

The prognostic significance of distinct psychosis symptom profiles in dementia: A cohort study using linked electronic health records

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Abstract

Background

Psychotic symptoms in dementia overall are associated with poorer outcomes, but the prognostic significance of different symptom profiles remains unclear. We aimed to evaluate the prognostic significance of distinct psychosis profiles in a large dementia cohort.

Methods

We used de-identified electronic health records from a large South London mental health and dementia care provider. The cohort included 21,108 patients with dementia diagnosed between 2008 and 2022. Psychosis was identified after dementia diagnosis and classified as hallucinations only (H + D-), delusions only (H-D+), co-occurring hallucinations and delusions (H + D+), or no psychosis (H-D-). Cox regression models estimated hazard ratios (HRs) for mortality, psychiatric admission, and general hospital admission comparing the different hallucination/delusions combinations with no psychosis. Logistic regression estimated odds ratios (ORs) for care home admission. Multivariate models were adjusted for sociodemographic factors, cognition, dementia subtype, mental health diagnoses, pharmacotherapy, and physical comorbidity.

Results

Psychotic symptoms were present in 34.8% of patients with dementia. In fully adjusted models, H + D+ showed the most consistent associations across all outcomes: mortality (aHR: 1.10, 95% CI: 1.04–1.17), general hospital admission (aHR: 1.13, 95% CI: 1.06–1.19), psychiatric admission (aHR: 2.15, 95% CI: 1.71–2.70), and long-term care admission (aOR: 1.23, 95% CI: 1.04–1.46). H + D- was associated with increases in mortality (aHR: 1.08, 95% CI: 1.03–1.13), general hospital admission (aHR: 1.06, 95% CI: 1.02–1.11), and psychiatric admission (aHR: 1.28, 95% CI: 1.02–1.61), but not long-term care admission. H – D+ was associated only with psychiatric admission (aHR: 1.41, 95% CI: 1.07–1.85).

Conclusions

The prognostic significance of psychosis in dementia differs by symptom profile. Combined hallucinations and delusions identify a particularly severe phenotype associated with consistently poorer outcomes and greater service need.

Background

Dementia is currently the seventh leading cause of death worldwide and a major cause of disability and dependency among older adults[1]. According to the World Health Organization, in 2021, 57 million people had dementia worldwide, and every year, there are nearly 10 million new cases[1]. Alongside cognitive decline, 90% of people with dementia are likely to experience some form of behavioural and psychological symptoms of dementia (BPSD)[2]. These symptoms often result in negative outcomes, such as prolonged hospitalisation, increased medical comorbidities, higher health and social care costs, and lower survival rates[2]. BPSD covers a variety of symptoms, such as depression, anxiety, apathy, aggression and psychosis. Psychosis is present in 34% to 63% of cases with dementia[3], and takes the form of delusions and hallucinations, with prevalences of 31% and 16% respectively[4, 5]. Delusions are fixed false beliefs that are incongruent with reality typically persecutory in content (theft, harm, or jealousy)[6]. Hallucinations are perceptual experiences occurring in the absence of an external stimulus, most commonly visual or auditory in nature, experienced with the vividness and sense of reality of a true perception[7].

Psychosis in dementia is associated with poorer outcomes, including increased risks of long-term care placement, emergency department visits, hospital admissions, infections and mortality[8–10]. Evidence suggests that hallucinations may confer a greater risk of adverse outcomes than delusions. In a multicentre longitudinal cohort of 456 individuals with early Alzheimer's disease (AD) followed for approximately four years, delusions were linked to faster cognitive and functional decline, whereas hallucinations were associated with institutionalisation and increased mortality[11]. A separate four-year longitudinal study of 410 individuals with AD found that baseline hallucinations—but not delusions—were associated with more rapid cognitive decline[12], supporting the suggestion that hallucinations may have particular prognostic significance and could inform more personalised dementia care.

However, recent work has emphasised that much of the evidence on psychosis in dementia derives from relatively small or highly selected specialist research cohorts which may not generalise to the broader population seen in routine care[13]. This highlights the need for large naturalistic cohorts with detailed clinical characterisation in order to clarify the independent contribution of psychosis to key outcomes across dementia subtypes[13]. Greater knowledge in this area may support more personalised care planning, facilitate discussions with families, and inform strategies to reduce pressures on health and social care systems[13].

This study aimed to address these gaps by evaluating the prognostic significance of distinct psychosis symptom profiles in dementia in a large naturalistic cohort. Specifically, we examined whether these psychosis subgroups showed differential associations with mortality, psychiatric admission, general hospital admission, and care home admission. By conceptualising psychosis not only as a behavioural complication but also as a potential prognostic marker, this study aims to improve the understanding of its role in dementia trajectories.

Methods

Data Source

We used the Clinical Record Interactive Search (CRIS) system from the South London and Maudsley (SLaM) NHS Foundation Trust, a de-identified electronic health records platform from an organisation serving over 1.36 million residents across four South London boroughs (i.e., Lambeth, Lewisham, Southwark, and Croydon)[14, 15]. The CRIS platform enables researcher access to all recorded clinical, demographic, and service-use data and is one of the most comprehensive mental health research databases in Europe, approved for secondary research use by the Oxford Research Ethics Committee (reference 23/SC/0257). Information was obtained from both structured fields in patient records and from free-text clinical notes. For the latter, natural language processing (NLP) tools were applied, using the General Architecture for Text Engineering (GATE) framework[14, 16], with a detailed description available in the CRIS NLP Applications Library[17].

Cohort definition

The cohort included all patients with a diagnosis of dementia recorded between 1st January 2008 and 31st December 2022. Dementia subtypes were identified from structured fields containing ICD-10 [18] diagnostic codes (i.e., F00–F03) and supplemented with NLP to capture diagnoses of dementia with Lewy bodies in unstructured clinical notes[19, 20]. Dementia subtypes were captured and classified into five categories: i) dementia in Alzheimer's disease (AD), ii) vascular dementia (VD), iii) mixed AD/VD, iv) dementia with Lewy bodies (DLB), and v) other/unspecified dementia if none of the aforementioned diagnoses were present. Dementia subtype was assigned using diagnoses recorded at any time in the patient record using the following hierarchical structure: a diagnosis of DLB was assigned if any DLB diagnosis was present; mixed-type AD/VD if an F00.2 or both F00 and F01 were recorded; AD if only F00 was recorded; VD if only F01 was recorded; and unspecified/other if none of these diagnoses were present.

Exposure

The main exposure variable was the presence of psychotic symptoms after the time of the first dementia diagnosis. These were ascertained using NLP applications to identify recorded instances of hallucinations of any modality and/or delusions of any type at the time of first dementia diagnosis [17, 21]. Patients were classified into four groups according to which psychotic symptom were recorded in a window from six months before to six months after first dementia diagnosis: Hallucinations and delusions present (H + D+), hallucinations present and delusions absent (H + D-), hallucinations absent and delusions present (H-D+), hallucinations and delusions absent (H-D-).

Outcomes

Four outcomes were examined: i) mortality was defined as death from any cause until a censoring point on 22/05/2025; ii) psychiatric hospital admission was defined as the first inpatient psychiatric hospitalisation recorded after dementia diagnosis with follow-up censored at the earlier of death or 22/05/2025; iii) general hospital admission was defined as the first inpatient admission to an acute (non-psychiatric) hospital after dementia diagnosis and was ascertained via a linkage to national Hospital Episode Statistics (HES)[22] from which data was available until 31/03/2023 and where follow-up was censored on this date or at death, if death occurred earlier; iv) long-term care admission was defined as a change of address to a care home after dementia diagnosis. Care home residence was determined using Lower Layer Super Output Areas (LSOAs). Patients were classified as living in a care home if their recorded LSOA matched an LSOA containing a registered care home [23]. For analyses of the move to long-term care outcome (iv), patients living in a care home at baseline and those with less than six months of follow-up were excluded. During follow-up, participants were classified as having moved to long-term care when their recorded LSOA changed to one containing a registered care home.

Covariates

Sociodemographic variables included age, sex, ethnicity (White, Black, Asian, Other), marital/cohabitation status, and neighbourhood-level deprivation measured using the Index of Multiple Deprivation (IMD)[24]. Level of cognitive impairment was measured from the recorded Mini-Mental State Examination (MMSE) score closest to dementia diagnosis[19, 25]. Mental health conditions prior to the dementia diagnosis were identified in structured fields on CRIS according to ICD-10 codes. We identified schizophrenia and other primary psychotic disorders (ICD-10: F20-F29), bipolar disorder (ICD-10: F30/F31) and depression (ICD-10: F32/F33). The Health of the Nation Outcome Scales (HoNOS[26]) was used to derive indicators of mental health symptoms and functioning excluding the subscales relating to psychosis or cognition. Each subscale is rated from 0 (no problem) to 4 (severe or very severe problem). We used the HoNOS score closest to the index date and dichotomised the relevant subscales to identify patients with difficulties (scoring 2–4) versus those without or with only minor problems (scoring 0–1). In addition to the HoNOS physical illness and disability subscale, physical health conditions were identified from the full mental health record using a suite of MedCAT NLP algorithms identifying the recorded presence of 21 different conditions[27]. Psychotropic medication receipt within a one-year exposure window surrounding the dementia diagnosis (index date) was ascertained from structured data supplemented by an NLP algorithm ascertaining this from text fields[19]. Use of each medication class was captured for the following: acetylcholinesterase inhibitors, memantine, antidepressants, and antipsychotics.

Statistical Analysis

All analyses were conducted in Stata (StataCorp, College Station, TX). We used Cox and logistic regression models to investigate the association between psychosis groups and subsequent outcomes. For mortality, psychiatric admission, and general hospital admission, we estimated hazard ratios (HRs) and 95% confidence intervals (CIs) using Cox proportional hazards regression models. The proportional hazards assumption was tested using Schoenfeld

residuals in the fully adjusted complete case model and time-varying covariates included where the proportional hazard assumptions were violated. For long-term care admission, only the occurrence (and not the exact timing) of admission was available; therefore, this outcome was analysed using logistic regression, with adjustment for available follow-up time. Odds ratios (ORs) and 95% CIs were estimated for the association between psychosis groups and later care home admission. The analytic sample comprised 11,176 individuals after exclusion of those already residing in care homes at baseline and those with < 6 months of follow-up. In addition to an unadjusted model (Model 1), the following multivariate models were generated. Model 2 was adjusted for demographics, the MMSE score and the dementia subtype. To capture the impact of other mental health difficulties, Model 3 was additionally adjusted for previous mental health diagnoses, HoNOS mental health and functional problems subscales and psychotropic pharmacotherapy. To assess the impact of co-morbid physical health problems in Model 4, Model 2 was additionally adjusted for problematic physical health according to HoNOS and the MedCAT co-morbidity score. A final fully adjusted model (Model 5) included all covariates described above. To assess whether psychotic symptoms due to previous mental health conditions affected the identified relationships, we conducted a sensitivity analysis excluding patients with previous diagnoses of schizophrenia and related disorders, bipolar disorder and depression (ICD-10: F20-29, F30-31, F32-33). Missing data were addressed using multiple imputation by chained equations. As 35% of the analysed sample had missing data on at least one of the covariates, a total of 35 imputed datasets were generated by replacing missing values through simulated values assembled from potential covariates and all outcome values. We judged missingness to be random in this sample and applied Rubin's rules to combine coefficients in final cox regression analyses.

Results

Sample characteristics

The study cohort comprised 21,108 individuals diagnosed with dementia between January 2008 and December 2022. Of these, 7,350 (34.8%) had evidence of psychotic symptoms (hallucinations and/or delusions) around the time of dementia diagnosis. Of the 7,350 experiencing psychosis, 45.7% (n = 3,362) had only hallucinations, 23.4% (n = 1,719) had only delusions, and 30.9% (n = 2,269) had both hallucinations and delusions.

Baseline characteristics

Characteristics at first dementia diagnosis for the full sample and by psychosis group are presented in Table 1. Patients experiencing both delusions and hallucinations (H + D+) were the youngest group, were most likely to live in the most deprived areas and had the highest prevalence of problematic living conditions. The H + D+ group also had the highest proportions of non-Alzheimer's and other/unspecified dementias, previous mental health conditions and additional mental diagnosis and antipsychotic prescribing. The highest proportions of patients from ethnic minority backgrounds and of married patients, as well as the highest mean number of MedCAT comorbidities, were observed in the groups experiencing delusions (H – D+ and H + D+). Groups experiencing hallucinations (H + D– and H + D+) had the lowest MMSE scores, the highest prevalence of impaired activities of daily living, and were most likely to be prescribed memantine and/or antidepressants. Baseline characteristics were broadly similar when psychosis was treated as a binary exposure (Supplementary Table 1), with patients with psychosis showing younger age at diagnosis, greater deprivation, lower MMSE scores, higher levels of functional and psychiatric morbidity, and greater psychotropic prescribing than those without psychosis.

Table 1
Baseline characteristics of the full sample and by psychotic symptom profile

Characteristics	Full Cohort (n = 21,108)	No psychosis (H-D-, n = 13,758)	Hallucinations only (H + D-, n = 3,362)	Delusions only (H-D+, n = 1,719)	Hallucinations and delusions (H + D+, n = 2,269)	P value ^a
Socio-demographic status and cognitive function^b						
Mean age at dementia diagnosis (SD)	81.1(9.0)	81.3 (8.7)	81.1 (9.2)	80.9 (9.1)	79.9 (9.9)	< 0.001
Female sex (%)	60.1%	60.4%	60.1%	59.3%	59.3%	0.480
Ethnicity (%)						< 0.001
White	71.5%	72.4%	71.7%	69.1%	67.7%	
Black	18.5%	17.3%	18.9%	20.5%	23.8%	
Asian	6.5%	6.5%	6.1%	7.5%	6.4%	
Other	3.5%	3.8%	3.3%	3.0%	2.1%	
Married or cohabiting status (%)	66.1%	65.3%	65.5%	68.7%	69.8%	< 0.001
Mean index of deprivation (SD) ^b	24.2 (10.2)	23.8 (10.3)	24.8 (10.1)	24.5 (10.3)	25.5 (9.9)	< 0.001
Mean MMSE score at diagnosis (SD)	17.9 (6.5)	18.1 (6.5)	17.0 (6.7)	18.3 (6.2)	17.2 (6.5)	< 0.001
Subtype of dementia (%)						< 0.001
Alzheimer Disease (AD)	45.0%	49.1%	38.3%	44.3%	31.3%	
Vascular Disease (VD)	17.1%	16.6%	16.8%	18.9%	19.1%	
Mixed (AD + VD)	19.9%	20.0%	20.2%	21.2%	17.2%	
Dementia with Lewy Bodies	3.2%	0.7%	7.6%	1.1%	13.1%	
Other/Unknown	14.8%	13.6%	16.9%	14.5%	19.4%	
Functional diagnoses prior to dementia						
Schizophrenia or other primary psychotic disorders (F20-F29)	2.5%	0.8%	2.0%	6.7%	10.8%	< 0.001
Bipolar affective disorder (F30, F31)	6.2%	5.3%	7.0%	6.6%	10.7%	< 0.001
Depressive episode/disorder (F32, F33)	5.6%	4.8%	6.5%	5.5%	8.7%	< 0.001
HoNOS mental or physical health problems (%)^{b,c}						
Agitated behaviour	18.1%	14.1%	24.0%	19.5%	31.8%	< 0.001
Non-accidental self-injury	1.4%	1.0%	1.8%	1.5%	2.9%	< 0.001
^a one-way ANOVA or chi2 test.						
^b closest to the time of dementia diagnosis.						
^c Health of the Nation Outcome Scale (HoNOS): Each item is rated on a scale from 0 to 4, where 0 indicates no difficulty and 4 indicates a very severe problem. Scores of 0–1 were grouped as “no or minor problems,” while scores of 2–4 were grouped as “clinically significant problems.”						
^d in a window from 6 months before to 6 months after dementia diagnosis.						
^e Physical health conditions identified across the whole patient’s medical records using natural language processing.						
MedCAT =Medical Concept Annotation						
Tool.						

Characteristics	Full Cohort (n = 21,108)	No psychosis (H-D-, n = 13,758)	Hallucinations only (H + D-, n = 3,362)	Delusions only (H-D+, n = 1,719)	Hallucinations and delusions (H + D+, n = 2,269)	P value ^a
Socio-demographic status and cognitive function^b						
Problem-drinking or drug taking	3.2%	3.1%	2.9%	3.2%	4.2%	0.031
Depressed mood	14.2%	12.8%	17.9%	13.7%	17.8%	< 0.001
Physical illness or disability	55.0%	52.2%	63.7%	49.7%	62.5%	< 0.001
HoNOS functional problems (%)^{b,c}						
Activities of daily living	58.8%	56.3%	65.3%	56.1%	65.7%	< 0.001
Living conditions	12.1%	10.9%	13.6%	12.7%	17.0%	< 0.001
Occupational / recreational activities	32.2%	29.2%	36.5%	35.3%	41.5%	< 0.001
Social relationships	14.8%	12.5%	16.2%	18.7%	23.3%	< 0.001
Pharmacotherapy (%)^d						
Acetylcholinesterase inhibitors	35.8%	35.3%	37.4%	34.8%	35.8%	0.021
Memantine	14.3%	12.4%	18.7%	15.2%	18.5%	< 0.001
Antidepressant	28.2%	24.7%	35.6%	28.8%	38.1%	< 0.001
Antipsychotic	12.0%	4.9%	16.7%	17.6%	43.8%	< 0.001
Mean of Number of MedCat comorbidities (SD) ^e	2.7 (2.0)	2.5 (1.9)	2.9 (2.0)	3.3 (2.0)	3.5 (2.3)	< 0.001
^a one-way ANOVA or chi2 test.						
^b closest to the time of dementia diagnosis.						
^c Health of the Nation Outcome Scale (HoNOS): Each item is rated on a scale from 0 to 4, where 0 indicates no difficulty and 4 indicates a very severe problem. Scores of 0–1 were grouped as “no or minor problems,” while scores of 2–4 were grouped as “clinically significant problems.”						
^d in a window from 6 months before to 6 months after dementia diagnosis.						
^e Physical health conditions identified across the whole patient’s medical records using natural language processing.						
MedCAT =Medical Concept Annotation Tool.						

Psychotic symptoms and risk of mortality

Of the whole sample 16,604 (78.6%) died in the follow-up period and the median survival time was 3.9 years after dementia diagnosis (interquartile range (IQR): 1.7-7.0 years). Any psychosis was associated with an increased risk of mortality (see Table 2). This association was most attenuated when adjusting for other functional and mental health difficulties (Model 3) but remained significant in the fully adjusted model. While the H + D- and H + D+ groups were consistently associated with higher mortality across all models, the H-D + was not associated with mortality in either crude or fully adjusted analyses.

Table 2

Risk of mortality, general hospitalisation, and psychiatric hospitalisation associated with any psychosis, hallucinations only, delusions only, and combined hallucinations and delusions, compared with no psychosis (n = 13,758) in Cox proportional hazards models (n = 21,108)

Group	Mortality (HR, 95% CI)					General hospital admission (HR, 95% CI)					Psychiatric hospital admission		
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 1	Model 2	Model 3	Model 4	Model 5	Model 1	Model 2	Model 3
Any psychosis (n = 7,350)	1.11 (1.07–1.15)	1.10 (1.06–1.14)	1.06 (1.02–1.10)	1.09 (1.05–1.13)	1.06 (1.02–1.10)	1.11 (1.08–1.15)	1.09 (1.06–1.13)	1.08 (1.04–1.12)	1.04 (1.01–1.08)	1.05 (1.01–1.08)	3.46 (2.97–4.04)	3.04 (2.60–3.58)	1.77 (1.48–2.11)
Hallucinations only (H + D-, n = 3,362)	1.17 (1.12–1.22)	1.12 (1.08–1.18)	1.09 (1.04–1.14)	1.10 (1.05–1.15)	1.08 (1.03–1.13)	1.14 (1.09–1.19)	1.11 (1.06–1.16)	1.10 (1.05–1.15)	1.06 (1.02–1.11)	1.06 (1.02–1.11)	2.09 (1.68–2.60)	1.88 (1.50–2.35)	1.32 (1.05–1.67)
Delusions only (H + D+, n = 1,719)	0.96 (0.91–1.02)	0.98 (0.92–1.03)	0.96 (0.90–1.02)	1.00 (0.94–1.06)	0.98 (0.92–1.04)	0.97 (0.92–1.02)	0.97 (0.91–1.03)	0.97 (0.91–1.03)	0.94 (0.89–1.00)	0.94 (0.89–1.00)	2.33 (1.79–3.03)	2.30 (1.76–3.00)	1.65 (1.25–2.16)
Hallucinations and delusions (H + D+, n = 2,269)	1.14 (1.09–1.21)	1.17 (1.10–1.23)	1.10 (1.03–1.16)	1.16 (1.09–1.22)	1.10 (1.04–1.17)	1.20 (1.14–1.26)	1.19 (1.13–1.25)	1.18 (1.11–1.25)	1.12 (1.06–1.18)	1.13 (1.06–1.19)	6.60 (5.54–7.88)	5.72 (4.75–6.89)	2.60 (2.09–3.24)
bold = p < 0.05													
Model 1: unadjusted													
Model 2: adjusted for demographics, MMSE score and dementia subtype													
Model 3: Model 2 plus previous mental health diagnoses, HoNOS mental health and functioning subscales, pharmacotherapy													
Model 4: Model 2 plus HoNOS physical illness and disability scale and MedCAT co-morbidity score													
Model 5: fully adjusted													

Psychotic symptoms and general hospital admission

Of the whole sample 17,098 (81.0%) had a general hospital admission in the follow-up period and the median time to first hospital admission was 10.9 months after dementia diagnosis (IQR: 3.3–28.7 months). Any psychosis was associated with an increased risk of general hospital admission (see Table 2). This association was most attenuated when adjusting for physical health problems according to HoNOS and MedCAT co-morbidities (Model 4) but remained significant in the fully adjusted model. Highest risk was observed in the H + D+ groups and remained elevated after full adjustment (Hazard ratio (HR): 1.13, 95% confidence interval (CI): 1.06–1.19). General hospitalisation risk was more modestly increased in the H + D- group (HR: 1.06, 95% CI: 1.02–1.11, after full adjustment), but not in the H-D+ group.

Psychotic symptoms and psychiatric hospital admission

In total 678 (3.2%) had a psychiatric hospital admission in the follow-up period. In those who had a psychiatric admission the median time between dementia diagnosis and admission was 8.6 months (IQR: 2.1–25.3 months). Any psychosis was strongly associated with psychiatric hospitalisation, with the effect most markedly attenuated after adjustment for other functional and mental health difficulties in Model 3 but remaining statistically significant in the fully adjusted model. Across all models, the strongest association with psychiatric admission was observed in the H + D+ group. In crude analyses, this group had a risk of psychiatric admission that was more than six times higher than that of the H-D- group (HR: 6.60, 95% CI 5.54–7.88). Although this association was attenuated after adjustment, the H + D+ had a higher risk of psychiatric hospitalisation (adjusted HR: 2.15, 95% CI: 1.71–2.70) than the H + D- (adjusted HR: 1.28, 95% CI: 1.02–1.61) and the H-D+ (adjusted HR: 1.41, 95% CI: 1.07–1.85) groups.

Psychotic symptoms and long-term care admission

This analysis included a sub cohort of 11,176 individuals who did not reside in a care home at baseline and had at least 6 months of follow-up time. Of those, 4,215 (37.7%) experienced psychosis and 2,189 (19.6%) were admitted to long-term care a median follow-up time (to the end of the observation window) of 2.3 years (IQR: 1.1–4.0 years). Any psychosis was associated with increased odds of long-term care admission (odds ratio (OR): 1.38, 95% CI: 1.25–1.52; see Table 3). However, this association was substantially attenuated after adjustment for functional and other mental health difficulties and was no longer statistically significant in the fully adjusted model (adjusted OR: 1.11, 95% CI: 0.99–1.24, p = 0.071). Similar patterns were observed for the H-D+ group, which was also no longer significantly associated with long-term care admission in the fully adjusted model (adjusted OR: 1.16, 95% CI: 0.98–1.38, p = 0.088). For the H + D- group, significant associations were observed only in Model 1. The strongest association with long-term care admission was seen in the H + D+ group, which remained statistically significant across all models, including the fully adjusted model (adjusted OR: 1.23, 95% CI: 1.04–1.46, p = 0.014).

Table 3
Associations between psychosis symptom groups (any psychosis, hallucinations only, delusions only, and combined hallucinations and delusions) and long-term care admission, compared with no psychosis (n = 6,961) in logistic regression models (total n = 11,176)

Group	Long-term care admission (Odds ratio, 95% confidence interval)				
	Model 1	Model 2	Model 3	Model 4	Model 5
Any psychosis (n = 4,215)	1.38 (1.25–1.52)	1.29 (1.16–1.42)	1.12 (1.00–1.24)	1.27 (1.14–1.40)	1.11 (0.99–1.24)
Hallucinations only (H + D-, n = 1,847)	1.16 (1.01–1.33)	1.07 (0.94–1.23)	1.00 (0.87–1.15)	1.09 (0.95–1.25)	1.02 (0.88–1.17)
Delusions only (H-D+, n = 986)	1.31 (1.11–1.55)	1.33 (1.12–1.57)	1.21 (1.02–1.44)	1.28 (1.08–1.51)	1.16 (0.98–1.38)
Hallucinations and delusions (H + D+, n = 1,382)	1.75 (1.53–2.01)	1.60 (1.38–1.85)	1.26 (1.07–1.49)	1.55 (1.34–1.80)	1.23 (1.04–1.46)
bold = p < 0.05					
Model 1: adjusted for follow-up time available					
Model 2: adjusted for demographics, MMSE score, dementia subtype and follow-up time available					
Model 3: Model 2 plus previous mental health diagnoses, HoNOS mental health and functioning subscales, pharmacotherapy					
Model 4: Model 2 plus HoNOS physical illness and disability score and MedCAT co-morbidity score					
Model 5: fully adjusted					

In sensitivity analyses excluding 1,737 patients with prior mental health conditions (resulting in an analytic sample of 19,371 patients) findings were broadly similar to those of the main analyses (see Supplementary Tables 2 and 3).

Discussion

The aim of this study was to determine whether distinct psychotic symptom profiles in dementia predict important outcomes, such as mortality, psychiatric admission, general hospital admission, and care home admission. A key finding was that combined H + D+ showed the most consistent pattern of adverse outcomes, with increased risks across mortality, psychiatric admission, general hospital admission, and higher odds of care home admission. The H + D- group was associated with more modest increases in mortality, general hospital admission and psychiatric admission. Meanwhile, the H - D+ group showed a more selective pattern: it was consistently associated with psychiatric admission, but not with mortality or general hospital admission, and its association with care home admission was attenuated after adjustment. To our knowledge, this is the first study to investigate different outcomes separately according to hallucinations, delusions, and their co-occurrence in people with dementia, which limits direct comparison with previous studies.

In terms of mortality, hallucinations appeared to have greater prognostic significance than delusions, with increased risk observed in both hallucination groups but not in the H-D+ group. In the fully adjusted model, the highest mortality risk was generally seen in the H + D+ group, although effect sizes were modest. Our findings are broadly consistent with those of Scarmeas et al. (2005), in suggesting that psychosis-related hallucinations were associated with a poorer prognosis than psychosis-related delusions, particularly with regard to mortality. Moreover, given the modest effect sizes observed, our results may still be regarded as compatible with a recent systematic review and meta-analysis that found no statistically significant association between psychotic symptoms and all-cause mortality, with pooled adjusted hazard ratios of 1.06 (95% CI 0.98–1.14) for psychotic symptoms overall, 1.15 (95% CI 0.95–1.39) for hallucinations, and 1.02 (95% CI 0.94–1.11) for delusions[28]. Thus, while hallucinations may be associated with a higher risk of mortality, the extent of this increased risk is likely to be limited.

The causal nature of these limited predictive associations is unknown, but there are several possible explanations. One possible reason is that hallucinations – and, to a lesser extent, delusions[29] – may occur as part of the clinical presentation of delirium, which is itself associated with increased mortality[30–32]. Another potential explanation is that hallucinations, especially visual hallucinations, are more closely linked to Lewy body pathology, including mixed AD and Lewy body co-pathology, which has been associated with greater disease burden, faster progression, and shorter survival[33–35]. In addition, a small proportion of hallucination-related psychosis in dementia may reflect unrecognised frontotemporal lobar degeneration with TAR DNA-binding protein 43 pathology (FTLD-TDP) associated with chromosome 9 open reading frame 72 (C9orf72) hexanucleotide repeat expansion (HRE), a condition often characterised by prominent psychotic symptoms and linked to shorter survival and faster disease progression[36, 37]. By contrast, “delusions only” may reflect a broader and more heterogeneous set of mechanisms, including neurodegenerative, affective, and environmental contributors, and their relationship with cognitive impairment appears to be less specific and less consistently linked to advanced neuropathology than that of hallucinations[38, 39].

The distinction between the mental health model (Model 3) and the physical health model (Model 4) enables an evaluation of the differential impact of covariate adjustment on these associations. As would be expected, mental health attenuates associations with psychiatric admission. For general hospital admission, the attenuation of associations after adjustment for physical comorbidity suggests that the excess hazard among patients with hallucinations may partly reflect greater underlying physical health burden, rather than psychosis alone. These findings may, once again, be partly explained by

superimposed delirium, which is associated with greater acute hospital use, including longer hospital stays and higher readmission rates[40, 41]. Findings are also consistent with broader evidence showing that dementia-related psychosis is associated with greater healthcare costs and service use[42]. At the same time, some previous work has reported lower emergency department utilisation among patients with psychosis and agitation in severe dementia, suggesting that the relationship between neuropsychiatric symptoms and acute care use may vary according to dementia severity, caregiver responses, and symptom context rather than simply symptom presence alone[43].

Overall, psychosis was associated with higher odds of long-term care admission in crude models, but this association was attenuated after adjustment and was no longer statistically significant in the most adjusted models, except in the H + D+ group. In this subgroup, the attenuation of the association after adjustment for pharmacological treatment and broader clinical covariates suggests that the link with long-term care admission may partly reflect greater clinical severity, treatment exposure, functional impairment, and behavioural complexity. Nevertheless, H + D+ remained significantly associated with long-term care admission after adjustment for a broad range of covariates, indicating that this profile may identify a subgroup with a greater likelihood of institutionalisation or psychiatric input after moving to a care home. This pattern differs somewhat from previous findings in an AD cohort, in which hallucinations at any time predicted both mortality and institutionalisation[11]. In our broader dementia cohort, hallucinations alone were associated with mortality but not with long-term care admission after adjustment; instead, the most consistent associations after extensive adjustment were observed among patients with co-occurring hallucinations and delusions. These differences may partly reflect methodological variation, as we examined mutually exclusive psychosis profiles recorded after dementia diagnosis, whereas Scarmeas et al. used broader 'hallucinations, any' and 'delusions, any' categories[11]. In addition, their institutionalisation outcome captured care needs irrespective of actual residence, whereas ours measured an observed transition to a care home after dementia diagnosis.

Finally, the markedly higher use of antipsychotic medication in the H + D+ group may also be relevant to the excess mortality observed in this subgroup[44, 45]. More broadly, psychotropic treatment was substantially more common in patients with psychosis. While this raises the possibility that treatment-related harms may contribute to poorer outcomes, antipsychotic use is also likely to act as a marker of greater symptom severity and clinical complexity[19]. Antipsychotic use was especially common in the H + D+ group, with 43.8% of patients receiving antipsychotics, almost three times the proportion observed in the hallucinations-only and delusions-only groups. This supports the view that co-occurring hallucinations and delusions may identify a more severe and clinically challenging psychosis phenotype. In the H + D+ group, the attenuation in the association with psychiatric admission after adjustment for pharmacological treatment suggests that medication use, particularly antipsychotic prescribing, may partly reflect greater clinical severity and complexity. However, antipsychotic prescribing was not restricted to patients with recorded hallucinations or delusions: 4.9% of patients without recorded psychosis were also prescribed antipsychotics, which may reflect prescribing for other behavioural and psychological symptoms of dementia, such as agitation, aggression, sleep disturbance, or distress, rather than for hallucinations or delusions per se.

Antipsychotic prescribing in older people with dementia without clear psychotic symptoms merits caution, as current guidelines restrict their use to severe distress, agitation, psychosis, or risk of harm, and recent population-based evidence has linked their use to multiple serious adverse outcomes[44, 46]. Acetylcholinesterase inhibitor use was relatively similar across groups, at around one third of patients, with only minor differences according to psychosis status. As these proportions were only slightly higher in groups with more AD and dementia with Lewy bodies, this pattern suggests that these drugs were prescribed mainly according to their established procognitive indications rather than for neuropsychiatric symptoms, including psychosis. Memantine use, however, was somewhat higher in the psychosis groups, especially in those with hallucinations. Although procognitive agents are not standard treatment for neuropsychiatric symptoms in dementia, recent evidence suggests possible benefits beyond cognition, with galantamine showing benefit for overall neuropsychiatric symptoms and memantine for psychotic symptoms[47].

Strengths and limitations

This study has several strengths. First, it draws on one of the largest dementia cohorts in Europe, including over 21,000 people, many of whom had follow-up all the way to death. The size of the dataset provided strong statistical power, making it possible to detect associations across different outcomes and dementia subgroups, and improving the precision of estimates. Second, the use of the CRIS platform allowed us to capture information from routine clinical practice, including people with multiple comorbidities, advanced cognitive impairment, and disadvantaged backgrounds—groups that are often excluded from traditional studies. As a result, the findings may better reflect the challenges faced in real-world care. Another strength lies in the decision to examine hallucinations and delusions separately rather than treating psychosis as a single construct, providing clearer evidence of the heterogeneity of psychosis. To our knowledge, this is the first study to take this approach across most of the outcomes assessed. A further strength is the breadth of outcomes assessed. By examining mortality, psychiatric admission, general hospitalisation, and care home placement, the study provides a multidimensional view of prognosis. The consistency of associations across outcomes strengthens confidence that the results are not simply driven by bias in any single measure. The breadth of covariate adjustment, including sociodemographic, clinical, functional, comorbidity, and treatment-related factors, also strengthens the interpretation of the findings. Finally, the consistency of the results after performing the sensibility analyses represents an additional strength of this study, supporting the robustness of the findings.

However, several limitations should be acknowledged. Diagnoses of psychosis, as well as the distinction between hallucinations and delusions, were based on clinician documentation rather than structured research assessments. In addition, limited clinical context meant that superimposed delirium could not be reliably excluded. Similarly, dementia subtype diagnoses in routine records may be less accurate than those made in specialist research settings, raising the possibility that psychosis prevalence was sometimes misattributed. Further, admission to long-term care was estimated using LSOA-based classification rather than confirmed care home addresses and may therefore have resulted in some misclassification. In addition, both long-term care admission and psychiatric hospital admission were ascertained from CRIS and would not capture admissions occurring outside the SLAM catchment, potentially leading to under-ascertainment of these outcomes, particularly among people with dementia who may relocate to residential care outside the area in later stages of

illness. Lastly, although hallucinations and delusions were analysed as separate symptom profiles, this approach still simplifies a complex phenomenon; differences in phenomenology, modality, severity, frequency, and context may be highly relevant to aetiology, treatment, and prognosis[48].

Conclusion

In conclusion, the prognostic significance of psychosis in dementia was not uniform across symptom profiles. Combined hallucinations and delusions emerged as the phenotype most consistently associated with adverse outcomes, with the strongest associations observed for psychiatric admission and more modest associations for mortality, general hospital admission, and long-term care admission. This suggests that this subgroup is particularly vulnerable from a psychiatric perspective and may therefore require more timely and effective clinical management. The marked attenuation of estimates after adjustment suggests that part of the increased risk may reflect differences in patients’ clinical characteristics and treatment exposure, rather than the effect of psychosis alone. Overall, our findings support the need for more tailored care for patients with psychosis and highlight the importance of integrating psychiatric expertise into dementia services, as well as planning resources capable of meeting the greater acute and long-term care needs of this population.

Abbreviations

- AD
- Alzheimer's disease
- aHR
- adjusted hazard ratio
- aOR
- adjusted odds ratio
- ARC
- Applied Research Collaboration
- BPSD
- behavioural and psychological symptoms of dementia
- C9orf72
- chromosome 9 open reading frame 72
- CRIS
- Clinical Record Interactive Search
- DLB
- dementia with Lewy bodies
- FTLD-TDP
- frontotemporal lobar degeneration with TAR DNA-binding protein 43 pathology
- GATE
- General Architecture for Text Engineering
- H + D+
- hallucinations and delusions present
- H + D–
- hallucinations present, delusions absent
- H – D+
- hallucinations absent, delusions present
- H – D–
- hallucinations and delusions absent (no psychosis)
- HDR UK
- Health Data Research UK
- HES
- Hospital Episode Statistics
- HoNOS
- Health of the Nation Outcome Scales
- HR
- hazard ratio
- HRE
- hexanucleotide repeat expansion
- ICD-10
- International Classification of Diseases, 10th revision
- IMD
- Index of Multiple Deprivation
- IoPPN
- Institute of Psychiatry, Psychology and Neuroscience
- IQR
- interquartile range

LSOA
Lower Layer Super Output Area
MedCAT
Medical Concept Annotation Toolkit
MMSE
Mini-Mental State Examination
NLP
natural language processing
OR
odds ratio
SLaM
South London and Maudsley NHS Foundation Trust
UKRI
UK Research and Innovation
VD
vascular dementia.

Declarations

Ethics approval: CRIS has received ethical approval as an anonymised data resource (Oxford Research Ethics Committee C, reference 23/SC/0257). The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent to participate: CRIS has received ethical approval as an anonymised data resource.

Consent for publication: not applicable.

Availability of data and materials: the datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: the authors declare that they have no competing interests.

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