



## ORIGINAL ARTICLE

## Drug treatment at the end of life: An epidemiologic study in nursing homes

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### Abstract

**Objective.** To examine drug treatment in nursing home patients at the end of life, and identify predictors of palliative drug therapy. **Design.** A historical cohort study. **Setting.** Three urban nursing homes in Norway. **Subjects.** All patients admitted from January 2008 and deceased before February 2013. **Main outcome measures.** Drug prescriptions, diagnoses, and demographic data were collected from electronic patient records. Palliative end-of-life drug treatment was defined on the basis of indication, drug, and formulation. **Results.** 524 patients were included, median (range) age at death 86 (19–104) years, 59% women. On the day of death, 99.4% of the study population had active prescriptions; 74.2% had palliative drugs either alone (26.9%) or concomitantly with curative/preventive drugs (47.3%). Palliative drugs were associated with nursing home, length of stay > 16 months (AOR 2.10, 95% CI 1.12–3.94), age (1.03, 1.005–1.05), and a diagnosis of cancer (2.12, 1.19–3.76). Most initiations of palliative drugs and withdrawals of curative/preventive drugs took place on the day of death. **Conclusion.** Palliative drug therapy and drug therapy changes are common for nursing home patients on the last day of life. Improvements in end-of-life care in nursing homes imply addressing prognostication and earlier response to palliative needs.

**Key Words:** Drug therapy, end of life care, general practice, Norway, nursing homes, palliation

### Introduction

In Norway, 47.5% of deaths occur in nursing homes (NHs), 32.5% in hospitals, and 14.5% at home [1]. About 95% of patients in long-term care will die in the institution [2]. NH patients are prescribed a wider range of medications than any other subpopulation [3,4]. For the dying patient, standing drug treatments must be reconsidered and often discontinued. The last days of life are often characterized by symptoms such as pain, respiratory distress, and anxiety, as well as inability to take oral medications [5]. These symptoms may be palliated by parenterally administered drugs [6].

Whereas palliative literature has a main focus on specialized care for patients with cancer in hospice and hospital, including a range of drug therapy options for the dying [6–8], international consensus on palliative end-of-life (EOL) drug treatment for

more heterogeneous NH populations is lacking. Derived from international and Norwegian guidelines [6–8], a shorter drug list has been recommended for use in NHs in Norway, comprising parenteral morphine, benzodiazepines, anticholinergics, and antipsychotics [2,5]. Previous studies on EOL care in NHs have reported on treatment with selected drug groups such as opioids and pulmonary agents [9], and pain relief [4] without a clearly defined palliative drug treatment.

Pharmacological treatment for dying patients is thus an important aspect of EOL care in NHs, of which we have little knowledge. Insight into initiation and discontinuation of drug therapy in this phase may shed light on the quality of EOL care and point to vulnerable patient groups. Our study aimed to examine drug treatment in NH patients at the EOL, and to identify predictors of a clearly defined palliative drug therapy.

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(Received 7 June 2014; accepted 23 September 2014)

ISSN 0281-3432 print/ISSN 1502-7724 online © 2014 The Author(s)  
DOI: 10.3109/02813432.2014.972068

End-of-life care guidelines are centred on cancer patients, while nursing home patients die from various illnesses.

- This study shows that palliative drugs were commonly prescribed for nursing home patients during the last days of life.
- A diagnosis of cancer and length of stay were associated with palliative drug therapy.
- Most initiations of palliative drugs, and most withdrawals of curative/preventive drug therapy, occurred on the day of death.

## Material and methods

### Study population

NHs in Norway accommodate around 41 000 beds, corresponding to 18% of the general population 80 years and older. All NHs provide EOL care, but only 42 institutions have specialized palliative care units. Most NH physicians in Norway are part-time engaged general practitioners [1]. The study population comprised all patients in three urban NHs in Norway admitted from January 2008 and deceased before February 2013. The institutions were selected on the basis of using an electronic patient record system optimized for data extraction [10].

### Data collection

We collected routinely registered data from the patients' final NH stay: demographic data (age, gender, date of NH admission and death, long- or short-term stay); diagnoses (ICD-10) [11]; medications (generic name, Anatomical Therapeutic Chemical (ATC) code [12], drug formulation, regular or as-needed schedule, indication, dates of initiation, alteration, or discontinuation). An external IT consultant extracted the data, and replaced ID-numbers with a running number, the key to which remained undisclosed to the research group.

### Drug therapy

We defined palliative EOL drug therapy in NHs on the basis of indication, drug, and formulation; (1) any drug prescription with an explicit EOL care indication key word was included: palliative, terminal, death, death rattle, Liverpool Care Pathway, or EOL; (2) we also included prescriptions of specifically recommended *injectable* palliative EOL drugs for use in NHs [2,5], regardless of missing EOL key words in the indication text (Table I). "Curative/preventive drug therapy", in contrast, was defined as medication for regular use without an explicit EOL care indication.

### Statistical analysis

User rates were established for drugs according to the above categories. We explored predictors of palliative EOL drug therapy by a chi-squared test, and subsequently by binary logistic regression analysis; dependent variable: palliative EOL drug therapy; independent variables: age, gender, length of stay, nursing home, diagnosis of cancer. All variables but age were analysed as categorical. Significance was determined at a level of 5%. IBM SPSS Statistics 20 (SPSS Inc., Chicago, Ill., USA) was used for statistical analyses.

## Results

### Patient characteristics

The study population comprised 524 deceased patients. Median (range) age at death was 86 (19–104) years, 59.4% were women, 68.1% in long-term care. The most common registered diagnoses were dementia (36.8% of the patients), congestive heart failure (29.6%), and cancer (23.7%) (Table II).

The three NH populations did not differ with regard to gender or number of diagnoses. Compared with the other NHs, more patients at NH C were 86 years and older, or had a diagnosis of infection or cancer,  $p < 0.01$ . Patients at NH A had longer stays

Table I. Injectable drugs recommended for palliative treatment for the dying in NHs in Norway [2,5], by proportion (%) of users on the day of death.

Drug name	ATC code	Common EOL use	Proportion (%) of patients
Morphine	N02AA01	Pain or dyspnoea	71.4
Glycopyrronium	A03AB02	Death rattle	46.9
Scopolamine	N05CM05	Death rattle	25.8
Morphine-scopolamine	N02AG01	Pain or dyspnoea and death rattle	12.2
Midazolam	N05CD08	Anxiety, agitation	55.0
Diazepam	N05BA01	Anxiety, agitation	1.0
Haloperidol	N05AD01	Nausea and terminal delirium	46.9

Table II. Patient characteristics (n = 524).

Median (range) age at death, years	86 (19–104)
Women, %	59.4
Median (range) length of stay, days	103 (0–1765)
Long-term care, %	68.1
Diagnoses:	
Dementia, %	36.8
Congestive heart failure, %	29.6
Cancer, %	23.7
Chronic pulmonary disease, %	18.5
Infections, %	20.0
Hip fracture, %	9.7

( $p < 0.01$ ), as the EPR data were collected from was used only in the long-term ward.

Patients with cancer more frequently died within two weeks of admission than patients without cancer (41.1% vs. 20.5%,  $p < 0.01$ ). Patients with dementia more frequently died after stays of longer than 16 months compared with patients without this diagnosis (40.4% vs. 16.0%,  $p < 0.01$ ).

#### Drug use on the day of death

On the day of death, 99.4% of the study population were on drug therapy. The most common regular and as-needed drugs are shown in Table III.

Of the 4736 standing prescriptions (regular and as-needed drugs) on the day of death, palliative EOL drugs comprised 1306 (27.6%) and curative/preventive drugs 2419 (51.1%), while 1011 (21.3%)

prescriptions were not classified in either category. Indication was documented for 99.6% of all drugs on the day of death.

Altogether 50.2% of patients were prescribed any drug with a specified EOL care indication. The most common palliative EOL drugs were morphine (71.4% of patients), midazolam (55.0%), glycopyrronium (46.9%), and haloperidol (46.9%) (see Table I). Palliative EOL drugs were prescribed to 74.2% of the study population, either alone (26.9%) or concomitantly with curative/preventive drugs (47.3%). Curative/preventive drugs were prescribed to 72.5% of patients (alone 25.2%). Some 95.7% of palliative EOL drugs were prescribed as needed. Patients had standing prescriptions of median (25th–75th percentile) three (zero–eight) palliative EOL drugs and three (zero–four) curative/preventive drugs on the date of death. There was a median period of two (zero–seven) days from prescription to death for palliative EOL drugs.

Having prescriptions of palliative EOL drugs at death was associated with length of stay  $> 16$  months (AOR 2.10, 95% CI 1.13–3.95), cancer (2.12, 1.19–3.76), age (1.03, 1.005–1.05), and being at NH B (3.53, 1.99–6.25) or NH C (4.20, 2.36–7.48) (Table IV).

Figure 1 shows that the proportion of patients for whom at least one palliative EOL drug was initiated, or at least one curative/preventive drug was discontinued, increased in the last week before death and peaked on the day of death.

Table III. Most common drugs on the date of death (% of patients).

ATC-code	Regular drugs Drug subgroup	Proportion (%) of patients	ATC-code	As-needed drugs Drug subgroup	Proportion (%) of patients
A06A	Laxatives	32.6	N02A	Opioid analgesics	82.6
N02A	Opioid analgesics	32.4	N05C	Hypnotics	70.4
N02B	Non-opioid analgesics and antipyretics	28.2	N05A	Antipsychotics	51.1
C03C	High-ceiling diuretics	26.7	N05B	Anxiolytics	30.9
B01A	Antithrombotic agents	24.0	N02B	Non-opioid analgesics and antipyretics	26.0
N06A	Antidepressants	19.1	A03A	Drugs for functional gastrointestinal disorders <sup>1</sup>	24.6
C07A	Beta-blocking agents	17.6	C03C	High-ceiling diuretics	16.8
A02B	Drugs for peptic ulcer and gastro-oesophageal reflux disease	15.1	A03F	Metoclopramide	13.4
B03B	Vitamin B12 and folic acid	14.3	A06A	Laxatives	13.0
N05C	Hypnotics	13.5	C01D	Vasodilators used in cardiac diseases	11.1
N05A	Antipsychotics	11.5	R03A	Adrenergic inhalants	6.3
N05B	Anxiolytics	11.1	A10A	Insulins and analogues	5.2
C09A	ACE inhibitors, plain	8.6	B05B	i.v. solutions	4.8
H02A	Corticosteroids for systemic use, plain	8.4	R05C	Expectorants, excl. combinations with cough suppressants	4.6
R03A	Adrenergic inhalants	8.4	R03B	Other drugs for obstructive airways disease, inhalants	4.4

Note: <sup>1</sup>Glycopyrronium represented 84.8% of prescriptions in this category.

Table IV. Associations between palliative EOL drug therapy and patient characteristics.

	Proportion of patients (%) prescribed palliative drugs	Chi-square, p	AOR	95% CI
<b>Nursing home:</b>				
A	52.7	< 0.01	1	Ref
B	78.7		3.53	1.91–6.00
C	80.4		4.20	2.26–7.08
<b>Length of stay (quartiles):</b>				
< 2 weeks	81.2	0.01	1.86	0.97–3.25
2 weeks–3 months	65.1		1	Ref
3–16 months	71.8		1.70	0.97–3.17
> 16 months	78.6		2.10	1.13–3.95
<b>Gender:</b>				
Women	75.8	0.31	1	Ref
Men	71.8		0.98	0.60–1.44
<b>Age:</b>				
86+	77.4	0.06	1.03	1.005–1.05
< 86	70.0			
<b>No. of diagnoses:</b>				
> 6	76.6	0.21	Variable not included	
< 6	71.7			
<b>Cancer:</b>				
No	71.5	0.01	1	Ref
Yes	83.1		2.12	1.30–4.13
<b>Dementia:</b>				
No	72.2	0.16	1	Ref
Yes	77.7		1.43	0.88–2.25
<b>Infections:</b>				
No	75.4	0.22	Variable not included	
Yes	69.5			
<b>Chronic pulmonary disease:</b>				
No	75.2	0.30	Variable not included	
Yes	70.1			
<b>Heart failure:</b>				
No	73.4	0.52	Variable not included	
Yes	76.1			
<b>Hip fracture:</b>				
No	74.6	0.53	Variable not included	
Yes	70.6			

Notes: Logistic regression model: chi-squared (8, 524) = 58.41,  $p < 0.001$ , Cox & Snell  $R^2 = 0.11$ , 74.4% correctly classified. The logistic regression was performed as a block analysis, each variable being adjusted by the effects of the others. Association strength is given as adjusted odds ratios (AORs), with 95% confidence intervals (CI). Only variables with a  $p < 0.20$  in the chi-squared test were included in the regression analysis, with the exception of gender which was included on the basis of being a common confounder. In the regression model, age was analysed as a continuous variable, all other included variables as categorical. Ref = reference value.

## Discussion

Our study shows that palliative EOL drugs were commonly prescribed for NH patients during the last days of life. NH, a diagnosis of cancer, and long stay were associated with palliative EOL drug therapy. Most initiations of palliative EOL drugs, and most withdrawals of curative/preventive drug therapy, occurred on the day of death.

### *Strengths and weaknesses*

The study population comprised patients from all types of wards, and although the diagnostic data are

not validated this broad diversity is expected to reflect NH populations in general.

With the exception of short-term care patients from NH A, all patients admitted and deceased in three NHs during the five-year study period were included, limiting selection bias. Only three institutions participated in the study, limiting statistical power and to some extent generalizability.

A complete set of medication data for all patients was collected. The electronic patient record did not include information on whether prescribed medication was actually taken, leading to possible overestimation of drug use. Prescribed medication, on the



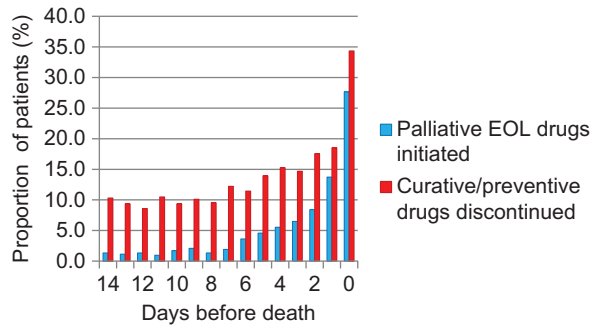


Figure 1. Proportion of patients (%) for whom at least one palliative EOL drug was initiated, or at least one curative/preventive drug was discontinued during the last 14 days of life.

other hand, may reflect the doctor's treatment decisions more appropriately than given medication. This point is particularly important for palliative drugs, which comprised almost exclusively as-needed drug prescriptions.

Use of indication text secured a comprehensive definition of palliative EOL drugs, while inclusion of specifically recommended palliative EOL drugs ensured that these prescriptions were not missed regardless of missing EOL key words in the indication text. Restricting the latter to injectables, we excluded prescriptions less specific to the dying patient, such as opioid tablets, oral suspensions, and patches. Injectable antipsychotics and benzodiazepines may on occasion be used to treat neuropsychiatric symptoms in dementia. A median of two days from prescription to death makes it less likely, though, that these prescriptions were issued for their non-palliative indications. Although anticholinergics have other indications, in injectable form, glycopyrronium and scopolamine are seldom used for non-palliative purposes in NHs.

#### Comparison with other studies

There are few other studies reporting on drug therapy at the EOL in the general NH population, and with considerably smaller sample sizes. Decreased overall treatment intensity has been found in patients perceived as dying, across NH, hospital, and general practice settings in the Netherlands [13]. Patients with dementia dying in American NHs were prescribed unchanged total numbers of drugs, palliative medications replacing other medications [9].

Our study adds to previous knowledge showing that NH patients with the longest duration of stay, or a diagnosis of cancer, were more likely to receive palliative EOL drugs on the day of death than those without these characteristics. More than 80% of long-term care patients have dementia [14], interfering

with the communication of suffering, analgesia, and EOL care [15–17]. Accurate survival prediction for patients with advanced dementia is difficult, and may hinder palliative care [18]. Longer NH stays may nevertheless allow time for advance care planning and staff familiarity with the patient, thus facilitating palliation, and perhaps explaining the association found with the longest stays. Patients with cancer often have expected deaths with a typically rapid functional decline, and are at the centre of palliative guidelines [7,19]. Palliative drug therapy for this group was therefore expected. A diagnosis of dementia, heart failure, chronic pulmonary disease, infection, or hip fracture was not associated with initiation of palliative drugs. This may indicate death coming unexpectedly. For respiratory distress in chronic pulmonary disease there may also be a reservation among physicians to prescribe morphine and benzodiazepines, as they inhibit respiration.

An evidence base for EOL care in non-malignant conditions, which are prevalent in the general NH population, is scarce [20]. We found a high treatment rate with palliative drugs (73.9% overall, 71.9% for morphine), in line with 77% of NH patients with advanced dementia in the Netherlands receiving opioids. Despite extensive prescribing, the Dutch study found that symptoms of pain, shortness of breath, and agitation were prevalent, suggesting that a prescribed drug is no guarantee of satisfactory symptom control [21]. For this, factors such as close symptom assessment as well as appropriate drug dosage and administration are required.

Palliative drug therapy increased and curative/preventive drug treatment decreased in the last week of life, most changes taking place on the day of death. A recent study in long-term care facilities in Canada found that care only changed substantially to palliative in nature during the last hours or days of life, calling for earlier awareness of impending death [22]. Initiation of palliative drugs is not to be expected for all dying patients, nor does it depend only on staff competence. Less palliative drug therapy could also come from less need for it, by having a shorter terminal phase, or less burdensome symptoms. Little is known about the identification and duration of the dying phase in NH patients and for how many it lasts long enough to allow for pharmacological response. Distinct death trajectories have been described for patients with different diseases [23], and timing of palliative care for patients with non-malignant diagnoses has been shown to be particularly challenging [24]. Yet, relatively accurate prediction of survival for these patients in NHs has been shown to be feasible, though only in the last seven days of life [25].

NH A had a lower proportion of patients prescribed palliative medications at death. Differences

in prescribing culture between doctors may be one explanation. For the present study we did not collect this variable.

### Meaning of the study

Palliative drug prescriptions and drug therapy changes are common for NH patients on the last day of life. Extensive curative/preventive drug therapy and comprehensive changes in drug treatment on the day of death may both point to the known prognostication difficulties in the multimorbidity characterizing NH populations. Improvements of EOL care in NHs must address prognostication and an early response to palliative needs.

### Acknowledgements

The authors would like to thank the Municipality of Bergen, and Magne Rekdal at Emetra, for data collection for this study. This study was supported by grants from the Municipality of Bergen, Kavli Research Centre for Ageing and Dementia, and the Foundation for Research in General Practice (PhD grant Kristian Jansen).

### Ethical approval

The Regional Committee for Medical and Health Research Ethics (2012/1748), and Norwegian Social Science Data Services (12/30691) approved the study.

### Declaration of interest

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

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