

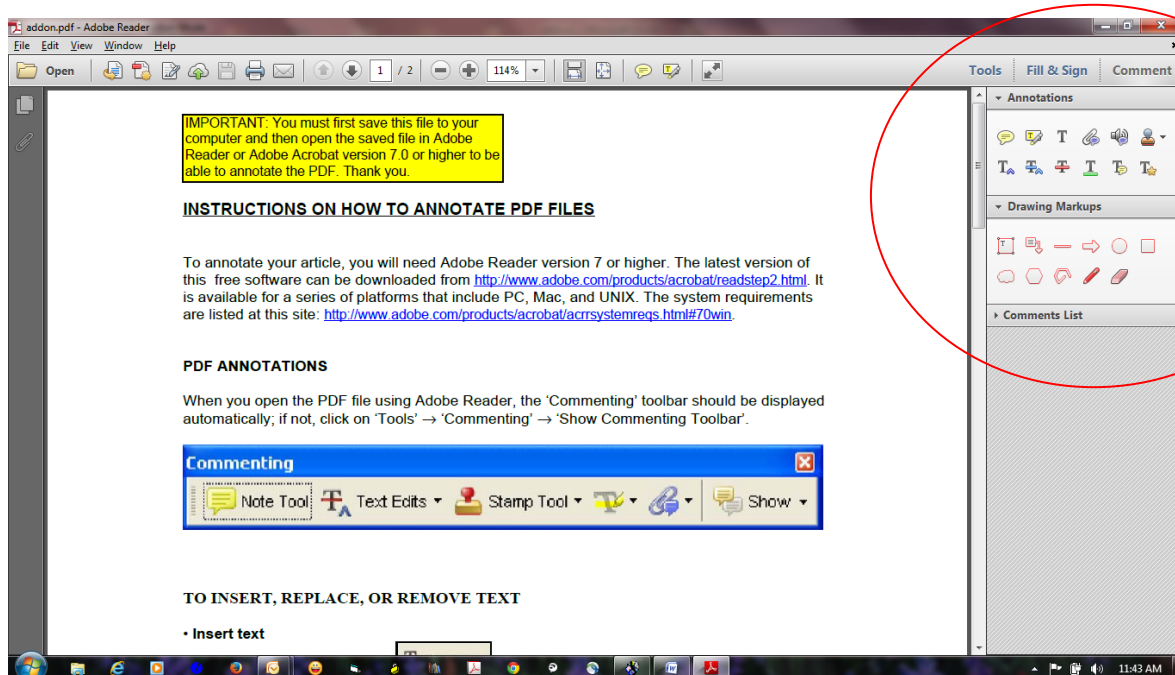
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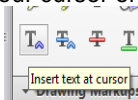
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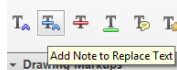
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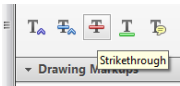
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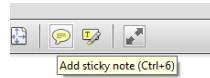
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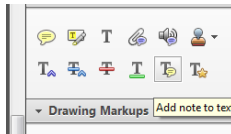
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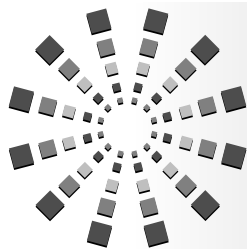
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AQ1

# Comorbid Dementia and Cancer in Residents of Nursing Homes

## Secondary Analyses of a Cross-Sectional Study

### KEY WORDS

Agitation

Cancer

Dementia

Neuropsychiatry

Nursing home

Sleep disturbances

**Background:** Life expectancy is increasing continuously, which increases the likelihood of developing dementia or cancer. Both dementia and cancer are serious conditions that give manifold symptoms. The interaction of these conditions is however complex and less explored. **Objectives:** The aim of this study was to identify the prevalence of cancer and differences regarding neuropsychiatric symptoms (NPS) and medication among nursing home (NH) patients with and without dementia and cancer. **Methods:** This is a cross-sectional study of Norwegian NH patients (N=1825). Participants were categorized according to degree of dementia (Clinical Dementia Rating > 1) and cancer diagnoses. Differences in NPS and other symptoms, as well as the use of medication, were explored. **Results:** Eighty-four percent of NH patients had dementia, and 5.5% had comorbid dementia and cancer. Patients with comorbid dementia and cancer received significantly more analgesics compared with patients without cancer but with dementia ( $P<.05$ ). Compared with patients without dementia but with cancer, patients with comorbid dementia and cancer had significantly more NPS, including sleep disturbances and agitation. **Conclusions:** Patients with comorbid dementia and cancer receive more analgesics than patients with dementia but still display more agitation and sleep disturbances than patients with cancer and patients with neither dementia nor cancer, suggesting that symptoms may

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not be treated adequately. **Implications for Practice:** The results indicate a considerable strain for patients with comorbid dementia and cancer and highlight essential challenges for the clinician who is responsible for treatment and care. Nurses should pay attention to agitation and sleep disturbances among patients with comorbid dementia and cancer.

Life expectancy is continuously increasing worldwide, and the likelihood of developing dementia is thereby growing dramatically.<sup>1</sup> Dementia, of which the most common cause is Alzheimer's disease, is an incurable and progressive condition. It affects 35 million people worldwide—a number expected to almost double in the next 2 decades.<sup>2,3</sup> In general, dementia results in the decline of the person's cognition and physical function. Up to 90% of people with dementia experience neuropsychiatric symptoms (NPS), such as agitation, depression, and delusion, during the course of their disease.<sup>4</sup> In total, 77 000 Norwegians are affected by this disease,<sup>5</sup> and approximately 14% of Norwegians older than 80 years receive institutional care.<sup>6</sup>

Cancer diseases affect approximately 10 million people in Europe,<sup>7</sup> and 30 000 new cases annually are expected.<sup>8</sup> As a result of the demographic development, the prevalence is expected to double during the next 10 years.<sup>9</sup> By the end of 2014, 242 398 Norwegians were registered with a cancer diagnosis, and the disease was the cause of death for 10 971 people.<sup>10</sup> In Norway, 3 of 4 cancer cases are diagnosed in those older than 60 years,<sup>10</sup> and a quarter of all terminal patients with cancer die in a nursing home (NH).<sup>11</sup> Previous studies indicate that from 14% to 26% of Norwegian NH patients are given a diagnosis of cancer,<sup>12</sup> and international studies show that approximately 5% were receiving active cancer treatment when being admitted to an institution.<sup>13</sup> It is unknown how many develop cancer during the time they live in an NH and how this is discovered and treated.

The likelihood of developing comorbid dementia and cancer increases with age. Cancer symptoms are potentially more onerous for people with both conditions because they are no longer able to give a valid self-report—a prerequisite for adequate treatment.<sup>14</sup> As suggested by symptom science, the management of symptoms needs to be based on an understanding of the individual, the condition, and the context in which the individual resides.<sup>15</sup> Ideally, the assessment of cancer-related pain and symptoms should be based on the individual's self-report with subsequent administration of analgesics and appropriate symptom management.<sup>16</sup> However, people with dementia express their pain in ways that are different from those without cognitive impairment, leading to agitation<sup>17,18</sup> and depression.<sup>19,20</sup> Furthermore, previous studies show that sleep disturbances are related to the presence of untreated pain<sup>21,22</sup> and to depression.<sup>23,24</sup> In light of recent research, which indicates that benzodiazepines have no effect on sleep time between users and nonusers,<sup>25</sup> there is a need for awareness around these circumstances because they can contribute to potentially meaningless treatment and widespread use of psychotropic drugs.<sup>26</sup>

In a recent review, our group summarized the evidence on cancer-related symptoms among NH patients<sup>11</sup> and highlighted

11 studies, which together confirmed high prevalence of pain and reduced analgesic drug prescription in NH patients with cancer. Only 1 smaller study (n=48) included patients with comorbid dementia and cancer, and this study found that people with severe dementia received less opioids and displayed less pain behavior compared with patients with mild cognitive impairment.<sup>27</sup> Another study by Monroe et al<sup>28</sup> found that patients with comorbid dementia and cancer were more likely to receive an opioid if they were enrolled in hospice. However, patients enrolled in hospice were more cognitively intact.

The overall purpose of the study is to investigate comorbid dementia and cancer among NH residents, with a particular emphasis on NPS and the medication thereof. The study has the following research objectives: (1) to investigate the prevalence of cancer among NH patients with and without dementia and (2) to compare patients with comorbid dementia and cancer with those without, with regard to the prevalence of NPS such as agitation, depression, and sleep disturbances and the daily use of medication, including analgesic drug prescription.

## ■ Method

### Design, Setting, and Procedure

The study builds on secondary analyses of a multicenter, cross-sectional study including 64 NHs, located in urban and rural areas in 5 of 19 counties of Norway. The data set includes standardized interviews with NH staff, as well as information from patients' medical records. The organization of the setting and the participants of the study have been previously described by Helvik et al<sup>29</sup> wherein this data set was used alongside data from 2004. In brief, Norway has around 34 000 long-term NH patients,<sup>30</sup> and the jurisdiction for public healthcare services is the responsibility of the municipalities. In the process of gaining a representative sample of small, medium-sized, and large municipalities from both urban and rural areas, 49 municipalities were approached, and the sample of NHs was selected.

The study was conducted from June 2010 to November 2011. All patients in the NHs were screened for inclusion, and all patients who had lived in the NH for at least 2 weeks were eligible. Project nurses were responsible for data collection. Before data collection, they participated in a 2-day session on the use of mapping instruments and standardized interviews, as well as on the purpose of the study. Data collection involved registering information from each patient's medical record, as well as performing standardized interviews with the patient's primary caregiver, who served as a proxy for the patient, regardless of the patient's degree of cognitive impairment.

## Measurements

We classified the patient's level of dementia by the Clinical Dementia Rating (CDR) scale (range, 0–3). The instrument consists of 6 categories with scores for no dementia of 0, possible dementia of 0.5, and mild, moderate, and severe dementia of 1, 2, and 3, respectively. The cutoff point for the presence of dementia is CDR of 1 or greater. The CDR scoring algorithm weights memory as the primary domain and the other domains as secondary.<sup>31</sup> Good validity and reliability of the scale have been reported (overall  $\kappa = 0.62$ ).<sup>32–34</sup>

Cancer diagnoses were collected from patients' records and coded by means of the *International Classification of Diseases, Tenth Revision*.<sup>35</sup> Ongoing medical treatment from patients' records was coded by the Anatomical Therapeutic Chemical (ATC) System—an international system for the classification of drugs.<sup>36</sup> We divided analgesics into 3 groups: (1) peripheral (ATC, N02B), (2) opioids (ATC, N02A), and (3) nonsteroidal anti-inflammatory drugs, namely, anti-inflammatory and anti-rheumatic drugs (ATC, M01). We similarly collected data on the following psychotropic drugs: antidepressants (ATC, N06A), anxiolytic drugs (ATC, N05B), sedatives (ATC, N05C), ant dementia drugs (ATC, N06D), and antipsychotics (ATC, N05A).

We assessed NPS related to dementia using the Neuropsychiatric Inventory-Nursing Home version (NPI-NH).<sup>37</sup> The NPI-NH maps 12 NPS associated with dementia: delusions, hallucinations, dysphoria/depression, anxiety, agitation/aggression, euphoria, disinhibition, irritability/lability, apathy, aberrant motor behavior, nighttime behavior, and appetite disturbances/eating change (all judged as no/yes). Each symptom was scored for frequency (score, 1–4) and severity (score, 1–3), and a product score (0–12) was calculated thereof for each symptom. In this study, we used a previously identified underlying 4-factor structure,<sup>38</sup> in which items are clustered into subsyndromes for agitation (agitation and irritability), affective symptoms (depression and anxiety), and psychosis (hallucination and delusions), whereas apathy is analyzed as a single symptom. In addition to the use of these NPS factors, sleep disturbances were identified using the nighttime behavior item from the NPI-NH. Scores of 1 or higher suggest impaired sleep, and in accordance with previous studies, anyone scoring higher than or equal to 4 on this item was judged as having clinically significant sleep disturbances.<sup>39</sup>

We used the Cornell Scale for Depression in Dementia (CSDD) to measure depression, an instrument that is found to be a reliable measure for depression in people with dementia (Cronbach's  $\alpha = .84$ ).<sup>40,41</sup> We used the General Medical Health Rating (GMHR) to assess patients' degree of somatic illness. It is a reliable and valid measure, with 1 item comprising 4 categories, which assesses medical comorbidity (weighted  $\kappa = 0.93$ ).<sup>42</sup> The 4 categories were excellent, good, fair, and poor. The rating was performed based on all available medical information. In addition, we used the Physical Self-Maintenance Scale (PSMS), a reliable measure of patients' level of function with regard to activities of daily living. A high score indicates a lower level of functioning.<sup>43,44</sup>

## Statistical Analyses

We calculated the mean, standard deviation (SD), and range for patient characteristics (number of diagnoses, regular drugs, and analgesics) and calculated the product score for the NPI-NH and its 4 subclusters and sum scores for the CSDD and the PSMS. For the GMHR, we created a binary variable from the 4 categories of the scale simply reflecting good or bad health. Patients who had excellent or good health were recorded as "good," whereas those with fair or poor health were recorded as "bad." For all variables, means were compared across patient groups, and the statistical significance of the differences was tested by means of analyses of variance and logistic regressions for continuous and categorical variables, respectively. In the analyses, we divided the final sample into 4 groups, which we refer to throughout the text and tables in the following way: patients with comorbid dementia and cancer (COMORBID), patients with cancer but without dementia (CANCER), patients with dementia but without cancer (DEMENTIA), and patients who have neither dementia nor cancer (NEITHER).

Finally, we conducted a multiple logistic regression investigating the likelihood of analgesic drug prescription to investigate the characteristics associated with the use of analgesics, while controlling for other variables. The dependent variable was a categorical variable indicating whether the patient received analgesics regularly. The independent variables were the following: cancer, dementia, comorbidity, GMHR, PSMS, CSDD, NPI-NH, regular drugs, use of sedatives, age, and gender. We conducted the statistical analyses in IBM SPSS Statistics 22.

## Ethical Approval

We obtained verbal and written information in direct conversation with the patient (if possible) and his/her legal guardian, usually a family member or an advocate, in accordance with local law. Depending on the patient's ability to give consent, the patient or next of kin made the decision of participation in the study after we explained the aims and protocol of the study. The Regional Committee for Medical and Health Research Ethics (REC West) in Norway approved the study (REC number 2010/1894).

## Results

There were 2385 residents eligible for inclusion. From this sample, 560 patients were excluded for the following reasons: the patient or next of kin declined participation ( $n=423$ ), serious somatic illness or terminal conditions ( $n=33$ ), death before data collection ( $n=17$ ), leaving the NH before assessment ( $n=1$ ), and either missing data or unlisted reasons ( $n=53$ ). In addition, 33 patients were excluded from the analyses because of the lack of CDR scores. The final sample was composed of 1825 participants. Seventy-one percent of the participants were women, and the mean (SD) age was 85.1 (8.04) years. Baseline clinical characteristics are reported in Table 1.

**Table 1 • Descriptive Statistics of the Study Sample**

	Total (N=1825)	COMORBID (n=100)	CANCER (n=33)	DEMENTIA (n=1435)	NEITHER (n=257)
Age, y	85.20 (7.99)	86.03 (7.30)	82.70 (9.50)	85.29 (7.72)	84.70 (9.36)
Female, %	71	68	76	71	68
Diagnoses	3.04 (1.71)	3.83 (1.85)	3.76 (1.90)	2.94 (1.65)	3.17 (1.84)
Bad health, %	44	54	35	45	37
Depression	4.97 (4.80)	5.83 (5.36)	3.61 (3.72)	5.34 (4.86)	2.86 (3.70)
Level of function	17.53 (5.36)	18.18 (5.18)	13.88 (5.16)	18.14 (5.20)	14.33 (5.08)
Neuropsychiatric symptoms	18.48 (19.46)	19.82 (18.40)	6.85 (7.73)	20.70 (19.94)	7.01 (12.44)
Agitation cluster	5.95 (8.23)	6.38 (8.22)	1.61 (3.56)	6.73 (8.59)	1.95 (4.43)
Psychosis cluster	2.68 (5.03)	2.57 (5.27)	0.73 (2.61)	3.08 (5.28)	0.73 (2.61)
Affective cluster	3.47 (5.15)	3.18 (4.84)	2.03 (3.57)	3.76 (5.32)	2.13 (4.13)
Apathy cluster	1.87 (3.32)	2.39 (3.76)	0.45 (1.54)	2.10 (3.44)	0.60 (2.04)
Sleep disturbances, %	17.6	19	9.1	19.4	8.6
Regular drugs	6.93 (3.25)	6.66 (3.02)	8.09 (2.98)	6.67 (3.11)	8.32 (3.73)
Analgesics, %	55	68	58	54	53
Peripheral analgesics, %	48	56	45	48	47
Opioids, %	23	35	36	22	25
NSAIDS, %	4	3	3	4	5
Antidepressants, %	37	38	30	37	35
Anxiolytic agents, %	22	21	24	21	28
Sedatives, %	31	30	48	29	39
Antidementia drugs, %	16	16	3	18	5
Antipsychotics, %	17	15	6	18	14

Each column describes means and SDs (in parentheses) for the full sample, as well as for the 4 subgroups: COMORBID (patients with comorbid dementia and cancer), CANCER (patients with only cancer), DEMENTIA (patients with only dementia), and NEITHER (patients with neither dementia nor cancer).

Bad health refers to the percentage of patients with bad health as measured by the General Medical Health Rating. Depression refers to the sum score for the Cornell Scale for Depression in Dementia. Level-of-function refers to the sum score for the Physical Self-Maintenance Scale. Neuropsychiatric symptoms refer to the product score for the Neuropsychiatric Inventory-Nursing Home Edition.

Abbreviations: COMORBID, patients with comorbid dementia and cancer; CANCER, patients with only cancer; DEMENTIA, patients with only dementia; NEITHER, patients with neither dementia nor cancer; NSAIDS, nonsteroidal anti-inflammatory drugs.

## Prevalence of Dementia and Cancer Among NH Patients

The total sample consisted of 1825 patients. One hundred thirty-three patients (7.3%) had cancer, of which 100 patients had comorbid dementia and cancer (5.5%) and 33 patients had a cancer diagnosis but no dementia (1.8%). Thus, the prevalence of cancer is significantly higher among patients without dementia than among those with dementia ( $P < .01$ ). Most common was breast cancer for women (45%) and prostate cancer for men (31%). Colorectal cancer was the second most common cancer diagnosis for both genders (17% of cancer cases overall). Cognitive impairment consistent with dementia ( $CDR \geq 1$ ) was found in 1535 patients (84%); 29% had moderate dementia, and 36% had severe dementia. The most frequent diagnoses from the NH medical record were unspecified dementia and Alzheimer's disease (29% and 12%, respectively), hypertension (27%), and apoplexia cerebri (15%). Regarding our first research objective, our findings reveal higher prevalence of cancer among patients without dementia than among those with dementia. Compared with cancer prevalence in NHs documented in previous research, the prevalence of cancer in this sample is quite low.

## Comparison of NPS and Medication Use for the Different Patient Groups

Compared with CANCER patients ( $n = 33$ ), COMORBID patients ( $n = 100$ ) displayed more NPS based on NPI-NH sum score ( $P < .01$ ) for the agitation cluster score ( $P < .05$ ) and the apathy item score ( $P < .05$ ). These individuals also displayed worse physical function ( $P < .01$ ) and had significantly more sleep disturbances ( $P < .01$ ). We found no differences between the groups regarding the use of medication or in socio-demographic characteristics (see Table 2).

Compared with DEMENTIA patients ( $n = 1435$ ), COMORBID patients had significantly more diagnoses ( $P < .01$ ) and received more analgesics ( $P < .05$ ), in particular, opioids ( $P < .05$ ). There were no other significant differences between the 2 groups (see Table 2).

Compared with NEITHER patients ( $n = 257$ ), COMORBID patients had significantly reduced physical function and more NPS as measured by the NPI-NH sum score and agitation and psychosis cluster scores ( $P < .01$ ) (see Table 2). Similarly, they had higher scores for singular behavioral disturbances such as apathy, sleep disturbances, and depression assessed by the CSDD. They also had more comorbidity and worse somatic health according to

**Table 2 • Differences in Mean Scores Between the 4 Groups**

	Difference Between COMORBID and CANCER	Difference Between COMORBID and DEMENTIA	Difference Between COMORBID and NEITHER	Difference Between CANCER and DEMENTIA
Age, y	3.33	-0.74	1.33	-2.59
Female, %	8	3	0	-5
Diagnoses	-0.07	0.89 <sup>a</sup>	0.66 <sup>a</sup>	0.82 <sup>a</sup>
Bad health, %	19	9	17 <sup>b</sup>	-10
Depression	2.22	0.49	2.97 <sup>a</sup>	-1.73
Level of function	4.30 <sup>a</sup>	0.04	3.85 <sup>a</sup>	-4.26 <sup>a</sup>
Neuropsychiatric symptoms	12.97 <sup>a</sup>	-0.88	12.81 <sup>a</sup>	-13.85 <sup>a</sup>
Agitation cluster	4.77 <sup>b</sup>	-0.35	4.43 <sup>a</sup>	-5.12 <sup>a</sup>
Psychosis cluster	1.84	-0.51	1.84 <sup>a</sup>	-2.35 <sup>b</sup>
Affective cluster	1.15	-0.58	1.05	-1.73
Apathy cluster	1.94 <sup>b</sup>	0.29	1.79 <sup>a</sup>	-1.65 <sup>b</sup>
Sleep disturbances, %	9.9 <sup>a</sup>	-0.4	10.4 <sup>a</sup>	-10.3
Regular drugs	-1.43	-0.01	-1.66 <sup>a</sup>	1.42
Analgesics, %	10	14 <sup>b</sup>	15 <sup>b</sup>	4
Peripheral analgesics, %	11	8	9	-3
Opioids, %	-1	13 <sup>b</sup>	12 <sup>b</sup>	14
NSAIDS, %	0	-1	-2	-1
Antidepressants, %	8	1	3	-7
Anxiolytic agents, %	-3	0	-7	3
Sedatives, %	-18	1	-9	19
Antipsychotics, %	9	-3	1	-12

The table shows differences in mean scores between the 4 patient groups (COMORBID, CANCER, DEMENTIA, and NEITHER) for each of the variables outlined in Table 1. For instance, the column “Difference Between COMORBID and CANCER” shows the difference in mean scores between the group with comorbid dementia and cancer (COMORBID) and the group with cancer only (CANCER). Positive values indicate that the former group has the higher mean score, whereas negative values indicate that the latter group has the higher mean score.

Depression refers to differences in the sum score for the Cornell Scale for Depression in Dementia. Level of function (daily activities) refers to differences in the sum score for the Physical Self-Maintenance Scale. Neuropsychiatric symptoms refer to differences in the product score for the Neuropsychiatric Inventory-Nursing Home Edition. Abbreviations: CANCER, Patients with only cancer; COMORBID, Patients with comorbid dementia and cancer; DEMENTIA, Patients with only dementia; NEITHER, Patients with neither dementia nor cancer; NSAIDS, nonsteroidal anti-inflammatory drugs.

<sup>a</sup>*P*<.01.

<sup>b</sup>*P*<.05.

GMHR. COMORBID patients received less medication (*P*<.01) but more analgesics (*P*<.05), than did NEITHER patients.

The regression model predicting the likelihood of using analgesics was statistically significant (*P*<.001) and explained 21.9% (Nagelkerke *R*<sup>2</sup>) of the variation in analgesic use. As shown in **T3** Table 3, the independent variables that were statistically significant were age, gender, use of sedatives, regular drugs, PSMS, CSDD, and cancer. The highest odds ratio was 1.974 for cancer. That is, patients with cancer were almost twice as likely to receive analgesics regularly as were patients without cancer. Regarding our second research objective, there is significantly a higher prevalence of NPS among COMORBID patients than among CANCER and NEITHER patients, but there is no significant difference between COMORBID and DEMENTIA patients. Furthermore, analgesic use is significantly more common among COMORBID patients than among DEMENTIA or NEITHER patients, but there is no difference between COMORBID and CANCER patients.

## Discussion

Our study found a 7.3% prevalence of cancer among all patients. Comorbid dementia and cancer were found among 5.5%, whereas

1.8% had only a cancer diagnosis. Compared with CANCER patients, COMORBID patients displayed significantly more NPS, such as agitation, depression, and sleep disturbances, as well as lower function levels regarding daily activities. COMORBID patients also received more analgesics, especially opioids, compared with CANCER and NEITHER patients.

The overall burden of the comorbid dementia and cancer group was even more evident when we compared COMORBID patients with people with neither cancer nor dementia: COMORBID patients were significantly reduced in their physical function and had increased intensity of NPS, such as agitation, psychosis, apathy, and depression, combined with worse overall health conditions. Interestingly, COMORBID patients received less medication, than did NEITHER patients, but more analgesics.

## Comorbid Dementia and Cancer

To our knowledge, few studies have investigated the comorbidity of dementia and cancer in NH patients. The study by Monroe et al<sup>27</sup> indicated that patients with severe Alzheimer’s disease and cancer have fewer pain behaviors and found severe Alzheimer’s disease to be negatively associated with total opioid medication.

**Table 3 • Multiple Logistic Regression Predicting the Likelihood of Using Analgesics**

	OR	SE	P
Cancer	1.974	0.219	<b>.002<sup>a</sup></b>
Dementia	1.000	0.158	.998
Comorbidity	1.001	0.034	.973
General medical health	1.206	0.127	.141
Level of function (daily activities)	1.065	0.012	<b>.000<sup>a</sup></b>
Depression	1.035	0.016	<b>.035<sup>b</sup></b>
Neuropsychiatric symptoms	1.004	0.003	.352
Regular drugs	1.261	0.021	<b>.000<sup>a</sup></b>
Use of sedatives	0.776	0.124	<b>.041<sup>b</sup></b>
Age, y	1.047	0.007	<b>.000<sup>a</sup></b>
Gender, male	0.624	0.120	<b>.000<sup>a</sup></b>
R <sup>2</sup>		0.219	

The table shows a multiple logistic regression predicting the likelihood of using analgesics. The binary variable analgesics (yes/no) is the dependent variable. The independent variables are listed in the first column. The model was statistically significant:  $\chi^2(11, N = 1825) = 300.4, P < .001$ , Nagelkerke  $R^2 = 21.9\%$ . Significant  $P$  values are shown in boldface, with  $P < .01$  indicated by the footnote letter a and  $P < .05$  with the footnote letter b.

General medical health refers to the percentage of patients with bad health as measured by the General Medical Health Rating. Depression refers to the sum score for the Cornell Scale for Depression in Dementia. Level of function (daily activities) refers to the sum score for the Physical Self-Maintenance Scale. Neuropsychiatric symptoms refer to the product score for the Neuropsychiatric Inventory-Nursing Home Edition. Abbreviations: OR, odds ratio; SE, standard error.

<sup>a</sup> $P < .01$ .

<sup>b</sup> $P < .05$ .

Another study by Monroe et al<sup>28</sup> found an association between hospice enrolment and more opioid pain treatment among patients with dementia and terminal cancer. However, no patients with severe dementia and cancer were admitted to hospice.<sup>28</sup> The study highlights that patients with severe dementia and cancer are at a great risk of having untreated advanced cancer pain because they are no longer able to account for their suffering.

The results of this study indicated that COMORBID patients have increased prevalence of NPS, including sleep disturbances, and reduced level of function with regard to activities of daily living compared with NEITHER and CANCER patients. However, COMORBID patients received more analgesics than DEMENTIA patients but displayed significantly more agitation than did CANCER and NEITHER patients. This could indicate that COMORBID patients experienced more pain compared with CANCER and NEITHER patients. However, there is no significant difference in NPS between COMORBID and DEMENTIA patients, and we do not have a measure of pain in our study. Thus, these findings should be interpreted with caution because it could be that the dementia is the source of the association.

Today, approximately 5550 patients with comorbid dementia and cancer are living in Norway, and the number is expected to increase rapidly. The results of our study provide important information for clinicians in their decision-making process regarding treatment and care for these individuals. Our results may support previous studies that showed that untreated pain is still common among NH patients with cancer.<sup>45–47</sup> To meet these challenges, pain management methods of high quality are necessary and should be used. In light of this, it is alarming that

recent findings show that, even when pain is identified through proper methods, people with cognitive impairment still do not receive pain treatment.<sup>47</sup>

Previous studies indicate that approximately 24% of people with cancer die in an NH.<sup>11</sup> From the perspective of symptom science, the treatment for such patients should be informed by the patient's symptom experience, relevant management strategies thereof, and measureable outcomes of the treatments.<sup>15</sup> To optimize care for dying adults in the last days of life, the National Institute for Health and Care Excellence recently published guidelines that give an evidence-based approach for all healthcare professionals involved in the care of a person who is nearing death.<sup>48</sup> Recommendations highlight the need for advanced care planning and assessment and treatment of pain and distressing symptoms. It is noteworthy that the care and treatment for dying people with dementia are not yet mentioned in this important document.

Interestingly, we did not find differences in NPS between COMORBID and DEMENTIA patients. Patients with comorbid dementia and cancer did however receive more analgesics than DEMENTIA patients, and the lack of differences in NPS could thus indicate that this treatment is somewhat effective in the COMORBID group. However, COMORBID patients expressed more potentially pain-related behavior such as agitation and sleep disturbance compared with CANCER patients. This is of key importance because it highlights the particularly vulnerable position of patients with comorbid dementia and cancer.

Our study reveals a cancer prevalence of 7.3% among NH patients, which is somewhat lower than previous estimates of 14% to 26%.<sup>11</sup> Results are closer to reports from the United States, wherein studies revealed cancer prevalence among NH patients varying from 4% to 14%.<sup>13</sup> It is beyond the scope of this study to explore the cause of the difference in cancer prevalence between people with and without dementia. However, previous research indicated that frailty status is associated with decreased cancer incidence.<sup>49</sup> Another interesting aspect is that cancer and cancer treatment on its own can lead to cognitive impairment, which highlights the need for more knowledge and guidelines about the particularities of this group and how it should be treated.<sup>50</sup>

## Depression and Sleep Disturbances Among People With Comorbid Dementia and Cancer

COMORBID patients also had higher CSDD scores than did NEITHER patients. There was, however, no difference between COMORBID and DEMENTIA patients, suggesting that dementia is the source of the association. Depression is associated with pain (pain-depression dyad), although the interaction between the phenomena is poorly understood.<sup>19,20</sup> As shown in the regression analyses, depression is associated with the use of analgesics, thus suggesting that patients who experience depression are more likely to receive such medication. However, the predictor with the highest odds ratio in the regression is cancer. This suggests a need for further investigation into the relationship between pain and depression: could, for instance, depression be a result of pain, in this case, cancer-related pain? This could be a fruitful topic for further research.



Furthermore, COMORBID patients had more sleep disturbances than did CANCER and NEITHER patients. This indicates that dementia is also the source of this association and implies that having comorbid dementia and cancer potentially can give sleep-related symptoms that are more burdensome. Our results also show a negative association between the use of sedatives and the use of analgesics, indicating that, if patients receive sedatives, they are less likely to be treated with analgesics. This is of interest because recent research indicates that intense anxiety and agitation are associated with sedative-hypnotic use.<sup>51</sup> Because agitation may be an expression of untreated pain among people with dementia,<sup>17,18</sup> our results may indicate that some people with comorbid dementia and cancer are given sedatives instead of pain treatment.

## Limitations

The main limitation of this study is the lack of a validated pain assessment instrument, which could have been used before and after pain treatment was initiated. Thus, we are not able to demonstrate the efficacy of analgesic treatment on pain intensity or to analyze how pain and symptom management affected related symptoms. For this reason, further research should be initiated, or alternatively, longitudinal data should be collected that allow for research on the relationship between treatment and patient characteristics. Another challenge is that there is potential for systematic differences between patients declining inclusion and the final sample, but our data do not allow us to investigate this. There is also a significant difference in sample sizes between the 4 patient groups. A third limitation is that the patients do not have a confirmed diagnosis of dementia. However, good validity and reliability of the CDR scale have been reported, and it therefore serves as a good substitute for a diagnosis. Our data do not reveal the cancer stage and actual cancer treatment and do not distinguish between current and historical diagnoses of cancer, that is, patients who already have received successful treatment of cancer. This may interfere with the analyses of DEMENTIA and CANCER patients. However, earlier studies indicated that approximately 5% of patients with cancer in NH were receiving active cancer treatment at the point of admission.<sup>13</sup>

## Conclusions and Implications for Practice

Our study reveals relatively low cancer prevalence in our sample, yet significantly higher prevalence of cancer among patients with dementia than among those without. Although we find higher levels of NPS among COMORBID patients than among CANCER and NEITHER patients, there are no significant differences in NPS between COMORBID and DEMENTIA patients. Similarly, we find significantly higher use of analgesics for COMORBID patients than for DEMENTIA and NEITHER patients but no significant difference between COMORBID and CANCER patients.

The fact that COMORBID patients receive more analgesics than DEMENTIA patients, but still display more agitation and

sleep disturbances than CANCER and NEITHER patients, raises the question of whether they receive adequate treatment. The lack of pain assessment in our study renders us unable to provide further evidence on this relationship.

Because COMORBID patients are often no longer able to give a valid self-report, a prerequisite for adequate treatment, our results suggest that healthcare professionals working at NHs should pay close attention to this patient group. Furthermore, our results highlight the importance of identifying patients at risk for developing sleep disturbances and other types of NPS. This could include screening of NPS using validated tools, in addition to the active use of pain assessment tools to optimize treatment.

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## References

1. National Institute on Aging. *Global health and aging*. <http://www.nia.nih.gov/research/publication/global-health-and-aging/living-longer>. Updated January 22, 2015. Accessed August 20, 2015.
2. World Health Organization and Alzheimer's Disease International. *Dementia: a public health priority*. <http://www.alz.co.uk/WHO-dementia-report>. Accessed January 22, 2014.
3. Ferri CP, Prince M, Brayne C, et al. Global prevalence of dementia: a Delphi consensus study. *Lancet*. 2005;366:2112–2117.
4. Selbaek G, Engedal K, Benth JS, Bergh S. The course of neuropsychiatric symptoms in nursing-home patients with dementia over a 53-month follow-up period. *Int Psychogeriatr*. 2014;26(1):81–91.
5. Norwegian Ministry of Health and Care Services. *Care Plan 2020*. Oslo, AQ2 Norway; 2015.
6. Statistics Norway. *Population 1 January 2013*. <http://www.ssb.no/en/befolkning/statistikker/folkemengde>. Accessed January 20, 2016.
7. International Agency for Research on Cancer. GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012. *International Agency for Research on Cancer Web site*. [http://globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx). Updated January 2015. Accessed August 13, 2015.
8. Engeland A, Bjørge T, Brunborg G. 2014. *Kreft i Norge. folkehelse rapporten 2014 [Cancer in Norway: the report on public health 2014]*. Norwegian Institute of Public Health. [www.fhi.no/artikler/?id=110413](http://www.fhi.no/artikler/?id=110413). Accessed April 12, 2016.
9. Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008–2030): a population-based study. *Lancet Oncol*. 2012;13(8):790–801.
10. Cancer Registry of Norway. Cancer in Norway 2014: cancer incidence, mortality, survival and prevalence in Norway. Oslo, Norway: Cancer Registry of Norway. [https://www.kreftregisteret.no/globalassets/cancer-in-norway/2014/cin2014-special\\_issue.pdf](https://www.kreftregisteret.no/globalassets/cancer-in-norway/2014/cin2014-special_issue.pdf). Accessed May 22, 2016.
11. Drageset J, Corbett A, Selbaek G, Husebo BS. Cancer-related pain and symptoms among nursing home residents: a systematic review. *J Pain Symptom Manage*. 2014;48(4):699.e1–710.e1.
12. Drageset J, Eide GE, Ranhoff AH. Cancer in nursing homes: characteristics and health-related quality of life among cognitively intact residents with and without cancer. *Cancer Nurs*. 2012;35(4):295–301.
13. Rodin MB. Cancer patients admitted to nursing homes: what do we know? *J Am Med Dir Assoc*. 2008;9(3):149–156.
14. Husebo BS, Strand LI, Moe-Nilssen R, et al. Mobilization-Observation-Behavior-Intensity-Dementia Pain Scale (MOBID): development and validation of a nurse-administered pain assessment tool for use in dementia. *J Pain Symptom Manage*. 2007;34(1):67–80.

15. Dodd M, Janson S, Facione N, et al. Advancing the science of symptom management. *J Adv Nurs*. 2001;33(5):668–676.
16. Corbett A, Smith J, Creese B, Ballard C. Treatment of behavioral and psychological symptoms of Alzheimer's disease. *Curr Treat Options Neurol*. 2012; 14(2):113–125.
17. Husebo BS, Ballard C, Sandvik R, Nilsen OB, Aarsland D. Efficacy of treating pain to reduce behavioural disturbances in residents of nursing homes with dementia: cluster randomised clinical trial. *BMJ*. 2011;343:d4065.
18. Husebo BS, Ballard C, Cohen-Mansfield J, Seifert R, Aarsland D. The response of agitated behavior to pain management in persons with dementia. *Am J Geriatr Psychiatry*. 2014;22(7):708–717.
19. Landi F, Onder G, Cesari M, et al. Pain and its relation to depressive symptoms in frail older people living in the community: an observational study. *J Pain Symptom Manage*. 2005;29(3):255–262.
20. Onder G, Landi F, Gambassi G, et al. Association between pain and depression among older adults in Europe: results from the Aged in Home Care (AdHOC) project: a cross-sectional study. *J Clin Psychiatry*. 2005; 66(8):982–988.
21. Chen Q, Hayman LL, Shmerling RH, Bean JF, Leveille SG. Characteristics of chronic pain associated with sleep difficulty in older adults: the Maintenance of Balance, Independent Living, Intellect, and Zest in the Elderly (MOBILIZE) Boston study. *J Am Geriatr Soc*. 2011;59(8):1385–1392.
- AQ3** 22. Flo E, Bjorvatn B, Corbett A, Pallese S, Husebo BS. Joint occurrence of pain and sleep disturbances in people with dementia: a systematic review. *Curr Alzheimer Res*. 2016.
23. Giron MST, Forsell Y, Bernsten C, et al. Sleep problems in a very old population drug use and clinical correlates. *J Gerontol A Biol Sci Med Sci*. 2002;57(4):M236–M240.
24. Ownby RL, Peruyera G, Acevedo A, Loewenstein D, Sevush S. Subtypes of sleep problems in patients with Alzheimer disease. *Am J Geriatr Psychiatry*. 2014;22(2):148–156.
25. Brown DT, Westbury JL, Schütz B. Sleep and agitation in nursing home residents with and without dementia. *Int Psychogeriatr*. 2015;27(12):1945–1955.
26. Ballard CG, Gauthier S, Cummings JL, et al. Management of agitation and aggression associated with Alzheimer disease. *Nat Rev Neurol*. 2009; 5(5):245–255.
27. Monroe T, Carter M, Feldt K, Tolley B, Cowan RL. Assessing advanced cancer pain in older adults with dementia at the end-of-life. *J Adv Nurs*. 2012;68(9):2070–2078.
28. Monroe TB, Carter MA, Feldt KS, Dietrich MS, Cowan RL. Pain and hospice care in nursing home residents with dementia and terminal cancer. *Geriatr Gerontol Int*. 2013;13(4):1018–1025.
29. Helvik AS, Engedal K, Benth JS, Selbæk G. Prevalence and severity of dementia in nursing home residents. *Dement Geriatr Cogn Disord*. 2015; 40(3–4):166–177.
30. Statistics Norway. *Nursing and care services 2013*. <http://ssb.no/en/helse/artikler-og-publikasjoner/pleie-og-omsorgstjenesten-2013>. Accessed February 22, 2016.
31. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993;43(11):2412–2414.
32. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. *Int Psychogeriatr*. 1997; 9(suppl 1):173–176.
33. Rockwood K, Strang D, MacKnight C, Downer R, Morris JC. Interrater reliability of the Clinical Dementia Rating in a multicenter trial. *J Am Geriatr Soc*. 2000;48(5):558–559.
34. Selbæk G, Kirkevold Ø, 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(9):843–849.
35. World Health Organization. *The ICD-10 Classification of Mental and Behavioral Disorders: Clinical Descriptions and Diagnostic Guidelines (Vol. 1)*. Geneva, Switzerland: World Health Organization; 1992.
36. WHO Collaborating Centre for Drug Statistics Methodology. *Guidelines for ATC Classification and DDD Assignment 2013*. Oslo, Norway: The Norwegian Institute of Public Health. [http://www.whocc.no/filearchive/publications/1\\_2013guidelines.pdf](http://www.whocc.no/filearchive/publications/1_2013guidelines.pdf). Accessed May 15, 2016.
37. Cummings JL. The neuropsychiatric inventory: assessing psychopathology in dementia patients. *Neurology*. 1997;48(5 suppl 6):10S–16S.
38. Selbæk G, Engedal K. Stability of the factor structure of the Neuropsychiatric Inventory in a 31-month follow-up study of a large sample of nursing-home patients with dementia. *Int Psychogeriatr*. 2012;24(1): 62–73.
39. García-Alberca JM, Lara JP, Cruz B, et al. Sleep disturbances in Alzheimer's disease are associated with neuropsychiatric symptoms and antedementia treatment. *J Nerv Ment Dis*. 2013;201(3):251–257.
40. Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell scale for depression in dementia. *Biol Psychiatry*. 1988;23(3):271–284.
41. Barca ML, Engedal K, Selbæk G. A reliability and validity study of the Cornell scale among elderly inpatients, using various clinical criteria. *Dement Geriatr Cogn Disord*. 2010;29(5):438–447.
42. Lyketos CG, Galik E, Steele C. The General Medical Health Rating: a bedside global rating of medical comorbidity in patients with dementia. *J Am Geriatr Soc*. 1999;47(4):487–491.
43. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9:179–186.
44. Hokoishi K, Ikeda M, Maki N, et al. Interrater reliability of the Physical Self-Maintenance Scale and the Instrumental Activities of Daily Living Scale in a variety of health professional representatives. *Aging Ment Health*. 2001; 5(1):38–40.
45. Buchanan RJ, Barkley J, Wang S, Kim M. Analyses of nursing home residents with cancer at admission. *Cancer Nurs*. 2005;28(5):406–414.
46. Duncan JG, Bott MJ, Thompson SA, Gajewski BJ. Symptom occurrence and associated clinical factors in nursing home residents with cancer. *Res Nurs Health*. 2009;32(4):453–464.
47. Pimentel CB, Briesacher BA, Gurwitz JH, et al. Pain management in nursing home residents with cancer. *J Am Geriatr Soc*. 2015;63(4):633–641.
48. NICE guideline. *Care of dying adults in the last days of life*. [nice.org.uk/guidance/ng31](http://nice.org.uk/guidance/ng31). Accessed June 20, 2016.
49. Kanapuru B, Simonsick EM, Ershler WB. Is cancer incidence decreased in the frail elderly? Evidence from a prospective cohort study. *J Geriatr Oncol*. 2013;4(1):19–25.
50. Von Ah D. Cognitive changes associated with cancer and cancer treatment: state of the science. *Clin J Oncol Nurs*. 2015;19(1):47–56.
51. Maust DT, Langa KM, Blow FC, Kales HC. Psychotropic use and associated neuropsychiatric symptoms among patients with dementia in the USA. *Int J Geriatr Psychiatry*. 2016. **AQ3**

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