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## ORIGINAL ARTICLE

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# Adherence to Pharmacological Pain Therapy in Patients with NonMalignant Pain: The Role of Patients' Knowledge of Pain Medication

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### ■ Abstract

**Background:** Nonadherence to pharmacological therapy is a common and underexposed problem in patients with chronic nonmalignant pain. It may lead to treatment failure and increased healthcare costs.

**Methods:** In this prospective observational study we analyzed the association between knowledge and adherence in the chronic nonmalignant pain population. We included 96 patients treated with a new pharmacological prescription. During the initial visit (T0), demographic variables, pain intensity, knowledge of the prescription (name, dose, and frequency), self-reported adherence to the prescription, and general knowledge of pharmacological pain therapy (according to the Pain Knowledge Questionnaire, Dutch Language Version (PKQ-DLV) were recorded. During two follow-up visits (T1, T2), apart from demographics, these parameters were measured again.

**Results:** Adherence rates were 42%, 42%, and 46% at T0, T1 and T2, respectively. 53%, 59%, and 48% of patients had knowledge of their current prescription, and mean scores on

the PKQ-DLV were 56, 55, and 52 percent of the maximum scores, respectively, at T0, T1 and T2. A multivariate binary logistic regression analysis resulted in a significant contribution of knowledge of the prescription and of age to the prediction of adherence.

**Conclusions:** Knowledge of the analgesic prescription is associated with adherence and significantly contributes to the prediction of adherence to analgesic therapy. An interventional study is needed to determine whether increasing knowledge will improve medication adherence and therapy outcome in patients with chronic nonmalignant pain. ■

**Key Words:** chronic pain, nonmalignant pain, analgesic use, medication adherence, patient education, patient knowledge, compliance

### INTRODUCTION

Chronic nonmalignant pain is a common health problem that leads to disability as well as high medical and societal costs. Although over 60% of pain sufferers use medication to relieve their pain, this therapy is often not effective. Nonadherence to the prescription is reported to play a major role in the suboptimal effect of chronic pharmacological therapy.<sup>1</sup> The prevailing definition of adherence is “the extent to which a person’s behavior (in terms of taking medication, following diets, or executing lifestyle changes) coincides with medical or health advice”.<sup>2</sup> Broekmans et al.<sup>3</sup> reported that in

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patients with chronic nonmalignant pain, nonadherence is common: 29.9% (range 2 to 53%) of the patients used less medication and 13.7% (range 3 to 21%) used more medication than prescribed.

Nonadherence to prescribed analgesics is an underexposed problem in chronic pain management. For other chronic conditions (eg HIV infection, asthma, diabetes and cardiovascular disease), much more is known about the prevalence and determinants of nonadherence and about interventions to improve adherence.<sup>1,2,4</sup> In general, poor adherence to medication accounts for a substantial worsening of disease, readmissions to the hospital, death, and increased healthcare costs.<sup>5</sup> Recently, it has been shown that adherence to prescribed medication is negatively associated with pain intensity.<sup>6</sup> However, it is still unknown whether a causal relationship exists between adherence and the outcome of chronic pain therapy. In some serious chronic conditions such as HIV infection, strict adherence is mandatory for positive treatment outcome.<sup>7</sup> In chronic pain management, some deviation from the prescription may be acceptable without serious consequences for treatment efficacy.

Knowledge of determinants of medication adherence contributes to the prediction and identification of nonadherent behavior in clinical practice. Furthermore, understanding why, when, and which patients are nonadherent is essential for developing strategies to improve medication-taking behavior. Adherence research in chronic pain management has, due to increasing reports of prescription medication abuse, been primarily focused on identification and prevention of opioid overuse and abuse.<sup>8,9</sup> However, most deviations from physician instructions are omissions, that is, underuse of medications.<sup>5</sup> Determinants of medication underuse that are reported in chronic pain management include age, psychological distress, poor communication with providers, lower affective pain ratings, poor clinical attendance,<sup>3</sup> active coping strategies, and use of selfmedication.<sup>10</sup> Furthermore, patients' concerns and beliefs about the prescribed therapy play an important role in their medication-taking behavior.<sup>11–13</sup>

Knowledge of the disease or the prescribed therapy was found to be positively correlated to medication adherence in other conditions, and patient education was successfully used to improve adherence.<sup>14–17</sup> The present study investigates the association between knowledge and adherence to a pharmacological prescription in patients with chronic nonmalignant pain.

## METHODS

### Design

Our study was a prospective observational study approved by the Institutional Review Board of the Erasmus Medical Center. All study participants gave written informed consent prior to any study procedure.

### Patients

Included were consenting outpatients with chronic nonmalignant pain persisting for at least 3 months who were treated with a new pharmacological pain prescription at the Center for Pain Medicine of the Erasmus Medical Center. Patients had to be aged  $\geq 18$  years and have adequate understanding of the Dutch language. Excluded from the study were patients receiving pain medication on an "as needed" basis.

### Measurements

Measurements were made during the first visit to our Center for Pain Medicine (T0) and during two consecutive follow-up visits after one (T1) and three months (T2), respectively. Patients underwent a structured interview by study personnel not involved in clinical care of the study participants. At T0 measurements included: demographic variables (age, gender, educational level); medical variables (location and duration of pain, mean pain intensity in the previous week using an 11-point numeric rating scale<sup>18</sup>) and medication adherence: the prescribed pain therapy was compared with the anamnestic use of medication the day before measurement: "which pain medication(s) did you use yesterday?". Knowledge of the prescription was determined by asking for the name, dose, and frequency of the therapy prescribed and comparing the result with the actual prescription as noted in the patient file. In addition, general knowledge on the pharmacological pain therapy was evaluated using a Dutch language version of Ferrell's Patient Pain Questionnaire.<sup>19</sup> This questionnaire consists of eight statements that could be answered on a five-point Likert scale (strongly agree, agree, not agree/not disagree, disagree, and strongly disagree). For ease of interpretation, all item scores were linearly transformed to a 0-to-100 scale and a total score was computed for overall pain knowledge. This Pain Knowledge Questionnaire (PKQ-DLV) was translated backward and forward and pretested in a group of 49

patients with chronic cancer pain. It demonstrated acceptable levels of validity and reliability.<sup>20</sup>

At T1 and T2, apart from demographics, location and duration of the pain, all the forementioned parameters were measured again. Knowledge of the prescription and adherence to it were assessed using the current pharmacological pain therapy.

### Data Analysis

Adherence to prescribed therapy was determined by recording adherence to: the drug, the dose of the drug, and the frequency of the prescribed dose regimen. Any deviation regarding the type, dose or frequency of medication in relation to the prescribed therapy was defined as nonadherence. Overall adherence was defined as adherence at T1 and T2 to all three aspects mentioned earlier. Knowledge of the name, dose, and frequency was recorded dichotomously and overall knowledge was defined as knowledge at T1 and T2 of all three aspects. T0 was left out of the analysis because knowledge measured at T0 concerned knowledge of the newly prescribed medication (and not knowledge of earlier prescribed therapy as at T1 and T2).

Item scores of the PKQ-DLV were linearly transformed to a 0-to-100 scale, after recoding five items, and a total score was computed for general pain knowledge.

### Statistical Analysis

Descriptive statistics were used to determine frequencies. Binary logistic regression analysis was used to evaluate the contribution of parameters to the prediction of adherence to the prescribed medication. To prevent overfitting of the model, we performed univariate binary logistic regression analyses of demographic parameters (gender, age, and education), overall knowledge of the prescription, general knowledge of pharmacological pain therapy at T0, and pain intensity in the previous week at T0. Only those parameters with a significance level of  $P \leq 0.2$  were entered into the final multivariate stepwise binary logistic regression analysis (method Backward Wald) with a probability out of  $P = 0.1$ . To prevent multicollinearity, pairwise correlations between the parameters to be entered into the final model were calculated. Of those with a bivariate correlation of  $\geq 0.7$ , only the parameter with the highest univariate significance level was entered into the final model. Analyses were performed with the Statistical Package for the Social Sciences (SPSS), version 16.0.

## RESULTS

### Demographics

Of the 112 patients initially included in the study, 17 later declined to participate.

At T0, T1 and T2, a total of 95, 88 and 79 patients, respectively, were participated in the study. At T0, there were 30 (31.6%) male and 65 (68.4%) female participants with a mean age of 52.5 (SD 15.1) years; details of their educational level are given in Table 1. In the week prior to T0, mean pain intensity was 7.8 (SD 1.5). At T0, 62 patients were unemployed (65.3%), 27 of them (43.5%) due to functional disability.

### Medication

Table 2 lists the analgesic therapy of patients before and after their first visit to the Center for Pain Medicine. Of all patients, 25% did not use any medication at all before their initial visit. Co-analgesics (antidepressants

**Table 1. Level of education at T0 according to the International Standard Classification of Education (1997)**

	n (%)
None	2 (2.4)
Primary education	12 (14.5)
Lower secondary education	44 (53.0)
Upper secondary education	14 (16.8)
Tertiary education	11 (13.3)
Total*	83 (100)

\*Data of 12 patients are missing.

**Table 2. Analgesic therapy before and after the first visit to the Center of Pain medicine**

	Medication before treatment n (%)	Medication after treatment n (%)
Step 1 WHO ladder	54 (57.4)	19 (20.2)
Step 2 WHO ladder	31 (33.0)	10 (10.6)
Step 3 WHO ladder	12 (12.8)	6 (6.4)
Anticonvulsants	15 (16.0)	24 (25.5)
Antidepressants	12 (12.8)	20 (21.3)
Anti-migraine medication	2 (2.1)	0
Hypnotics, sedatives, anxiolytic medication	18 (19.1)	1 (1.1)
Sympatholytic medication	1 (1.1)	1 (1.1)
Muscle relaxants	3 (3.2)	0
Topical medication	1 (1.1)	0
Vasodilator therapy	1 (1.1)	2 (2.1)
Other	3 (3.2)	1 (1.1)
Unknown	4 (4.3)	28 (29.8)
No analgesic therapy	25 (26.6)	0
Total*	182 (193.6)	112 (119.1)

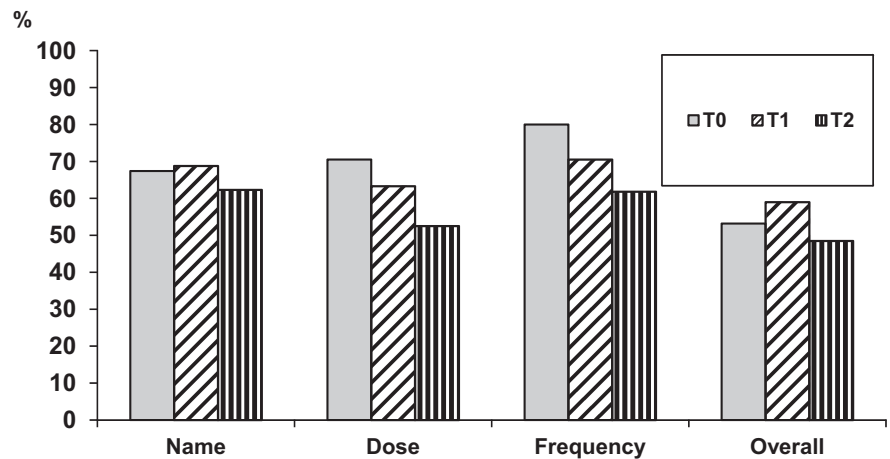
\*Data of one patient are missing. Total score exceeds 100%, indicating that some patients used more than one analgesic drug.



**Table 3. General knowledge on analgesic therapy according to the PKQ-DLV. Data are shown as mean scores (SD) on the eight questions on pain therapy. Higher scores indicate better pain knowledge**

	T0	T1	T2
Pain can be treated effectively	52.6 (30.4)*,†	60.8 (29.8)*	56.6 (31.4)†
Pain therapy should only be considered in case of severe pain‡	49.7 (39.0)	45.2 (41.3)	42.4 (35.9)
Most patients who use analgesic medication will develop some sort of addiction over time‡	43.2 (32.1)	37.2 (34.1)	39.2 (33.9)
In analgesic therapy it is important to use the lowest dose possible. Higher doses can then be reserved for more severe complaints‡	36.3 (41.9)*,†	27.3 (36.1)†	15.2 (26.4)*,†
It is advised to use analgesic therapy on a regular basis, instead of dosing on an "as needed" basis	80.3 (30.3)	79.3 (33.3)	78.5 (33.7)
There are other ways to treat pain besides analgesic medication.	66.6 (31.7)	71.0 (31.0)	70.6 (31.2)
Too many patients receive too much analgesic medication‡	40.8 (34.0)	43.2 (35.9)	41.8 (34.1)
I can easily change the prescribed analgesic regimen myself, without consulting my doctor‡	70.8 (38.2)	72.4 (35.0)	67.4 (38.3)
Total score	55.9 (14.4)*,†	54.8 (16.1)†	51.7 (14.2)*,†

\*,†Significant difference between groups are indicated by identical superscripts ( $P < 0.05$ ).  
‡Items were recoded.



**Figure 2.** Percentage of patients with knowledge on the different aspects and overall knowledge of the prescription.

**Table 4. Results of the multivariate binary logistic regression analysis**

	B (SE) [P-value]	95% CI for Odds Ratio		
		Lower	Odds Ratio	Upper
<b>Included</b>				
Constant	2.05 (1.68) [0.22]			
Age	-0.08 (0.04) [0.02]	0.86	0.92	0.99
Knowledge	2.09 (0.04) [0.02]	1.73	8.05	37.51

$R^2 = 0.28$  (Cox & Schnell), 0.39 (Nagelkerke). Model  $\chi^2_{(2)} = 15.45$ ,  $P < 0.001$ .

adherence, that is, self-report, can be susceptible to misinterpretation as patients often overestimate their compliance to prescribed therapy.<sup>5</sup> For this reason, it is unlikely that this method is responsible for the low levels of adherence found in this and earlier studies.<sup>11,23</sup> We defined every single deviation from the prescribed therapy as nonadherent behavior. This strict definition,

which is used in most adherence research in chronic pain, may partly account for the high levels of nonadherence found in this and other studies. Medication adherence is difficult to operationalize, firstly because it is not a dichotomous variable but varies from 0 to more than 100% as people may overuse their medications.<sup>5</sup> Secondly, it is a dynamic process, as it can change over time. We measured adherence the day before their visit, but this does not guarantee the same level of adherence on other days. "White coat adherence" is a phenomenon that has to be accounted for when interpreting the results: patients may follow prescriptions better just before and after a follow-up visit.<sup>24</sup>

In the present study, about 50% of the patients had no knowledge of one or more aspects of the medical prescription. The regression analysis showed a significant relationship between knowledge of and adherence to prescribed analgesic therapy. To depict the association

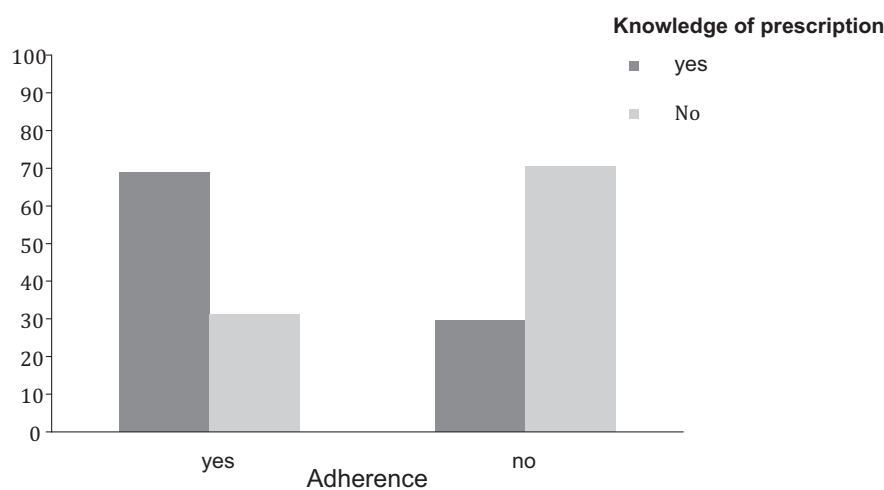
between overall knowledge of the prescription and adherence, we performed a post hoc univariate analysis. Of those who were adherent, the proportion of patients with overall knowledge of the prescription (compared to those who had not) was found to differ substantially; this difference was significant ( $P < 0.02$ , Fisher's Exact test) (Figure 3). Of those patients who did not know the name, dose or frequency of their analgesic regimen, 86.1% was nonadherent compared to 54.2% of those who had this knowledge. In other words, patients who did not have knowledge of their prescription were significantly less adherent to their therapy.

In this correlational study, we cannot draw conclusions about the causality of the relationship between adherence and knowledge, but it seems plausible that knowledge of the prescription increases the chance of adherence to analgesic therapy. Asking for prescription details gives insight in the risk of nonadherence during clinical evaluation of a chronic pain patient. Even though it is possible to take medication correctly without knowing its' exact name or dose, it is more likely if these items are known to the patient. Furthermore, it is almost impossible not knowing the dosing frequency and still use medication properly. This emphasizes that healthcare professionals should provide adequate information about the prescription. We defined knowledge of a prescription as knowledge of the name, dose, and frequency. These basic items might not be the most important goals for an educational intervention. It seems unlikely that people who do not know which medication they actually use will have sufficient knowledge of important properties of the prescribed therapy. Experiences in other chronic conditions demonstrate that education on prescribed medica-

tion alone might be ineffective.<sup>2,25</sup> Communication should also address personal barriers and beliefs on pain medication, and education should focus on any specific concerns about prescribed medication.<sup>13</sup> When pain treatment is started in an informed patient by shared decision after concerns have been addressed, the patient may be more likely to adhere to the therapy.<sup>12</sup>

The results of the PKQ-DLV, in which only 56% of the maximum score was reached, suggest that basic knowledge on pharmacological pain therapy was low in this study population. The relationship between medication adherence and the results of the PKV-DLV was not significant in the final analysis. The PKV-DLV was designed and validated to test knowledge in patients with cancer. Although nonmalignant pain differs from cancer pain, it is assumed that the statements made on pain therapy can be used for nonmalignant pain therapy as well. It has been used previously to test knowledge on nonmalignant pain care in nurses,<sup>26</sup> and the questionnaire appears suitable for use in a nonmalignant pain population. Some statements, however, may not hold in this population, for example, "pain can be treated effectively". In nurses and in patients with cancer, an educational intervention positively affected the total PKQ-DLV score.<sup>20,26</sup>

Our study demonstrated a negative association between age and adherence. This might be the result of polymedication being more prevalent in older adults. Polymedication has been shown to be an independent risk factor for nonadherence.<sup>27</sup> Furthermore, decreased clearance of drugs due to organ failure can increase the risk of adverse effects in elderly patients, resulting in premature cessation of prescribed therapy. However, previous studies reported a positive association between



**Figure 3.** Percentage of patients with and without knowledge of their prescription in relation to adherence.

age and pain medication adherence.<sup>28,29</sup> These studies had a different design and performed adherence measurements in a more stable treatment phase, after initial dose finding had been performed. Psychological factors and active coping strategies, that are more prevalent in younger patients, are reported to predict non-adherence and may play a more important role after the initial treatment phase.<sup>10,30,31</sup>

In conclusion, the present study confirms that medication adherence of patients with chronic, nonmalignant pain is low, with only about 50% complying with the prescribed therapy. In addition, knowledge of the prescription is low as well. Importantly, our study showed that knowledge of the prescription significantly contributes to the prediction of the level of adherence to analgesic therapy. This finding could be used as a tool to define the risk of nonadherence during evaluation of a chronic pain patient. Further study is needed to determine whether an educational intervention aimed at increasing knowledge of prescribed medication increases compliance with pain treatment and, most importantly, improves treatment outcome.

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