

SCREENING FOR DEPRESSION IN PARKINSON’S DISEASE: THE PERFORMANCE OF TWO SCREENING QUESTIONS.

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Word count: 2498

Running title: Depression screening in PD using two questions

Keywords: Parkinson’s disease, Depression, Screening, Geriatric Depression Scale,

Conflict of interest: None of the authors have any conflict of interest to report.

ABSTRACT

Background - The study objective was to evaluate the validity of the two questions recommended by the U.K. National Institute for Health and Clinical Excellence for depression screening in Parkinson's disease (PD).

Methods - One hundred and twenty patients attending a PD out-patient clinic were interviewed in a standardised manner using relevant sections of the Present State Examination- Schedules for Clinical Assessment in Neuropsychiatry to identify depression according to Diagnostic and Statistical Manual (4th edition) criteria. Participants then completed the two depression screening questions and the 15-item Geriatric Depression Scale (GDS-15).

Results - Sensitivity, specificity, positive and negative predictive values of the two questions and GDS-15 for major and minor depression combined were calculated for different cut-off scores and a receiver operating characteristics (ROC) analysis was conducted. A threshold of one or more positive responses to the two screening questions gave a sensitivity of 100% and specificity of 84% (positive predictive value 54%, negative predictive value 100%). The area under the ROC curve was 0.95. The optimal cut-off for the GDS-15 was 5/6, which gave a sensitivity of 84% and specificity of 89% (positive predictive value 59%, negative predictive value 97%), and the area under the curve was 0.92.

Conclusion - This study shows that the two depression screening questions can be used as an initial screen for depression in patients with PD who have no significant cognitive impairment. A positive response to either of the questions would indicate that further diagnostic assessment may be warranted.

INTRODUCTION

Parkinson's disease (PD) affects over 120,000 people in the UK, with about 10,000 newly diagnosed each year [1]. Although PD is defined by its motor symptoms, non-motor symptoms such as depression are also common. Research indicates that approximately 19% of PD patients meet DSM-

IV diagnostic criteria for major depression whilst 35% have clinically relevant depressive symptoms [2].

Depression has a negative impact on the quality of life of the PD patient and their family [3], has a negative effect upon motor symptoms [4], cognitive functioning [5], and functional ability [6] and is associated with increased mortality [7] and greater medical and psychiatric co-morbidity [8].

Diagnosis of depression in PD is not straight-forward because several clinical features of depression and PD overlap. Symptoms of depression such as tiredness, lack of energy, psychomotor retardation, mental slowing, impaired concentration, reduced appetite and insomnia occur in both depression and PD making it difficult for clinicians to identify when depression is present. As a result depression in PD is poorly recognised in clinical practice and depressive symptoms are frequently missed during specialist reviews [9].

The U.K. National Institute for Health and Clinical Excellence (NICE) [10] recommend screening for depression in patient groups at higher risk of depression, and suggest the use of two screening questions [11]:

- *During the past month, have you often been bothered by feeling down, depressed or hopeless?*
- *During the past month, have you often been bothered by having little interest or pleasure in doing things?*

In light of this recommendation and growing evidence that antidepressant treatment in PD is effective [12], it is important that clinicians consider routine screening of PD patients. This study aimed to investigate the effectiveness of these questions for screening for depression in a PD outpatient setting. As a comparator we used the 15 item version of the Geriatric Depression Scale

(GDS-15) [13]. The GDS-15 has previously been shown to be effective in screening for depression in PD [14].

METHODS

Study participants were 136 patients attending the PD outpatient clinic at Leicester General Hospital. Patients were either newly diagnosed or attending the clinic for review. All met the UK Parkinson's Disease Society Brain Bank diagnostic criteria for Parkinson's disease [15], were able to give informed consent, and could speak English. Each participant was visited at home and first completed section 21 of the Present State Examination - Schedules for Clinical Assessment in Neuropsychiatry (SCAN) [16] which incorporates the Mini-Mental State Examination (MMSE). Those scoring less than 24 on the MMSE were excluded from the remainder of the study – this cut-off was chosen because a score of 24 or less is the most widely used cut-off used in research to exclude patients with dementia [17]. The researcher then completed the sections of the SCAN interview pertaining to depression (sections 6, 7 and 8) with the participant, to establish the Diagnostic and Statistical Manual (4th edition) (DSM-IV) diagnosis of depression [18], which was used as the gold standard in this study. These researchers were psychiatrists who had received formal training in the SCAN interview technique. Participants were identified as having either major, minor or no depression. The major depression diagnosis was produced using the diagnostic algorithm of the SCAN software, which applies the DSM-IV diagnostic criteria. This software does not include an algorithm for a diagnosis of minor depression, so the algorithm was adapted manually to apply the DSM-IV criteria for minor depression. Within five days of the initial SCAN assessment the participant was visited by another researcher (SB), who was blind to the outcome of the SCAN interview, and administered the two NICE screening questions and the 15-item Geriatric Depression Scale. The severity of PD at the participant's most recent PD clinic appointment, as indicated by the Hoehn and Yahr scale [19], was retrieved from their clinic notes. The project was approved by the Leicester Research Ethics Committee and received no specific funding.

Sensitivity (Se), specificity (Sp), positive and negative predictive value (PPV, NPV), positive and negative likelihood ratio (LR+, LR-) and the diagnostic odds ratio (DOR) were calculated. Receiver operating characteristic (ROC) curve analyses were carried out using the methods described by Altman [20] and the areas under the curves (AUC) were compared using the methods described by Hanley and McNeil [21]. Analyses were performed using SPSS v18.

RESULTS

A total of 136 patients participated in the study between 2007 and 2011 - 15 were excluded due to scoring less than 24 on the MMSE and one patient declined to continue following the SCAN interview. Data were therefore available for 120 participants (Table 1). Hoehn and Yahr ratings were only available for 59 (50%) participants; 55 (93% of cases where a Hoehn and Yahr rating was recorded) were stage 1-2, indicating minimal disability. The prevalence of major depression was 11.7%, and prevalence of any depression (minor or major) was 15.8%. No participant received a diagnosis of dysthymia.

Table 1. Characteristics of the study participants (N = 120)

Gender	Male : Female	67 (55.1%) : 53 (44.9%)
Age	Mean (SD)	73.1 yrs (9.4)
Time since diagnosis of PD	Mean (SD)	48.6 months (52.1)
	Range	1-249 months
MMSE Score	Mean (SD)	27.9 (1.7)
DSM-IV diagnosis, N (%)	No depression	101 (84.2%)
	Minor depression	5 (4.2%)
	Major depression	14 (11.7%)
Antidepressant medication	N (% Yes)	22 (18.3%)

A total of 17 participants responded positively to one of the two NICE screening questions, and 18 responded positively to both. A threshold score of 1 (i.e. a positive response to one or more of the questions) gave optimal performance for the purpose of screening for depression in PD patients (Table 2). Table 3 shows the results for different cut-off scores for the GDS-15; the optimal screening cut-off was 5/6.

Table 2. Operating characteristics of the two NICE screening questions for the identification of DSM-IV minor or major depression, and for the identification major depression

Cut-off	Se (95% CI)	Sp (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+	LR-	Diagnostic Odds Ratio
Minor or major depression							
0/1	1.00 (0.83-1.0)	0.84 (0.76-0.90)	0.54 (0.38-0.70)	1.00 (0.96-1.0)	6.31	0	--
1/2	0.68 (0.46-0.85)	0.95 (0.89-0.98)	0.72 (0.49-0.88)	0.94 (0.88-0.97)	13.82	0.33	41.60
Major depression							
0/1	1.00 (0.79-1.0)	0.80 (0.72-0.87)	0.40 (0.26-0.56)	1.00 (0.96-1.0)	5.05	0	--
1/2	0.64 (0.39-0.84)	0.92 (0.85-0.96)	0.50 (0.29-0.71)	0.95 (0.89-0.98)	7.57	0.39	19.40

128 **Table 3.** Operating characteristics of the GDS-15 for the identification of DSM-IV minor or major
129 depression, and for the identification of major depression

Cut-off	Se (95% CI)	Sp (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+	LR-	Diagnostic Odds Ratio
Minor or major depression							
3/4	0.95 (0.75-0.99)	0.71 (0.62-0.79)	0.38 (0.26-0.53)	0.99 (0.93-1.0)	3.30	0.07	44.69
4/5	0.89 (0.69-0.97)	0.76 (0.67-0.84)	0.41 (0.28-0.57)	0.97 (0.91-0.99)	3.77	0.14	27.27
5/6	0.84 (0.62-0.95)	0.89 (0.82-0.94)	0.59 (0.41-0.76)	0.97 (0.91-0.99)	7.73	0.18	43.64
6/7	0.79 (0.57-0.92)	0.94 (0.88-0.97)	0.71 (0.50-0.86)	0.96 (0.90-0.98)	13.29	0.22	59.38
7/8	0.68 (0.46-0.85)	0.96 (0.90-0.98)	0.76 (0.53-0.90)	0.94 (0.88-0.97)	17.28	0.33	52.54
8/9	0.58 (0.36-0.77)	0.97 (0.92-0.99)	0.79 (0.52-0.92)	0.92 (0.86-0.96)	19.49	0.43	44.92
Major depression							
3/4	1.00 (0.79-1.0)	0.69 (0.60-0.77)	0.30 (0.19-0.44)	1.00 (0.95-1.0)	3.21	0	--
4/5	0.93 (0.69-0.99)	0.74 (0.65-0.81)	0.32 (0.20-0.47)	0.99 (0.93-1.0)	3.52	0.10	36.21
5/6	0.86 (0.60-0.96)	0.86 (0.78-0.91)	0.44 (0.28-0.63)	0.98 (0.93-0.99)	6.06	0.17	36.40
6/7	0.79 (0.52-0.92)	0.91 (0.84-0.95)	0.52 (0.32-0.72)	0.97 (0.92-0.99)	8.33	0.24	35.20
7/8	0.64 (0.39-0.84)	0.92 (0.86-0.96)	0.53 (0.31-0.74)	0.95 (0.89-0.98)	8.52	0.39	22.05
8/9	0.64 (0.39-0.84)	0.95 (0.89-0.98)	0.64 (0.39-0.84)	0.95 (0.89-0.98)	13.63	0.37	36.36

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131 The AUC for the identification of both minor and major depression, calculated from the ROC curve,
132 was 0.950 (p<0.001, 95% confidence interval 0.914 to 0.987) for the NICE screening questions and for
133 the GDS-15 it was 0.922 (p<0.001, 95% confidence interval 0.849 to 0.996). These AUC were not

statistically different for minor and major depression combined ($z=0.713$, 95% confidence interval -0.049 to 0.105, $p=0.476$) or major depression alone ($z=0.166$, 95% confidence interval -0.058 to 0.069, $p=0.867$).

NICE guidelines [22] suggest using a two-stage screening process in which the two questions are the initial screen, followed by a second screening measure for those who respond positively to either or both of the questions, in order to reduce the numbers of false-positives who are subjected to further assessment for depression. We used data from this study to simulate this two-stage screening process. 35/120 participants responded positively to one or both of the screening questions. Examination of the responses of these 35 participants on the GDS-15, and application of the 6/7 threshold (which has the higher diagnostic odds ratio than a 5/6 cut-off), resulted in the correct identification of 15/19 depressed (79% sensitivity) and 12/16 non-depressed participants (75% specificity). This reduced the original false-positive rate after the NICE questions from 16/35 (46%) to 4/35 (11%). However this would be at the cost of 'missing' 4/19 (21%) depressed participants who were incorrectly identified by the GDS-15 as non-depressed. At the lower threshold of 5/6 on the GDS-15, 16/19 depressed participants and 10/16 non-depressed participants were correctly identified (sensitivity 84%, specificity 63%). This reduced the number of false-positives to 6/35 (17%), at the cost of 'missing' 3/19 (16%) depressed participants.

DISCUSSION

This study was designed to assess the validity of the two depression screening questions recommended by NICE [22] in PD patients attending a hospital out-patient PD clinic. The two-question measure appears to be a useful tool to identify participants with major or minor depression in this setting. With a threshold of a 'Yes' response to either of the two questions, all cases of depression were correctly identified in this study sample (100% sensitivity) and two 'No' responses correctly identified 84% of all non-depressed (84% specificity). This detection rate should come as no surprise, as the two screening questions reflect the core symptoms of major depression in DSM-IV (that is, at least one of these symptoms is required to be present when making a diagnosis of depression).

In our study the GDS-15 also demonstrated good test characteristics – at a threshold score of 5/6 for major and minor depression it showed 84% sensitivity, 89% specificity and PPV of 59%. The GDS-15 is already established as a valid tool for screening for depression in PD [23], and although relatively brief still takes longer to complete and to score than the two-question measure. The brevity of the two questions recommended by NICE lends itself to easy integration into routine clinical assessment and review. The high sensitivity of these questions means that most cases of depression will be identified, but a PPV of 54%, shows that nearly half the people who tested positive on the two questions were false-positives. In a screening programme in a clinical setting this could lead to unnecessary further investigation in many non-depressed patients. Depending on the action taken following a positive depression screening result (e.g. a diagnostic interview performed by the clinic doctor or referral for specialist assessment) this may not be acceptable. At the very least, if a patient responds positively to either of the NICE screening questions it should prompt the clinician to question them further regarding their mood. In our study half of the non-depressed participants identified as depressed by the NICE screening questions had sub-threshold depression or other mental health issues (e.g., significant anxiety symptoms or unresolved bereavement). These participants would benefit from further investigation or support despite not meeting diagnostic

criteria for depression, and would clearly be worth identifying in a clinical context especially as co-morbid anxiety and depression are common in PD [24].

NICE guidelines for depression [22] recommend that if a person responds positively to either of the screening questions, an appropriate clinician should review their mental state and associated functional, interpersonal and social difficulties (p108). This assessment may include use a second depression scale with better overall psychometric properties. As all participants completed both screening measures it was possible to simulate this two-stage screening process. . Using the GDS-15 as a second screening measure for participants who screened positive to the NICE questions reduced the number of false-positives substantially but at the cost of ‘ruling out’ a number of depressed participants. This analysis was based on a small number of participants so further investigation of the relative benefits of this process would be worthwhile. Use of the second depression scale should be in the context of a more holistic assessment of the patient’s mood and functioning.

There are limitations to this study – there is some debate regarding the use of standard criteria for depression in patients who have chronic illnesses such as PD due to the overlap of many symptoms between the medical illness and depression [25]. DSM-IV criteria were applied in this study as they are the criteria most frequently used in studies of this nature, therefore symptoms were discounted only if the interviewer was confident that they were attributable to physical illness rather than to depression.

Hoehn and Yahr ratings were not available for all participants making characterisation of the sample difficult. Length of time since receiving their diagnosis of PD was obtained for all participants but this does not lend itself to easy interpretation for the purpose of describing the study sample.

Additionally, it may have been preferable to have balanced the order of the study assessments to avoid the possibility of any priming effect of the SCAN on the subsequent assessments, or to have

completed the screening scales followed by the SCAN interview in order to replicate the order of presentation in practice but for practical reasons neither were possible.

Although comparable with most other studies validating depression screening measures in PD patients, this study included a relatively small sample. Patients who scored less than 24 on the MMSE were excluded so it is not possible to generalise use of this screening measure to PD patients who have dementia, which may be a significant proportion of patients with PD. Similarly the sample included few patients with severe PD. Further research would need to be conducted to validate these questions in these patient groups. However it is important to validate a screening measure in the setting in which it would be used. A PD outpatient clinic is the most likely setting for routine screening and, in this hospital at least, few patients with severe PD or dementia in PD attend the clinic.

A systematic review of depression rating scales [26] has indicated that several are useful measures in PD. Observer-rated scales demonstrated better psychometric properties than self-rated scales but are less practical for use as routine screening measures. A recent paper by Williams et al. [27] evaluated the performance of nine depression scales in the identification of both minor and major depression in a community-based sample of PD patients and demonstrated similar levels of sensitivity and specificity for all of the scales. The authors felt that the GDS-30 was the most efficient scale for screening in clinic because it was a self-report measure and had favourable psychometric properties (sensitivity 72%, specificity 82%, PPV 73% and NPV 81%). The GDS-15 and the two NICE screening questions have shown slightly better performance in this study, except in terms of PPV, and have the advantage of being shorter scales than the GDS-30. One recent study has investigated the utility of an ultra-short scale - the PHQ-2 [28]. This scale uses the same two items from the PRIME-MD [29] as the NICE questions. In the PHQ-2 the reference time period is two weeks rather than the last month, and items are rated on a scale from 0 (not at all) to 3 (nearly every day). The study found the two-item scale to be a valid screening measure in PD (sensitivity 75%, specificity

89%, PPV 70% and NPV 91% at a cut-off score of 3 out of 6) but although the scale is short the scoring is less simple than the yes/no response used for the NICE screening questions. The data here indicates that the two NICE questions may offer good psychometric properties as well as being extremely quick to complete, with a threshold that is very easy to apply.

Evidence suggests that screening for depression improves recognition of depression but does not necessarily lead to improvement in depression symptoms for the patient [30]. Screening needs to take place in the context of a system which enables accurate diagnosis following positive screening, effective treatment and appropriate follow-up in order to achieve positive clinical benefits [31]. This study shows that the two questions recommended for screening for depression in the NICE guidelines are a useful means of identifying depression in patients with PD, who do not have significant cognitive impairment. They could be easily assimilated into routine practice and their brevity suggests they would be more acceptable to clinician and patients compared to longer instruments. If widespread use of the screening questions is adopted, the clinical challenge will be ensuring the accurate diagnosis of patients that screen positive; whether it is by the PD specialist themselves, or by a mental health professional. An intermediate stage of a second instrument for those that screen positive may assist with this process, in the context of a wider assessment of the patient's mental state and associated functioning. Furthermore, effective treatment with appropriate follow-up care needs to be provided by health care providers.

3-5 KEY POINTS

- The two questions recommended by NICE for screening for depression perform well in identifying depression in patients with PD who do not have significant cognitive impairment.
- The two questions could easily be assimilated into routine assessment and review of patients with PD.
- A two-stage screening process, with a scale such as the GDS-15, can reduce the number of false-positives.

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264 **ACKNOWLEDGEMENTS**

265 We are very grateful to Drs Pravin Prabhakaran, Oli Hands, Jonathan Murray, Suzanne Stacey,
266 Sandhya Gaur, Aniruddha Rajkonwar, Jayaraj Padmanabhan, Deepak Shukla and Santanu Chakrabarti
267 who conducted the patient interviews. We would also like to thank Dr Richard Abbott, Dr Peter
268 Critchley and Jean Martey for referring patients to the study.

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