Published in final edited form as:

Hemodial Int. 2015 April ; 19(2): 216–224. doi:10.1111/hdi.12247.

Longitudinal Associations of Depressive Symptoms and Pain with Quality of Life in Patients Receiving Chronic Hemodialysis

Linda Y. Belayev, MD¹, Maria K. Mor, PhD^{3,4}, Mary Ann Sevick, ScD, RN⁵, Anne Marie Shields, MSN, RN³, Bruce L. Rollman, MD, MPH⁶, Paul M. Palevsky, MD^{1,2}, Robert M. Arnold, MD^{6,7}, Michael J. Fine, MD, MSc^{3,6}, and Steven D. Weisbord, MD, MSc^{1,2,3}

¹Renal-Electrolyte Division, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA

²Renal Section, Medicine Service Line, VA Pittsburgh Healthcare System, Pittsburgh, PA

³Center for Health Equity Research and Promotion, VA Pittsburgh Healthcare System, Pittsburgh, PA

⁴Department of Biostatistics, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA

⁵Department of Population Health, New York University School of Medicine, New York, NY

⁶Division of General Internal Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA

⁷Division of Palliative Care, University of Pittsburgh School of Medicine, Pittsburgh, PA

⁸Nephrology Department, Geisinger Medical Center, Danville, PA

Abstract

Background—Depressive symptoms and pain are common in patients on chronic hemodialysis (HD), yet their associations with quality of life (QOL) are not fully understood. We sought to characterize the longitudinal associations of these symptoms with QOL.

Methods—As part of a trial comparing two symptom management strategies in patients receiving chronic HD, we assessed depressive symptoms using the Patient Health Questionnaire-9 (PHQ-9), and pain using the Short-Form McGill Pain Questionnaire (SF-MPQ) monthly over 24 months. We assessed health-related QOL (HR-QOL) quarterly using the Short Form 12 (SF-12) and global QOL (G-QOL) using a single item survey. We used random effects linear regression to analyze the independent associations of depressive symptoms and pain, scaled based on 5 point increments in symptom scores, with HR-QOL and G-QOL.

Direct correspondence and reprint requests to: Steven D. Weisbord MD, MSc, 7E Room 120, VA Pittsburgh Healthcare System, 111F-U, Pittsburgh, PA 15240, weisbordsd@upmc.edu, Tel: 412-360-3911, Fax: 412-360-6908. SDW and MKM contributed equally to this work.

Conflict of interest statement - None of the authors has any conflicts of interest to disclose

Disclosure: The opinions expressed in this article are those of the authors and do not represent the views of the Department of Veterans Affairs or the United States Government.

Results—Overall, 286 patients completed 1,417 PHQ-9 and SF-MPQ symptom assessments, 1,361 SF-12 assessments, and 1,416 G-QOL assessments. Depressive symptoms were independently and inversely associated with SF-12 physical HR-QOL scores ($\beta = -1.09$; 95% CI: -1.69, -0.50, $p < 0.001$); SF-12 mental HR-QOL scores ($\beta = -4.52$; 95% CI: -5.15, -3.89, $p < 0.001$); and G-QOL scores ($\beta = -0.64$; 95% CI: -0.79, -0.49, $p < 0.001$). Pain was independently and inversely associated with SF-12 physical HR-QOL scores ($\beta = -0.99$; 95% CI: -1.30, -0.68, $p < 0.001$) and G-QOL scores ($\beta = -0.12$; 95% CI: -0.20, -0.05, $p = 0.002$); but not with SF-12 mental HR-QOL scores ($\beta = -0.16$; 95% CI: -0.050, 0.17, $p = 0.34$).

Conclusion—In patients receiving chronic HD, depressive symptoms and to a lesser extent pain, are independently associated with reduced HR-QOL and G-QOL. Interventions to alleviate these symptoms could potentially improve patients' HR-QOL and G-QOL.

Keywords

depressive symptoms; depression; quality of life; pain; symptoms

Introduction

Patients with chronic kidney disease and those with end-stage renal disease (ESRD) receiving chronic hemodialysis (HD) experience a large burden of psychological and physical symptoms that are potentially treatable.¹⁻¹⁵ Depression is the most common psychological condition in patients receiving chronic HD with a prevalence of approximately 20-25%.^{7,16-20} Preliminary studies suggest that anti-depressant medication and cognitive behavioral therapy are effective in depressed patients on chronic HD.²¹⁻²⁴ Pain is among the most common symptoms in this population with several studies demonstrating a prevalence rate of approximately 50%.^{4,14,25} While there are limited data on the treatment of pain in patients on chronic HD, one prior study suggests that analgesic therapy is efficacious.²⁶

Data demonstrating the high prevalence and potential treatability of these two symptoms is important given empirical studies documenting their association with impaired health-related quality of life (HR-QOL).²⁷⁻³³ For example, a recent study by Preljevic *et al.* found that the presence of depression in patients on chronic dialysis was associated with lower scores on several domains of HR-QOL. Similarly, Harris *et al.* reported that both inter- and intra-dialytic pain were associated with impaired HR-QOL.³⁴ However, these and most other studies of symptoms and HR-QOL in the dialysis population used cross-sectional designs with measurement of symptoms and HR-QOL at a single point in time. The presence and severity of depression and pain likely fluctuate considerably due to life circumstances, treatment factors, and other issues. Thus, single assessments of these symptoms may not accurately capture their longitudinal associations with HR-QOL. Moreover, some investigators have advocated the importance of patient-perceived “global” QOL, yet there is a paucity of data on the associations of these symptoms with ‘global’ rather than ‘health-related’ QOL.^{35,36} Our understanding of the nature, magnitude, and independence of the associations of depressive symptoms and pain with HR-QOL and G-QOL would be enhanced substantially by analyses that utilized sequential longitudinal measurements of these patient-related domains. Identifying the presence of longitudinal

associations of depression and pain with HR-QOL and G-QOL may serve to encourage renal providers to aggressively treat these symptoms. In this study, we sought to characterize the independent associations of depressive symptoms and pain with HR-QOL and global QOL based on prospective, serial measurements of these domains.

Materials and Methods

Patient Population

This study used data collected in the Symptom Management Involving End-Stage Renal Disease (SMILE) study, a multi-center, randomized trial that compared the effectiveness of 2 management strategies for pain, depression, and sexual dysfunction in patients with ESRD receiving chronic outpatient HD.^{25,37} Participants were cognitively intact, English-speaking adults, who were not undergoing work up for living donor kidney transplant or considering peritoneal dialysis, but were receiving thrice weekly HD at 9 outpatient dialysis units in Western Pennsylvania. The Institutional Review Boards of the University of Pittsburgh and Veterans Administration Pittsburgh Healthcare System and the Western Institutional Review Board approved the SMILE trial and all patients provided informed consent prior to enrollment.

Baseline data collection and assessments of depression and pain

At baseline, study personnel (research personnel and trained nurses) conducted patient interviews and reviewed medical records to assess participants' demographic characteristics including age, race, sex, income, and educational status, as well as dialysis vintage, form of vascular access, and burden of comorbid illness. After enrollment, and then on a monthly basis for up to 24 months, depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9). Scores on the PHQ-9 range from 0 to 27, with higher scores denoting more severe depressive symptoms.³⁸ Pain was assessed on the same monthly schedule using the Short Form McGill Pain Questionnaire (SF-MPQ), which includes 15 descriptors of pain scored from 0 (no pain) to 3 (severe pain). Total pain scores range from 0 to 45, with higher scores denoting greater levels of pain.^{26,39}

Study outcome assessments

The primary outcomes for this study were HR-QOL and global QOL (G-QOL). We assessed HR-QOL quarterly using the Short Form 12 (SF-12), which has been validated in patients on HD.⁴⁰⁻⁴² The SF-12 includes 12 questions that generate physical (PCS) and mental component summary (MCS) scores that reflect physical and mental domains of HR-QOL, respectively. The PCS and MCS scores range from 0 denoting the lowest level of HR-QOL to 100 denoting the highest level of HR-QOL. We evaluated G-QOL on a quarterly basis using a single item QOL scale that asks patients to answer the question: "Considering all parts of my life-physical, emotional, social, spiritual, and financial--over the past 2 days, the quality of my life has been ..." using a Likert scale from 0 (very bad) to 10 (excellent).^{35,36} Prior research has validated this scale in the chronic HD population.^{36,43,44}

Statistical analyses

As many study variables had a skewed distribution and the median/IQR is an accepted way to present normally distributed continuous data, we used medians and interquartile ranges [IQRs] to describe all continuous variables. We used frequencies/proportions for categorical variables. We assessed the internal consistency of the SF-12, PHQ-9, and SF-MPQ by calculating Cronbach's alpha. We used random effects linear regression to model the associations of depressive symptoms and pain with HR-QOL and G-QOL, utilizing a random intercept for each patient and a linear effect of time in all analyses. Although we assessed depressive symptoms and pain on a monthly basis as part of the parent trial, the current study is based on analyses that only utilized symptom scores from the assessments performed the month prior to the quarterly HR-QOL and G-QOL assessments. Our primary analyses considered depressive symptoms and pain as continuous variables based on 5-point increments in symptom scores. We scaled the symptom scores as such because 5 point increments on the PHQ-9 denote an increase in the level of depressive symptoms and likely reflect a clinically significant increase in SF-MPQ score. We performed secondary analyses in which we categorized depressive symptoms based on PHQ-9 scores ≥ 10 denoting the presence of moderate to severe depressive symptoms. We categorized pain as severe versus not severe based on the presence versus absence of a report of severe pain (score of 3) on any of the 15 pain descriptors on the SF-MPQ. All models were adjusted for the following potential confounders: age, sex, race, employment, income, comorbid illness burden, time on dialysis, and type of vascular access. The analyses also included a fixed effect for the dialysis unit and an indicator variable for the dialysis schedule (Monday/Wednesday/Friday vs. Tuesday/Thursday/Saturday), which allowed us to account for the unit of randomization in the parent SMILE trial.³⁷ In addition, because of the relationship between pain and depression, analyses for each symptom included the other symptom in the analytical models.

We report the beta coefficients (β) with corresponding 95% confidence intervals from the multivariable models. For the primary analyses, these β coefficients reflect the magnitude decrease in SF-12 PCS, SF-12 –MCS, and G-QOL scores for each 5-point increment in PHQ-9 and SF-MPQ scores. For the secondary analyses, these β coefficients reflect the magnitude of decrease in SF-12 PCS, SF-12 MCS, and G-QOL scores associated with the presence of moderate to severe depressive symptoms (PHQ-9 ≥ 10) and the presence of severe pain (score on at least 1 SF-MPQ item of 3). P-values <0.05 were considered statistically significant. All analyses were conducted using SAS 9.3 (Cary, NC) and Stata 12 (College Station, TX).

Results

Study population and study instruments

Of 288 patients enrolled in the SMILE trial, 259 (90%) completed at least one SF-12 and/or G-QOL assessment and PHQ-9 and SF-MPQ the previous month. These 259 patients comprised the analytic study sample. The median patient age was 63 years [IQR 56, 72], 39% were African Americans, 56% were male, and 53% had comorbid diabetes mellitus (Table 1). Patients were followed for a median of 640 days [IQR 420, 721]. The

standardized Cronbach's alpha was 0.90 for the SF-12, 0.83 for the PHQ-9, and 0.93 for the SF-MPQ.

Depressive symptoms, pain, HR-QOL, and G-QOL

Patients in the analytic sample completed a total of 1,417 PHQ-9 and SF-MPQ assessments. At least mild depressive symptoms (PHQ-9 score of ≥ 5) were reported on 601 (42%) assessments while moderate to severe depressive symptoms (PHQ-9 score of ≥ 10) were reported on 238 (17%) assessments. Ninety-two patients (36%) reported moderate to severe depressive symptoms on at least one assessment and 32 (12%) reported moderate to severe depressive symptoms on at least 75% of all assessments. Pain was reported on 1,119 (79%) assessments. The maximum level of pain reported on any of the assessments was severe (score of 3 on any of the 15 pain descriptors) on 367 (26%), moderate (score of 2 on any of the 15 pain descriptors) on 404 (29%), and mild (maximum score of 1 on any of the 15 pain descriptors) on 351 (25%). Pain was reported on at least one assessment by 246 (95%) patients, and 190 (73%) patients reported pain on 75% or more of their assessments. Patients completed a median of 6 [IQR 3, 8] SF-12 assessments and 6 [IQR 4, 8] G-QOL assessments. The mean SF-12 PCS score was 37.5 ± 11.5 ; mean SF-12 MCS score was 50.2 ± 11.0 ; and mean G-QOL score was 6.8 ± 2.4 . Mean longitudinal symptom and QOL scores are depicted in the Figure.

Associations of depressive symptoms with HR-QOL and global QOL

In the unadjusted longitudinal analyses, depressive symptoms were inversely associated with SF-12 PCS and MCS scores and G-QOL scores (Table 2). After multivariable adjustment, depressive symptoms were independently and inversely associated with SF-12 PCS scores ($\beta = -1.09$; 95% CI: -1.69, -0.50, $p < 0.001$); SF-12 MCS scores ($\beta = -4.52$; 95% CI: -5.15, -3.89, $p < 0.001$); and G-QOL scores ($\beta = -0.64$; 95% CI: -0.79, -0.49, $p < 0.001$) (Table 2). In unadjusted analyses that considered depressive symptoms as a dichotomous variable, the presence of moderate to severe depressive symptoms was inversely associated with SF-12 PCS, SF-12 MCS, and G-QOL scores (Table 2). In multivariable analyses, the presence of moderate to severe depressive symptoms was independently and inversely associated with SF-12 PCS scores ($\beta = -1.50$; 95% CI: -2.83, -0.17, $p = 0.03$); SF-12 MCS scores ($\beta = -8.81$; 95% CI: -10.30, -7.33, $p < 0.001$); and G-QOL scores ($\beta = -1.32$; 95% CI: -1.66, -0.97, $p < 0.001$) (Table 2). In sensitivity analyses that assessed higher orders (quadratic and cubic) of time, patient-level random slopes for time and depressive symptoms, and interactions between depressive and pain symptoms, the estimated associations between depressive symptoms and study outcomes were virtual unchanged (data not shown).

Associations of pain with HR-QOL and global QOL

In unadjusted analyses, pain was inversely associated with SF-12 PCS, SF-12 MCS, and G-QOL scores (Table 3). After multivariable adjustment, pain was independently and inversely associated with SF-12 PCS scores ($\beta = -0.99$; 95% CI: -1.30, -0.68, $p < 0.001$) and G-QOL scores ($\beta = -0.12$; 95% CI: -0.20, -0.05, $p = 0.002$), but not with SF-12 MCS scores ($\beta = -0.16$; 95% CI: -0.50, 0.17, $p = 0.34$) (Table 3). In unadjusted analyses that considered pain as a categorical variable, the presence of severe pain was inversely associated with SF-12 PCS, SF-12 MCS, and G-QOL scores (Table 3). In multivariable analyses, the presence of severe

pain was independently and inversely associated with SF-12 PCS scores ($\beta = -1.78$; 95% CI: -2.82, -0.74, $p=0.001$) and SF-12 MCS scores ($\beta = -1.20$; 95% CI: -2.83, -0.01, $p=0.048$); but not with G-QOL scores ($\beta = -0.27$; 95% CI: -0.55, 0.01, $p=0.05$) (Table 3). These results were unchanged in the sensitivity analyses described above (data not shown).

Discussion

This longitudinal study of patients with ESRD on chronic HD demonstrates that depressive symptoms and, to a lesser extent pain, are independently associated with impairments in health-related and global QOL in patients receiving chronic in-center HD. The validity of our findings are strengthened by the multiple longitudinal assessments of these domains and suggest that symptom alleviating treatment, particularly targeting depressive symptoms, may favorably affect patients' mental and global well-being.

Prior studies that were principally cross-sectional in design demonstrated associations of depression with decrements in HR-QOL in patients on chronic dialysis. Drayer *et al.* studied 62 patients on chronic HD and found that patients with depression had lower SF-36 MCS and PCS scores, although this later difference was not statistically significant.²⁸ Sacks *et al.* assessed depression and HR-QOL with the Beck Depression Inventory and Illness Effects Questionnaire, respectively, in 57 patients receiving chronic dialysis and demonstrated an association of higher BDI scores (i.e., greater levels of depression) with increased IEQ scores (i.e., greater patient perception of their illness interfering with their personal and social behavior).³⁰ These and other studies measured depression and HR-QOL at a single time point.^{27,29,44} However, depressive symptoms (and potentially HR-QOL and global QOL) fluctuate over time due to patient-specific circumstances, illness burden, and treatment effects. By utilizing data from multiple serial quarterly assessments, the current study builds upon prior research by characterizing the magnitude and independence of the associations of depressive symptoms with HR-QOL and global QOL, accounting for changes in these domains over time. Our findings also confirm that depressive symptoms have considerably stronger associations with mental HR-QOL and global QOL than with physical HR-QOL.

Preliminary research also suggests that pain is associated with impaired HR-QOL.^{45,46} Davison *et al.* assessed pain using the Edmonton Symptom Assessment Scale and HR-QOL using the Kidney Disease Quality of Life Short Form on 2 occasions 6 months apart among 591 patients on chronic dialysis.⁴⁵ Similar to the SF-12 used in the current study, the KDQOL-SF generates PCS and MCS scores ranging from 0 to 100. Pain was reported by 72% of patients and was independently associated with baseline PCS and MCS scores. Change in pain at 6 months was independently associated with change in PCS scores at this time point, but not with change in MCS scores. The nature of these associations is congruent with those seen in our study. However, the coefficients characterizing the strength of the association of pain with HR-QOL, both in the study by Davison and our study, were of very small magnitude. This suggests that while increases in pain and the presence of severe pain have statistically significant associations with decrements in HR-QOL, the associations may not be clinically significant. Moreover, these associations are of lower magnitude than the associations for depressive symptoms. Our results also suggest that pain does not have a

clinically significant association with global QOL. Whether these findings are related to the subjective nature of pain, the manner in which pain was assessed in these studies, or the fact that pain may not contribute significantly to impaired health-related or global QOL are not known; however, these findings clearly warrants further investigation.

Multiple studies have documented the marked decrements in HR-QOL among patients dependent on chronic dialysis.^{9,47-53} Unfortunately, few interventions other than renal transplantation have been shown to mediate improvements in HR-QOL in this patient population. Trials to date investigating anti-depressant medication and cognitive behavioral therapy in patients treated with chronic dialysis suggest that in addition to alleviating depressive symptoms, these treatments may improve HR-QOL.^{22,54,55} However, small patient populations and the lack of long-term follow up are key limitations to these trials. Consequently, the sustained effects of anti-depressant therapy and cognitive behavioral therapy on HR-QOL, particularly mental HR-QOL are unknown, as are their effects on G-QOL. The robust associations of depressive symptoms with mental HR-QOL and global QOL in our study suggest that practitioners should consider anti-depressant medication and/or non-pharmacological therapy as potential means to improve patients' mental and global sense of well-being, although adequately powered trials are needed to determine whether the associations seen in our study translate into clinically meaningful improvements in HR-QOL and global QOL with anti-depressant treatment. There is a dearth of data on the potential impact of analgesic therapy on HR-QOL. A recent cross-over trial studied the efficacy of gabapentin and pregabalin in 40 patients on chronic HD and demonstrated statistically significant improvements in pain and multiple domains of HR-QOL with these medications.⁵⁶ While these findings are promising, this study was limited by the very small number of patients and issues with study design. Our results suggest that analgesic therapy (pharmacological or non-pharmacological) may not have meaningful effects on health-related or global QOL, although alleviation of pain is sufficiently important to warrant treatment. Well-designed, adequately powered trials of analgesic therapy will have to be conducted to determine if the alleviation of pain meaningfully enhances health-related and/or global QOL.

Our study has several limitations. First, our patient population was comprised of individuals participating in a clinical trial and was drawn from a single geographic area, which may reduce the generalizability of the findings. Second, the SF-12 and G-QOL are generic instruments that are not specific to patients with ESRD on chronic HD. Third, the PHQ-9 is not considered the gold-standard for the diagnosis of 'major depression'. As such, our findings reflect the associations of depressive symptoms rather than 'major depression' with health-related and global QOL. Fourth, our use of continuous pain scores based on summing responses on the 15 SF-MPQ items may not be a valid approach in all patients as individuals who report mild pain on multiple SF-MPQ items may have higher summary pain scores than patients who report severe pain on a small number of items. However, our analyses that considered pain as a continuous predictor variable are consistent with those that considered pain as a categorical variable (severe pain v. no severe pain). Fifth, our analyses were based on the symptom scores from the month prior to the outcome assessments. In sensitivity analyses that utilized the two most recent monthly symptom scores prior to the outcome assessment, the results were inconsistent as to which lagged score had a stronger association

with the outcomes and did not provide sufficient insight into the data to justify presenting these more complex models. Sixth, in certain analyses, a greater difference was observed between “no to minimal” and “mild” symptoms than between “mild” and “moderate” symptoms than would be predicted by a linear model. However, for ease of interpretation, our results reflect the average linear association between symptoms and study outcomes. Lastly, this study was observational and cannot establish causal associations of symptoms with health-related and global QOL.

In conclusion, depressive symptoms, and to a considerably lesser degree pain, are independently associated with impaired HR-QOL and global QOL in patients with ESRD receiving chronic in-center HD. The strength and validity of these findings are based on the prospective, longitudinal assessments of these symptoms and of HR-QOL and G-QOL. Considering the marked burden of depressive symptoms and pain in patients dependent on chronic HD, our findings underscore the strong need to evaluate multi-disciplinary approaches to implement symptom alleviating therapy in order to improve the mental and physical well-being of this chronically ill patient population.

Acknowledgments

Funding disclosure - SDW was supported by a Department of Veterans Affairs Health Services Research and Development Merit Review award (IIR 07-190) and LYB was supported by NIH/NIDDK grant T32 DK061296.

References

1. Barrett BJ, Vavasour HM, Major A, Parfrey PS. Clinical and psychological correlates of somatic symptoms in patients on dialysis. *Nephron*. 1990; 55:10–5. [PubMed: 2352574]
2. Carreon M, Fried LF, Palevsky PM, Kimmel PL, Arnold RM, Weisbord SD. Clinical correlates and treatment of bone/joint pain and difficulty with sexual arousal in patients on maintenance hemodialysis. *Hemodialysis international*. 2008; 12:268–74. [PubMed: 18394062]
3. Curtin RB, Bultman DC, Thomas-Hawkins C, Walters BA, Schatell D. Hemodialysis patients' symptom experiences: effects on physical and mental functioning. *Nephrol Nurs J*. 2002; 29:562, 7–74. discussion 75, 98. [PubMed: 12596605]
4. Davison SN. Pain in hemodialysis patients: prevalence, cause, severity, and management. *Am J Kidney Dis*. 2003; 42:1239–47. [PubMed: 14655196]
5. Hedayati SS, Grambow SC, Szczech LA, Stechuchak KM, Allen AS, Bosworth HB. Physician-diagnosed depression as a correlate of hospitalizations in patients receiving long-term hemodialysis. *Am J Kidney Dis*. 2005; 46:642–9. [PubMed: 16183419]
6. Kimmel PL. Psychosocial factors in adult end-stage renal disease patients treated with hemodialysis: correlates and outcomes. *Am J Kidney Dis*. 2000; 35:S132–40. [PubMed: 10766011]
7. Kimmel PL. Psychosocial factors in dialysis patients. *Kidney international*. 2001; 59:1599–613. [PubMed: 11260433]
8. Kimmel PL. Depression in patients with chronic renal disease: what we know and what we need to know. *J Psychosom Res*. 2002; 53:951–6. [PubMed: 12377308]
9. Kimmel PL, Cohen SD, Weisbord SD. Quality of life in patients with end-stage renal disease treated with hemodialysis: survival is not enough! *Journal of nephrology*. 2008; 21(Suppl 13):S54–8. [PubMed: 18446733]
10. Kimmel PL, Peterson RA, Weihs KL, et al. Psychosocial factors, behavioral compliance and survival in urban hemodialysis patients. *Kidney international*. 1998; 54:245–54. [PubMed: 9648085]
11. Merkus MP, Jager KJ, Dekker FW, de Haan RJ, Boeschoten EW, Krediet RT. Physical symptoms and quality of life in patients on chronic dialysis: results of The Netherlands Cooperative Study on

- Adequacy of Dialysis (NECOSAD). *Nephrol Dial Transplant*. 1999; 14:1163–70. [PubMed: 10344356]
12. Weisbord SD. Symptoms and their correlates in chronic kidney disease. *Advances in chronic kidney disease*. 2007; 14:319–27. [PubMed: 17904498]
 13. Weisbord SD, Carmody SS, Bruns FJ, et al. Symptom burden, quality of life, advance care planning and the potential value of palliative care in severely ill haemodialysis patients. *Nephrol Dial Transplant*. 2003; 18:1345–52. [PubMed: 12808172]
 14. Weisbord SD, Fried LF, Arnold RM, et al. Prevalence, severity, and importance of physical and emotional symptoms in chronic hemodialysis patients. *J Am Soc Nephrol*. 2005; 16:2487–94. [PubMed: 15975996]
 15. Abdel-Kader K, Unruh ML, Weisbord SD. Symptom burden, depression, and quality of life in chronic and end-stage kidney disease. *Clin J Am Soc Nephrol*. 2009; 4:1057–64. [PubMed: 19423570]
 16. 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; 18:365–74. [PubMed: 3235282]
 17. Cukor D, Rosenthal DS, Jindal RM, Brown CD, Kimmel PL. Depression is an important contributor to low medication adherence in hemodialyzed patients and transplant recipients. *Kidney international*. 2009; 75:1223–9. [PubMed: 19242502]
 18. Hedayati SS, Finkelstein FO. Epidemiology, diagnosis, and management of depression in patients with CKD. *Am J Kidney Dis*. 2009; 54:741–52. [PubMed: 19592143]
 19. Kimmel PL, Peterson RA, Weihs KL, et al. Multiple measurements of depression predict mortality in a longitudinal study of chronic hemodialysis outpatients. *Kidney international*. 2000; 57:2093–8. [PubMed: 10792629]
 20. Kimmel PL, Thamer M, Richard CM, Ray NF. Psychiatric illness in patients with end-stage renal disease. *The American journal of medicine*. 1998; 105:214–21. [PubMed: 9753024]
 21. Cukor, D. Psychiatric services. Vol. 58. Washington, DC: 2007. Use of CBT to treat depression among patients on hemodialysis; p. 711-2.
 22. Duarte PS, Miyazaki MC, Blay SL, Sesso R. Cognitive-behavioral group therapy is an effective treatment for major depression in hemodialysis patients. *Kidney international*. 2009; 76:414–21. [PubMed: 19455196]
 23. Blumenfeld M, Levy NB, Spinowitz B, et al. Fluoxetine in depressed patients on dialysis. *Int J Psychiatry Med*. 1997; 27:71–80. [PubMed: 9565715]
 24. Levy NB, Blumenfeld M, Beasley CM Jr, et al. Fluoxetine in depressed patients with renal failure and in depressed patients with normal kidney function. *Gen Hosp Psychiatry*. 1996; 18:8–13. [PubMed: 8666216]
 25. Weisbord SD, Mor MK, Green JA, et al. Comparison of symptom management strategies for pain, erectile dysfunction, and depression in patients receiving chronic hemodialysis: a cluster randomized effectiveness trial. *Clin J Am Soc Nephrol*. 2013; 8:90–9. [PubMed: 23024159]
 26. Barakzoy AS, Moss AH. Efficacy of the world health organization analgesic ladder to treat pain in end-stage renal disease. *J Am Soc Nephrol*. 2006; 17:3198–203. [PubMed: 16988057]
 27. Cruz LN, Fleck MP, Polanczyk CA. Depression as a determinant of quality of life in patients with chronic disease: data from Brazil. *Soc Psychiatry Psychiatr Epidemiol*. 2010; 45:953–61. [PubMed: 19771379]
 28. Drayer RA, Piraino B, Reynolds CF 3rd, et al. Characteristics of depression in hemodialysis patients: symptoms, quality of life and mortality risk. *Gen Hosp Psychiatry*. 2006; 28:306–12. [PubMed: 16814629]
 29. Prelicjevic VT, Osthus TB, Os I, et al. Anxiety and depressive disorders in dialysis patients: association to health-related quality of life and mortality. *Gen Hosp Psychiatry*. 2013; 35:619–24. [PubMed: 23896282]
 30. Sacks CR, Peterson RA, Kimmel PL. Perception of illness and depression in chronic renal disease. *Am J Kidney Dis*. 1990; 15:31–9. [PubMed: 2294731]

31. Garcia-Llana H, Remor E, Selgas R. Adherence to treatment, emotional state and quality of life in patients with end-stage renal disease undergoing dialysis. *Psicothema*. 2013; 25:79–86. [PubMed: 23336548]
32. Son YJ, Choi KS, Park YR, Bae JS, Lee JB. Depression, symptoms and the quality of life in patients on hemodialysis for end-stage renal disease. *American journal of nephrology*. 2009; 29:36–42. [PubMed: 18679023]
33. Santoro D, Satta E, Messina S, Costantino G, Savica V, Bellinghieri G. Pain in end-stage renal disease: a frequent and neglected clinical problem. *Clin Nephrol*. 2013; 79(Suppl 1):S2–11. [PubMed: 23249527]
34. Harris TJ, Nazir R, Khetpal P, et al. Pain, sleep disturbance and survival in hemodialysis patients. *Nephrol Dial Transplant*. 2012; 27:758–65. [PubMed: 21771748]
35. Gill TM, Feinstein AR. A critical appraisal of the quality of quality-of-life measurements. *JAMA*. 1994; 272:619–26. [PubMed: 7726894]
36. Kimmel PL, Emont SL, Newmann JM, Danko H, Moss AH. ESRD patient quality of life: symptoms, spiritual beliefs, psychosocial factors, and ethnicity. *Am J Kidney Dis*. 2003; 42:713–21. [PubMed: 14520621]
37. Weisbord SD, Shields AM, Mor MK, et al. Methodology of a randomized clinical trial of symptom management strategies in patients receiving chronic hemodialysis: the SMILE study. *Contemporary clinical trials*. 2010; 31:491–7. [PubMed: 20601163]
38. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine*. 2001; 16:606–13. [PubMed: 11556941]
39. Melzack R. The short-form McGill Pain Questionnaire. *Pain*. 1987; 30:191–7. [PubMed: 3670870]
40. Resnick B, Parker R. Simplified scoring and psychometrics of the revised 12-item Short-Form Health Survey. *Outcomes Manag Nurs Pract*. 2001; 5:161–6. [PubMed: 11898312]
41. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care*. 1996; 34:220–33. [PubMed: 8628042]
42. Lacson E Jr, Xu J, Lin SF, Dean SG, Lazarus JM, Hakim RM. A comparison of SF-36 and SF-12 composite scores and subsequent hospitalization and mortality risks in long-term dialysis patients. *Clin J Am Soc Nephrol*. 2010; 5:252–60. [PubMed: 20019120]
43. Kimmel PL, Patel SS. Quality of life in patients with chronic kidney disease: focus on end-stage renal disease treated with hemodialysis. *Seminars in nephrology*. 2006; 26:68–79. [PubMed: 16412831]
44. Patel SS, Shah VS, Peterson RA, Kimmel PL. Psychosocial variables, quality of life, and religious beliefs in ESRD patients treated with hemodialysis. *Am J Kidney Dis*. 2002; 40:1013–22. [PubMed: 12407647]
45. Davison SN, Jhangri GS. Impact of pain and symptom burden on the health-related quality of life of hemodialysis patients. *Journal of pain and symptom management*. 2010; 39:477–85. [PubMed: 20303025]
46. Amro A, Waldum B, Dammen T, Miaskowski C, Os I. Symptom clusters in patients on dialysis and their association with quality-of-life outcomes. *J Ren Care*. 2014; 40:23–33. [PubMed: 24438743]
47. Evans RW, Manninen DL, Garrison LP Jr, et al. The quality of life of patients with end-stage renal disease. *The New England journal of medicine*. 1985; 312:553–9. [PubMed: 3918267]
48. Evans RW, Rader B, Manninen DL. The quality of life of hemodialysis recipients treated with recombinant human erythropoietin. Cooperative Multicenter EPO Clinical Trial Group. *Jama*. 1990; 263:825–30. [PubMed: 2404150]
49. Johnson JP, McCauley CR, Copley JB. The quality of life of hemodialysis and transplant patients. *Kidney international*. 1982; 22:286–91. [PubMed: 6757524]
50. Kutner NG, Devins GM. A comparison of the quality of life reported by elderly whites and elderly blacks on dialysis. *Geriatr Nephrol Urol*. 1998; 8:77–83. [PubMed: 9893215]
51. Simmons RG, Abress L. Quality-of-life issues for end-stage renal disease patients. *Am J Kidney Dis*. 1990; 15:201–8. [PubMed: 2305760]
52. Unruh ML, Weisbord SD, Kimmel PL. Health-related quality of life in nephrology research and clinical practice. *Seminars in dialysis*. 2005; 18:82–90. [PubMed: 15771650]

53. Weisbord SD, C S, Bruns FJ, Rotondi AJ, Cohen LM, Zeidel ML, Arnold RM. Symptom Burden, Quality-of-Life and Advance Care Planning in Highly Comorbid Hemodialysis Patients: Is There a Role for Palliative Care? *Nephrol Dial Transplant*. 2003; 18:1345–52. [PubMed: 12808172]
54. Atalay H, Solak Y, Biyik M, et al. Sertraline treatment is associated with an improvement in depression and health-related quality of life in chronic peritoneal dialysis patients. *International urology and nephrology*. 2010; 42:527–36. [PubMed: 19953347]
55. Cukor D, Ver Halen N, Asher DR, et al. Psychosocial Intervention Improves Depression, Quality of Life, and Fluid Adherence in Hemodialysis. *J Am Soc Nephrol*. 2013
56. Atalay H, Solak Y, Biyik Z, Gaipov A, Guney F, Turk S. Cross-over, open-label trial of the effects of gabapentin versus pregabalin on painful peripheral neuropathy and health-related quality of life in haemodialysis patients. *Clin Drug Investig*. 2013; 33:401–8.

Figure. Mean Longitudinal Symptom and QOL Scores

Table 1
Baseline Patient Characteristics

Characteristic	(n=259)
Age (years)	63 [56, 72]
Sex (male)	144 (56)
Race (African-American)	102 (39)
Education level ^b	
< High school	36 (14)
High school equivalent	84 (33)
>High school	138 (54)
Income	
<\$30,000/yr	132 (51)
\$30,000/yr	83 (32)
Unknown	44 (17)
Married/living with partner	125 (48)
Employed	28 (11)
Time on dialysis (years)	2.2 [0.9, 4.3]
Dialysis schedule (MWF)	168 (65)
Dialysis access	
Catheter	50 (19)
AV fistula or graft	209 (81)
CCI score ^b	
1-2	59 (23)
3-4	103 (40)
5	97 (37)
Diabetes	137 (53)
Peripheral vascular disease	32 (12)
Hemoglobin (g/dL)	11.6 [10.9, 12.3]
Albumin (g/dL)	3.8 [3.5, 4.1]
Calcium (mg/dL)	8.9 [8.5, 9.3]
Phosphorous (mg/dL)	5.0 [4.3, 5.9]
iPTH (pg/mL)	253 [175, 392]
Kt/V	1.5 [1.4, 1.6]

Abbreviations: MWF, Monday Wednesday Friday; AV, arteriovenous; CCI, Charlson Comorbidity Index; iPTH, intact parathyroid hormone

^a Continuous variables presented as median [IQR] and categorical variables as n (%)

^b Totals do not sum to 286 due to missing data from 1 patient

Table 2
Associations of Depressive Symptoms with Quality of Life Outcomes

Outcomes	Depression defined using PHQ-9 as continuous variable		Depression defined using PHQ-9 as categorical variable	
	Unadjusted association	Adjusted association	Unadjusted association	Adjusted association
SF-12 PCS	-1.47 [-2.05, -0.90]	-1.09 [-1.69, -0.50]	-1.71 [-3.01, -0.40] ^a	-1.50 [-2.83, -0.17] ^b
SF-12 MCS	-4.61 [-5.20, -4.03]	-4.52 [-5.15, -3.89]	-9.06 [-10.51, -7.61]	-8.81 [-10.30, -7.33]
G-QOL	-0.70 [-0.84, -0.56]	-0.64 [-0.79, -0.49]	-1.36 [-1.70, -1.02]	-1.32 [-1.66, -0.97]

Data denote β coefficient [95% CI]

p<0.001 unless otherwise denoted

^a
p=0.01

^b
p=0.03

Table 3
Associations of Pain with Quality of Life Outcomes

Outcome	Pain defined using MPQ-SF as continuous variable		Pain defined using MPQ-SF as categorical variable	
	Unadjusted association	Adjusted association	Unadjusted association	Adjusted association
SF-12 PCS	-1.11 [-1.41, -0.82]	-0.99 [-1.30, -0.68]	-2.06 [-3.08, -1.03]	-1.78 [-2.82, -0.74]
SF-12 MCS	-0.82 [-1.16, -0.48]	-0.16 [-0.50, 0.17] ^a	-2.26 [-3.47, -1.05]	-1.20 [-2.83, -0.01] ^b
G-QOL	-0.22 [-0.30, -0.15]	-0.12 [-0.20, -0.05]	-0.46 [-0.74, -0.19]	-0.27 [-0.55, 0.01] ^c

Data denote β coefficient [95% CI]

p<0.01 unless otherwise denoted

^a
p=0.34

^b
p=0.048

^c
p=0.05