# Post-dialysis recovery time is extended in patients with greater self-reported depression screening questionnaire scores


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Abstract

Introduction

Most patients take time to recover after a haemodialysis session. It has been suggested that recovery time is associated with intra-dialytic hypotension and rapid solute clearances. Other studies have reported a linkage to depression. We investigated the association between recovery time and intra-dialytic hypotension and depression.

Methods

In five UK haemodialysis units, we screened for depressive symptoms using the Beck Depression Inventory-II (BDI-II), Public Health Questionnaire (PHQ-9), and recorded sessional blood pressures and Kt/Vurea.

Findings

701 HD patients were studied; 63.6% male, mean age 64.1±16.6 years, 33.5% diabetic. 24.1% recovered in < 1 hour, 27% 1-4 hours, 15.4% 4-8 hours, 10.7 8-12 hours, and 22.8 after 12 hours. Systolic blood pressure (SBP) fell by ≥20 mmHg in 30.9% post-dialysis, and to <100 mmHg in 7.6%. In multivariate analysis, patients with recovery times >1 hour were more likely to be female, have high self-reported BDI-II scores, a past medical history of depression, and be living without a partner. Longer recovery times were also associated with very low post-dialysis systolic blood pressures (<100 mmHg), and higher body weight. However, the model predicted only 18% of the variation in recovery times. We found no association between recovery times and short- term mortality risk.

Discussion

Prolonged post-dialysis recovery times are associated with higher self-reported depression scores, and very low post-dialysis blood pressure. Future studies investigating changes in dialysis practice and recovery times will need to target strategies to prevent intra-dialytic hypotension and adjust for patient psychological status.

Introduction

Despite the technological advances in haemodialysis (HD)[1] , patients attending for outpatient treatments may suffer hypotension and take time to recover post-dialysis. Symptomatic hypotension is the most common complication of out-patient HD treatments[2] , and intra-dialytic hypotension is now recognised to reduce the blood supply to the heart and other vital organs [3,4] . Changing from standard thrice weekly to shorter daily haemodialysis sessions has been reported to reduce the time to recover from dialysis [5,6].

Although some reports have suggested that dialysis factors are the most important in determining post-dialysis fatigue [7] , others have suggested that patient factors, including age [8] , additional co-morbidity, including cerebrovascular disease [9] , contribute to post-dialysis fatigue [10]. As with many chronic diseases, HD patients have higher rates of self-reported depression [11].

To investigate whether there was an association between the time to recover post-dialysis and depressive symptoms we studied this in a cohort of haemodialysis patients screened for depressive symptoms as part of the ASSERTID study [12], using the Beck Depression Inventory (BDII) [13], and the Patient Health Questionnaire (PHQ-9) [14,15].

## Materials and Methods

### Patients

701 haemodialysis patients attending for outpatient haemodialysis, dialysing under the care of five UK dialysis centres were recruited into a screening trial for depression. Patients over the age of 18 years old who had been receiving haemodialysis for more than 3 months were eligible for inclusion. Patients who could not read and speak English and those with cognitive impairment were excluded according to the Folstein Mini mental status examination [16].

### Data collection

1. Patient demographics were obtained from computerised medical records

2. The following data were collected during the course of a routine haemodialysis session

By questionnaire

i. Depression symptoms - patients completed the BDI-II and PHQ-9 questionnaires

ii. Time taken to recover post-dialysis - by questionnaire – categorised into following time intervals < 1 hour. 1-4 hours, 4-8 hours, 8-12 hours, >12 hours

iii. Co-morbidity – using a validated self-report scale [17] .

iv. Self-report ethnicity

v. Self-reported highest educational achievement

vi. Self-reported living status: including marital and residential status

Clinical data

i. Pre- and post-haemodialysis blood pressure

ii. Target weight.

iii. Intra-dialytic hypotension - was defined as a fall in systolic blood pressure (SBP) ≥20 mmHg or a fall in mean arterial blood pressure (MAP) of ≥ 10 mmHg.

3. Routine biochemical and haematological data

The results of routine monthly investigations were obtained closest to the day on which the questionnaires were completed. Parameters included haemoglobin, serum albumin, calcium, phosphate, and normalized urea clearance (Kt/Vurea).

4. Follow-up data

Patients were followed up for a minimum 12 months after completion of questionnaires. Date of death, transplantation, and transfer to other centres during follow-up were recorded.

## Ethics

All patients provided appropriate informed consent in keeping with the Helsinki agreement, prior to receiving questionnaires. The study received ethical approval (National Research Ethics Service Committee London - Bentham, reference 12/LO/1554), and was registered (ISRCTN06146268).

## Statistical analysis

Data is reported as mean and standard deviation, or median and interquartile range, or percentage and intergroup analysis was by ANOVA, or Kruskal Wallis test, or Chi square analysis with correction for repeated tests and for small numbers, where appropriate. Univariate association was with Spearman correlation. Multivariate logistic analysis was used for determinants of time to recover post haemodialysis including variables significant on univariate analysis <0.1, and those thought to be clinically relevant. Variables were then excluded if not significant, or did not improve model fit, and models were checked for collinearity. Cox proportional models were used for survival analysis. Analyses were performed with Graph Pad Prism (Graph Pad Prism V6.0, San Diego, USA) and SPSS 24 (SPSS 24, University Chicago, Illinois, USA). Statistical significance was taken as $p<0.05$.

Results

709 patients were screened for depression, patients with dementia and those unable to understand English were excluded, and 701 completed the time to recover post-haemodialysis questionnaire, 63.6% male, mean age 64.1±16.6 years. 697 patients completed the PHQ9 questionnaire, 695 the BDI-II. Patient demographics are set out in table 1. Using standard cut off values for the self-reported depression, BDI-II (score ≥ 16) and PHQ-9 (score ≥ 10), 33.2% and 28% respectively, were considered at high risk of depression.

Time to recover post dialysis was less than 1 hour for 24.1% of the cohort, but > 12 hours for 22.8% (Figure 1). In univariate analysis, there were no differences in recovery time with patient age, weight, dialysis vintage, haemoglobin, serum albumin, calcium, phosphate or dialysis Kt/V (table 2). Median BDI-II and PHQ-9 scores increased with increasing recovery time ($p < 0.001$ in both cases: table 2). The major differences in these parameters occurred between recovery times < 1 hour and > 1-hour (6 (9) vs 12 (15) for BDI-II and 2.3 (6) v 6 (9) for PHQ-9)

Male patients, and those passing more than a cupful of urine daily reported shorter recovery times of < 1-hour post dialysis (table 3). Longer time to recover post-dialysis was associated with high BDI-II and PHQ-9 scores (figure 2, table 3). There was no statistically significant association between co-morbidity and time to recover, nor with ethnicity and educational achievement.

During dialysis MAP fell by ≥10 mmHg in 36% of patients, and SBP by ≥20 mmHg in 30.9%, but there was no association with time to recover ($X^2$ 3.2, $p=0.52$, $X^2$ 5.0, $p=0.29$ respectively). Systolic blood pressure dropped to < 100 mmHg post-dialysis in 7.6% of cases. Such low blood pressures were measured in 2.4% of patients reporting the shortest recovery time (table 2), which was significantly fewer compared to those patients with recovery times > 1 hour ($X^2=8.3$, $p=0.004$). Three dialysis centres used haemodiafiltration as the standard

of treatment and two haemodialysis. Although fewer patients reported recovery within one hour in the haemodialysis centres (16.1% vs 25.6%), the differences in self-reported recovery times were not significantly different (table 2).

Apart from self-reported depression, time to recover post-dialysis was greater in patients taking antidepressant medication, those who had a previous renal transplant, those passing minimal amounts of urine, those living alone and those of younger age (table 3).

On univariate analysis, longer recovery times greater than 1-hour were associated with both self-reported BDI-II and PHQ-9 scores ($r=0.26$, $p<0.001$), and younger age ($r=-0.09$, $p=0.02$). Regression models were constructed comparing patients who recovered within one hour and those who took longer to recover. In the best model those with longer recovery times were more likely to have high self-reported BDI-II scores, be of female gender, have a past medical history of depression, and living without a partner (table 4). In addition, longer recovery times were also associated with very low post-dialysis systolic blood pressures (<100 mmHg), and higher body weight. However, the model predicted only 18% of the variation in recovery times.

The median follow-up was 19 (13-25) months. During the first 12 months 77 patients died (11%) and 55 were transplanted (8.3%). There was no relationship of recovery time to mortality by Kaplan Meier analysis or after adjustment for age, gender, comorbidity and depression scores, hazard ratio 0.8 (0.54-1.19).

## Discussion

Dialysis patients are less physically active compared to healthy patients [18,19], with fatigue being a commonly reported symptom with a reported prevalence ranging between 42% to 89% [20]. Besides generally feeling fatigued, patients may also report fatigue specifically post-dialysis, which then improves during the inter-dialytic interval [5], We wished

to determine whether there are specific factors which are associated with post-dialysis fatigue, as potentially these may be modifiable and so allow patients to have shorter post-dialysis recovery times . Previous studies have differed in the methodology of asking patients about recovery times, with some studies simply asking patients to estimate the time taken to recovery post-dialysis, whereas others have used visual analogue or Likert scales [6,7] , As open ended questions his may lead to vague answers, we favoured anumerical visual analogue rating scale, similar to a five point Likert scale [7] . The findings of our large multicentre study are in keeping with those of previous smaller single centre reports in that around a quarter of patients recover rapidly from dialysis, and just under a quarter taking more than 12 hours to recover [8,21]].

We found that there was a strong association between higher BDI-II and PHQ-9 scores and longer post-dialysis recovery times, and patients living without the support of a partner were also more likely to report longer recovery times. This association between self-reported depression scores and post-dialysis recovery times is in keeping with a previous report, although this was in a younger, less co-morbid cohort of HD patients from Brazil, with some 70% reporting immediate recovery post-dialysis and a median recovery time of only 60 minutes [9].

The BDI-II [12], which has been used in most studies of depression in HD patients, has two essential elements, one cognitive and the other physical somatic [22], and includes some items which are not uniquely related to depression. As such, for some patients the mean score for the somatic-affective factors may be significantly different to the cognitive factors [23]. Similarly, the PHQ-9, which is used as a screening tool in primary care also depends on cognitive function and there is a potential overlap between 4 of the 9 PHQ questions and fatigue [14,24], which may have accounted for the association we found between the time to recover post-dialysis and the self-reported PHQ-9 scores. As such, we cannot exclude some

overlap between self-reported depression and general fatigue. However, there is no consensus that patients reporting more fatigue similarly report longer post-dialysis recovery times, or similarly that patients with greater self-reported depression scores report more fatigue or longer post-dialysis recovery times.

An earlier study reported that intra-dialytic hypotension was a major difference between those who required time to recover post-dialysis compared to those who needed no recovery time [9], and greater cardiovascular stability during HD has been reported to reduce recovery time [5,25]. We only recorded the pre- and post-dialysis blood pressures of a single dialysis session, at the time of the questionnaire. We accept that changes in blood pressure may vary during the dialysis week, and from week to week. However most centres report groups of patients more susceptible to intra-dialytic hypotension and on the other hand those with stable dialysis. In keeping with the UK Renal registry, we recorded blood pressures with a single dialysis session rather than averaging dialysis sessions over time. Although we found no difference between the fall in sessional SBP or MAP with dialysis and recovery times, fewer patients had post-dialysis SBPs of < 100 mmHg in the group with the shortest recovery time compared to those with longer recovery times. This would support hypo-perfusion to vital organs, including the brain and heart affecting recovery times. In keeping with hypo-perfusion and hypotension, bioimpedance studies have shown patients to be dehydrated post-dialysis [26,27], which may account for the association between longer recovery times. Others have suggested that a longer recovery time and post-dialysis fatigue could be due to greater relative changes in serum and intracellular osmolality [5,20]. However, we did not observe any association with sessional Kt/Vurea, but noted that fewer women had shorter recovery times, which would be in keeping with both greater prevalence of hypotensive episodes and osmolar shifts. We also noted that more patients who were passing urine reported recovery within an hour. Patients with residual renal function are more likely to have

shorter dialysis sessions and less ultrafiltration requirements. Unfortunately, pre- and post-dialysis weight and ultrafiltration rates were not recorded for this study. The Frequent Hemodialysis Network have shown that patients dialysing more frequently reported both a greater visual analogue health score and shorter recovery time [7] . The more frequent cohort would have been expected to have both less ultrafiltration requirements and lower osmolar shifts. When they compared, patients dialysing at home with longer dialysis session times, then those dialysing more frequently self-reported shorter recovery times but similar health scores compared to the thrice weekly group [6] . As the health scores did not differ in the more frequent home dialysis patients, this would suggest that dialysis factors determine recovery time. However, the more frequent trials recruited a much younger and less co-morbid group of patients compared to our study.

Other studies have reported longer recovery times, and post-dialysis fatigue linked to inflammation, increased serum phosphate and calcium [20,28] . We found no such associations. Previously we have demonstrated that CRP is not strongly linked with self-reported depression scores [29]. It has also been suggested that haemodiafiltration, possibly by improving cardiovascular stability during treatment or removing middle molecules could reduce recovery times [30]. Comparing results from the 3 centres which provided haemodiafiltration as their standard treatment with the two centres providing haemodialysis, we found no significant differences.

Likewise, we found no association between age, dialysis vintage or physical co-morbidities and recovery time, which supports results from other studies [19]. A much smaller study from 20 years ago reported an increased mortality risk with longer recover times [30], but as with more recent studies we were unable to confirm this association [5,21]. As our patients with longer times to recover post-dialysis also had higher self-reported depression scores, and higher self-reported depression scores are associated with increased risk of mortality [31], then

this may explain previous reports of an association between post-dialysis recovery times and survival [30].

In our study, we found that patients who self-reported greater depression scores also reported longer post-dialysis recovery times. Whereas the more frequent haemodialysis studies reported that more frequent daytime dialysis resulted in both better patient wellbeing and shorter post-dialysis recovery times [5,9]. We did not find any association between sessional Kt/Vurea, or dialysis modality and recovery times. Although we did not observe a direct association between intra-dialytic hypotension, in terms of 10 mmHg fall in MAP or 20 mmHg fall in SBP and recovery times, those patients with recorded post-dialysis systolic blood pressures below 100 mmHg reported longer recovery times. As such measurement of post-dialysis recovery times appear to be more complex than simple assessment of the physical effects of the dialysis session. Although interventions are required to prevent patients developing severe low systolic blood pressures with dialysis to improve recovery times and patient experience, future studies need to additionally consider the general physical and psychological health of the patient when interpreting changes in recovery times.

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Figure 1. Proportion of patients reporting time to recover after their haemodialysis session between less than an hour to more than twelve hours.

Figure 2. Beck Depression Inventory (BDI-II) and Public Health Questionnaire (PHQ-9) self-reported scores in patients reporting time to recover after their haemodialysis session between less than an hour to more than twelve hours. Median (interquartile range). *** $p<0.001$ vs patients with recovery time of < 1 hour.

Table 1. Study baseline Patient demographics of the 701 participants

| variable | Percentage of patients |
|---|---|
| Male gender | 63.6 |
| Caucasian | 69.5 |

| | |
|---|---|
| Asian | 11.1 |
| African-Afro-Caribbean | 7.7 |
| Mixed race | 9.6 |
| Other | 2.1 |
| Married | 48.6 |
| Living with civil partner | 3.0 |
| Separated but not divorced | 2.3 |
| Divorced | 10.6 |
| Single | 21.4 |
| Widowed | 13.8 |
| Living alone | 30.2 |
| Living with spouse or partner | 38.2 |
| Living with family | 29.5 |
| Living in nursing home | 1.1 |
| Living with friends | 0.7 |
| No educational qualifications | 29.7 |
| Qualifications aged 16 | 25.0 |
| Qualifications aged 18 | 9.1 |
| University education | 10.3 |
| Postgraduate qualification | 7.1 |
| History of heart disease | 34.8 |
| History of diabetes | 33.5 |
| History of stroke | 8.1 |
| Previous amputation | 3.3 |
| History of cancer | 10.7 |
| History of chronic liver disease | 2.4 |
| History of lung disease | 6.6 |
| Previous renal transplant | 30.8 |
| Prescription of antidepressants | 19.7 |

Table 2. Patients divided according to post-dialysis recovery times. between < 1 hour and 12 hours or more.
Results as numbers, mean ± standard deviation, or median (interquartile range), or percentage. Body mass index (BMI), Pre- dialysis (Pre), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP). Analysis by ANOVA or Kruskal-Wallis with appropriate post hoc testing (Tukey or Dunn's). p vs 1-hour, no significant differences (NS) vs < 1-hour recovery cohort (NS)

| Recovery time | < 1 hour | 1-4 hours | 4-8 hours | 8-12 hours | ≥ 12 hours | Overall p-value |
|---|---|---|---|---|---|---|
| Age year | 66±16 | 66±16 | 60±17* | 64±16 | 63±17 | 0.015 |
| Weight kg | 74±17 | 75±18 | 81±23 | 78±16 | 74±17 | 0.015 |
| BMI kg/m$^2$ | 25.7±4.9 | 26.6±5.6 | 28.4±12.5* | 27.6±6.6 | 27.0±6.1 | 0.041 |
| Dialysis Vintage months | 27(60) | 32(60) | 37(57) | 31(71) | 35(47) | NS |
| Hemoglobin g/L | 112±12 | 111±12 | 112±12 | 112±13 | 111±13 | NS |
| Albumin g/L | 37±5 | 37±4 | 38±4 | 38±4 | 37±4 | NS |
| Calcium mmol/L | 2.26±0.18 | 2.26±0.17 | 2.27±0.23 | 2.29±0.17 | 2.25±0.18 | NS |
| Phosphate mmol/L | 1.6±0.5 | 1.6±0.5 | 1.6±0.5 | 1.7±0.6 | 1.6±0.4 | NS |
| Kt/Vurea | 1.42±0.31 | 1.45±0.34 | 1.42±0.25 | 1.42±0.27 | 1.42±0.25 | NS |
| Pre SBP mmHg | 142±24 | 144±26 | 142±25 | 142±27 | 142±25 | NS |
| Pre DBP mmHg | 72±15 | 74±14 | 75±17 | 72±20 | 72±16 | NS |
| Pre MAP mmHg | 95.4±16.1 | 97.3±15.4 | 93.2±16.3 | 88.4±16.9 | 89.6±16.5 | NS |
| Post SBP mmHg | 134±24 | 133±25 | 134±28 | 132±26 | 132±27 | NS |
| Post DBP mmHg | 69±14 | 69±14 | 73±15 | 66±14 | 68±15 | 0.043 |
| Post MAP mmHg | 90.4±14.3 | 90.3±15.4 | 93.2±16.3 | 88.4±16.9 | 89.6±16.5 | NS |
| Intra-dialytic hypotension % | 22.4 | 34.4 | 12.0 | 13.0 | 22.7 | NS |
| Post SBP <100 mmHg % | 2.4 | 9.0 | 9.4 | 9.2 | 8.0 | NS |

Table 3. Percentage of patients reporting post haemodialysis recovery times from < 1 hour to > 12 hours and self-reported depression or previous medical history of depression

. Beck Depression Inventory (BDI-II) and Public Health Questionnaire (PHQ-9), haemodiafiltration (HDF), haemodialysis (HD). Chi square analysis with p values comparing groups.

| Recovery time | < 1 hour | 1-4 hours | 4-8 hours | 8-12 hours | ≥ 12 hours | X2 |
|---|---|---|---|---|---|---|
| Male | 27.8 | 26.6 | 16.7 | 10.2 | 18.7 | 17.2 |
| Female | 17.8 | 27.9 | 12.8 | 12.0 | 29.5** | p 0.002 |
| BDI-II > 16 | 11.9 | 31.2 | 17.4 | 14.2 | 29.8 | 32.6 |
| BDI-II ≤ 16 | 30.7 | 25.5 | 14.5 | 9.1 | 20.1 | p <0.001 |
| PHQ-9 ≥ 10 | 12.9 | 27.8 | 16.0 | 15.5 | 27.8 | 24.2 |
| PHQ-9 ≤10 | 28.6 | 26.4 | 15.1 | 9.1 | 20.7 | p <0.001 |
| Past history of depression | 10.3 | 28.2 | 27.2 | 13.9 | 30.5 | 24.2 P< 0.001 |

| | | | | | | |
|---|---|---|---|---|---|---|
| No depression | 28.6 | 25.4 | 15.1 | 9.1 | 21.5 | |
| Prescribed antidepressants | 12.3 | 26.8 | 15.9 | 14.5 | 30.4 | 16.6 p =0.001 |
| No antidepressants | 27.0 | 27.2 | 15.1 | 9.9 | 20.8 | |
| Living with partner/spouse | 28.7 | 27.3 | 14.9 | 9.9 | 19.1 | 11.3 p =0.024 |
| No partner/ spouse | 19.4 | 25.6 | 15.5 | 11.9 | 25.6 | |
| Urine output > cupful | 24.7 | 26.2 | 12.5 | 12.5 | 24.1 | 13.2 p =0.010 |
| Urine output < cupful | 21.1 | 28.2 | 21.1 | 6.1 | 23.0 | |
| Previous transplant | 21.1 | 16.8 | 18.6 | 16.8 | 26.5 | 12.0 p =0.017 |
| No transplant | 24.7 | 29.1 | 14.6 | 9.7 | 21.9 | |
| HDF centre % | 25.6 | 26.8 | 14.8 | 9.8 | 22.9 | 6.7 p =0.15 |
| HD centre % | 16.1 | 28.6 | 17.9 | 16.1 | 21.4 | |

Table 4. Logistical regression model comparing patients with longer post-dialysis recovery time (> 1 hour) to those with shortest recovery times (< 1 hour).
Past medical history of depression (PMH), Beck Depression Inventory score [14], post-dialysis systolic blood pressure (Post SBP). Model fit Nagelkerke $r^2$=0.18.

| variable | β | StE β | Wald | p value | Odds ratio | 95% CL |
|---|---|---|---|---|---|---|
| BDI score | 0.06 | 0.01 | 24.9 | 0.000 | 1.06 | 1.04-1.09 |
| Post SBP < 100 mmHg | 1.37 | 0.01 | 6.4 | 0.011 | 3.76 | 1.29-10.99 |
| PMH depression | 0.68 | 0.29 | 5.6 | 0.018 | 2.01 | 1.13-3.58 |
| Gender (male) | 0.49 | 0.21 | 5.2 | 0.022 | 0.58 | 0.38-0.89 |
| Dry weight kg | 0.12 | 0.01 | 4.3 | 0.039 | 1.01 | 1.00-1.03 |
| Living with partner | -0.39 | 0.20 | 4.0 | 0.047 | 0.66 | 0.44-0.96 |

Figure 1

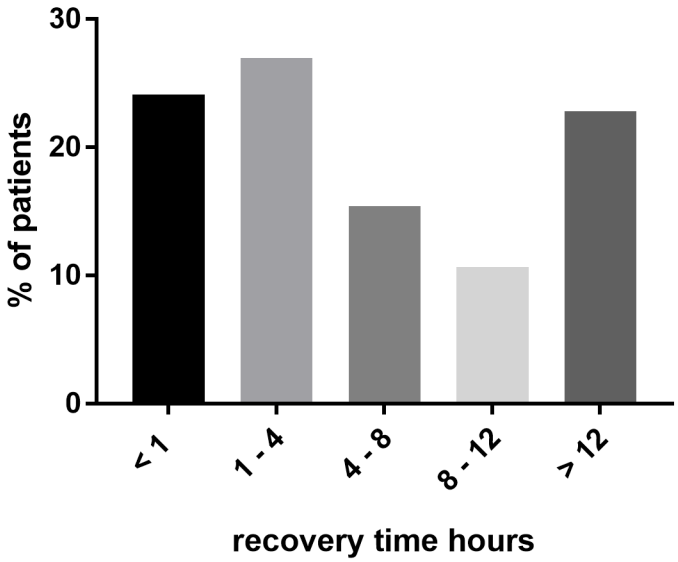
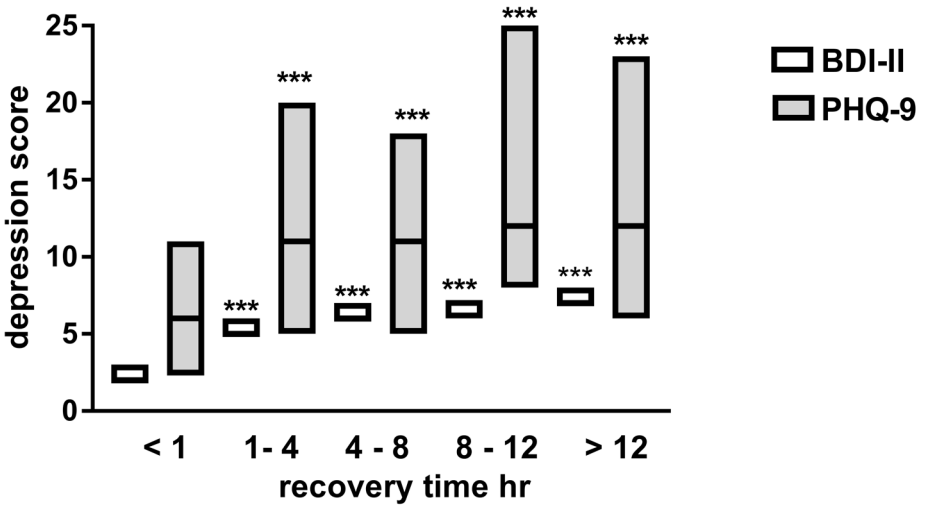


Figure 2


depression score
25
20
15
10
5
0
***
***
***
***
***
***
< 1
1- 4
4 - 8
8 - 12
> 12
recovery time hr
BDI-II
PHQ-9