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Original Study

Impact of Psychotic Symptoms and Concurrent Neuropsychiatric Symptoms on the Quality of Life of People With Dementia Living in Nursing Homes

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A B S T R A C T

Objectives: The aim of the present study was to determine whether psychotic symptoms in people with dementia (PwD) living in nursing homes were associated with reduced quality of life and to understand the additional impact of other concurrent neuropsychiatric symptoms on QoL.
Design: Cross-sectional cohort study (using data from WHELD cohort).
Settings and participants: 971 PwD living in nursing homes participating in the WHELD study.
Methods: The Neuropsychiatric Inventory–Nursing Home (NPI-NH) version was completed by informant interview. We compared mean differences in proxy-rated QoL scores (DEMQOL-Proxy) for PwD experiencing or not experiencing delusions and for PwD experiencing or not experiencing hallucinations. Backward multiple regression was used to determine the added contributions of agitation (Cohen-Mansfield Agitation Inventory), anxiety (NPI-NH-Anxiety), depression (Cornell Scale for Depression in Dementia), dementia severity (Clinical Dementia Rating-sum of boxes score), pain (Abbey Pain Scale), and antipsychotic prescription. Mediation analysis was conducted for agitation, anxiety, and depression.
Results: Presence of both delusions ($P < .001$, $B = -8.39$) and hallucinations ($P < .001$, $B = -7.78$) was associated with poorer QoL. Both associations remained significant after controlling for other factors. Agitation, anxiety, and depression partially mediated the relationship between each psychotic symptom and QoL.
Conclusions and Implications: Delusions and hallucinations in PwD are associated with poorer QoL among PwD living in nursing homes. The effects remain significant after adjusting for confounding variables. Direct effects of each symptom maintained significance despite significant mediation by concurrent neuropsychiatric symptoms.

Around one-third of people with dementia (PwD) live in nursing homes.[1] Compared with PwD living in the community, these individuals typically have more severe cognitive and functional difficulties, higher rates of comorbidity, and substantially higher rates of neuropsychiatric symptoms, including psychosis.[1,2]

Psychotic symptoms such as delusions and hallucinations are common in PwD and become more prevalent as dementia progresses,[3] with an estimated prevalence of 22% for delusions and 14% for hallucinations among nursing home residents with dementia.[4] Psychotic symptoms are impactful and are associated with a number of detrimental outcomes such as accelerated cognitive and functional decline and increased mortality.[5,6] Moreover, psychotic symptoms in PwD often occur in conjunction with other neuropsychiatric symptoms such as agitation, anxiety, and depression,[7,8] which may have further adverse effects.[9–12] Pharmacologic treatments such as atypical antipsychotics are commonly prescribed to treat neuropsychiatric

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symptoms but have been linked to various potentially harmful outcomes for PwD.[13–15] Understanding the mediating impact of frequently comorbid neuropsychiatric symptoms on quality of life (QoL) in PwD experiencing psychotic symptoms is an important gap in our current knowledge and may provide new avenues for developing nonpharmacologic treatments to improve QoL in PwD-related psychotic symptoms.

Measures of QoL are frequently used to determine subjective life experience and ability to live well when experiencing dementia and the various symptoms resulting from dementia.[12,16–18] In the context of psychotic symptoms, previous studies have indicated that the presence of psychotic symptoms is associated with lower QoL in PwD living in the community[8,19] and PwD living in nursing homes.[12,20–24] Several studies have investigated delusion and hallucinations in PwD and did not find an association with QoL; these studies however had relatively small sample sizes.[25,26] Other studies that focus on the association between psychotic symptoms and QoL investigated the symptoms as a singular phenomenon rather than delusions and hallucinations separately.[21,27] Only 2 studies with a large sample cohort have examined the independent impact of delusions and hallucinations on QoL in PwD living in nursing homes, and each study concluded that both delusions and hallucinations were significantly associated with reduced QoL.[23,24]

Although there appears to be a clear association between reduced QoL and the occurrence of psychotic symptoms in PwD living in nursing homes, what is less clear is whether this is a direct effect or whether other key factors associated with psychotic symptoms and impaired QoL, such as concurrent neuropsychiatric symptoms, dementia severity, chronic pain,[28–30] and antipsychotic medications,[13–15] may have an additive role. Crucially, neuropsychiatric symptoms commonly comorbid with psychotic symptoms such as agitation, anxiety, and depression have shown to be heavily associated with reduced QoL in PwD.[12,21] It is therefore important to understand whether these neuropsychiatric symptoms fully mediate the impact of psychotic symptoms on QoL. If psychotic symptoms do not show to have independent association in the presence of other neuropsychiatric symptoms, focus on developing treatment methods for psychotic symptoms in dementia should be secondary to these other neuropsychiatric symptoms.

The aim of the present study is to determine the independent effects of delusions and hallucinations on QoL for PwD living in nursing homes and to elucidate the role of concurrent factors such as concurrent neuropsychiatric symptoms, dementia severity, pain, and antipsychotic prescription in mediating or adding to detrimental impacts on QoL.

Methods

Study Population

In this study, we analyzed baseline data collected as part of the Improving Well-being and Health for People with Dementia (WHELD) study,[31] a 9-month cluster randomized controlled trial conducted in 69 nursing homes in England, recruited from 3 recruitment hubs: South London, North London, and Buckinghamshire. Residents of identified nursing homes were eligible for inclusion if they met criteria for dementia, defined as a score of 1 or greater on the Clinical Dementia Rating (CDR). At baseline, the WHELD cohort comprised 971 PwD. Written consent was provided by PwD when they had mental capacity to provide consent for their own participation. Written consent was provided by next of kin when individuals did not have mental capacity to consent for themselves. Data on PwD were collected through assessments conducted by trained researchers. All measures, except where stated, were completed by members of staff from contributing care homes, subsequently referred to as "informants," who provided details about the PwD in their care. The WHELD study was reviewed and approved by the Oxford C National Research Ethics Committee (Ref: 13/SC/0281). This study is registered with the ISRCTN Registry (Ref: ISRCTN62237498). Further details are available in the published protocol and trial findings.[32,33]

Measures

Psychotic symptoms

Delusions and hallucinations were measured using the Neuropsychiatric Inventory–Nursing Home version (NPI-NH).[34,35] In the NPI-NH informants were asked whether the person with dementia they were caring for was experiencing symptoms in 12 discrete behavioral domains: delusions, hallucinations, agitation and aggression, depression and dysphoria, anxiety, euphoria and elation, apathy and indifference, disinhibition, irritability and lability, aberrant motor behavior, nighttime behavioral disturbances, and appetite and eating changes. For each NPI-NH domain endorsed, the informant was asked to complete a corresponding rating for frequency (1-4) and severity (1-3) within the past week, with higher scores indicating more frequency and severity. For the purposes of this study, the delusions and hallucinations domains were considered as binary categorical variables; that is, we noted the absence or presence of each symptom.

Anxiety

The NPI-NH was also used to evaluate anxiety. Unlike psychotic symptoms, the present study used the NPI ordinal score to assess anxiety.[35] This approach was undertaken to acknowledge the fact that presence of some anxiety is normal,[36] whereas the presence of any psychotic symptoms would be construed as an abnormal experience.

QoL

The primary method of assessing QoL in PwD was with the DEMQOL-Proxy,[37] a 31-item interviewer-administered questionnaire. Scores ranged between 31 and 124, with higher scores indicating better QoL.

Agitation

The Cohen-Mansfield Agitation Inventory (CMAI)[38] was used to rate agitated behavior. The CMAI comprises 29 items related to agitated behavior, each of which is rated on a 7-point scale of frequency, with a total score range of 29 to 203. Higher scores indicate more severe agitation.

Depression

The Cornell Scale for Depression in Dementia (CSDD)[39] was used to assess signs and symptoms of major depression in PwD, with a score range from 0 to 38, with higher scores indicating more severe depression.

Pain

The Abbey Pain Scale was used as an observational brief indicator of pain for PwD. The scale is rated on 6 nonverbal indicators of pain, with a total score range of 0 to 18. Higher scores indicate more severe pain experienced.[40]

Dementia severity

The CDR is a scale used to quantify the severity of symptoms of dementia. Scores are obtained through semistructured interviews of residents and informants, and cognitive functioning is rated in 6 domains of functioning: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. For the purpose of the present study, we used the CDR sums of boxes score, which was obtained by summing each of the domain box scores.

The range of scores for CDR sums of boxes is 0-18.[41] Higher scores indicate more severe dementia.

Antipsychotic prescription

Information on antipsychotic prescription over the previous 12 months was taken from participants' medication charts at each nursing home.[32] The present analysis uses a binary measure of whether individuals were prescribed antipsychotic drugs at the time of the baseline assessment.

Data Analysis

All statistical analyses were carried out using IBM SPSS Statistics v26. For the first research question, unadjusted linear regressions were used to determine whether the presence of delusions and hallucinations respectively was associated with a lower QoL score.

For the second research question, a backwards stepwise multiple regression was used to determine the best overall predictive model of impaired QoL based on delusions, hallucinations, agitation, depression, anxiety, dementia severity, antipsychotic usage, and pain. To correct for multiple comparisons, findings were only reported if they were significant at the 5% level after Holm-Bonferroni correction.

For the third research question, parallel multiple mediator analyses were used to determine the mediating effect of agitation, anxiety, and depression on the relationship between each psychotic symptom and QoL. The analyses were performed using PROCESS macro.[42]

Results

Of the 971 participants, 687 (70.1%) were female and the mean age was 84.57 (SD 8.98). The prevalence of delusions and hallucinations was 17.5% and 14.6%, respectively, and 20% of participants were prescribed atypical antipsychotics. People who were experiencing delusions did not significantly differ in age [$t(968) = -0.25$, $P = .278$] or sex [$\chi^2(1) = 0.447$, $P = .504$]. Similarly, people experiencing hallucinations did not differ in age [$t(969) = -0.87$, $P = .098$] or sex [$\chi^2(1) = 0.497$, $P = .487$]. The full characteristics are summarized in Table 1, and a characteristic difference in those who experience psychotic symptoms are summarized in Supplementary Table 1.

Association of Psychotic Symptoms With Impaired QoL

The first research question focused on whether there were associations between the presence of informant-rated delusions and hallucinations, respectively, and the DEMQOL-Proxy total score. In the unadjusted model, the presence of both delusions and hallucinations, respectively, were both strongly associated with lower DEMQOL-Proxy scores (delusions $B = -8.39$, $P < .001$; hallucinations $B = -7.78$, $P < .001$; see Tables 2 and 3).

In the backwards stepwise regression model (including dementia severity, other concurrent neuropsychiatric symptoms, pain, and antipsychotic prescriptions), the main effect for delusions remained statistically significant but the beta coefficient was attenuated by nearly 3 points. The model explained 29% of the variance, with concurrent depression the biggest predictor for reduced QoL. Antipsychotic prescription was dropped from the final model; see Table 2. All variables included in the final model remained significant after Holm-Bonferroni adjustment.

Similarly, the main effect for hallucinations also remained statistically significant in the adjusted model, but the beta coefficient was attenuated by nearly 3 points. The model explained 29% of the variance, with concurrent depression as the biggest predictor of reduced QoL. The backwards stepwise model did not include antipsychotic medication in the final model; see Table 3. All variables included in the final model remained significant after Holm-Bonferroni adjustment.

Table 1
Characteristics of the People With Dementia (N = 971)

Demographic Characteristic	n (%) or Mean (SD); n
Sex	
Male	284 (29.2)
Female	687 (70.8)
Ethnicity	
Asian	9 (0.9)
African	11 (1.1)
Black Caribbean	25 (2.6)
White	916 (94.4)
Mixed	6 (0.6)
Other	4 (0.4)
Marital status	
Single	120 (12.4)
Married	205 (21.1)
Divorced	58 (6.0)
Separated	7 (0.7)
Widowed	563 (58.0)
Long-term partnership	7 (0.7)
Missing	11 (1.1)
Delusions	
No	800 (82.4)
Yes	170 (17.5)
Missing	1 (0.1)
Hallucinations	
No	829 (85.4)
Yes	142 (14.6)
Antipsychotic prescription within the last 12 mo	
Yes	194 (20.0)
No	755 (77.8)
Missing	22 (2.2)
Age	84.57 (8.98); 971
DEMQOL-Proxy	101.48 (12.93); 964
Clinical Dementia Rating–sum of boxes score	13.78 (3.55); 971
Cohen-Mansfield Agitation Inventory	48.32 (19.36); 969
NPI-NH–Anxiety	1.45 (2.80); 970
Cornell Scale for Depression in Dementia	6.22 (5.07); 960
Abbey Pain Scale	2.29 (2.81); 967

Therefore, the individual effect of delusions and hallucinations on QoL were similar.

Following on from the regression model, the key question was how the experience of other neuropsychiatric symptoms mediated the relationship between psychotic symptoms and QoL in dementia. Delusions, agitation, anxiety, and depression had a negative and significant direct effect on QoL, but there were also indirect effects (IEs) of delusions on QoL mediated via agitation (IE = −1.56, 95% CI −2.5, −0.72), anxiety (IE = −1.21, 95% CI −1.89, −0.62), and depression (IE = −2.34, 95% CI −3.25, −1.57) (see Figure 1).

Similarly, hallucinations, agitation, anxiety, and depression had a negative and significant direct effect on QoL, but again there were indirect effects of hallucinations on QoL mediated via agitation (IE = −1.70, 95% CI −2.72, −0.84), anxiety (IE = −1.13, 95% CI −1.80, −0.58), and depression (IE = −2.46, 95% CI −3.51, −1.54) (see Figure 2).

Table 2
Unadjusted and Adjusted Multiple Linear Regression on the Relationship of Delusions to QoL Scores as Measured by the DEMQOL-Proxy

	B	SE	β	*t*	*P*
Unadjusted					
Delusion	−8.39	1.06	−0.25	−7.901	<.001
Adjusted					
Delusion	−2.79	1.00	−0.08	−2.79	.005
Agitation	−0.1	0.02	−0.15	−4.41	<.001
Anxiety	−0.68	0.15	−0.15	−4.60	<.001
Depression	−0.74	0.09	−0.29	−7.94	<.001
Dementia severity	0.46	0.10	0.13	4.57	<.001
Pain	−0.30	0.14	−0.07	−2.18	.029

$R^2 = 0.293$ (adjusted $R^2 = 0.289$).

Table 3
Unadjusted and Adjusted Multiple Linear Regression on the Relationship of Hallucinations to QoL Scores as Measured by the DEMQOL-Proxy

	B	SE	β	*t*	*P*
Unadjusted					
Hallucination	−7.78	1.15	−0.21	−6.77	<.001
Adjusted					
Hallucination	−2.83	1.07	−0.08	−2.65	.008
Agitation	−0.10	0.02	−0.15	−4.47	<.001
Anxiety	−0.69	0.15	−0.15	−4.71	<.001
Depression	−0.74	0.09	−0.29	−8.03	<.001
Dementia severity	0.51	0.10	0.14	4.00	<.001
Pain	−0.28	0.14	−0.06	−2.01	.044

$R^2 = 0.290$ (adjusted $R^2 = 0.286$).

Discussion

The present study investigated the impact of delusions and hallucinations on proxy-rated QoL in a large cohort of PwD living in nursing homes. Both delusions and hallucinations were significantly associated with lower QoL, in the unadjusted and adjusted regression models. Key concurrent neuropsychiatric symptoms such as increased agitation, anxiety, and depression were associated with delusions and hallucinations and were important mediating factors in the relationship between psychotic symptoms and reduced QoL. To our knowledge this is the first study to examine the mediating effects of agitation, anxiety, and depression on the relationship between psychotic symptoms and QoL in PwD.

The findings confirm the association reported in previous studies between psychotic symptoms and impaired QoL in PwD living in nursing homes.[20–24] Additionally, the present research attempts to address the need for urgent development of treatments to target psychotic symptoms. The mediation analyses were conducted to determine whether psychotic symptoms were still impactful on quality of life when frequently comorbid neuropsychiatric symptoms may be present within a chain of associations. If psychotic symptoms did not have independent negative association to quality of life, then an argument can be made to focus treatment efforts primarily on other neuropsychiatric symptoms. The significant direct effect of psychotic symptoms on QoL in the mediation analysis suggests that the contribution of delusions and hallucinations does not merely impact through intermediary neuropsychiatric symptoms. However, the substantial impact of concurrent agitation, anxiety, and depression clearly indicates the importance of taking a more holistic view of the relationship between neuropsychiatric symptoms and QoL. This is important when considering the optimal approach to interventions aiming to improve QoL in PwD experiencing neuropsychiatric symptoms. Chronic pain also showed a significant association with reduced QoL, consistent with previous studies.[28,29]

Antipsychotic medications were not associated with impaired QoL in the current analysis, contrary to previous findings.[13–15] This is probably explained by the lower and hopefully more targeted prescription of antipsychotics in current practice compared to the period when previous studies were undertaken.[18,43] Indeed, recent findings have indicated low prevalence of antipsychotic prescription in PwD living in the community and as a result a reduced impact on QoL.[8] In view of the significant adverse events associated with antipsychotic prescription in PwD, the use of these agents should remain as sparing as possible.[13–15] The overall model accounted for 29% of the variance. This is relatively lower to previous studies investigating predictors of QoL in PwD.[11,21,25] This is likely due to focusing on selected neuropsychiatric symptoms that have been known to be strongly associated to reduced QoL rather than including all neuropsychiatric symptoms.

The strengths of the present study include the use of an analysis model incorporating dementia severity, concurrent neuropsychiatric symptoms, antipsychotic prescription, and pain, the large sample size, and the use of mediation analyses,

The study was limited by the use of a proxy-rated instrument for measuring QoL rather than a self-rated tool, as this does not give a direct insight into the perspective of PwD on their QoL; however, modest levels of agreement have been found between ratings by caregivers and PwD using DEMQOL-Proxy and DEMQOL[44] and the use of proxy ratings is a more feasible method of eliciting QoL in a sample that includes people with severe dementia, many of whom have communication and language difficulties. The use of a dichotomized delusion and hallucination variable limits the ability of the study to fully capture the varied frequency and severity of these symptoms. However, this was necessary to prevent biasing the data toward more severe symptom experience as the focus of the study was to determine if any experience of psychotic symptom would be associated with reduced QoL.

The cross-sectional nature of the study limits the interpretations that can be drawn, and causal relationships cannot be determined.

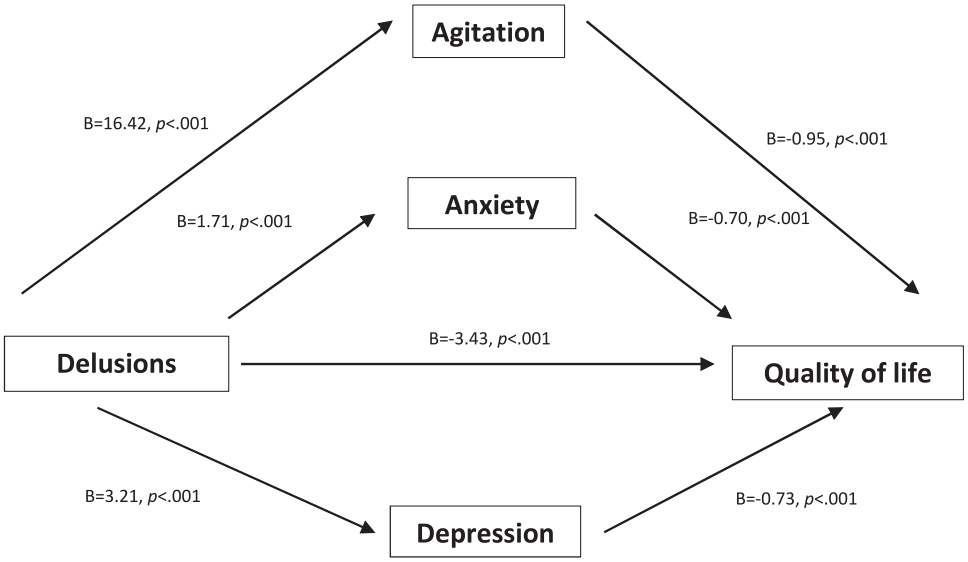

Fig. 1. Relationship between delusions and QoL mediated by agitation, anxiety, and depression in PwD living in nursing homes.

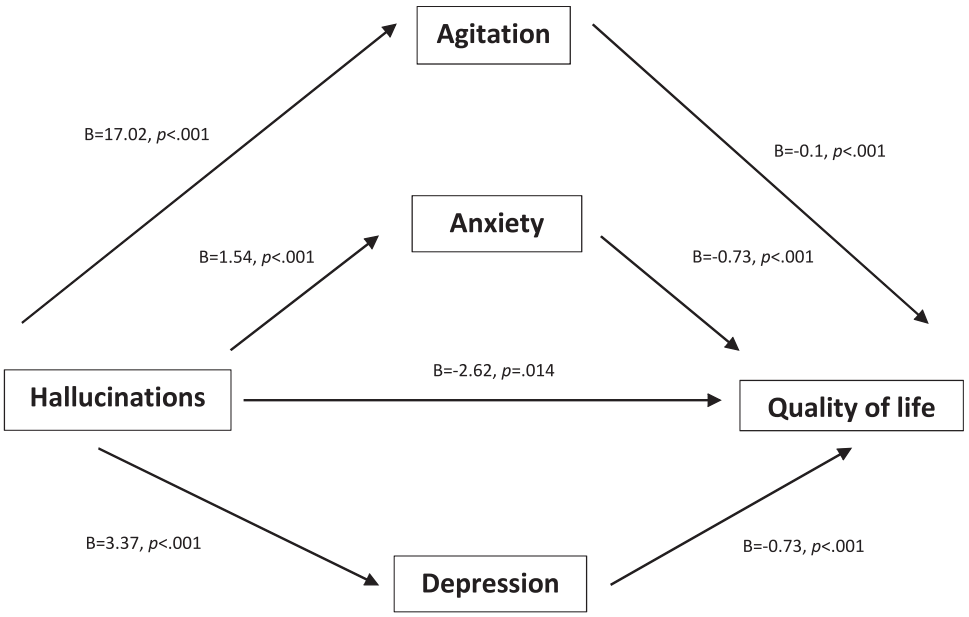

Fig. 2. Relationship between hallucinations and QoL mediated by agitation, anxiety, and depression in PwD living in nursing homes.

Additionally, the mediation analysis does not draw any conclusions of directionality. The analyses show that given the possibility of a serial line of neuropsychiatric symptom causality that results in reduced QoL, psychotic symptoms remain a key independent association. Hence, focus on developing treatments directed toward psychotic symptoms is an important priority for researchers and clinicians. It should also be acknowledged that CDR is a staging classification, not a formal classification system for diagnosing dementia, and not all participants therefore had a formal diagnosis of dementia.

Conclusions and Implications

The present findings highlight the impact of psychotic symptoms on reduced QoL in PwD living in nursing homes independent of confounding factors and implicates the urgent need for safe and effective methods of treatment and management. Additionally, the findings of the mediation analyses provide clearer insight into the role of comorbid neuropsychiatric symptoms and in turn will bolster future development of nonpharmacologic treatments for psychotic symptoms and other concurrent neuropsychiatric symptoms in PwD.

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Supplementary Table 1
Characteristic of People With and Without Psychotic Symptoms

	Delusions, n or Mean (SD)		Hallucinations, n or Mean (SD)	
	No	Yes	No	Yes
Sex				
Male	237	46	246	38
Female	563	124	583	104
Ethnicity				
Asian	8	1	9	0
African	9	2	9	2
Black Caribbean	18	7	24	1
White	757	158	777	139
Mixed	5	1	6	0
Other	3	1	4	0
Marital status				
Single	105	15	107	13
Married	167	37	170	35
Divorced	48	10	53	5
Separated	7	0	6	1
Widowed	459	104	476	87
Long-term partnership	6	1	6	1
Antipsychotic drug prescription				
Yes	149	44	155	39
No	633	122	658	97
Age, y	84.54 (9.15)	84.73 (8.22)	84.67 (8.81)	84.00 (9.93)