#### ORIGINAL REPORT

# Prescribing quality for older people in Norwegian nursing homes and home nursing services using multidose dispensed drugs

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#### ABSTRACT

**Purpose** To examine and compare the quality of drug prescribing for older patients in nursing homes and home nursing services.

**Methods** Cross-sectional study comprising 11 254 patients aged  $\geq$ 65 years in nursing homes (*n*=2986) and home nursing services (*n*=8268). Potentially inappropriate medications were identified by using the Norwegian General Practice criteria and drug–drug interactions through a Norwegian Web-based tool. The impact of care setting on exposure to selected drug groups, potentially inappropriate medications, and drug interactions was calculated, adjusting for patients' age, gender, and number of drugs used.

**Results** Patients in nursing homes and home nursing services used on average 5.7 (SD = 2.6) multidose dispensed regular drugs. Twentysix percent used at least one potentially inappropriate medication, 31% in nursing homes and 25% in home nursing services, p < .001. Concomitant use of three or more psychotropic and/or opioid drugs was the criterion most commonly identified in nursing homes (18%) and home nursing services (9%), p < .001. Compared with nursing homes, more patients in home nursing services used cardiovascular drugs and fewer patients used psychotropic drugs. Altogether, 8615 drug–drug interactions were identified in 55% of patients, 48% in nursing homes and 57% in home nursing services, p < .001.

**Conclusions** There are significant differences in the quality of drug prescribing in nursing homes compared with home nursing services. Explanations as to why these differences exist need to be further explored. Copyright © 2011 John Wiley & Sons, Ltd.

KEY WORDS-frail older adults; nursing homes; home nursing services; inappropriate prescribing; drug interactions; multidose dispensed drugs

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#### **INTRODUCTION**

In Norway, older persons receiving professional health-related assistance from home nursing services (HNS), or living in nursing homes (NHs), commonly use multiple medications for complex health problems. However, age-related changes and drug interactions put these people at increased risk of adverse drug events and hospitalization.<sup>1</sup> Therefore, evidence-based treatment recommendations are needed that target older patients with co-morbidity.

Inappropriate drug prescribing occurs when risks outweigh benefits.<sup>2</sup> Various sets of explicit prescribing quality indicators are developed to assess quality of prescribing for older people.<sup>3</sup> Studies using Beers' criteria<sup>4</sup> revealed 18%–42% potentially inappropriate medications (PIMs) use in the community and 18%–35% in NHs.<sup>3</sup> Although Beers' criteria are widely used, about half of the listed drugs are unavailable outside the USA. To compensate, criteria corresponding to European drug formularies have been developed, such as the French consensus panel list of PIMs in older persons,<sup>5</sup> the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP),<sup>6</sup> and the Norwegian General Practice (NORGEP) criteria.<sup>7</sup>

To meet older patients' need of drug safety and effective medication management, multidose dispensed drug (MDD) systems have been implemented in Norway during the last decade. MDDs are usually dispensed for 1 or 2 weeks at a time. For NH patients, drug lists are sent from the NH directly to an MDD

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supplier, and drugs are dispensed without further intervention of a pharmacy. For patients in HNS, all prescriptions issued by the patients' general practitioner and other prescribers are ordered through a local pharmacy, which electronically forwards the total orders to an MDD supplier. The pharmacist may make interventions before the total order is submitted. Dispensed drugs are returned to the pharmacy, and the HNS deliver the MDDs to patients as a part of their assistance.

In 2009, approximately 35 000 people received MDDs, primarily older persons living in NHs and those receiving HNS.<sup>8</sup> Only solid drug formulations (i.e., tablets and capsules) can be packaged in MDDs. Drugs prescribed "as required" can be dispensed separately, if requested.

Inappropriate drug prescribing may be critical for frail older people taking multiple medications. So far, little is known about the quality of drug treatment for older persons receiving MDDs. We conducted a cross-sectional study aiming to examine and compare the quality of drug prescribing for older persons in NHs and HNS, based on explicit prescribing quality indicators.

# METHODS

#### Study population

Patients in NHs and HNS aged  $\geq 65$  years and receiving MDDs from one of three suppliers of MDDs in Norway on September 9, 2009, were eligible for this study. For each patient, we obtained the following variables from the supplier: age, gender, setting (NH or HNS), and all dispensed medications (drug name, strength, formulation, dosage, and if the drug is used regularly or as required). Data were provided anonymously, that is, patients' identity (name and social security number) was replaced by consecutive running numbers.

We excluded patients when information regarding gender was missing (n = 47). Further, drug formulations not dispensed as MDDs (i.e., inhalators, ointments, mixtures, suppositories, and injectables, n = 217), medications exclusively prescribed "as required" (n = 25), herbal remedies (n = 6), and medications with unclear dosage (n = 3) were excluded. All drugs were coded according to the Anatomical Therapeutic Chemical classification system.<sup>9</sup>

# Potentially inappropriate medications

Each patient's drug list was screened for PIMs by means of the NORGEP criteria.<sup>7</sup> NORGEP is composed of 36 items, that is, 21 single medications and

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15 drug–drug combinations to be avoided in older people (Table 1). After publication of NORGEP in 2009, carisoprodol and chlorpromazine have been withdrawn from the Norwegian market. MDDs are commonly dispensed for a 1- or 2-week period; medications requiring close monitoring (such as warfarin), and those susceptible of contamination (such as antiinfectives and cytostatics), are usually not dispensed as MDDs. Consequently, we excluded the six NOR-GEP items addressing warfarin as well as Anatomical Therapeutic Chemical groups J (anti-infectives) and L (antineoplastic and immunomodulating agents). Excluding these items left a subset of 28 NORGEP criteria for assessing PIMs in this study (Table 1).

# Drug-Drug interactions

In addition to the nine drug–drug combinations included in NORGEP, patients' drug lists were systematically screened for drug–drug interactions (DDIs) using a Norwegian Web-based tool, DRUID,<sup>10</sup> where DDIs are classified according to a 4-point severity scale: (A) of academic interest, (B) take precautions, (C) should be administered 2–3 hours apart, and (D) should not be combined. DRUID includes mostly pharmacokinetic DDIs, whereas pharmacodynamic DDIs caused by counteracting drugs, or drugs with similar mechanism of action, do not systematically trigger a DDI count. Screening for DDIs was performed by the enterprise responsible for development and support of the Web-based tool (Emetra AS).

# Ethics and approvals

The Regional Committee for Medical and Health Research Ethics presented no objections regarding the study design and concluded that committee clearance was not required. The Norwegian Social Science Data Services approved the study.

# Statistical analysis

Student's *t*-test was applied to compare means (continuous data; age, number of drugs used) and  $\chi^2$  test to compare proportions (categorical data; gender, setting). Logistic regression was performed to examine the impact of care setting (NH or HNS) on exposure to selected drug groups, PIMs or DDIs, adjusting for patients' age and gender and number of drugs used. Effect estimates are presented as prevalence odds ratio (OR) with 95% confidence interval. Pearson's correlation coefficient (*r*) was calculated (one-tailed) to examine associations between patients' age, number of drugs used, PIMs, and DDIs, respectively. We considered

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Table 1. Use of PIMs according to NORGEP criteria (n and proportion per 1000) among patients in nursing homes and home nursing services

NORGEP criteria <sup>7</sup>		All patients		ng homes	Home nursi	ing services		
	( <i>n</i> = 11 254)		( <i>n</i> =	2986)	(n = 8268)			
	n	‰	n	‰	n	‰	OR	CI
1. Amitriptyline	194	17	37	12	157	19	1.59	1.10-2.29
2. Doxepine	44	4	9	3	35	4	1.52	0.73-3.20
3. Clomipramine	18	2	4	1	14	2	0.94	0.31-2.90
4. Trimipramine	53	5	15	5	38	5	0.91	0.50-1.68
5. Chlorpromazine			Wi	ithdrawn fr	om the Norwe	gian market		
6. Chlorprothixene	138	12	45	15	93	11	0.59	0.41-0.85
7. Levomepromazine	157	14	43	14	114	14	0.84	0.59-1.21
8. Prochlorperazine	51	5	13	4	38	5	1.19	0.63-2.27
9. Diazenam	256	23	92	31	164	20	0.61	0.47-0.80
10. Nitrazepam	317	28	79	26	238	29	1.17	0.90 - 1.52
11 Flunitrazenam	56	5	17	6	39	5	0.94	0.52 - 1.68
12 Oxazenam $30 \text{ mg}/24 \text{ h}$	0	_	0	-	0	-	-	-
13. Zoniclone $7.5 \text{ mg}/24 \text{ h}$	40	4	5	2	35	4	0.40	0 15-1 01
14 Carisoprodol	10		Wi		om the Norwe	oian market	0.10	0.15 1.01
15 Devtropropovuphene	23	2	10	3	13	2 2	0.47	0.20-1.09
16. Theophylline	23	2	10	6	58	27	1.03	0.61 1.75
17 Sotalol	80	8	14	5	75	9	2.00	1 17_3 73
18 Develorfeniramine	28	2	2	3	20	2	0.06	0.42 2.21
10. Devemonterina 10. Devemonterina	20	4	12	1	20	2	0.90	0.42 - 2.21 0.46 1.67
20. Hudrouvine	246	22	10	4	125	4	0.00	0.40-1.07
20. Hydroxy2life	240	22	121	41	123	13	0.57	0.26 - 0.46
22. Warfarin - NSAID	200	23	30	19 Not analy	202 rod duo to inco	24 mulata data	1.15	0.80-1.50
22. Wallalli + NSAID				not analy	zeu que to mco	inpiete data		
23. Wartarin + Onoxacin or cipronoxacin								
24. Wartarin + Erythromycin or clarithromycin								
25. Warrann + SSKI	1.45	10	20	0	117	14	1.64	1.07.0.50
26. NSAID (or coxib) + ACE inhibitor (or ARB)	145	13	28	9	117	14	1.64	1.07-2.50
27. NSAID + Diuretic	179	16	52	17	127	15	1.02	0.73–1.42
28. NSAID + Glucocorticoid	41	4	8	3	33	4	1.65	0.75-3.63
29. NSAID+SSRI	116	10	43	14	73	9	0.59	0.40-0.87
30. Erythromycin or clarithromycin + statin				Not analy	zed due to inco	mplete data		
31. ACE inhibitor + potassium/potassium-sparing diuretic	297	26	49	16	248	30	2.20	1.60 - 3.02
32. Fluoxetine or fluvoxamine + TCA	1	0	0	0	1	0	-	-
33. Beta blocker + cardioselective calcium antagonist	37	3	5	2	32	4	2.54	0.98–6.58
34. Diltiazem + lovastatin or simvastatin	23	2	1	0	22	3	8.07	1.08-60.33
35. Erythromycin or clarithromycin + carbamazepine				Not analy	zed due to inco	mplete data		
36. Concomitant prescription of three or more drugs within the groups centrally acting analgesics, antipsychotics, antidepressants, and/or benzodiazepines	1274	113	528	177	746	90	0.40	0.35-0.45
Any NORGEP criterion (%)	2971	(26.4)	937	(31.4)	2034	(24.6)	0.67	0.61 - 0.74

Note: The impact (OR) and 95%CI of care setting on use of PIMs, adjusted for patients' age, gender, and number of drugs; nursing homes were used as reference.

PIMs, potentially inappropriate medications; OR, odds ratio; CI, confidence interval; NORGEP, Norwegian General Practice; NSAID, non-steroidal antiinflammatory drug; SSRI, selective serotonine reuptake inhibitor; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; TCA, tricyclic antidepressant.

p < .05 statistically significant. Analysis was performed using PASW Version 18.

#### RESULTS

The study population was composed of 11254 patients, 2986 in NHs (72% women) and 8268 in HNS (69% women; Table 2). Patients in NHs were on average older than those in HNS (85.3 vs. 83.0 years, p < .001). Women were generally older than men in NHs (86.3 vs. 82.9, p < .001) and HNS (83.8 vs. 81.1, p < .001).

#### Drug use

The dataset was composed of 63936 drug items. The mean number of regular drugs per patient in NHs and HNS combined was 5.7 (SD = 2.6), with no difference between the groups. Women and men in NHs used 5.8 and 5.7 drugs (p = .43), respectively, and women and men in HNS use 5.7 and 5.5 drugs (p < .001), respectively. The number of drugs used was weakly inversely correlated with patients' age in both NHs and HNS (r < .16). Drugs for the cardiovascular and musculoskeletal systems were more frequently

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Table 2. Patient characteristics of the total study population and nursing home and home nursing service groups; drug utilization by ATC first level

	Total group			Nursing homes				Home nursing service					Difference				
	n	n	n	%	Both g	enders	N	len	Wo	men	Both g	genders	М	en	Wo	men	$p^*$
			n	%	n	%	n	%	n	%	п	%	n	%			
n	11 254	100	2986	26.5	843	7.5	2143	19.0	8268	73.5	2566	22.8	5702	50.7			
Age, M (SD)	83.6	(7.4)	85.3	(7.3)	82.9	(7.4)	86.3	(7.0)	83.0	(7.3)	81.1	(7.6)	83.8	(7.0)	<.01		
Drugs, M (SD)	5.9	(2.7)	5.9	(3.0)	6.0	(2.8)	5.9	(3.0)	5.9	(2.6)	5.7	(2.6)	6.0	(2.7)	.45		
ATC first level																	
Α	6426	57.1	1787	59.8	477	56.6	1310	61.1	4639	56.1	1375	53.6	3264	57.2	.09		
B	6353	56.5	1568	52.5	497	59.0	1071	50.0	4785	57.9	1567	61.1	3218	56.4	.12		
С	8960	79.6	1994	66.8	586	69.5	1408	65.7	6966	84.3	2170	84.6	4796	84.1	<.01		
D	10	0.1	3	0.1	1	0.1	2	0.1	7	0.1	6	0.2	1	< 0.1	_		
G	1251	11.1	310	10.4	108	12.8	202	9.4	941	11.4	390	15.2	551	9.7	.92		
H	2142	19.0	509	17.0	100	11.9	409	19.1	1633	19.8	300	11.7	1333	23.4	.65		
J	806	7.2	303	10.1	62	7.4	241	11.2	503	6.1	118	4.6	385	6.8	.17		
L	175	1.6	45	1.5	2	0.2	43	2.0	130	1.6	39	1.5	91	1.6	.48		
Μ	1939	17.2	385	12.9	77	9.1	308	14.4	1554	18.8	346	13.5	1208	21.2	.03		
N	7752	68.9	2555	85.6	712	84.5	1843	86.0	5197	62.9	1451	56.5	3746	65.7	<.01		
Р	16	0.1	2	0.1	0	0	2	0.1	14	0.2	1	< 0.1	13	0.2	_		
R	1253	11.1	415	13.9	137	16.3	278	13.0	838	10.1	247	9.6	591	10.4	.43		
S	4	< 0.1	1	< 0.1	1	0.1	0	0	3	< 0.1	0	0	3	0.1	_		
V	9	0.1	0	< 0.1	0	0	0	0	9	0.1	4	0.2	5	0.1	_		
Total	37 096		9877		2760		7117		27 219		8014		19 205				

ATC, Anatomic Therapeutic Chemical.

\*Chi-square test for group differences.

used, and psychotropic drugs were less frequently used, by patients in HNS compared with those in NHs (Tables 2 and 3).

Table 3 shows that antithrombotics (49% of patients), diuretics (44%), beta-blockers (40%), drugs affecting the renin-angiotensin system (37%), and antidepressants (31%) were the therapeutic subgroups most commonly prescribed. Compared with patients in NHs, more patients in HNS received cardiovascular drugs, and fewer used psychotropic drugs. More patients in NHs than in HNS used opioid (N02A) and non-opioid analgesic (N02B) drugs (Table 3). Paracetamol with codeine compounds was the opioid drug most frequently prescribed (5.9% of patients in NHs vs. 3.5% in HNS, p < .001), whereas paracetamol accounted for >99% of all non-opioid analgesics prescribed (40.3% in NHs vs. 14.8% in HNS, p < .001). Non-steroidal anti-inflammatory drugs (NSAIDs) were dispensed to 4.0% of patients in NHs and 3.7% of patients in HNS, p = .64 (not shown in table).

# Potentially inappropriate medications

Concomitant use of three or more psychotropic and/or opioid drugs was the criterion most commonly identified in both NHs (17.7%) and HNS (9.0%). Of all other PIMs, only the prevalence in NHs of hydroxyzine (4.1%) and diazepam (3.1%) exceeded 3%. Significantly different prevalence figures for patients in NHs and HNS were

found for five single PIMs and five drug–drug combinations (Table 1). PIMs including psychotropic drugs were more prevalent in NHs.

Totally, 26% used at least one PIM according to the NORGEP criteria, 31% in NHs and 25% in HNS, p < .001. Although more women than men in HNS used PIMs (26.3% vs. 20.9%, p < .001), no difference between the genders was found in NHs (31.4%). Mean numbers of PIMs per patient were significantly (p < .01) correlated with numbers of drugs used (all patients, r = .38; NHs, r = .42; HNS, r = .36) and weakly inversely correlated with patients' age in both NHs and in HNS (r < .13).

When excluding concomitant use of three or more psychotropic and/or opioid drugs, 21% of the study population were prescribed PIMs, with no difference between the groups.

# Drug–Drug interactions

The screening for DDI using DRUID revealed 8615 DDIs in 55% of patients, 48% in NHs and 57% in HNS, p < .001 (all patients, M = .77 DDIs per patient; NH, M = .65 DDIs per patient; HNS, M = .81 DDIs per patient). More women in HNS compared with men were exposed to DDI (58.5% vs. 54.0%, p < .001); however, no significant difference between genders was found in NHs (48.2% vs. 46.7%, p = .51). The number of DDIs per patient was significantly (p < .01)

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ATC code		<b>All patients</b> ( <b>n</b> = 11 254)		Nursin (n=	<b>g homes</b> 2986)	Home nursing services (n = 8268)		OR	CI
	Therapeutic drug group	п	%	п	%	n %			
A02B	H <sub>2</sub> blockers and proton pump inhibitors	2399	21.3	637	21.3	1762	21.3	1.05	0.94-1.17
A10B	Oral antidiabetics	1270	11.3	269	9.0	1001	12.1	1.41	1.21-1.63
A11E	Vitamin B complex	1861	16.5	539	18.1	1322	16.0	0.84	0.75-0.94
A12A	Calcium	1450	12.9	288	9.6	1162	14.1	1.71	1.48-1.97
B01A	Antithrombotic agents	5464	48.6	1255	42.0	4209	50.9	1.57	1.44-1.72
B03A	Iron preparations	908	8.1	255	8.5	653	7.9	1.03	0.88-1.20
B03B	Vitamin $B_{12}$ and folic acid	804	7.1	312	10.4	492	6.0	0.54	0.47-0.63
C01A	Cardiac glycosides	1106	9.8	246	8.2	860	10.4	1.54	1.32-1.80
C01D	Vasodilators	1184	10.5	225	7.5	959	11.6	2.36	2.00-2.78
C03	Diuretics	4971	44.2	1290	43.2	3681	44.5	1.26	1.15-1.38
C07A	Beta-blocking agents	4513	40.1	785	26.3	3728	45.1	2.71	2.45-2.99
C08	Calcium channel blockers	2023	18.0	315	10.5	1708	20.7	2.42	2.12-2.76
C09	Agents acting on the renin-angiotensin system	4113	36.5	690	23.1	3423	41.4	2.61	2.36-2.89
C10A	Lipid-lowering drugs, statins	3153	28.0	365	12.2	2788	33.7	3.99	3.51-4.53
H03A	Thyroid preparations	1508	13.4	348	11.7	1160	14.0	1.33	1.17-1.52
M05B	Bisphosphonates	990	8.8	151	5.1	839	10.1	2.40	2.00-2.89
N02A	Opioid analgesics	1067	9.5	370	12.4	697	8.4	0.68	0.59-0.78
N02B	Non-opioid analgesics	2442	21.7	1215	40.7	1227	14.8	0.25	0.23-0.28
N03A	Antiepileptics	882	7.8	245	8.2	637	7.7	0.78	0.67-0.92
N05A	Antipsychotics	1345	12.0	543	18.2	802	9.7	0.39	0.35-0.45
N05B	Anxiolytics	1554	13.8	733	24.5	821	9.9	0.32	0.28-0.36
N05C	Hypnotics and sedatives	3069	27.3	914	30.6	2155	26.1	0.85	0.77-0.94
N06A	Antidepressants	3534	31.4	1227	41.1	2307	27.9	0.50	0.45-0.55
N06D	Antidementia drugs	1037	9.2	368	12.3	669	8.1	0.61	0.53-0.69
R06A	Antihistamines	897	8.0	287	9.6	610	7.4	0.70	0.60-0.82

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Table 3	The 25 most frequently	v used drug groups	among natients in	nursing homes ar	nd home nursing s	ervices
rable 5.	The 25 most neguenti	y used drug groups	s among patients m	nurshig nomes a	ia nome naising s	

The impact (OR) and 95%CI of care setting on use of drug groups, adjusted for patients' age, gender, and number of drugs used; nursing homes were used as reference.

OR, odds ratio; CI, confidence interval; ATC, Anatomical Therapeutic Chemical.

correlated with the number of drugs used (all patients, r=.61; NHs, r=.61; HNS, r=.62) and weakly inversely correlated with patient's age in both NHs and in HNS (r < .13). Most DDIs were assigned low severity levels: (A) 27% and (B) 39% of all patients. DDIs of all four severity levels were more prevalent in HNS than in NHs (Table 4).

#### DISCUSSION

Older patients in NHs and HNS used 5.7 MDDs regularly. Compared with patients in NHs, more patients in

Table 4.	DDIs among	patients in	nursing	homes	and	home	nursing	services
	-	*						

HNS used cardiovascular drugs, and fewer patients used psychotropic drugs; fewer patients in HNS were exposed to PIMs, and more patients were exposed to DDIs.

#### Methodological considerations

To the best of our knowledge, this is the first study comparing the quality of MDD prescribing for older patients in NHs and HNS. The study population was composed of numerous NHs and HNS throughout the country, representing about 10% of the total NH

Severity level	All patients ( <i>n</i> = 11 254)		Nursing	homes	Home nursi	ng services		
			( <i>n</i> = 2986)		(n=8)	268)	OR	CI
	n	%	n	%	n	%		
A	3030	27	631	21	2399	29	1.77	1.58-1.98
В	4380	39	1103	37	3277	40	1.20	1.09-1.33
С	1010	9	178	6	832	10	2.05	1.72-2.45
D	195	2	29	1	166	2	2.09	1.40-3.14
Any DDI*	6147	55	1426	48	4721	57	1.75	1.58-1.95

The impact (OR) and 95%CI of care setting on DDIs, adjusted for patients' age, gender, and number of drugs used; nursing homes were used as reference. DDI, drug-drug interactions; OR, odds ratio; CI, confidence interval.

\*Sum does not add up as one patient can be exposed to several DDIs. Severity level: (A) of academic interest, (B) take precautions, (C) should be administered 2–3 hours apart, and (D) should not be combined.

and HNS population aged  $\geq 65$  years in Norway, and contributing to external validity. Comprehensive information on drug use in large groups of these patients provided by the MDD supplier is otherwise unavailable because patients in NHs are not included. and those in HNS cannot specifically be identified in the Norwegian prescription database.<sup>11</sup> The MDD records are probably a true picture of both drug prescribing and drug ingestion in NHs, because nursing staff in charge of drug administration ensures good compliance. Furthermore, NORGEP and DRUID provide the advantage of being based on the national drug formulary. However, NORGEP was originally intended for use among community-dwelling older people. Therefore, the criteria may possibly underestimate PIMs in particularly vulnerable older patients in NHs. Based on DRUID, mostly pharmacokinetic DDIs were identified, which are predictable and thus preventable, whereas clinically relevant pharmacodynamic DDIs may have been underestimated.

Limitations of using MDD prescribing data are lack of information on drugs used "as required" and exclusion of drug formulations other than tablets and capsules. This applies for drugs such as lactulose mixture extensively used in NHs; warfarin, which has potential for dangerous interactions with other drugs; and anxiolytics, hypnotics, and analgesics commonly used "as required." This means that our data represent a certain underestimation of overall drug use, PIMs, and DDIs. Lack of access to clinical information limits assessment of prescribing quality for specific diagnoses. With such access, we could have performed analysis using screening tools<sup>6,12</sup> that would have provided a more comprehensive picture.

# Drug utilization

Comparison of drug utilization studies among older people is hampered by heterogeneity in study population (the general population of older people, patients in hospital, NHs, or HNS), data sources (medical record, prescription database, or MDD), and prescribing indicators (such as Beers, STOPP, and NORGEP); prevalence figures should therefore be interpreted with caution.

The age and gender distribution of the study population is in line with recent Scandinavian studies of older people in NHs and the community.<sup>8,13,14</sup> The 5.7 regular drugs prescribed for patients in NHs and HNS reflect similar and substantial complex health problems in both groups of older people.

The different patterns of drug use in NHs and HNS (Tables 2 and 3) are consistent with previous studies, <sup>14–16</sup> but we were not able to identify comparative studies. More use of psychotropic drugs in NHs

compared with HNS probably reflects extensive symptomatic treatment of behavioral and psychiatric symptoms in dementia that are prevalent among patients in NHs.<sup>17</sup> In contrast, more use of cardiovascular drugs in HNS is possibly explained by greater emphasis on preventive and curative treatment for non-institutionalized older people. The large difference between the groups regarding lipid-modifying agents (NHs = 12.2%; HNS = 33.7%) may reflect compliance with treatment recommendations that advice against these drugs for patients with life expectancy fewer than 5 years, which applies for most patients in NHs.<sup>12</sup> More use of all types of analgesics in NHs, particularly non-opioid analgesics such as paracetamol (NHs 40.7%; HNS 14.8%), is possibly due to higher prevalence of pain, better diagnostics, or more rational pain treatment.

# Potentially inappropriate medications

Based on 28 of the 36 original NORGEP criteria, this study revealed PIMs in 31% of patients in NHs compared with prevalence rates from 18% to 35% in studies based on Beers' criteria.<sup>3</sup> The prevalence of PIMs among patients in HNS was 25% in the present study and 21% in an Irish study based on the STOPP criteria<sup>18</sup> and ranged from 18% to 42% in studies based on Beers' criteria.<sup>3</sup> Two Norwegian studies conducted on relatively healthier older people in general practice reported 14% PIMs during 1 month<sup>19</sup> and 19% PIMs during 1 year.<sup>20</sup> Swedish studies on older people receiving MDDs revealed 74% prevalence of PIMs and DDIs combined in NHs<sup>15,21</sup> and 40% in the community.<sup>15,21</sup> Both studies showed an inverse correlation between prescribing quality and patients' age, supported by a German NH study<sup>22</sup> as well as our findings.

The prevalence of PIMs in NHs in this study was lower compared with that in previous NH studies in Norway<sup>23,24</sup> and other Nordic countries regarding long-acting benzodiazepines, anticholinergic drugs, and multiple psychotropic drugs.<sup>14,15,25</sup> However, concomitant use of three or more psychotropic drugs in our study was more prevalent than reported in previous Norwegian cross-sectional studies in the community<sup>20</sup> and in NHs.<sup>26</sup>

Considering all NORGEP criteria combined, prescribing quality in this study appears to be poorer in NHs than in HNS. Differences between the settings are mainly due to the far most prevalent criterion, concomitant use of three or more psychotropic and/or opioid drugs (NHs = 18%, HNS = 9%), and reflect different drug use patterns toward more use of psychotropic drugs in NHs. This particular criterion puts emphasis on polypharmacy with increased risk of gait instability, falls, fractures, and cognitive decline in frail older people. However, the criterion has the disadvantage of double counting psychotropic drugs already included in 15 other criteria (Nos. 1–4, 6–13, 20, 29, and 32; Table 1) and thus overestimating inappropriate prescribing in NHs.

Although most single criteria had less than 3% prevalence, they must be regarded clinically significant due to increased risk of adverse side effects, such as hyperkalemia with combinations of angiotensin-converting enzyme inhibitors and potassium/potassium-sparing diuretics, or compromised kidney function with use of NSAIDs.

# Drug–Drug interactions

A study from Taiwan reported DDIs in 25% of NH patients<sup>27</sup> versus 48% in our study. Two Swedish NH studies examining drugs used regularly and "as required" revealed 41%–45% DDIs assigned Class C and 8%–12% DDIs assigned Class D, <sup>14,15</sup> compared with 6% Class C and 1% Class D DDIs of regular MDDs in the present study. The 58% DDIs prevalence in HNS in our study exceeds the 45%–46% prevalence reported in two European studies.<sup>28,29</sup> Variations between countries may probably be explained by different drug interaction databases and computerized detection programs.

One might question the clinical relevance of the DDIs identified in our study, as serious interactions were scarce. Further, we are not aware if prescribers took clinical considerations and precautions such as increasing intervals between drug doses regarding Class C interactions.

Prescribed equal average numbers of drugs, more patients in HNS than in NHs were exposed to DDIs. Differences between the settings can be explained by different drug use patterns, as more patients in HNS used cardiovascular drugs that are involved in DDIs more frequently than psychotropic drugs.<sup>30</sup> Physicians might have considered DDIs more carefully when initiating additional drugs for particularly frail older patients in NHs compared with general practitioners prescribing for patients in HNS. Web-based interaction tools connected to electronic patient record systems should be used systematically by prescribers to avoid DDIs.

#### Implications

Compared with previous research, this study suggests that the use of several PIMs has decreased in Norwegian NHs. However, increased co-prescribing of multiple psychotropic and opioid drugs is of great concern.

The Norwegian General Practice is a suitable tool for screening large databases for PIMs. To increase the eligibility for particularly frail older patients in NHs and HNS, special NORGEP criteria should be developed with even stricter indicators for use of drugs such as NSAIDs. Further, we suggest including a criterion for cardiovascular polypharmacy, addressing the risk of hypotension, gait instability, and falls.

Our study suggests that MDD systems have potential for systematically identifying PIMs and DDIs by means of explicit prescribing indicators such as NORGEP and DRUID. When MDDs are introduced on a large scale, screening of patients' drug list and feedback to the prescribers should be mandatory to assure prescribing quality. Two Swedish studies revealed that community-dwelling older persons receiving MDDs were more prone to PIMs and less susceptible to DDIs, compared with those receiving their drugs from a pharmacy.<sup>21,31</sup> We can only speculate if the ordination system for MDDs is leading to less contact between the patients and their physicians, especially in HNS, and subsequently poorer monitoring of regular drug treatment. Our findings emphasize the need for control mechanisms that ensure prescribing quality for MDD users.

Nursing homes have often been criticized for suboptimal drug therapy. This study demonstrates that the quality of drug prescribing differs significantly between older patients in NHs and HNS. MDD systems have only recently been implemented on a larger scale in Norway, and therefore, it is important to evaluate the prescribing quality prospectively. Future studies should evaluate whether the MDD systems may contribute to improve prescribing quality.

# CONFLICT OF INTEREST

Farmaka AS provided data for this study. Farmaka AS is one of the suppliers of multidose dispensed drugs in Norway.

# **KEY POINTS**

- Older patients in NHs and HNS used on average 5.7 MDDs.
- Patients in NHs used fewer cardiovascular drugs and more psychotropic drugs, compared with those in HNS.
- In total, one in four patients was prescribed PIMs and one in nine patients used three or more psy-chotropic drugs concomitantly.
- In HNS, fewer patients received PIMs, and more patients were exposed to DDIs.

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#### REFERENCES

- Beijer HJ, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. *Pharm World Sci* 2002; 24: 46–54.
- Hanlon JT, Schmader KE, Ruby CM, et al. Suboptimal prescribing in older inpatients and outpatients. J Am Geriatr Soc 2001; 49: 200–209.
- Chang CB, Chan DC. Comparison of published explicit criteria for potentially inappropriate medications in older adults. *Drugs Aging* 2010; 27: 947–957.
- Fick DM, Cooper JW, Wade WE, et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med 2003; 163: 2716–2724. DOI: 10.1001/ archinte.163.22.2716.
- Laroche ML, Charmes JP, Merle L. Potentially inappropriate medications in the elderly: a French consensus panel list. *Eur J Clin Pharmacol* 2007; 63: 725–731.
- Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. *Age Ageing* 2008; **37**: 673–679. DOI 10.1093/ ageing/afn197.
- Rognstad S, Brekke M, Fetveit A, *et al.* The Norwegian General Practice (NOR-GEP) criteria for assessing potentially inappropriate prescriptions to elderly patients. A modified Delphi study. *Scand J Prim Health Care* 2009; 27: 153–159. DOI: 10.1080/02813430902992215.
- Wekre LJ, Spigset O, Sletvold O, et al. Multidose drug dispensing and discrepancies between medication records. *Qual Saf Health Care* 2010; 19: e42. DOI: 10.1136/qshc.2009.038745.
- WHO. Collaborating Centre for Drug Statistics Methodology ATC/DDD Index. 2011; Available from: http://www.whocc.no/atc\_ddd\_index/.
- DRUID. Drug information database. 2011; Available from: www.interaksjoner.no.
  The Norwegian Institute of Public Health. The Norwegian Prescription Database. Oslo 2011; Available from: http://www.norpd.no/.
- Barry PJ, Gallagher P, Ryan C, *et al.* START (screening tool to alert doctors to the right treatment) an evidence-based screening tool to detect prescribing omissions in elderly patients. *Age Ageing* 2007; **36**: 632–638. DOI 10.1093/ageing/ afm118
- Ruths S, Straand J, Nygaard HA. Multidisciplinary medication review in nursing home residents: what are the most significant drug-related problems? The Bergen District Nursing Home (BEDNURS) study. *Qual Saf Health Care* 2003; 12: 176–180.
- Olsson J, Bergman A, Carlsten A, et al. Quality of drug prescribing in elderly people in nursing homes and special care units for dementia: a cross-sectional computerized pharmacy register analysis. Clin Drug Investig 2010; 30: 289–300.
- Bergman Å, Olsson J, Carlsten A, *et al.* Evaluation of the quality of drug therapy among elderly patients in nursing homes. *Scand J Prim Health Care* 2007; 25: 9–14.

- Barry PJ, O'Keefe N, O'Connor KA, et al. Inappropriate prescribing in the elderly: a comparison of the Beers criteria and the improved prescribing in the elderly tool (IPET) in acutely ill elderly hospitalized patients. J Clin Pharm Ther 2006; **31**: 617–626.
- Selbaek G, Kirkevold O, Engedal K. The prevalence of psychiatric symptoms and behavioural disturbances and the use of psychotropic drugs in Norwegian nursing homes. *Int J Geriatr Psychiatry* 2007; 22: 843–849. DOI: 10.1002/ gps.1749.
- Ryan C, O'Mahony D, Kennedy J, *et al.* Potentially inappropriate prescribing in an Irish elderly population in primary care. *Br J Clin Pharmacol* 2009; **68**: 936–947. DOI: 10.1111/j.1365-2125.2009.03531.x.
- Straand J, Rokstad KS. Elderly patients in general practice: diagnoses, drugs and inappropriate prescriptions. A report from the More & Romsdal Prescription Study. *Fam Pract* 1999; 16: 380–388.
- Brekke M, Rognstad S, Straand J, et al. Pharmacologically inappropriate prescriptions for elderly patients in general practice: How common? Baseline data from The Prescription Peer Academic Detailing (Rx-PAD) study. Scand J Prim Health Care 2008; 26: 80–85. DOI: 10.1080/02813430802002875.
- Johnell K, Fastbom J. Multi-dose drug dispensing and inappropriate drug use: A nationwide register-based study of over 700,000 elderly. *Scand J Prim Health Care* 2008; 26: 86–91. DOI: 10.1080/02813430802022196.
- Kolzsch M, Kopke K, Fischer T, et al. Prescribing of inappropriate medication in nursing home residents in Germany according to a French consensus list: a crosssectional cohort study. *Pharmacoepidemiol Drug Saf* 2011; 20: 12–19. DOI: 10.1002/pds.2005.
- Nygaard HA, Naik M, Ruths S, *et al.* Nursing-home residents and their drug use: a comparison between mentally intact and mentally impaired residents. The Bergen district nursing home (BEDNURS) study. *Eur J Clin Pharmacol* 2003; 59: 463–469. DOI: 10.1007/s00228-003-0646-7.
- Ruths S. Evaluation of prescribing quality in nursing homes based on drugspecific indicators: The Bergen district nursing home (BEDNURS) study. Nor J Epidemiol. 2008; 18: 173–178.
- Hosia-Randell HM, Muurinen SM, Pitkala KH. Exposure to potentially inappropriate drugs and drug-drug interactions in elderly nursing home residents in Helsinki, Finland: a cross-sectional study. *Drugs Aging* 2008; 25: 683–692.
- Ruths S, Straand J, Nygaard HA. Psychotropic drug use in nursing homesdiagnostic indications and variations between institutions. *Eur J Clin Pharmacol* 2001; 57: 523–528.
- Liao HL, Chen JT, Ma TC, et al. Analysis of drug-drug interactions (DDIs) in nursing homes in Central Taiwan. Arch Gerontol Geriatr 2008; 47: 99–107. DOI: 10.1016/j.archger.2007.06.007.
- Tulner LR, Frankfort SV, Gijsen GJ, et al. Drug-drug interactions in a geriatric outpatient cohort: prevalence and relevance. Drugs Aging 2008; 25: 343–355.
- Bjorkman IK, Fastbom J, Schmidt IK, et al. Drug-drug interactions in the elderly. Ann Pharmacother 2002; 36: 1675–1681.
- Rosholm JU, Bjerrum L, Hallas J, *et al.* Polypharmacy and the risk of drug-drug interactions among Danish elderly. A prescription database study. *Dan Med Bull* 1998; 45: 210–213.
- Lesen E, Petzold M, Andersson K, et al. To what extent does the indicator "concurrent use of three or more psychotropic drugs" capture use of potentially inappropriate psychotropics among the elderly? Eur J Clin Pharmacol 2009; 65: 635–642. DOI: 10.1007/s00228-009-0623-x.