## Depressive and anxiety symptoms in Dutch chronic kidney disease patients

Loosman, W.L.

2016

***document version***
Publisher's PDF, also known as Version of record

# Chapter 2

# Validity of the Hospital Anxiety and Depression Scale and the Beck Depression Inventory for use in end-stage renal disease patients

W. L. Loosman, C. E. H. Siegert, A. Korzec, and A. Honig

British Journal Clinical Psychology. 2010 Nov;49:507-16

## ABSTRACT

**Objective** To validate the Hospital Anxiety and Depression Scale (HADS) and the Beck Depression Inventory (BDI) for use in patients with end-stage renal disease (ESRD) and to compare the outcome of both screening measures with each other.

**Design** The study had a cross-sectional and between-subjects design. The independent variable was the diagnosis depression by the Mini International Neuropsychiatric Interview (MINI). The dependent variables were the HADS and BDI.

**Methods** All 130 patients with ESRD who were treated with haemodialysis (HD) or peritoneal dialyses (PD) in the Sint Lucas Andreas Hospital in Amsterdam were eligible for this study, and were asked to fill out both HADS and BDI. The outcomes of both rating scales were compared with the diagnosis major depressive episode based on the MINI, which was seen as the gold standard. Receiver operating characteristic curves were used to choose optimal cut-off values.

**Results** Of 62 enrolled subjects, 21 (34%) were diagnosed with a depressive disorder. Optimal cut-off values were ≥ 12 (HADS) and ≥ 13 (BDI). Sensitivity was 81.0% (HADS) and 75.0% (BDI). Specificity was 90.2% for both.

**Conclusions** Both HADS and BDI are valid screening instruments for the diagnosis depression in ESRD patients but there is no statistical difference found between both rating scales.

## INTRODUCTION

Depression is underdiagnosed and undertreated in patients with end-stage renal disease (ESRD).[1;2] It appears to be an independent risk factor for increased morbidity and mortality in ESRD patients.[3-5] The estimated prevalence of depression in ESRD patients is 20–30%[6], but varies with the diagnostic tool employed.[1;2;7]

Complaints of uraemia may overlap with somatic complaints of depression, thereby hampering screening for depression.[8;9] Inclusion of such overlapping somatic symptoms in screening methods for depression may therefore not be preferable.

Self-report rating scales are a simple way for screening of depression. Two well-known self-report rating scales are Hospital Anxiety and Depression Scale (HADS)[10] and Beck Depression Inventory (BDI).[11] HADS contains an anxiety subscale (anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A), seven items with a score from 0 to 21) and depressions subscale (depression subscale of the Hospital Anxiety and Depression Scale (HADS-D), seven items with a score from 0 to 21). BDI contains 21 items with a total score from 0 to 63. HADS and BDI take 2–5 min to complete. It will take a researcher maximally 2 min per questionnaire to score. The questionnaires are widely available via Internet and/or paper versions. As far as we are aware there are no costs involved for the use of these questionnaires.

Both scales measure depression. An important difference between the two scales is that BDI measures both cognitive and somatic symptoms of depression.[11] HADS, on the other hand, was specially developed for somatic ill patients and avoids inclusion of somatic items of depression. HADS measures predominantly cognitive and anxiety symptoms of depression.[10]

HADS has proven to be a valid instrument for use in somatic patients[12-17] as well as in the general population.[18] It has been suggested that HADS may be a suitable instrument for the assessment of anxiety and depression in ESRD patients.[19] However, there have been questions on the use of HADS in patients with ESRD treated with peritoneal dialyses (PD).[20] Another study suggests that although HADS could be used for screening of depression, more research is necessary to determine its validity.[21] Also, a recent study compared HADS with a gold standard for an anxiety disorder in ESRD patients but the use of the HADS as a screening tool for anxiety in patients with ESRD is questionable.[22] As yet, HADS has never been validated as a screening measure for detecting depression in ESRD patients.

BDI is validated in several patients groups[12;17;23;24] and three studies validated BDI in ESRD patients.[25-27] The aim of this study is to validate HADS as a screening measure for detecting depression in ESRD and to compare the outcome with the validation data of BDI.

## METHOD

### Participants

All patients with ESRD who were treated with haemodialysis (HD) or PD in the Sint Lucas Andreas Hospital in Amsterdam between February 2008 and June 2008 were eligible for participation in this study. Patients who were unable to read or understand the Dutch language were excluded from this study.

### Design

To validate both self-report rating scales, a structured interview called the Mini International Neuropsychiatric Interview (MINI)[28] was used. This interview is based on the Diagnostic and Statistical Manual – Fourth Edition criteria, and was used as gold standard. The diagnosis major depressive episode based on the MINI was compared with the outcome of both self-report rating scales. Major depressive episode was diagnosed if participants fulfilled at least one core symptom (depressed mood or anhedonia) and three additional criteria within the last 2 weeks.

### Procedure

All patients were asked to fill out both HADS and BDI self-report rating scales. HD patients did so while receiving hospital-based treatment. The PD patients were asked to fill out the rating scales while visiting the out-patient clinic of the dialysis department.

Between 1 and 7 days after completing the questionnaires, all patients returned to the hospital for the diagnostic interview. These interviews were carried out by a medical resident (W. L. L.) who was extensively trained in the MINI by a psychiatrist (A. H.). Both the medical resident and the psychiatrist were blinded for the outcome of HADS and BDI. All individual MINI interviews were reviewed by A. H. At random, in 1:7 patients, MINI interviews were performed by both the medical resident (W. L. L.) and the psychiatrist (A. H.). Inter-rater reliability proved optimal (100%).

This study was approved by the local ethical committee. All patients gave written informed consent before participation.

### Statistical analysis

To determine the validity of HADS and BDI, an optimal cut-off score was detected using a receiver operating characteristics (ROC) curve. This curve plots the sensitivity against the '1-specificity'. The differentiating value of a diagnostic test is optimal when a cut-off value is chosen at the point where the ROC curve is in the nearest left upper corner. We choose that cut-off in order to minimize the total of false positive and false negative misdiagnoses. Also the area under the curve (AUC) was determined to give a judgment of diagnostic accuracy of HADS and BDI. In addition, positive predictive values (PPV), negative predictive values (NPV), positive likelihood ratio (+LR), and negative likelihood ratio (-LR) were measured for the optimal cut-off scores. Cronbach's alphas were calculated as a measure of internal consistency. Differences between-groups were analysed by using Mann–Whitney U tests. The p values $< 0.05$ were considered to be statistically significant. The results were analysed by means of the Statistical Package for Social Sciences release 15.0.

## RESULTS

Between February 2008 and June 2008, 130 patients were receiving treatment in the dialyses department of the Sint Lucas Andreas Hospital. One hundred and two patients were treated with HD and 28 with PD. Twenty-five of the HD and 11 of the PD patients were not eligible for participation because they could not speak or understand the Dutch language. Two HD patients died before they could be included and one patient was not eligible for participation because of documented psychological retardation. Two PD patients were to severely ill to participate.

Of the remaining 74 HD patients, 51 agreed to sign consent and of the remaining 15 PD patients, 11 agreed to sign consent. In total, 62 patients agreed to participate in this study and 27 refused participation. Baseline characteristics of all patients are shown in Table 1. Significant differences between both treatment groups were found for albumin, parathyroid hormone (PTH), and residual renal function. The other differences between the patients groups were statistically not significant.

**Table 1.** Demographic, psychiatric and clinical characteristics of included ESRD patients (N = 62).

| | **All patients (± SD) (N = 62)** | **Haemodialysis (± SD) (N = 51)** | **Peritoneal dialysis (± SD) (N =11)** |
|---|---|---|---|
| Demographic characteristics | | | |
| Age (years) | 63.5 ± 14.9 | 63.2 ±15.7 | 64.8 ± 11.7 |
| Male gender (%) | 53.2 | 64.6 | 36.4 |
| Dutch ethnicity (%) | 64.5 | 57.1 | 81.8 |
| Living alone (%) | 48.4 | 66.3 | 63.6 |
| Living together or married (%) | 51.6 | 80.5 | 36.4 |
| Employment (%) | 12.9 | 18.5 | 9.1 |
| | | | |
| Psychiatric characteristics | | | |
| Previous depression (%) | 9.7 | 7.8 | 18.2 |
| Use of anti-depressants (%) | 3.2 | 2.0 | 9.1 |
| | | | |
| Causes of ESRD | | | |
| Diabetes Mellitus | 21.0 | 21.6 | 18.2 |
| Hypertension | 21.0 | 23.5 | 9.1 |
| Other | 59.7 | 56.9 | 72.7 |
| | | | |
| Treatment characteristics | | | |
| Number of active somatic diagnosis | 2.4 ± 1.8 | 2.4 ± 1.9 | 2.3 ± 1.1 |
| Number of medications | 9.7 ± 3.3 | 9.6 ± 3.3 | 10.3 ± 3.4 |
| | | | |
| Biochemical parameters | | | |
| Haemoglobin (mmol/l) | 7.4 ± 0.8 | 7.4 ± 0.9 | 7.5 ± 0.8 |
| Albumin (mmol/l) | 40.0 ± 5.5 | 40.9 ± 5.2* | 35.9 ± 5.3* |
| Phosphate (mmol/l) | 1.66 ± 0.49 | 1.68 ± 0.52 | 1.57 ± 0.25 |
| PTH (pmol/l) | 27.7 ± 28.9 | 30.7 ± 30.6* | 14.2 ± 12.9* |
| | | | |
| Renal parameters | | | |
| Time on dialysis (months) | 46 ± 65 | 51 ± 71 | 23 ± 17 |
| Residual renal function (ml/min) | 2.3 ± 3.3 | 1.7 ± 2.5* | 5.0 ± 4.8* |

ESRD, End-Stage Renal Disease; SD, Standard Deviation; PTH, parathyroid hormone.
* Difference statistically significant -> $p < 0.05$.

All 62 patients completed HADS and 61 patients completed BDI. All patients who completed HADS or BDI were interviewed by means of the MINI. Twenty-one patients (34%) met criteria for depression.

ROC curves show the optimum cut-off scores of HADS and BDI for detecting a depressive episode according to the MINI (Figure 1). For the HADS-A subscale, the optimum cut-off score was 7/8 (sensitivity = 47.6%; specificity = 90.2%; PPV = 47.6%; NPV = 90.2%)

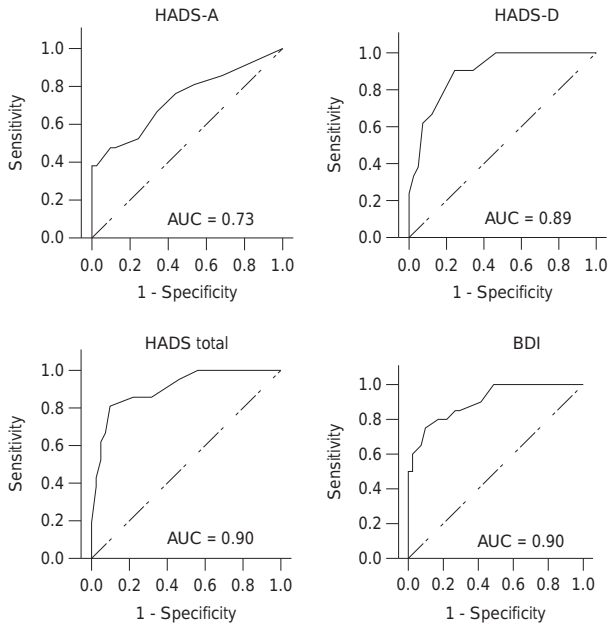


**Figure 1.** ROC curve of the HADS-A, HADS-D, HADS total, and BDI.
AUC, area under the curve; BDI, Beck Depression Inventory; HADS-A, anxiety subscale of the Hospital Anxiety and Depression Scale; HADS-D, depression subscale of the Hospital Anxiety and Depression Scale; HADS total, total score of the Hospital Anxiety and Depression Scale.

and the AUC was 0.73. For the HADS-D subscale, the optimum cut-off value was 6/7 (sensitivity = 90.5%; specificity = 75.6%; PPV = 85.7%; NPV = 75.6%) and the AUC was 0.89. For the HADS total score, the optimum cut-off score was 12/13 (sensitivity = 81.0%; specificity = 90.2%; PPV = 80.9%; NPV = 90.2%) and the AUC was 0.90. For the BDI total score, the optimum cut-off score was 13/14 (sensitivity = 75.0%; specificity = 90.2%; PPV = 75.0%; NPV = 90.2%) and the AUC was 0.90.

A +LR and -LR was also determined. The HADS-A had a +LR of 4.86 and a -LR of 0.58. The HADS-D had a +LR of 3.71 and a -LR of 0.13. The HADS total score had a +LR of 8.27 and a -LR of 0.21. The BDI had a +LR of 7.65 and a -LR of 0.28. The results are shown in Table 2.

The average score on HADS-A was 6.2 (SD = 4.6, range 0–14) for depressed and 2.5 (SD = 2.5, range 0–8) for not depressed patients. The average score on HADS-D was 9.6 (SD = 3.8, range 4–19) for depressed and 3.6 (SD = 2.9, range 0–11) for not depressed patients. The average score on HADS total score was 15.8 (SD = 5.9, range 6–29) for depressed and 6.1 (SD = 4.7, range 0–19) for not depressed patients. The average score

**Table 2.** Screening abilities at optimal cut-off values of the HADS-A subscale, HADS-D subscale, HADS total score, and the BDI total score.

| | HADS-A | HADS-D | HADS total | BDI |
|---|---|---|---|---|
| | (N = 62) | (N = 62) | (N = 62) | (N = 61) |
| Optimal cut-off point | ≥ 7 | ≥ 6 | ≥ 12 | ≥ 13 |
| Sensitivity | 47.6 | 90.5 | 81.0 | 75.0 |
| Specificity | 90.2 | 75.6 | 90.2 | 90.2 |
| +LR | 4.86 | 3.71 | 8.27 | 7.65 |
| -LR | 0.58 | 0.13 | 0.21 | 0.28 |
| PPV | 47.6 | 85.7 | 80.9 | 75.0 |
| NPV | 90.2 | 75.6 | 90.2 | 90.2 |
| AUC | 0.73 0.59–0.88* | 0.89 0.82–0.97* | 0.90 0.83–0.98* | 0.90 0.83–0.98* |

AUC, area under the curve; BDI, Beck Depression Inventory; HADS total, total score of the Hospital Anxiety and Depression Scale; HADS-A, anxiety subscale of the Hospital Anxiety and Depression Scale; HADS-D, Depression subscale of the Hospital Anxiety and Depression Scale; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.
* Ninety-five per cent confidence interval.

on BDI was 17.9 (SD = 7.9, range 7–35) for depressed and 6.5 (SD = 4.3, range 0–16) for not depressed.

All differences between depressed and not depressed patients using HADS and BDI (sub) scores were statistically significant ( $p < 0.0001$). The results of the self-report rating scales are shown in Table 3. The internal consistency was high for all scales. Cronbach's alpha was 0.83 (HADS-D), 0.80 (HADS-A), 0.85 (HADS total score), and 0.85 (BDI).

**Table 3.** Result of the HADS-A subscale, HADS-D subscale, and HADS total score with and without a depressive disorder by diagnosis of the MINI.

| | Depressed (± SD) (N = 21)* | Not depressed (± SD) (N = 41) |
|---|---|---|
| HADS-A | 6.2 ± 4.6 | 0.71 – 0.78 |
| Range | 0 - 14 | 0 - 8 |
| HADS-D | 9.6 ± 3.8 | 3.6 ± 2.9 |
| Range | 4 - 19 | 0 - 11 |
| HADS total | 15.8 ± 5.9 | 6.1 ± 4.7 |
| Range | 6 - 29 | 0 - 19 |
| BDI | 17.9 ± 7.9 | 6.5 ± 4.3 |
| Range | 7 - 35 | 0 - 16 |

BDI, Beck Depression Inventory; HADS total, total score of the Hospital Anxiety and Depression Scale; HADS-A, anxiety subscale of the Hospital Anxiety and Depression Scale; HADS-D, depression subscale of the Hospital Anxiety and Depression Scale; MINI, Mini International Neuropsychiatric Interview; SD, standard deviation.
* BDI (N = 20).

## DISCUSSION

The aim of this study was to validate HADS and BDI self-report rating scales as screening measures for the detection of depression in ESRD patients. HADS, which has not previously been validated in this patient group, was compared with BDI, which was validated three times in ESRD patients.[25-27] Both scales were compared to the diagnosis major depressive episode based on the MINI.

Results show different cut-off values for the self-report scales. The optimal cut-off value for HADS is ≥ 12 (sensitivity: 81.0; specificity: 90.2) and for BDI ≥ 13 (sensitivity: 75.0; specificity: 90.2). The AUC for HADS is 0.90 and for BDI is 0.90. Any scale with the largest AUC is superior for distinguishing between depressed and non-depressed patients. Conclusively, there is not a difference between HADS and BDI.

As opposed to BDI, HADS was originally developed for somatically ill patients.[10] Although the original author had not intended to combine the two subscales of HADS, the results show that the combination of the two scales gives better results although the difference was statistical not significant. For daily clinical practice, it is important to be able to clarify whether symptoms of anxiety are related to a current depressive episode. When using previously reported cut-off values for HADS in our study group, results would not be optimal. The generally used cut-off. Greater than or equal to 15 for HADS total score[18], in comparison with ≥ 12 found in our study, would result in a decreased sensitivity (52.4%) and an increased specificity (95.1%). Therefore, we recommend using the cut-off values found in our study.

BDI has been validated in this patient group several times. Cut-off scores found in these studies vary from ≥ 13 (our study), ≥ 14, ≥ 15, and ≥ 16.[25-27] All cut-off scores give adequate sensitivity, specificity, and AUC for use of the BDI in ESRD patients. Therefore, it is difficult to recommend which BDI cut-off value is the best to use.

A common reason to use a self-report scale is screening. For screening purposes, a high sensitivity and NPV are more important than a high specificity and PPV. HADS total score has a sensitivity of 81.0% and a NPV of 90.2%. BDI has a sensitivity of 75.0% and NPV of 90.2%. When trying to optimize sensitivity and NPV by choosing lower cut-off values (HADS total = 5/6; BDI = 6/7), specificity would decrease to low levels (HADS total = 43.9%; BDI = 51.2%). We conclude that both HADS and BDI rating scales are comparable for screening purposes in ESRD patients.

Apart from screening purposes, self-report rating scales can also be used as a diagnostic evidence tool. To this end, a high specificity and PPV are most important. The prevalence of the disorder in the population is a factor to determine the PPV. Due to the relatively high prevalence of depression, PPV of both HADS and BDI are comparable to NPV and relatively high. Both self-report rating scales are therefore not adequate diagnostic tools. In addition, when validating a test against a gold standard it is important to emphasize the significance of the likelihood ratios (LRs). The LRs, unlike the NPV and PPV, do not depend on the prevalence of the disease. LRs express the odds that a given cut-off of the test would be expected in a patient with depression as opposed to without a depression.[29] By knowing the pre-test probability, the LRs predict the post-test probability of depression in a patient based on their score of the test. HADS total score and BDI show much higher +LR then HADS subscores, which makes HADS total sore and BDI acceptable screening tools.

Following the screening process, further diagnostic work up and if appropriate treatment should be offered to those patients scoring above the cut-off. For this purpose, the patients should be referred to a psychiatrist or clinical psychologist for diagnosis and treatment. Preferred treatment can be either pharmacotherapy and/or cognitive therapy.[30;31]

Limitations of this study are the sample size and the combination of dialysis modalities in a single centre study. However, most patient characteristics (Table 1) show that HD patients and PD patients are comparable patient groups. Nevertheless, different dialyses modalities may influence patient's perception of daily life. Finally, it is difficult to generalize our findings because this study does not include data regarding those patients who did not give consent.

In sum, the HADS self-report rating scale, which does not have somatic items, has been demonstrated to be a valid screening tool for detecting depression in ESRD patients and performs equally well as the BDI, a self-report rating scale which includes somatic items.

## REFERENCES


(1) Kimmel PL. Depression in patients with chronic renal disease: what we know and what we need to know. J Psychosom Res 2002;53:951-956.

(2) Lopes AA, Albert JM, Young EW. Screening for depression in haemodialysis patients: associations with diagnosis, treatment, and outcomes in the DOPPS. Kidney Int 2004;66:2047-2053.

(3) Kimmel PL, Peterson RA, Weihs KL et al. Multiple measurements of depression predict mortality in a longitudinal study of chronic haemodialysis outpatients. Kidney Int 2000;57:2093-2098.

(4) Kimmel PL, Patel SS, Peterson RA. Depression in African-American patients with kidney disease. J Natl Med Assoc 2002;94:92S-103S.

(5) Kimmel PL, Weihs K, Peterson RA. Survival in haemodialysis patients: the role of depression. J Am Soc Nephrol 1993;4:12-27.

(6) Wuerth D, Finkelstein SH, Finkelstein FO. The identification and treatment of depression in patients maintained on dialysis. Semin Dial 2005;18:142-146.

(7) Lopes AA, Bragg J, Young E. Depression as a predictor of mortality and hospitalization among haemodialysis patients in the United States and Europe. Kidney Int 2002;62:199-207.

(8) Cukor D, Peterson RA, Cohen SD, Kimmel PL. Depression in end-stage renal disease haemodialysis patients. Nat Clin Pract Nephrol 2006;2:678-687.

(9) O'Donnell K, Chung JY. The diagnosis of major depression in end-stage renal disease. Psychother Psychosom 1997;66:38-43.

(10) Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361-370.

(11) Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-571.

(12) Aben I, Verhey F, Lousberg R, Lodder J, Honig A. Validity of the beck depression inventory, hospital anxiety and depression scale, SCL-90, and hamilton depression rating scale as screening instruments for depression in stroke patients. Psychosomatics 2002;43:386-393.

(13) Herrmann C. International experiences with the Hospital Anxiety and Depression Scale—a review of validation data and clinical results. J Psychosom Res 1997;42:17-41.

(14) Kuijpers PM, Denollet J, Lousberg R, Wellens HJ, Crijns H, Honig A. Validity of the hospital anxiety and depression scale for use with patients with noncardiac chest pain. Psychosomatics 2003;44:329-335.

(15) Poole NA, Morgan JF. Validity and reliability of the Hospital Anxiety and Depression Scale in a hypertrophic cardiomyopathy clinic: the HADS in a cardiomyopathy population. Gen Hosp Psychiatry 2006;28:55-58.

(16) Stafford L, Berk M, Jackson HJ. Validity of the Hospital Anxiety and Depression Scale and Patient Health Questionnaire-9 to screen for depression in patients with coronary artery disease. Gen Hosp Psychiatry 2007;29:417-424.

(17) Strik JJ, Honig A, Lousberg R, Denollet J. Sensitivity and specificity of observer and self-report questionnaires in major and minor depression following myocardial infarction. Psychosomatics 2001;42:423-428.

(18) Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 2002;52:69-77.

(19) Martin C.R., Thompson D.R. The hospital anxiety and depression scale in patients undergoing peritoneal dialysis: Internal and test-retest reliability. Clinical Effectiveness in Nursing 2002;6:78-80.

(20) Martin C.R., Thompson D.R. Utitlity of the Hospital Anxiety and Depression Scale in patients with end-stage renal disease on continuous ambulatory peritoneal dialysis. Psychology, Health and Medicine 1999;4:369-376.

(21) Martin CR, Tweed AE, Metcalfe MS. A psychometric evaluation of the Hospital Anxiety and Depression Scale in patients diagnosed with end-stage renal disease. Br J Clin Psychol 2004;43:51-64.

(22) Cukor D, Coplan J, Brown C et al. Anxiety disorders in adults treated by haemodialysis: a single-center study. Am J Kidney Dis 2008;52:128-136.

(23) Richter P, Werner J, Heerlein A, Kraus A, Sauer H. On the validity of the Beck Depression Inventory. A review. Psychopathology 1998;31:160-168.

(24) Steer RA, Cavalieri TA, Leonard DM, Beck AT. Use of the Beck Depression Inventory for Primary Care to screen for major depression disorders. Gen Hosp Psychiatry 1999;21:106-111.

(25) Craven JL, Rodin GM, Littlefield C. The Beck Depression Inventory as a screening device for major depression in renal dialysis patients. Int J Psychiatry Med 1988;18:365-374.

(26) Hedayati SS, Bosworth HB, Kuchibhatla M. The predictive value of self-report scales compared with physician diagnosis of depression in haemodialysis patients. Kidney Int 2006;69:1662-1668.

(27) Watnick S, Wang PL, Demadura T, Ganzini L. Validation of 2 depression screening tools in dialysis patients. Am J Kidney Dis 2005;46:919-924.

(28) Overbeek T., Schruers K, Griez E. Dutch Translation of the Mini International Neuropsychiatric Interview version 4.4. Maastricht 1997.

(29) Sackett D., Haynes R., Guyatt G., Tugwell P. Clinical epidemiolgy: A basic science for clinical medicine (2nd ed., pp. 77085, 119-125). Philidelphia. PA: Lippincott Williams Wilkins, 1991.

(30) Duarte PS, Miyazaki MC, Blay SL. Cognitive-behavioral group therapy is an effective treatment for major depression in haemodialysis patients. Kidney Int 2009;76:414-421.

(31) Wuerth D, Finkelstein SH, Kliger AS, Finkelstein FO. Chronic peritoneal dialysis patients diagnosed with clinical depression: results of pharmacologic therapy. Semin Dial 2003;16:424-427.