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Original Study

Quality of Life and Pain Medication Use in Persons With Advanced Dementia Living in Long-Term Care Facilities

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A B S T R A C T

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Objectives: In residents with dementia living in a long-term care facility (LTCF), un(der)treated pain may trigger behavioral disturbances, mood syndromes, and deterioration of physical functioning and self-maintenance. Because these factors can have considerable impact on the quality of life (QoL), this study aimed to (1) compare characteristics of persons with advanced dementia living in LTCFs with and without pain medication; (2) compare QoL in these persons with and without pain, stratified by type of pain medication use; and (3) explore associations between the use of paracetamol and QoL in persons with advanced dementia living in LTCFs.

Design and setting: This study analyzed baseline data from the Communication, Systematic Assessment and Treatment of Pain, Medication Review, Occupational Therapy, and Safety Study; a multicenter, cluster-randomized effectiveness-implementation clinical hybrid trial in 67 Norwegian LTCF clusters.

Participants: In total, 407 LTCF residents (rural and urban areas) aged ≥ 65 years, with Functional Assessment Staging scores of 5–7 (ie, moderate to advanced dementia).

Main outcome measure: QoL as assessed by the 6 QUALIDEM (validated questionnaire to measure QoL in persons with dementia living in LTCF) domains applicable to persons with moderate to severe dementia. The association between QoL and paracetamol was estimated using linear mixed-effect models, adjusting for confounding variables.

Results: 62.0% used pain medication (paracetamol, opioids, or both). QoL was lower in residents using pain medication, compared with those without pain medication [mean QUALIDEM score 68.8 (standard deviation 17.4 vs) 75.5 (standard deviation 14.6), respectively, $P < .001$]. Multilevel analysis showed that paracetamol use was not associated with QoL.

Conclusions and Implications: Persons with advanced dementia living in LTCF using pain medication have a lower QoL compared with those not using pain medication. These results are of key importance for the clinician because they stress the need for regular medication review and pain management. When measured cross-sectionally, use of paracetamol is not associated with increased QoL.

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According to the World Health Organization (WHO), at present 47.5 million people worldwide have dementia. This number is expected to increase to 75.6 million by 2030 and to 135.5 million by

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2050.¹ Pain is a common symptom among persons with dementia living in long-term care facilities (LTCFs), with a prevalence ranging from 40% to 60%.^{2–5} A more accurate prevalence rate is difficult to establish, as persons with advanced stages of dementia cannot always express their feelings and needs (such as help for pain) compared with persons without dementia.^{6–8} Therefore, undertreatment of pain remains a threat in this population. Moreover, un(der)treated pain may trigger behavioral disturbances, (ie, aggression, apathy, agitation),^{5,6,9} mood syndromes (ie, depression),¹⁰ and sleeping disorders^{11,12} in persons with dementia. In addition, these symptoms may decrease the quality of life (QoL) of persons with dementia.^{13–15}

QoL is defined by the WHO as individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns.¹⁶ Because persons with dementia are often unable to show/explain their own goals, expectations, standards, and concerns, healthcare professionals may need to maintain QoL for them. A major component of this latter aim is to adequately treat symptoms that may have an impact on QoL, such as pain.¹⁷

Several pain treatments have been evaluated regarding their influence on behavioral and mood problems of persons with dementia, irrespective of whether or not the person has pain. One such treatment is the use of paracetamol; the world's most frequently used analgesic and the first step of pain treatment in accordance with the WHO pain relief ladder.¹⁸ One study showed that persons with dementia were less socially isolated and more active during the intervention period with paracetamol compared with the placebo period.¹⁹ In another study on pain treatment conducted in Norway, agitation and depression rates dropped significantly in the intervention group who received pain medication in a stepwise way.^{9,20,21} Moreover, staff distress diminished because of a reduction in residents' agitation and apathy.²² Finally, another study showed that pain treatment improved sleeping disturbances over a short period of time in persons with dementia and depression.²³

Research on the relationship between pain, pain medication, and QoL in persons with dementia is relatively scarce. Therefore, the aims of this study were to (1) compare characteristics of persons with advanced dementia living in LTCFs with and without pain medication; (2) compare QoL in these persons with and without pain, stratified by pain medication use (paracetamol, opioids, both paracetamol and opioids, or no pain medication); and (3) explore associations between the use of paracetamol and QoL in persons with advanced dementia living in LTCFs.

Our hypothesis was that persons with advanced dementia that use pain medication would have less pain and, consequently, would have a better QoL.

Methods

Study Design

This study made a cross-sectional secondary analysis of data from baseline measurements of the Communication, Systematic Assessment and Treatment of Pain, Medication Review, Occupational Therapy, and Safety (COSMOS) study; a multicenter, cluster randomized effectiveness-implementation clinical hybrid trial in 67 Norwegian LTCF clusters (conducted between August 2014 and December 2015).²⁴ The main purpose of that study was to ameliorate QoL of individuals both with and without dementia by improving advance care planning, adequate assessment, and treatment of pain, implementing systematic medication reviews to reduce administration of unnecessary medication and systematic organization of individual activities. The intervention lasted 4 months with a follow-up period of 9 months post-baseline.

The COSMOS trial was approved by the Regional Committee for Medical and Health Research Ethics, West Norway (REK 2013/1765), and registered at clinicaltrials.gov (NCT02238652).

Verbal and written informed consents were acquired in direct conversation with the resident (if possible) and his or her legal representative.

Inclusion criteria for this cross-sectional study were LTCF residents (in both rural and urban areas) aged ≥ 65 years, with Functional Assessment Staging (FAST) scores of 5–7 (ie, moderate, moderate severe and severe dementia).²⁵

Patients with a life expectancy ≤ 6 months, or having schizophrenia were excluded.

Measurements

Information on age, sex, and marital status were collected by nurses. To extract data on pain medication use (paracetamol and opioids), the treating elderly care physician provided a "Topical Medication Overview" (ie, a sheet with only the current prescribed and used medications, including dose). This medication overview was provided in the same week as the other data were collected. Use of paracetamol and/or opioids was defined as the use of paracetamol, opioids, or both on a continuous basis (ie, at least once a day).

The stage of dementia was obtained by the FAST measure.²⁵ This is a tool to assess functional deterioration in different stages of dementia.²⁶ FAST scores range from 1 (no objective or subjective functional decrement/normal aging) to 7 (severe dementia).

For the primary outcome, QoL, the validated questionnaire to measure QoL in persons with dementia living in LTCF (QUALIDEM) was used.²⁷ For the primary outcome, QoL, the validated questionnaire, specifically developed to measure QoL in persons with dementia living in LTCF.²⁸ Moreover, of an established set of QoL instruments, it is considered to have the best-studied measurement properties.²⁹ The instrument consists of 8 subscale domains (care relationship, positive affect, negative affect, restless tense behavior, social relations, social isolation, feeling at home, and occupation). For the present study, 19 of 37 items were deleted as recommended by the authors of the QUALIDEM manual for people with advanced dementia.³⁰ Consequently, 6 domains were used for analysis (care relationship, positive affect, negative affect, restless tense behavior, social relationships, and social isolation). To compare different domain scores and to calculate an overall mean score, the scores were rescaled to a maximum of 100 points per domain by dividing the score by the maximum score of the domain and multiplying by 100. In this way, the new value represents the original score as a percentage of the maximum value. An overall mean score (QUALIDEM 6-domain overall score, QUALIDEM 6D) was calculated by adding the domain scores, and dividing by 6 (the number of domains). Mean domain scores and an overall mean score range from 0 (worst QoL possible) to 100 (best QoL possible). This process of transformation has been successfully applied in previous studies.^{31–33}

The Mobilization-Observation-Behavior-Intensity-Dementia-2 (MOBID-2) Pain Scale^{34–36} is a 2-part tool used to measure pain intensity. This pain scale was developed to capture pain expressed verbally, with facial expression, and/or with showing defense by a person with dementia. The nurse grades the overall pain intensity with an overall score (ranging from 0 to 10). An overall score of ≥ 3 indicates that a resident has clinically relevant pain intensity.^{34,35}

The Cornell Scale for Depression in Dementia, with 19 symptoms and signs distributed among 5 domains (mood-related signs, behavioral disturbance, physical signs, cyclic functions, and ideational disturbance), was used to assess depressive symptoms.³⁷ A score > 12 is indicative of probable major depressive disorder.³⁷

Neuropsychiatric symptoms were measured by the Neuropsychiatric Inventory-Nursing Home version (NPI-NH).^{38,39} It consists of 10 domains of behavior (delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability/lability, and aberrant motor behavior), and 2 types of neurovegetative changes (sleep and night-time behavior disorders, and appetite and eating disorders). For each domain, frequency (rarely, sometimes, often, very often) and severity (mild, moderate, severe) are multiplied to form a domain score. The total NPI-NH score was calculated by adding all 12 domain scores, ranging from 144 (extreme neuropsychiatric symptoms) to 0 (no neuropsychiatric symptoms). Furthermore, 8 domains were clustered into 3 factors, (ie, psychosis, delusion, hallucination). Agitation (agitation, disinhibition, and irritability) and affective symptoms (depression,

anxiety), as was carried out with Norwegian data,⁴⁰ based on the study of Selbæk et al.⁴¹

The Physical Self-Maintenance Scale was used to assess physical functioning in terms of activities of daily living (ADL).⁴² This encompasses 6 aspects (toilet, feeding, dressing, grooming, physical ambulation, and bathing) in which professional caregivers rate the level of self-maintenance. Total scores range from 0 (no physical self-maintenance) to 6 (complete physical self-maintenance).

Statistical Analysis

To compare characteristics of persons with and without pain medication and QoL for persons with and without pain, independent samples *t*-tests were used to compare numerical, normally distributed characteristics, whereas Mann-Whitney U-tests were used to compare numerical, non-normally distributed characteristics. Categorical characteristics were compared using χ^2 tests. The association between QoL and paracetamol use was estimated by linear mixed-effect models, using restricted maximum likelihood. To account for correlation among residents within LTCFs, we included a random intercept for LTCF units. Confounding was minimized by adjusting for opioid use, age, sex, stage of dementia, ADL functioning, neuropsychiatric behavior, mood, and interaction between paracetamol and opioids.

For the QUALIDEM-6D and for each of the 6 QUALIDEM domains, 4 models were computed: (1) in the first model, the effect of paracetamol use on QoL was estimated; (2) the second model contained items from the first model plus confounding variables (age, sex, behavior, mood, stage of dementia); (3) in the third model opioid use was added; and (4) in the final model interaction between paracetamol and opioids was added.

Descriptive analyses were performed with SPSS statistical software, v 23 (IBM Corp., Armonk, NY), and linear mixed-effect analyses were performed with STATA/IC15 (StataCorp 2017 Stata Statistical Software, Release 15; StataCorp LLC, College Station, TX).

Results

COSMOS data were available for 545 nursing home residents. Of these, 32 residents were excluded because of missing FAST scores, 86

were excluded as they had FAST scores of 1–4, and an additional 20 persons were removed due to missing QUALIDEM data.

Data for 407 persons with dementia were available for analysis (Table 1).

Mean age was 86.6 (standard deviation [SD] 7.3) years and 72.2% was female. Of all residents, 54.1% used paracetamol and 32.7% used 1 or more opioids on a continuous basis. Of these, there was a 25% overlap of participants using both paracetamol and opioids (62.7% used paracetamol, opioids, or both). When stratified into 2 groups (using any pain medication daily and not using any pain medication), the mean age, sex, and marital status did not differ between the 2 groups (Table 1). In the group that used pain medication, the percentage of residents with FAST scores of 7 was significantly higher (24.7%) than in those not using pain medication (15.8%); $P = .042$.

In the total group, the QUALIDEM-6D was 71.3 (SD 16.7). Of the 6 individual QUALIDEM domains, care relationship 76.9 (SD 23.8), positive affect 75.4 (SD 22.4), social relationships 73.5 (SD 21.4), and social isolation 75.2 (SD 23.7) scored above the QUALIDEM-6D mean. "Negative affect" and "restless tense behavior" scored below the QUALIDEM-6D mean (67.0 [SD 26.8] and 59.6 [SD 30.3], respectively).

Compared with the group without pain medication, those who used pain medication had significantly lower QUALIDEM scores on all domains, with the exception of "social relationships" (Table 1).

In the total group, (1) 43.3 had clinically relevant pain scores (MOBID-2 score ≥ 3) and (2) the MOBID-2 total pain score was (on average) 2.5 (SD 2.6) (Table 1). The group that used pain medication had a total pain score more than twice that of those not using pain medication [3.2 (SD 2.7) vs 1.4 (SD 2.0), $P < .001$]; moreover, the proportion of clinically relevant pain scores showed a significant difference between these 2 groups (54.0% vs 25.4%, $P < .001$).

The mean Cornell total score of the total group was 7.3 (SD 6.1) (Table 1). The mean Cornell score in the group that used pain medication was significantly higher [8.2 (SD 6.6)] than that of the group without pain medication [5.6 (SD 5.2)] (Table 1).

The median of the NPI-NH total score was 12.0 [interquartile range (IQR) 3.0–26.0]. The NPI-NH total score and the subscores on psychosis, agitation, and affective symptoms, were significantly higher in

Table 1
Characteristics of and Measurements in the Total Group of Persons With Advanced Dementia, Stratified by Pain Medication Use

	Total (n = 407)	Pain Medication (n = 255)	No Pain Medication (n = 152)	P Value
Mean age (SD), y	86.6 (7.3)	86.5 (7.2)	86.6 (7.4)	.878
Female (%)	294 (72.2)	189 (74.1)	105 (69.1)	.272
Marital status (%)				.605
Unmarried	47 (12.3)	31 (11.8)	18 (11.8)	
Married	101 (26.4)	62 (23.6)	40 (26.3)	
Widow	234 (61.3)	159 (60.5)	80 (52.6)	
FAST score 7 (%)	86 (21.1)	62 (24.3)	24 (15.8)	.042*
QUALIDEM-6D 0–100 (SD)	71.3 (16.7)	68.8 (17.4)	75.5 (14.6)	<.001
A Care relationship 0–100	76.9 (23.8)	74.6 (25.3)	80.9 (20.4)	.009
B Positive affect 0–100	75.4 (22.4)	73.1 (22.7)	79.1 (21.3)	.010
C Negative affect 0–100	67.0 (26.8)	63.2 (27.6)	72.9 (24.0)	.001
D Restless tense behavior 0–100	59.6 (30.3)	55.3 (31.3)	66.0 (27.8)	.001
F Social relationships 0–100	73.5 (21.4)	72.4 (21.5)	75.3 (20.9)	.196
G Social isolation 0–100	75.2 (23.7)	73.4 (24.7)	78.4 (21.3)	.034
MOBID-2 overall pain intensity, 0–10 (SD)	2.5 (2.6)	3.2 (2.7)	1.4 (2.0)	<.001
MOBID-2 ≥ 3 (%) [†]	155 (43.3)	121 (54.0)	34 (25.4)	<.001
Cornell total score 36–0 (SD)	7.3 (6.1)	8.2 (6.6)	5.6 (5.2)	<.001
NPI-Nursing Home total score, 0–144 (IQR)	12.0 (3.0–26.0)	13.0 (4.0–32)	9.0 (2.0–20.0)	.012
Psychosis (delusion, hallucination) (0–24)	0.0 (0.0–3.0)	0.0 (0.0–4.0)	0.0 (0.0–1.0)	.035
Agitation (agitation, disinhibition, irritability) (0–48)	3.0 (0.0–11.0)	4.0 (0.0–12.3)	2.0 (0.0–9.0)	.019
Affective symptoms (depression, anxiety) (0–24)	1.0 (0.0–6.0)	2.0 (0.0–8.0)	0.0 (0.0–4.5)	.016
Physical self-maintenance scale, 0–6 (IQR)	1.0 (0.0–1.0)	1.0 (0.0–1.0)	1.0 (0.0–2.0)	.003

*Compared with FAST 5/6 group.

[†]Clinically relevant pain.

the group with pain medication than in the group without pain medication (Table 1).

The median ADL functioning on the Physical Self-maintenance Scale was 1.0 (IQR 0.0–1.0). The group without pain medication had better ADL functioning [1.0 (IQR 0.0–2.0)] compared with those using pain medication [1.0 (IQR 0.0–1.0)]; $P = .003$.

Figure 1 shows QoL of persons with dementia with and without pain, stratified by pain medication use. In the group with pain (MOBID-2 total score ≥ 3), persons with dementia that were using no pain medication had better overall QoL according to the QUALIDEM-6D [75.6 (SD 15.8)], compared with persons with paracetamol only [68.2 (SD 15.4)], opioids only [65.9 (SD 11.4)] and persons that used both paracetamol and opioids [64.6 (SD 18.6)]; $P = .021$. The group that used only paracetamol had significantly lower overall QoL when they were (still) in pain (68.2%) compared with having no pain (74.8%; $P = .031$).

Because there were no significant differences in QoL between the groups with and without pain using opioids, both opioids and paracetamol, or no pain medication, only the association between paracetamol and QoL was estimated. The final model of the linear mixed-effects model to estimate the association between paracetamol use and QoL is presented in Table 2. When adjusted for confounding variables and interaction between paracetamol and opioids, no significant association was found between paracetamol and overall QoL or in the 6 QoL subdomains.

Discussion

The main goal of this study was to gain insight into (1) differences in the characteristics of persons with advanced dementia with and without pain medication, (2) the QoL of these persons, and (3) the association between paracetamol use and QoL.

Contrary to our hypothesis, this study shows that, compared with the QoL of persons with dementia who did not use pain medication, the QoL of persons with dementia was lower when they use pain medication daily. This was the case for all QoL domains, with the exception of “social relationships.” In addition, this study shows that (1) the pain score of persons with dementia using pain medication was more than twice as high as those without pain medication, and (2) that these individuals had a significantly lower ADL function.

Finally, the results show that paracetamol use was not independently associated with QoL of persons with dementia. Our results are of key importance for the clinician because they stress the need for regular medication review and pain management. Clinicians should not automatically assume that persons with dementia that are

already using pain medication are relieved from their pain, or that they will be relieved from their pain once (any) pain medication is started. Periodical pain assessment and adjustment of pain medication prescriptions are important to diminish under- and over-prescription, and side-effects of pain medication as much as possible, to establish or maintain the best possible QoL in persons with advanced dementia.

In this study, the number of pain medications used is comparable to that of a previous study performed in Norway.²⁰ However, in the present study, the overall number of people having clinically relevant pain scores (MOBID-2 ≥ 3) was lower (43.3%) compared with the Norwegian study (>55%). A possible explanation for this difference could be that, in the Norwegian study, only people with behavioral disturbances were included, whereas in our study this was not the case. Pain could have caused these behavioral disturbances, leading to the higher number in the Norwegian study.

Our data on pain medication use and pain are also comparable with those of studies in other countries.^{6,43} Moreover, the higher number of people using pain medication and still in pain, compared with those that use pain medication without pain, was also found in a study conducted in the United Kingdom.⁴⁴

A major strength of the present study is that, to our knowledge, it is the first to explore the association between pain medication and QoL in this population. A recent study on the implementation of a stepwise multidisciplinary intervention concluded that effective pain management would be of vital importance to establish an optimal QoL.⁴⁵

Another strength is that we used the 18-item QUALIDEM questionnaire, rather than the 37-item version, to measure QoL. As we only included people in severe stages of dementia and did not compare them with individuals in lower stages of dementia, we think that the 18-item version of the QUALIDEM is the most appropriate for our group of participants. Also, this avoids including items that are not applicable to be filled in by nurses about persons with advanced dementia, as was also applied in earlier studies.^{43,46,47} Finally, we included all LTCF residents with FAST scores of 5–7 and aged ≥ 65 years irrespective of having pain or not, whereas other studies had stricter inclusion criteria besides (severe) dementia (eg, behavioral problems^{20,36} or depression).²³

A limitation of our study is that we used data from a study that was not specifically designed to address our research questions. For example, we only had information on what medication participants used at baseline, so we do not know how (adequately) the identification and assessment of pain were established before the baseline measurement, and consequently, how adequate the analgesic treatments were prescribed. Moreover, we had no information on what might have changed in the prescriptions of pain medication over time between baseline and the other measurement points at 4 and 9 months in the COSMOS study, so we were unable to examine the association between paracetamol use and QoL over time. Finally, another limitation of our study is that we could not control for the relative presence of painful conditions, because data on these were not present. This might have caused an underestimated the QoL in the pain medication group, because simply having a painful condition could cause more pain and a lower QoL in a person with dementia and presumably there might have been more persons with a painful condition in the pain medication group than in the nonmedication group.

Our comparison of data on the QoL in persons with advanced dementia with and without pain revealed a lower QoL when an individual used paracetamol daily and was (still) in pain. For the other pain medication groups (opioids, opioids and paracetamol, and no pain medication) the same trend was seen; however, this difference was not significant. Either this trend could be based on coincidence, or the groups using opioids or both paracetamol and opioids were

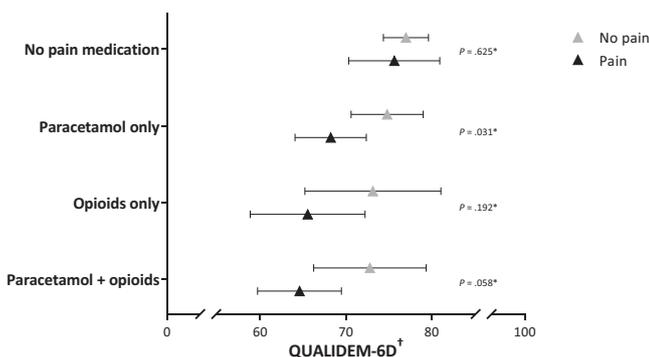


Fig. 1. Quality of life of persons with dementia with and without pain (MOBID-2 score ≥ 3), stratified by pain medication use.

*Independent samples t-test. †Range 0–100. No pain medication no pain: $n = 100$, pain: $n = 34$. Paracetamol only no pain: $n = 57$, pain: $n = 53$. Opioids only no pain: $n = 18$, pain: $n = 12$. Paracetamol and opioids; no pain: $n = 28$, pain: $n = 56$.

Table 2
Final Linear Mixed-Effects Model of the Association Between Paracetamol Use and Quality of Life*

	Coefficient	Standard Error	z	P Value	95% Confidence Interval	
QUALIDEM domains						
QUALIDEM-6D	–1.181	1.362	–0.87	.386	–3.850	1.488
A - Care relationship (SD)	–1.755	2.353	–0.75	.456	–6.367	2.857
B - Positive affect (SD)	–0.668	2.606	–0.26	.798	–5.775	4.440
C - Negative affect (SD)	–2.421	2.726	–0.89	.374	–7.764	2.922
D - Restless tense behavior (SD)	–3.639	2.969	–1.23	.220	–9.458	2.181
F - Social relationships (SD)	0.871	2.675	0.33	.745	–4.371	6.113
G - Social isolation (SD)	0.963	2.254	0.43	.669	–3.455	5.382

*Adjusted for opioid use, interaction between paracetamol and opioids, age, sex, stage of dementia, ADL functioning, neuropsychiatric behavior, and mood

underpowered. A possible explanation for the lower QoL could be that a person experiences (unpleasant) side-effects (as seen with opioids in a recent study⁴⁸), and/or the effects are insufficient. Also, the pain score of persons with dementia using pain medication in our study was more than twice as high as those without pain medication, which can be caused by badly dosed pain medication. Since this specific population is at increased risk for comorbidity, there is an increased chance of needing pain medication and being at risk to develop side-effects which can, in turn, decrease ADL function and QoL. This should be borne in mind by physicians when prescribing and evaluating pain medication in persons with advanced dementia.

Conclusions/Relevance

Persons with dementia living in LTCF who use pain medication have a lower QoL compared with persons with dementia who do not use any pain medication. These results are of key importance for the clinician because they stress the need for regular medication review and pain management. Periodical pain assessment and adjustment of pain medication prescriptions are important to diminish under- and overprescription, and side-effects of pain medication as much as possible to establish or maintain the best possible QoL in persons with advanced dementia. When measured cross-sectionally, the use of paracetamol is not associated with QoL. More research is needed to further explore the effects of paracetamol use on QoL over time.

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