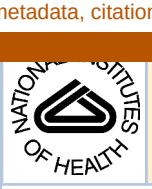

Published in final edited form as:

Res Social Adm Pharm. 2009 June ; 5(2): 143–153. doi:10.1016/j.sapharm.2008.06.004.

Pre-Dialysis Chronic Kidney Disease: Evaluation of Quality of Life in Clinic Patients Receiving Comprehensive Anemia Care

Richard A. Hansen, PhD,
Assistant Professor of Pharmacy, University of North Carolina; School of Pharmacy, Division of Pharmaceutical Outcomes and Policy, Center for Pharmaceutical Outcomes and Policy, Chapel Hill, NC 27599, Phone: (919) 966-7517, Fax: (919) 966-8486, Email: rahansen@unc.edu

Hyunsook Chin, MPH,
Statistician, University of North Carolina; School of Medicine, Division of Nephrology and Hypertension, UNC Kidney Center, Chapel Hill, NC 27599

Susan Blalock, PhD, MPH, and
Associate Professor of Pharmacy, University of North Carolina; School of Pharmacy, Division of Pharmaceutical Outcomes and Policy, Chapel Hill, NC 27599

Melanie S. Joy, Pharm.D., FCCP
Associate Professor of Medicine and Pharmacotherapy and Experimental Therapeutics, University of North Carolina; School of Medicine, Division of Nephrology and Hypertension, UNC Kidney Center, Chapel Hill, NC 27599

Abstract

Background—Anemia is common in chronic kidney disease (CKD), and suboptimal management of anemia can lead to serious health complications and poor quality of life.

Objectives—1) To describe health-related and overall quality of life among patients entering a clinic focused on anemia management; 2) to compare their baseline quality of life with other relevant populations; 3) to explore predictors of quality of life prior to anemia management; and 4) to explore changes in quality of life over 1 year for patients managed in the clinic.

Methods—The Kidney Disease Quality of Life questionnaire – short form (KDQOL™-SF) was used to measure kidney disease specific and overall quality of life in a cohort of pre-dialysis CKD patients (n=79) enrolled in the clinic from January 2003 to September 2004. Baseline measures were compared to previously published measurements. The influence of demographic and clinical characteristics on baseline quality of life was explored. Changes in quality of life were evaluated over time.

Results—Patients with CKD entering the clinic had lower overall quality of life compared with estimates from the general US population (physical composite 35.7 vs. 48.4 and mental composite

Correspondence to: Richard A. Hansen.

Authors' contributions: RA conducted the quality of life analysis and drafted the manuscript. HC performed statistical analyses. SB participated in the design of the study. MJ conceived of the study and participated in its design and coordination. All authors read and approved the final manuscript.

Competing interests: The authors declare they have no competing interests.

46.0 vs. 50.2, respectively). Clinic patients had better kidney disease specific scores than patients with end stage kidney disease. General quality of life scores were similar regardless of kidney disease severity, with the exception of physical functioning which was lowest for patients with end-stage disease. Hemoglobin was the only factor predictive of quality of life. Over time, quality of life improved among patients managed in the CKD clinic, with statistically significant improvements in sleep (change of 6.2 ± 15.2; $p < 0.05$) and social function (change of 11.6 ± 27.7; $p < 0.05$).

Conclusions—Patients with anemia of chronic kidney disease reported reduced quality of life compared to populations without kidney disease, but better quality of life compared to populations with end stage kidney disease on dialysis. Quality of life generally improved among patients managed in the multidisciplinary anemia clinic.

Keywords

Quality of life; chronic kidney disease; anemia; SF-36; KDQOL; multidisciplinary

BACKGROUND

Approximately 20 million people in the US have chronic kidney disease (CKD),[1] and at least eight million of these are classified as having moderate to severe disease (CKD Stages 3 through 5),[2] which is defined by reduced kidney function measured by glomerular filtration rate (Table 1). Pre-dialysis CKD patients often exhibit many of the complications of end stage kidney disease (ESRD), including metabolic bone disease, fluid and electrolyte disorders, and anemia. Anemia complications generally are present after the glomerular filtration rate drops to less than 60 ml/minute (i.e., ≥ stage 3), and the prevalence becomes greater as renal function is lost.

Inadequate management of anemia in patients on dialysis has been associated with negative health outcomes, including left ventricular hypertrophy, decreased mental capacity,decreased quality of life, and increased risk of hospitalizations.[3–7] Some of these negative outcomes can be avoided through administration of erythropoietic proteins (e.g., epoetin alfa or darbepoetin alfa) and correction of anemia.[8,9] Unfortunately, only one-third of CKD patients ever receive treatment for anemia in the pre-dialysis time frame, as shown by publications reviewing clinical characteristics of incident dialysis patients. [10] Furthermore, the average hematocrit at dialysis initiation is approximately 30%, which is significantly less than that recommended by the National Kidney Foundation.[9,10] these data suggest that the effects of inadequate control of anemia in the CKD population (pre-dialysis) requires additional study.

Reasons for inappropriate control of anemia may include such factors as high cost of recombinant erythropoietins, failure of clinicians to screen for anemia in CKD, and lack of integrated, multidisciplinary practice approaches. Integrated, multidisciplinary practice approaches are particularly important in managing anemia, because related drug therapy requires frequent assessments of hemoglobin levels, adjustments of doses/frequencies, and adequate documentation to obtain insurance coverage.

We have previously described our Institution's multidisciplinary approach to managing pre-dialysis CKD-related anemia.[11] Given the practicality and the improved clinical outcomes of the multidisciplinary CKD clinic, we sought to explore health-related quality of life outcomes for patients enrolled in the clinic. In light of recent controversies over hemoglobin targets and potential cardiovascular adverse events with erythropoietic stimulating proteins, it is important to note that at the time of this study our Institution had adapted hemoglobin targets consistent with current recommendations.[12,13] Thus, quality of life among patients managed in our Institution's multidisciplinary clinic is likely to be reflective of the current environment.

The objectives of this paper are as follows:

1. to describe kidney disease-related and general health-related quality of life among patients entering a clinic focused on anemia management;
2. to compare quality of life among our sample to estimates from the general US population and previous studies of patients with varying degrees of kidney disease;
3. to explore whether certain demographic and clinical characteristics are predictive of quality of life among patients beginning anemia management therapy; and
4. to explore changes in quality of life over 1 year for patients managed in the clinic.

To our knowledge, our study is the first to provide benchmark data for the kidney disease specific scales using the Kidney Disease Quality of Life instrument – short form (KDQOL-SF™, Rand Corporation, Santa Monica, CA).[14] Further, our exploratory analyses provide insights into important predictors of quality of life and the benefits of appropriate management of anemia among patients with CKD.

METHODS

Study subjects and procedures

A study to collect clinical and quality of life outcomes in a CKD clinic was approved by the University's Committee on the Protection of the Rights of Human Subjects and conducted in accordance with the Good Clinical Practice guidelines and the Declaration of Helsinki. Data were collected from patients participating in the CKD clinic between January 2003 and September 2004. The qualification for entry into the CKD clinic was the presence of anemia requiring erythropoietic stimulating agents and not currently requiring renal replacement therapy (i.e., pre-dialysis).[11] The mean (SD) GFR for patients in this clinic was 29.3 (18.1) mL/min, with most patients being classified as Stages 3 and 4 CKD. To be included in the current study, patients had to have completed the KDQOL-SF™ at least once after entering the clinic. Changes in the KDQOL-SF™ over time were assessed only for patients that returned at 6 and/or 12 months.

Measures

The KDQOL-SF™ is a self report measure originally developed for individuals with kidney disease and on dialysis.[14] We excluded dialysis-specific questions because our patient population did not have severe enough kidney disease to require dialysis.. This instrument previously has been used in CKD,[15, 16] although formal validation work has not been conducted. Our analysis focused on 9 domains of health-related concerns of individuals with kidney disease, including 1) symptoms/problems, 2) effects of kidney disease, 3) burden of kidney disease, 4) work status, 5) cognitive function, 6) quality of social interaction, 7) sexual function, 8) sleep, and 9) social support. The internal consistency reliability estimates [17] for domains of the scale range from 0.61 to 0.90, while correlations with the KDQOL™ Long-Form (criterion validity) range from 0.91 to 1.00.[18] Numeric responses to the KDQOL-SF™ are pre-coded so that higher numbers reflect better health. Raw scores are then transformed to a 0 to 100 scale, so that the lowest possible score is set at 0 and the highest score set at 100. Items within each domain are averaged together to create a summary scale score. We chose not to report an overall health score because our modified scale (deleting specific domains) has not been previously validated.

The KDQOL-SF™ also includes a 36-item health survey (SF-36) [19, 20] which consists of 8 multi-item measures assessing 1) physical functioning, 2) role limitations caused by physical health problems, 3) role limitations caused by emotional health problems, 4) social functioning, 5) emotional well-being, 6) pain, 7) energy/fatigue, and 8) general health perceptions. We calculated overall physical and mental health status composites for this portion of the scale.

Based on the Medical Outcomes Study, internal consistency reliability estimates were 0.78 or greater for each domain of the SF-36,[20] and multiple studies have supported its construct validity.[21, 22] Similar to the KDQOL-SF™ scales, SF-36 scale scores are transformed linearly into a 0 to 100 point scale with higher values representing better health. We used the modified RAND scoring algorithm to calculate scores.[14, 20] The RAND algorithm is similar to the Medical Outcomes Study algorithm with the exception of slightly higher pain scale scores for the RAND algorithm.[20]

Statistical analysis

Patient demographic data and key laboratory data were abstracted and compared according to whether they completed only a baseline KDQOL-SF™ or completed at least one follow-up KDQOL-SF™. Differences in baseline characteristics for these groups were assessed using Chi Square or Fisher's Exact test for categorical data and unpaired T-test or the Mann Whitney U test for continuous variables. After calculating means and standard deviations for individual KDQOL-SF™ scale domains and composite scores, the group completing only a baseline assessment was compared to the group that completed at least one follow-up assessment using an unpaired T-test.

Baseline kidney disease specific scales and individual domains of the SF-36 from the study CKD population and several reference populations were graphed and visually inspected to evaluate similarity and differences among populations. US estimates from the Dialysis Outcomes and Practice Patterns Study (DOPPS) [23] and a publication by Manns et al.[24] were used as benchmarks to compare kidney disease specific scales in patients with ESRD to our population. In this comparison, the 9 scales reflect the same items included in the original version of the KDQOL-SF™. Since we modified the instrument by deleting the dialysis staff encouragement scale and the patient satisfaction scale, we do not report these values. General health-related QOL (i.e., SF-36) in ESRD, pre-dialysis CKD, and the U.S. population were compared to our CKD clinic patients. DOPPS [23] was used to compare quality of life in ESRD to our CKD population. The Renal Research Institute-CKD Study [25] provided estimates of health-related quality of life for 505 patients with CKD not requiring renal replacement therapy. Finally, health-related quality of life estimates for the US population from the 1990 National Survey of Functional Status (NSFHS) [26] were used.

As an exploratory analysis, multivariate analysis of variance (MANOVA) was used to evaluate the impact of demographic and clinical characteristic variables on baseline assessment of 9 kidney disease specific domains of health-related concerns. Effects associated with a p-value less than or equal to 0.05 were considered of interest. After obtaining a borderline significant multivariate test for a hemoglobin effect, univariate ANOVA was conducted to identify the specific domain that contributed to the significant overall effect.

Although our study was not statistically powered to assess changes over time, we explored trends in QOL among patients who had at least one follow-up visit at which they completed a QOL survey. Among these patients, some patients completed the KDQOL-SF™ assessment at both 6 and 12 months (n=23) and some patients completed the instrument only at 6 months (n=10) or 12 months (n=10). Therefore, we used both an observed cases approach (i.e., using all assessments available) and an intention-to-treat (ITT) approach. In the more conservative ITT analysis, we focused on the 12 month assessment. If a 12 month assessment was not available, we used the last observation (i.e., 6 months) carried forward. Because both methods provided similar results, we report the ITT analysis. Repeated measures analysis of variance (ANOVA) was used to test whether mean scores changed statistically from baseline to follow-up. Post hoc analyses using Duncan's multiple range test were conducted to explore group differences for variables deemed to be significant ($P<0.05$) in the repeated measures ANOVA. SAS (version 9.1.2, Cary, NC) was used for statistical analyses.

RESULTS

Seventy-nine patients seen in the CKD clinic from January 2003 to September 2004 provided baseline KDQOL-SF™ data (Table 2). More than 50 percent of patients were female. The mean patient age was more than 60 years and nearly half of patients were African American. The primary cause of kidney disease was either hypertension or diabetes mellitus. Of the 79 patients with a baseline KDQOL-SF™ assessment, 43 of these patients (54%) had at least one follow-up KDQOL-SF™ assessment. A comparison of the baseline clinical characteristics (Table 1) between patients with (n = 43) and without (n = 36) a follow-up KDQOL-SF™ assessment demonstrated that only serum calcium was significantly different between the baseline only group and the follow-up group, respectively (8.6 ± 0.9 mg/dL versus 9.1 ± 0.5 mg/dL ($p < 0.05$)). For all other baseline characteristics, patients with followup measures did not differ statistically from patients without KDQOL-SF™ followup measures.

Baseline quality of life scores were comparable for patients with only a baseline KDQOL™ assessment and patients who had at least one followup assessment (Table 3), with two exceptions. Patients with followup KDQOL™ data had higher baseline quality of life scores than patients without followup data on two kidney disease-targeted scales; effect of kidney disease (mean 78.6 vs. 68.8, respectively, ($p < 0.05$)) and burden of kidney disease (mean 72.8 vs. 66.6, respectively ($p < 0.05$)). The 36-item health survey scale scores and overall health status (physical and mental component) were similar between patients with only a baseline and those with at least one follow-up assessment ($p > 0.05$)

Compared to two larger cohorts,[23,24] mean scores on the kidney disease specific scales from the KDQOL-SF™ showed a trend toward higher values for patients in the CKD clinic (Figure 1). Although we did not have access to estimates of variance to make statistical comparisons of the means from our population with means from the US dialysis population,[23] we did have confidence bounds for a study in Canadian dialysis patients.[24] Comparing these groups, our CKD population had significantly higher ratings on the domains for “effects of kidney disease” and “burden of kidney disease”. This is illustrated by the non-overlapping 95% confidence intervals for these domains in Figure 1.

A plot of the mean scores for the SF-36 component (overall health status) domains from our study and three additional studies was also evaluated (Figure 2). These data showed that compared to the general US population,[26] patients with kidney disease have lower general QOL values – as seen in our CKD study, the RRI-CKD study,[25] and the DOPPS ESRD study (Figure 2).[23] Mean domain specific estimates from our CKD population appeared lower than the previously reported CKD estimates from the Perlman, et al study.[25] However, our population was smaller and had wider confidence intervals. Our confidence intervals overlapped with the previous CKD study in all domains except social functioning, whereby our mean score was lower. Patients in our CKD clinic had similar general health domain scores as compared to estimates from patients with ESRD on hemodialysis, with the exception of physical functioning which was greater in our CKD population. The mean results from the general health domains between populations were not tested statistically since the raw data from the comparative studies were not available.

In exploring whether certain demographic and clinical characteristics impacted baseline assessment of the 9 kidney disease specific domains of the KDQOL-SF™, we found a borderline significant effect of hemoglobin ($p=0.06$). Work status ($p = 0.02$), cognitive function ($p = 0.06$),and quality of social interaction ($p = 0.08$) were identified as contributing factors to the significant overall effect of hemoglobin (data not shown).

A comparison of the change in kidney disease specific and general health domains of the KDQOL-SF™ was made from baseline to follow-up in our patients who completed a follow-

up survey (n = 43). In general, quality of life scales showed numerical improvement at followup in our CKD population (Table 4). Statistically significant improvements ($p < 0.05$) were observed with regard to sleep (change of 6.2 ± 15.2) and social function (change of 11.6 ± 27.7). The social support and physical function scales showed slight numerical declines, although changes were not statistically significant.

DISCUSSION

A previous publication highlighting our multidisciplinary clinic demonstrated the feasibility and clinical effectiveness of a model to deliver anemia management to patients with CKD. In the clinic model, the target hemoglobin (11 to 12 g/dL) for erythropoietic stimulating agent treatment was based on guidelines endorsed by the National Kidney Foundation. [27] In this manuscript, we provide baseline and follow-up estimates of quality of life (as measured by the KDQOL-SF™) for a cohort of our clinic patients with CKD receiving anemia management with erythropoietic proteins. Overall, our kidney disease specific estimates (as assessed by the kidney disease components in the KDQOL™) demonstrated better quality of life as compared to patients with ESRD.[23,24] Our baseline measures of kidney disease specific quality of life are useful as a benchmark in CKD patients. This benchmark is useful to help gauge the effectiveness of anemia interventions and to put the negative effects of CKD into perspective. Our baseline measures suggest that CKD is especially detrimental with regard to ability to work (i.e., work status = 31.7) and role limitations caused by physical health problems (i.e., role-physical = 39.0).

Because the KDQOL-SF™ is designed specifically for kidney disease, quality of life measured on this scale cannot be compared to a healthy population. However, the SF-36 – a generic measure of health status – has been used as a measure of quality of life in healthy populations. [26] Compared to healthy populations, patients with pre-dialysis CKD demonstrated significantly lower health status scores on the SF-36 – as shown in Figure 2. Compared to populations with ESRD,[23, 24] patients with pre-dialysis CKD had similar health status. This finding of similar QOL score for general health domains, as measured by the SF-36 for CKD and ESRD patients, suggests that the SF-36 may not be sensitive enough to detect kidney disease stage specific measures of QOL. Our data also suggested this - showing a trend toward disparate scores in several measures of the kidney disease specific questions of the KDQOL-SF™ between CKD and ESRD and a lack of disparate scores in similar domains of the SF-36 component between these groups. The implications of this observation may be that specific reductions in QOL attributed to kidney disease will be overlooked in the SF-36. Hence, centers that use this latter measure only may not have the sensitivity to find true reductions in QOL in the CKD patient population. Additionally, as patients move from one stage of CKD to another, it may not be practical to detect QOL changes that may be apparent from less severe to more severe disease staging. Therefore, the impact of stage of kidney disease on QOL may best be assessed by the kidney specific component of the KDQOL-SF™. Further validation of this assertion is needed since the KDQOL-SF™ has not previously been validated in CKD, even though it has been used in previous studies of CKD.[15, 16]

In the subset of our patients who provided longitudinal assessments of quality of life, we found general trends towards improvement in quality of life while enrolled in the CKD clinic. With regard to the kidney disease specific domains, improvements in QOL were statistically significant with regard to sleep and social functioning. It is difficult to expand on why these factors improved, and future work should consider further exploration of this area. We did not see any statistically significant improvements (only trends in improvements) in the general health domains of the KDQOL-SF™. We also did not assess changes in KDQOL-SF™ scores in relationship to changes in CKD stage since our follow-up time period was ≤ one year in duration. A study that tested KDQOL™ in a longitudinal approach from CKD to ESRD showed

that patients who transitioned to dialysis had significant decreases in the domain scores for burden and effects of kidney disease.[28] This suggests that changes in kidney function may obscure clinical and QOL improvements that result from other interventions such as management of anemia.

The slightly lower reported general SF-36 scores in our population versus the previous publication needs to be explored. There are at least two possible explanations for this observation. The first being differences in the racial make-up of the two studies. Our study had ~50% African-Americans and the previous CKD study had ~25% of patients in this race category.[25] While it has been reported in hemodialysis patients that African-American patients report higher QOL scores in most domains,[29] one needs to consider the effect of changes in kidney function (consistent with the CKD process) and its effect on QOL. Hence, the second factor is the effect of changes in kidney function (i.e. changes in CKD staging). Declines in kidney function may occur at different rates in different racial backgrounds and hence may effect QOL self-reports. [28] If patients were evaluated in a relative state of a more rapid decline, it is reasonable to entertain the prospect that this may result in a lower reported QOL value across many domains. This would potentially reduce the positive impact that race may have had on QOL score (as in an African-American population). We did not assess changes in kidney function over time to enable an assessment in this regard. Additionally, trends in follow-up QOL values in the Perlman, et al study were not reported.[25]

Although not an initial aim of our study, we retrospectively evaluated patient demographic and clinical parameters to assess their impact on predicting baseline QOL. While most clinical measures (calcium, phosphorus, parathyroid hormone, glomerular filtration rate, serum creatinine, transferrin saturation, and ferritin) did not appear to have a significant effect on QOL, their contribution cannot be ruled out since our study was not adequately powered for this analysis. Hemoglobin trended towards significance (i.e., $P = 0.06$) as a predictor of kidney specific domains. Since previous studies have reported that anemia – assessed by low hemoglobin – is related to lower quality of life,[25,30] we hypothesize that untreated baseline anemia is a contributing factor to the low QOL estimates we found in the CKD clinic. Our mean ± standard deviation follow-up hemoglobin values for these patients (11.7 ± 0.7) [11] were within the planned target range and are consistent with the currently recommended range by the Food and Drug Administration for patients receiving erythropoiesis stimulating agents.[13] A recent CKD study showed QOL values in low (11.5 g/dL) and high (13.5 g/dL) hemoglobin arms to be relatively consistent after therapy with erythropoietin beta for two years.[12] Hence correction of hemoglobin levels to within the acceptable range appears to provide similar scores for QOL without enhanced risk for cardiovascular complications.[12,31] Although we did not have sufficient statistical power to actually test whether longitudinal improvements in hemoglobin were correlated with improvements in quality of life, this presents an opportunity for future research.

Our study has several other limitations that need to be considered. First and foremost, it was observational in nature and was not powered to detect statistically significant changes. Future studies should use our preliminary effect size estimates to conduct a randomized, controlled study to test (a priori) the factors, such as hemoglobin and/or changes in CKD staging, that may predict improved quality of life. The baseline estimates of quality of life are limited by our relatively small convenience sample. Patients were not randomly selected, but rather were eligible due to their participation in our CKD clinic and their willingness to complete quality of life surveys. Furthermore, our study population was derived from one clinical site. We conducted hypothesis tests among a subset of patients that had endpoint assessments to determine whether quality of life changed over time; these tests should be interpreted in light of the fact that our study was not designed to test hypotheses. Multivariate analysis should be viewed strictly as exploratory given the small sample size. Sample size also limited our ability

to make stage-specific inferences. Still, this study provides insight for a pre-dialysis CKD population that has not been well studied in terms of QOL assessments by the KDQOL-SF™.

CONCLUSIONS

Patients with kidney disease have significantly decreased quality of life compared to healthy populations as assessed by the SF-36. QOL measures that assess effect of kidney disease, such as the KDQOL-SF™, may be most useful to detect changes in QOL associated with progression of kidney disease. Patient reported improvements in QOL can be realized in a multidisciplinary CKD clinic that incorporates management of anemia to an accepted target range.

Acknowledgements

Dr. Hansen is supported by grant K12RR023248. Dr. Joy is supported by grant K23DK064888.

List of abbreviations used

CKD, Chronic kidney disease
KDQOL^{TM}-SF, Kidney Disease Quality of Life questionnaire – short form
ESRD, End stage kidney disease
SF-36, Medical Outcomes Study 36-item short form survey instrument
DOPPS, Dialysis outcomes and practice patterns study
NSFHS, National survey of functional health status
QOL, Quality of life
ITT, Intention to treat
ANOVA, Analysis of variance
MANOVA, Multivariate analysis of variance
RRI-CKD, Renal research institute - chronic kidney disease

REFERENCES

1. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis 2003;41:1–12. [PubMed: 12500213]
2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002;39:S1–S266. [PubMed: 11904577]
3. Marsh JT, Brown WS, Wolcott D, et al. rHuEPO treatment improves brain and cognitive function of anemic dialysis patients. Kidney Int 1991;39:155–163. [PubMed: 2002629]
4. Goicoechea M, de Vinuesa SG, Gomez-Campdera F, Luno J. Predictive cardiovascular risk factors in patients with chronic kidney disease (CKD). Kidney Int Suppl 2005:S35–S38. [PubMed: 15613066]
5. Jurkovitz CT, Abramson JL, Vaccarino LV, Weintraub WS, McClellan WM. Association of high serum creatinine and anemia increases the risk of coronary events: results from the prospective community-based atherosclerosis risk in communities (ARIC) study. J Am Soc Nephrol 2003;14:2919–2925. [PubMed: 14569102]
6. Foley RN. Anaemia: cardiovascular adaptations and maladaptive responses in chronic kidney disease. Nephrol Dial Transplant 2002;17:32–34. [PubMed: 12386255]
7. 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;263:825–830. [PubMed: 2404150]
8. Collins AJ, Roberts TL, St Peter WL, Chen SC, Ebben J, Constantini E. United States Renal Data System assessment of the impact of the National Kidney Foundation-Dialysis Outcomes Quality Initiative guidelines. Am J Kidney Dis 2002;39:784–795. [PubMed: 11920345]

9. National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease. Am J Kidney Dis 2006;47:S11–S145. [PubMed: 16678659]
10. United States Renal Data System. USRDS 2005 annual data report. Bethesda, MD: The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2005.
11. Joy MS, Candiani C, Vaillancourt BA, Chin H, Hogan SL, Falk RJ. Reengineering clinical operations in a medical practice to optimize the management of anemia of chronic kidney disease. Pharmacotherapy 2007;27:734–744. [PubMed: 17461709]
12. Drueke TB, Locatelli F, Clyne N, et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med 2006;355:2071–2084. [PubMed: 17108342]
13. U.S. Food and Drug Administration Center for Drug Evaluation and Research. Information on erythropoiesis stimulating agents (ESA)(marketed as Procrit, Epogen, and Aranesp). [Accessed December 12, 2007]. Available at: http://www.fda.gov/cder/drug/infopage/RHE/default.htm.
14. Hays RD, Kallich JD, Mapes DL, Coons SJ, Carter WB. Development of the kidney disease quality of life (KDQOL) instrument. Qual Life Res 1994;3:329–338. [PubMed: 7841967]
15. Alexander M, Kewalramani R, Agodoa I, Globe D. Association of anemia correction with health related quality of life in patients not on dialysis. Curr Med Res Opin 2007;23:2997–3008. [PubMed: 17958944]
16. Abu-Alfa AK, Sloan L, Charytan C, et al. The association of darbepoetin alfa with hemoglobin and health-related quality of life in patients with chronic kidney disease not receiving dialysis. Curr Med Res Opin 2008;24:1091–1100. [PubMed: 18328118]
17. Cronbach LJ. Coefficient alpha and the internal structure of tests. Psychometrika 1951;16:297–334.
18. Hays, RD.; Kallich, JD.; Mapes, DL., et al. Kidney disease quality of life short form (KDQOL-SF), version 1.3: A manual for use and scoring. Santa Monica, CA: 1997.
19. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). II. Conceptual framework and item selection. Med Care 1992;30:473–483. [PubMed: 1593914]
20. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item Health Survey 1.0. Health Econ 1993;2:217–227. [PubMed: 8275167]
21. McHorney CA, Ware JE Jr, Rogers W, Raczek AE, Lu JF. The validity and relative precision of MOS short- and long-form health status scales and Dartmouth COOP charts. Results from the Medical Outcomes Study. Med Care 1992;30:S253–S265.
22. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31:247–263. [PubMed: 8450681]
23. Fukuhara S, Lopes AA, Bragg-Gresham JL, et al. Health-related quality of life among dialysis patients on three continents: the Dialysis Outcomes and Practice Patterns Study. Kidney Int 2003;64:1903–1910. [PubMed: 14531826]
24. Manns B, Johnson JA, Taub K, Mortis G, Ghali WA, Donaldson C. Quality of life in patients treated with hemodialysis or peritoneal dialysis: what are the important determinants? Clin Nephrol 2003;60:341–351. [PubMed: 14640240]
25. Perlman RL, Finkelstein FO, Liu L, et al. Quality of life in chronic kidney disease (CKD): a cross-sectional analysis in the Renal Research Institute-CKD study. Am J Kidney Dis 2005;45:658–666. [PubMed: 15806468]
26. McHorney CA, Kosinski M, Ware JE Jr. Comparisons of the costs and quality of norms for the SF-36 health survey collected by mail versus telephone interview: results from a national survey. Med Care 1994;32:551–567. [PubMed: 8189774]
27. National Kidney Foundation. IV. NKF-K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease: update 2000. Am J Kidney Dis 2001;37:S182–S238. [PubMed: 11229970]
28. Gorodetskaya I, Zenios S, McCulloch CE, et al. Health-related quality of life and estimates of utility in chronic kidney disease. Kidney Int 2005;68:2801–2808. [PubMed: 16316356]
29. Unruh M, Miskulin D, Yan G, et al. Racial differences in health-related quality of life among hemodialysis patients. Kidney Int 2004;65:1482–1491. [PubMed: 15086492]

30. Revicki DA, Brown RE, Feeny DH, et al. Health-related quality of life associated with recombinant human erythropoietin therapy for predialysis chronic renal disease patients. Am J Kidney Dis 1995;25:548–554. [PubMed: 7702049]

31. Singh AK, Szczech L, Tang KL, et al. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med 2006;355:2085–2098. [PubMed: 17108343]

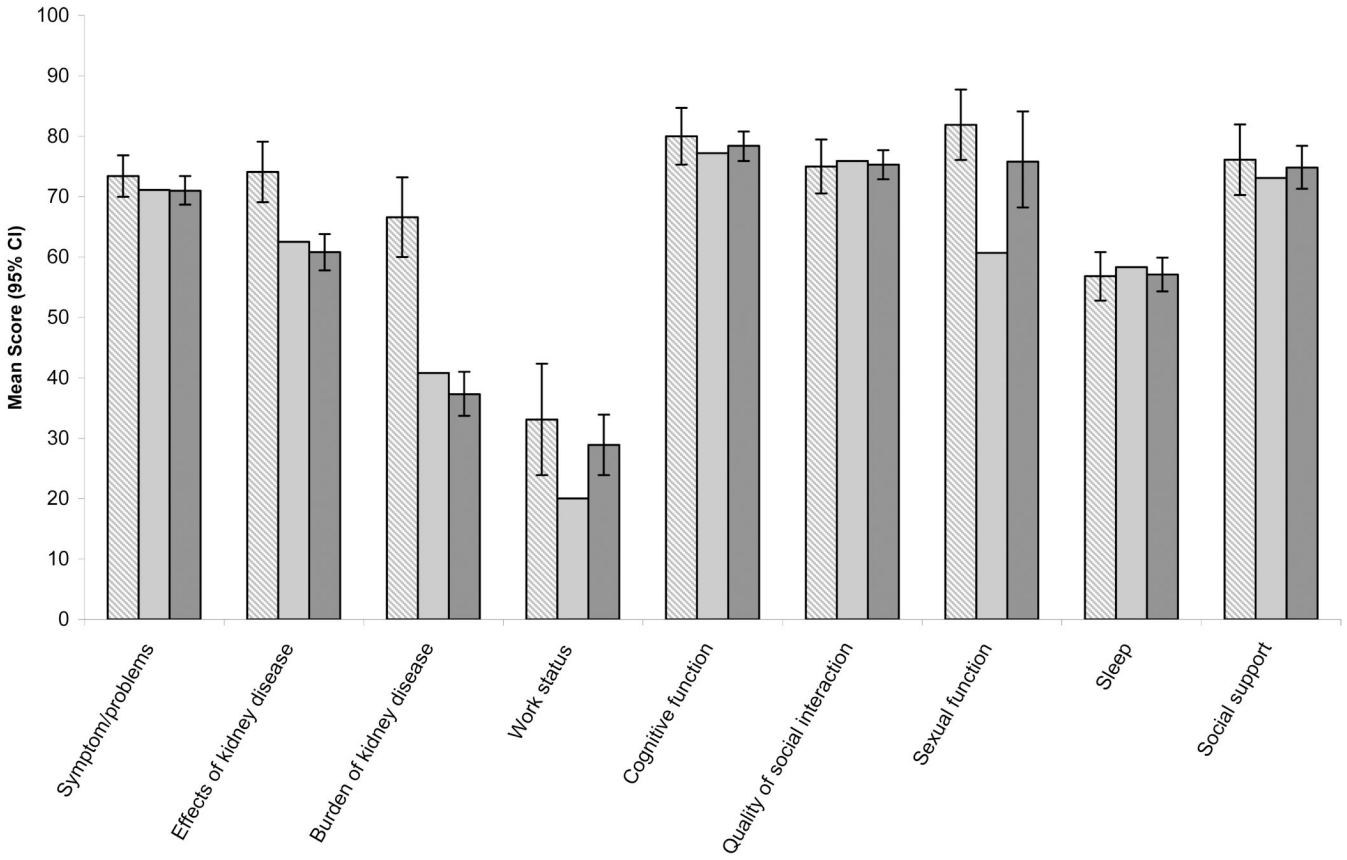

Figure 1. Comparison of kidney disease specific scales chronic kidney disease populations

CKD Clinic (n=79)

US dialysis patients [23] (n=2,885)a

Canadian dialysis patients [24] (n=192)

[a] 95% confidence intervals not available for this study

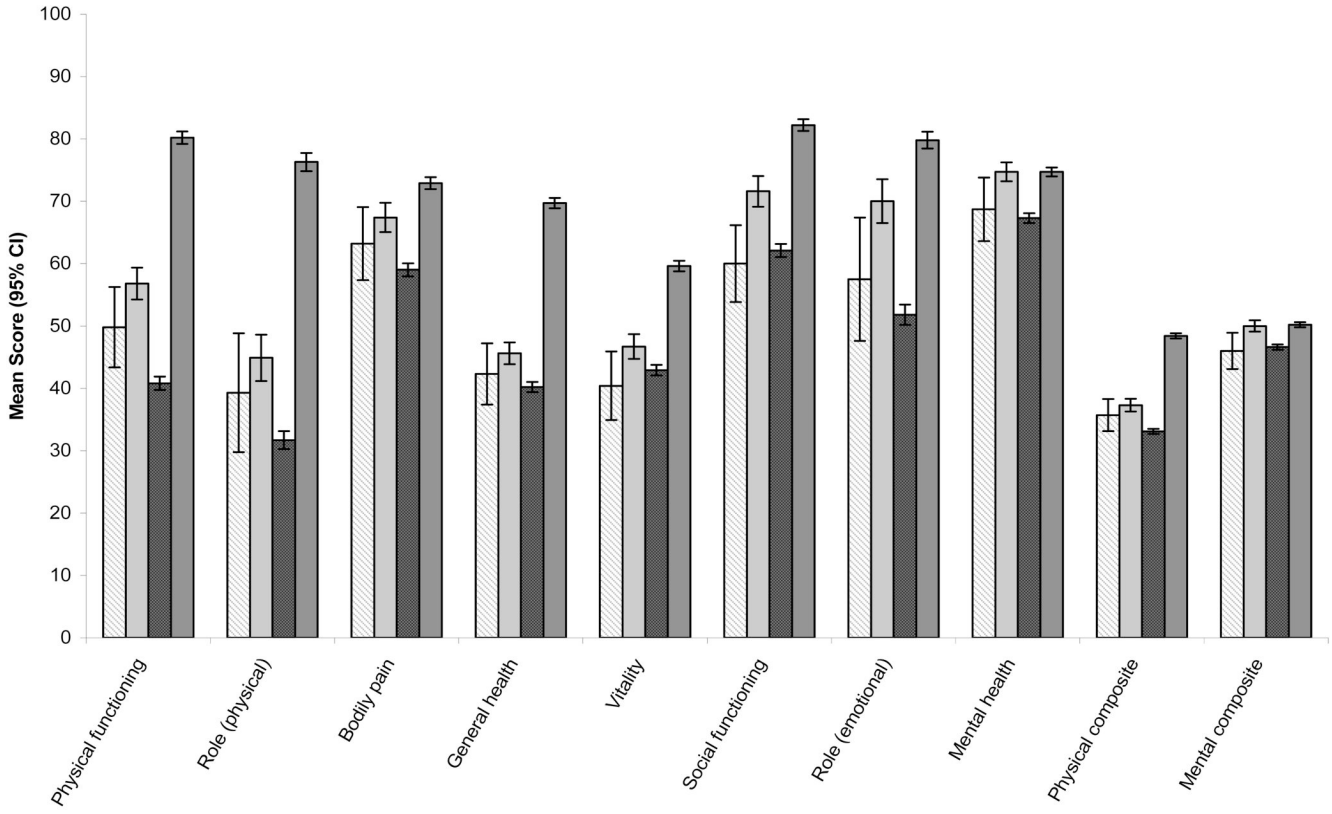

Figure 2. Comparison of SF-36 domains for pre-dialysis chronic kidney disease, end-stage kidney disease, and the general US population

CKD Clinic (n=79)
RRI-CKD Study [25] (n=505)
US Dialysis Patients [23] (n=2,885)
US Population Average [26] (n=192)

Table 1

Chronic kidney disease staging and projected prevalence

CKD Stage	Stage Definition	Projected prevalence in US population [a]	
		(N)	(%)
1	Kidney damage with GFR ≥ 90	5,900,000	3.3
2	Kidney damage with GFR 60–89	5,300,000	3.0
3	GFR 30–59	7,600,000	4.3
4	GFR 15–29	400,000	0.2
5	GFR < 15	300,000	0.1

CKD – chronic kidney disease

GFR (ml/min/1.73m^2) – glomerular filtration rate

[a] Number and percentage based on estimates from the National Kidney Foundation[2]

Table 2

Baseline patient characteristics

Patient Characteristic	**All patients n = 79**	**Patients with only a baseline assessment n = 36**	**Patients with at least one follow-up assessment n = 43**
	n (%)	***n (%)***	***n (%)***
Sex			
Male	37 (47%)	19 (53%)	18 (42%)
Female	42 (53%)	17 (47%)	25 (58%)
Race			
Caucasian	40 (51%)	19 (53%)	21 (49%)
African American	37 (47%)	17 (47%)	20 (46%)
Other	2 (2%)	0 (0%)	2 (5%)
Cause of kidney disease			
Hypertension	30 (38%)	15 (41.7%)	15 (35%)
Diabetes Mellitus	28 (35%)	12 (33.3%)	16 (37%)
Other	39 (49%)	22 (61%)	17 (40%)
Unknown	1 (1.3%)	1 (2.8%)	0 (0%)
	mean ± sd	***mean ± sd***	***mean ± sd***
Age (years)	62.2 ± 15.3	59.4 ± 17.3	64.6 ± 13.1
Hb (g/L)	11.0 ± 1.4	11.1 ± 1.5	10.9 ± 1.4
TSAT (%)	25.9 ± 14.5	26.9 ± 16.5	25.1 ± 12.7
Ferritin (mcg/L)	180.3 ± 156.3	161.4 ± 132.1	196.0 ± 173.8
iPTH (pg/mL)	190.4 ± 180.7	233.4 ± 241.0	158.6 ± 111.4
Calcium (mg/dL)	8.9 ± 0.8	8.6 ± 0.9	9.1 ± 0.5[a]
PO4 (mg/dL)	4.2 ± 1.1	4.2 ± 1.1	4.2 ± 1.1
Creatinine (mg/dL)	3.1 ± 1.4	3.2 ± 1.5	3.0 ± 1.4

Hb – Hemoglobin; g – grams; L – Liter; TSAT – transferring saturation; mcg – micrograms; iPTH – intact parathyroid hormone; pg - picograms; mL – milliliter; mg – milligram; dL – deciliter; PO4 - phosphate

[a] $P < 0.05$ for comparing baseline scores for patients with a baseline measure and at least one endpoint assessment to patients with only a baseline measure; calcium is not adjusted for albumin.

Table 3

Baseline values [a] on the KDQOL-SF™

Measure	All patients n = 79	Patients with only a baseline assessment n = 36	Patients with at least one follow-up assessment n = 43
	mean (sd)	*mean (sd)*	*mean (sd)*
Kidney disease-targeted scales			
Symptom/problems	73.4 (15.6)	70.4 (15.9)	76.0 (15.3)
Effects of kidney disease [b]	74.1 (22.7)	68.8 (23.0)	78.6 (22.2)
Burden of kidney disease [b]	66.6 (29.9)	59.4 (31.6)	72.8 (27.2)
Work status	33.1 (41.8)	34.7 (44.4)	31.7 (39.9)
Cognitive function	80.0 (21.3)	77.6 (21.2)	82.1 (21.6)
Quality of social interaction	75.0 (20.3)	73.3 (20.0)	76.4 (20.7)
Sexual function	81.9 (26.4)	81.7 (30.9)	88.5 (21.1)
Sleep	56.8 (18.2)	56.1 (17.7)	57.3 (18.8)
Social support	76.1 (26.5)	72.9 (25.3)	78.7 (27.5)
36-Item health survey scales			
Physical functioning	49.8 (29.2)	46.6 (28.9)	52.5 (29.6)
Role-physical	39.3 (43.2)	39.7 (44.0)	39.0 (43.1)
Pain	63.2 (26.5)	62.6 (25.6)	63.7 (27.6)
General health perceptions	42.3 (22.2)	41.5 (23.8)	42.9 (21.0)
Emotional well-being	68.7 (23.1)	63.7 (22.5)	72.9 (23.1)
Role-emotional	57.5 (44.8)	54.9 (45.6)	59.5 (44.5)
Social function	60.0 (28.0)	56.6 (29.2)	62.8 (26.9)
Energy/fatigue	40.4 (24.9)	34.6 (22.3)	45.4 (26.2)
Overall health status			
SF-36 Physical Composite	35.7 (11.7)	35.9 (11.8)	35.5 (11.8)
SF-36 Mental Composite	46.0 (13.2)	43.5 (13.0)	48.1 (13.2)

[a] All scales have a possible range of 0–100, with higher transformed scores always reflecting better quality of life

[b] $P < 0.05$ for t-test comparing mean baseline scores for patients with a baseline measure and at least one endpoint assessment to patients with only a baseline measure

Table 4

Baseline, follow-up, and mean change values [a] on the KDQOL-SF™ (n=43)

Measure	Patients (n=43) with a baseline measure and at least one follow-up measure (ITT)		
	Baseline *mean (sd)*	**Follow-up** *mean (sd)*	**Change** *mean (sd)*
Kidney disease-targeted scales			
Symptom/problems	76.0 (15.3)	77.0 (16.1)	1.0 (12.2)
Effects of kidney disease	78.6 (22.2)	80.5 (18.3)	1.4 (17.8)
Burden of kidney disease	72.8 (27.2)	74.5 (25.2)	0.9 (24.8)
Work status	31.7 (39.9)	34.1 (42.5)	3.8 (31.2)
Cognitive function	82.1 (21.6)	84.7 (15.6)	2.6 (20.5)
Quality of social interaction	76.4 (20.7)	81.6 (15.6)	5.2 (20.9)
Sexual function	88.5 (21.1)	89.8 (17.4)	0.3 (16.5)
Sleep [b]	57.3 (18.8)	63.4 (16.7)	6.2 (15.2)
Social support	78.7 (27.5)	77.8 (34.7)	–0.4 (43.2)
36-Item health survey scales			
Physical functioning	52.5 (29.6)	51.7 (28.9)	–0.5 (19.3)
Role-physical	39.0 (43.1)	44.4 (43.2)	5.8 (36.3)
Pain	63.7 (27.6)	67.0 (24.1)	2.6 (21.4)
General health perceptions	42.9 (21.0)	43.8 (18.9)	0.9 (14.0)
Emotional well-being	72.9 (23.1)	77.1 (13.8)	4.5 (18.8)
Role-emotional	59.5 (44.5)	61.0 (42.1)	0.8 (28.7)
Social function [b]	62.8 (26.9)	74.4 (24.8)	11.6 (27.7)
Energy/fatigue	45.4 (26.2)	46.1 (22.8)	1.3 (20.9)
Overall health status			
SF-36 Physical Composite	35.5 (11.8)	35.6 (11.1)	0.2 (8.5)
SF-36 Mental Composite	48.1 (13.2)	50.3 (9.4)	2.0 (10.1)

[a] All scales have a possible range of 0–100, with higher transformed scores always reflecting better quality of life

[b] $P < 0.005$ for repeated measures F-statistic.