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RESEARCH ARTICLE

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Drug-related problems and changes in drug utilization after medication reviews in nursing homes in Oslo, Norway

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ABSTRACT

Objective: We describe the drug-related problems (DRPs) identified during medication reviews (MRs) and the changes in drug utilization after MRs at nursing homes in Oslo, Norway. We explored predictors for the observed changes.
Design: Observational before-after study.
Setting: Forty-one nursing homes.
Intervention: MRs performed by multidisciplinary teams during November 2011 to February 2014.
Subjects: In all, 2465 long-term care patients.
Main outcome measures: DRPs identified by explicit criteria (STOPP/START and NORGEP) and drug–drug interaction database; interventions to resolve DRPs; drug use changes after MR.
Results: A total of 6158 DRPs were identified, an average of 2.6 DRPs/patient, 2.0 for regular and 0.6 for pro re nata (prn) drugs. Of these patients, 17.3% had no DRPs. The remaining 82.7% of the patients had on average 3.0 DRPs/patient. Use of unnecessary drugs (43.5%), excess dosing (12.5%) and lack of monitoring of the drug use (11%) were the most frequent DRPs. Opioids and psychotropic drugs were involved in 34.4% of all DRPs. The mean number of drugs decreased after the MR from 6.8 to 6.3 for regular drugs and from 3.0 to 2.6 for prn drugs. Patients with DRPs experienced a decrease of 1.1 drugs after MR (0.5 for regular and 0.6 for prn drugs). The reduction was most pronounced for the regular use of antipsychotics, antidepressants, hypnotics/sedatives, diuretics, antithrombotic agents, antacid drugs; and for prn use of anxiolytics, opioids, hypnotics/sedatives, metoclopramide and NSAIDs.
Conclusion: The medication review resulted in less drug use, especially opioids and psychotropic drugs.

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KEYWORDS
Drug-related problems; medication review; nursing home; elderly; discontinuation

Introduction

In Norway, the nursing home (NH) sector comprising 42,000 beds provide care for both physically disabled and psychogeriatric patients. About 80% of NH patients are cognitively impaired and most have at least one significant neuropsychiatric symptom [1,2]. A typical NH patient is an old (mean age, 86 years) and frail female with short life expectancy [3]. Because of multiple comorbidities, they use around eight drugs on a regular basis [1,4,5] and have thus an increased risk of drug–drug interactions [4] and adverse drug reactions [6]. Frailty, cognitive impairment [3] and age-related changes in pharmacokinetics and pharmacodynamics add further to these risks [7].

A drug-related problem (DRP) is 'an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes' [8]. Previous Norwegian studies using different tools for identifying drug–drug interactions [9] and potentially inappropriate prescriptions for the elderly [10,11] have reported that NH patients are frequently exposed to DRPs [1,12,13].

In the NH setting, medication reviews (MRs) are recommended for improving the quality and the follow-up of the drug therapy by substantiating needs for continued use or for better balancing risks with potential benefits [14,15]. However, although MRs may identify and resolve DRPs, there is a lack of evidence about their effects on 'hard' patient outcomes such as adverse drug events, hospital admissions or death [15]. MRs involving collaboration between physicians, pharmacists and nurses have been used in NH settings in several

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countries [1,13,16–18] and such collaboration is recommended in the Norwegian national guideline [14].

The aims of this study were to describe the DRPs identified at multidisciplinary MRs and the interventions that were carried out to resolve them, as well as changes in drug use that followed the MRs. We explored some predictors for the observed changes.

Methods

Patients

Of the 51 NHs in Oslo with long-term care patients ($n = 4020$), 41 accepted to participate in a MR project involving one or more units in their institutions. The project took place between November 2011 and February 2014. Except for those terminally ill, all patients (next of kin for patients with dementia) at the participating units were asked to participate in the MR project ($n = 2625$ patients). Eighteen refused and 142 scheduled MRs were not performed because the patient either died ($n = 32$), became terminally ill ($n = 33$), moved to another institution ($n = 18$), or for some other logistical reasons ($n = 59$). Therefore, a total of 2465 patients (on average 60 patients/NH, range 19–136) had their medication use reviewed by a multidisciplinary team.

Medication reviews

The MRs were conducted as a structured evaluation of each patient's drug use by the NH physician and a registered nurse employed at the unit in collaboration with an externally hired clinical pharmacist. Training sessions were held for the involved physicians, nurses and pharmacists before project start.

From the patient's anonymized medication lists, the pharmacist identified potential DRPs using explicit criteria for pharmacological inappropriateness listed in the STOPP/START criteria [10] and the Norwegian general practice (NORGEP) criteria for assessing potentially inappropriate prescribing to older persons [11] together with the drug–drug interaction database DRUID [9]. At the MR meeting, the physician provided supplementary clinical information from the patient's medical record. The medication and the possible DRPs were discussed aiming at consensus on measures to improve the patient's medication use. In case of disagreement, the physician held the final decision. DRPs and interventions on the drug use were classified according to a consensus-based classification system [8] (see Box 1). Medication lists for about eight patients were reviewed at each meeting that lasted about two hours. The interventions accepted by the patient (next of kin for patients with dementia) were thereafter implemented.

Box 1. Classification of DRPs [8]:

1. Drug choice problem, with subcategories: 1(a) need for additional drug, 1(b) unnecessary drug, 1(c) inappropriate drug choice;
2. Dosing problem, with subcategories: 2(a) too high, 2(b) too low, 2(c) suboptimal dosing scheme, 2(d) suboptimal formulation;
3. Adverse drug reactions;
4. Interactions;
5. Inappropriate drug use, with subcategories 5(a) administered by health personnel, 5(b) administered by patient;
6. Other, with subcategories: 6(a) monitoring of drug use required, 6(b) unclear documentation, 6(c) not classified.

Classification of interventions to resolve DRPs:

1. Stop the drug
2. Drug switch
3. Start new drug
4. Adjust the drug dose
5. Monitor the drug use
6. Other measures

Data retrieval for the present study

The following variables were recorded in our data set: NH identification number, patient's age and gender, patient's drugs in use before and after the MR (drug name, regular or prn use), DRPs (category linked to the drug involved) and interventions implemented (category linked to the drug involved).

Drugs were categorized according to the Anatomical Therapeutic Chemical (ATC) classification system [19]. Drug items without ATC codes (e.g. nutritional supplements, multivitamins) were not included. A drug–drug interaction was recorded as only one DRP.

Statistics

Descriptive statistical analyses were performed using IBM SPSS Statistics v.24 (IBM Corp., Armonk, NY). We explored whether DRPs or the change in the number of drugs after the MR were associated with the patients' age or gender using a Poisson regression model with NH random effects (RE) in Stata SE 14 (Stata Corp LP, College Station, TX). The model was fitted to the individual data of each patient with MR ($n = 2465$), grouped at the level of the NHs ($n = 41$) and further adjusted for drug counts at baseline. Model estimates in terms of incidence rate ratios (IRR)

Table 1. Baseline characteristics of the long-term care patients participating in the medication review project.

Variables	All patients	Age <80 years	Age 80–89 years	Age ≥90 years
Patients with MR, *n* (%)	2465 (100)	463 (18.8)	1023 (41.5)	979 (39.7)
Gender, *n* (%)				
Female	1828 (74.2)	274 (59.2)	752 (73.5)	802 (81.9)
Male	630 (25.6)	188 (40.6)	267 (26.1)	175 (17.9)
Number of drugs, *n* (%)				
Regular drugs	16,634 (69.3)	3324 (68.3)	6960 (70.7)	6350 (68.3)
Prn drugs	7369 (30.7)	1540 (31.7)	2881 (29.3)	2948 (31.7)
Total drugs	24,003 (100)	4864 (100)	9841 (100)	9298 (100)
Mean drugs/patient(±SD)				
Regular drugs	6.8 ± 3.3	7.2 ± 3.6	6.8 ± 3.3	6.5 ± 3.1
Prn drugs	3.0 ± 2.1	3.3 ± 2.3	2.8 ± 2.0	3.0 ± 2.2
Total drugs	9.8 ± 4.4	10.5 ± 4.7	9.6 ± 4.3	9.5 ± 4.3

Missing gender data (7 patients).
The mean numbers of drugs by gender were similar: 6.8 for regular drugs and 3.0 for prn drugs.

Table 2. Categories of drug-related problems and the three drugs (therapeutic groups) most commonly involved in the problem listed.

Drug-related problems (*n* = 6158)		The three drugs most commonly involved in the drug-related problems listed					
Problem	*n* (%)	No. 1	*n* of drugs	No. 2	*n* of drugs	No. 3	*n* of drugs
Unnecessary drug	2680 (43.5)	Hypnotics/sedatives	296	Opioids[b]	249	Anxiolytics	213
Excess dosing	770 (12.5)	Paracetamol	108	Antacid drugs	103	Hypnotics/sedatives	92
Monitoring of drug use required	680 (11.0)	Antidepressants	103	Antidementia drugs	48	Renin–angiotensin system	46
Inappropriate drug choice	503 (8.2)	Opioids	80	Anxiolytics	56	Hypnotics/sedatives	43
Need for additional drug	453 (7.4)	Anti-anaemia drugs[a]	130	B-complex vitamins	62	Paracetamol	43
Adverse drug reaction	287 (4.7)	Hypnotics/sedatives	37	Anxiolytics	32	Antipsychotics	28
Drug–drug interactions	271 (4.4)	Antidepressants	124	Antithrombotic agents	66	Opioids	50
Under-dosing	169 (2.7)	Paracetamol	27	Opioids	26	Thyroid therapy	23
Suboptimal dosing/formulation	141 (2.4)	Beta-blockers	21	Paracetamol	18	Hypnotics/sedatives	6
Other	127 (2.0)	Anti-thrombotic agents[d]	17	Opioids	7	Anxiolytics	7
Inappropriate drug use	77 (1.2)	Paracetamol	12	COPD drugs[c]	9	Opioids	4

[a]iron supplements, B_{12} vitamin and folate.
[b]ATC-N02A comprising weak opioids (codeine, tramadol) and strong opioids.
[c]Chronic obstructive pulmonary disease drugs comprising adrenergic/anti-cholinergic drugs (systemic or inhalation use) and glucocorticoids (inhalation use).
[d]ATC-B01A (mainly warfarin, acetylsalicylic acid and heparin).

and their 95% confidence intervals for numbers of DRPs and drugs after MR were calculated for both genders and different age groups (≥90 years as reference group). The significance level was set at $\alpha = 0.05$.

Ethics

After reviewing the research study protocol, the Regional Committee in Medical Research Ethics in South-East Norway (reference no. 2015/786) and the Norwegian Centre for Research Data (reference no. 2015/43659) concluded that their approvals were not needed.

Results

The mean age of the 2465 patients was 85.9 years (range 36–108) and women were older than men (mean 86.9 and 82.8 years, respectively). Patients' baseline characteristics are presented in Table 1.

In total, the MR identified 6158 DRPs, an average of 2.6 DRPs/patient (range 0–14), 2.0 for regular and 0.6 for prn drugs. In total, 17.3% of the patients had no DRP at the MR. The 82.7% of the patients with DRPs had an average of 3.0 DRPs/patient, 2.3 for regular and 0.7 for prn drugs. Female gender (IRR with 95% CI: 1.11 [1.04–1.17]) was associated with an increased risk of DRPs, but not age.

The DRPs and the drugs most commonly related to them are listed in Table 2. Overall, 6409 drugs were involved in the DRPs (75.2% regular drugs and 24.8% prn drugs). Drugs used prn were most commonly involved in the DRP categories unnecessary drug use (43%), inappropriate drug choice (25%) and excess dosing (11%) and they most commonly consisted of opioids (20.7%), anxiolytics (15.6%) and hypnotics/sedatives (11.8%).

The 6158 DRPs led to 6283 interventions to change the drug therapy, including 125 drug–drug interactions that led to changes in the use of both drugs (Table 3). Of the 2662 discontinued drugs, 47.6% were drugs for prn use, most commonly opioids (20.6%), anxiolytics (14.5%) and hypnotics/sedatives (12.9%). Dosage adjustments and needs for closer monitoring the drug use involved almost exclusively drugs for regular use (96%). The proposed changes in drug therapy were implemented, except for 31 that were

Table 3. Interventions to resolve drug-related problems (DRPs) and the three drugs (therapeutic groups) most commonly involved in changes to the drug therapy regimens.

Interventions to resolve DRPs ($n = 6283$)		The three drugs most commonly involved in the interventions listed					
Intervention	*n* (%)	No. 1	*n* of drugs	No. 2	*n* of drugs	No. 3	*n* of drugs
Stop drug	2662 (42.4)	Opioids[a]	293	Hypnotics/sedatives	242	Anxiolytics	217
Monitor drug use	1455 (22.7)	Antidepressants	182	Antithrombotic agents[b]	112	Hypnotics/sedatives	84
Dose adjustment	1141 (17.8)	Hypnotics/sedatives	131	Paracetamol	128	Antacid drugs[c]	112
Drug switch	438 (6.8)	Opioids	68	Hypnotics/sedatives	41	Diuretics	32
Start new drug	436 (6.8)	Anti-anaemia drugs[d]	124	B-complex vitamins	62	Paracetamol	41
Other	151 (2.4)	Paracetamol	17	Beta-blockers	13	Hypnotics/sedatives	8

[a]ATC-N02A comprising weak opioids (codeine, tramadol) and strong opioids.
[b]ATC-B01A (mainly warfarin, acetylsalicylic acid and heparin).
[c]Mainly proton pump inhibitors.
[d]Iron supplements, B_{12} vitamin and folate.

declined by the patient (next of kin for patients with dementia).

After the MR, the total number of drugs used by all patients went down by 9.3% (from 24,003 to 21,777 drugs; $p < .01$). The mean number of drugs per patient went down from 9.8 to 8.9 ($p < .001$) and the decrease was significant ($p < .001$) for both regular (from 6.8 to 6.3) and prn drugs (from 3.0 to 2.6). For the 82.7% of the patients who had any DRPs, the average decrease in the number of drugs was 1.1 (0.5 for regular and 0.6 for prn drugs). No associations were found between the change in the number of drugs (regular or prn) and the patients' age or gender. The changes in the drug use following the MRs are presented for regular and prn drugs in Tables 4 and 5, respectively. Individual drugs for regular use, which were most commonly discontinued after the MR, were zopiclone (from 23.4% to 20.4%, $p < .01$) and furosemide (from 14.7% to 11.8%, $p < .001$). The prn drugs most often discontinued were oxazepam (from 37.5% to 32.8%, $p < .001$), zopiclone (from 15.6% to 12.9%, $p < .01$), metoclopramide (from 12.5% to 9%, $p < .001$), and clomethiazole (from 7.1% to 4.8%, $p < .001$).

Discussion

To our knowledge, this is the first study to report the effect of multidisciplinary MRs at NHs in terms of DRPs and drug use changes related to both regular and prn drugs.

We found on average 2.6 DRPs/patient (3.0 for patients with DRPs) and that regular drugs contributed to 77% of all DRPs. Psychotropic drugs and opioids were most commonly involved in all types of DRPs and the subsequent interventions. The use of all therapeutic drug groups went down after MR, except for thyroid therapy. In the 82.7% of the patients with DRPs, the number of drugs was reduced with on average 1.1 drugs; most discontinued medications comprised opioids and psychotropic drugs, which should be used with caution in frail elderly.

Our study has some limitations that warrant consideration. We have analysed data from a pragmatic project without random patient selection or a control group for comparison. However, we consider the validity of the results to be reasonable high because 82% of all NHs included 61% of all long-term care patients in the municipality, and because terminal illness was the only exclusion criterion. Furthermore, the patients' age and sex distribution correspond well with that of the total NH population in the city and country [4,12,13,20–22]. Similar MR procedures at the various sites were ensured through training of the MR teams, standardized tools and classification systems [8–11] and because each pharmacist participated in several hundred MRs. The use of the NORGEP criteria [11] may be questioned because they were not developed in particular for nursing home settings and because more recent criteria tailored for the nursing home setting, the NORGEP-NH criteria [23] are now available. However, the NORGEP-NH criteria had not been published when this study started and it was the STOPP-START and NORGEP criteria that were included in in the national guideline for MRs in nursing homes [14].

Although direct comparison with other studies is challenged by differences in MR procedures or drugs targeted, the distribution of the DRPs is comparable to other studies [1,13,16], with problems most frequently associated with unnecessary drug use, excess dosing or inadequate monitoring/follow-up of the drug therapy. The lower prevalence of DRPs as compared to other Norwegian studies reporting 2.5–3.5 DRPs/patient [1,12,13], might be related to more staffing with full-time rather than part-time physicians in Oslo and an increased focus in recent years on safer prescribing practice for the elderly. The average number of drug used per patient before the MR compares well or is slightly lower than in other studies reporting 6.1–9.8 regular [1,4,5,13,16,20,24,25] and 2.8–3.8 prn

Table 4. The proportion of patients using regular drugs before and after the medication review and reductions in drug use after the medication review.

	All patients, $n = 2465$ % of patients using the drug		
Therapeutic group	Before MR	After MR	Reduction (95% CI)[a]
Laxatives	82.0	81.6	0.4
Antithrombotic agents	46.2	43.5	2.7 (–1.0–5.5)
Paracetamol	44.5	43.7	0.8
Antidepressants	37.2	33.3	3.9 (1.2–6.6)
Opioids	34.3	33.1	1.2
Hypnotics/sedatives	32.6	28.9	3.7 (1.1–6.3)
Diuretics	32.0	27.3	4.7 (2.2–7.2)
Anti-anaemia drugs	27.1	26.2	0.9
Beta-blockers	24.9	23.9	1.0
Anxiolytics	21.4	20.2	1.2
Antacid drugs	21.0	18.9	2.1 (–0.1–4.3)
Osteoporosis drugs	20.3	19.5	0.8
Thyroid therapy	20.2	20.2	–
COPD drugs	18.8	17.4	1.4
Antipsychotics	18.3	16.5	1.8 (–0.3–3.9)
Drugs for glaucoma	15.6	15.4	0.2
Antiepileptic drugs	12.4	12.4	–
Drugs used in diabetes	11.9	11.4	0.5
Digitalis and nitrates	11.9	10.8	1.1
Antidementia drugs	11.6	10.5	1.1
Antibiotics	9.8	9.1	0.7
Calcium blockers	8.6	7.5	1.1
Antihistamines	6.4	5.0	1.4
Lipid modifying agents	6.0	5.1	0.9
Oral corticosteroids	6.2	6.0	0.2
Anti-Parkinson drugs	5.4	5.2	0.2
Others	86.5	77.7	8.8 (6.4–11.2)
Total *n* of drugs	16,634	15,563	6.4 (2.2–4.4)

[a]The 95% confidence interval is shown only if significant.

Table 5. The proportion of patients using pro re nata drugs before and after the medication review and reductions in drug use after the medication review.

	All patients, $n = 2465$ % of patients using the drug		
Therapeutic group	Before MR	After MR	**Reduction (95% CI)[a]**
Paracetamol	49.0	48.0	1.0
Anxiolytics	48.1	41.0	7.1 (4.3–9.9)
Opioids	38.9	27.7	11.2 (8.6–13.8)
Laxatives	29.1	26.3	2.8 (0.3–5.3)
Hypnotics/sedatives	24.9	19.1	5.8 (3.5–8.1)
Expectorants	12.9	10.2	2.7 (0.9–4.5)
Nitrates	12.7	11.8	0.9
Metoclopramide	12.5	9.0	3.5 (1.8–5.2)
NSAIDs	6.8	3.9	2.9 (1.6–4.2)
Diuretics	5.7	5.1	0.6
Drugs used in diabetes	5.2	5.0	0.2
Antipsychotics	4.9	3.4	1.5 (0.4–2.6)
Others	48.0	42.2	5.8 (1.7–9.9)
Total *n* of drugs	7369	6214	15.3 (6.6–10.0)

[a]The 95% confidence interval is shown only if significant.

drugs [4,20]. The high drug utilization at NHs may also partly reflect that the drug regiments are based on guidelines developed for younger patients with less comorbidity and the lack of consensus on best practice for pharmacotherapy in the oldest old.

The higher use of opioids in our population as compared with findings in a previous Norwegian study [22] may be related to less use of NSAIDs and increased use for chronic pain. In NH patients with dementia, chronic pain is commonly communicated in terms of neuropsychiatric symptoms [2] and treatment of pain can reduce both agitation and other neuropsychiatric symptoms [26]. This may therefore also explain the more use of analgesics in our study.

Compared to other studies, we found a slightly higher use of hypnotics/sedatives [20,21], but less use of antidepressants [13,20,21] and antipsychotics [20,21] and a comparable use of anxiolytics [20,21]. Although reduced, their utilization was still high after the MR, possibly reflecting the patients' need for continued treatment or reluctance among physicians and nursing staff to discontinue the drugs [27]. Studies of withdrawing long-term use of antipsychotics [28] or anti-depressants [29] in Norwegian NHs have shown that in most cases, discontinuation does not result in more NPS or relapse of depression. We do not know of any studies on discontinuing anxiolytics in NH residents. However, based on their questionable therapeutic long-term effects on anxiety symptoms [30], we consider that these drugs probably are still overused in frail NH patients who are at particular risk of falls and fractures [6].

Based on the results of this study, we support that MRs should be part of the regular clinical follow up of NH residents [14].

Conclusions

The MR resulted in overall less drug use, most pronounced for psychotropic drugs and opioids, and in a closer follow-up to optimise the potential benefits of the drug use. Future research on MRs should include patient-related clinical outcomes.

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The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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