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## DEPRESSION & ANXIETY TRAJECTORIES IN HED-SMART

### **Title:**

The Effect of Brief Self-Management Intervention for Hemodialysis Patients (HED-SMART) on Trajectories of Depressive and Anxious Symptoms

### **Short Title (for Running Head):**

Depression & Anxiety Trajectories in HED-SMART

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**Abstract**

**Objective:** Depression is often comorbid with End-Stage Renal Disease, and associated with poor adherence and clinical outcomes but course of symptoms is variable. This study sought to describe the long-term trajectories of anxiety and depression in hemodialysis patients, to identify predictors of these trajectories over 12 months and to evaluate the effectiveness of the HEMoDialysis Self-Management Randomized Trial (HED SMART) against usual care on symptoms of anxiety and depression.

**Methods:** A secondary analysis of data from a randomized controlled trial that contrasted HED SMART ( $n=101$ ) against usual care ( $n=134$ ). Depressive and anxious symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS) at baseline, 1 week and at 3 and 9 months post-intervention. Latent class growth analysis identified trajectories of depression and anxiety, and their sociodemographic and clinical predictors.

**Results:** Symptoms of depression and anxiety over 12 months were characterized by two trajectories: low stable (depression: 55%; anxiety: 59%) with non-clinical levels of distress, and high stable (depression: 45%; anxiety: 41%) with clinical levels of distress. HED SMART predicted significant reductions in depression relative to usual care. A similar trend was noted for anxiety. Younger age, Chinese ethnicity, and more comorbidities were associated with persistent high depression. Younger age and shorter dialysis vintage was associated with persistent high anxiety.

**Conclusion:** A brief self-management intervention designed to support behavioral change can also lead to significant reductions in symptoms of depression and may be of great value for younger HD patients shown to be at greater risk for persistent distress.

*Keywords:* depression; hemodialysis; trajectories; intervention

Trial registration: ISRTN31434033

**The Effect of Brief Self-Management Intervention  
for Hemodialysis Patients on Trajectories of Depressive and Anxious Symptoms**

Depression is a frequent and pernicious comorbid condition amongst patients with End Stage Renal Disease (ESRD), with prevalence rates between 23% to 29% [1,2]. Estimates of subclinical distress, using self-report measures rather than diagnostic assessments, are even higher. Most research, however, has measured distress at one time. Of the limited longitudinal research that has been conducted, it has been established that symptoms of distress vary markedly across patients with respect to their severity, longitudinal course and response to treatment [3,4]. It is important to understand symptom course and individual variability to guide more targeted intervention efforts in ESRD.

Support programs for ESRD related distress are much needed as symptoms of emotional distress have been shown to be associated with poor clinical outcomes, including higher morbidity and mortality rates, and higher health care costs [5,6]. Studies have also noted that trends over time (i.e., persisting or worsening of symptoms over time) are associated with increased cardiovascular and overall mortality risk [7,8]. Small-scale randomized controlled trials of Cognitive Behavioral Therapy (CBT), an evidence-based treatment for depression, have been shown to reduce distress in patients on dialysis [9,10]. Considerations however, related to high costs, intensity and the need for additional resources (e.g., specialist CBT therapists) for CBT programs coupled with a shortage of healthcare staff with psychological skills training constrain their availability and wide implementation in routine renal care [11].

Self-management based programs have been widely advocated as an effective and cost-efficient means to deliver patient education and provide patients with self-management skills and strategies to promote and change their behavior as well increase their confidence in

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dealing with their long-term condition [12]. In ESRD, such programs, delivered and implemented by health care staff have demonstrated improvements in several outcomes including self-efficacy [13], quality of life [14], and self-report adherence and clinical markers [15].

Although it is generally hoped that broader benefits may also be achieved, little is known about the effectiveness of these interventions in reducing distress. This raises the question of whether these less resource-intensive interventions, where the focus is mainly on behavioral change, would bring about other gains notably in mental health. This is particularly pertinent in Asian settings where the stigma attached to mental health and related-services may hinder the acceptability, participation or retention in CBT programs [16–18]. The HED-SMART intervention (HEmoDialysis Self-Management Randomized Trial) is a brief self-management intervention developed through formative work in Singapore to improve treatment adherence and clinical outcomes in ESRD [15,19]. Delivered by renal health professionals over 4 group sessions, the program was designed to support behavior change using the principles of Social Learning Theory, self-monitoring, and goal setting. Analyses of primary outcomes indicated significant benefits for HED-SMART in clinical markers, namely interdialytic weight gains (markers of fluid control) and potassium and phosphate levels with only modest loss of effects at nine months post intervention [15].

The aims of the present study were (1) to identify the trajectories of depressive and anxious symptoms over 12 months (2) to examine the effects sociodemographic and medical parameters on these trajectories and (3) to evaluate the effects of HED-SMART on the course of these emotional outcomes.

### **Methods**

#### **Study Design**

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The data presented in this paper are part of the Hemodialysis Self-Management Randomized Trial (HED-SMART), a pragmatic cluster RCT (Trial Registration: ISRTN31434033), which used dialysis shift within each dialysis center as the unit of randomization. The methods have been described in detail previously [15]. In summary, **this is a 12 month 2-group randomised controlled trial, to compare the HED SMART intervention in addition to usual care, with usual care alone. Study endpoints included clinical markers of disease control, i.e. interdialytic weights gain, potassium, phosphate levels and patient-reported outcomes, i.e. adherence, self-efficacy, self-management skills, quality-of-life and distress collected at baseline, and at 2 weeks, 3 months and 9-month follow up.** The primary objectives of the trial were to determine if this brief group-based self-management intervention could improve short- and long-term, self-management skills, behavioral and clinical outcomes [15]. Part of the secondary objectives which constitute the foci of this paper, were to determine the impact of this intervention on psychological outcomes.

### **Setting and Participants**

**The trial was undertaken between 2009 to 2013.** The recruiting centers were dialysis centers operated by National Kidney Foundation (NKF), Singapore. **NKF Singapore is a nonprofit charitable organization that caters for the lower and middle-income patients with ESRD in Singapore. NKF Singapore dialysis centres are located within the community, island wide, and run by nurses with a team of nephrologists working in rotation.** The target population comprised adults, aged 21 years and above, receiving hemodialysis in one of the 11 participating National Kidney Foundation dialysis centers in Singapore for a minimum duration of six months. Participants were excluded if they were not fluent in either English, Mandarin or Malay, or had conditions that would hinder full participation in the trial (i.e., functional psychosis, organic brain disorder), learning disabilities, dementia, life-limiting

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medical disorders or significant hearing or visual impairments uncorrected with hearing or visual aids). **Inclusion/ exclusion criteria were assessed by senior nurse through patients' medical records.**

### **Recruitment and Randomization**

Patients were randomly allocated to the intervention or control condition based on their dialysis shifts to minimize contamination across patients within the same shift. Those in the intervention condition received HED-SMART over and above standard renal care, while those in the control condition received only standard renal care. Patients were informed of the results of the randomization only after having provided informed consent and completing the baseline assessment. All staff at the dialysis centers, and research personnel administering the questionnaires, remained blind to patients' study arm allocation (Figure 1).

The intervention was then implemented at 3 weeks post-baseline, **in a group format** over 3 core sessions (1 to 3) and 1 booster session [19]. **HED-SMART was guided by social cognitive theory and aimed to improve capability for disease management. Sessions targeted knowledge, attitudes, skills and self-management behaviours: fluid intake, diet and medication. The content and delivery format was established following rigorous process including focus groups and interviews, training and extensive piloting to develop a theory-based program that is tailored to needs of patients in local context [20]. The sessions were delivered in groups of 5-7 patients, in either English, Chinese or Malay (as per patients' preference). They were facilitated by two renal health professionals (medical social worker, renal dietician or nurse) unrelated to direct patients' care and took place over weekends (non-dialysis days) to avoid interference with dialysis center workflow and to allow more flexibility in patients' and facilitators' availability. Non-dialysis days were also preferred as cognitive abilities over dialysis cycle are shown to be better at 24-hours post dialysis [21].**

### **Measures**

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Sociodemographic information, including age, gender, ethnicity, employment status, education, and marital status, were collected at baseline. Medical/serological data, including Kt/V, nPCR, hemoglobin, albumin, comorbidities, primary cause of ESRD, and duration of hemodialysis (in months), were abstracted from medical records. The Charlson Comorbid Index (CCI) [22] was used to consolidate co-morbidity burden, and subsequently scored based on previous recommendations [23]. Higher scores indicate greater comorbid burden. The CCI has been validated for use in ESRD patients [24].

Emotional distress was measured using the Hospital Anxiety and Depression Scale (HADS) [25], a well-established self-report measure of anxiety and depression. The HADS was selected not only because its omission of somatic items makes it an appropriate measure for a chronically ill population, but also because it has been linguistically validated in both Mandarin [26] and Malay [27], an important consideration for use in the multi-ethnic context of Singapore. HADS assesses symptoms of anxiety (7 items; score range=0 to 21) and depression (7 items; score range=0 to 21) within the past week. Higher scores indicate higher levels of depressive and anxious symptoms – with scores  $\geq 8$  for each subscale signifying caseness as per internationally validated criteria across a range of patient populations and cultures [28,29]. In the present study, both the HADS-D and HADS-A demonstrated good internal consistency across all assessments ( $\alpha > .70$ ). Participants self-completed the study questionnaire. The researcher provided assistance when required.

Emotional distress was measured at baseline (Time 1), immediately after the end of HED-SMART (Time 2; 1week post), and at 3 months (Time 3), and at 9 months (Time 4) post-HED-SMART.

### **Data Analysis**

Latent Class Growth Analysis (LCGA) [30,31] was employed using Mplus version 6.12 [32]. Unlike conventional growth curve modelling [33], LCGA does not assume that all

individuals within the sample can be adequately characterized by a single set of growth parameters (i.e., intercepts and slopes) [34]. As such, this technique allows researchers to examine if a population comprises multiple growth trajectories [34], and to subsequently model covariates as predictors of trajectory membership and growth parameters [35].

**Unconditional model.** To select the optimal number of trajectories, one through four classes of linear growth models were fit without covariates in a series of iterative steps [36,37]. Based on previous recommendations, this selection was guided by substantive interpretation [38] and the following fit statistics [39]: Bayesian Information Criterion (BIC) [40] and Bootstrapped Likelihood Ratio Test (BLRT) [41,42]. Lower BIC, and significant BLRT, values indicate better model fit. However, if the lowest BIC value corresponded to the model with the largest number of classes, “elbow” plots were examined in a method similar to the use of scree plots in Exploratory Factor Analysis (EFA) [36]. Entropy, a measure of classification quality, was also obtained. Its values range from zero to one, and values closer to one indicate better classification of individuals into classes [36,43]. The resultant linear growth model was compared against a corresponding quadratic growth model using  $\chi^2$  difference tests to investigate if the inclusion of a quadratic growth parameter would significantly improve model fit [37].

**Conditional model.** To model covariates as predictors of trajectory membership and growth parameters, selected sociodemographic and medical variables, and the intervention variable, were included into the unconditional model [37]. Class membership was regressed on key sociodemographic and medical variables. Given the risk for model instability as result of too many covariates [44], **only the following variables, shown to be significantly associated with depression or anxiety in previous work on hemodialysis (HD), were included: age, gender, ethnicity, education, dialysis vintage, and co-morbidity burden.** The linear growth factor within each class was also regressed on the dummy-coded intervention variable

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(1 = intervention; 0 = usual care). In order to determine if the intervention effect varied according to latent class membership,  $\chi^2$  difference tests were employed to compare (a) a model in which the intervention effect was invariant across latent classes, against (b) a model in which the intervention effect was constant across latent classes.

### **Missing Data**

The Mplus software package used Full Information Maximum Likelihood (FIML) estimation. This approach has been widely regarded as appropriate for handling missing data [45,46], and assumes that the data were Missing At Random (MAR) [47]. In order to assess the appropriateness of this assumption, sensitivity analyses were conducted to compare the LCGA model against a pattern mixture model in which the data were Not Missing At Random (NMAR) [48]. These analyses suggested the appropriateness of the MAR assumption: there were no significant improvements in the BIC for both depressive symptoms and anxious symptoms, and the trajectories remained substantively unchanged.

## **Results**

### **Participants**

Figure 1 shows a flowchart of the recruitment process. Of the 956 patients screened between January 2009 and June 2012, 532 patients fulfilled the criteria, and were therefore invited to participate. Among these patients, 235 provided informed consent and completed the baseline assessment (response rate: 44%). These patients were subsequently randomized to either the HED-SMART intervention ( $n = 101$ ) or usual care ( $n = 134$ ) based on their dialysis shifts. Across the subsequent follow-up assessment points over the ensuing 12 months, 91% ( $n = 214$ ) were captured at Time 2; 88% ( $n = 206$ ) at Time 3; and 82% ( $n = 193$ ) at Time 4. A total of 80% ( $n = 189$ ) were captured across all four time points.

[Insert Figure 1]

Table 1 shows the baseline sociodemographic and medical characteristics based on participants' trial arm allocation. These characteristics, including emotional distress, were adequately balanced across both arms (no significant difference noted). On average, participants were  $53.5 \pm 10.4$  years of age. Approximately 41.7% were female, and 56.8% identified as Chinese. Mean dialysis adequacy and biochemical markers were within accepted clinical targets [49], and CCI was moderate [23].

[Insert Table 1]

### Symptoms of Depression

**Unconditional model.** According to the fit indices in Table 2, successive linear growth models continued to demonstrate improved fit through four classes. An examination of the “elbow” plot for the BIC revealed a bend at two classes, which suggested that the two-class solution fit the data best. Comparing the four- and two-class solutions, the former was relatively uninformative because it merely split each of the trajectories from the two-class solution based on intercept values. Therefore, based on a combination of statistical indicators and substantive interpretation, the four-class solution was rejected in favor of the two-class solution. The inclusion of a quadratic growth parameter did not significantly improve model fit ( $\chi^2 [2, N = 235] = .34, p = 0.85$ ).

**Conditional model.** After having identified the optimal number of trajectories, the seven sociodemographic and medical variables, as well as the intervention variable, were included in the unconditional model. The inclusion of the sociodemographic and medical variables significantly improved model fit ( $\chi^2 [7, N=218] = 120.45, p < 0.001$ ), although the sample size was slightly reduced due to missing data on these covariates. A model in which the intervention effect varied across latent classes did not fit the data significantly better than a model in which the intervention effect was constant ( $\chi^2 [1, N = 218] = 1.44, p = 0.23$ ). As shown in Figure 2, the two-class solution identified two substantively distinct groups of

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trajectories of depressive symptoms. The first class ( $n = 120$ ; 55%) was characterized by consistently low levels of depressive symptoms. This class was thus termed the low stable class. The second class ( $n = 98$ ; 45%) was characterized by consistently high levels of depressive symptoms. This class was thus termed the high stable class.

[Inset Figure 2]

The results indicated that age, ethnicity, and comorbid burden significantly predicted latent class membership (Table 4): patients who were either younger, Chinese, or had higher CCI scores, were more likely to demonstrate the high stable, as compared to the low stable, trajectory of depressive symptoms. The intervention was also associated with a statistically significant reduction in symptoms of depression, over 12 months, in both the low stable and the high stable classes ( $B = -1.44$ ,  $SE = 0.64$ ,  $p = 0.03$ ; Figure 2).

**Dialysis vintage was not associated with depression trajectories.**

### Symptoms of Anxiety

**Unconditional model.** A similar model-fitting process was followed for symptoms of anxiety. In line with the findings for symptoms of depression, the two-class model was selected based on an examination of the “elbow” plot for the BIC, and because the four-class solution was relatively uninformative as it merely split each of the trajectories from the two-class solution based on intercept values. The inclusion of a quadratic growth parameter did not significantly improve model fit ( $\chi^2 [2, N = 235] = 1.84$ ,  $p = 0.40$ ).

**Conditional model.** The inclusion of the same sociodemographic and medical variables further improved model fit ( $\chi^2 [7, N = 218] = 123.54$ ,  $p < 0.001$ ). A model in which the intervention effect varied across latent classes did not fit the data significantly better as compared to one in which the intervention effect was constant ( $\chi^2 [1, N = 218] = 0.013$ ,  $p = 0.91$ ). As shown in Figure 2, the two-class solution identified two substantively distinct groups of trajectories of anxious symptoms. The first class ( $n = 129$ ; 59%) was characterized

by consistently low levels of anxious symptoms. This class was thus termed the low stable class. The second class ( $n = 89$ ; 41%) was characterized by consistently high levels of anxious symptoms. This class was thus termed the high stable class.

The findings indicated significant effects of age and dialysis vintage (Table 4). Patients who were either younger, **or had a shorter dialysis vintage, were more likely to demonstrate the high stable, as compared to the low stable, trajectory of anxious symptoms.** The intervention was also associated with a marginal reduction in symptoms of anxiety, over 12 months, in both the low stable and the high stable classes – but the effect did not reach statistical significance ( $B = -1.23$ ,  $SE = 0.65$ ,  $p = 0.06$ ; Figure 2).

### Discussion

Depression and anxiety are growing health concerns in ESRD. However, the majority of previous studies are observational, and have not examined the heterogeneity in the course of change in symptoms. To the best of our knowledge, the present study is the first to show distinct trajectories of depressive and anxious symptoms within the context of an RCT and the effects of a self-management intervention on these symptoms.

Study findings showed that symptoms of anxiety and depression over 12 months follow two distinct courses. In each case a low stable class (i.e., no depression [55%]; no anxiety [59%]) characterized by consistently low symptoms within the normal range or below cut offs for a clinical classification. Second a high stable class characterized by persistently high symptoms of depression (45%) or anxiety (41%) throughout the 12-month study window. Previous studies have also noted this polarized pattern of few or no symptoms of distress or high distress in HD patients [4,50]. However, these findings differ from prior work on incident HD patients which identified low-reducing (62%), moderate-increasing (22%), and high-reducing (16%) trajectories for depression [3]. Nonetheless, because the abovementioned study comprised incident HD patients while the present study examined

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prevalent patients, and because fluctuations in emotional distress tend to stabilize over time [51], it is possible that both the moderate-increasing and the high-reducing classes may eventually collapse into one of the two classes identified for the established HD patients in our study.

Analyses found a range of variables that distinguished the trajectory groups. Patients who were either younger, Chinese, or had a greater number of co-morbidities, were more likely to demonstrate a high stable, as compared to a low stable, trajectory of depressive symptoms. Trajectories of anxious symptoms were predicted by age and dialysis vintage with patients who were either younger or had a shorter dialysis vintage more likely to demonstrate a high stable, as compared to a low stable, trajectory of anxious symptoms. These variables have not been included in other trajectory studies although some, namely age and comorbid burden have been found by some to be related to depression or anxiety [3,52]. Life on dialysis may be particularly disruptive for younger patients who are more likely to be occupationally active, in pursuit of life/personal goals, or with responsibilities towards family and dependents [3]. Culture-related views and stigma around mental health may explain the effects of ethnicity [16] found in this study. The Chinese culture traditionally views mental illnesses as weaknesses of character, those who hold these beliefs might be less likely to engage in help-seeking behavior, and are therefore at an increased risk of depression [17]. Familialism and collectivism beliefs, dominant among Chinese, may also intensify perceptions of burden and emotional distress when in ill health especially in local context of decreasing household sizes among Singaporean Chinese [53]. Similar effects have been noted for emotional QOL in cohort studies in Singapore [54] favoring Malay respondents (noted to have larger household sizes) over Chinese or Indian despite their lower socioeconomic resources and worse clinical profile. Although replication of these findings is essential, these analyses suggest that individual-level factors (e.g., younger age, Chinese ethnicity) appear to

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be predictive of persistently high depressive and anxious symptoms – and could serve to identify at risk populations to be targeted.

Study findings showed that the HED-SMART intervention, despite focusing primarily on behavior change, yielded significant benefits by reducing symptoms of depression for both the low stable and high stable groups. This has been shown for self-management programs in other patient group [55]. A similar trend was noted for reduced anxiety, although this failed to reach significance. These patterns of results provide preliminary support that theory-informed self-management programs which extend the role of renal health care professionals to deliver minimal psychologically-informed behavior change interventions may also be useful in improving emotional distress and psychosocial adjustment. It is noteworthy that improvements were noted across all the trajectories.

It is interesting to speculate how the emotional gains may have been brought about, especially as there was no component in HED-SMART to directly target emotional management. Although the mechanisms of these effects were not examined, several pathways are possible and suggest directions for future studies. First, HED-SMART might have impacted patients' depressive symptoms by building personal resources (self-management skills; self-efficacy) that promote resilience, adherence to treatment and in turn improved clinical outcomes as shown in (15). HED SMART has shown benefits in clinical markers and adherence behaviors (15). These may in turn have lowered distress by reducing symptoms such as breathlessness or itchiness due to poor fluid intake or phosphate control (15) or reinforcing more adaptive attitudes towards illness and treatment. Such improvements may also translate to improved or more rewarding doctor-patient interactions as they imply less need for discussions related to adherence lapses that could generate distress and tension to patients. Moreover, better disease management, as shown in clinical endpoints may have provided further positive reinforcement for adaptive behaviors (e.g., self-care) [15]. Such

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changes would be expected to lessen depressive symptoms by decreasing helplessness and hopelessness and further increasing self-efficacy.

Second, participation in group-based HED-SMART might have created more opportunities for more effective peer support among patients and greater attention from healthcare professionals. These newly forged or more consistent relationships among HED-SMART participants and facilitators might have provided additional social reinforcement and stress-buffering social support, both of which would be expected to reduce depressive symptoms [4]. Other processes (i.e., social comparisons or modelling) may also be involved in the observed psychological benefits. Considering the evidence on adverse effects of ESRD and hemodialysis on social life and activities [56], the potential of group-based intervention to build or expand interpersonal resources should be noted.

There are several strengths to the present analyses. These include an adequately powered, RCT design, the recruitment of ethnically diverse representative sample of patients, a wide range of demographic and clinical parameters as predictors of latent class membership, as well as the employment of formal statistical models to identify heterogeneous trajectories of change.

Nevertheless, some limitations should be mentioned. First, a convenience sample rather than a probability-based sample was used, which may limit generalizability to other populations. Although the current sample represents fairly well the national HD registry [57], the rate of diabetes was lower in this sample. The ethnic profile of sample differs from other cohorts such as the US Renal Data System (USRDS) that includes other ethnic groups not represented in our study sample. Replication is therefore warranted. Second, even though participants were randomly selected, self-selection bias by patients cannot be excluded. Although HADS is a validated measure and has been linguistically validated in both Mandarin [26] and Malay [27], its effectiveness as a screening tool for anxiety disorders has

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been criticized [58]. Moreover, as no data were collected beyond 12 months post baseline, the longer-term trajectories, and effects of HED-SMART, are therefore not known. Last, although statistically significant effects were noted, their clinical relevance warrants further evaluation as minimal important difference in HADS has not been established. It is however encouraging that a brief, low intensity psychological intervention showed reduction in severity of depression and anxiety symptoms.

In conclusion, this study is the first to use a formal statistical model such as LCGA to assess emotional distress trajectories in a cohort of prevalent HD patients in Singapore. The findings indicated two markedly distinct classes of symptom progression that remained stable over time. Further analyses revealed that HED-SMART, a brief, low intensity self-management intervention designed to support behavior change, led to reductions in depressive and anxious symptoms, and could be of great value for younger patients shown to be at a greater risk for persistent distress. Given the high prevalence of primary/illiterate education status (>25%) in our sample, the HED-SMART intervention may also be well suited for populations with low health literacy.

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### **Competing Interests**

The authors have no competing interests to report.

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Table 1.

Participants' Characteristics

	<b>Total sample (N=235)</b>	<b>HED-SMART (n=101)</b>	<b>Usual Care (n=134)</b>	<b><i>p</i></b>
Age (years)	53.5 ± 10.4	53.1 ± 10.5	53.9 ± 10.4	0.5 <sup>a</sup>
Age at diagnosis (years)	43.4 ± 13.5	42.9 ± 13.3	43.7 ± 13.8	0.7 <sup>a</sup>
Age when left formal education, (years)	16.7 ± 6.0	17.1 ± 7.4	16.4 ± 4.7	0.3 <sup>a</sup>
Education level				0.1 <sup>b</sup>
Illiterate/primary	71 (30.2%)	28 (27.7%)	43 (32.1%)	
Secondary	147 (62.6%)	69 (68.3%)	78 (58.2%)	
Tertiary	17 (7.2%)	4 (4%)	51 (38.3%)	
Female sex	98 (41.7%)	47 (46.1%)	51 (38.3%)	0.3 <sup>b</sup>
Ethnicity				0.9 <sup>b</sup>
Chinese	133 (56.8%)	57 (55.9%)	76 (57.6%)	
Malay	80 (34.2%)	36 (35.3%)	44 (33.3%)	
Indian	15 (6.4%)	7 (6.9%)	8 (6.1%)	
Others	6 (2.5%)	2 (2%)	4 (3.1%)	
Relationship status: married	155 (66.5%)	68 (67.3%)	87 (65.9%)	0.9 <sup>b</sup>
Employment status: employed <sup>c</sup>	87 (42.6%)	33 (37.5%)	54 (46.6%)	0.2 <sup>b</sup>
Perceived ability to work (able)	129 (56.8%)	52 (51.0%)	77 (61.6%)	0.1 <sup>b</sup>
Income <sup>d,e</sup>				0.1 <sup>e</sup>
S\$0- S\$2,000	119 (51.5%)	59 (58.4%)	60 (46.2%)	
S\$2,001 - S\$4,000	49 (21.2%)	16 (15.8%)	33 (25.4%)	
S\$4,001 - S\$6,000	11 (4.8%)	5 (5.0%)	6 (4.6%)	
> S\$6,000	9 (3.9%)	5 (5.0%)	4 (3.1%)	
Dialysis vintage category				0.8 <sup>b</sup>
6-12 months	20 (8.5%)	9 (8.8%)	11 (8.3%)	
13-24 months	34 (14.5%)	16 (15.7%)	18 (13.5%)	
> 24 months	181 (77.0%)	77 (75.5%)	104 (78.2%)	
Dialysis vintage, years	5.68 ± 4.76	5.83 ± 5.09	5.81 ± 4.53	0.9 <sup>a</sup>
Dialysis shift				0.7 <sup>b</sup>

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Mon-Wed-Fri	129 (54.9%)	57 (56.4%)	72 (53.7%)	
Tue-Thu Sat	106 (45.1%)	44 (43.6%)	62 (46.3%)	
Primary Cause of ESRD				0.7 <sup>b</sup>
Glomerulonephritis	68 (28.9%)	27 (26.5%)	41 (30.8%)	
Diabetic Nephropathy	61 (25.9%)	28 (27.5%)	33 (24.8%)	
Hypertension	22 (9.4%)	9 (8.9%)	13 (9.7%)	
Polycystic Kidney Disease	19 (8.1%)	9 (8.8%)	10 (7.5%)	
Charlson Comorbidity Index	4.89 ± 2.23	4.88 ± 2.19	4.90 ± 2.27	0.9 <sup>a</sup>
Kt/V	1.61 ± 0.20	1.63 ± 0.18	1.60 ± 0.22	0.4 <sup>a</sup>
nPCR g/kg/d	1.01 ± 0.26	1.01 ± 0.21	0.99 ± 0.30	0.6 <sup>a</sup>
Hemoglobin, g/dL	11.54 ± 1.47	11.55 ± 1.27	11.54 ± 1.61	0.9 <sup>a</sup>
Albumin, g/dL	34.81 ± 2.99	34.62 ± 3.03	34.95 ± 2.97	0.4 <sup>a</sup>
No. of medications	9.57 ± 3.65	9.67 ± 4.08	9.53 ± 3.62	0.9 <sup>a</sup>
Medication use				
Phosphate binders	209 (94.1%)	86 (91.5%)	122 (95.3%)	0.7 <sup>b</sup>
Calcium carbonate	80 (33.9%)	31 (30.7%)	49 (36.6%)	0.4 <sup>b</sup>
Calcium acetate	127 (53.8%)	55 (54.5%)	72 (53.7%)	0.7 <sup>b</sup>

Abbreviations: ESRD, end-stage renal disease; HED-SMART, Hemodialysis Self-Management Intervention Randomized Trial; nPCR, normalized protein catabolic rate.

<sup>a</sup>Use of independent-samples t test.

<sup>b</sup>Use of  $\chi^2$ -test.

<sup>c</sup>N = 204 because 31 participants did not provide information on employment,

<sup>d</sup>N = 189 because 14 participants ticked option “do not wish to answer” for income and 32 indicated “do not know.”

<sup>e</sup>Income brackets are equivalent to US dollars as follows: S\$2,000 = US\$1,600; S\$4,000 = US\$3,200; S\$6,000 = US\$4,800. The median monthly household income of the Singapore population was S\$3,770 in 2014 (Ministry of Manpower, Singapore).<sup>33</sup>

<sup>e</sup>Use of Fisher exact test because the number of expected count is less than 5.



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**Table 2**

*Fit Indices for One- to Four-Class Unconditional Models for Depressive Symptoms*

Number of Classes	Number of Parameters	Log-Likelihood	BIC	BLRT <i>p</i> value	Entropy
1	6	-2387.32	4807.41	-	-
2	9	-2265.36	4579.85	< 0.001	.74
3	12	-2218.00	4501.46	< 0.001	.79
4	15	-2203.93	4489.76	< 0.001	.77

*Note.* BIC = Bayesian Information Criterion; BLRT = Bootstrapped Likelihood Ratio Test.

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**Table 3**

*Fit Indices for One- to Four-Class Unconditional Models for Anxious Symptoms*

Number of Classes	Number of Parameters	Log-Likelihood	BIC	BLRT <i>p</i> value	Entropy
1	6	-2479.97	4992.69	-	-
2	9	-2333.02	4715.17	< 0.001	.80
3	12	-2299.09	4663.69	< 0.001	.78
4	15	-2286.57	4655.04	< 0.001	.75

*Note.* BIC = Bayesian Information Criterion; BLRT = Bootstrapped Likelihood Ratio Test.

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**Table 4**

*Multinomial Logistic Regression for Sociodemographic and Medical Predictors of Latent Class Membership (N=218)*

	Depressive Symptoms			Anxious Symptoms		
	Low Stable <sup>a</sup> vs. High Stable			Low Stable <sup>a</sup> vs. High Stable		
	B	SE	<i>p</i>	B	SE	<i>p</i>
Age	-.082	.028	0.003	-.055	.021	0.009
Gender						
Female	-.227	.365	0.5	.288	.329	0.3
Male	0	–	–	0	–	–
Ethnicity						
Chinese	1.012	.370	0.006	.047	.325	0.9
Non-Chinese <sup>b</sup>	0	–	–	0	–	–
Marital Status						
Married	-.411	.399	0.3	-.038	.347	0.9
Not Married	0	–	–	0	–	–
Education	-.008	.330	0.9	-.013	.296	0.9
<b>Dialysis Vintage</b>	<b>-.039</b>	<b>.038</b>	<b>0.3</b>	<b>-.085</b>	<b>.037</b>	<b>0.02</b>
Comorbidities	.265	.106	0.01	.129	.089	0.1

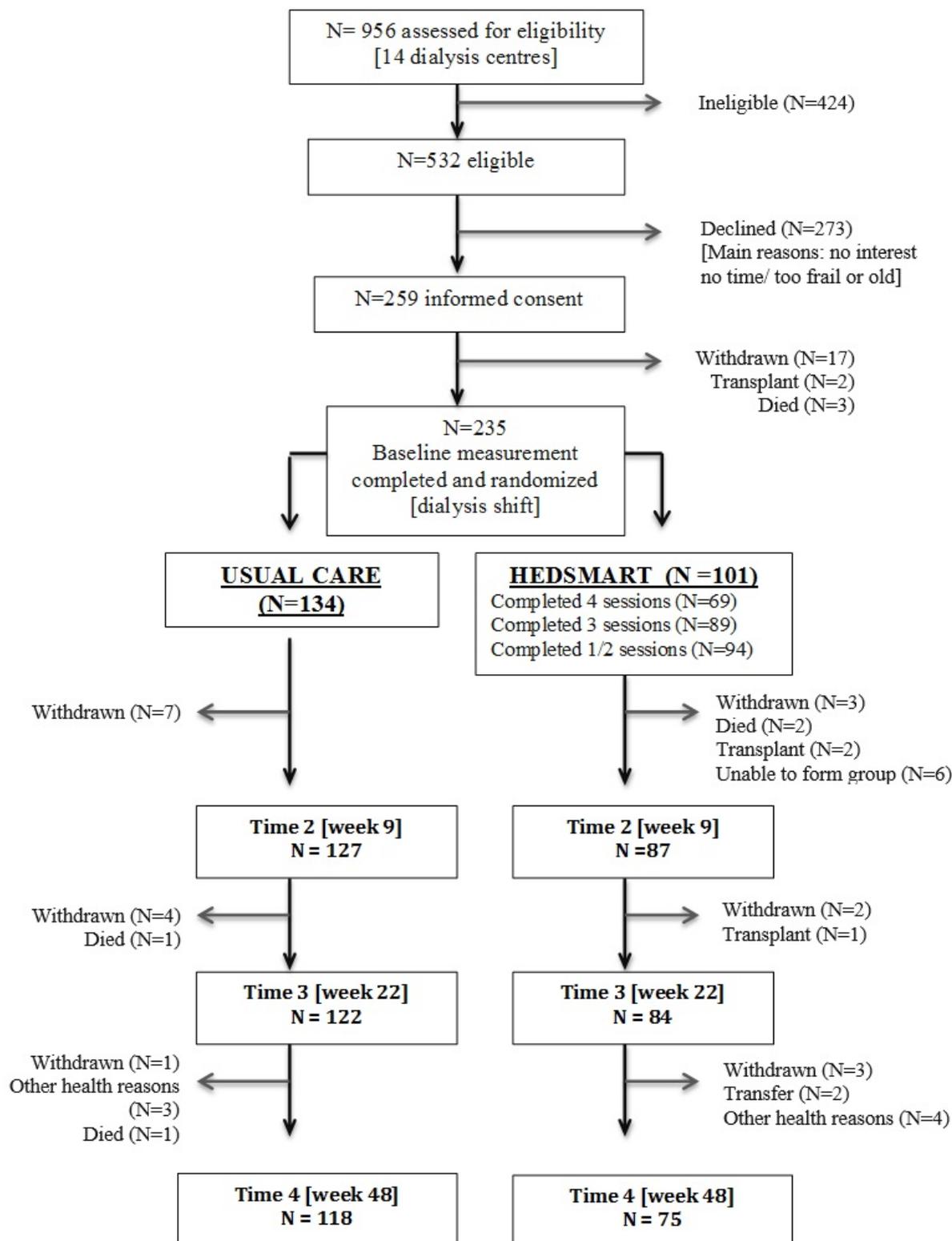
*Notes.* B = Logit, SE = Standard Error.

<sup>a</sup> Reference Class. <sup>b</sup> Non-Chinese comprise Malay, Indian, and Other ethnic minorities.

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*Figure 1.* Flowchart of Recruitment Process.

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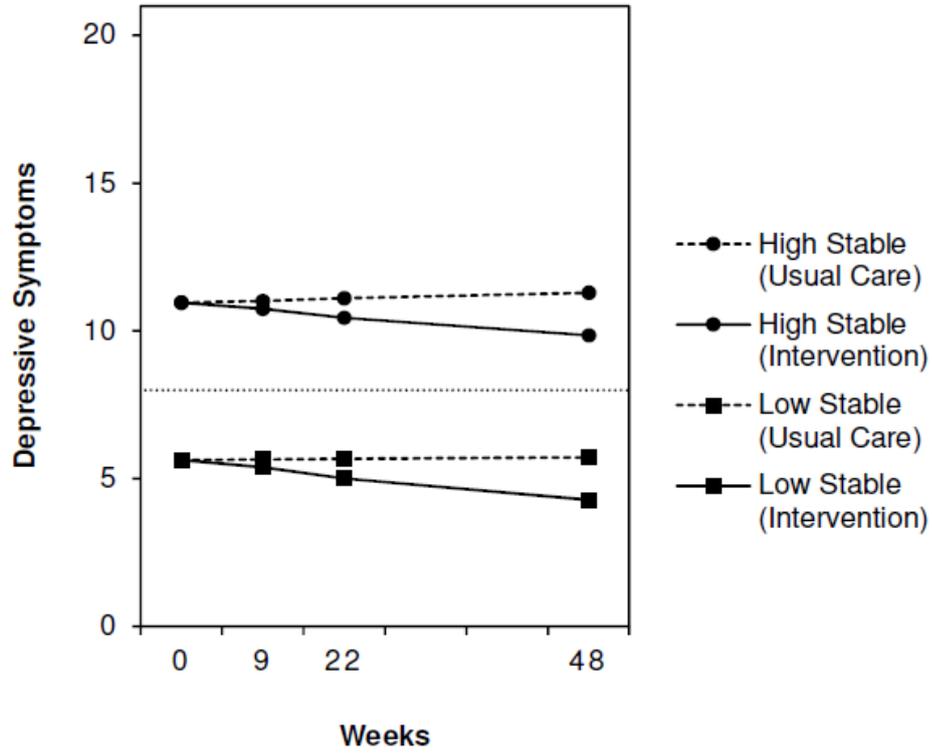


## DEPRESSION & ANXIETY TRAJECTORIES IN HED-SMART

*Figure 2.* Estimated trajectories of depressive symptoms (Panel A) and anxious symptoms (Panel B). Latent Class Growth Analysis (LCGA) identified two substantively distinct groups of trajectories of depressive symptoms and anxious symptoms: low stable (■) and high stable (●). Within each group, HED-SMART intervention (continuous lines), as compared to usual care (dashed lines), was associated with reductions in depressive symptoms ( $p = .025$ ) and anxious symptoms ( $p = .057$ ). Scores  $\geq 8$  (dotted lines) signified caseness.

# DEPRESSION & ANXIETY TRAJECTORIES IN HED-SMART

A



B

