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Original Research Article

Trajectories of Depressive Symptomatology in Rural Memory Clinic Patients between Baseline Diagnosis and 1-Year Follow-Up

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Key Words

Alzheimer's disease · Dementia · Mild cognitive impairment · Depression · Depressive symptoms · Rural population · Memory clinic

Abstract

Background/Aims: To investigate the prevalence and trajectories of depressive symptomatology at 1-year follow-up, and the severity of depressive symptoms, by dementia diagnostic group, as well as to determine the predictors of depressive symptomatology at 1-year follow-up. ***Methods:*** In rural and remote patients of an interdisciplinary memory clinic between 2004 and 2014, 144 patients diagnosed with no cognitive impairment (NCI), mild cognitive impairment, dementia due to Alzheimer's disease (AD), or non-AD dementia completed the Center for Epidemiologic Studies of Depression Scale to assess depressive symptomatology at both time points. ***Results:*** Among patients with data at both time points, persistence of depressive symptomatology at follow-up occurred in 22.2%, remission in 17.4%, incidence in 13.2%, and absence in 47.2%. The prevalence of depressive symptomatology at baseline and persistence at follow-up were significantly greater in the NCI group than in the other diagnostic groups, but there were no differences in severity. Depressive symptomatology at follow-up was independently associated with depressive symptomatology, lower independence in activities of daily living, and lower self-rating of memory at baseline, as well as with decreased independence in activities of daily living between time points. ***Conclusion:*** Future studies should further examine short-term postdiagnostic trajectories in depressive symptomatology in multiple dementia diagnostic groups to inform prognoses and treatment decisions.

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Introduction

The prevalence of depression varies widely among noninstitutionalized (i.e., community-based) individuals who have diagnoses of either mild cognitive impairment (MCI) or dementia. Among individuals diagnosed with MCI, the prevalence of depression (depressive symptoms, minor and major depression) ranges from 3 to 63% [1–3]; and the prevalence ranges from 20 to 66% among those diagnosed with dementia [2, 4–8]. Differences in study design and methods partly account for the variations observed in depression prevalence [3, 9].

Studies have shown that the prevalence of depression is associated with specific dementia diagnoses. Higher rates of depression have been found in those diagnosed with non-Alzheimer's disease (AD) dementias versus AD dementia; specifically in those diagnosed with vascular dementia [10–13], ischemic vascular disease [14], and dementia with Lewy bodies (DLB) [2, 4, 7]. Moreover, the prevalence of depression was higher in memory clinic patients diagnosed with dementia due to AD compared to those diagnosed with MCI [5]. We previously observed that the prevalence of elevated depressive symptoms (depressive symptomatology) did not differ significantly between memory clinic patients with non-AD dementia versus those with AD dementia (38.2 vs. 27.3%); however, we found a significantly higher prevalence and severity of elevated depressive symptoms in patients with MCI than in those with dementia due to AD and non-AD dementia (51 vs. 23.9%) [15].

A small number of studies have compared depressive symptoms among noninstitutionalized patients with possible dementia at initial diagnosis and at follow-up of 3 months [16], 6 months [11], 1 year [7, 11, 17, 18], and at regular intervals over periods of 2 years or longer [6, 19–22]. Four distinct trajectories in postdiagnostic depressive symptomatology (or in major depression) have been investigated: *persistence* (presence of elevated depressive symptoms at both baseline and follow-up) [7, 11, 17–19, 21], presence at baseline diagnosis followed by *remission* at follow-up [7, 11, 17, 21], absence at baseline followed by *incidence* or emergence at follow-up [7, 17, 18, 21, 22], and *absence* of elevated depressive symptoms at both time points [7, 17].

Few studies, however, have assessed short-term postdiagnostic (<2 year) depressive symptoms in multiple diagnostic groups [7, 11]. Rather, most studies have examined short-term postdiagnostic depressive symptoms in patients with a diagnosis of dementia due to AD [6, 16–18, 20, 22] or in patients with dementia due to different causes, but without diagnostic group comparisons [19, 21]. Moreover, to the best of our knowledge, only one of these studies has included rural or remote (rural/remote) populations in their investigations [21].

It is important to understand trajectories in depressive symptomatology given that elevated depressive symptoms are associated with a higher prevalence and greater severity of behavioral symptoms (e.g., anxiety and diurnal rhythm disturbances) in those diagnosed with AD dementia or MCI [5]. Mild and major depression are also associated with higher levels of impairment in activities of daily living in patients with AD dementia [23]. Moreover, major depression has been found to be an independent risk factor for early long-term care admission within 1 year of diagnosis [11]. Studies suggest that psychosocial interventions (e.g., reminiscence therapy, caregiver strategies) may be more effective than pharmacologic (e.g., antidepressant) and nonpharmacologic therapies (e.g., physical activity) in patients with dementia and concomitant depressive symptoms [2, 9]. Therefore, awareness, timely recognition, and monitoring of depressive symptoms by health care professionals in the short-term period following initial diagnosis may facilitate access to the necessary medical and social supports where they exist, potentially mitigating caregiver stress and delaying institutionalization.

Using a sample of rural and remote individuals with suspected dementia referred to a memory clinic for the assessment and diagnosis of rural and remote patients, the study objec-

tives were (1) to determine whether the prevalence of elevated depressive symptoms and the severity of depressive symptoms, at baseline and at 1-year follow-up, varied within or between diagnostic groups and changed in the interval between baseline and follow-up; (2) to identify the trajectories of depressive symptomatology between baseline and 1-year follow-up (persistence, remission, incidence, and absence) by diagnostic group; and (3) to explore the sociodemographic and clinical predictors of elevated depressive symptoms (persistence and incidence) at 1-year follow-up.

Methods

Study Population and Sample

This study uses data from the Rural and Remote Memory Clinic (RRMC) located in the city of Saskatoon (population 260,600) [24], based on 450 patients enrolled from March 2004 to July 2014 (the clinic's 7th data release). Data collection for the larger RRMC study is ongoing. Patients living more than 100 km from the two census metropolitan areas in the province of Saskatchewan (Saskatoon and Regina) receive referrals to the clinic from their primary health care provider and attend an in-person clinic day evaluation, with their caregiver(s), by a clinical team of a neurologist, physical therapist, and dietitian, as well as by a neuropsychology team. At clinic day evaluation (hereafter known as baseline), patients have an interdisciplinary interview and complete a questionnaire consisting of sociodemographic and clinical measures; further, collateral informants are interviewed and complete standardized clinical measures. In addition, patients complete a standardized neuropsychological battery, physical therapy assessment, a CT head scan, blood work, and a neurological examination. Follow-up assessments are conducted by the neurologist and take place via telehealth at 6 weeks, 12 weeks, and 6 months. Subsequent follow-up assessments are conducted in person by the full clinical team 1 year after baseline (hereafter known as 1-year follow-up), and the subsequent follow-up is based on clinical need. Further details can be found in Morgan et al. [25, 26].

Of 450 patients enrolled between March 2004 and July 2014, 371 completed a baseline questionnaire. A total of 144 patients completed the 20-item Center for Epidemiologic Studies of Depression Scale (CES-D) at both baseline and 1-year follow-up (fig. 1) and were included in the sample for the present study. A total of 201 noncompleters included patients who completed a baseline questionnaire and had been enrolled in the study for 1 year, but were excluded from the study sample given that they completed fewer than 19 CES-D items at baseline (n = 41) or at the 1-year follow-up (n = 5), or had incomplete or missing 1-year follow-up data (n = 155) due to reasons that included moving to another province or nursing home, quitting the study, or death.

The 144 patients in the present study were separated into four groups for this analysis: no cognitive impairment (NCI; n = 28), MCI (n = 40), dementia due to AD (n = 45), and non-AD dementia (n = 31). Of the 40 patients in the MCI diagnostic group, 16 were diagnosed with MCI amnestic (single or multiple domain), 15 with MCI nonamnestic (single or multiple domain) or vascular cognitive impairment, and 9 with MCI not specified. Of the 31 patients included in the non-AD dementia diagnostic group, 13 were diagnosed with frontotemporal dementia, 5 with DLB, 7 with vascular dementia, 2 with dementia due to multiple etiologies, 2 with Parkinson's disease dementia, 1 with dementia not otherwise specified, and 1 with Huntington's disease dementia.

Ethical Considerations

Ethical approval for the larger ongoing RRMC study was received from the University of Saskatchewan Behavioural Research Ethics Board. Written informed consent was

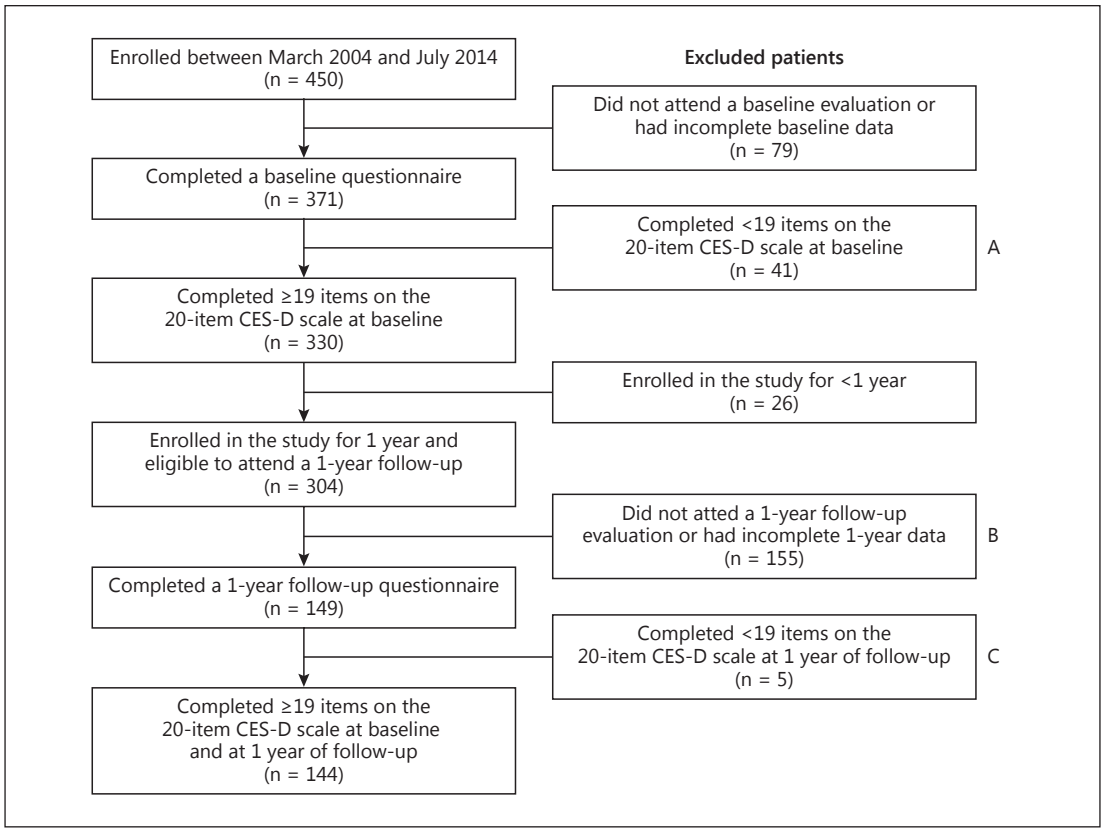

Fig. 1. Flow chart of patients included in the study sample. Note: A + B + C = 201 (noncompleters).

provided by patients and caregivers to allow their clinical data to be used for research. Caregiver informants also provided proxy consent for patients in the event of diminished patient capacity.

Measures

During the clinic day and follow-up evaluations, caregivers and/or RRMC clinic staff assist patients to complete the questionnaires containing clinical and sociodemographic measures. For instance, caregivers assist to ensure that reverse-scored items are properly understood. The RRMC neuropsychology team also checks for likely errors in reverse-scored items and revisits errors with patients and caregivers.

Sociodemographic measures consisted of age, gender, education (years), marital status, and living alone (vs. not living alone). Clinical measures included total number of current chronic conditions, Quality of Life-Alzheimer's Disease (QOL-AD), instrumental activities of daily living (IADL), self-rating of memory scale (SRMS), and Modified Mini-Mental State (3MS) examination.

The self-rated QOL-AD consists of 13 items scored on a 4-point scale from 1 (poor), 2 (fair), 3 (good), to 4 (excellent). Total QOL scores range from 13 to 52, with higher scores suggesting higher current patient QOL [27]. The self-rated IADL scale contains 9 items, each scored 1 (total dependence), 2 (some assistance required), or 3 (total independence) [28]. Total IADL scores range from 9 to 27, with higher scores indicating greater independent functioning on daily activities. The SRMS [29] assesses current memory ability versus memory

ability 4 years previously. Higher SRMS scores suggest greater current memory ability, with total scores ranging from –30 to +30 based on 15 items rated on a 5-point scale from –2 to +2. Total scores on the 3MS examination range from 0 to 100 based on 15 questions. Lower 3MS scores indicate greater cognitive impairment [30]. Where a patient's scale was missing less than 25% of the items in the QOL, IADL, or SRMS scale, the case mean was imputed for those missing items; the scale for that patient was discarded where a patient's scale was missing 25% or more of the items [31, 32].

The 20-item CES-D [33, 34] was used to assess depressive symptoms, the outcome measure for the current study. The CES-D measures the frequency and severity of depressive symptoms experienced during the previous week and may be used to identify depressive symptoms in older adults and individuals with AD dementia [3, 4]. Depression in AD dementia may be assessed with other instruments as well; because the diagnostic criteria for depression and dementia are not fully independent, there is no scientific agreement on the most valid instrument to measure depression in AD dementia [23]. Four dimensions of symptoms are measured with the CES-D: depressed affect, lack of positive affect, somatic complaints, and interpersonal difficulties. Scores from 0 (rarely or none of the time) to 3 (most or all of the time) are assigned to negatively worded items, and reverse scoring is applied to positively worded items. Higher scores on a scale of 0–60 indicate higher levels of depressive symptomatology. A score of '0' was applied to one missing item, and the entire scale was discarded for that patient if 2 or more items were missing [34]. Elevated depressive symptoms (depressive symptomatology) were considered to be present for scores of ≥16, as in previous studies of older adults [35, 36]. This cut point may be used to identify those at high risk for major depressive disorder [37]. *Persistence* of elevated depressive symptoms was defined as CES-D ≥16 at both baseline and 1-year follow-up; *remission* as CES-D ≥16 at baseline and <16 at 1-year follow-up; *incidence* as CES-D <16 at baseline and ≥16 at 1-year follow-up; and *absence* as CES-D <16 at both baseline and 1-year follow-up. Internal consistency reliability for the CES-D was indicated by a Cronbach's α of 0.84 at baseline and 0.86 at 1-year follow-up.

Statistical Analyses

Statistical analyses employed SPSS version 23.0. Sociodemographic and clinical characteristics of the sample were assessed with frequencies and means, with characteristics of completers and noncompleters assessed separately.

The frequency and severity of depressive symptoms (median, mean) were compared across the four diagnostic groups and between pairs of diagnostic groups. Differences were compared for significance within each diagnostic group (e.g., MCI), between each pair of groups (e.g., MCI vs. AD), and across the four groups using the χ^2 test or Fisher's exact test for nominal variables, Cohen's d effect sizes [38] (small, $0.20 \leq d < 0.50$; medium, $0.50 \leq d < 0.80$; large, $d \geq 0.80$), and where appropriate, the independent samples t test, Mann-Whitney U test, or Kruskal-Wallis H test for interval variables.

Within each diagnostic group and within each trajectory group (e.g., persistence), the paired sample t test was used to evaluate the significance of change in the mean CES-D score between baseline and 1-year follow-up. For each pair of diagnostic groups, the Mann-Whitney U test was used to evaluate the significance of change in the mean CES-D score between baseline and 1-year follow-up.

The unadjusted odds ratios (OR) of elevated depressive symptoms (CES-D ≥16) at 1-year follow-up are reported for each independent variable. Based on bivariate analyses, independent variables with a p value <0.25 were selected for inclusion in the final multiple logistic regression analysis [39]. All independent variables associated at the bivariate level ($p < 0.25$) with elevated depressive symptoms at 1-year follow-up were assessed for multicollinearity. Highly collinear variables (variance inflation factor >2.0) were excluded from the multiple

Table 1. Baseline sociodemographic and clinical characteristics of completers and noncompleters of the CES-D at 1-year follow-up

	Completers (n = 144)	Noncompleters (n = 201)	p value[a]
Female, n	81 (56.3) [144]	201 (58.7) [201]	0.660
Age, years	69.7±10.3 [144]	71.3±12.6 [199]	0.190
Education, years	11.4±2.8 [136]	10.7±3.3 [189]	0.049
Married, n	113 (81.3) [139]	129 (64.8) [199]	0.001
Living alone, n	20 (14.4) [139]	43 (21.6) [199]	0.118
Chronic conditions, n	3.9±1.4 [144]	3.9±1.6 [201]	0.791
QOL-AD score	36.1±5.4 [134]	34.4±6.4 [166]	0.016
IADL score	23.6±3.9 [137]	21.6±5.2 [182]	<0.001
SRMS score	–11.6±7.5 [134]	–11.7±8.8 [165]	0.988
3MS score	82.6±12.9 [140]	74.4±17.6 [174]	<0.001
CES-D ≥16	57 (39.6) [144]	64 (40) [160]	0.941
CES-D score	13.6±8.8 [144]	15.4±10.8 [160]	0.119

Values denote means ± SD unless otherwise specified. Figures in parentheses are percentages, and data given in brackets indicate the total sample size. [a] Calculated by the χ^2 test for nominal variables and the independent samples t test for interval variables.

logistic regression analysis [40]. Although the 3 independent variables based on the CES-D measure demonstrated variance inflation factors >2.0, CES-D ≥16 at baseline was retained because it produced the best fitting final model of the 3 variables. Age was also included as a possible confounder.

Results

Sociodemographic and Clinical Characteristics

Compared to noncompleters of the CES-D at both time points, completers were more likely to be married (p = 0.001) and have higher levels of education (p = 0.049), QOL (p = 0.016), independence in activities of daily living (p < 0.001), and cognitive function (p < 0.001) at baseline (table 1). Overall, the two groups were not significantly different on baseline prevalence of depressive symptomatology (p = 0.941) or severity of depressive symptoms (p = 0.119). Within the NCI group, depressive symptoms were significantly more severe among noncompleters than among completers (22.0 ± 11.6 and 15.5 ± 8.6; p = 0.012); however, the prevalence did not differ significantly. Prevalence and severity did not significantly differ between completers and noncompleters within the other three diagnostic groups. Overall, individuals whose functioning was more impaired, in terms of both cognition and independence in daily activities, were less likely to complete the CES-D at both time points.

Approximately 38% of the sample with valid baseline data reported that they were using at least one antidepressant medication at baseline (n = 47/121). Of these patients, 46.8% reported elevated depressive symptoms at baseline, compared to 35.1% of those using no antidepressant medications (p = 0.201).

As shown in table 2, the majority of the sample was female, married, and lived with others. The patients were an average of 69.7 years of age (SD 10.3, range 42–89) and had an average of 11.4 years of education (SD 2.8, range 5–18). Patients in the AD group were oldest, and patients in the NCI group were youngest, on average (p < 0.005). The highest level of

Table 2. Baseline sociodemographic and clinical characteristics of RRMC patients, by diagnostic group

	Total (n = 144)	NCI (n = 28)	MCI (n = 40)	AD (n = 45)	Non-AD (n = 31)	p value[a]
Female, n	81 (56.3) [144]	16 (57.1) [28]	27 (67.5) [40]	27 (60.0) [45]	11 (35.5) [31]	0.051
Age, years	69.7±10.3 [144]	64.5±10.2 [28]	68.9±11.1 [40]	73.9±8.3 [45]	69.3±9.9 [31]	0.005
Education, years	11.4±2.8 [136]	12.6±3.3 [27]	11.0±2.7 [39]	10.9±2.6 [44]	11.5±2.4 [26]	0.122
Married, n	113 (81.3) [139]	23 (88.5) [26]	30 (76.9) [39]	33 (75.0) [44]	27 (90.0) [30]	0.260
Living alone, n	20 (14.4) [139]	3 (11.1) [27]	6 (15.4) [39]	9 (20.9) [43]	2 (6.7) [30]	0.360
Chronic conditions, n	3.9±1.4 [144]	3.9±1.5 [28]	3.9±1.4 [40]	3.8±1.4 [45]	4.2±1.4 [31]	0.539
QOL-AD score	36.1±5.4 [134]	34.9±5.2 [27]	37.1±4.9 [36]	36.8±4.9 [42]	35.0±6.4 [29]	0.121
IADL score	23.6±3.9 [137]	25.0±2.2 [27]	25.1±2.3 [38]	23.1±4.3 [42]	21.2±5.0 [30]	0.001
SRMS score	–11.6±7.5 [134]	–12.0±10.9 [26]	–12.1±5.4 [37]	–11.7±6.6 [43]	–10.6±7.6 [28]	0.653
3MS score	82.6±12.9 [140]	92.0±10.6 [28]	87.7±6.3 [39]	71.7±13.0 [43]	82.7±10.2 [30]	<0.001

Values denote means ± SD unless otherwise specified. Figures in parentheses are percentages, and data given in brackets indicate the total sample size. Sample sizes vary due to missing values. [a] Calculated by the χ^2 test for nominal variables and the Kruskal-Wallis H test for interval variables.

Table 3. Prevalence of elevated depressive symptoms (CES-D ≥16) and the severity of depressive symptoms in RRMC patients at baseline and 1-year follow-up, by diagnostic group at baseline

	Total (n = 144)	NCI (n = 28)	MCI (n = 40)	AD (n = 45)	Non-AD (n = 31)	p value[a]
Baseline						
Elevated depressive symptoms	57 (39.6%)	16 (57.1%)	17 (42.5%)	15 (33.3%)	9 (29.0%)	0.115[b]
Median CES-D score	13.0	16.5	14.5	10.0	10.0	
Mean CES-D score ± SD (range)	13.6±8.8 (0–38)	15.5±8.6 (0–33)	14.3±8.0 (1–30)	12.4±9.8 (0–38)	12.6±8.4 (0–31)	0.290[c]
1-year follow-up						
Elevated depressive symptoms	51 (35.4%)	12 (42.9%)	14 (35.0%)	11 (24.4%)	14 (45.2%)	0.227[d]
Median CES-D score	12.0	13.0	12.5	12.0	14.0	
Mean CES-D score ± SD (range)	13.5±9.1 (0–46)	14.5±9.7 (0–35)	12.8±8.0 (0–31)	12.6±9.3 (0–34)	14.9±9.9 (0–46)	0.639[c]
Mean CES-D score Δ[e] ± SD (range)	–0.1±9.2 (–25 to 31)	–1.1±7.5 (–16 to 15)	–1.5±10.3 (–25 to 15)	0.1±9.5 (–20 to 19)	2.3±8.7 (–18 to 31)	0.452[c, f]

[a] Across the 4 groups, calculated by the χ^2 test for nominal variables and the Kruskal-Wallis H test for interval variables. [b] Calculated by the x^2 test and Cohen's d within each pair of groups. [c] Calculated by the Mann-Whitney U test and Cohen's d within each pair of groups. [d] Calculated by the χ^2 test and Cohen's d between baseline and 1-year follow-up within each group, and within each pair of groups. [e] CES-D score at 1 year – CES-D score at baseline. [f] Calculated by the paired sample t test between baseline and 1-year follow-up within each group.

independent functioning on daily activities was found in the NCI and MCI groups, and the lowest level was observed in the non-AD group (p = 0.001). The NCI group had the lowest degree of cognitive impairment, and the AD group had the highest degree of cognitive impairment (p < 0.001).

Prevalence of Elevated Depressive Symptoms and Severity of Depressive Symptoms at Baseline and 1-Year Follow-Up

Table 3 shows that the prevalence of elevated depressive symptoms in the total sample was 39.6% at baseline and 35.4% at 1-year follow-up. At baseline, elevated depressive symptoms were significantly more prevalent in the NCI than in the AD (p = 0.045; d = 0.482) and non-AD groups (p = 0.029; d = 0.593). At 1-year follow-up, significant differences in the prevalence of elevated depressive symptoms between diagnostic groups were not apparent; however, the difference between the non-AD and AD groups approached significance (p = 0.059; d = 0.444). The severity of depressive symptoms did not vary significantly between diagnostic groups at either baseline or 1-year follow-up.

Table 4. Trajectories of elevated depressive symptoms (CES-D ≥16) between baseline and 1-year follow-up in RRMC patients, by diagnostic group at baseline

	Total (n = 144)				NCI (n = 28)	MCI (n = 40)	AD (n = 45)	Non-AD (n = 31)	p value[b]
	n	mean baseline CES-D score	mean 1-year CES-D score	p value[a]					
Persistence	32 (22.2)	23.9±6.0	23.8±6.6	0.982	11 (39.3)	7 (17.5)	6 (13.3)	8 (25.8)	0.057
Remission	25 (17.4)	21.0±4.3	8.1±4.5	<0.001	5 (17.9)	10 (25.0)	9 (20.0)	1 (3.2)	0.104
Incidence	19 (13.2)	11.2±3.8	22.6±7.3	<0.001	1 (3.6)	7 (17.5)	5 (11.1)	6 (19.4)	0.250
Absence	68 (47.2)	6.7±4.2	8.1±4.6	0.037	11 (39.3)	16 (40.0)	25 (55.6)	16 (51.6)	0.386

Figures in parentheses are percentages. [a] Calculated by the paired samples t test between baseline and 1-year follow-up. [b] Calculated by the χ^2 test across the 4 groups, and by the χ^2 test (or Fisher's exact test) and Cohen's d within each pair of groups.

Change in Depressive Symptoms between Baseline and 1-Year Follow-Up

Table 3 also shows that elevated depressive symptoms may have been more prevalent at baseline than at 1-year follow-up within all but one diagnostic group (non-AD group); however, these differences were not significant ($p > 0.05$). In addition, the mean CES-D score may have decreased between baseline and 1-year follow-up within the NCI and MCI groups, and increased in the AD and non-AD groups; however, these differences were nonsignificant ($p > 0.05$). Significant differences between diagnostic groups also did not emerge in the change in mean CES-D score between baseline and 1-year follow-up either.

Trajectories of Depressive Symptomatology between Baseline and 1-Year Follow-Up

Between baseline and 1-year follow-up, elevated depressive symptoms persisted in 22.2% of all patients with data at both time points, were in remission in 17.4%, incident in 13.2%, and absent in 47.2% (table 4). The proportion of patients with persistent elevated symptoms was significantly higher in the NCI than in the MCI ($p = 0.045$; $d = 0.501$) and AD groups ($p = 0.011$; $d = 0.626$). The proportion of patients with elevated symptoms in remission was significantly lower in the non-AD than in the MCI ($p = 0.018$; $d = 0.625$) and AD groups ($p = 0.041$; $d = 0.503$). The proportion of patients with incident and absent elevated depressive symptoms did not significantly differ between diagnostic groups.

Unadjusted and Adjusted OR of Elevated Depressive Symptoms at 1-Year Follow-Up

As shown in the unadjusted OR presented in table 5, elevated depressive symptoms at 1-year follow-up were significantly associated ($p < 0.25$) with elevated depressive symptoms at baseline, a higher CES-D score at baseline, an increased CES-D score in the interval between baseline and 1-year follow-up, a lower QOL at baseline, a decreased QOL between baseline and 1-year follow-up, a lower independence in IADL at baseline, a decreased independence in IADL between baseline and 1-year follow-up, and a lower self-rated memory at baseline. Elevated depressive symptoms at 1-year follow-up did not differ significantly ($p < 0.05$) by diagnostic group.

In the final multivariable model (table 6), significant independent associations with elevated depressive symptoms at 1-year follow-up were preserved for elevated depressive symptoms at baseline ($p < 0.001$), lower SRMS at baseline ($p = 0.033$), lower independence in IADL at baseline ($p = 0.03$), and decreased independence in self-rated IADL between baseline and 1-year follow-up ($p = 0.003$).

Table 5. Unadjusted OR of elevated depressive symptoms (CES-D ≥16) at 1-year follow-up

	Sample size (n = 144)	Elevated depressive symptoms (CES-D ≥16)[a]	Unadjusted OR (95% CI)	p value
Male, n (%)	63	24 (38.1)	1.23 (0.62–2.45)	0.554
Female, n (%)	81	27 (33.3)	1.00	
Age, years	144	68.5±10.6	0.98 (0.95–1.02)	0.294
CES-D ≥16 at baseline, n (%)	57	32 (56.1)	4.58 (2.21–9.50)	<0.001
CES-D <16 at baseline, n (%)	87	19 (21.8)	1.00	
CES-D score at baseline	144	19.1±8.1	1.14 (1.08–1.20)	<0.001
CES-D Δ score between baseline and 1-year follow-up	144	4.3±9.4	1.10 (1.05–1.15)	<0.001
QOL-AD score at baseline	134	33.7±4.7	0.87 (0.80–0.94)	<0.001
QOL-AD Δ score between baseline and 1-year follow-up	132	–2.4±5.1	0.87 (0.80–0.94)	0.001
IADL score at baseline	137	22.9±4.4	0.93 (0.85–1.02)	0.115
IADL Δ score between baseline and 1-year follow-up	124	–1.1±3.2	0.91 (0.81–1.03)	0.124
SRMS score at baseline	134	–14.7±6.1	0.90 (0.85–0.96)	0.001
SRMS Δ score between baseline and 1-year follow-up	133	3.3±8.9	0.98 (0.95–1.02)	0.428
3MS score at baseline	140	83.3±13.2	1.01 (0.98–1.04)	0.593
3MS Δ score between baseline and 1-year follow-up	116	–1.2±5.4	1.01 (0.96–1.07)	0.614
Diagnosis at baseline, n (%)				
NCI	28	12 (42.9)	1.00	
AD	31	14 (45.2)	1.10 (0.39–3.08)	0.859
MCI	40	14 (35.0)	0.718 (0.27–1.93)	0.512
Non-AD	45	11 (24.4)	0.431 (0.16–1.19)	0.103

Values denote means ± SD unless otherwise specified. Sample sizes vary due to missing values. [a] n = 51 patients with persistent or incident elevated depressive symptoms.

Table 6. Adjusted OR of elevated depressive symptoms (CES-D ≥16) at 1-year follow-up (n = 115)[a]

	B	SE	Wald	OR	95% CI	p value
Age	–0.02	0.03	0.33	0.99	0.94–1.04	0.569
CES-D ≥16 at baseline	0.14	0.04	13.38	1.15	1.07–1.24	<0.001
QOL-AD score at baseline	–0.02	0.06	0.14	0.98	0.88–1.09	0.705
IADL score at baseline	–0.19	0.09	4.69	0.87	0.70–0.98	0.030
IADL Δ score between baseline and 1-year follow-up	–0.25	0.09	8.80	0.78	0.66–0.92	0.003
SRMS score at baseline	–0.10	0.05	4.54	0.90	0.83–0.99	0.033

[a] Twenty-nine missing cases. Hosmer and Lemeshow: $\chi^2 = 6.29$, p = 0.615, c statistic = 0.855.

Discussion

Four key findings emerged from the present study of depressive symptoms in rural and remote individuals referred to a memory clinic for dementia assessment and diagnosis.

Prevalence of Elevated Depressive Symptoms and Severity of Depressive Symptoms at Baseline and 1-Year Follow-Up

First, the prevalence of depressive symptomatology at baseline was significantly greater in the NCI group than in the other diagnostic groups (AD and non-AD); however, the prevalence did not vary by diagnostic group at 1-year follow-up. The overall prevalence was 39.6% at baseline and 35.4% at follow-up. Moreover, the diagnostic group was not associated with

the severity of depressive symptoms at either baseline or 1-year follow-up. To the best of our knowledge, comparable data on variations in the severity of depressive symptoms by diagnostic group, at multiple time points, have not been reported in previous studies.

The baseline prevalence of elevated depressive symptoms in non-AD (29%) and AD dementia patients (33.3%) was within the range of baseline depression prevalence reported in 7 longitudinal studies of noninstitutionalized patients with dementia (20.5–69%) [7, 11, 19, 21] and AD dementia (40–53%) [6, 17, 18], which used 6 different instruments to assess depressive symptomatology. Our results indicated that baseline prevalence was not significantly different between the AD and non-AD dementia groups. In contrast, the first of 2 previous longitudinal studies of multiple diagnostic groups found the baseline prevalence of major depression to be significantly higher in a non-AD than in an AD dementia group [11], whereas the second study did not report on the significance of group differences at baseline [7]. Our findings also showed that the baseline prevalence of elevated depressive symptoms was significantly higher in the NCI group (57.1%) than in the AD and non-AD groups. Other studies showed similarly high levels of depressive symptomatology ranging from 32 to 56.8% [41–43] in memory clinic patients who presented without evidence of objective cognitive impairment.

Our findings and those of previous studies suggest that depressive symptomatology is not uncommon in patients seen in memory clinics [17–19, 44–46]. In a retrospective study of over 1,400 patients referred to 12 memory or outpatient clinics across Norway, Knapskog et al. [46] found depression in 50% of all patients. Since memory clinics specialize in early diagnosis and treatment of memory and other cognitive disorders, including dementia [44, 47], it is to be expected that the scope of medical conditions seen in memory clinics will be wide [45]. Thus, Hejl et al. [48] found that 29% of the first 1,000 patients referred to a Danish neurology-based memory clinic lacked evidence of objective cognitive impairment, with depression being the most common of numerous reversible conditions seen in the clinic. Such patients are seen in memory clinics due partly to 'dementia worry', i.e., that they may have or may develop dementia [43]. Requiring medical referral should minimize the number of patients without evidence of objective cognitive impairment in memory clinics. However, physicians face considerable challenges in diagnosing individuals with complex or atypical presentation [49], particularly in rural communities with reduced access to specialists and dementia-specific continuing education [50]. Memory clinics such as ours, which is the only memory clinic in a province of more than 1 million population and serves only rural and remote individuals, has strong diagnostic capabilities and may therefore expect to see a wide range of conditions responsible for cognitive symptoms that are not exclusive to MCI or dementia.

Change in Depressive Symptoms between Baseline and 1-Year Follow-Up

Second, our results indicated that the prevalence of elevated depressive symptoms and the severity of depressive symptoms at baseline and 1-year follow-up did not significantly differ within or between any of the diagnostic groups. Several other community-based studies also found prevalence to be relatively steady at 1-year follow-up [6, 7, 19]. Our finding is in line with the results from the only available study that reported change in depression severity between baseline and follow-up in different diagnostic groups of noninstitutionalized patients with dementia [7], showing no significant diagnostic group differences (AD vs. DLB) in average change in depression severity between baseline and 1-year follow-up. In a study of memory clinic patients with dementia, depression severity decreased between baseline and 1-year follow-up and remained consistently low at 2-year follow-up [19]. Furthermore, Mormont et al. [16] found that the severity of depressive symptoms in noninstitutionalized patients who received a diagnosis of mild or moderate AD dementia did not significantly increase or decrease by 3-month follow-up. Evidence suggests this trend continues in the long

term, as Zahodne et al. [51] found that the severity of depressive symptoms in noninstitutionalized patients with AD dementia did not significantly vary over a 5.5-year follow-up period. Taken together, these findings suggest that depressive symptoms may not become more severe in the year following diagnosis, regardless of the dementia diagnostic group, and that patients may expect a consistent level of depressive symptomatology over the disease course.

Trajectories of Depressive Symptomatology between Baseline and 1-Year Follow-Up

Third, in patients with data at both time points, persistent and incident depressive symptomatology at 1-year follow-up occurred in more than one third of patients overall (22.2 and 13.2%, respectively). The relatively low incidence at follow-up compared to the prevalence at baseline (39.6%) suggests that depressive symptomatology may be more likely to present at diagnosis than in the postdiagnostic period.

Persistent depressive symptomatology occurred in 56.1% (n = 32/57) of patients with elevated depressive symptoms at baseline. Previous community-based studies have reported similar findings, with persistence at 1-year occurring in 39–68.1% of patients with dementia who were also diagnosed with depression at baseline [7, 17, 18]. Persistence was significantly higher in the NCI than in the MCI or AD dementia group in the present study. Persistence did not vary between the AD and non-AD dementia groups, consistent with a previous study, which found that persistent depression did not significantly vary between AD and DLB groups [7]. Possibly, depressive symptomatology is an outcome of awareness of memory dysfunction or insight into the implications of memory impairment [17, 46, 52]. Studies have shown that depressive symptoms decrease with cognitive decline (as assessed with an objective measure such as the Mini-Mental State Examination) [19–21]. Therefore, our finding that persistence was significantly more prevalent in the NCI than in the AD dementia group prompts several possible explanations. One possibility is that the absence of an expected diagnosis of dementia or MCI at baseline led to ongoing depressive symptomatology in NCI patients. These patients may be in a pre-MCI stage 'when the patient knows, but presently the doctor doesn't know' that lasts an average of 15 years before the patient is identified with MCI and eventually AD dementia [53, p. S98]. Another possibility is that NCI patients retain their ability to express negative emotion with time, whereas MCI and AD dementia patients tend to lose this capacity with disease progression [20]. Also, NCI patients possibly remain aware of their subjective memory limitations for a longer period of time than MCI and AD dementia patients [54], causing depressive symptomatology to persist to a greater degree in NCI than in MCI and AD patients.

The incidence of depressive symptomatology occurred in 21.8% (n = 19/87) of patients without elevated depressive symptoms at 1-year follow-up in the present study. This finding is consistent with previous studies of noninstitutionalized patients that found incident depression at 1-year follow-up in 20–23% of patients with dementia diagnosed with no depression at baseline [7, 17, 18]. Significant diagnostic group variations were not apparent in incident depressive symptomatology, a finding consistent with Fritze et al. [7].

Remission of depressive symptomatology in the present study took place in 43.9% (n = 25/57) of patients with elevated depressive symptoms at baseline. This finding is consistent with previous studies that found remission at 1-year follow-up in 32–61% of noninstitutionalized patients with dementia diagnosed with depression at baseline [7, 17, 18]. In the present study, remission was significantly more prevalent in the AD dementia and MCI groups than in the non-AD group; however, this finding is limited by the small cell size of the remission non-AD group (n = 1). In comparison, Fritze et al. [7] found no significant differences in remission between the AD and DLB groups.

More than three quarters of patients without elevated depressive symptoms at baseline experienced an absence of depressive symptomatology at 1-year follow-up (78.2%; n =

68/87). This finding is consistent with previous studies that reported an absence of depression at 1-year follow-up in 77–80% of noninstitutionalized patients with dementia diagnosed with no depression at baseline [7, 17]. Absence of depressive symptomatology did not significantly vary between diagnostic groups, consistent with Fritze et al. [7].

Adjusted OR of Elevated Depressive Symptoms at 1-Year Follow-Up

Fourth, depressive symptomatology at 1-year follow-up (i.e., persistence and incidence) was independently associated with the presence of depressive symptomatology at baseline, confirming a similar finding in noninstitutionalized patients with dementia at 2-year follow-up [21]. Our findings also showed that persistence and incidence were significantly independently related to a lower subjective rating of memory (SRMS score) at baseline. This finding points to a possible bidirectional relationship between subjective memory status and depressive symptomatology. Incidence at 1-year follow-up may reflect a delayed emotional reaction to lower self-rated memory. At the same time, persistence may indicate that depression tends to accompany subjective memory complaints, and, in some patients, causes lower self-assessment of memory at initial diagnosis. Lower self-assessment of memory in these patients may be due to an underestimation of memory capabilities as a result of elevated depressive symptoms [55], or lower self-assessment of memory may lead to overreporting of depressive symptoms. Studies suggest that conditions other than the onset of AD dementia, such as depressive symptomatology, lead to subjective memory impairment [45, 53]. For instance, Lehrner et al. [42] found that memory clinic patients with depressive symptomatology were significantly more likely to report subjective memory complaints than controls, regardless of objective cognitive status.

The baseline score on the objective measure of cognitive impairment included in the present study (3MS examination), and the change in this measure, were not found to be independently associated with depressive symptomatology at 1-year follow-up. Other studies found that depressive symptoms decreased with increased cognitive impairment (as assessed with an objective measure such as the Mini-Mental State Examination) [19–21]. However, our findings are in line with a previous study, which showed that the cognitive status as measured by the 3MS was not a risk factor for depressive symptoms at 1-year follow-up [6]. Our finding may be partly attributable to the short interval between baseline and follow-up in the present study, as Aalten et al. [19, p. 528] notes that '…there may be a shift from self-reported psychological symptoms towards symptoms that are assessed by observation of overt behaviour' as dementia progresses.

Our finding of an independent association between lower independence in daily activities at baseline and depressive symptomatology at 1-year follow-up supports previous findings of a positive association between functional dependence and depressive symptomatology in noninstitutionalized patients with AD dementia at 1-year follow-up [17]. Other studies have found similar associations several years after baseline in patients with AD dementia [6, 51]. Zahodne et al. [51] suggests that a bidirectional relationship exists between depressive symptoms and functional abilities in patients with AD dementia: a decline in functioning abilities triggers depressive symptoms, and depressive symptoms predict a subsequent decline in functional abilities. Our findings provide further evidence that a decline in functional abilities in noninstitutionalized patients over a 1-year period may cause depressive symptomatology to persist and emerge, independent of the dementia diagnostic group and the changes in cognitive functioning.

Limitations

The small sample size of the diagnostic groups may have limited the statistical power of this study to identify genuinely true effects, increasing the chance of false negatives [56]. Also,

the study sample of memory clinic patients may not be representative of community-based individuals assessed for dementia given that individuals with suspected cognitive impairment plus depressive symptoms may be more likely to be referred to a memory clinic than individuals with suspected cognitive impairment alone. Moreover, patients with less impairment in functional abilities and cognition at baseline were more likely to complete the CES-D at both time points, as were NCI patients with lower depressive symptom severity at baseline. Thus, our findings may be biased toward patients with a higher cognitive status and functional abilities, consequently overestimating depressive symptomatology, and toward NCI patients with a lower severity of depressive symptoms. It is also possible that patients without persistent and incident depressive symptomatology were more likely to participate in the follow-up than patients with depressive symptomatology. If so, the findings of the present study may represent an overestimate of remission and absence and an underestimate of persistence and incidence. The use of antidepressant medication may also have resulted in an underestimation of the baseline prevalence of depressive symptomatology, and an overestimation of remission and absence. However, only 50% of patients (n = 72/144) reported on their use of antidepressants at 1-year follow-up and, therefore, it was not possible to examine the association between antidepressant use and trajectories of elevated depressive symptoms.

Conclusions

The present study examined the prevalence of depressive symptomatology as well as the severity and trajectories in depressive symptomatology between baseline and 1-year follow-up in a sample of rural and remote memory clinic patients, within and between diagnostic groups (NCI, MCI, AD, and non-AD). A recent review suggested that early-life depression is a risk factor for dementia; in late life, depression is a prodrome of dementia [57]. Applying a trajectory approach to investigating the temporal relationship between depression and dementia recognizes the chronic nature of depressive symptoms as well as the association that such chronicity may have with cognitive decline [58]. More research is needed to further examine trajectories of depressive symptomatology, and the factors associated with these trajectories, in noninstitutionalized individuals in the short-term (<2 years) period following diagnosis. Comparisons of the trajectories across multiple diagnostic groups are also warranted given that most studies to date have focused on single diagnostic groups. Such studies would contribute to the knowledge base of clinicians as well as of patients and families in terms of treatment decisions, prognosis, and ongoing monitoring [59].

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