review, feedback and agreement for change (SÄKLÄK).

2. The aim of the second paper was to see if SÄKLÄK had any impact on the prescribing of potentially inappropriate medications (PIMs).

3. The third paper aimed to evaluate the effect of medication reviews in elderly patients regarding occurrence and types of drug-related problems, as well as the effects on potentially inappropriate drug use.

4. The last paper was an evaluation of the effects of medication reviews of antipsychotic drug use in nursing homes and home care.

Methods

An overview of the studies is presented in table 1.

Table 1
Overview of the papers.

Paper	I	II	III	IV
Design	Qualitative	RCT	Cross-sectional	Cross-sectional
Participants	17 employees from 5 primary care centers	5+5 primary care centers	Nursing home residents and patients with home care (n=1720)	Nursing home residents and patients with home care (n=1683)
Outcomes	Experiences of the method (SÄKLÄK)	Changes in prescription of PIMs	Occurrence of DRPs, types of DRPs, effect on PIMs	Effects of medication reviews on use of antipsychotics
Data collection method	Semi-structured interviews	Data collected from the Swedish Prescribed Drug Register	Data collected from medication reviews	Data collected from medication reviews
Data collection period	2014	2012-2015	2011-2012	2011-2012
Data analysis	Qualitative Content Analysis	Chi^2-test Hypotheses testing using 95% CI	Student's t-test Chi^2-test	Multiple logistic regression analysis Chi^2-test

Study settings, participants and recruitment

Papers I and II

Papers I and II are evaluations of the SÄKLÄK pilot study. All primary care centers in Sweden (approximately 1200) were invited to participate. Invitations were emailed to managers and information about the study was also given at the congress of the Swedish College of General Practice in May 2014. A total of 20 primary care centers responded and they were stratified according to urban or rural location. Using Excel, ten of these were randomly assigned to intervention group (five) or

control group (five) keeping the distribution between rural and urban location. For paper I, participating staff from the intervention primary care centers were asked for willingness to be interviewed about their perception of the intervention method.

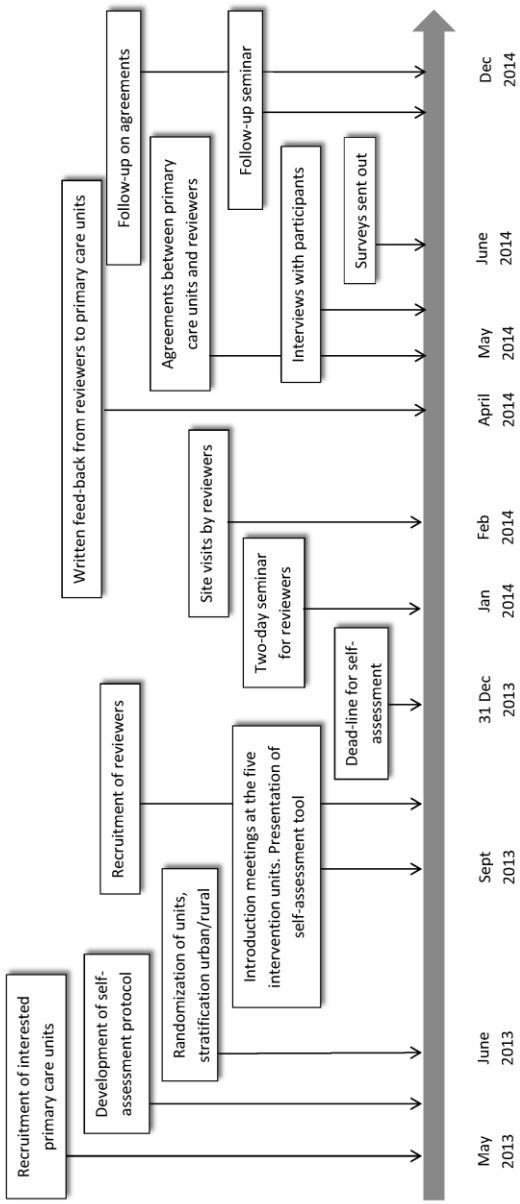


Figure 1.
Overview of the time schedule for the SÄKLÄK project.

Papers III and IV

During 2011-2012 pharmacists from the Department of Medicines Management and Informatics aided private primary care centers in Skåne with medication reviews. Of 65 eligible primary care centers, 25 asked for the service. Seven clinical pharmacists, all with at least three years' experience of medication reviews, were involved. Patients aged 75 years or older, living at nursing homes or in their own homes with municipally provided home care were included in the analysis. Data from these medication reviews were collected in an Access database.

Procedure

Paper I

The participants were interviewed using a semi-structured interview guide. Examples of questions asked were: Tell me something positive/negative about participating in the project? How did you perceive the four steps of the project? How did you perceive co-operation with other health professionals and staff? Each question was followed by exploring questions like "Can you give me an example of that?" The interviews lasted between 8 and 36 minutes.

A survey including similar questions was sent to the managers at the five intervention primary care centers. The responses were triangulated with the results from the interviews.

Paper II

Data were collected from the Swedish Prescribed Drug Register [27]. The register includes data on all drugs dispensed by Swedish community pharmacies since 2005 and is managed by the National Board of Health and Welfare. It includes data for individual patients on substance, brand name, formulation, package and date of prescription and dispensing. All drugs are classified according to the Anatomical Therapeutic Chemical (ATC) Classification System [54]. Multi-dose drug dispensing, i.e. all drugs which are to be ingested at the same time are machine-dispensed in unit bags are included in the register. The multi-dose drug dispensing system is very common in nursing homes in Sweden. All other prescriptions were defined as ordinary prescriptions. Drugs used in hospitals and OTC (over-the-counter) drugs are not included. Since data is only available for dispensed drugs, these were used as a proxy for prescribed drugs in this study. All prescriptions for

patients 65 years and older from the participating primary care centers (five interventions and five control) for the following ATC-groups: antipsychotics, drugs with anticholinergic effects, long-acting benzodiazepines, tramadol, propiomazine and NSAIDs (see Table 2) was collected. Data were collected for two periods: 12 months before (June 2012-May 2013) and 12 months after (June 2014-May 2015) the intervention.

Table 2.
Potentially inappropriate medications according to the Swedish National Board of Health and Welfare.

PIM group	ATC-group	Substance (examples)	May cause:
NSAIDs	M01A	Ibuprofen Diclofenac Naproxen	Gastric ulcer and haemorrhage, fluid retention, heart decompensation, reduced renal function
Long acting benzodiazepines	N05BA01 N05CD02 N05CD03	Nitrazepam Flunitrazepam Diazepam	Prolonged half-lives in elderly may cause hangover, cognitive impairment and falls
Anticholinergics	R06AD G04 N05BB	Promethazine Urologic spasmolytics (e.g. tolterodin) Hydroxyzine	Cognitive impairment, confusion, impaired functional status
Propiomazine	N05CM	Propiomazine	Daytime sedation, extrapyramidal symptoms
Tramadol	N02AX	Tramadol	Confusion
Antipsychotics	N05A exluding lithium	Risperidon Haloperidol Quetiapin	Cognitive impairment, sedation, orthostatism

Analysis comparing age groups (65-79 years and 80+) and gender were performed. Total number of patients and change in number of patients using PIMs before and after the intervention were examined as well as differences in the change between the intervention and the control group. Total number of prescriptions of PIMs and mean number of prescriptions per patient were also analyzed. Mean Defined Daily Dose (DDD) per patient (combined for all PIMS) were examined in the same way as well as differences between ordinary prescriptions and multi-dose drug dispensing.

Paper III

Medication reviews in primary care according to the LIMM model [55]

A symptom assessment tool (PHASE-20) [56, 57] was used to assess the patient's health status. This includes medical information such as blood pressure, pulse,

current diagnosis, weight (measured by the nurse) and creatinine levels, as well as questions about symptoms such as anxiety, dizziness and constipation. The PHASE-20 is a validated tool to use in connection with medication reviews for identifying possible drug-related symptoms in older people and has been recommended by the Swedish National Board of Health and Welfare [16]. The PHASE-20 together with a copy of the medication list was sent to the pharmacist for evaluation of potential DRPs. Identified DRPs and possible actions to solve them were noted and thereafter discussed at a team-meeting with the patient-responsible GP, the nurse, the pharmacist and sometimes a carer. Based on these discussions and his/her knowledge of the patient, the GP then decided on a course of action. Changes in patient status were to be followed-up in 4-8 weeks by the nurse and forwarded to the pharmacist.

Information about identified and discussed DRPs, on actions taken and if any follow-up was recorded, was collected from the Access database and from the paper records: medication lists, symptom assessments and notes from the medication review. We also measured the percentage of patients taking 10 or more medications (regularly or as needed) and the percentage of patients taking three or more psychotropic drugs (from the following Anatomical Therapeutic Chemical Classification System (ATC) [54] groups; N05A (antipsychotics), N05B (anxiolytics), N05C (hypnotics and sedatives) and N06A (antidepressants)).

Paper IV

Information about age, gender, type of housing, number of medications, antipsychotic drug use, indication/diagnosis for this, as well as symptoms (from PHASE-20) was collected from the paper records of the medication review (medication list, symptom assessment and notes from the medication review). We had no access to the medical record during data collection or analysis.

Review of the medication lists identified all patients receiving antipsychotics. Antipsychotics in this study included the following ATC groups [54]: all drugs in N05A, except for lithium, and R06AD01 (alimemazine). The reason/indication for treatment with antipsychotics was identified using the symptom assessment form, the medication list and the list of suggested recommendations from the pharmacist. A judgement whether the reason/indication was appropriate or not was done. Indications regarded as appropriate according to the Swedish quality indicators [16] were the following: Psychotic conditions, other disease with psychotic symptoms and dementia with BPSD such as severe aggressiveness. All other indications were regarded as potentially inappropriate. All indications were regarded as inappropriate for patients with Lewy body dementia. If no reason/indication could be found this was registered.

If the use of antipsychotics was discussed during the medication review or not, and whether any changes to therapy were made was also noted.

Qualitative analysis (paper I)

All interviews were recorded and transcribed verbatim, and then subjected to qualitative content analysis [58]. The analysis was started as soon as the first interview was transcribed, i.e. before all interviews were completed. After 15 interviews saturation was reached. The analysis was performed in several steps and commenced by reading through the text several times to get a sense of the whole. The text was then divided into meaning units, which could be words, sentences or paragraphs containing aspects related to each other through their content and context. The meaning units were then condensed and after that coded. The codes were then sorted into categories. Thereafter a deeper analysis to find the latent meaning of the interviews was performed, giving a theme [59].

Statistical analysis

The data were analyzed using IBM SPSS version 22 (paper II-III) and IBM SPSS version 23 (paper IV) [60] as well as an online Chi-square calculator [61]. A significance level (α) of 0.05 was used.

Paper II

Hypothesis testing using 95% confidence interval for the mean difference was used to compare groups before and after intervention. Hypothesis testing using Chi-square test was used to compare percentages of different PIM groups for ordinary prescriptions and multi-dose dispensing. Other hypothesis testing was not possible due to the data set containing a mix of dependent and independent observations.

Paper III

Student's t-test was used to compare groups and multiple significance was tested according to the suggestion by Bland, Altman [62]. Chi-square was used to compare medication use before and after medication review as well as to compare follow-up between groups.

Paper IV

Categorical versions of continuous variables in the PHASE-20 were made by dichotomizing these variables into 'No or Small problems' (none or small problems in the original data) and 'Moderate or Severe problems' (moderate or severe in the original data). Differences in the proportion of symptoms between patients who were/were not prescribed antipsychotics, was tested using a Chi-square test on a two-way table. Resident characteristics were assessed for their association with prevalent antipsychotic use in univariable logistic regression models. Variables with p-values under 0.20 were used in an adjusted multivariable logistic regression model and we used the likelihood ratio test to produce p-values.

Ethical considerations

Ethical considerations for paper I-II

The study protocol for SÄKLÄK was approved by the Regional Ethics Review Board at Lund University (date: 23 May, 2013; case number: 2013/333). The decision from the board was that the study did not need ethical approval.

All participating primary care centers received oral and written information about the study, and all managers at the centers provided written consent to participate. During the interviews the data were collected with a digital recorder and made anonymous before transcription. The results were presented in such a way that no individual could be identified. The extraction of data for paper II was done by the Swedish National Board of Health and Welfare with no possibility for the research team to identify any individual patient.

Ethical considerations for paper III-IV

The study protocol was approved by the Regional Ethics Review Board at Lund University (date: 29 October, 2013; case number: 2013/649).

Medication reviews were not considered to expose the patients to any harm. Patients and/or next of kin had the possibility to be excluded from the analysis. All data were unidentified and presented on a group level.

Results

Main findings

- The SÄKLÄK method is a feasible process to use in primary care and the participants perceived the multi-professional approach as very positive. However, it was time-consuming but was also deemed as an investment and an opportunity to share knowledge. (Paper I)
- The SÄKLÄK method had some impact on the prescription of potentially inappropriate medications, such as antipsychotics, NSAIDs, tramadol, propiomazine, anticholinergic drugs and long-acting benzodiazepines. (Paper II)
- Medication reviews are one way to improve drug use in elderly primary care patients. The use of potentially inappropriate medications and use of three or more psychotropic drugs decreased after the medication review. Drug use is extensive in nursing home residents and elderly patients with homecare, and unnecessary drug therapy is a common problem. (Paper III)
- The use of antipsychotic drugs is high in elderly patients in nursing homes. They are often given for indications that are not officially approved, or poorly documented. Medication reviews appear to offer one useful strategy for reducing excessive use of these drugs. (Paper IV)

SÄKLÄK – the participants' experiences (Paper I)

The qualitative content analysis of the interviews yielded six categories. (Table 3).

Table 3.

Examples of how findings were yielded from the analytical process, showing some of the many meaning units that built up the categories and the theme.

Meaning unit	Condensed meaning unit	Code	Category	Theme
To see all this and to listen to other people participating, to listen to their ways of seeing things	Listen to other people's way of seeing things	Co-operation	Multi-professional co-operation	Medication safety is a large area. In order to make improvements time needs to be invested and different professions must contribute
I cannot make progress in this matter, but is there someone else who has managed it, and if so, how?	Helping each other	Knowledge sharing	The joy of sharing knowledge	
It was quite comprehensive, so it took a lot of time to go through it all and answer all the questions	Comprehensive form and time-consuming to answer	Time-consuming	Spend time to save time	
It costs energy right now, but if we can improve our routines and follow them… then I think it will pay off in the long run	Investing time now will save time later	Time-saving		
Not that I clearly felt that we were talking about the answers in our self-assessment report	Not talking about the same things	Disappointment	Disappointment with the focus of the feedback	
I think it was really good to see it in print, what's working and what's not, and what we can improve	What's working and what's not, and improvements	Strengths and weaknesses	A focus on areas of improvement	
Yes, concerning medication reviews I think so […] we can surely perform many more of these	Perform many more of these	Change of routines	Impact on work	

Based on these categories, a theme emerged: "Medication safety is a large area. In order to make improvements time needs to be invested and different professions must contribute."

Multi-professional co-operation

The project's multi-professional approach was expressed as something very positive by the participants. It was an opportunity to invite people from the hospital, the pharmacy and municipal home care to engage in closer co-operation and to meet face-to-face.

> "…the most positive part has been working with the self-assessment, working multi-professionally and getting a better understanding of each other's work." (primary care unit head, C4)

The multi-professional approach seems to have given the participants a chance to meet in person to discuss questions of importance for medication safety. Many of them said that they had been working "together" for a long time, but now realized it was more side-by-side than real co-operation.

> "…I have thought one step further: we need to help each other…" (nurse, E40)

A focus on areas of improvement

The self-assessment process highlighted specific areas for improvement, but also showed strengths of the primary care center, according to the participants. Identified areas for improvement included: keeping an accurate medication list, factors affecting the prescribers' choice of therapy and factors affecting patients' ability to contribute to drug safety. Examples of identified strengths were: committed leadership, climate open to discussion, existing routines and access to consultants (geriatricians, psychiatrists, pharmacists). The written feedback also highlighted areas for improvement, which was appreciated by the participants. One person pointed out that many questions in the self-assessment concerned monitoring and that monitoring a lot of things could distract from the aim to increase patient safety.

> "…seeing what we have done and what we need to improve, presented in a clear and concise way, is positive." (primary care unit head, U15)

> "I look at the medicines in another way now." (nurse, E7)

The joy of sharing knowledge

The peer review team visits were viewed as mostly enjoyable and exciting, with no feeling of being investigated. The reviewers, with working experience from different areas, were perceived as being able to bring a lot of knowledge to the primary care center, but they could also learn some new things to take home.

> "…it's great to have a peer review team from different parts of the country with different viewpoints. […] Sometimes they said this is not how we do it, but you seem to have found a good solution…" (primary care unit head, J112)

> "…they were interested and had questions. We had a good discussion…" (primary care unit head, V11)

Disappointment with the focus of the feedback

Some respondents had hoped for a short summary of their strengths and weaknesses by the end of the peer review visit and expressed slight disappointment with the lack of this. The written feedback did not always focus on the primary care unit; it was sometimes more of a discussion on a higher level, according to many of the participants.

> "…some feedback at the end of the visit. But I didn't get that with me, it was more of a general discussion of Swedish health care…" (primary care unit head, C14)

> "…these are things outside our influence." (GP, B106)

Spend time to save time

According to the participants, the project took more time than expected. It was more time-consuming than expected finding interested participants outside the primary care center and explaining the aim of the project to them. The self-assessment form was felt to be too long and filling it out online took a lot of time.

> "…to include people outside the primary care unit took a lot of time" (primary care unit head, U4)

> "It took longer than I had initially expected" (primary care unit head, L9)

On the other hand, some of the participants pointed out that the time invested in the short-term may save time later on through improved routines for safe use of medications.

"…it costs energy right now, but if we can improve our routines and follow these […] then I think it will pay off in the long-run…" (GP, G117)

Impact on work

The participants viewed written agreements as something positive; a reminder to keep focused on medication safety. But it was also perceived as a little stressful. The follow-up was six months later and summer was coming in between. The self-assessment led to a change of routines right away at some primary care units, while others stated that changes would be made in the future.

"Yes, it has already [started to yield change]…" (GP, B167)

"It can only get better. More structure, get more routines…" (nurse, H62)

Surveys

All five managers at the intervention primary health care centers completed the survey, and four of them also participated in the interviews. The responses from the surveys correspond in general with the interviews. The multi-professional approach was pointed out by the respondents as being very positive. The self-assessment was said to be worthwhile to identify strengths and weaknesses. One respondent thought this was the only useful part of the project, even though it took more time than expected. At one of the participating primary care units they felt criticized by the reviewers, according to the survey, but this did not come up during the interviews.

Validation

The results of the survey and the qualitative analysis of the interviews were discussed at a follow-up seminar. The participants agreed with the findings.

Effects of SÄKLÄK on prescription of PIMs (Paper II)

At baseline, 63% of the prescriptions were dispensed to women and almost 68% to patients in the age group 65-79 years. Multi-dose dispensing accounted for 13.8% of these prescriptions and ordinary prescriptions for 84.7%.

In the intervention group, a decrease of 22.2% was seen for prescriptions (from 19,796 to 15,400), compared to a decrease of 8.8% in the comparison group (from

12,770 to 11,641). The average number of prescriptions increased in the comparison group after the intervention period (7.64 to 8.81) while it remained unchanged in the intervention group (7.48 to 7.48). The difference was however not significant.

The most common groups of PIMs in the intervention group was anticholinergics, antipsychotics and NSAIDs, and this remained after the intervention. The largest decrease was seen for propiomazine and tramadol. In the comparison group, the most common groups of PIMs were anticholinergics, NSAIDs and antipsychotics. In this group, all PIMs decreased except for antipsychotics and propiomazine where an increase was seen. Regarding the number of patients receiving PIMs, this decreased for all groups of PIMs except for antipsychotics in the comparison group.

Ordinary prescriptions vs multi-dose dispensing

The number of patients with multi-dose dispensing increased from 13.8% to 16.4% after the intervention. There was a significant difference between the two groups regarding prescription of PIMs (Table 4). The most common PIMs for patients with multi-dose dispensing were antipsychotics, anticholinergics and long-acting benzodiazepines. This remained the same after the intervention, including a 13.6% increase in prescriptions of antipsychotics. In the group with ordinary prescriptions, NSAIDs, anticholinergics and tramadol were the most common groups.

Table 4.
Number of prescriptions of different potentially inappropriate medications (PIMs) before the intervention, divided into ordinary prescriptions and multi-dose dispensing. Number and percentage of total.

	Ordinary prescriptions N= 7712	Multi-dose N=1264	p-value*
NSAIDs number (%)	3132 (40.6%)	132 (10.4%)	<0.001
Anticholinergics number (%)	1564 (20.3%)	319 (25.2%)	<0.001
Tramadol number (%)	1298 (16.8%)	87 (6.9%)	<0.001
Long-acting benzodiazepines number (%)	772 (10.0%)	204 (16.1%)	<0.001
Antipsychotics number (%)	219 (2.8%)	420 (33.2%)	<0.001
Propiomazine number (%)	727 (9.4%)	102 (8.1%)	0.122

*Chi-square test
PIM = Potentially Inappropriate Medication
NSAID = Non-Steroidal Anti-Inflammatory Drug

Medication reviews (Paper III)

The study included 1720 patients with a mean age of 87.5 years and used on average 11.3 drugs (range 1-35). See also Table 5. The medication reviews decreased the number of drugs per patient to 10.5.

Table 5.
Baseline characteristics

	Nursing home n= 1508	Home care n= 212	p-value
Age, mean (SD)	87.7 (5.8)	86.3 (5.7)	<0.01[a]
Female n (%)	1123 (74.5)	142 (67.0)	0.02[b]
Number of drugs per patient, mean (SD) continuous drugs, mean (SD) drugs as needed, mean (SD)	11.2 (4.6) 8.5 (3.6) 2.8 (2.1)	11.4 (4.3) 9.2 (3.3) 2.2 (2.0)	0.59[a] <0.01[a] <0.01[a]
Number of potentially inappropriate drugs, mean (SD) Antipsychotics, mean (SD) Long-acting benzodiazepines, mean (SD) Anticholinergics, mean (SD) Propiomazine, mean (SD) Tramadol, mean (SD)	0.30 (0.46) 0.12 (0.33) 0.06 (0.24) 0.09 (0.29) 0.02 (0.15) 0.05 (0.23)	0.27 (0.44) 0.05 (0.21) 0.10 (0.31) 0.09 (0.29) 0.05 (0.21) 0.04 (0.20)	0.35[a] <0.01[a] 0.04[a] 0.90[a] 0.09[a] 0.49[a]
Patients with ≥ 1 PIM, n (%)	453 (30.0)	57 (26.9)	0.35[b]
Patients with ≥ 3 psychotropics, n (%)	367 (24.3)	28 (13.2)	<0.01[b]
DRPs, mean (SD)	2.2 (1.9)	2.4 (1.8)	0.21[a]

SD standard deviation

[a] t-test, [b] Chi square test

Drug-related problems

In 84% of the patients, DRPs were identified, with a total of 3868 DRPs, giving a mean of 2.2 DRPs per patient. The most common types of DRPs were unnecessary drug therapy (39%), dose too high (21%) and wrong drug (20%). The most common group of drugs causing DRPs were drugs acting on the nervous system (33%) and cardiovascular drugs (27%).

Of the DRPs 12% (485 of 3868) were attributable to PIMs.

Suggested intervention recommendations

Almost all identified DRPs (3860 of 3868) received an intervention recommendation. The most common interventions suggested by the pharmacist to the GP were withdrawal of drug therapy (47%), decreased dose (21%) and change of drug therapy (9%).

Acceptance of suggested recommendations

Acceptance or not was not recorded for 410 "for information/notification" recommendations. From the remaining 3450 recommendations, the GPs accepted 80%, giving a mean of 1.6 changes per patient. In 9% of the cases, the GP did not accept the pharmacists' suggestions.

Potentially Inappropriate Medications

The proportion of patients with least one PIM was reduced significantly ($p<0.001$) by the medication review. Nearly 23% (395 of 1720) of the population used ≥ 3 psychotropics before the medication review, and this decreased to 17% (296 of 1720) after the review ($p<0.001$). Table 6.

Table 6.
Number of patients using potential inappropriate medications before and after medication review. (n= 1720 patients)

	Before medication review	After medication review	p-value[a]
Patients with antipsychotics, n (%)	194 (11.3)	136 (7.9)	<0.001
Patients with anticholinergics, n (%)	158 (9.2)	72 (4.2)	<0.001
Patients with propriomazine, n (%)	43 (2.5)	16 (0.9)	<0.001
Patients with tramadol, n (%)	90 (5.2)	41 (2.4)	<0.001
Patients with long-acting benzodiazepines, n (%)	112 (6.5)	62 (3.6)	0.001
Patients with ≥ 1 PIM*, n (%)	510 (30)	299 (17)	<0.001
Patients with ≥ 3 psychotropics, n (%)	395 (23)	296 (17)	<0.001

*PIM Potentially Inappropriate Medication (antipsychotics, anticholinergics, propiomazine, tramadol and long-acting benzodiazepines)

[a] Chi square test between total numbers (nursing home and home care together)

Effects of medication reviews on antipsychotics (Paper IV)

A total of 1683 patients were included in the analysis and 12% of these (n=206) used antipsychotics. The use of antipsychotics among patients in nursing homes was more common (13.4%) than in patients with home care (3.8%) ($p<0.001$). Among patients with antipsychotics the use of ≥10 drugs was more common (65.5%) than in patients without (57%) (p=0.02). In the group receiving antipsychotics, cognitive impairment, depressive symptoms, anxiety and feeling tired was more common in the symptom assessment than among those not on antipsychotics.

The odds of being prescribed antipsychotics decreased by age [OR=0.96 (0.94-0.99)], while nursing home residents had higher odds [OR=4.20 (2.03-8.66)]. Increased number of drugs was also associated with higher odds of being prescribed antipsychotics [OR=1.06 (1.03-1.09)].

The treatment with antipsychotics was brought up as a potential problem during the medication review in 80% (n=166) of the cases. The most common DRPs were wrong drug (60%), unnecessary drug therapy (18%) and adverse events (16%). The most common advice offered was to evaluate the efficacy and possible adverse effects of the drug therapy (48%), followed by withdrawal of drug (19%) and progressive lowering of dose (19%). This advice was acted upon by the doctor in about one quarter of the cases. The use of antipsychotics decreased after the medication review by 23%, from 206 patients to 157 patients.

Of the patients using antipsychotics, only 43% had an approved indication while no indication was given for 15% (Table 7).

Table 7.
Indications for use of antipsychotics. n= 215, with nine patients having two antipsychotics (i.e. 206 patients)

	n (%)	Approved indication[a]
Psychosis or psychotics symptoms	80 (37)	77[b]
BPSD	11 (5)	11
Nausea	4 (2)	-
Anxiety	61 (28)	-
Depression	1 (0.5)	-
Dementia	19 (9)	-
Bipolar disease	6 (3)	5[c]
Sleep	1 (0.5)	-
None specified	32 (15)	-

[a]According to Swedish National Board of Health and Welfare. (2010). [Indicators for the evaluation of quality in drug use of the elderly].

[b]3 Patients with Lewy body dementia treated with antipsychotics for psychotic symptoms

[c]Olanzapine approved

The most common indications recorded were psychosis or psychotic symptoms (n=80), anxiety (n=61), none specified (n=32) and dementia (n=19). Risperidone (n=92), haloperidol (n=45), olanzapine (n=26) and alimemazine (n=21) were the most commonly used antipsychotics.

Discussion

This thesis shows that excessive drug use is common among elderly patients and that unnecessary drug therapy is a common problem. Antipsychotic drug use is frequent in nursing homes, often without a proper indication. Medication reviews are one way of addressing these problems. An intervention method consisting of self-assessment, peer review, feedback, and agreement for change is another way to affect prescription of PIMs to elderly patients and the method is well accepted by health care personnel.

Findings compared to other studies and literature

Polypharmacy is increasing among the elderly and with that the risk for drug-related problems such as adverse drug events, interactions or over/underuse [63, 64]. Methods to overcome these problems include medication reviews, deprescribing, education, electronic aids for prescribers and projects like SÄKLÄK.

In a Norwegian study, an electronic decision system significantly reduced the use of antipsychotics in nursing home residents [65]. It has also been shown that educational outreach visits to GPs can affect prescribing patterns regarding PIMs [66]. A review article on deprescribing concluded that generalized educational programs did not affect mortality for older patients, but patient-specific interventions can [67].

Paper I-II

The aim of the SÄKLÄK project was to improve medication safety for elderly primary care patients by using a method consisting of self-assessment, peer review, feedback, and written agreements for change. The care of elderly people is fragmented [68] and the cooperation between health care professionals involved needs to be improved to enhance medication safety [34]. Self-assessment is a useful tool to identify areas of improvement and to clarify strengths and weaknesses [46, 69] and was appreciated by the participating primary care centers. For the self-assessment to be successful and achieve acceptance, both management and

employees should be involved [69]. In order to answer all the questions on the SÄKLÄK self-assessment, it was necessary to get input from different health professionals. In other words, one person could not answer all the questions by him or herself. Since collaborations imply more than just working side-by-side as health professionals [70], the self-assessment may facilitate communication between different professionals. Peer review can be explained as knowledge sharing [71] and has been shown to be useful to shed light on provider-related errors and associated safety concerns [72]. The sharing of knowledge was useful both for the reviewed unit and the reviewers in SÄKLÄK and was highlighted as a positive part of the method.

From 2005 to 2014, there has been a 44% decrease in the use of PIMs according to national Swedish data [73]. Beyond this, the SÄKLÄK intervention led to a decrease of 22% on prescription of PIMs in the intervention group but only 8% in the comparison group. We could also see that fewer patients received PIMs and the mean DDD/patient was significantly lower in the intervention group post intervention. No significant differences were seen in mean DDD/patient between men and women, but women received more PIMs than men did in this study. It is known that women use more medications than men and this seems to be true for PIMs as well, which also is supported by other studies [74, 75].

Younger patients (65-79 years) received a higher mean DDD/patient than did the older patients (+80 years). This could indicate that the older patients are getting lower doses or shorter treatment, which is appropriate. Other studies have shown contradictory results with both an increased risk of getting PIMs [76, 77] and a lower risk [78] for older patients.

Paper III-IV

Medication reviews can be performed at hospital, in primary care or in nursing homes. It can be discussed at a multi-professional meeting or left as a note to the doctor, with or without patient participation. However, many different methods and study designs can make it difficult to compare results and conclude on effectiveness [79].

Medication reviews at hospitals have been shown to improve drug use [38, 39], reduce the length of hospital stay [80] and to reduce repeat visits to hospitals [40]. In primary care, medication reviews can reduce the total number of drugs, decrease prescription of PIMs, reduce falls and maintain self-rated health [41, 42, 81].

In paper III, almost 30% of the nursing home residents used a least one PIM before medication review. This is in line with other Swedish studies (26-33%) [41, 82] but slightly more than in a Swiss study (22.5%) [83]. When compared with the general

population aged 75 years or older in Skåne, the use of a least one PIM was higher in the study group: 30% vs around 10% [73]. This indicates that the studied population is less healthy than the general population. In recent years there has been a decrease in the use of PIMs among the older Swedish population [73] but the decrease is more distinct after medication reviews, which is in line with other studies [41, 82].

In paper III, the total number of drugs and usage of PIMs were decreased by medication reviews. This is in line with other studies [41, 64, 81] and could in some way affect health care utilization. However, for frail elderly patients, other factors like multimorbidity, can influence their health care utilization [84-86]. We saw a high incidence of polypharmacy with 61% of the patients using 10 drugs or more. This is much higher than for the total 75+ population in Skåne (10.2% in 2013 [73]), which indicate a more ill study population at nursing homes. Swedish nursing homes are usually for patients that are not able to care for themselves anymore, often because of multimorbidity and thereby polypharmacy.

The study also shows that DRPs are common in this population with 84% having at least one. This is less than in other studies [41, 64, 85] and could be due to a larger, non-selected patient group in this study. Unnecessary medication was the most common DRP and drugs from ATC-classes "N – Nervous system", "C – Cardiovascular system" and "A – alimentary tract and metabolism" cause the majority of DRPs, which is in line with other studies [63, 64]. Multi-dose dispensing is very common in Swedish nursing homes and almost all residents receive help with drug administration; therefore compliance was not a common DRP.

Withdrawal of medication was the most common result of the medication reviews and resulted in a decrease in both total number of drugs per patient and in PIMs. In this study the GPs accepted 80% of the clinical pharmacists' suggestions, indicating that this is a feasible method to use in primary care. Another study, which rate the clinical importance of a sample of these DRPs and suggestions, showed a significant clinical importance in the vast majority of them [87].

One PIM of special interest is antipsychotics, where the use is high and not always on correct indications. In paper IV, 13% of the nursing home residents had a prescription for antipsychotics, which is in line with other studies [88, 89]. However, there are also studies indicating a higher use of antipsychotics [90-92].

Nursing home patients are elderly, use many medications and are susceptible to the negative effects of antipsychotics [16]. Despite warnings, like the one from FDA about increased morbidity and mortality in dementia patients on antipsychotics [25], the use is frequent [90, 93]. Around 57% of the patients receiving antipsychotics in our study did not use it for an approved indication. Our figures are lower in comparison to a Canadian study [94], where 70-80% of the use was regarded as

potentially inappropriate. The Canadian data were, however, collected before the FDA-warnings.

We could see that the use of antipsychotics decreased with age, but increased with nursing home residency and number of drugs. Nursing home residents are usually sicker and patients with for example severe BPSD often have to move to a nursing home, which could be an explanation for this. Cognitive impairment was more common in the group receiving antipsychotics, which is in line with other studies [95, 96]. We could not see any differences between men and women regarding the use of antipsychotics. There are studies reporting both higher use in men [97] and the opposite [88].

A difficulty in comparing different studies concerning PIMs, is the different definitions used. Settings (assisted living or patients living at home) and what is being measured (individuals, prescriptions or DDD) can also differ. In our studies, we used the definition by the Swedish quality indicators [16] and included anticholinergics, tramadol, propiomazine, long-acting benzodiazepines, antipsychotics and NSAIDs.

Strengths

Paper I and II

The method used (self-assessment, peer review, feedback, and agreement for change) was developed and successfully implemented in hospital care. Even though this was a small pilot study, the participants came from both urban and rural areas in Sweden.

For paper I all interviews were done by the same interviewer, i.e. there was no need to calibrate answers from different interviewers. The answers from the interviews were also validated by triangulation with the surveys. The findings from the qualitative analysis were also reported back to the participants to see if they agreed, which they did.

The data in paper II came from the Swedish Prescribed Drug Register; a register that provides complete national data on the number of individuals exposed to dispensed drugs in the Swedish population. This register covers all prescription drugs, irrespective of reimbursement status.

Paper III and IV

The analyzed medication reviews were performed in everyday care using a standardized method (LIMM). The participants came from different primary care units all over Skåne, thus involving a non-selected group of patients as well as many GPs, nurses and pharmacists. Nurses with direct contact with the patients did the symptom assessment (PHASE-20), which ensure a correct description of their symptoms. All medication reviews were performed as team-based discussions, i.e. a GP, nurse, pharmacist and sometimes a carer met. A majority of the nursing home residents receive multi-dose dispensed drugs and help with administration, which ensures correct medication lists and high compliance. This gave the pharmacist the possibility to give accurate advice on medication changes. Identification of DRPs was done according to a well-documented method (LIMM) using both medication lists and symptom assessments (PHASE-20).

Limitations

Paper I and II

The SÄKLÄK project was a small pilot study conducted within 10 primary care centers to evaluate if a method developed in hospital care is useful in primary care to improve medication use. This limits the opportunities to directly apply these results to primary care centers in Sweden or other countries.

The Swedish Prescribed Drug Register does not provide information on diagnosis or indication for the treatment. Therefore, even though PIMs are classified as inappropriate on a group level, there may be a rationale behind some of the "inappropriate" treatments found in the study.

NSAIDs are also available OTC in Sweden so the figures in paper II do not show the real use. However, since the intervention also targeted nurses and pharmacists, not only doctors, it might also have affected the OTC-use of NSAIDs. This remains yet to be proved.

The data delivered from the drug register contained a mix of dependent and independent observations, and therefore the possible hypothesis testing was somewhat restricted.

Paper III and IV

The pharmacist did not meet the patients and the preparation of the medication reviews was done without access to patient records, thus identifying potential DRPs. However, during the team-meeting, the GP had access to the patient records. Another limitation is the lack of follow-up in a majority of the medication reviews. The nurses were supposed to do this as a part of ordinary care. The evaluation might have been performed, but forwarding the results to the pharmacist was forgotten about. Since this was an evaluation of medication reviews in everyday practice, there were no extra resources for things such as reminders to nurses. Regarding follow-up, there is also a difficulty on how to decide on a suitable timeframe for this. For example, antipsychotics require a slow dosage tapering and this might not be possible in 4-8 weeks. These patients are also elderly and many other things, like for example infections, might influence the possibility to perform changes and do follow-up.

Another limitation could be the absence of a commonly used method for performing medication reviews and identifying PIMs. We used the Swedish quality indicators [16] as the base for our analysis since this was an evaluation of medication reviews performed according to a well-documented Swedish method (LIMM). These indicators are well-known and generally well accepted by Swedish GPs. On the other hand, criteria like STOPP/START, is not well-known in Sweden and according to a Dutch study [98], many identified DRPs were not associated with these criteria.

Conclusions

Drug-related problems are a big issue resulting in both decreased quality of life for affected patients and increased health care utilization, and thereby increased costs for society. Methods to improve the medication treatment of elderly patients are needed. We could show that unnecessary treatment is a common drug-related problem in nursing home residents. It is not uncommon for these patients to use 10 or more medications regularly; often potentially inappropriate medications. One way to improve the situation is multi-professional medication reviews. Antipsychotic drug use without an approved indication is also common in this group, despite the risks involved, and medication reviews can correct this.

Another problem for elderly patients is the lack of co-operation and information sharing between different levels of care. A method involving self-assessment, peer review, feedback and written agreements for change may promote this.

Future research

Since the population is getting older, further studies on how to optimize medication use among the elderly is important for future health care in general. Larger randomized controlled trials comparing different settings are needed, including studies addressing possible effects of medication reviews on health care utilization.

In Sweden medication reviews are mandatory for some groups but so far there is a lack of information on how patients and their relatives perceive medication reviews. If they are reluctant to participate in the intervention and the following changes, the doctors and nurses interest in medication reviews could diminish. On the other hand, if patients and their relatives appreciate the medication reviews, this might be a reason to further implement the intervention.

With more treatments available, both preventive and curative, elderly patients receive more medications and polypharmacy is prevalent. How elderly patients think about preventive medications is another area to explore.

Svensk sammanfattning

Över hela världen ökar den äldre befolkningen, så även i Sverige. Med ökad ålder ökar risken för sjukdomar och detta resulterar ofta i mer läkemedel. Vilket kan orsaka läkemedelsrelaterade problem, som in sin tur kan leda till ökat sjukvårdsutnyttjande. Detta kostar både i form av mänskligt lidande, t ex nedsatt livskvalitet, och i form av stora kostnader för samhället. Det är därför viktigt att utveckla och utvärdera metoder som kan förbättra läget.

Syftet med avhandlingen är att utvärdera metoder för att förbättra läkemedelsanvändningen hos äldre patienter i primärvård.

Delarbete I-II

De första två arbetena handlar om utvärdering av projektet Säker läkemedelsanvändning i primärvård (SÄKLÄK). SÄKLÄK är en metod bestående av självvärdering, extern kollegial granskning, feedback och överenskommelse om åtgärder. Metoden riktar sig till verksamhetsledningar på vårdcentraler, men förutsätter samarbete med specialistvård/sjukhus, apotek och kommun för genomförande. Totalt deltog tio vårdcentraler, fem i interventionsgruppen och fem i kontrollgruppen, spridda över Sverige.

Delarbete I är en kvalitativ utvärdering av deltagarnas uppfattning om metoden där 17 deltagare intervjuades. Texterna från intervjuerna tolkades med kvalitativ innehållsanalys. Deltagarna lyfte fram det tvärprofessionella arbetssättet som mycket positivt. Den externa granskningen sågs som en möjlighet att utbyta erfarenheter. Dock tog projektet mer tid än förväntat, bland annat att svara på självvärderingen och att hitta intresserade samarbetspartners. Samtidigt kunde tid investerad under interventionen ses som en möjlighet att senare spara tid genom tex bättre rutiner. Man upplevde också att en del av feedbacken handlade om en nivå över vårdcentralen, dvs sådant som de ej kunde påverka.

I delarbete II sågs en påverkan av SÄKLÄK på förskrivning av potentiellt olämpliga läkemedel (PIMs). Interventionen ledde till en minskning av PIMs på 22 % i interventionsgruppen, medan de i kontrollgruppen minskade 9 %. Alla grupper av PIMs minskade förutom antipsykotiska läkemedel i kontrollgruppen. En signifikant

minskning av medeldos/patient sågs i interventionsgruppen, men inte i kontrollgruppen.

Delarbete III-IV

Delarbete III-IV är analyser av läkemedelsgenomgångar gjorda i skånsk primärvård, framför allt på patienter i särskilt boende. Alla gjordes i form av teamgenomgångar, dvs läkare, sjuksköterska, apotekare och vissa fall även vårdpersonal, träffades för att diskutera potentiella problem och möjliga åtgärder.

I delarbete III var fokus på vanliga läkemedelsrelaterade problem (LRP), föreslagna åtgärder och genomförande av dessa. Patienterna var i genomsnitt 87,5 år, använde i snitt 11,3 läkemedel (variation mellan 1 och 35) och 61 % använde minst 10 läkemedel. Av dessa hade 84 % åtminstone ett LRP med ett snitt på 2,2 LRP/patient. De vanligaste LRP var onödig läkemedelsbehandling (39 %), för hög dos (21 %) och fel läkemedel (20 %). Den vanligaste åtgärden var utsättning av läkemedel. Läkemedelsgenomgångarna minskade andelen patienter med minst ett PIM ($p<0,001$) samt användningen av 3 eller fler psykofarmaka samtidigt ($p<0,001$).

Mycket talar för att det används för mycket neuroleptika på särskilda boenden, och ofta på oklar indikation. I delarbete IV analyseras effekten av läkemedelsgenomgångar på neuroleptikaanvändningen, samt även av hur mycket neuroleptika som används och på vilka indikationer. Läkemedelsgenomgångar minskade användningen av neuroleptika med 23 %. Av patienterna som använde neuroleptika var det 43 % som hade en godkänd indikation medan det för 15 % saknades indikation. Neuroleptikaanvändning var vanligare hos patienter på särskilt boende än hos hemmaboende patienter ($p<0,01$) och med ökat antal läkemedel ($p=0,001$). Det var också vanligare att patienter med nedsatt kognition, depressiva symtom och sömnproblem fick neuroleptika.

Patientnytta

Samhället och vården står inför en stor utmaning framöver, nämligen att möta behovet av vård och omsorg för gruppen multisjuka äldre, som beräknas öka de närmaste åren. Multisjuka äldre använder många läkemedel och utnyttjar sjukvården i hög utsträckning. Till stor del sköts dessa av primärvården och insatser där är därför viktiga. Läkemedelsgenomgångar kan vara ett sätt att förbättra situationen, metoder såsom SÄKLÄK ett annat.

Acknowledgements

I wish to express my sincere gratitude to all that have inspired and supported me during my work with this thesis, and especially to

Patrik Midlöv, my main supervisor, for guiding me through this journey with patience, intelligence and reliability.

Åsa Bondesson, my co-supervisor, for careful review of all my work and giving me other perspectives.

Nina Viberg, my co-supervisor, for support and valuable comments.

Kerstin Troein, for always being there to help and with time for a word.

The National Research School of General Practice: Lars Hjalmar Lindholm, Olov Rolandsson, Sigvard Mölstad, Cecilia Björkelund, Kristina Bengtsson Boström, Mats Foldevi, Maria Boström, Simon Griffin and Stuart Spencer and fellow PhD-students of the school. Thank you for interesting seminars and the possibility to international co-operation.

Professor John Chalmers, my Australian supervisor at the George Institute for Global Health. Thank you for your hospitality and all interesting discussions during my stay in Sydney. The visit in Sydney introduced me to a lot of interesting research and interesting people, and gave me new energy and interest both in my own research and in research in general.

My fellow PhD-students Beata, Moa, Mia, Helena for friendship and all our discussions about everything and anything.

Ulf Jacobsson, Anders Beckman and Kris Rogers, my co-authors and statistical gurus, for your patience with my questions and for helpful explanations.

Steven Gilliver and Patrick Reilly for language expertise.

My colleagues at the Department of Medicines Management and Informatics in Region Skåne, for your understanding and encouraging words along the way.

Näsets Läkargrupp, the primary care center where I work, for the flexibility with my schedule and encouragement along the way.

Ewa Karlsson and Maud Aronsson, previous managers, for encouragement during my early years of work.

Birgitta Danielsson and Jan Hasselström, co-authors in my first scientific paper, for introducing me to primary care research.

Lena Lennartsson for excellent aid in transcribing the interviews for paper I.

Margareta Troein Töllborn, my mother, for being my greatest supporter and for invaluable professional feedback on my work, including numerous proof readings.

Claes Lenander, my father, for love and support.

Karin Luton, my sister, for all support and invaluable help with the English language.

My family and friends, for giving me other perspectives and a helping hand.

Julius and Gustav, my sons, for being my everything and reminding me what is really important in life.

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. **Statistics Sweden,** Available from: [http://scb.se/sv_/Hitta-statistik/Statistik-efter-amne/Befolkning/Befolkningens-sammansattning/Befolkningsstatistik/25788/25795/Helarsstatistik---Riket/26040/] Accessed January 20, 2017.
3. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B: **Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study**. *Lancet* 2012, **380**(9836):37-43.
4. Strand LM, Morley PC, Cipolle RJ, Ramsey R, Lamsam GD: **Drug-related problems: their structure and function**. *DICP* 1990, **24**(11):1093-1097.
5. Beijer HJ, de Blaey CJ: **Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies**. *Pharm World Sci* 2002, **24**(2):46-54.
6. Davies EC, Green CF, Mottram DR, Rowe PH, Pirmohamed M: **Emergency re-admissions to hospital due to adverse drug reactions within 1 year of the index admission**. *Br J Clin Pharmacol* 2010, **70**(5):749-755.
7. Conforti A, Costantini D, Zanetti F, Moretti U, Grezzana M, Leone R: **Adverse drug reactions in older patients: an Italian observational prospective hospital study**. *Drug Healthc Patient Saf* 2012, **4**:75-80.
8. Franceschi M, Scarcelli C, Niro V, Seripa D, Pazienza AM, Pepe G, Colusso AM, Pacilli L, Pilotto A: **Prevalence, clinical features and avoidability of adverse drug reactions as cause of admission to a geriatric unit: a prospective study of 1756 patients**. *Drug safety* 2008, **31**(6):545-556.
9. Mannesse CK, Derkx FH, de Ridder MA, Man in 't Veld AJ, van der Cammen TJ: **Contribution of adverse drug reactions to hospital admission of older patients**. *Age Ageing* 2000, **29**(1):35-39.
10. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM: **Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients**. *BMJ* 2004, **329**(7456):15-19.
11. Baena MI, Fajardo PC, Pintor-Marmol A, Faus MJ, Marin R, Zarzuelo A, Martinez-Olmos J, Martinez-Martinez F: **Negative clinical outcomes of medication resulting in emergency department visits**. *Eur J Clin Pharmacol* 2014, **70**(1):79-87.
12. Tjia J, Velten SJ, Parsons C, Valluri S, Briesacher BA: **Studies to reduce unnecessary medication use in frail older adults: a systematic review**. *Drugs Aging* 2013, **30**(5):285-307.

13. Maher RL, Hanlon J, Hajjar ER: **Clinical consequences of polypharmacy in elderly**. *Expert Opin Drug Saf* 2014, **13**(1):57-65.
14. Patterson SM, Cadogan CA, Kerse N, Cardwell CR, Bradley MC, Ryan C, Hughes C: **Interventions to improve the appropriate use of polypharmacy for older people**. *Cochrane Database Syst Rev* 2014(10):CD008165.
15. Swedish National Board of Health and Welfare: **Öppna jämförelser.** Availbale from: [http://oppnajamforelser.socialstyrelsen.se/halsoochsjukvard/Sidor/default.aspx] Accessed January 20, 2017.
16. Swedish National Board of Health and Welfare: **[Indicators for the evaluation of quality in drug use of the elderly]**. 2010.
17. **American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults**. *J Am Geriatr Soc* 2015, **63**(11):2227-2246.
18. Fick DM, Semla TP: **2012 American Geriatrics Society Beers Criteria: new year, new criteria, new perspective**. *J Am Geriatr Soc* 2012, **60**(4):614-615.
19. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P: **STOPP/START criteria for potentially inappropriate prescribing in older people: version 2**. *Age Ageing* 2015, **44**(2):213-218.
20. Rognstad S, Brekke M, Fetveit A, Spigset O, Wyller TB, Straand J: **The Norwegian General Practice (NORGEP) criteria for assessing potentially inappropriate prescriptions to elderly patients. A modified Delphi study**. *Scand J Prim Health Care* 2009, **27**(3):153-159.
21. Renom-Guiteras A, Meyer G, Thurmann PA: **The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries**. *Eur J Clin Pharmacol* 2015, **71**(7):861-875.
22. Hanlon JT, Schmader KE, Samsa GP, Weinberger M, Uttech KM, Lewis IK, Cohen HJ, Feussner JR: **A method for assessing drug therapy appropriateness**. *J Clin Epidemiol* 1992, **45**(10):1045-1051.
23. Samsa GP, Hanlon JT, Schmader KE, Weinberger M, Clipp EC, Uttech KM, Lewis IK, Landsman PB, Cohen HJ: **A summated score for the medication appropriateness index: development and assessment of clinimetric properties including content validity**. *J Clin Epidemiol* 1994, **47**(8):891-896.
24. Schneider LS, Dagerman KS, Insel P: **Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials**. *Jama* 2005, **294**(15):1934-1943.
25. US Food and Drug Administration: **Information for Healthcare Professionals: Conventional Antipsychotics.** Available from: [http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124830.htm] Accessed January 20, 2017.
26. Swedish National Board of Health and Welfare: **Quality of drug use in elderly patients [Kvaliteten i äldres läkemedelsanvändning - KÄLLA-projektet]**. 2004.
27. 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.

28. Shah SM, Carey IM, Harris T, Dewilde S, Cook DG: **Antipsychotic prescribing to older people living in care homes and the community in England and Wales**. *Int J Geriatr Psychiatry* 2011, **26**(4):423-434.
29. Seitz DP, Gill SS, Herrmann N, Brisbin S, Rapoport MJ, Rines J, Wilson K, Le Clair K, Conn DK: **Pharmacological treatments for neuropsychiatric symptoms of dementia in long-term care: a systematic review**. *Int Psychogeriatr* 2013, **25**(2):185-203.
30. Midlov P, Bergkvist A, Bondesson A, Eriksson T, Hoglund P: **Medication errors when transferring elderly patients between primary health care and hospital care**. *Pharm World Sci* 2005, **27**(2):116-120.
31. Midlov P, Holmdahl L, Eriksson T, Bergkvist A, Ljungberg B, Widner H, Nerbrand C, Hoglund P: **Medication report reduces number of medication errors when elderly patients are discharged from hospital**. *Pharm World Sci* 2008, **30**(1):92-98.
32. The Swedish Council on Technology Assessment in Health Care: **[Use of medications in elderly: how can it be improved? A systematic litterature review.]**. SBU; 2009.
33. Anell A, Glenngard AH, Merkur S: **Sweden health system review**. *Health Syst Transit* 2012, **14**(5):1-159.
34. Al-Jumaili AA, Doucette WR: **Comprehensive Literature Review of Factors Influencing Medication Safety in Nursing Homes: Using a Systems Model**. *J Am Med Dir Assoc* 2017.
35. Scott IA, Hilmer SN, Reeve E, Potter K, Le Couteur D, Rigby D, Gnjidic D, Del Mar CB, Roughead EE, Page A *et al*: **Reducing inappropriate polypharmacy: the process of deprescribing**. *JAMA Intern Med* 2015, **175**(5):827-834.
36. Cassels A: **"Can I ever stop even one of these pills?" The developement of a tool to make deprescribing easier**. *Eur J Hosp Pharm* 2017, **24**:3-4.
37. Cipolle RJ, Strand LM, PC M: **Pharmaceutical care practice.** New York: The McGraw-Hill Companies Inc; 1998.
38. Bergkvist A, Midlov P, Hoglund P, Larsson L, Eriksson T: **A multi-intervention approach on drug therapy can lead to a more appropriate drug use in the elderly. LIMM-Landskrona Integrated Medicines Management**. *J Eval Clin Pract* 2009, **15**(4):660-667.
39. Spinewine A, Swine C, Dhillon S, Lambert P, Nachega JB, Wilmotte L, Tulkens PM: **Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial**. *J Am Geriatr Soc* 2007, **55**(5):658-665.
40. Gillespie U, Alassaad A, Henrohn D, Garmo H, Hammarlund-Udenaes M, Toss H, Kettis-Lindblad A, Melhus H, Morlin C: **A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial**. *Arch Intern Med* 2009, **169**(9):894-900.
41. Milos V, Rekman E, Bondesson A, Eriksson T, Jakobsson U, Westerlund T, Midlov P: **Improving the Quality of Pharmacotherapy in Elderly Primary Care Patients Through Medication Reviews: A Randomised Controlled Study**. *Drugs Aging* 2013.

42. Lenander C, Elfsson B, Danielsson B, Midlov P, Hasselstrom J: **Effects of a pharmacist-led structured medication review in primary care on drug-related problems and hospital admission rates: a randomized controlled trial**. *Scand J Prim Health Care* 2014, **32**(4):180-186.
43. Malet-Larrea A, Goyenechea E, Gastelurrutia MA, Calvo B, Garcia-Cardenas V, Cabases JM, Noain A, Martinez-Martinez F, Sabater-Hernandez D, Benrimoj SI: **Cost analysis and cost-benefit analysis of a medication review with follow-up service in aged polypharmacy patients**. *Eur J Health Econ* 2016.
44. Frankenthal D, Israeli A, Caraco Y, Lerman Y, Kalendaryev E, Zandman-Goddard G, Lerman Y: **Long-Term Outcomes of Medication Intervention Using the Screening Tool of Older Persons Potentially Inappropriate Prescriptions Screening Tool to Alert Doctors to Right Treatment Criteria**. *J Am Geriatr Soc* 2016.
45. **Socialstyrelsens föreskrifter om ändring i föreskrifterna och allmänna råden (SOSFS 2000:1) om läkemdelshantering i hälso- och sjukvården [Elektronisk resurs]**: Socialstyrelsen; 2012.
46. Nystrom ME, Westerlund A, Hoog E, Millde-Luthander C, Hogberg U, Grunewald C: **Healthcare system intervention for prevention of birth injuries - process evaluation of self-assessment, peer review, feedback and agreement for change**. *BMC Health Serv Res* 2012, **12**:274.
47. W-Dahl A, Robertsson O, Stefansdottir A, Gustafson P, Lidgren L: **Timing of preoperative antibiotics for knee arthroplasties: Improving the routines in Sweden**. *Patient Saf Surg* 2011, **5**:22.
48. Swedish National Board of Health and Welfare: **[Statistics on assisted living]**. Stockholm; 2016.
49. Lagergren M: **The systems of care for frail elderly persons: the case of Sweden**. *Aging Clin Exp Res* 2002, **14**(4):252-257.
50. Katz PR: **An international perspective on long term care: focus on nursing homes**. *J Am Med Dir Assoc* 2011, **12**(7):487-492.e481.
51. Tolson D, Rolland Y, Katz PR, Woo J, Morley JE, Vellas B: **An international survey of nursing homes**. *J Am Med Dir Assoc* 2013, **14**(7):459-462.
52. Bergstrand BO, Staaf A: **Socialtjänstlagen 2016**. Helsingborg: Komlitt; 2016.
53. Swedish National Board of Health and Welfare: **Öppna Jämförelser 2016: Vård och omsorg om äldre - jämförelser mellan kommuner och landsting**. 2017.
54. WHO: **Anatomical Therapeutic Chemical Classification System [online]** Available from: [http://www.who.int/classifications/atcddd/en] Accessed January 20, 2017.
55. Hellstrom LM, Bondesson A, Hoglund P, Midlov P, Holmdahl L, Rickhag E, Eriksson T: **Impact of the Lund Integrated Medicines Management (LIMM) model on medication appropriateness and drug-related hospital revisits**. *Eur J Clin Pharmacol* 2011, **67**(7):741-752.
56. Hedström M, Lidström B, Hulter-Åsberg K: **PHASE-20: a new instrument for assessment of possible therapeutic drug-related symptoms among elderly in nursing homes [in Swedish]**. *Nordic Journal of Nursing Research and Clinical Studies (Vård i Norden)* 2009, **4**:9-14.

57. **PHASE-20** Available from: [http://www.lul.se/phase-20english] Accessed January 20, 2017.
58. Hsieh HF, Shannon SE: **Three approaches to qualitative content analysis**. *Qual Health Res* 2005, **15**(9):1277-1288.
59. Graneheim UH, Lundman B: **Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness**. *Nurse Educ Today* 2004, **24**(2):105-112.
60. IBM Corp.: **IBM SPSS Statistics for Windows, Version 22.0.** Armonk, NY; 2013.
61. Social Science Statistics: **Chi-square Calculator** Available from: [http://www.socscistatistics.com/tests/chisquare/default2.aspx] Accessed May 06, 2015.
62. Bland JM, Altman DG: **Multiple significance tests: the Bonferroni method**. *BMJ* 1995, **310**(6973):170.
63. Brulhart MI, Wermeille JP: **Multidisciplinary medication review: evaluation of a pharmaceutical care model for nursing homes**. *Int J Clin Pharm* 2011, **33**(3):549-557.
64. Finkers F, Maring JG, Boersma F, Taxis K: **A study of medication reviews to identify drug-related problems of polypharmacy patients in the Dutch nursing home setting**. *J Clin Pharm Ther* 2007, **32**(5):469-476.
65. Kruger K, Strand L, Geitung JT, Eide GE, Grimsmo A: **Can electronic tools help improve nursing home quality?** *ISRN nursing* 2011, **2011**:208142.
66. Midlov P, Bondesson A, Eriksson T, Nerbrand C, Hoglund P: **Effects of educational outreach visits on prescribing of benzodiazepines and antipsychotic drugs to elderly patients in primary health care in southern Sweden**. *Fam Pract* 2006, **23**(1):60-64.
67. Page AT, Clifford RM, Potter K, Schwartz D, Etherton-Beer CD: **The feasibility and effect of deprescribing in older adults on mortality and health: a systematic review and meta-analysis**. *Br J Clin Pharmacol* 2016, **82**(3):583-623.
68. Sinnott C, Mc Hugh S, Browne J, Bradley C: **GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research**. *BMJ open* 2013, **3**(9):e003610.
69. Zink K, Schmidt A: **Practice and implementation of self-assessment**. *Int J Qual Sci* 1998, **3**(2):147-170.
70. Davies C: **Getting health professionals to work together**. *BMJ* 2000, **320**(7241):1021-1022.
71. Bergquist M, Ljungberg J, Lundh-Snis U: **Practising peer review in organisations: a qualifier for knowledge dissemination and legitimization**. *J Info Tech* 2001, **16**:99-112.
72. Meeks DW, Meyer AN, Rose B, Walker YN, Singh H: **Exploring new avenues to assess the sharp end of patient safety: an analysis of nationally aggregated peer review data**. *BMJ quality & safety* 2014, **23**(12):1023-1030.
73. Swedish National Board of Health and Welfare: **[Open comparisons Drug use]**. Stockholm; 2014.

74. Aparasu RR, Mort JR: **Inappropriate prescribing for the elderly: beers criteria-based review**. *Ann Pharmacother* 2000, **34**(3):338-346.

75. Johnell K, Weitoft GR, Fastbom J: **Sex differences in inappropriate drug use: a register-based study of over 600,000 older people**. *Ann Pharmacother* 2009, **43**(7):1233-1238.

76. Maio V, Yuen EJ, Novielli K, Smith KD, Louis DZ: **Potentially inappropriate medication prescribing for elderly outpatients in Emilia Romagna, Italy: a population-based cohort study**. *Drugs Aging* 2006, **23**(11):915-924.

77. 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.

78. Bergman A, Olsson J, Carlsten A, Waern M, Fastbom J: **Evaluation of the quality of drug therapy among elderly patients in nursing homes**. *Scand J Prim Health Care* 2007, **25**(1):9-14.

79. Hohl CM, Wickham ME, Sobolev B, Perry JJ, Sivilotti ML, Garrison S, Lang E, Brasher P, Doyle-Waters MM, Brar B *et al*: **The effect of early in-hospital medication review on health outcomes: a systematic review**. *Br J Clin Pharmacol* 2015, **80**(1):51-61.

80. Hohl CM, Partovi N, Ghement I, Wickham ME, McGrail K, Reddekopp LN, Sobolev B: **Impact of early in-hospital medication review by clinical pharmacists on health services utilization**. *PloS one* 2017, **12**(2):e0170495.

81. Zermansky AG, Alldred DP, Petty DR, Raynor DK, Freemantle N, Eastaugh J, Bowie P: **Clinical medication review by a pharmacist of elderly people living in care homes--randomised controlled trial**. *Age Ageing* 2006, **35**(6):586-591.

82. 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.

83. Reich O, Rosemann T, Rapold R, Blozik E, Senn O: **Potentially inappropriate medication use in older patients in Swiss managed care plans: prevalence, determinants and association with hospitalization**. *PloS one* 2014, **9**(8):e105425.

84. Palladino R, Lee JT, Millett C: **Association between multimorbidity and healthcare utilisation and health outcomes among elderly people in Europe**. In: *7th European Public Health Conference: 20 November, 2014; Glasgow, Scotland*. 2014.

85. Gheewala PA, Peterson GM, Curtain CM, Nishtala PS, Hannan PJ, Castelino RL: **Impact of the pharmacist medication review services on drug-related problems and potentially inappropriate prescribing of renally cleared medications in residents of aged care facilities**. *Drugs Aging* 2014, **31**(11):825-835.

86. Bahler C, Huber CA, Brungger B, Reich O: **Multimorbidity, health care utilization and costs in an elderly community-dwelling population: a claims data based observational study**. *BMC Health Serv Res* 2015, **15**:23.

87. Modig S, Holmdahl L, Bondesson A: **Medication reviews in primary care in Sweden: importance of clinical pharmacists' recommendations on drug-related problems**. *Int J Clin Pharm* 2016, **38**(1):41-45.

88. Vidal X, Agusti A, Vallano A, Formiga F, Moyano AF, Garcia J, Lopez-Soto A, Ramirez-Duque N, Torres OH, Barbe J *et al*: **Elderly patients treated with psychotropic medicines admitted to hospital: associated characteristics and inappropriate use**. *Eur J Clin Pharmacol* 2016, **72**(6):755-764.

89. Breining A, Bonnet-Zamponi D, Zerah L, Micheneau C, Riolacci-Dhoyen N, Chan-Chee C, Deligne J, Harlin JM, Boddaert J, Verny M *et al*: **Exposure to psychotropics in the French older population living with dementia: a nationwide population-based study**. *Int J Geriatr Psychiatry* 2016.

90. Frankenthal D, Zandman-Goddard G, Ben-Muvhar Y, Porat-Katz BS: **The impact of facility characteristics on the use of antipsychotic medications in nursing homes: a cross-sectional study**. *Isr J Health Policy Res* 2016, **5**:12.

91. Taxis K, Kochen S, Wouters H, Boersma F, Jan Gerard M, Mulder H, Pavlovic J, Stevens G, Andrew M, Pont LG: **Cross-national comparison of medication use in Australian and Dutch nursing homes**. *Age Ageing* 2017.

92. Azermai M, Elseviers M, Petrovic M, van Bortel L, Stichele RV: **Assessment of antipsychotic prescribing in Belgian nursing homes**. *Int Psychogeriatr* 2011, **23**(8):1240-1248.

93. Ballard C, Howard R: **Neuroleptic drugs in dementia: benefits and harm**. *Nat Rev Neurosci* 2006, **7**(6):492-500.

94. Stock KJ, Amuah JE, Lapane KL, Hogan DB, Maxwell CJ: **Prevalence of, and Resident and Facility Characteristics Associated With Antipsychotic Use in Assisted Living vs. Long-Term Care Facilities: A Cross-Sectional Analysis from Alberta, Canada**. *Drugs Aging* 2016.

95. Kruger K, Folkestad M, Geitung JT, Eide GE, Grimsmo A: **Psychoactive drugs in seven nursing homes**. *Prim Health Care Res Dev* 2012, **13**(3):244-254.

96. Jacquin-Piques A, Sacco G, Tavassoli N, Rouaud O, Bejot Y, Giroud M, Robert P, Vellas B, Bonin-Guillaume S: **Psychotropic Drug Prescription in Patients with Dementia: Nursing Home Residents Versus Patients Living at Home**. *J Alzheimers Dis* 2015, **49**(3):671-680.

97. Kamble P, Chen H, Sherer J, Aparasu RR: **Antipsychotic drug use among elderly nursing home residents in the United States**. *Am J Geriatr Pharmacother* 2008, **6**(4):187-197.

98. Verdoorn S, Kwint HF, Faber A, Gussekloo J, Bouvy ML: **Majority of drug-related problems identified during medication review are not associated with STOPP/START criteria**. *Eur J Clin Pharmacol* 2015, **71**(10):1255-1262.

99. Prince RL, Devine A, Dhaliwal SS, Dick IM: **Effects of calcium supplementation on clinical fracture and bone structure: results of a 5-year, double-blind, placebo-controlled trial in elderly women**. *Arch Intern Med* 2006, **166**(8):869-875.

100. Hansen RA, Kim MM, Song L, Tu W, Wu J, Murray MD: **Comparison of methods to assess medication adherence and classify nonadherence**. *Ann Pharmacother* 2009, **43**(3):413-422.

101. Osterberg L, Blaschke T: **Adherence to medication**. *New Engl J Med* 2005, **353**(5):487-497.

102. The Model of Care Polypharmacy Working Group: **Polypharmacy Guidance**. NHS Scotland; 2012.

103. Swedish Association of Local Authorities and Regions: **A Better Life for Elderly Sick People**. Stockholm; 2014.

104. Sjoberg C, Ohlsson H, Wallerstedt SM: **Association between multi-dose drug dispensing and drug treatment changes**. *Eur J Clin Pharmacol* 2012, **68**(7):1095-1101.

105. Sorensen L, Stokes JA, Purdie DM, Woodward M, Elliott R, Roberts MS: **Medication reviews in the community: results of a randomized, controlled effectiveness trial**. *Br J Clin Pharmacol* 2004, **58**(6):648-664.

106. Bergkvist Christensen A, Holmbjer L, Midlov P, Hoglund P, Larsson L, Bondesson A, Eriksson T: **The process of identifying, solving and preventing drug related problems in the LIMM-study**. *Int J Clin Pharm* 2011, **33**(6):1010-1018.

107. Blix HS, Viktil KK, Moger TA, Reikvam A: **Characteristics of drug-related problems discussed by hospital pharmacists in multidisciplinary teams**. *Pharm World Sci* 2006, **28**(3):152-158.

108. **American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults**. *J Am Geriatr Soc* 2012, **60**(4):616-631.

109. Berdot S, Bertrand M, Dartigues JF, Fourrier A, Tavernier B, Ritchie K, Alperovitch A: **Inappropriate medication use and risk of falls--a prospective study in a large community-dwelling elderly cohort**. *BMC Geriatr* 2009, **9**:30.

Appendix

Appendix 1. Interview guide.

1. Tell me something positive about participating in this project?

2. Tell me something negative about participating in this project?

3. How did you perceive the four steps of the process?

    - Self-assessment
    - Peer-review
    - Written feedback
    - Agreement for change

4. How did you perceive the co-operation with other professionals and staff?

5. How do you think participation in this project will affect work at your primary care centre?

6. If you had the power to decide, how would you organize the care for frail elderly with many diseases?

7. Do you have anything else you would like to add?

Each question was followed by exploring questions, for example “Can you tell me more about that?” or “Can you give me an example?”

Paper I

Lenander et al. BMC Family Practice (2015) 16:117
DOI 10.1186/s12875-015-0334-6

BMC Family Practice

RESEARCH ARTICLE Open Access

Healthcare system intervention for safer use of medicines in elderly patients in primary care—a qualitative study of the participants' perceptions of self-assessment, peer review, feedback and agreement for change

Cecilia Lenander[1*], Åsa Bondesson[2], Patrik Midlöv[1] and Nina Viberg[1,3]

Abstract

Background: The elderly population is increasing and with advanced age comes a higher risk for contracting diseases and excessive medicine use. Polypharmacy can lead to drug-related problems and an increased need of health care. More needs to be done to help overcome these problems. In order for new models to be successful and possible to implement in health care they have to be accepted by caregivers. The aim of this study was to evaluate participants' perceptions of the SÄKLÄK project, which aims to enhance medication safety, especially for elderly patients, in primary care.

Methods: This is a qualitative study within the SÄKLÄK project. The SÄKLÄK project is a multi-professional intervention in primary care consisting of self-assessment, peer review, feedback and written agreements for change. A total of 17 participants from the intervention's primary care units were interviewed. Most of the interviews were done on a one-to-one basis. The interviews were recorded and transcribed verbatim. A survey was also sent to the primary care unit heads. Qualitative content analysis was used to explore the participants' perceptions.

Results: The analysis of the interviews yielded six categories: *multi-professional co-operation*, *a focus on areas of improvement*, *the joy of sharing knowledge*, *disappointment with the focus of the feedback*, *spend time to save time and impact on work*. From these categories a theme developed: "Medication safety is a large area. In order to make improvements time needs to be invested and different professions must contribute."

Conclusions: This study shows that our studied intervention method is feasible to use in primary care and that the multi-professional approach was perceived as being very positive by the participants. Multi-professional co-operation was time consuming, but was also deemed as an investment and an opportunity to share knowledge. Some points of improvement of the method were identified such as simplification of the self-assessment form and clearer instructions for reviewers. In addition, to have an impact on work the focus must lie in areas within the primary care units' scope.

* Correspondence: cecilia.lenander@med.lu.se
[1]Department of Clinical Sciences in Malmö, Lund University, Jan Waldenströms gata 35, SE-205 02 Malmö, Sweden
Full list of author information is available at the end of the article

Background

The elderly population is increasing worldwide and statistical demographic data suggest that ~22 % of the global population will be older than 65 years of age by 2050 [1]. In Sweden, the proportion of the population aged 65 years or older was 19.4 % in 2013 [2]. Ageing is known to be associated with an increased prevalence of multiple chronic diseases and as a result the use of more medications. Elderly patients with multiple diseases and polypharmacy risk suffering from drug-related problems. Previous studies have found that a significant proportion of hospital admissions among elderly people are due to adverse drug events (ADEs) [3–7]. Indicators of prescribing quality for drug treatment in the elderly have been developed in Sweden [8], as is the case in other countries [9] Elderly patients with multiple diseases and polypharmacy often have several prescribers. With many different systems for documentation, there is a big risk of medication errors, especially when these elderly patients are transferred from, for example, hospital care to primary care [10, 11]. General practitioners (GPs) are central to this work since they often have overall responsibility for these patients. If they do not have information about current drug use and take it in to account when prescribing, the risk of ADEs increases and compliance can decrease. Noncompliance can increase morbidity and thereby increase health care utilisation [12–14]. Different approaches to overcoming these problems have been tried [15], but more must be done in terms of, for example, co-operation between primary care and municipally provided home care [16]. A multidisciplinary approach to managing polypharmacy has been recommended in other countries, such as the United Kingdom [17]. No single intervention will solve all problems. Multiple interventions are needed instead [18].

The present study aimed to elucidate participants' perceptions of the SÄKLÄK project, an intervention model created to improve medication safety for elderly patients in primary care.

The intervention model was originally developed for, and successfully implemented in, hospital care, to prevent birth injuries [19]. The model was then tested in orthopaedic surgery (PRISS) [20] and also in an ongoing project to improve abdominal surgery. For an intervention to be successful and possible to implement in health care it has to be accepted by the health care staff. The rationale for performing the entire SÄKLÄK project was to see if an improvement methodology, i.e. internal quality monitoring followed by external audit/peer review, can be applied in different settings. The intervention was adapted to primary care by the participating professional organisations (The Swedish College of General Practice, The Swedish Pharmaceutical Society, Geriatric Medicine in Sweden, Riksföreningen för Medicinskt Ansvariga Sjuksköterskor (a Swedish association of authorised nurses), Sweden's National Organisation of District Nurses and The Swedish Society of Clinical Pharmacology and Therapeutics) and consists of self-assessment followed by peer review, feedback and a written agreement for change.

The aim of this study was to elucidate how the participants perceived a multi-professional intervention consisting of self-assessment, peer review, feedback and agreement for change.

Methods

We did a qualitative study based on individual, semi-structured interviews supplemented with a survey. The interviews were analysed by manifest and latent qualitative content analysis to derive the participants' experiences of a multi-professional project to enhance medication safety in elderly patients. The results from the interviews were triangulated with the survey responses.

Setting

The interviews were performed with participants in the intervention group of the SÄKLÄK project. The survey was sent to the managers at the five intervention primary care units.

Intervention model (SÄKLÄK project)

The SÄKLÄK project was initiated by the Swedish Association of Local Authorities and Regions (SALAR) and The Patient Insurance LÖF. The steering committee of the project consisted of one delegate each from six professional organisations (The Swedish College of General Practice, The Swedish Pharmaceutical Society, Geriatric Medicine in Sweden, Riksföreningen för Medicinskt Ansvariga Sjuksköterskor (a Swedish association of authorised nurses), Sweden's National Organisation of District Nurses and The Swedish Society of Clinical Pharmacology and Therapeutics). The SÄKLÄK project was a pilot study to determine whether an intervention model (see Table 1), developed in hospital care, could be used in primary care to enhance medication safety in elderly patients. Based on previous studies [19, 20] it was concluded that self-assessment was valuable, that external peer reviews prevent postponing of the self-assessment and that the review process supports ongoing improvement and encourages new improvement projects. It was also noted that reviewers learn a lot, become aware of patient safety risks in their clinics and bring improvement ideas back to their clinics. However, the reviewers need to receive clear instructions to focus on achievable goals.

The aim of the SÄKLÄK project was to reduce medication errors and drug-related problems.

Table 1 Description of the different parts of the tested intervention model (SÄKLÄK)

1. Introductory meeting	Representatives from the steering committee[a] visited the primary care units, gave a structured introduction and presented the intervention model for unit managers and staff representatives, including nurses working in home care and pharmacists. The involvement of all professional categories was presented as a prerequisite for the self-assessment process.
2. Structured self-assessment	The self-assessment was developed by an expert group, appointed by the steering committee[a]. It contained 12 questions covering areas of importance for safe use of medications in primary care, with focus on elderly patients with multiple diseases. The areas covered were: prescribing of drugs, follow-up, medication reviews, environmental aspects, co-operation with specialized care, pharmacies and communal home care. For each of the 12 questions, five follow-up questions were asked: 1. What methods/routines/guidelines do you have? 2. How do you provide conditions to ensure compliance? 3. How do you measure compliance? 4. How do you give feedback on the results to the staff? 5. What ideas do you have for improvement?
3. Peer review	A group of doctors, nurses and pharmacists selected by the professional organisations[b] served as reviewers. For each primary care unit, a peer-review team consisting of five to six reviewers with different professions was formed at a seminar 4 months after the project was initiated. At this meeting the teams discussed the answered self-assessments and how to conduct the site visits. The primary care units were visited by a peer-review team 5 months after the project was initiated. A document based on the questions used in the self-assessment procedure served as support for the peer review. New or updated information arising during the visit or in dialogue with the primary care unit was noted in this document.
4. Written feedback and agreement for change	The peer-review team presented a written feedback report regarding their view on strengths and weaknesses, priority areas for improvement and proposed measures to be taken. Eventually, a written contract consisting of a detailed action plan was jointly produced by the primary care unit and the peer-review team.
5. Follow-up seminar	A seminar for the steering committee, the reviewers and all managers at the intervention primary care units.
6. Follow up on accomplishment of agreements	The agreements for change were to be followed up on 6 months after they were signed.

[a]The steering committee comprised representatives from the Swedish Association of Local Authorities and Regions (SALAR) and The Patient Insurance LÖF and one delegate each from the six professional organisations listed below
[b]The Swedish College of General Practice, The Swedish Pharmaceutical Society, Geriatric Medicine in Sweden, Riksföreningen för Medicinskt Ansvariga Sjuksköterskor (a Swedish association of authorized nurses), Sweden's National Organisation of District Nurses and The Swedish Society of Clinical Pharmacology and Therapeutics

The first step of the intervention was a self-assessment questionnaire, with questions on how patient safety is secured during prescribing of medication, medication use and follow up, at the primary care centre and in co-operation with pharmacies/hospitals/municipally provided home care. The questions were focused on frail elderly people, on how conditions are to be provided for different measures of importance and, not least, how it is ensured that these measures are being followed. A group of selected doctors, nurses and pharmacists, with vast experience in elderly care, served as reviewers in the second step of the intervention. The assessment by the reviewers comprised of:

- Receiving and analysing of self-assessment forms, and discussion of these
- Visits to primary care units with opportunities to ask questions and share their views
- Feedback and agreement for change

Supported by written instructions, documents and continuous contact with the project management the reviewers analysed the self-assessments and any additional material supplied by the primary care units. They had the possibility to get clarifications on their questions during site visits. Thereafter the reviewers produced a written feedback report for the primary care unit, and the reviewers and the management at the primary care unit agreed on an action plan for improvements. The procedures of the intervention model are described in Table 1 and Fig. 1. Invitations to participate were emailed to all primary care units in Sweden (approximately 1200) and participation was open to all. A total of 20 units applied and they were stratified according to urban or rural location. A random sample of 10 units was drawn using Excel. Five units were randomised to the intervention group and five to the control group, keeping the distribution between urban and rural units. The control units were recruited for later comparison on quantitative data (not yet available).

Interviews

At the five intervention primary care centres, the managers were asked to identify individuals who had had an active role in answering the self-assessment questions and to invite them to be interviewed. A total of 17 persons

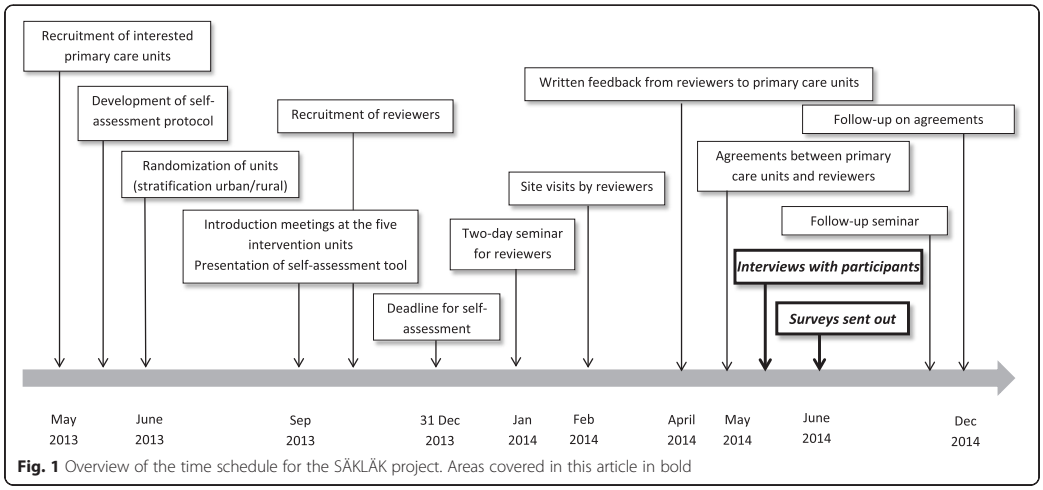


Fig. 1 Overview of the time schedule for the SÄKLÄK project. Areas covered in this article in bold

participated in 15 interviews (two interviews were held with two subjects together). Furthermore, 13 of the interviews were performed face-to-face at the primary care centres and two were conducted via telephone (see Table 2 for more information).

All interviews were performed by the first author (C.L.). The interviews were conducted with an interview guide (Additional file 1) and lasted for between 8 and 36 min. Questions were asked regarding, for example, positive and negative experiences of participating in the project, perceptions of the different steps of the project and collaboration between different professionals. The interviewer is a clinical pharmacist and has 15 years of experience working with elderly patients and their medication use at pharmacies, in hospital care and in primary care. Prior to the interview process the interviewer completed a course for doctoral students in qualitative methods, including interview techniques. One of the authors (NV) is experienced in interview studies and provided supervision. All interviews were recorded and transcribed verbatim.

Table 2 Presentation of the interviewees

Occupation	Years in current position	Gender	Interview	Location
General practitioner	17	Female	Face-to-face	Urban
Head of primary care centre	1	Female	Face-to-face	Urban
District nurse	30	Female	Face-to-face	Urban
District nurse working in municipally provided home care	6	Female	Face-to-face	Urban
Pharmacist working at a pharmacy	20	Female	Face-to-face	Urban
Pharmacist working at primary care centre	1	Female	Face-to-face	Urban
General practitioner	14	Male	Face-to-face	Urban
District nurse	42	Female	Face-to-face	Urban
General practitioner	25	Male	Face-to-face	Urban
Head of primary care centre	4.5	Female	Face-to-face	Urban
Two district nurses working in municipally provided home care	4	Females	Face-to-face	Urban
Head of primary care centre	4.5	Female	Face-to-face	Rural
District nurse	3	Female	Face-to-face	Rural
MAS[a] (nurse)	12	Female	Telephone	Rural
Head of primary care centre	-	Female	Telephone	Urban
Administrator	-	Female		

[a]A nurse with responsibility for health care in the municipality

Analysis of interviews

The transcribed interviews were subjected to qualitative content analysis, a research method for interpreting the content of text data through systematic classification by coding and identifying themes or patterns [21]. The analysis was performed in several steps and was initiated before all interviews had been conducted. After reading the text several times to get a sense of the whole, the text was divided into meaning units. These meaning units could be words, sentences or paragraphs containing aspects related to each other through their content and context. The meaning units were condensed and thereafter coded. The codes were then sorted into categories. A deeper analysis was thereafter performed to find the latent meaning of the interviews, giving a theme [22]. The analysis started as soon as the first interview was transcribed. Thereafter the analysis ran parallel to the interviews and after 15 interviews saturation was reached. The codes and categories were not predefined, but instead developed during the analysis (Table 3). To enhance trustworthiness, the codes and categories were discussed within the research group throughout the analysis process. The findings are illustrated by citations from the interviews to show that the findings derive from the data. The citations have been translated from Swedish. All citations can be tracked by a letter identifying the interviewed individual, and a number indicating the line in the transcribed interview.

Surveys

At the end of the SÄKLÄK project a survey was sent to the heads of each of the five intervention primary care units. The survey was a web questionnaire and contained questions about how the heads perceived the initial information regarding the project, the different components of the project and the support available. It included both multiple choice and open-ended questions (Additional file 2). The survey was based on the survey questions used in the birth injury-project [19] in order to make a comparison between the projects possible. The survey responses were carefully read and compared with the findings from the interviews.

Validation

The results of the qualitative analysis were reported to the managers, the reviewers representing different professional organisations, and the SÄKLÄK project steering committee at a follow-up seminar.

Ethical considerations

Approval was granted by the Research Ethics Review Board in Lund (reference no. 2013/333). Participation in the study was based on informed consent. Consent to publish was obtained from all interviewees (Table 2).

Results

Based on identified categories a theme emerged: "Medication safety is a large area. In order to make improvements time needs to be invested and different professions must contribute." (Table 3).

Table 3 Example of how findings were yielded from the analytical process, showing some of the many meaning units that built up the categories and the theme

Meaning unit	Condensed meaning unit	Code	Category	Theme
To see all this and to listen to other people participating, to listen to their ways of seeing things	Listen to other people's way of seeing things	Co-operation	Multi-professional co-operation	Medication safety is a large area. In order to make improvements time needs to be invested and different professions must contribute
I cannot make progress in this matter, but is there someone else who has managed it, and if so, how?	Helping each other	Knowledge sharing	The joy of sharing knowledge	
It was quite comprehensive, so it took a lot of time to go through it all and answer all the questions	Comprehensive form and time-consuming to answer	Time-consuming	Spend time to save time	
It costs energy right now, but if we can improve our routines and follow them… then I think it will pay off in the long run	Investing time now will save time later	Time-saving		
Not that I clearly felt that we were talking about the answers in our self-assessment report	Not talking about the same things	Disappointment	Disappointment with the focus of the feedback	
I think it was really good to see it in print, what's working and what's not, and what we can improve	What's working and what's not, and improvements	Strengths and weaknesses	A focus on areas of improvement	
Yes, concerning medication reviews I think so […] we can surely perform many more of these	Perform many more of these	Change of routines	Impact on work	

Interviews

The qualitative content analysis of the interviews yielded six categories.

Multi-professional co-operation

The participants noted the project's multi-professional approach as something very positive. It was an opportunity to invite people from the pharmacy, the hospital and municipal home care to engage in closer co-operation, to meet face to face.

As one respondent said:

"…the most positive part has been working with the self-assessment, working multi-professionally and getting a better understanding of each other's work." (primary care unit head, C4)

The multi-professional approach seems to have given the participants a chance to meet in person and discuss questions of importance for medication safety. Many of them said that they had been working "together" for a long time, but now realised it was more side-by-side than real co-operation.

"…I have thought one step further: we need to help each other…" (nurse, E40)

A focus on areas of improvement

According to the participants, the self-assessment process highlighted specific areas for improvement, but also showed strengths of the primary care centre. Examples of identified areas for improvement were: keeping an accurate medication list, factors affecting the prescribers' choice of therapy and factors affecting patients' ability to contribute to drug safety. Identified strengths included: committed leadership, climate open to discussion, existing routines and access to consultants (geriatricians, psychiatrists, pharmacists). Areas for improvement were also highlighted in the written feedback, which was appreciated by the participants. One person pointed out that many questions in the self-assessment concerned monitoring, and that monitoring a lot of things could distract from the aim to increase patient safety.

"…seeing what we have done and what we need to improve, presented in a clear and concise way, is positive." (primary care unit head, U15)
"I look at the medicines in another way now." (nurse, E7)

The joy of sharing knowledge

The visits by the peer review teams were viewed as mostly enjoyable and exciting, with no feeling of being investigated. The group of reviewers, with working experience from different areas, were perceived as being able to bring a lot of knowledge to the primary care centre, but also to learn some new things to take home.

"…it's great to have a peer review team from different parts of the country with different viewpoints. […] Sometimes they said this is not how we do it, but you seem to have found a good solution…" (primary care unit head, J112)
"…they were interested and had questions. We had a good discussion…" (primary care unit head, V11)

Disappointment with the focus of the feedback

Some respondents expressed slight disappointment that the peer review visits sometimes lacked a summary at the end of the day. They had hoped for a short summary of their strengths and weaknesses. Many of the participants felt that the written feedback did not always focus on the primary care unit; it was sometimes more of a discussion at a higher level.

"…some feedback at the end of the visit. But I didn't get that with me, it was more of a general discussion of Swedish health care…" (primary care unit head, C14)
"…these are things outside our influence." (GP, B106)

Spend time to save time

The project took more time than expected, according to the participants. Finding interested participants outside the primary care centre and explaining the aim of the project to them was more time-consuming than expected. The self-assessment form was felt to be too long and filling it out online took a lot of time.

"…to include people outside the primary care unit took a lot of time" (primary care unit head, U4)

"It took longer than I had initially expected" (primary care unit head, L9)

On the other hand, some of the participants pointed out that the time invested in the short-term may save time later on through improved routines for safe use of medications.

"…it costs energy right now, but if we can improve our routines and follow these […] then I think it will pay off in the long run…" (GP, G117)

Impact on work

The participants viewed written agreements as something positive – a reminder to keep focused on medication safety – but also perceived it as a little stressful. The follow-up was six months later and summer was coming in between. At some primary care units the self-

assessment led to a change of routines right away, while others stated that changes would be made in the future.

"Yes, it has already [started to yield change]..." (GP, B167)
"It can only get better. More structure, get more routines..." (nurse, H62)

Surveys

All five managers completed the survey. Four of them also participated in the interviews. The responses from the surveys concur in general with the interviews. The respondents pointed out the multi-professional approach as being very positive. The self-assessment was said to be worthwhile to identify strengths and weaknesses. According to one respondent this was the only useful part of the project, even though it took more time than expected. At one of the participating primary care units they felt criticised by the reviewers, according to the survey. This did not come up during the interviews.

Validation

The results of the qualitative analysis of the interviews were discussed at the follow-up seminar. The participants agreed with the findings.

Discussion

One of the most positive experiences of the intervention, according to the participants, was the focus on multi-professional co-operation. It seemed as though the project opened the eyes of the participants to the importance of working together on the big issue of medication safety. Other ways to improve medication safety in the elderly population, such as medication reviews and medication reports, involve multiple professions and have been shown to reduce drug-related problems [10, 17, 23]. Still, the care of the elderly remains fragmented [18] and co-operation between all health care professionals involved in the care of the elderly needs to be improved. This is something this method might contribute to, since the multi-professional approach was pointed out as being something very positive by the participants.

The self-assessment was an appreciated and useful tool to identify areas of improvement for medication safety at primary care units and to clarify strengths and weaknesses. Other studies, both in the health care system and in other areas, have shown similar results [19, 24]. It is also important to involve both management and employees for the self-assessment to achieve acceptance and success [24]. The self-assessment in the SÄKLÄK project was constructed in such a way that no person could answer all questions by himself or herself, but had to include other health professionals. And since there's more to collaboration than simply working side by side as health professionals [25], the self-assessment may serve as a tool to facilitate communication between different professionals. The British National Institute for Health and Care Excellence (NICE) has acknowledged that "no-one who works alone can stay at the forefront of knowledge given the speed of organisational and clinical change".

The focus of the feedback was sometimes on general problems rather than specific problems at the primary care unit, which disappointed many participants. The reviewers were criticised for proposing solutions that were not applicable. These problems were also seen when testing the method at Swedish maternity units [19], despite instructions for the reviewers involved to be humble and to have realistic expectations on feasible measures of actions within the healthcare system. These aspects raise questions about how to use the peer review process in other interventions, and how peer reviewers should be selected, trained and instructed. Peer review can be explained as knowledge sharing [26] and is not only useful for the reviewed unit but also for the reviewers. The sharing of knowledge was highlighted as a positive part of this project by some participants. Peer review has been shown by others to be useful to shed light on provider-related errors and associated safety concerns, some of which may be modifiable [27]. This is of course useful for a single primary care unit, but also at an aggregated level to see patterns at, for example, the national level [27]. In this study all units got suggestions in their written feedback that they felt was at a higher level and not within their scope. These suggestions will be analysed and used to improve the health care system.

The participants perceived some parts of the intervention, i.e. self-assessment, as time-consuming. In a pilot study like this, finding out what works and what does not is part of the evaluation. On the other hand, according to some participants the time invested in the short-term may be recouped later in form of, for example, better routines. Almost all respondents felt that participating in this project would affect their work, and thereby were in support of efforts to improve medication safety in the elderly. One interviewee expressed some annoyance over the fact that many of the questions in the self-assessment included monitoring. This could take focus from more important things, for example improving medications safety, according to the interviewee. It is important to select variables focusing on medication safety if monitoring should be a part of the routines.

This interview study indicates that a program consisting of self-assessment, peer review and feedback can be a valued tool to assess patient safety. This is supported by the findings of Meeks et al. [27], who found that health care organisations could renew their peer review programs to enable self-assessment, feedback and improvement and thereby increase patient safety.

Participation in this project was not mandatory; rather, it was to be seen as an opportunity to improve medication safety. Most of the participants seemed to agree that primary care units have a responsibility to help solve the problems concerning medication safety. But, again, focus in the feedback from reviewers must be on goals within the primary care units' scope.

Methodological discussion

As the design is qualitative it should be assessed by means of trustworthiness, which includes credibility, transferability and dependability. Credibility deals with the focus of the research and refers to confidence in how well data and analytical processes address the intended focus [22]. The participants represented different professions within Swedish primary care and had varying working experience. All but one received their medical education in Sweden. The interviews resulted in large amounts of material. We performed 15 interviews with 17 participants, and the parallel analysis showed that saturation was reached in the data. The number of participants interviewed varied between primary care units, with two units providing the majority of interviewees. This may have influenced the results since these units were very engaged in the project and both had an urban location. To improve trustworthiness, the results from the interviews and from the surveys were triangulated. This process revealed that one primary care unit felt questioned by the reviewers, which was not mentioned during the interviews. We also reported the findings from the qualitative analysis back to the participants to see if they agreed, which they did. To increase credibility, the analysis was discussed within the research group and the analytical process is shown in Table 3. Illustrative quotations from the interviews have been provided to show that the categories come from the data.

The original plan was to conduct the interviews after all units had completed every step of the intervention. However, due to an unexpected delay in providing written feedback to some units a few of the interviews were performed before the agreements for change had been signed. This might have affected the results. However, the surveys were sent out after the agreements had been signed and the answers concur with the interviews.

Dependability concerns the degree to which data change over time and alterations made in the researcher's decisions during the analysis process. Data were collected using a semi-structured interview guide, and according to Graneheim and Lundman [22] this can strengthen trustworthiness. The guide ensured that all participants were asked the same questions.

Transferability refers to the extent to which the findings can be transferred to other settings and groups, and it is up to the reader to judge it [22]. We elucidated the participants' perceptions of a multi-professional intervention model to enhance medication safety in primary care. A potential limitation is that although participation was open to all primary care units in Sweden, we do not know if the selected units are an accurate representation of Swedish primary care. A total of 20, out of the 1200 possible primary care units in Sweden, applied for participation in the study. These health care units were from different parts of the country in both urban and rural locations. However, this was a qualitative evaluation of a pilot study and the aim was to explore the perceptions of the method from the participants. A strength of this study is the use of the same interviewer for each interview, which meant there was no need to calibrate answers from different interviewers.

This research group has extensive experience from health care, especially elderly and medications. CL is a pharmacist and PhD-student, ÅB a pharmacist and PhD, PM an MD and associate professor, NV is a pharmacist and PhD.

Future research

This method needs further development. Potential modifications can be made based on the results of this pilot study. These include simplifying the self-assessment process and offering clearer instructions to reviewers and primary care management. It would also be beneficial for more primary care units to be given the opportunity to participate in similar studies in the future. Different models for improving medication safety in the elderly population need to be compared, and for these models to be successful we must know that the participants accept, or even welcome, the intervention.

Conclusion

This study shows that our studied intervention method is feasible to use in primary care and that the multi-professional approach was perceived as being very positive by the participants. Multi-professional co-operation was time consuming, but was also deemed as an investment and an opportunity to share knowledge. Some points of improvement of the method were identified, such as simplification of the self-assessment forms and clearer instructions for reviewers. Furthermore, in order to have an impact on work the focus must lie in areas within the primary care units' scope.

Additional files

Additional file 1: Interview guide. (DOCX 14 kb)

Additional file 2: Survey to primary care centres. (DOCX 17 kb)

Competing interests
The authors declare that they have no competing interests.

Authors' contributions
CL, NV and PM designed the study with input from ÅB. CL collected the data and conducted the analyses with confirmatory analysis by NV. CL drafted the manuscript with help from NV. PM and ÅB made substantial contributions to the manuscript and its conclusions. All authors read, contributed to and approved the final manuscript.

Acknowledgements
We would like to thank the interview participants, the steering committee and Torbjörn Schultz at The Patient Insurance LÖF for their time and assistance in setting up the study. This study was funded by The Swedish Association of Local Authorities and Regions and The Patient Insurance LÖF. We are grateful to Lena Lennartsson who transcribed the interviews. We are indebted to Stephen Gilliver and Patrick Reilly for their expertise and invaluable advice in editing the manuscript.

Author details
[1]Department of Clinical Sciences in Malmö, Lund University, Jan Waldenströms gata 35, SE-205 02 Malmö, Sweden. [2]Department of Medicines Management and Informatics, Region Skåne, Sweden. [3]Department for Public Health Sciences, Karolinska Institutet, Stockholm, Sweden.

Received: 5 December 2014 Accepted: 28 August 2015
Published online: 04 September 2015

References

1. Shi S, Morike K, Klotz U. The clinical implications of ageing for rational drug therapy. Eur J Clin Pharmacol. 2008;64(2):183–99.
2. The Swedish Bureau of Statistics. [http://scb.se/sv_/Hitta-statistik/Statistik-efter-amne/Befolkning/Befolkningenssammansattning/Befolkningsstatistik/25788/25795/Helarsstatistik—Riket/26040/] Accessed November 15, 2014.
3. Beijer HJ, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. Pharm World Sci. 2002;24(2):46–54.
4. Davies EC, Green CF, Mottram DR, Rowe PH, Pirmohamed M. Emergency re-admissions to hospital due to adverse drug reactions within 1 year of the index admission. Br J Clin Pharmacol. 2010;70(5):749–55.
5. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. BMJ. 2004;329(7456):15–9.
6. Mannesse CK, Derkx FH, de Ridder MA, Veld AJ M i 't, van der Cammen TJ. Contribution of adverse drug reactions to hospital admission of older patients. Age ageing. 2000;29(1):35–9.
7. Franceschi M, Scarcelli C, Niro V, Seripa D, Pazienza AM, Pepe G, et al. Prevalence, clinical features and avoidability of adverse drug reactions as cause of admission to a geriatric unit: a prospective study of 1756 patients. Drug Saf. 2008;31(6):545–56.
8. Swedish National Board of Health and Welfare. [Indicators for the evaluation of quality in drug use of the elderly]. Sweden: Stockholm; 2010.
9. American Geriatrics Society. updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;60(4):616–31.
10. Midlov P, Holmdahl L, Eriksson T, Bergkvist A, Ljungberg B, Widner H, et al. Medication report reduces number of medication errors when elderly patients are discharged from hospital. Pharm World Sci. 2008;30(1):92–8.
11. Midlov P, Bergkvist A, Bondesson A, Eriksson T, Hoglund P. Medication errors when transferring elderly patients between primary health care and hospital care. Pharm World Sci. 2005;27(2):116–20.
12. Prince RL, Devine A, Dhaliwal SS, Dick IM. Effects of calcium supplementation on clinical fracture and bone structure: results of a 5-year, double-blind, placebo-controlled trial in elderly women. Arch Intern Med. 2006;166(8):869–75.
13. Hansen RA, Kim MM, Song L, Tu W, Wu J, Murray MD. Comparison of methods to assess medication adherence and classify nonadherence. Ann Pharmacother. 2009;43(3):413–22.
14. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005;353(5):487–97.
15. The Swedish Council on Technology Assessment in Health Care (SBU). [Use of medications in elderly: how can it be improved? A systematic litterature review.]. Sweden: Stockholm; 2009.
16. Anell A, Glenngard AH, Merkur S. Sweden health system review. Health Syst Transit. 2012;14(5):1–159.
17. The Model of Care Polypharmacy Working Group. Polypharmacy Guidance. Scotland: NHS Scotland; 2012.
18. Sinnott C, Mc Hugh S, Browne J, Bradley C. GPs' perspectives on the management of patients with multimorbidity: systematic review and synthesis of qualitative research. BMJ open. 2013;3(9):e003610.
19. Nystrom ME, Westerlund A, Hoog E, Millde-Luthander C, Hogberg U, Grunewald C. Healthcare system intervention for prevention of birth injuries - process evaluation of self-assessment, peer review, feedback and agreement for change. BMC Health Serv Res. 2012;12:274.
20. W-Dahl A, Robertsson O, Stefansdottir A, Gustafson P, Lidgren L. Timing of preoperative antibiotics for knee arthroplasties: Improving the routines in Sweden. Patient Saf Surg. 2011;5:22.
21. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res. 2005;15(9):1277–88.
22. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Educ Today. 2004;24(2):105–12.
23. Milos V, Rekman E, Bondesson A, Eriksson T, Jakobsson U, Westerlund T, et al. Improving the Quality of Pharmacotherapy in Elderly Primary Care Patients Through Medication Reviews: A Randomised Controlled Study. Drugs Aging. 2013.
24. Zink K, Schmidt A. Practice and implementation of self-assessment. Int J Qual Sci. 1998;3(2):147–70.
25. Davies C. Getting health professionals to work together. BMJ. 2000;320(7241):1021–2.
26. Bergquist M, Ljungberg J, Lundh-Snis U. Practising peer review in organisations: a qualifier for knowledge dissemination and legitimization. J Info Tech. 2001;16:99–112.
27. Meeks DW, Meyer AN, Rose B, Walker YN, Singh H. Exploring new avenues to assess the sharp end of patient safety: an analysis of nationally aggregated peer review data. BMJ qual saf. 2014;23(12):1023–30.

Paper II

Family Practice Advance Access published December 5, 2016

Family Practice, 2016, 1–6
doi:10.1093/fampra/cmw121

Health Service Research

Effects of an intervention (SÄKLÄK) on prescription of potentially inappropriate medication in elderly patients

Cecilia Lenander[a,*], Åsa Bondesson[a,b], Nina Viberg[a,c], Ulf Jakobsson[a,d], Anders Beckman[a] and Patrik Midlöv[a]

[a]Department of Clinical Sciences in Malmö, Lund University, Malmö, Sweden, [b]Department of Medicines Management and Informatics, Region Skåne, Sweden, [c]Department of Public Health Sciences, Karolinska Institute, Sweden and [d]Center for Primary Health Care Research (CPF), Lund University/Region Skåne, Malmö, Sweden.

*Correspondence to Cecilia Lenander, Department of Clinical Sciences in Malmö, Lund University, Jan Waldenströmsgata 35, S-20502 Malmö, Sweden; E-mail: cecilia.lenander@med.lu.se

Abstract

Background. Polypharmacy is known to increase the risk for drug-related problems, and some drugs, potentially inappropriate medications (PIMs), are especially troublesome.
Objective. To analyse the effects on prescription of PIMs of the SÄKLÄK project, an intervention model created to improve medication safety for elderly patients in primary care.
Method. The SÄKLÄK project was a multiprofessional intervention in primary care consisting of self-assessment, peer review, feedback and written agreements for change. Five Swedish primary care centres participated in the intervention and five served as comparison group. Data were collected from the Swedish Prescribed Drug Register on PIMs (long-acting benzodiazepines, anticholinergics, tramadol, propiomazine, antipsychotics and non-steroidal anti-inflammatory drugs) prescribed to patients aged 65 years and older. Total number of patients and change in patients using PIMs before and after intervention with-in groups was analysed as well as differences between intervention and comparison group.
Results. A total of 32566 prescriptions of PIMs were dispensed before the intervention, 19796 in the intervention group and 12770 in the comparison group. After intervention a decrease was seen in both groups, intervention—22.2% and comparison—8.8%. All groups of PIMs decreased, except for antipsychotics in the comparison group. For the intervention group, a significant decrease in mean dose/patient was seen after the intervention but not in the comparison group.
Conclusion. Our study shows this method has some effects on prescription of PIMs.The evaluation indicates this is a feasible method for improvement of medication use in primary care and the method should be tested on a larger scale.

Key words: Aged, frail elderly, inappropriate prescribing, peer review—health care, primary health care, self-assessment.

Introduction

Worldwide, the elderly population is increasing, and demographic data estimate that 22% of the global population will be older than 65 years by 2050 (1). Ageing is known to be associated with an increased prevalence of multiple chronic diseases and thereby the use of an increased number of medications. Elderly patients with multiple diseases and polypharmacy risk suffering from drug-related problems (DRPs). Some drugs, such as potentially inappropriate medications (PIMs), are especially troublesome. These can be defined as medications for which the risks outweigh the benefits for elderly patients (2).

Different criteria for classifying inappropriate prescriptions have been proposed. The Medication Appropriateness Index (MAI) (3) is an instrument used to determine a drug's suitability to an individual, which has been validated for evaluating drug use in the elderly (4). Beer's criteria (5) list medications to be avoided in elderly patients. However, since many of these medications are unavailable in Europe, criteria corresponding to European drug formularies have been developed, such as the EU(7)-PIM list (6) and the Swedish quality indicators developed by the Swedish National Board of Health and Welfare (2).

The use of PIMs, defined according to the Swedish quality indicators, has decreased in Sweden between 2005 and 2014. The decrease could be explained by focused efforts by the Swedish county councils and a national improvement strategy (7). It should however be noted that 8.1% of the population aged 75 years or older still used PIMs in 2014 (8). Furthermore, according to a Swedish study, 26.4% of elderly adults in nursing homes used at least one PIM (9). Other international studies report different figures, depending on classification of PIMs, type of living (own home or nursing homes) and country for example (10,11).

The present pilot study analysed effects of the SÄKLÄK project, an intervention model created to improve medication safety for elderly patients in primary care, on the prescription of PIMs. The intervention model was originally developed for, and successfully implemented in, Swedish hospital care, to improve patient safety (12,13). The intervention was adapted to primary care by the six participating professional organizations and consists of self-assessment followed by peer review, feedback and a written agreement for change. The participants' experiences of the method and an analysis of identified improvement needs and agreements for changes have already been studied (14).

The aim of this study was to assess the effect of the SÄKLÄK project on prescription of PIMs in elderly primary care patients.

Method

Setting

Ten Swedish primary care centres participated in the SÄKLÄK pilot project. Participation was open to all primary care units in Sweden (~1200). Information about the study was presented at the Swedish College of General Practice yearly congress, in some regional information materials, as well as by email to managers at primary care centres. Despite a short application timeline and no reimbursement for participation, a total of 20 units applied, and they were stratified according to urban (12 units) or rural location (8 units). Within these groups, there were no major differences. We therefore randomized among all 12 units and all 8 units, respectively. Using Excel, five units were randomized to the intervention group and five to the comparison group, keeping the distribution between urban and rural units. The participating primary care centres varied in size between 2400 and 13 700 patients. The intervention took place between September 2013 and May 2014, with follow-up in October 2014.

Intervention model (SÄKLÄK project)

The overall aim of the SÄKLÄK project was to reduce medication errors and DRPs.

The SÄKLÄK project was initiated by the Swedish Association of Local Authorities and Regions (SALAR) and the Patient Insurance LÖF. This was a pilot study of the SÄKLÄK project to determine whether an intervention model, developed in hospital care, could be used in primary care to enhance medication safety for elderly patients.

The intervention consisted of several steps. The first step was a self-assessment questionnaire, to be answered by the primary care centres together with pharmacies, hospitals and municipally provided home care. It consisted of questions regarding how patient safety is maintained during prescription of medication, medication use and follow-up, and specifically frail elderly patients at the primary care centre. The focus of the questions was on how the primary care centres currently handle medication reviews, cooperation with pharmacies and secondary care, and, not least, how to ensure these measures are followed. In the second step of the intervention, a group of selected doctors, nurses and pharmacists, with vast experience in elderly care, served as reviewers. With support from the project management team and written instructions and documents, the reviewers analysed the self-assessment questionnaires and any additional material supplied by the primary care units. They had opportunity to get clarifications regarding any questions during site visits. Thereafter, the reviewers produced a written feedback report for the primary care unit and, together with the management at the primary care unit, agreed on an action plan for improvements. The improvement plan was followed-up after 6 months.

For further details, please see previously published article (14).

Potentially inappropriate medications

The project selected and analysed six drug-specific quality indicators, in accordance with the indicators described by the Swedish National Board of Health and Welfare (2). These included 'anticholinergic drugs', 'long-acting benzodiazepines', 'tramadol', 'propiomazine', 'antipsychotic drugs' and 'non-steroidal anti-inflammatory drug (NSAID)' (Table 1). According to the quality indicators, the use of 'anticholinergic drugs', 'long-acting benzodiazepines', 'tramadol' and 'propiomazine' should be as low as possible, regardless of indication, for older patients. For 'antipsychotic drugs' and 'NSAID', it is of particular importance to ensure correct and current indication. However, as the indication was not captured by the dispensing database in the present study and side effects of these drugs are common, antipsychotic drugs and NSAID were also classified by the same quality indicator, i.e. for the dose to be as low as possible, regardless of indication.

Morphine-scopolamine and glycopyrrolate were excluded from the analysis (mainly palliative use).

Data collection

Data were collected from the Swedish Prescribed Drug Register (15) that includes all drugs dispensed at Swedish community pharmacies since 2005. The register is managed by the National Board of Health and Welfare and includes data for individual patients on substance, brand name, formulation, package and date of prescription and dispensing. All drugs are classified according to the Anatomical Therapeutic Chemical (ATC) Classification System. Multi-dose drug dispensing, i.e. all drugs that are to be ingested at the same time are machine dispensed in unit bags, is included in the register. The system with multi-dose drug dispensing is very common in nursing homes in Sweden. All other prescriptions were defined as ordinary prescriptions. Drugs used in hospitals and over-the-counter (OTC) drugs are not included. Dispensed drugs were used here as a proxy for prescribed drugs in this study, since data only are available for dispensed drugs.

Information about all dispensed prescriptions for patients aged 65 years and older from the participating primary care centres (five

intervention and five comparison) was collected from the registry for: antipsychotics, drugs with anticholinergic effects, long-acting benzodiazepines, tramadol, propiomazine and NSAIDs (see Table 1). These data were collected for two periods, 12 months before (June 2012–May 2013) and 12 months after (June 2014–May 2015) the intervention.

Data analysis

Comparisons between age groups (65–79 years and 80+) and gender were performed.

Total number of patients and change in number of patients using PIMs before and after the intervention were analysed as well as differences in the change between the intervention and the control group. Total number of prescriptions of PIMs and mean number of prescriptions per patient were also presented. Mean defined daily dose (DDD) per patient (combined for all PIMs) were analysed in the same way as well as differences between ordinary prescriptions and multi-dose drug dispensing.

Data were analysed using IBM SPSS version 22. Hypothesis testing using 95% confidence interval for the mean difference was used to compare groups before and after intervention. Hypothesis testing using chi-square test was used to compare percentages of different PIM groups for ordinary prescriptions and multi-dose dispensing. Other hypothesis testing was not possible due to the data set containing a mix of dependent and independent observations. A significance level (α) of 0.05 was used.

Results

At baseline, almost 68% of the prescriptions were dispensed to patients in the age category 65–79 years and 63% to women. The vast majority (84.7%) of the patients had ordinary prescriptions, 13.8% had multi-dose drug dispensing and 1.5% had both.

For all 10 centres, a total of 32 566 prescriptions of PIMs were dispensed before the intervention period, which decreased to 27 041 after the intervention. A decrease of 22.2% in the intervention group (from 19 796 to 15 400) compared to a decrease of 8.8% in the comparison group (from 12 770 to 11 641) (Table 2).

The average number of prescriptions per patient remained unchanged in the intervention group (7.48–7.48), while it increased in the comparison group after the intervention period (7.64–8.81); however, this difference was not significant.

The overall most common group of PIMs before the intervention was anticholinergics, followed by antipsychotics and NSAIDs. This did not change after the intervention. In the intervention group, the largest decrease was seen for propiomazine and tramadol. In the comparison group, long-acting benzodiazepines, NSAIDs and tramadol decreased while antipsychotics and propiomazine

Table 1. Potentially inappropriate medications according to the Swedish National Board of Health and Welfare

Potentially inappropriate medication group	Anatomical Therapeutic Chemical group	Substance (examples)	May cause
NSAIDs	M01A	Ibuprofen Diclofenac Naproxen	Gastric ulcer and haemorrhage, fluid retention, heart decompensation, reduced renal function
Long-acting benzodiazepines	N05BA01 N05CD02 N05CD03	Nitrazepam Flunitrazepam Diazepam	Prolonged half-lives in elderly adults may cause hangover, cognitive impairment and falls
Anticholinergics	R06AD G04 N05BB	Promethazine Urologic spasmolytics (e.g. tolterodin) Hydroxyzine	Cognitive impairment, confusion, impaired functional status
Propiomazine	N05CM	Propiomazine	Daytime sedation, extrapyramidal symptoms
Tramadol	N02AX	Tramadol	Confusion
Antipsychotics	N05A excluding lithium	Risperidon Haloperidol Quetiapin	Cognitive impairment, sedation, orthostatism

NSAID, non-steroidal anti-inflammatory drug.

Table 2. Number of prescriptions of potentially inappropriate medications, before and after an intervention in 10 Swedish primary care centres

Potentially inappropriate medication groups	Intervention (n = 5 centres)			Comparison (n = 5 centres)		
	Before	After	Change	Before	After	Change
NSAID	3787	2974	–21.5%	2540	1978	–22.1%
Long-acting benzodiazepines	1860	1449	–22.0%	2084	1507	–27.7%
Anticholinergics	4513	3824	–15.3%	3183	2888	–9.3%
Propiomazine	2074	1368	–34.0%	1184	1240	+4.7%
Tramadol	3520	2449	–30.4%	1460	1147	–21.4%
Antipsychotics	4038	3336	–17.4%	2319	2881	+24.2%
Total	19 796	15 400	–22.2%	12 770	11 641	–8.8%

NSAID, non-steroidal anti-inflammatory drug.

Table 3. Number of patients using potentially inappropriate medications, divided into groups, before and after an intervention consisting of self-assessment, peer review, feedback and agreement for change

Potentially inappropriate medication groups	Intervention			Comparison		
	Before	After	Change	Before	After	Change
NSAID	1872	1598	−14.6%	1407	1098	−22.0%
Long-acting benzodiazepines	469	381	−18.7%	532	382	−28.2%
Anticholinergics	1156	1122	−2.9%	772	719	−6.9%
Propiomazine	534	388	−27.3%	311	278	−10.6%
Tramadol	883	648	−26.6%	502	354	−29.5%
Antipsychotics	407	353	−13.2%	264	285	+8.0%
Total	5321	4490	−15.6%	3788	3116	−17.7%

NSAID, non-steroidal anti-inflammatory drug.

increased (Table 2). Regarding number of patients receiving PIMs, this decreased for all groups of PIMs, except for antipsychotics in the comparison group (Table 3).

For all centres, the most common PIMs before the intervention were tramadol, diclofenac, propiomazine and naproxen. After intervention, this changed slightly to tramadol, naproxen, diclofenac and hydroxyzine. Tramadol and propiomazine showed major reductions as mentioned above, while hydroxyzine decreased only by 1.5% for example.

For all 10 primary care centres, the number of patients with multi-dose drug dispensing increased from 13.8% to 16.4%, but the group with both kinds of dispensing decreased after the intervention. There was a significant difference between the two groups regarding prescriptions of PIMs (Table 4). The most common PIM groups in patients with ordinary prescriptions were NSAIDs, anticholinergics and tramadol. This segmentation remained after the intervention even though the number of patients receiving PIMs decreased. For patients with multi-dose drug dispensing, the most common drug group was antipsychotics, anticholinergics and long-acting benzodiazepines. After intervention, the segmentation remained the same, including a 13.6% increase in prescriptions of antipsychotics.

For four of the five primary care centres in the intervention group, fewer patients received PIMs and the mean DDD/patient was lower after the intervention. Of the centres in the control group, only one had more patients on PIMs after, but three demonstrated an increase in mean DDD/patient. In total, the intervention group showed a significant decrease in mean DDD/patient, whereas the control group did not (Table 5).

For the total study population, no significant differences between men and women in mean DDD/patient were seen. In general, the age group 65–79 years received a higher mean DDD/patients than did the 80+ group, and this was significant ($P < 0.05$) for long-acting benzodiazepines, anticholinergics, tramadol and antipsychotics before the intervention. After intervention, the difference remained but was significant only for long-acting benzodiazepines and antipsychotics.

Table 4. Number of prescriptions of different potentially inappropriate medications before the intervention, divided into ordinary prescriptions and multi-dose dispensing

	Ordinary prescriptions	Multi-dose	*P*-value*
	N = 7712	*N* = 1264	
NSAIDs number (%)	3132 (40.6%)	132 (10.4%)	<0.001
Anticholinergics number (%)	1564 (20.3%)	319 (25.2%)	<0.001
Tramadol number (%)	1298 (16.8%)	87 (6.9%)	<0.001
Long-acting benzodiazepines number (%)	772 (10.0%)	204 (16.1%)	<0.001
Antipsychotics number (%)	219 (2.8%)	420 (33.2%)	<0.001
Propiomazine number (%)	727 (9.4%)	102 (8.1%)	0.122

Number and percentage of total.
*Chi-square test.

Discussion

In the intervention group, there was a significant decrease of the prescription of PIMs in primary care, but not in the control group. This indicates that the SÄKLÄK intervention is an effective way to reduce potential DRPs.

We noted that the intervention led to a significant lower mean DDD/patient in the intervention group, whereas the comparison group showed a much smaller change. According to national Swedish data, there has been a decrease in use of PIMs in Sweden of 44% from 2005 to 2014 (8). This could be explained by focused efforts by the Swedish county councils and a national improvement strategy. However, the studied intervention led to a difference between intervention and comparison centres, indicating something beyond the national improvement strategy.

The SÄKLÄK intervention was a multiprofessional intervention model created to improve medication safety for elderly patients in primary care and consisted of self-assessment followed by peer review, feedback and a written agreement for change. Earlier studies have shown that educational outreach visits to GPs can affect prescribing patterns regarding PIMs (16). In a register study by Hovstadius *et al.* (17), all PIM groups except anticholinergics decreased, and in our study, anticholinergics showed the smallest decrease. This could be attributed to the fact that there are few or no alternative therapies available for anticholinergics compared to the other groups.

There is a difficulty comparing studies since the definitions of PIMs and what is being measured (prescriptions, individuals, DDD) as well as the setting (assisted living or patients living at home) differ. We included long-acting benzodiazepines, anticholinergics, tramadol, propiomazine, antipsychotics and NSAIDs. Regarding NSAIDs, the real use might be higher than shown here, since they also are available OTC. We did not have data on OTC use but since the intervention was not only targeting doctors but also for example nurses and pharmacists, it might potentially have affected the use of OTC drugs (for example NSAIDs) as well. This however remains to be concluded.

We know from previous evaluations of the intervention method that the multiprofessional approach was perceived as something very positive (14), and this could be the part of the intervention

Table 5. Patients receiving at least one potentially inappropriate medication and mean defined daily dose per patient for each primary care centre

Primary care centres	Patients[a]		Defined daily dose/patient mean		
	Before	After	Before	After	Diff (95% confidence interval)
Intervention 1	1348	1032	134	108	−25.7 (−47.3 to −4.1)[b]
Intervention 2	885	639	110	104	−6.5 (−27.9 to 14.9)
Intervention 3	552	593	118	98	−20.4 (−48.4 to 7.65)
Intervention 4	949	863	111	106	−4.5 (−26.4 to 17.3)
Intervention 5	1587	1363	114	113	−0.9 (−19.3 to 17.6)
Intervention total	5321	4490	118	107	−10.9 (−20.7 to −1.22)[b]
Comparison 1	646	628	137	111	−26.1 (−56.0 to 3.8)
Comparison 2	908	771	110	116	6.5 (−14.3 to 27.4)
Comparison 3	1178	825	108	112	4.4 (−17.2 to 25.9)
Comparison 4	768	583	124	144	19.9 (−8.1 to 47.9)
Comparison 5	288	309	129	112	−17.0 (−49.9 to 15.9)
Comparison total	3788	3116	120	119	−1.0 (−12.6 to 10.5)

[a]Patients can occur more than once by receiving drugs from more than one group of potentially inappropriate medications.
[b]Significance at 5% level.

that makes the difference in PIMs between the groups (i.e. reaching broader than previous efforts). The self-assessment helped the centres to identify areas of improvement, and prescription of PIMs might be one of these, and the agreement for change set a timetable for when to do it. The impact of reviewers could be on how to do it.

Although women constitute 54.2% of the Swedish 65+ population according to Statistics Sweden, they receive around 63% of the PIMs in this study before the intervention. It is known that women use more medications than men, and this seems to be true for PIMs as well. This has also been shown in other studies (11,18).

We saw a difference in mean DDD/patient for some PIMs between the two age groups, indicating that the older patients are getting lower doses or shorter treatments, which is as it should be. Other studies have shown no clear evidence, with both a higher risk for getting PIMs prescribed with older age (10,17) and more PIMs to younger nursing home residents than to older ones (19).

The differences we saw in prescription of PIMs between ordinary prescriptions and multi-dose drug dispensing, antipsychotics are more common in the latter group for example, are likely due to the fact that patients with multi-dose dispensed medications are sicker and more often nursing home residents. There are also studies showing that these patients have fewer changes of their therapy than patients with ordinary prescriptions (20), which could lead to longer periods of treatment with PIMs.

One strength of this study was the representation of participating primary care centres from different parts of Sweden and from both urban and rural areas. Another strength is the data from the Swedish Prescribed Drug Register that provides complete national data on the number of individuals exposed to dispensed drugs in the Swedish population. In contrast to some other countries, all prescription drugs, irrespective of reimbursement status, are included in the register.

This study has some important limitations. It was a small pilot study with 10 primary care centres with the aim to evaluate if a method developed in hospital care is useful in primary care. This limits the opportunities to directly apply these results to primary care centres in Sweden or other countries.

Due to the limitations of the data, we were unable to analyse whether the intervention led to a decrease in number of PIMs per patient for example, but the study shows an overall decrease of PIMs. However, it is not certain that this is due to the intervention. The Drug Register does not provide information on diagnosis or indication for treatment. Therefore, we must assume there may be a rationale behind some of the 'inappropriate' treatments found, even though these PIMs are classified as inappropriate on a group level.

Further studies with more centres are needed to establish the effects of the SÄKLÄK project on prescription of PIMs, as well as studies of other interventions to optimize medication treatment of older patients in primary care.

Conclusion

Our study shows some positive effects on prescription of PIMs. This evaluation indicates this is a feasible method for improvement of medication use in primary care and the method should be tested on a larger scale.

Acknowledgements

We thank the participating primary care centres, the steering committee and Torbjörn Schultz at the Patient Insurance LÖF for their time and assistance in setting up the study. We are indebted to Karin Luton for her expertise and valuable advice in editing the manuscript.
Authors' contributions: C.L., N.V. and P.M. designed the study with input from Å.B. C.L. collected the data and conducted the analyses with help from A.B. and U.J. C.L. drafted the manuscript with assistance from P.M., and Å.B. and N.V. made substantial contributions to the manuscript and its conclusions. All authors read, contributed to and approved the final manuscript.

Declaration

Funding: the Swedish Association of Local Authorities and Regions; the Patient Insurance LÖF; the Swedish Society of Medicine (LSLS-408541); Fromma Foundation (201509-fromma-foundation); ALF (F 2015/121) funding from Region Skåne (awarded to P.M.).
Ethical approval: Regional Ethical Review Board in Lund (application number 2013/333; the extraction of data was done by the National Board of Health and Welfare with no possibility for the research team to identify any individual patient).
Conflict of interest: none.

References

1. Statistics Sweden. Statistics Sweden. http://scb.se/sv_/Hitta-statistik/Statistik-efter-amne/Befolkning/Befolkningens-sammansattning/Befolkningsstatistik/25788/25795/Helarsstatistik---Riket/26040/ (accessed on 15 January 2016).

2. Swedish National Board of Health and Welfare. *Indicators for the Evaluation of Quality in Drug Use of the Elderly*. Stockholm, Sweden: Swedish National Board of Health and Welfare, 2010.
3. Hanlon JT, Schmader KE, Samsa GP *et al*. A method for assessing drug therapy appropriateness. *J Clin Epidemiol* 1992; 45: 1045–51.
4. Samsa GP, Hanlon JT, Schmader KE *et al*. A summated score for the medication appropriateness index: development and assessment of clinimetric properties including content validity. *J Clin Epidemiol* 1994; 47: 891–6.
5. American Geriatrics Society. 2015 Updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2015; 63: 2227–46.
6. Renom-Guiteras A, Meyer G, Thürmann PA. The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. *Eur J Clin Pharmacol* 2015; 71: 861–75.
7. Swedish Association of Local Authorities and Regions. *A Better Life for Elderly Sick People*. Stockholm, Sweden: Swedish Association of Local Authorities and Regions, 2014.
8. Swedish Association of Local Authorities and Regions. *Open Comparisons Drug Use*. Stockholm, Sweden: Swedish National Board of Health and Welfare, 2015.
9. Gustafsson M, Sandman PO, Karlsson S *et al*. 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: 507–15.
10. Maio V, Yuen EJ, Novielli K, Smith KD, Louis DZ. Potentially inappropriate medication prescribing for elderly outpatients in Emilia Romagna, Italy: a population-based cohort study. *Drugs Aging* 2006; 23: 915–24.
11. Aparasu RR, Mort JR. Inappropriate prescribing for the elderly: beers criteria-based review. *Ann Pharmacother* 2000; 34: 338–46.
12. Nystrom ME, Westerlund A, Hoog E *et al*. Healthcare system intervention for prevention of birth injuries—process evaluation of self-assessment, peer review, feedback and agreement for change. *BMC Health Serv Res* 2012; 12: 274.
13. W-Dahl A, Robertsson O, Stefansdottir A, Gustafson P, Lidgren L. Timing of preoperative antibiotics for knee arthroplasties: improving the routines in Sweden. *Patient Saf Surg* 2011; 5: 22.
14. Lenander C, Bondesson Å, Midlöv P, Viberg N. Healthcare system intervention for safer use of medicines in elderly patients in primary care-a qualitative study of the participants' perceptions of self-assessment, peer review, feedback and agreement for change. *BMC Fam Pract* 2015; 16: 117.
15. Wettermark B, Hammar N, Fored CM *et al*. The new Swedish Prescribed Drug Register—opportunities for pharmacoepidemiological research and experience from the first six months. *Pharmacoepidemiol Drug Saf* 2007; 16: 726–35.
16. Midlöv P, Bondesson A, Eriksson T, Nerbrand C, Höglund P. Effects of educational outreach visits on prescribing of benzodiazepines and antipsychotic drugs to elderly patients in primary health care in southern Sweden. *Fam Pract* 2006; 23: 60–4.
17. Hovstadius B, Petersson G, Hellström L, Ericson L. Trends in inappropriate drug therapy prescription in the elderly in Sweden from 2006 to 2013: assessment using national indicators. *Drugs Aging* 2014; 31: 379–86.
18. Johnell K, Weitoft GR, Fastbom J. Sex differences in inappropriate drug use: a register-based study of over 600,000 older people. *Ann Pharmacother* 2009; 43: 1233–8.
19. Bergman A, Olsson J, Carlsten A, Waern M, Fastbom J. Evaluation of the quality of drug therapy among elderly patients in nursing homes. *Scand J Prim Health Care* 2007; 25: 9–14.
20. Sjöberg C, Ohlsson H, Wallerstedt SM. Association between multi-dose drug dispensing and drug treatment changes. *Eur J Clin Pharmacol* 2012; 68: 1095–101.

Paper III

Effects of medication reviews on drug-related problems in elderly patients; a cross-sectional study in primary care

Cecilia Lenander[1,2]*, Åsa Bondesson[1,2], Nina Viberg[1,3], Anders Beckman[1], Patrik Midlöv[1]

[1] Department of Clinical Sciences in Malmö, Lund University, Jan Waldenströms gata 35, SE-205 02 Malmö, Sweden

[2] Department of Medicines Management and Informatics, Region Skåne, Sweden

[3] Department of Public Health Sciences, Karolinska Institutet, Sweden

*Correspondence: cecilia.lenander@med.lu.se

Asa.c.bondesson@skane.se, anders.beckman@med.lu.se, nina.viberg@mail.com, patrik.midlov@med.lu.se

ABSTRACT

Background

In general, drug use in the elderly population is extensive and use of potentially inappropriate medications (PIMs) is common, which increases the risk for drug-related problems (DRP). Medication reviews are one method to improve drug therapy by identifying, preventing and solving DRPs.

The aim of this study was to evaluate the effect of medication reviews in elderly patients regarding occurrence and types of drug-related problems, as well as the effects of potentially inappropriate drug use.

Method

This was a cross-sectional analysis to examine medication reviews conducted by trained clinical pharmacists followed by team-based discussions with general practitioners (GPs) and nurses, for elderly patients listed at private primary healthcare centres in Skåne, Sweden. Patients ≥ 75 years living in nursing homes or in their own homes with home care, who received a medication review during 2011-2012, were included. Documented DRPs were described as both the type of DRPs and as pharmacists' recommendation to the GP. The usage of ≥ 3 psychotropics and PIMs (antipsychotics, anticholinergics, long-acting benzodiazepines, tramadol and propiomazine) at baseline and after medication review were also studied.

Results

A total of 1720 patients were included in the analysis. They were on average 87.5 years, used typically 11.3 drugs (range 1-35) and 61% of them used 10 drugs or more. Of the patients, 84% had at least one DRP with a mean of 2.2 DRPs/patient. The most common DRP was unnecessary drug therapy (39%), followed by dose too high (21%) and wrong drug (20%). Withdrawal of drug was the most common result. Of the DRPs, 12% were attributable to PIMs. The proportion of patients with at least one PIM was reduced significantly ($p<0.001$), as was the use of ≥ 3 psychotropics ($p<0.001$).

Conclusion

This study shows that medication reviews performed in everyday care are one way of improving drug use among elderly patients. The use of potentially inappropriate medications and use of three or more psychotropic drugs decreased after the medication review. It also shows that drug use is extensive in nursing home residents and elderly patients with homecare, and that unnecessary drug therapy is a common problem.

Key words: elderly, primary care, medication review, drug-related problems, potential inappropriate medication, clinical pharmacist

BACKGROUND

Demographic data estimates that 22% of the global population will be older than 65 by 2050 [1]. In Sweden, the proportion of the population aged 65 years or older was 19.8% in 2015 and the proportion is estimated to 23% in 2050 [2]. Elderly patients with multiple diseases and polypharmacy risk suffering from drug-related problems [3-5], and a substantial proportion of hospital admissions among elderly are due to adverse drug events (ADEs) [5-7]. The majority of these hospital admissions are avoidable [5, 8].

A previous study conducted in primary care by our group showed that as many as 93% of the studied elderly patients had at least one drug-related problem (DRP). Among these patients the average number of DRPs was 2.5 per patient [9]. Studies from primary care in other countries found an average of 3.5-5.5 DRPs per patient [3, 4, 10], while studies at hospital report 2.6-6.4 DRPs per patient [11-13]. One way of preventing and solving DRPs among the elderly is performing medication reviews. A medication review is a method to analyse, follow-up and review an individual's drug therapy. The review is done in a structured and systematic way, according to local guidelines and routines [14]. Potentially inappropriate medications (PIMs) are one cause of DRPs. In many countries, guidelines concerning potentially inappropriate medication have been developed. The most well-known is Beers criteria [15, 16]. Since many of the drugs listed as PIMs in Beers criteria are unavailable in Europe, criteria corresponding to European drug formularies have been developed, such as the Swedish quality indicators developed by the Swedish National Board of Health and Welfare [17], the STOPP/START criteria [18] and the EU(7)-PIM list [19]. These guidelines point out inappropriate medications in the elderly on a population basis, but there are still individuals that might need them. Another way of identifying inappropriate medications is Medication Appropriateness Index (MAI) [20], an instrument that determines a drug's suitability to an individual, and has been validated for evaluating drug use in the elderly [21]. However, the MAI is a time consuming instrument and less convenient to use in everyday care.

In a hospital setting, medication reviews have been reported to improve drug use [22, 23] and to reduce repeat visits to hospital [11]. Medication reviews in primary care can reduce total number of drugs, reduce falls and maintain self-rated health [24, 25]. The Lund Integrated Medicine Management (LIMM) [26] is an in-hospital intervention model with multi-professional teams, including clinical pharmacists. It has been shown to reduce potentially inappropriate medications and unscheduled drug-related re-visits to hospital [26]. Medication reviews have been conducted in primary care in Skåne County for over 10 years in different projects including to improve patient safety and medication use in the elderly. A study evaluating the

LIMM model adapted for primary care has shown a decrease in total number of drugs and prescription of potentially inappropriate medications for the elderly [9].

There is still need for further analysis of the extent of elderly patients in primary care suffering from drug-related problems and what type of problems they present. Also needed is additional data from a larger patient group on how medication reviews affect the use of potentially inappropriate medications in elderly in primary care.

The aim of this study was to evaluate the effect of medication reviews according to LIMM of elderly patients in primary care regarding occurrence and types of drug-related problems, as well as effects on total drug use and potentially inappropriate drug use.

METHOD

This was a cross-sectional analysis to examine the process of multi-professional medication reviews on elderly patients listed at private primary healthcare centres in Skåne, Sweden. It was based on everyday clinical practice in primary care with regular GPs, nurses and clinical pharmacists.

Setting

Almost all patients in Sweden are registered with a general practitioner (GP) as their primary care provider. The GP treat patients in all ages with a range of health problems, including patients in nursing homes. Skåne County, located in southernmost Sweden, have 1.3 million inhabitants with the majority of them living close to the western coast. Primary care in Skåne is provided by public or private primary care centres, which are all funded by the county council and financed by taxes. There were 150 primary care centres in Skåne and slightly over 40% of these were private during the time of the study. During 2011-2012, the private primary care centres in Skåne were offered medication reviews guided by a clinical pharmacist. A total of 25 centres accepted. Seven clinical pharmacists were involved in the medication reviews and all had at least three years' experience of performing medication reviews. Medication reviews performed in patients aged 75 years or older, living in nursing homes or their own homes with municipally provided home care, were included in this study. For patients receiving more than one medication review, only the first one was included in the analysis.

Patients

For all patients, age, gender, type of housing (nursing home or in their own home with home care), number of medications and types of PIMs was recorded. Some patients (or relatives) refused participation, in some cases the GP or nurse selected patients with the greatest need for medication review if resources didn't allow for all patients to have one, at a nursing home for example.

Potentially inappropriate medications

PIMs were identified according to the Swedish National Board of Health and Welfare's quality indicators for drug use in the elderly [17]. In these usage of ≥1 PIM, ≥3 psychotropics or ≥ 10 medications is classified as an indicator of higher risk for adverse events.

Medication reviews according to the LIMM model

A symptom assessment scale, Pharmacotherapeutical Symptom Evaluation, 20 questions (PHASE-20) [27, 28], was used to estimate the current health status of the patient. This includes medical information such as current diagnosis, blood pressure, pulse, weight (measured by the nurse) and creatinine levels, as well as questions about symptoms such as dizziness, pain and constipation. PHASE-20 is a validated tool for use in connection with medication reviews for identifying possible drug-related symptoms in older people. The tool has been recommended by the Swedish National Board of Health and Welfare [17] for use in medication reviews. The nurse filled out the evaluation together with the patient. For patients unable to do this, the nurse would get assistance from the nursing assistants. This information and a copy of the medication list were sent to the pharmacist one to two weeks prior to the team-meeting.

To identify DRPs, the pharmacist initiated medication reviews based on the background information (symptom assessment form, including some medical information, and the medication list), but had no access to the medical record during this phase. The process was carried out in a structured way using forms from the LIMM model [26].

The following predetermined risk categories for identifying DRPs were used by the pharmacist to ensure structure and consistency [26]:

1. Drugs requiring therapeutic monitoring

2. Potentially inappropriate drugs for elderly according to The Swedish National Board of Health and Welfare (PIMs)
3. Drugs that are not recommended according to the regional drug and therapeutics committee
4. Problems with administration/handling of the drug (crush, cut, inhalation technique)
5. C/D drug–drug interactions (C interactions are those involving a drug combination that could require dose adjustment; D interactions are those involving a drug combination that ought to be avoided)
6. Drug type or drug dosage not adjusted for the patient (renal or liver function)
7. Unclear indication for drug treatment
8. Suboptimal treatment
9. Drugs causing potential adverse drug reaction

After identification, the DRPs were classified by the pharmacist into seven categories of DRPs defined by Cipolle, Strand and Morley [14]:

1. Need for additional therapy
2. Unnecessary drug therapy
3. Wrong drug
4. Dose too low
5. Adverse drug reaction
6. Dose too high
7. Adherence problems

To aid the pharmacists to classify in a similar way, examples for each group was produced.

Based on the identified DRPs and the information sent by the nurse, the pharmacist suggested intervention recommendations. These were predefined and included [26]:

1. For information/notification
2. Initiation of drug therapy

3. Withdrawal of drug therapy
4. Decreased dose
5. Increased dose
6. Dose regimen adjustment
7. Change in drug formulation
8. Change of drug therapy
9. Evaluation of drug therapy

At a team meeting at the primary care centre, or at the nursing home, the identified DRPs and possible interventions were discussed by the patient-responsible GP, the nurse, the pharmacist and in some cases the caregiver. The pharmacist identified and selected which DRPs to discuss, but the GP and nurse was able to add to the list. At this meeting the team had access to the medical record and, if it was held at the nursing home, the nurse had access to the nursing journal. Based on these discussions and his/her clinical knowledge of the patient, the GP then decided on interventions. The changes in patient status (better, worse or unchanged) were to be followed-up in 4-8 weeks by the nurse and forwarded to the pharmacist.

For each patient, age, gender, number of medications and type of PIM was recorded by the pharmacist. If a prescription was for both continuous use and as needed, it was counted as one drug. Drugs for topical use such as eye drops, moisturisers and topical steroids were included; short-term antibiotic prescriptions were not. Information about DRPs discussed, suggested recommendations, agreed upon interventions and follow-up were also recorded.

Data collection

All parts of the medication reviews, as described above, was performed by the participating pharmacists. Finally, the pharmacists entered all information into an Access database. The research team retained the paper records: medication lists, symptom assessments, notes on identified and discussed DRPs, on actions taken and if any follow-up was recorded as well as the Access database.

Data analysis

Descriptive analysis included average age and sex distribution of the patients, as well as the average number of drugs per patient. ”Before medication review” indicates the treatments used prior to performing of medication review. ”After

medication review" is the result of changes in therapy decided upon during the team meeting. In accordance with the Swedish quality indicators [17] the percentage of patients taking 10 or more medications (regularly or as needed) and the percentage of patients taking three or more psychotropic drugs (from one or more of the following Anatomical Therapeutic Chemical Classification System (ATC) [29] groups; N05A (antipsychotics), N05B (anxiolytics), N05C (hypnotics and sedatives) and N06A (antidepressants)) was measured.

Occurrence of DRPs, distribution of types of DRPs, suggested intervention recommendations and the related treatment adjustments, and outcomes of follow-up were determined.

Change in the proportion of patients taking PIMs, as defined in the Swedish quality indicators [17] and including one or more of the following drugs were analysed: antipsychotics (N05A, excluding lithium (N05AN)), drugs with anticholinergic effects (R06AD, G04 and N05BB; for example promethazine, urologic spasmolytics and hydroxyzine), long-acting benzodiazepines (N05BA01, N05CD02 and N05CD03; nitrazepam, flunitrazepam and diazepam), tramadol (N02AX) and propiomazine (N05CM).

Data was analysed using IBM SPSS version 22 [30]. Student's t-test was used to compare groups (nursing home residents vs patients living at home with home care). Multiple significance was tested according to the suggestion by Bland, Altman [31]. Online Chi-square Calculator [32] was used to compare medication use before and after medication review as well as to compare follow-up between groups.

A significance level of 0.05 was used.

RESULTS

A total of 1720 patients were included in the analysis.

The included patients had a mean age of 87.5 years and used on average 11.3 drugs (range 1-35). A majority of the patients were females and lived in nursing homes, Table 1.

Before the medication review 96% of the patients used five drugs or more and 61% used 10 drugs or more. Patients with home care used more drugs for continuous use (9.2) compared to nursing home residents (8.5) ($p=0.004$), while the latter group had more drugs for use as needed (2.8 vs 2.2, $p<0.001$). No significant difference in total number of drugs or usage of ≥ 1 PIM between the groups was seen at baseline. Almost a quarter of the patients in nursing homes used ≥ 3 psychotropics before the medication review, which was significantly more than patients with home care

(13%) (p<0.001). The use of antipsychotics among patients in nursing homes was more common (12.2%) compared to patients with home care (4.7%) (p<0.001), but the use of long-acting benzodiazepines was lower in nursing homes (6.0% vs 10.4%, p=0.045), Table 1.

After medication review the mean number of drugs per patient decreased from 11.3 to 10.5.

Drug-related problems

DRPs were identified in 84% (1447 of 1720) of the patients. A total of 3868 DRPs were identified and presented (range 0-15 per review), giving a mean of 2.2 DRPs per patient (Figure 1). No significant difference was seen between the number of presented DRPs in patients at nursing homes (mean 2.2 (SD 1.9)) and patients with home care (mean 2.4 (SD 1.8)) (p=0.21).

The most common drugs to cause DRPs (n=3868) were those in the 1st level ATC categories "N – Nervous system" (33%), "C – Cardiovascular system" (27%) and "A – Alimentary tract and metabolism" (12%). The single most common drugs to cause DRPs were low dose ASA (4.9%) followed by folic acid (4.8%), citalopram (3.6%) and simvastatin (3.3%).

Of the DRPs 12% (485 of 3868) were attributable to PIMs.

The most common types of DRPs (n=3868) were unnecessary drug therapy (39%), dose too high (21%) and wrong drug (20%), Figure 2.

Suggested intervention recommendations

Of the 3868 identified DRPs, 3860 received an intervention recommendation. The most common interventions suggested by the pharmacist to the GP were withdrawal of drug therapy (47%), decreased dose (21%) and change of drug therapy (9%). Figure 3. For a total of 285 PIMs, therapy was discontinued, which constituted almost 16% of the "withdrawal of drug therapy" group.

Acceptance of suggested recommendations

For the 410 "for information/notification" recommendations acceptance or not by the GP, was not recorded. Of the remaining 3450 recommendations, the GPs accepted 80% (2760 of 3450) of the recommendations suggested by the clinical pharmacist, giving a mean of 1.60 changes per patient (range 1-15). In 9% (301 of

3450) of the cases the GP needed more information before making a decision and in 2% (77 of 3450) the GP solved the DRP in another way than suggested. In 9% (312 of 3450) of the cases the GP did not accept the pharmacists' suggestions.

Follow-up

For 29% (n=1195) of the changes a result at follow-up was recorded. Of these 93% (n=932) led to improved (16.6%) or unchanged (76.4%) status for the patient. However, there was a significant difference between nursing homes and patients with home care. For home care patients 31% of the changes led to an improvement in patient status compared to 15% for nursing home patients ($p<0.0001$).

Potentially Inappropriate Medications

The proportion of patients with least one PIM was reduced significantly ($p<0.001$), Table 2. There was a significant decrease for all subgroups (anticholinergics, tramadol etc.). Before medication review 9 patients used ≥3 PIMs and this decreased to 5 patients after medication review.

Nearly 23% (395 of 1720) of the population used ≥ 3 psychotropics before the medication review, and this decreased to 17% (296 of 1720) after the review ($p<0.001$).

DISCUSSION

This study based in everyday clinical practice in Swedish primary care, shows that the medication reviews decreased the use of potentially inappropriate medications and the use of three or more psychotropic drugs. It also shows that drug-related problems are frequent among older patients with multimorbidity and their most common problem is unnecessary medication.

At baseline, almost 30% of the patients in this study used at least one PIM. This is a slightly more than a Swiss study (22.5%) [33] but comparable to other Swedish studies (26-33%) [9, 34]. Compared to the general population, aged 75 years or older in the county of Skåne, use of at least one PIM was considerably higher in the study population; 30% vs around 10%, indicating that the study population is less healthy than the general population [35]. The use of PIMs in the older population has decreased in recent years in Sweden [35], but the reduction is more distinct in our study. The decrease in use of PIMs after a medication review is in line with other

studies [9, 34]. There are also studies showing a correlation between usage of PIMs and falling [36].

We saw a decrease in total number of drugs and usage of PIMS. Other studies have shown that medication reviews can decrease the total number of drugs [4, 9, 25] and the use of PIMs [9] as well as reduce the incidence of falls [25]. This may in some way affect health care utilisation. However, these patients are frail and elderly and other factors, like the fact that most of them suffer from multimorbidity, can influence their health care utilisation [37, 38].

In our study 61% of the patients used 10 drugs or more, which is much higher than for the total 75+ population in Skåne (10.2% in 2013 [35]). In Sweden, nursing homes are usually for patients who are not able to care for themselves anymore, often because of multimorbidity and thereby polypharmacy, which is supported by this study. With the high number of patients using 10 drugs or more, and unnecessary drug treatment being a common problem, effective ways to improve medication use in the elderly should be highly prioritised.

The population in this study is of similar age and had the same number of medications as in other studies [3, 4, 9, 39] performed in primary care. But compared to these studies [4, 9, 39] fewer patients had at least one DRP in our study, 84% compared to 87%, 93% and 98% respectively. This could be due to a larger, non-selected patient group in this study. As a result of this the mean number of DRPs in this study was lower (2.2) than in the other studies mentioned above (2.5-3.5). In this study the most common DRP was unnecessary medication, which could be any kind of medication including PIMs. Unnecessary medication being the most common DRP is in line with other studies [3, 4], as well as medications from Anatomical Classification System classes "N- Nervous system", "C - Cardiovascular system" and "A - Alimentary tract and metabolism", causing the majority of DRPs. Changes in guidelines or recommendations during this time period, e.g. for folic acid and low dose ASA, may explain some of the DRPs in this study. Since almost all patients at Swedish nursing homes receive assistance with administration of drugs, compliance was not a common DRP in our study. The most common result of the medication reviews was withdrawal of drug therapy, which resulted in a decrease in both total number of drugs per patients and in PIMs.

Seven clinical pharmacists participated in the medication reviews together with many GPs and nurses. The GPs accepted 80% of the clinical pharmacists' suggestions, which indicates that this is a feasible method to use in primary care. A study rating the clinical importance of a sample of these DRPs and suggestions showed a significant clinical importance in the vast majority of them [40]. The study also included a non-selected group of patients, with many patients and GPs from 25 different primary care centres, from all over Skåne. Identification of DRPs was done according to a well-documented method (LIMM) using both the medication list and

the symptom assessment (Phase-20). Another strength is that all medication reviews were conducted as team-based discussions.

There are some limitations to this study. Not all patients at the included primary care centres received a medication review due to lack of resources (i.e. clinical pharmacists) and the medication reviews were done in everyday clinical practice. The pharmacist did not meet the patients and had no access to the patient records when preparing the medication reviews. At the team-meeting the team had access to the patient records and with the GPs knowledge of the patient, the actual DRPs were clarified. Another limitation is the lack of follow-up in a majority of the medication reviews. This was supposed to be done by the nurses as a part of ordinary care. The evaluation might have been performed, but forwarding the results to the pharmacist forgotten. As we evaluated medication reviews in everyday practice, there were no extra resources for such things as reminders to nurses. Another limitation could be the absence of a commonly used method for performing medication reviews and identifying PIMs. Since this was an evaluation of medication reviews performed according to a well-documented Swedish method (LIMM), we used the Swedish quality indicators [17] as the base for our analysis. These indicators are well-known and generally well accepted among Swedish GPs. The STOPP/START criteria on the other hand, is not well-known in Sweden and according to a study by Verdoorn et al [41], many identified DRPs were not associated with these criteria.

To avoid mass significance we checked, by multiplying the observed p-values with the number of tests, that our results where significant at the 0.05 level according to Bland, Altman [31].

Further studies, like a larger randomised controlled study comparing different settings, are needed, especially to see possible effects of medication reviews on health care utilisation.

CONCLUSION

This study confirms that medication reviews performed in everyday care are one way of improving drug use among elderly patients. The use of potentially inappropriate medications and use of three or more psychotropic drugs decrease after a medication review. The study also confirms that drug use is extensive in nursing home residents and elderly patients with homecare, and unnecessary drug therapy is a common problem in this population.

DECLARATIONS SECTION

List of abbreviations

PIM – Potentially Inappropriate Medication

DRP – Drug-Related Problem

GP – General Practitioner

ADE – Adverse Drug Event

MAI – Medication Appropriateness Index

LIMM – Lund Integrated Medicines Management

PHASE-20 – Pharmacotherapeutical Symptom Evaluation, 20 questions

ATC - Anatomical Therapeutic Chemical Classification System

Ethics

The study was approved by the Regional Ethical Review Board in Lund (application number 2013/649). Patient anonymity was accomplished by using a non-traceable id-number.

Availability of data and materials

Since sharing of data was not included in the approval from the ethics committee, data will not be made public.

Consent to participate

No informed consent was obtained from the patients included in the study. The patients were not exposed to any harm by participating, all data are published on group level, and the Ethical Review Board approved the setup.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by a grant from The Swedish Society of Medicine, Fromma foundation as well as ALF funding from Region Skåne awarded to Patrik Midlöv.

Authors' contributions

CL and ÅB designed the study with input from PM. CL and ÅB collected the data and CL conducted the analyses with help from AB. CL drafted the manuscript with help from PM and ÅB. AB and NV made substantial contributions to the manuscript and its conclusions. All authors read, contributed to and approved the final manuscript.

Thanks to the pharmacists performing the medication reviews (Nadia Al-Omar, Linda Andersson, Sara Andersson, Emma Brogård, Karolina Engvall and Emma Lundgren), the participating municipal care nurses, and general practitioners.

We are indebted to Patrick Reilly and Karin Luton for expertise and valuable advice in editing the manuscript.Introduction (chapter headline)

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. Statistics Sweden, [http://scb.se/sv_/Hitta-statistik/Statistik-efter-amne/Befolkning/Befolkningens-sammansattning/Befolkningsstatistik /25788/25795/Helarsstatistik---Riket/26040/]. Access date June 21, 2015.
3. Brulhart MI, Wermeille JP: Multidisciplinary medication review: evaluation of a pharmaceutical care model for nursing homes. Int J Clin Pharm 2011, 33(3):549-557.
4. Finkers F, Maring JG, Boersma F, Taxis K: A study of medication reviews to identify drug-related problems of polypharmacy patients in the Dutch nursing home setting. J Clin Pharm Ther 2007, 32(5):469-476.
5. Beijer HJ, de Blaey CJ: Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. Pharm World Sci 2002, 24(2):46-54.
6. Davies EC, Green CF, Mottram DR, Rowe PH, Pirmohamed M: Emergency re-admissions to hospital due to adverse drug reactions within 1 year of the index admission. Br J Clin Pharmacol 2010, 70(5):749-755.
7. Conforti A, Costantini D, Zanetti F, Moretti U, Grezzana M, Leone R: Adverse drug reactions in older patients: an Italian observational prospective hospital study. Drug Healthc Patient Saf 2012, 4:75-80.
8. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM: Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. BMJ 2004, 329(7456):15-19.
9. Milos V, Rekman E, Bondesson A, Eriksson T, Jakobsson U, Westerlund T, Midlov P: Improving the Quality of Pharmacotherapy in Elderly Primary Care Patients Through Medication Reviews: A Randomised Controlled Study. Drugs Aging 2013, 30:235-246.
10. Sorensen L, Stokes JA, Purdie DM, Woodward M, Elliott R, Roberts MS: Medication reviews in the community: results of a randomized, controlled effectiveness trial. Br J Clin Pharmacol 2004, 58(6):648-664.
11. Gillespie U, Alassaad A, Henrohn D, Garmo H, Hammarlund-Udenaes M, Toss H, Kettis-Lindblad A, Melhus H, Morlin C: A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. Arch Intern Med 2009, 169(9):894-900.
12. Bergkvist Christensen A, Holmbjer L, Midlov P, Hoglund P, Larsson L, Bondesson A, Eriksson T: The process of identifying, solving and preventing drug related problems in the LIMM-study. Int J Clin Pharm 2011, 33(6):1010-1018.

13. Blix HS, Viktil KK, Moger TA, Reikvam A: Characteristics of drug-related problems discussed by hospital pharmacists in multidisciplinary teams. Pharm World Sci 2006, 28(3):152-158.
14. Cipolle RJ SL, Morley PC.: Pharmaceutical care practice. New York: The McGraw-Hill Companies Inc; 1998.
15. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012, 60(4):616-631.
16. Fick DM, Semla TP: 2012 American Geriatrics Society Beers Criteria: new year, new criteria, new perspective. J Am Geriatr Soc 2012, 60(4):614-615.
17. Swedish National Board of Health and Welfare: [Indicators for the evaluation of quality in drug use of the elderly]. 2010.
18. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P: STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age ageing 2015, 44(2):213-218.
19. Renom-Guiteras A, Meyer G, Thurmann PA: The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. Eur J Clin Pharmacol 2015, 71(7):861-875.
20. Hanlon JT, Schmader KE, Samsa GP, Weinberger M, Uttech KM, Lewis IK, Cohen HJ, Feussner JR: A method for assessing drug therapy appropriateness. J Clin Epidemiol 1992, 45(10):1045-1051.
21. Samsa GP, Hanlon JT, Schmader KE, Weinberger M, Clipp EC, Uttech KM, Lewis IK, Landsman PB, Cohen HJ: A summated score for the medication appropriateness index: development and assessment of clinimetric properties including content validity. J Clin Epidemiol 1994, 47(8):891-896.
22. Bergkvist A, Midlov P, Hoglund P, Larsson L, Eriksson T: A multi-intervention approach on drug therapy can lead to a more appropriate drug use in the elderly. LIMM-Landskrona Integrated Medicines Management. J Eval Clin Pract 2009, 15(4):660-667.
23. Spinewine A, Swine C, Dhillon S, Lambert P, Nachega JB, Wilmotte L, Tulkens PM: Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial. J Am Geriatr Soc 2007, 55(5):658-665.
24. Lenander C, Elfsson B, Danielsson B, Midlov P, Hasselstrom J: Effects of a pharmacist-led structured medication review in primary care on drug-related problems and hospital admission rates: a randomized controlled trial. Scand J Prim Health Care 2014, 32(4):180-186.
25. Zermansky AG, Alldred DP, Petty DR, Raynor DK, Freemantle N, Eastaugh J, Bowie P: Clinical medication review by a pharmacist of elderly people living in care homes--randomised controlled trial. Age ageing 2006, 35(6):586-591.
26. Hellstrom LM, Bondesson A, Hoglund P, Midlov P, Holmdahl L, Rickhag E, Eriksson T: Impact of the Lund Integrated Medicines Management (LIMM) model on medication appropriateness and drug-related hospital revisits. Eur J Clin Pharmacol 2011, 67(7):741-752.
27. Hedström M, Lidström B, Hulter-Åsberg K: PHASE-20: a new instrument for assessment of possible therapeutic drug-related symptoms among elderly in nursing

homes [in Swedish]. Nordic Journal of Nursing Research and Clinical Studies (Vård i Norden) 2009, 4:9-14.

28. PHASE-20 [http://www.lul.se/Global/Extran%c3%a4t/V%c3%a5rdgivare/L%c3%a4kemedelsenheten/Dokument/Phase-20/PHAS_20_pat_eng.pdf]. Access date March 29, 2016.
29. Anatomical Therapeutic Chemical Classification System [online] [http://www.who.int/classifications/atcddd/en]. Access date May 15, 2015.
30. IBM Corp.: IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY; 2013.
31. Bland JM, Altman DG: Multiple significance tests: the Bonferroni method. BMJ 1995, 310(6973):170.
32. Chi-square Calculator [http://www.socscistatistics.com/tests/chisquare/default2.aspx]. Access date May 6, 2015.
33. Reich O, Rosemann T, Rapold R, Blozik E, Senn O: Potentially inappropriate medication use in older patients in Swiss managed care plans: prevalence, determinants and association with hospitalization. PloS one 2014, 9(8):e105425.
34. 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.
35. The Swedish National Board of Health and Welfare: [Open comparisons Drug use]. Stockholm; 2015.
36. Berdot S, Bertrand M, Dartigues JF, Fourrier A, Tavernier B, Ritchie K, Alperovitch A: Inappropriate medication use and risk of falls--a prospective study in a large community-dwelling elderly cohort. BMC Geriatr 2009, 9:30.
37. Bahler C, Huber CA, Brungger B, Reich O: Multimorbidity, health care utilization and costs in an elderly community-dwelling population: a claims data based observational study. BMC Health Serv Res 2015, 15:23.
38. Palladino R, Lee JT, Millett C: Association between multimorbidity and healthcare utilisation and health outcomes among elderly people in Europe. In: 7th European Public Health Conference: 20 November, 2014; Glasgow, Scotland. 2014.
39. Gheewala PA, Peterson GM, Curtain CM, Nishtala PS, Hannan PJ, Castelino RL: Impact of the pharmacist medication review services on drug-related problems and potentially inappropriate prescribing of renally cleared medications in residents of aged care facilities. Drugs Aging 2014, 31(11):825-835.
40. Modig S, Holmdahl L, Bondesson A: Medication reviews in primary care in Sweden: importance of clinical pharmacists' recommendations on drug-related problems. Int J Clin Pharm 2016, 38(1):41-45.
41. Verdoorn S, Kwint HF, Faber A, Gussekloo J, Bouvy ML: Majority of drug-related problems identified during medication review are not associated with STOPP/START criteria. Eur J Clin Pharmacol 2015, 71(10):1255-1262.

Tables

Table 1. Baseline characteristics of included patients (n=1720).

	Nursing home n= 1508	Home care n= 212	p-value
Age, mean (SD)	87.7 (5.8)	86.3 (5.7)	<0.01[a]
Female n (%)	1123 (74.5)	142 (67.0)	0.02[b]
Number of drugs per patient, mean (SD) **continuous drugs, mean (SD)** **drugs as needed, mean (SD)**	11.2 (4.6) 8.5 (3.6) 2.8 (2.1)	11.4 (4.3) 9.2 (3.3) 2.2 (2.0)	0.59[a] <0.01[a] <0.01[a]
Number of potentially inappropriate drugs, mean (SD) **Antipsychotics, mean (SD)** **Long-acting benzodiazepines, mean (SD)** **Anticholinergics, mean (SD)** **Propiomazine, mean (SD)** **Tramadol, mean (SD)**	0.30 (0.46) 0.12 (0.33) 0.06 (0.24) 0.09 (0.29) 0.02 (0.15) 0.05 (0.23)	0.27 (0.44) 0.05 (0.21) 0.10 (0.31) 0.09 (0.29) 0.05 (0.21) 0.04 (0.20)	0.35[a] <0.01[a] 0.04[a] 0.90[a] 0.09[a] 0.49[a]
Patients with ≥ 1 PIM, n (%)	453 (30.0)	57 (26.9)	0.35[b]
Patients with ≥ 3 psychotropics, n (%)	367 (24.3)	28 (13.2)	<0.01[b]
DRPs, mean (SD)	2.2 (1.9)	2.4 (1.8)	0.21[a]

SD standard deviation

[a] t-test, [b] Chi square test

Table 2. Number of patients using potential inappropriate medications before and after medication review. (n= 1720 patients)

	Before medication review			After medication review			p-value[a]
	Total	Nursing home	Home care	Total	Nursing home	Home care	
Patients with antipsychotics, *n* (%)	194 (11.3)	184 (12.2)	10 (4.7)	136 (7.9)	128 (8.5)	8 (3.8)	<0.001
Patients with anticholinergics, *n* (%)	158 (9.2)	139 (9.2)	19 (9.0)	72 (4.2)	60 (4.0)	12 (5.7)	<0.001
Patients with propriomazine, *n* (%)	43 (2.5)	33 (2.2)	10 (4.7)	16 (0.9)	10 (0.7)	6 (2.8)	<0.001
Patients with tramadol, *n* (%)	90 (5.2)	81 (5.2)	9 (4.2)	41 (2.4)	39 (2.6)	2 (0.9)	<0.001
Patients with long-acting benzodiazepines, *n* (%)	112 (6.5)	90 (6.0)	22 (10.4)	62 (3.6)	51 (3.4)	11 (5.2)	0.001
Patients with ≥ 1 PIM*, *n* (%)	510 (29.7)	453 (30.0)	57 (26.9)	299 (17.4)	266 (17.6)	33 (15.6)	<0.001
Patients with ≥ 3 psychotropics, *n* (%)	395 (23.0)	367 (24.3)	28 (13.2)	296 (17.2)	274 (18.2)	22 (10.4)	<0.001

*PIM Potentially Inappropriate Medication (antipsychotics, anticholinergics, propiomazine, tramadol and long-acting benzodiazepines)

[a] Chi square test between total numbers (nursing home and home care together)

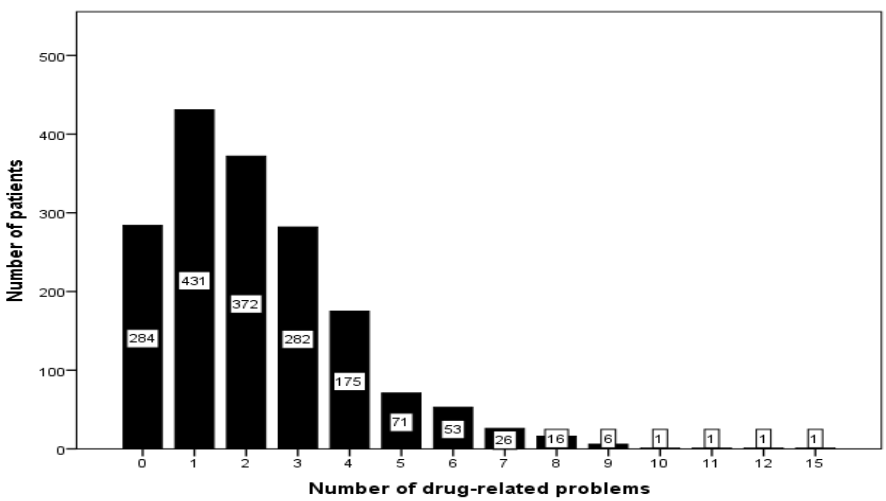


Figure 1. Distribution of drug-related problems (n=1720 patients)

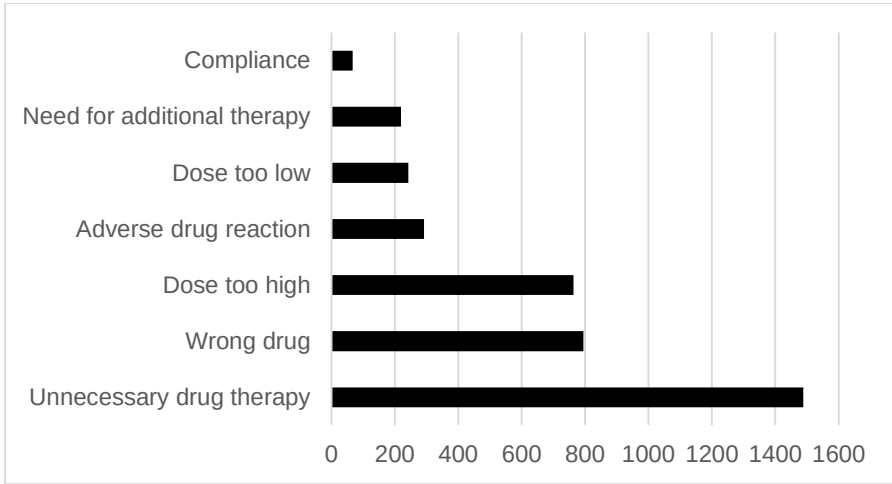


Figure 2. Distrubution of types of drug-related problems (DRP) according to Strand, Cipolle and Morleys definition. (n= 3868 DRPs)

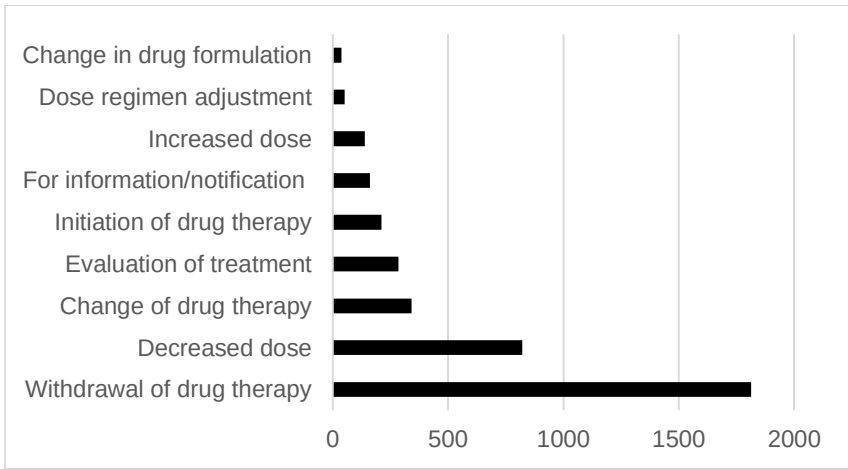


Figure 3. Distribution of types of suggested intervention recommendations (n=3860)

Paper IV

Use of antipsychotic drugs by elderly primary care patients and the effects of medication reviews

Cecilia Lenander[1,2]*, Patrik Midlöv[1], Nina Viberg[1,3], John Chalmers[4], Kris Rogers[4], Åsa Bondesson[1,2]

[1] Department of Clinical Sciences in Malmö, Lund University, Jan Waldenströms gata 35, SE-205 02 Malmö, Sweden

[2] Department of Medicines Management and Informatics, Region Skåne, Sweden

[3] Department of Public Health Sciences, Karolinska Institutet, Sweden

[4] The George Institute of Global Health, University of Sydney, Australia

*Correspondence: cecilia.lenander@med.lu.se

ABSTRACT

Background

Antipsychotics form a class of drugs which should be used with caution in the elderly due to a high risk of adverse events. Despite the risks and the modest effects their use is estimated to be high, especially in nursing homes. This study aimed to explore the effects of medication reviews on antipsychotic drug use for elderly primary care patients and describe the extent of, and reasons for, the prescription of antipsychotics.

Methods

In this cross-sectional study in primary care in Skåne, Sweden, patients ≥ 75 years living in nursing homes or in their own homes with home care were included. The effects of medication reviews were documented, as were the use of antipsychotics and the differences in characteristics between patients receiving or not receiving antipsychotics.

Results

A total of 1683 patients aged 87.6 (±5.7) was included in the analysis. Medication reviews reduced the use of antipsychotics by 23% in this study. Of the 206 patients using antipsychotics, 43% (n=93) had an approved indication while for 15% (n=32) the indication was not given. Antipsychotic drug use was more common with increasing number of drugs ($p=0.001$), and in nursing home residents ($p<0.01$). It was also more frequent in patients with cognitive impairment, depressive symptoms or sleeping problems.

Conclusion

The use of antipsychotic drugs is high in elderly patients in nursing homes. They are often given for indications that are not officially approved, or poorly documented. Medication reviews appear to offer one useful strategy for reducing excessive use of these drugs.

KEY POINTS:

- Potentially inappropriate antipsychotic drug use is high among elderly patients in nursing homes.
- The use correlates with age and number of drugs.
- Medication reviews reduced the antipsychotics drug use by 23% in this study and could be one way of addressing the problem.

INTRODUCTION

The Swedish Board of Health and Welfare published a report in 2010 with quality indicators for treatment of elderly patients [1]. The report points to antipsychotics as a medication group which should be used with caution in the elderly. Prescription of antipsychotics should be limited to patients with psychotic events and perhaps to aggressive patients with dementia [1]. Antipsychotics have a high risk of adverse events, such as extra-pyramidal symptoms, cognitive impairment, sedation and orthostatic hypotension as well as an increased risk of stroke and premature death in patients with dementia [2]. The use of antipsychotics for treatment of behavioral and psychological symptoms in dementia (BPSD) is still high, despite warnings from, for example, the US Food and Drug Administration (FDA), concerning the use of antipsychotics in patients with dementia [3]. Moreover, the evidence for the efficacy of antipsychotics for treating BPSD is at best modest for aggression, and very weak for other symptoms [4].

Prescription of antipsychotics for elderly patients with multiple co-morbidities seems to be high and often for indications that are not officially approved. A Swedish study from 2004 [5], supported by the findings from other studies [3, 2, 6, 7] reporting that 25-30% of patients in nursing homes were given antipsychotics, often without a clear indication.

Medication reviews provide a possible strategy to improve the situation. A medication review is a method to analyse, review and follow-up an individual's drug therapy. The review is done in a structured and systematic way, according to local guidelines and routines [8].

The aim of the present study was to study the effects of medications reviews on antipsychotic drug use in elderly patients. We also wished to explore the extent and justification for the prescription of antipsychotics for elderly patients in everyday practice and whether there were significant differences between patients receiving antipsychotics and those not so treated.

METHOD

This was a cross-sectional study to examine the use of antipsychotics in elderly patients listed at private primary healthcare centres in Skåne, Sweden and also to see if medication reviews could impact the antipsychotic drug use. It was based on

everyday clinical practice in primary care with regular general practitioners (GPs), nurses and clinical pharmacists.

Setting

Almost all patients in Sweden are registered with a general practitioner (GP) as their primary care provider. Primary care in Skåne (region in southern Sweden) is provided by public or private primary care centres, which are all funded by the county council and financed by taxes. At the time of the study, there were 151 primary care centres in Skåne and 43% of these were private. During 2011-2012, the private primary care centres in Skåne were offered medication reviews guided by a clinical pharmacist. A total of 25 out of 65 centres accepted. Seven clinical pharmacists were involved in the medication reviews and they all had at least three years' experience of performing medication reviews. Patients aged 75 years or older, living in nursing homes or their own homes with municipally provided home care who received a medication review were included in this study. For patients having more than one medication review, only the first one was included in the analysis.

Medication reviews according to the LIMM model

The LIMM (Lund Integrated Medication Management) model has been described earlier [9, 10] so the principal features are only briefly outlined here. A nurse did a symptom assessment using PHASE-20 (Pharmacotherapeutical Symptom Evaluation, 20 questions) [11], including medical information such as current diagnosis, blood pressure, pulse, weight (measured by the nurse) and creatinine levels, as well as questions about symptoms such as dizziness, cognitive impairment and anxiety. This was sent together with a medication list to the pharmacist. The pharmacist used this information to identify drug-related problems and suggest recommendations to overcome these problems. All this was then discussed at a team-meeting with the GP caring for the patient, the pharmacist, the nurse and in some cases the carer. Based on the discussion, notes in the medical record and his/her clinical knowledge, the GP then decided on appropriate measures. The results of the changes were followed up at 4-8 weeks by the nurse and forwarded to the pharmacist.

All data were collected in an Access database. Patient anonymity was accomplished by using a non-traceable id-number.

Data collection

For all patients, age, gender, type of housing (nursing home or ordinary home with home care), number of medications, use of antipsychotics, indications for this and symptoms (from PHASE-20) were recorded. As this was a retrospective analysis, the information available was from the medication review/the team meeting, i.e. symptom assessment form, medication list and suggested recommendations from the pharmacist. We had no access to the medical record during the analysis.

All patients receiving antipsychotics were identified by review of the medication lists. Antipsychotics in this study included the following Anatomical Therapeutic Chemical Classification System (ATC) [12] groups: all drugs in N05A, except for lithium, and R06AD01 (alimemazine). For all patients treated with antipsychotics the reason/indication was identified using the symptom assessment form, the medication list and the list of suggested recommendations from the pharmacist. A judgement whether the reason/indication was appropriate or not was done. According to the Swedish quality indicators [1] the following indications were regarded as appropriate: Psychotic conditions, other disease with psychotic symptoms and dementia with BPSD such as severe aggressiveness. All other indications were regarded as potentially inappropriate. For patients with Lewy body dementia, all indications were regarded as inappropriate. If no reason/indication could be found this was registered.

We also noted whether the use of antipsychotics was discussed during the medication review, and whether any changes to therapy were made.

Data analysis

Descriptive analysis included average age and sex distribution of the patients, number of drugs, type of living, use of antipsychotics and the type of antipsychotics drugs used. Percentage of patients with an appropriate indication for antipsychotics was analysed and for what indications. Distribution of types of DRPs, suggested intervention recommendations and the related treatment adjustments were also determined.

Data were analyzed using IBM SPSS version 23 [13]. Categorical versions of continuous variables in the PHASE-20 were dichotomizing these variables into 'No or Small problems' (none or small problems in the original data) and 'Moderate or Severe problems' (moderate or severe in the original data). Differences in proportion of symptoms between patients who were/were not prescribed antipsychotics, was tested using a x2-test on a two-way table. Resident characteristics were assessed for their association with prevalent antipsychotic use in univariable logistic regression models. Variables with p-values under 0.20 were

used in an adjusted multivariable logistic regression model and we used the likelihood ratio test to produce p-values.

A significance level of 0.05 was used.

RESULT

A total of 1683 patients were included in the analysis and of these 12% (n=206) used antipsychotics. The patients included had a mean age of 87.6 years and on average, used 10.9 drugs (range 1-29). Polypharmacy was frequent with 95% using 5 or more drugs and 58% using 10 or more drugs. A majority of the patients were females and lived in nursing homes (Table 1).

During the medication review, the pharmacist brought up the treatment with antipsychotics as a problem for all patients in home care (n=8) and in 80% (n=158) of the cases in nursing homes. The most common drug related problems (DRPs) were wrong drug (60%), unnecessary drug therapy (18%) and adverse events (16%). The most common advice offered was to evaluate the efficacy and possible adverse effects of the drug therapy (48%), followed by withdrawal of drug (19%) and progressive lowering of dose (19%). This advice was acted upon by the doctor in about one quarter of the cases, both in nursing homes and home care.

Before medication review 206 patients used antipsychotics, 198 in nursing homes and 8 in home care. After medication review this had decreased to 157 patients, i.e. a decrease of 23%. For two of the patients receiving two antipsychotics drugs, one was withdrawn following the medication review.

Of the 206 patients using antipsychotics, only 43% (n=93) had an approved indication while for 15% (n=32) no indication was given (Table 2). The most common indications recorded were psychosis or psychotic symptoms (n=80), anxiety (n=61), none specified (n=32) and dementia (n=19). Nine patients were prescribed two antipsychotic drugs at the same time. Of the patients on antipsychotics, 66.5% of those in nursing homes had used the antipsychotic drug for more than three months, compared to 50% in the home care-group.

The antipsychotics most commonly used were risperidone (n=92), haloperidole (n=45), olanzapine (n=26) and alimemazine (n=21).

The use of antipsychotics among patients in nursing homes was more common (13.4%) than in patients with home care (3.8%) ($p<0.001$). There was a no significant difference between the sexes in the use of antipsychotics, men 14.3% compared to women 11.4% ($p=0.12$). Among patients with antipsychotics the use

of ≥10 drugs were more common (65.5%) than in patients without (57%) (p=0.02). Fewer of the patients using antipsychotics could participate (fully or partly) in answering the symptom assessment compared to those not using antipsychotics (43.0% vs 57%, p<0.001). In the group receiving antipsychotics, cognitive impairment, depressive symptoms, anxiety and feeling tired was more common in the symptom assessment than among those not on antipsychotics (Table 3).

Older patients had lower odds of being prescribed antipsychotics [OR=0.96 (0.94-0.99)], while nursing home resident had higher odds [OR=4.20 (2.03-8.66)]. Increased number of drugs was also associated with higher odds of being prescribed antipsychotics [OR=1.06 (1.03-1.09)] (Table 1).

DISCUSSION

Our study shows that medication reviews offer a useful strategy for reducing excessive use of antipsychotic drugs. We found that the use of antipsychotics in nursing homes is common, often without an approved indication and that in many cases the patients had had the treatment for more than three months. We also found that patients on antipsychotics more often reported symptoms such as anxiety, depressive symptoms and cognitive impairment. The use of antipsychotics decreased with age, but increased with nursing home residency and number of drugs.

In the majority of the medication reviews for patients with antipsychotic drugs, the use was discussed during the team-meeting. Action was taken by the doctor in 25% of the cases and the use of antipsychotics was decreased by 23%. Compared to acceptance rates to pharmacist recommendations during medication reviews including all kinds of drugs, 25% is a small percentage [14-16, 10]. This could be due to the need of tapering antipsychotics slowly or perhaps the doctors need more time to consider the suggestions before acting. Since this was a study in everyday practice with no extra resources for follow-up, the only decisions recorded were those taken at the team-meeting. It is possible, however, that the doctor acted upon given advice, some time after the team meeting.

In our study 13% of patients in nursing homes had a prescription for antipsychotics. This is in line with other studies [17, 18]. However, an American study showed variations between 14.8-70.6% [19] depending on setting.

According to a study by Kamble et al one third of dementia patients in nursing homes get antipsychotics, men more often than women [20]. Another study [17] reported that the use of antipsychotics was higher for women, patients with

polypharmacy and those with decreased functional status. In our study, antipsychotic use was more prevalent in nursing home residents, in patients with many drugs and in younger patients. Around 57% of the patients using antipsychotics in this study did not receive the drug for an approved indication. This is lower than in a recent Canadian study, where 70-80% of the use was regarded as potentially inappropriate [21]. However, the Canadian data was collected in 2006-2007, i.e. before the FDA-warnings about antipsychotic drugs use in dementia patients. The most common drugs used were risperidone and haloperidole, which is in line with the recommendations for the use of antipsychotics in Sweden [1].

We know that patients in nursing homes are old, use many medications and that they are susceptible to the negative effects of antipsychotic drugs [1]. FDA (US Food and Drug Administraion) has issued a warning for increased morbidity and mortality in patients with dementia treated with antipsychotics [3]. Antipsychotics are however frequently used to treat psychiatric symptoms in patients with dementia [22, 19].

According to the Swedish indicators [1], treatment effects of antipsychotics should be evaluated and attempts at lowering the dose should be undertaken within two weeks after initiation of therapy. There are studies showing that multi-dose dispensing leads to increased treatment times in general [23] and that multi-dose dispensing is common at Swedish nursing homes which could be one explanation to the higher rates of antipsychotic use in the nursing homes. It is also possible that patients with conditions such as severe BPSD cannot stay at home but are instead moved into a nursing home. This is in line with a French study [24] indicating that for Alzheimers patients, treatment with antipsychotics is more common in nursing home than in home care.

The study included a non-selected group of patients, with many patients and GPs from 25 different primary care centres, in the Skåne region. There were seven clinical pharmacists who participated in the team-based medication reviews. The study was done in everyday practice, reflecting the actual use of antipsychotics and the problems associated with that use.

Our study has some limitations. Antipsychotics were not the only focus in the medication reviews, even though their use was discussed as a problem in the vast majority of the reviews. The participating doctors and pharmacists may have had different priorities. The medication reviews were conducted in everyday clinical practice, with limited resources, including the number of clinical pharmacists, so that not all patients at the included primary care centres received a medication review and follow-up information was not routinely collected. Nor did we have access to patient records during the analysis and therefore we could not establish the connection between onset of symptoms and the timing of the prescription of antipsychotics. Furthermore, as this was a cross sectional observational study, the

findings are limited to reporting associations and cannot infer causality, as for example, in relation to the link between the use of antipsychotics and the frequency of cognitive impairment, depressive symptoms and sleeping disorders.

Future studies with improved follow-up are needed to evaluate the long-term effects of medication reviews on antipsychotic use as well as to establish the link between polypharmacy and antipsychotics drug use.

CONCLUSION

The use of antipsychotic drugs was high in this population of elderly patients in nursing homes in Sweden, particularly in those with cognitive impairment, depression or difficulty in communication. They are often prescribed for indications that are not officially approved, or poorly documented. Medication reviews appear to offer a useful strategy for reducing excessive use of these drugs, and should be explored in subsequent studies.

COMPLIANCE WITH ETHICAL STANDARDS

Acknowledgements

Thanks to the pharmacists performing the medication reviews (Nadia Al-Omar, Linda Andersson, Sara Andersson, Emma Brogård, Karolina Engvall and Emma Lundgren), the participating municipal care nurses and general practitioners.

Authors' contributions

CL and ÅB designed the study with input from PM. CL collected the data and conducted the analyses with help from KR. CL drafted the manuscript with help from PM and ÅB. JC and NV made substantial contributions to the manuscript and its conclusions. All authors read, contributed to and approved the final manuscript.

Conflict of interest

All authors declare that they have no conflict of interest.

Ethical approval

The study was approved by the Regional Ethical Review Board in Lund (application number 2013/649).

Funding

This study was supported by a grant from The Swedish Society of Medicine, Gyllenstierna Krapperup foundation, Fromma foundation as well as ALF funding from Region Skåne awarded to Patrik Midlöv and by the Department of Medicines Management and Informatics, Region Skåne, Sweden.

REFERENCES

1. Swedish National Board of Health and Welfare. [Indicators for the evaluation of quality in drug use of the elderly]. 2010.
2. Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. Jama. 2005;294(15):1934-43.
3. US Food and Drug Administration. Information for Healthcare Professionals: Conventional Antipsychotics. 2008. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124830.htm.
4. Seitz DP, Gill SS, Herrmann N, Brisbin S, Rapoport MJ, Rines J et al. Pharmacological treatments for neuropsychiatric symptoms of dementia in long-term care: a systematic review. International psychogeriatrics / IPA. 2013;25(2):185-203.

5. Swedish National Board of Health and Welfare. Quality of drug use in elderly patients [Kvaliteten i äldres läkemedelsanvändning - KÄLLA-projektet] 2004.

6. Wettermark B, Hammar N, Fored CM, Leimanis A, Otterblad Olausson P, Bergman U et al. The new Swedish Prescribed Drug Register--opportunities for pharmacoepidemiological research and experience from the first six months. Pharmacoepidemiology and drug safety. 2007;16(7):726-35.

7. Shah SM, Carey IM, Harris T, Dewilde S, Cook DG. Antipsychotic prescribing to older people living in care homes and the community in England and Wales. International journal of geriatric psychiatry. 2011;26(4):423-34.

8. Cipolle RJ SL, Morley PC. Pharmaceutical care practice. New York: The McGraw-Hill Companies Inc; 1998.

9. Hellstrom LM, Bondesson A, Hoglund P, Midlov P, Holmdahl L, Rickhag E et al. Impact of the Lund Integrated Medicines Management (LIMM) model on medication appropriateness and drug-related hospital revisits. Eur J Clin Pharmacol. 2011;67(7):741-52.

10. Milos V, Rekman E, Bondesson A, Eriksson T, Jakobsson U, Westerlund T et al. Improving the Quality of Pharmacotherapy in Elderly Primary Care Patients Through Medication Reviews: A Randomised Controlled Study. Drugs Aging. 2013.

11. Hedström M, Lidström B, Hulter-Åsberg K. PHASE-20: a new instrument for assessment of possible therapeutic drug-related symptoms among elderly in nursing homes [in Swedish]. Nordic Journal of Nursing Research and Clinical Studies (Vård i Norden). 2009;4:9-14.

12. WHO. Anatomical Therapeutic Chemical Classification System [online]. http://www.who.int/classifications/atcddd/en.

13. IBM Corp. IBM SPSS Statistics for Windows, Version 22.0. . Armonk, NY2013.

14. Gheewala PA, Peterson GM, Curtain CM, Nishtala PS, Hannan PJ, Castelino RL. Impact of the pharmacist medication review services on drug-related problems and potentially inappropriate prescribing of renally cleared medications in residents of aged care facilities. Drugs Aging. 2014;31(11):825-35.

15. Finkers F, Maring JG, Boersma F, Taxis K. A study of medication reviews to identify drug-related problems of polypharmacy patients in the Dutch nursing home setting. Journal of clinical pharmacy and therapeutics. 2007;32(5):469-76.

16. Brulhart MI, Wermeille JP. Multidisciplinary medication review: evaluation of a pharmaceutical care model for nursing homes. Int J Clin Pharm. 2011;33(3):549-57.

17. Vidal X, Agusti A, Vallano A, Formiga F, Moyano AF, Garcia J et al. Elderly patients treated with psychotropic medicines admitted to hospital: associated characteristics and inappropriate use. Eur J Clin Pharmacol. 2016;72(6):755-64.

18. The Swedish National Board of Health and Welfare. [Open comparisons Drug use]. Stockholm 2015.

19. Frankenthal D, Zandman-Goddard G, Ben-Muvhar Y, Porat-Katz BS. The impact of facility characteristics on the use of antipsychotic medications in nursing homes: a cross-sectional study. Isr J Health Policy Res. 2016;5:12.

20. Kamble P, Chen H, Sherer J, Aparasu RR. Antipsychotic drug use among elderly nursing home residents in the United States. The American journal of geriatric pharmacotherapy. 2008;6(4):187-97.

21. Stock KJ, Amuah JE, Lapane KL, Hogan DB, Maxwell CJ. Prevalence of, and Resident and Facility Characteristics Associated With Antipsychotic Use in Assisted Living vs. Long-Term Care Facilities: A Cross-Sectional Analysis from Alberta, Canada. Drugs Aging. 2016.

22. Ballard C, Howard R. Neuroleptic drugs in dementia: benefits and harm. Nature reviews Neuroscience. 2006;7(6):492-500.

23. Sjoberg C, Ohlsson H, Wallerstedt SM. Association between multi-dose drug dispensing and drug treatment changes. Eur J Clin Pharmacol. 2012;68(7):1095-101.

24. Jacquin-Piques A, Sacco G, Tavassoli N, Rouaud O, Bejot Y, Giroud M et al. Psychotropic Drug Prescription in Patients with Dementia: Nursing Home Residents Versus Patients Living at Home. J Alzheimers Dis. 2015;49(3):671-80.

Table 1. Baseline characteristics.

	Antipsychotic drug use		Overall	Unadjusted		Adjusted[a]	
	Yes n=206	**No n=1477**		**OR (CI)**	**p-value**	**OR (CI)**	**p-value**
Female, n (%)	140 (68.0)	1080 (73.1)	1220 (72.5)	1.29 (0.94;1.77)	0.11	0.80(0.60; 1.11)	0.17
Age, mean (SD)	86.3 (5.9)	87.8 (5.7)	87.6 (5.7)	0.96 (0.94;0.98)	0.001	0.96 (0.94;0.99)	0.02
Nursing home residents, n (%)	198 (96.1)	1276 (86.4)	1474 (87.6)	0.26 (0.13;0.53)	<0.001	4.20 (2.03;8.67)	<0.0001
Number of drugs per patient (except antipsychotics), mean (SD)	12.2 (4.6)	10.9 (4.5)	10.9 (4.5)	1.01 (0.98;1.04)	0.56	1.06 (1.03;1.10)	0.001

[a]Nagelkerke R2 0.05, Hosmer-Lemeshow goodness-of-fit p=0.58

Table 2. Indications for use of antipsychotics. n= 215, with 9 patients having 2 antipsychotics (i.e. 206 patients)

	n (%)	Approved indication[a]
Psychosis or psychotics symptoms	80 (37)	77[b]
BPSD	11 (5)	11
Nausea	4 (2)	-
Anxiety	61 (28)	-
Depression	1 (0.5)	-
Dementia	19 (9)	-
Bipolar disease	6 (3)	5[c]
Sleep	1 (0.5)	-
None specified	32 (15)	-

[a]According to Swedish National Board of Health and Welfare. (2010). [Indicators for the evaluation of quality in drug use of the elderly].

[b]3 patients with lewy body dementia treated with antipsychotics for psychotic symptoms

[c]olanzapine approved

Table 3. Symptoms from PHASE-20a assessment and their frequencies in patients with or without antipsychotic drugs.

Symptoms	Antipsychotic use (n=206)	No antipsychotic	p-value[b]
Sleeping problems	24.9%	18.6%	0.025
Depression	41.0%	27.6%	<0.001
Fatigue	60.0%	50.5%	<0.01
Cognitive impairment	69.8%	56.0%	<0.001
Anxiety	51.7%	30.0%	<0.001
Irritability	41.0%	27.6%	<0.001
Dizziness	37.1%	36.3%	n.s.
Participation in answering symptom assessment	43.0%	57.0%	<0.001

[a] Pharmacotherapeutical Symptom Evaluation, 20 questions

[b] Chi-square test

Printed by Media-Tryck, Lund 2017 NORDIC ECOLABEL, 3041 0903

As the demographics in Sweden and across the world are shifting, the proportion of elderly patients with multiple diseases is increasing. This can lead to the use of more medications, which may increase the risk of drug-related problems. Since this is costly both for society and those affected, something must be done to address this situation. In this thesis different methods to improve drug use among elderly patients in primary care were studied, aiming to evaluate the effects of potentially inappropriate medications and of antipsychotics.

LUND UNIVERSITY
Faculty of Medicine

Department of Clinical Sciences, Malmö

Lund University, Faculty of Medicine
Doctoral Dissertation Series 2017:54
ISBN 978-91-7619-434-8
ISSN 1652-8220