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Self-reported depression symptoms in haemodialysis patients: Bi-factor structures of two common measures and their association with clinical factors

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Running Head: Measuring self-reported depression in HD patients

ABSTRACT

Objective: To validate the factor structure of two common self-report depression tools in a large sample of haemodialysis (HD) patients and to examine their demographic and clinical correlates, including urine output, history of depression and transplantation.

Methods: Factor structures of the Beck Depression Inventory (BDI-II) and Patient Health Questionnaire (PHQ-9) were evaluated using confirmatory factor analysis (CFA). Data was utilised from the screening phase (n=709) of a placebo-controlled feasibility randomised control trial (RCT) of sertraline in HD patients with mild to moderate Major Depressive Disorder. Alternative factor models including bi-factor models for the BDI-II and PHQ-9 were evaluated. Coefficient omega and omega-hierarchical were calculated.

Results: For both measures, bi-factor measurement models had the overall best fit to the data, with dominant general depression factors. Omega-hierarchical for the general BDI-II and PHQ-9 factors was 0.94 and 0.88 respectively. Both general factors had high reliability (coefficient omega = 0.97 and 0.94 respectively) and explained over 85% of the explained common variance within their respective models. BDI-II and PHQ-9 general depression factors were negatively associated with age and urine output and positively with a history of depression, antidepressant use within the last 3 months, and a history of failed transplantation. In adjusted regression models, age, urine output and a history of depression remained significant.

Conclusions: These data suggest that both the BDI-II and PHQ-9 are sufficiently unidimensional to warrant the use of a total score. Younger age, lower urine output and a history depression appear consistent correlates of depression severity among HD patients.

INTRODUCTION

Efforts to develop a core set of outcomes for haemodialysis (HD) trials are well underway with both clinical and patient reported outcomes being identified as important [1]. It is well established that depression remains one of the most common symptoms among individuals with End-Stage Kidney Failure (ESKF), with 30-40% of patients experiencing significant depressive symptomology [2]. Depression symptoms are associated with adverse outcomes among dialysis patients with increased mortality being the most consistently reported [3–5]. Evaluating which self-report depression tools are most suited for regular screening and serving as appropriate outcome measures in intervention trials is therefore warranted.

Two depression measures, the Beck Depression Inventory (BDI-II) [6] and the Patient Health Questionnaire-9 (PHQ-9) [7], have been commonly used to evaluate depression symptoms among HD patients. Whilst these measures appear valid within this clinical population, only a few studies in dialysis patients have examined their underlying factor structures [8,9]. Within the renal literature there remains a tendency to consider cognitive/affective symptoms vs. somatic symptoms of depression, in an attempt to try and separate physical symptoms that might overlap with kidney disease. Despite this rationale to reduce criterion contamination, physical and cognitive/affective symptoms often correlate highly. Given this, bi-factor measurement models might be more appropriate in this setting, allowing underlying general and subgroup depression factors to be identified and used in research as outcome measures.

Within kidney patients, two studies have reported that for both the BDI-II and PHQ-9, bi-factor measurement models provide the best fitting and most conceptually acceptable interpretation [10,11]. In both of these studies, the general depression factors explained over 73% and 81% of the common variance between items for the PHQ-9 and BDI-II respectively, with smaller subgroup cognitive and somatic factors explaining less than 10% of the explained

variance. From this data it would appear that both tools are sufficiently unidimensional to warrant the use of a total severity depression score. However, further evaluation of these screening tools is warranted in order to better understand their psychometric performance in kidney patients and identify appropriate underlying latent factors. Accordingly, the aim of this study was to examine the underlying latent factor structures of the BDI-II and PHQ-9 in a large sample of HD patients using Confirmatory Factor Analysis (CFA). Depression screening data used to select patients into a multicentre placebo controlled feasibility randomised control trial (RCT) of sertraline in HD patients with mild to moderate Major Depressive Disorder [12,13] was used here. In line with past findings we hypothesized that bi-factor models, with dominant general depression factors would provide the best fitting and most appropriate interpretation of the BDI-II and PHQ-9. Since this was a secondary data analysis, we also had the opportunity to explore demographic and clinical correlates of the identified latent depression factors.

MATERIALS AND METHODS

Design: BDI-II and PHQ-9 depression screening data (n=709) used to select patients into a multicentre placebo controlled feasibility randomised control trial (RCT) of sertraline in HD patients with mild to moderate Major Depressive Disorder [12,13] were analysed here (trial registration number: ISRCTN06146268).

Patients: Prevalent HD patients treated across five UK dialysis centres were screened for depression using both the BDI-II and PHQ-9. Patients were eligible for screening providing they had been receiving HD for at least 3 months, were over 18 years of age and could speak and read English well enough to complete the screening measures. 1353 patients were approached for depression screening, with 243 excluded due to inability to read or understand English. Of the remaining 1110, 64% consented to be screened (n=709). The majority of the

sample was male (63.3%) with a median dialysis vintage of 33 months (inter quartile range = 59). The average age was 64.1 (16.4) years. Mean depression scores at screening were 13.5 (s.d= 11.4) and 6.9 (s.d=6.2) for the BDI-II and PHQ-9 respectively. 33% (95% confidence interval 30 – 37) had a BDI-II ≥16 and 28 % (95% confidence interval 25 – 31) scored ≥ 10 on the PHQ-9. A self-reported past history of depression was noted in 25% of patients. Antidepressant use within the 3 months prior to screening was 11%. 16% of the sample had at least one failed transplant, with the remaining 84% with no history of transplantation. A summary of clinical factors is provided in table 1.

Clinical and demographic factors: Presence of comorbidities (diabetes, heart disease, stroke, cancer, limb amputation, liver disease, lung disease), dialysis vintage (length of time on HD, months), haemoglobin (g/L), serum albumin (g/L), the number of past transplants (actual number and recoded as history of failed transplantation yes=1/no=0), urine output (passing more than cup per day; self-reported yes=1/no=1) and dialysis treatment adequacy (Kt/V) were collected from medical records. C-reactive protein (CRP, mg/L) was only available in a subset of the sample (n=396) since it is not commonly measured as part of routine practice. Due to its skewed distribution it was handled here as categorical variable using a clinical cut-off (CRP>5 mg/L). Self-reported clinical history of depression and antidepressant use within the last 3 months (on an antidepressant or not) was collected via a research nurse and was coded as yes=1, and no=1 for both variables. Demographic factors were collected from a questionnaire including age, gender and ethnicity (white vs. non-white).

Statistical analysis: CFA was used to evaluate the factor structures of the BDI-II and PHQ-9 using Weighted Least-Squares with Mean and Variance adjustment (WLSMV) estimation. Missing data was small (less than 2% for all items). Given this and the estimator

used (WLSMV) available case data was used in the models. Alternative one, two and bi-factor models were tested for both measures. In the bi-factor PHQ-9 model, all 9 items were loaded onto a general depression factor (figure 1). Two smaller group factors – somatic (3-items) and affective/cognitive (6-items) were also specified. Correlations between all latent factors were fixed to zero and variances of the latent factors fixed. A two factor PHQ-9 model comprising of correlated physical (3-items) and cognitive/somatic factors (6-items) was tested, in line with past analyses of the PHQ-9 in other clinical settings [14]. A one factor PHQ-9 model was also evaluated with all items loaded onto a single depression factor.

A bi-factor BDI-II model based upon Ward [15], and supported in past studies of HD [10] and myocardial infarction patients [16], was tested (figure 2). This model contains a general factor with all 21 items loaded upon it, and two smaller cognitive (8 items) and somatic (5 items) group factors. A two factor BDI-II model comprising of correlated cognitive-affective and somatic factors was also evaluated [6]. A one factor model was also evaluated with all items loaded onto a single depression factor.

Assessment of goodness-of-fit was based upon a confirmatory fit index (CFI) >.95, root mean squared error of approximation (RMSEA) <.08, and the Tucker-Lewis index (TLI) >.95 [17]. Reliability of the total and subscale scores was assessed using the omega index (coefficient omega [ω]), accompanied by omega-hierarchical, which is an indicator of the saturation of a multidimensional scale by a general factor [18,19]. For the subgroup factors relative omega was computed which controls for the part of the reliability attributable to the general factor. Demographic and clinical correlates of the identified general latent depression factors were also explored using univariate correlational analysis. Variables that demonstrated a significant univariate association with the general latent depression factors were then examined together in adjusted regression models which also controlled for gender and dialysis vintage. For these adjusted regression models unstandardized and standardised model

coefficients are presented accompanied by 95% confidence intervals (CI). The same adjusted models were rerun for the cognitive/affective and somatic subgroup factors for both the BDI-II and PHQ-9. All analyses were conducted in MPlus version 7.3.

RESULTS

CFA: A summary of competing factor models for the BDI-II and PHQ-9 is shown in table 2. The correlation between the cognitive/affective and somatic factors was high within both measures (BDI-II r=0.85, p<0.01; PHQ-9 r=0.89, p<0.01). All of the examined factor models had relatively good fit, with the bi-factor models having marginally better fit as indicated by their fit indices. Figures 1 and 2 show the bi-factor models for the BDI-II and PHQ-9 respectively, accompanied by their standardised factor loadings (with standard errors). All factor loadings on the general factor were above 0.50 and all factor loadings across the general and subgroup factors were significant (all p-values ≤0.01).

For the BDI-II the general factor accounted for 88% of the explained common variance and had high reliability (coefficient omega = 0.97). The smaller subgroup cognitive and somatic factors accounted for 6.0% and 5.0% of the explained variance respectively. Reliability of the subgroup factors was high (coefficient omega = 0.92 and 0.95 respectively), reducing to 0.12 and 0.15 after controlling for the part of the reliability attributable to the general depression factor. Omega-h for the general depression factor was 0.94 indicating that the total score across all items included in the scale predominantly reflects a general depression factor.

The general PHQ-9 factor accounted for 85% of the explained common variance and had high reliability (coefficient omega = 0.94). The subgroup cognitive/affective and somatic factors accounted for 11.3% and 3.4 % of the explained variance respectively, and also had high reliabilities (coefficient omega = 0.93 and 0.79 respectively). After controlling for the part of the reliability attributable to the general depression factor the subgroup coefficients drop to

0.11 and .10, respectively. Omega hierarchical was 0.88, again indicating that for the PHQ-9, the total score across all items predominantly reflects a general depression factor.

In summary, these data suggest that both the BDI-II and PHQ-9 are sufficiently unidimensional to warrant the use of a total score. As expected both general latent factors correlated highly (r=0.9, p<0.01).

Correlates of the BDI-II and PHQ-9 general factors:

Both general factors negatively correlated with age (standardized estimate [correlation]= -0.24, p<0.01 and -0.184, p<0.01). Urine output was negatively associated with both general depression factors (see table 3). A self-reported history of depression, having had a failed transplant and antidepressant use during the past 3 months were all positively associated with both general depression factors (table 3). Neither depression general factor was associated with gender, ethnicity, comorbidities, Haemoglobin, serum albumin, CRP>5 mg/L, dialysis vintage, the number of past transplants and Kt/V.

In adjusted regression models that controlled for all the variables shown in table 3 and also gender and dialysis vintage; age, urine output and a self-reported history of depression remained significantly associated with both general factors.

Correlates of the BDI-II and PHQ-9 subgroup factors:

The cognitive/affective and somatic subgroup factors from both the BDI-II and PHQ-9 were regressed upon the variables shown in table 3 (in separate analyses for both measures). For the BDI-II, the adjusted models revealed significant associations between the cognitive/affective subgroup factor with age (unstandardized estimate = -0.04, 95% CI -0.05, -0.02; p<0.01) and a past history of depression (unstandardized estimate = 1.9, 95% CI 1.30, 2.50; p<0.01) but not with failed transplantation, antidepressant use or urine output. The

somatic subgroup factor was associated with urine output (unstandardized estimate = -0.60, 95% CI -0.92, -0.27; p<0.01) and a past history of depression (unstandardized estimate = 0.96, 95% CI 0.48, 1.43 p<0.01) but not with failed transplantation, antidepressant use or age.

For the PHQ-9, the somatic subgroup factor was only associated with past history of depression (unstandardized estimate =0.62, 95% CI 0.36, 0.89; p<0.01). The cognitive/affective subgroup factor was associated with urine output (unstandardized estimate = -0.13, 95% CI -0.24, -0.02; p<0.05) and a past history of depression (unstandardized estimate = 0.34, 95% CI 0.21, 0.47 p<0.01).

DISCUSSION

Depression is uncontroversially present in a significant proportion of patients on haemodialysis [2]. Measuring depression routinely and offering appropriate evidenced based interventions is therefore a clinical priority. In an attempt to further evaluate two common depression screening tools, we found that both the BDI-II and PHQ-9 have dominant general depression factors and thus are sufficiently unidimensional to warrant a total severity score. These results support previous work [10,11] and suggest that both measures have high reliably for a general factor. Either measure would be suitable for regular depression screening among dialysis patients, or as outcome measures in clinical trials. The PHQ-9 might well be preferred for its relative brevity. If researchers and clinicians wish to have a broader measure of distress, then the Patient Health Questionnaire Anxiety and Depression Scale (PHQ-ADS) [20] (which a composite measure of depression and anxiety symptoms using the Patient Health Questionnaire-9 and Generalised Anxiety Disorder Scale [21]) is recommended [11].

With regards to correlates of depression, our findings support past data revealing a negative relationship between age and depression symptoms among dialysis patients [22]. Furthermore, we observed an association between urine output and depression symptoms,

findings which replicate a smaller study which showed a negative association between residual renal function and depression symptoms among HD patients [23]. Patients passing less than 1 cup of urine per day by their own estimate, had higher depressive symptoms than those passing more. This may reflect the restrictions imposed on the anuric patient in terms of diet and fluid intake, lack of any residual renal function and the potential for longer hours of dialysis and increased medication. Of course, this association could also be explained by increased somatic symptom reporting in anuric patients. Analysis of the BDI-II subgroup factors partially support this explanation since urine output was associated with the somatic subgroup factor but not the cognitive/affective factor. However, the opposite was evident for the PHQ-9, where the cognitive/affective subgroup factor was associated with urine output but not the somatic factor. This could be the consequence of more somatic items featuring in the BDI-II. Taken together, the association observed between depression severity and urine output is likely the combination of increased somatic symptoms, greater dietary restrictions and treatment related impact. Although longitudinal studies are needed to further examine the relationship between urine output and mood in order to infer causality, it is possible that preserving residual function has some advantages beyond identified clinical outcomes [24]; possibly being beneficial for mental health.

Unsurprisingly having a history of depression was associated with increased depression symptoms in our sample, results with mirror findings in renal transplant recipients [25]. A novel finding of particular interest was the association between depression and failed transplantation. The impact of a failed previous transplant necessitating a return to dialysis on depressive symptoms has been infrequently reported before and only in small numbers [26], the return to haemodialysis especially after a short duration of graft function being associated with depression [27].The current study did not identify if patients had been transplanted pre-emptively or had previously experienced dialysis, but the loss of a transplant had a significant

association with increased depressive symptoms. There are many potential reasons for this, loss of expectation, sense of failure, lack of future prospects for re-transplantation and additional complications arising from immunosuppression. However, this study did not differentiate between live donor recipients or deceased donor recipients, a previous study has shown that even with a functioning transplant recipients of a deceased donor kidney may exhibit more symptoms associated with depression than one from a live donor [28]. In adjusted analyses, the effect of failed transplantation was no longer significant, a likely result of failed transplantation being associated with a history of depression (odds ratio= 1.6, p=0.02). Accordingly, the process of returning to dialysis with a failing transplant and the point at which intervention into depressive symptoms is an area worth exploring further.

This study has some key strengths which include a large sample size and overall completeness of data. However, limitations of this study include the lack of a full psychometric evaluation (including for example test retest validity and testing model invariance over time). Furthermore, the study was restricted to English speaking patients therefore limiting generalizability. Clinical histories of depression and antidepressant treatment were also self-reported by the patients since it was not possible here to verify from clinical records. Furthermore, urine output was also self-reported. We also had limited available demographic information, missing potentially important data such as social economic status. Lastly, correlates of the latent depression general factor were explored cross-sectionally and were limited to clinical data collected from medical records therefore excluding other potentially important clinical and psychological factors [29].

In conclusion the BDI-II and PHQ-9 are sufficiently unidimensional to warrant the use of a total depression score. Younger age, lower urine output and a clinical history of depression appear to be consistent correlates of depression severity among HD patient and should be considered risk factors in this population.

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Table 1: Clinical characteristics.

Variable	Statistic
Heart disease (%)	31.7
Diabetes (%)	33.3
Cancer (%)	10.6
Liver disease (%)	2.4
Lung disease (%)	6.4
Amputation of limbs (%)	3.2
Stroke (%)	8.0
Haemoglobin g/L (mean, s.d)	11.1 (1.2)
Serum Albumin g/L (mean, s.d)	37.4 (4.4)
Dry weight (mean, s.d, kg)	75.5 (18.3)
CRP (>5 mg/L, %)	52%
Kt/V (mean, s.d)	1.4 (0.3)

Table 2: Alternative CFA models for the BDI-II and PHQ-9

Model	Chi-square (df), p-value	Number of free parameters	CFI	TLI	RMSEA
BDI-II					
1-factor	835.7 (189), p<0.01	84	0.963	0.959	0.070
2-factor	633.1 (188), p<0.01	85	0.976	0.972	0.058
Bi-factor	420.9 (176), p<0.01	97	0.986	0.983	0.044
PHQ-9					
1-factor	129.2 (27), p<0.01	36	0.984	0.978	0.073
2-factor	92.6 (26), p<0.01	37	0.989	0.985	0.060
Bi-factor	37.0 (19), p<0.01	45	0.997	0.994	0.040

Root mean squared error of approximation (RMSEA); Confirmatory Fit Index (CFI); Tucker-Lewis index (TLI); Degrees of freedom (df)

Table 3: Unadjusted and adjusted associations with the BDI-II and PHQ-9 general factors.

Variables	BDI-II general factor		PHQ-9 general factor	
	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
Age (years)	-4.0 (-5.30, -2.70)**	-0.01 (-0.02, -0.01)**	-3.0 (-4.3, -1.7)**	-0.01 (-0.02, -0.01)*
Urine output	-0.14 (-0.24, -0.04)**	-0.20 (-0.38, -0.01)*	-0.18 (-0.28, -0.08)**	-0.27 (-0.46, -0.08)**
History of depression	0.54 (0.46, 0.63)**	0.80 (0.56, 1.01)**	0.49 (0.40, 0.58)**	0.75 (0.50, 1.0)**
Anti-depressants use	0.46 (0.35, 0.58)**	0.25 (-0.08, 0.58)	0.41 (0.28, 0.53)**	0.13 (-0.21, 0.46)
Failed transplant	0.19 (0.07, 0.31)**	0.10 (-0.22, 0.42)	0.16 (0.04, 0.29)*	0.10 (-0.22, 0.42)

Estimates shown are unstandardized with 95% confidence intervals in parentheses

[a]adjusted for all the variables listed in the table and also dialysis vintage and gender.

history of failed transplantation (no=0/yes=1); urine output (passing more than cup per day; self-reported no=0/yes=1);

Self-reported clinical history of depression (no=0/yes=1) and antidepressant use within the last 3 months (on an antidepressant no=0/yes=1).
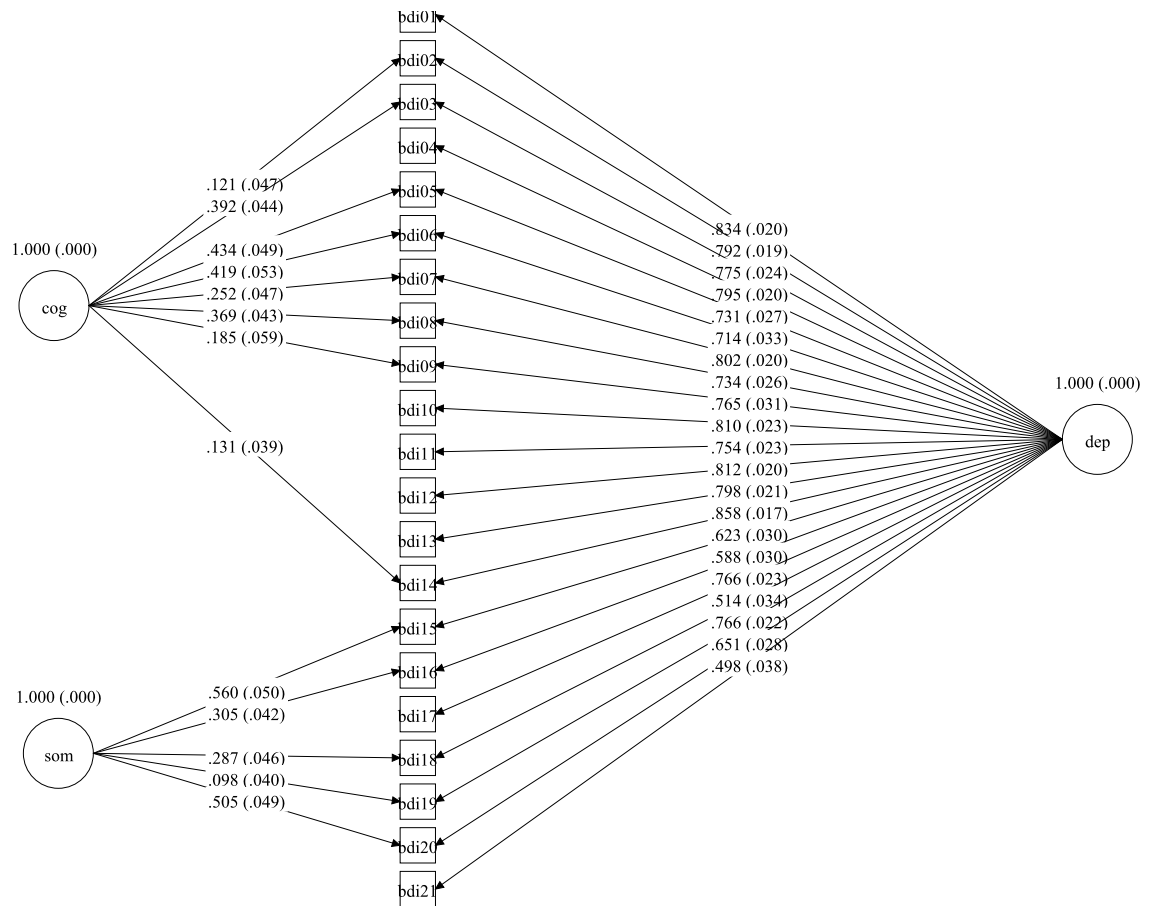
*$p<0.05$

*$p<0.01$

Figure 1: BDI-II bi-factor model (cog: cognitive-affective; som: somatic; dep: general depression factor). Standardised estimates shown.
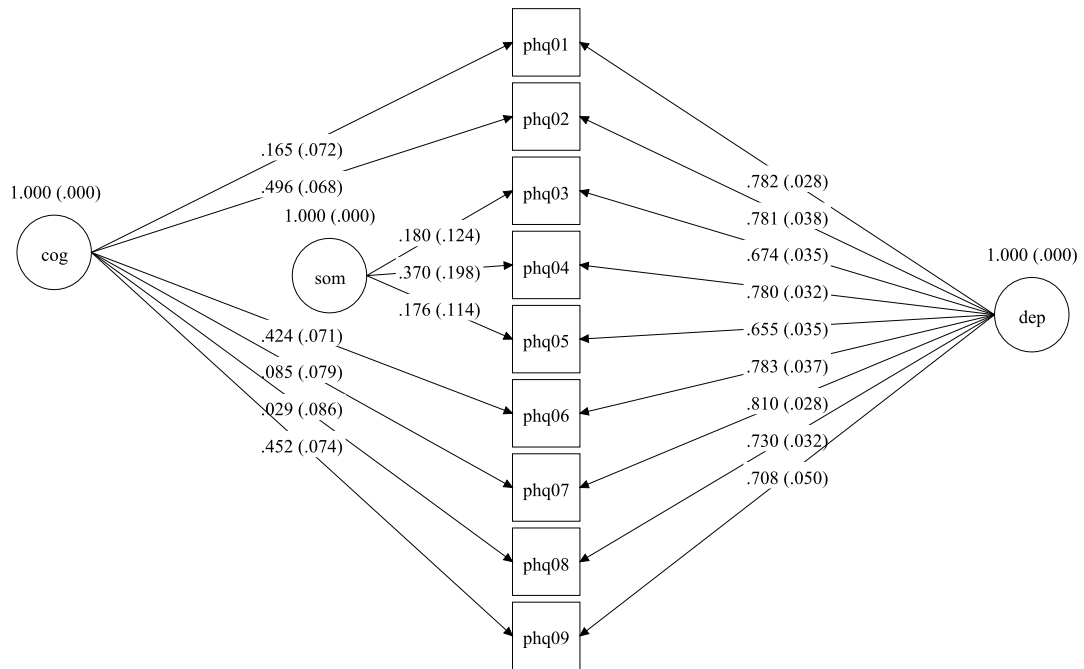
Figure 2: PHQ-9 bi-factor model (cog; cognitive; som: somatic; dep: general depression factor). Standardised estimates shown.