

## Research article Ερευνητική εργασία

# Assessing depression in Greek dementia patients: Which scale to use?

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**D**epression in dementia is known to deteriorate patients' cognitive function and Quality of Life and to increase the burden of care. Although detecting depression in dementia is crucial, there is no gold standard for its screening and diagnosis. We examined the psychometric properties of 3 different scales in detecting depression in dementia. Results will be useful as community services for dementia in the country are developing and the need for reliable detection of depression in dementia patients is urgent. Our sample consisted of 136 Greek dementia patients who consulted a memory clinic. For the diagnosis of depression, DSM-IV criteria for major depression and 3 different depression measures were used: a self-assessment scale (Geriatric Depression Scale; GDS), a caregiver assessment scale (Neuropsychiatric Inventory-Depression; NPI-D) and a clinician rated scale (Cornell Scale for Depression in Dementia; CSDD). For the evaluation of the screening performance of the three depression scales receiver operating characteristic curve (ROC) analysis was applied. The DSM-IV criteria served as the gold standard method for the diagnosis of major depression. CSDD showed the best psychometric properties for the diagnosis of depression in dementia. The ROC curve analysis revealed that among the three measures, the CSDD had the wider AUC (0.919), second in the width of the AUC was the GDS (0.871), and last was the NPI-D (0.812). The prevalence of depression ranged from 18.4% according to DSM-IV criteria to 42.6% using the NPI-D. Using the GDS (cut off point: 7/8) and the CSDD (cut off point: 6/7), depression was present in 26.9% and 33.1% of the patients, respectively. Correlations between scales used were significant ( $r$  from 0.432 to 0.660;  $p < 0.001$ ). Caregivers tend to report more depressive symptoms in dementia compared to patients' and clinicians' ratings. CSDD should be used in specialized centers, but GDS may be an alternative in patients able to complete the assessment. The need to establish valid criteria for the diagnosis of depression in dementia is urgent.

**Key words:** Depression, Alzheimer's disease, Cornell scale for depression in dementia, geriatric depression scale, neuropsychiatric inventory.

## Introduction

Depression in dementia is known to deteriorate patients' cognition, functional status,<sup>1</sup> behavioral and psychological symptoms<sup>1</sup> and Quality of Life.<sup>2</sup> Moreover, depression is an independent predictor of early institutionalization of dementia patients,<sup>3</sup> of increases in the burden of care<sup>4</sup> and of caregiver's depression.<sup>5</sup> There is a debate over whether late-life depression is a prodrome to dementia<sup>6</sup> or whether depression is an independent risk factor for dementia.<sup>7</sup>

Although systematically detecting depression in dementia with suitable instruments is crucial, there is no gold standard for its diagnosis, and its prevalence differs substantially between studies. In one study,<sup>8</sup> the prevalence of depression was found from 0 to 86%, depending on the diagnostic criteria employed. In fact, depression and dementia share a common clinical picture; it is very difficult to distinguish whether physical and autonomic symptoms are secondary to depression or constitute dementia symptoms. Furthermore, apathy is commonly confused with depression, especially from inexperienced raters. As a result, depression remains undiagnosed in about half of demented patients.<sup>9</sup>

The main aims of the study were to estimate the prevalence of depression in a Greek dementia population using three different scales, as well as to evaluate their validity by calculating their inter-correlations and by applying a receiver operating characteristic curve (ROC) analysis that uses as gold standard the DSM-IV criteria for the diagnosis of major depression. In addition, the study examines the reliability of the scales used by calculating their internal consistency. This is one of the first studies of depression in dementia patients in Greece. Results will be useful as community services for dementia in the country are developing and the need for reliable detection of depression in dementia patients is urgent. Furthermore, we discuss important matters concerning the proper detection of depression in dementia in Greece.

## Material and method

### *Participants and procedures*

A consecutive series of consenting 136 patient-caregiver couples who visited two memory clinics

between January and May 2008 were studied. All patients met diagnostic criteria for dementia according to DSM-IV-TR. Caregivers were primary, helping the patients for at least two hours, twice a week. The study took place in two memory clinics of the Non-Profit Organization "Nestor" Psychogeriatric Association in Athens, Greece. All services are free of charge for both patients and families. Informed consent was obtained from all caregivers and patients before their enrollment in the study.

Patients and caregivers were seen separately when they visited one of the consultation clinics for the first time. Demographic data were obtained and depression scales were administered to the patients by a neuropsychologist; caregiver demographic data and scales were completed by a senior psychiatrist. A geriatric psychiatrist who was unaware of the above completed the Cornell Scale for Depression in Dementia and made diagnoses of dementia and probable depression. All three professionals had at least 4 years working experience with dementia patients and received special training for scale administration.

### *Measures*

For the diagnosis of major depression, the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) Axis I Disorders was used. Furthermore three different depression scales were used:

- a. Geriatric Depression Scale (GDS;<sup>10</sup> is a self-rated depression scale. Its original form contained 30 items, but Sheikh et al,<sup>11</sup> developed a shorter, 15-item version of the scale. Fountoulakis et al<sup>12</sup> validated the scale for the Greek population and found excellent psychometric properties for cognitively intact persons. These properties were lost in those having a Mini Mental State Examination (MMSE) score of less than 18.
- b. NPI-D, the depression item of the Neuropsychiatric inventory.<sup>13</sup> As with other items of the scale, the frequency and the intensity of depressive symptoms are rated on the basis of scripted questions administered to the patient's caregiver. The product of frequency and intensity gives a final score of item severity.

c. Cornell Scale for Depression in Dementia (CSDD).<sup>14</sup> CSDD is a 19-item instrument for measuring depressive symptoms in dementia. Both the patient and the caregiver are interviewed by a psychiatrist and the scale is clinician-rated. A score >12 is strongly correlated with a psychiatric diagnosis of a major depressive episode.<sup>15</sup>

In addition, basic demographic data were collected for patients and caregivers, as well as specific disease characteristics. The type of Dementia was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders criteria (DSM-IV<sup>16</sup>) for the diagnosis of Alzheimer's disease (AD) and vascular dementia (VD), consensus criteria<sup>17</sup> for the diagnosis of dementia with Lewy bodies (DLB) and<sup>18</sup> criteria for the diagnosis of Frontotemporal dementia (FTD). We used the Greek version of validated scales, in order to assess patients' cognitive (MMSE);<sup>19,20</sup> functional (Katz Activities of Daily Living;<sup>21</sup> and behavioural (Neuropsychiatric Inventory (NPI);<sup>13,22</sup> status.

### Data analyses

The Statistical Package for Social Sciences (SPSS), version 17 for Windows, was used for the analyses of the data. To analyse demographic factors and to investigate the prevalence of cognitive and psychiatric symptoms in persons with dementia and their caregivers, mean scores and standard deviations were calculated. Cronbach's alpha was estimated to assess the internal consistency of the scales used.

For the evaluation of the screening performance of the three depression scales, namely of the GDS, the NPI-D and the CSDD, receiver operating characteristic curve (ROC) analysis was applied. The DSM-IV criteria served as the gold standard method for the diagnosis of major depression. The ROC curve plots the sensitivity and the specificity of a measure on the Y-axis and the X-axis, respectively. The area under the ROC curve (AUC) is the most important summary index of the ROC curve, and its evaluation is performed by comparing it with the AUC of the diagonal line, which represents classification by chance (AUC=0.50). When the value of the AUC is above 0.8, the corresponding scale is considered to be an accurate measure. Moreover, as the AUC becomes bigger, the accuracy of the scale increases. Optimal cut-off points of the three depression scales regarding the degree of sensitivity and speci-

ficity were estimated from the empirical ROC curves. This was performed by selecting, for each scale, the combination of sensitivity and specificity values that have the minimal Euclidean distance from the ideal point (1.1). Sensitivity was defined as the probability of a positive screening for depression given that the individual met the DSM-IV criteria for major depression. Specificity was defined as the probability of a negative screening for depression given that the individual did not meet the DSM-IV criteria for major depression.

### Results

All 136 patients included were community residing dementia patients. Their characteristics are listed in table 1. The study population was of advanced age (average age greater than 75 years old), a low educational level (less than 9 years of education on the average), and the majority of the patients were female (66.9%). Patients had dementia for an average of about 4 years, with 46.3% suffering from moderate (n=63) and 39.0% suffering from severe (n=53) de-

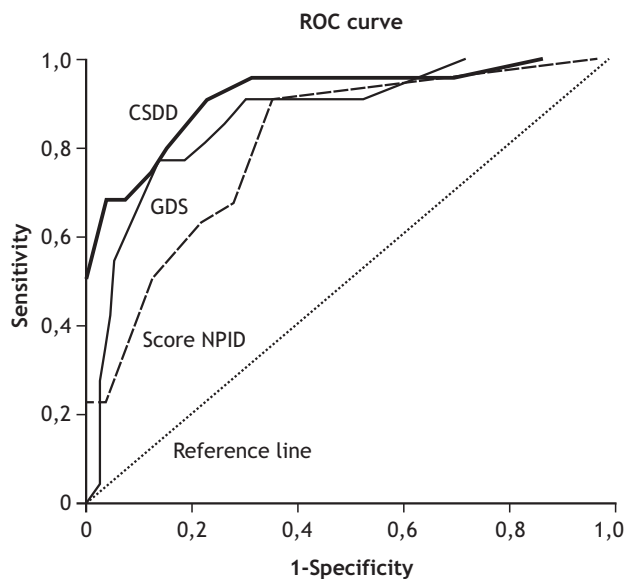
**Table 1.** Sociodemographic and clinical characteristics of patients with dementia (n=138).

Female patients (%)	91 (66.91)
Age (SD)	76.72 (7.15)
Married (%)	70 (51.47)
Years of education (SD)	8.58 (4.42)
Months with Dementia (SD)	46.15 (28.25)
Dementia type (%)	
AD	90 (66.18)
VD	26 (19.12)
DLB	9 (6.62)
FTD	9 (6.62)
PD	2 (1.47)
MMSE (SD)	11.50 (7.16)
ADL	4.05 (1.93)
NPI (SD)	28.09 (19.70)
GDS (SD)	4.86 (3.97)
NPI (SD)	2.37 (3.48)
CSDD (SD)	5.11 (4.58)

AD: Alzheimer's Disease, VD: Vascular Dementia, DLB: Dementia with Lewy Bodies, FTD: Frontotemporal Dementia, MMS: Mini Mental State Examination, ADL: Activities of Daily Living, GDS: Geriatric Depression Scale, NPI: Neuropsychiatric Inventory, CSDD: Cornell Scale for Depression in Dementia

mentia according to the MMSE scores (0–9 for severe and 10–19 for moderate dementia). Most caregivers were females (69.1%), patients' wives or daughters (28.7% and 30.9% respectively), and involved in the caregiving role for 73.32 hours per week on average.

The ROC curve analysis revealed that the AUC for the three depression scales is significantly greater than the diagonal line ( $p < 0.001$ ). Among the three measures, the CSDD the wider AUC (0.919), second in the width of the AUC was the GDS (0.871), and last was the NPI-D (0.812) (figure 1). Additionally the CSDD curve came closest to the left upper angle of the graph in comparison to the curves of the two other depression scales (figure 1). For distinguishing between depressed and non-depressed individuals the score of 6/7 was the ultimate cut-off point for the CSDD with 88.0% sensitivity and 79.3% specificity. With regards to the GDS the more accurate discrimination between depressed and non-depressed individuals was achieved at the cut-off score of 7/8 with 77.3% sensitivity and 86.6% specificity. Finally, the best cut-off score for the NPI-D was 0/1 with 88.0% sensitivity and 67.6% specificity.



**Figure 1.** ROC curves (receiver operating characteristics curves) of the Geriatric Depression Scale (GDS,  $n = 104$ ), the Cornell Scale for Depression in Dementia (CSDD,  $n = 136$ ), and the Neuropsychiatric Inventory-Depression scale (NPI-D,  $n = 136$ ), for the detection of major depression in patients with dementia. DSM-IV criteria were used as the gold standard).

The prevalence of depression ranged from 18.4% according to DSM-IV criteria to 42.6% using the NPI-D. Using the GDS (cut off point: 7/8) and the CSDD (cut off point: 6/7), depression was present in 26.9% and 33.1% of the patients, respectively (table 2). Correlations between scales used were significant ( $r$  from 0.432 to 0.660,  $p < 0.001$ ) (table 3).

The internal consistency of the three depression scales was measured by using Cronbach's alpha. The values obtained are the following: GDS Cronbach's alpha=0.867; CSDD Cronbach's alpha=0.777; and NPI-D Cronbach's alpha=0.841. One hundred and four out of 136 patients (76.47%) completed the GDS. The mean MMSE of the non-completers was 3.65. All patients with MMSE > 10 completed the scale. Cronbach's alphas were similar for completers with MMSE above 17 and below 18 (0.889 and 0.856, re-

**Table 2.** Internal consistency of three depression scales and prevalence of depression.

Scale	n	Dep. (%)	Cut-off	Cronbach's alpha
GDS (self-rated)	104	28 (26.9)	7/8	0.867
NPI-D (caregiver rated)	136	58 (42.6)	0/1	0.841
CSDD (clinician rated)	136	45 (33.1)	6/7	0.777
DSM-IV (clinician rated)	136	25 (18.4)		

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders (used as the gold standard), GDS: Geriatric Depression Scale, CSDD: Cornell Scale for Depression in Dementia, NPI-D: Neuropsychiatric Inventory-Depression

**Table 3.** Pearson correlation coefficients between depression scales.

Scale	CSDD	GDS	NPI-D
CSDD	1	0.555**	0.660**
GDS	0.555**	1	0.432**
NPI-D	0.660**	0.432**	1

GDS: Geriatric Depression Scale, CSDD: Cornell Scale for Depression in Dementia, NPI-D: Neuropsychiatric Inventory-Depression. \* $p < 0.05$ , \*\* $p < 0.01$

Correlation analysis between CSDD and NPI-D was performed in 136 individuals. Correlations between GDS and the two other scales were performed in 104 individuals that managed to complete the GDS scale

spectively). Correlations between the GDS and the other scales used were significant for those patients with MMSE<18 ( $r=0.385$ ,  $p\leq 0.001$  between GDS and NPI-D;  $r=0.559$ ,  $p\leq 0.001$  between GDS and CSDD).

## Discussion

The CSDD seems to have better psychometric properties, compared to the GDS and the NPI-D in the diagnosis of depression in dementia. The GDS may have better properties than previously thought, especially for not severely demented patients. In our study its specificity was excellent (86.6%), higher than that found for the CSDD. We also found that the prevalence of depression varied widely according to the scale used for its diagnosis. The prevalence was higher with the caregiver-rated NPI-D and lower with the application of the DSM-IV criteria.

In our sample, the prevalence of depression varied from 18.4% to 42.6%, according to the scale used. This confirms the great variation in the prevalence of depression reported in previous dementia studies.<sup>23,24,8</sup> WHO reported that the prevalence of depression in dementia varied from 0 to 86%, in the studies that they reviewed. A similar variation has been found in studies investigating the prevalence of depression amongst cognitively intact elderly people.<sup>25</sup> The great range of variation in the prevalence of depression may be attributed, among other factors, to differences in the definition of depression, the scales applied and the intrinsic characteristics of the populations studied. Moreover, as we will discuss subsequently, we are not fully aware of what constitutes depression in dementia.

Parza et al<sup>26</sup> reported that depression, mild cognitive impairment and dementia could represent a clinical continuum. In fact, dementia and depression share common symptoms, e.g. memory complaints, irritability, insomnia, fatigue and weight loss. Moreover, differentiating between the symptoms of depression and dementia can be difficult. Apathy, for example, one of the most common behavioral symptoms of dementia, is often misinterpreted as a symptom of depression. This substantial overlap in key symptoms, between dementia and depression, makes diagnosis of depression in dementia patients difficult. The picture is further obscured by the fact that antidepressants show good results in treating psychiatric symp-

toms of dementia,<sup>27</sup> while their effectiveness in treating depression in dementia is limited, at best.<sup>28</sup>

We used DSM-IV criteria as a gold standard, in order to examine the psychometric properties of three different scales. However, the use of DSM-IV criteria for the diagnosis of depression in dementia patients is largely criticized. According to Landes et al,<sup>29</sup> DSM criteria may increase the prevalence of major depression in dementia, since a depressed mood is not a prerequisite for a depression diagnosis and many DSM criteria for depression are symptoms of dementia as well. These factors may explain the observed increased prevalence of depression in dementia, more than 10% in most studies,<sup>30,31</sup> compared to the less than 5% prevalence of depression in the non-demented elderly.<sup>25</sup> On the other hand, the National Institute of Mental Health Provisional Diagnostic Criteria for Depression in Alzheimer disease,<sup>32</sup> largely overestimates the prevalence of depression.<sup>30</sup> The criteria include, for example irritability, an independent item in the NPI, which is very common in dementia, especially in severe stages of the disease.<sup>33</sup> If it is considered as a symptom of depression, inevitably it will increase its prevalence.

CSDD has been developed specifically to diagnose depression in dementia patients. Our results are in agreement with other studies<sup>34</sup> showing that CSDD is superior to other scales for diagnosing depression in dementia. Moreover, CSDD has been found to be more sensitive in detecting effects of drug treatment than other scales.<sup>35</sup> Physicians in Greece should be trained in CSDD administration, since its items take into account the unique symptoms of depression in dementia. On the other hand, CSDD is time consuming and can be administered only by physicians.

The use of the GDS in elders with cognitive impairment remains a controversial issue. In our study, GDS showed good psychometric properties for those who managed to complete the assessment. All patients with an MMSE above 10 completed the scale, with good sensitivity, specificity and internal consistency. Thus, in contrast with the findings of Fountoulakis et al,<sup>12</sup> our results support the use of the GDS in patients with moderate cognitive impairment. Also the optimal cut-off score of GDS in our study was 7/8, while Fountoulakis et al<sup>12</sup> reported a cut-off score of 6/7. This may be due to the fact that the optimal cut-off score of the GDS may be shifted



to higher values when moving from mild to the more advanced dementia, as Lam et al<sup>36</sup> noticed. Several other studies reported that the GDS can be used in patients with moderate dementia.<sup>37</sup> However, other studies showed exactly the opposite.<sup>23</sup> Concluding, our results support the use of the GDS in patients with dementia, when they manage to complete the assessment. Taking into consideration that the GDS is widely used, is less time consuming than the CSDD and can be administered by less experienced raters, GDS can offer an alternative to the CSDD, especially in primary health care settings.

NPI-D, as in other studies,<sup>24</sup> largely overestimated the prevalence of depression in dementia. This is probably because caregivers cannot reliably differentiate between the symptomatology of depression and dementia. Moreover, caregivers may incorporate in their assessments their own feelings. Depressed and highly burdened caregivers may report higher depressive symptoms for the patients they care for. On the other hand, NPI-D showed a very high sensitivity of 88%, for the diagnosis of depression. This indicates that caregivers should always be asked for the presence of depressive symptoms in the patients, although physicians should bear in mind that caregivers may overestimate their presence.

This study has a number of limitations. Our sample may not be representative of community patients with dementia because the study was conducted in a referral setting. The sample size, although large, did not allow us to explore depression diagnosis and scales psychometric properties between different degrees of dementia severity. DSM-IV criteria and CSDD were administered by the same rater and this may have overestimated the agreement between a DSM-IV and CSDD diagnosis. As mentioned above, the concept of depression is not fully understood in dementia. DSM-IV criteria and other scales have been criticized for their ability to accurately assess depressive symptoms in dementia. Moreover, these scales have been developed with the aim of screening or monitoring the depressive symptoms and not for diagnosing depression.

This is the first study evaluating depression in the context of dementia in Greece. Caregivers tend to overestimate depressive symptoms in dementia compared to patients' and clinicians' ratings. GDS may be reliable even in patients with severe dementia who are able to complete the assessment. CSDD shows the best psychometric properties and is the scale of choice for properly diagnosing depression in dementia.

## **Εκτίμηση της κατάθλιψης σε Έλληνες ασθενείς με άνοια: Ποια κλίμακα πρέπει να χρησιμοποιούμε;**

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Η κατάθλιψη στην άνοια επιδεινώνει τη γνωστική λειτουργία του ασθενούς και την ποιότητα ζωής του. Ταυτόχρονα, αυξάνει την επιβάρυνση της φροντίδας που απαιτείται και συμβάλλει πολλές φορές στην πρόωρη ιδρυματοποίηση του ασθενούς. Παρόλο που η ανίχνευση της κατάθλιψης στην άνοια είναι καθοριστική και για πολλούς ένα πρόδρομο σημάδι της ασθένειας, δεν υπάρχει κάποιος χρυσός κανόνας για τον έλεγχο και τη διάγνωσή της. Εξετάστηκαν οι ψυχομετρικές ιδιότητες, η ε-

γκυρότητα και η αξιοπιστία τριών διαφορετικών κλιμάκων για την ανίχνευση της κατάθλιψης στην άνοια, σε ελληνικό πληθυσμό. Το δείγμα αποτέλεσαν 136 Έλληνες ασθενείς με άνοια και οι φροντιστές τους, οι οποίοι επισκέφθηκαν τα δύο εξειδικευμένα κέντρα ελέγχου μνήμης της Ψυχογριατρικής Εταιρείας «Ο Νέστωρ» στην Αθήνα. Για τη διάγνωση της κατάθλιψης, χρησιμοποιήθηκαν τα κριτήρια κατά DSM-IV για τη μείζονα κατάθλιψη, καθώς και 3 διαφορετικές κλίμακες κατάθλιψης: μία κλίμακα αυτοαξιολόγησης του ασθενούς (Geriatric Depression Scale, GDS), μία κλίμακα εκτίμησης καταθλιπτικών συμπτωμάτων από τον φροντιστή (Neuropsychiatric Inventory-Depression, NPI-D) και μία κλίμακα εκτίμησης από τον κλινικό ιατρό (Cornell Scale for Depression in Dementia, CSDD). Οι ασθενείς ήταν κυρίως γυναίκες (67%), άνω των 75 ετών (μ.ο. 77), με χαμηλό μορφωτικό επίπεδο (8,6 έτη εκπαίδευσης κατά μ.ο.). Η μέση τιμή του Mini Mental State Examination ήταν 11,5. Παρουσιάστηκε στατιστικώς σημαντική συσχέτιση μεταξύ των τριών κλιμάκων ( $r$  από 0,432 έως 0,660,  $p < 0,001$ ). Σύμφωνα με την κλίμακα GDS το 26,9% του δείγματος έπασχε από κατάθλιψη, σύμφωνα με τη CSDD το 33,1%, ενώ με τη χρήση της κλίμακας NPI-D, το 42,6% παρουσίαζε κατάθλιψη. Η κλίμακα με τις καλύτερες ψυχομετρικές ιδιότητες για τη διάγνωση της κατάθλιψης στο πλαίσιο της άνοιας ήταν η CSDD. Οι φροντιστές τείνουν να υπερεκτιμούν τα συμπτώματα της κατάθλιψης στην άνοια σε σύγκριση με τις αξιολογήσεις των ίδιων των ασθενών και των κλινικών ιατρών. Καταθλιπτικά συμπτώματα στους ίδιους τους φροντιστές και δυσκολία στη διαφοροδιάγνωση ανάμεσα στην κατάθλιψη και την απάθεια πιθανώς σχετίζονται με την υπερεκτίμηση αυτή. Η κλίμακα CSDD θα πρέπει να χρησιμοποιείται σε εξειδικευμένα κέντρα άνοιας για ασθενείς σοβαρότερου σταδίου, αλλά η GDS μπορεί να είναι μια εναλλακτική λύση σε ασθενείς που είναι σε θέση να αυτοαξιολογηθούν και βρίσκονται σε μεσαίο στάδιο άνοιας. Η ανάγκη για τη δημιουργία έγκυρων κριτηρίων για τη διάγνωση της κατάθλιψης στην άνοια είναι επιτακτική.

**Λέξεις ευρητηρίου:** Κατάθλιψη, νόσος Alzheimer, κλίμακα Cornell για την εκτίμηση της κατάθλιψης στην άνοια, γριατρική κλίμακα κατάθλιψης, ερωτηματολόγιο καταγραφής ψυχιατρικών συμπτωμάτων.

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