Kidney Disease Quality of Life Questionnaire (KDQOL)-36 Items Associated with Anemia Severity
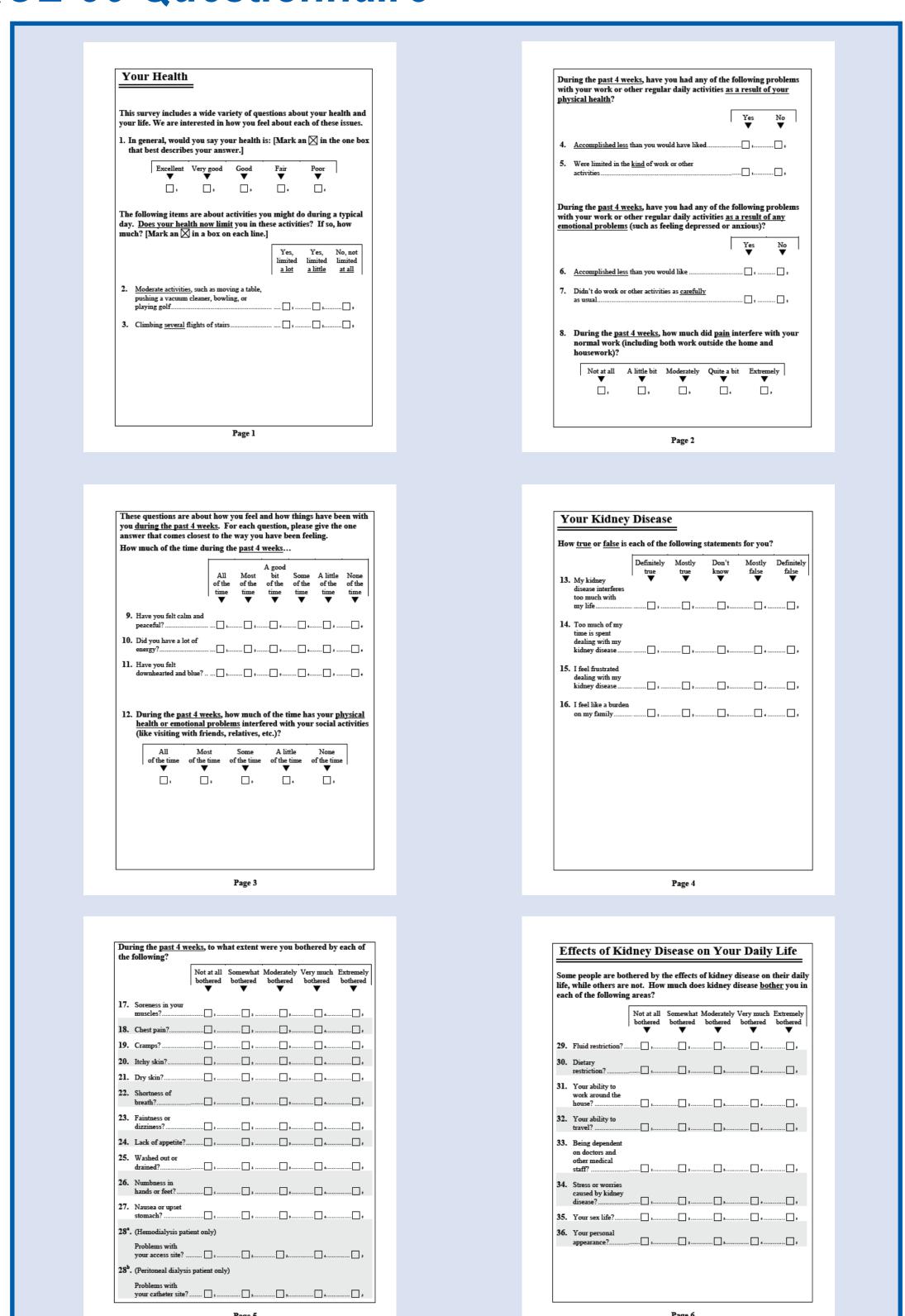
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INTRODUCTION

- More than 90% of hemodialysis patients are on an erythropoiesis stimulating agent (ESA) to treat anemia[1]
- Studies have shown that anemia symptoms increase as hemoglobin levels decrease;[2-7] however, few studies in this area were generalizable to contemporary dialysis patients.
  - Anemia symptoms include fatigue, shortness of breath, muscle weakness, dizziness, poor sleep, and leg cramps[8]
- Kidney Disease Quality of Life (KDQOL)-36 is the primary tool to assess end stage renal disease (ESRD) health-related quality of life, and Centers for Medicare and Medicaid Services (CMS) mandated that KDQOL-36 be administered to every dialysis patient once a year as part of the conditions of coverage[9]
- This has provided the opportunity to analyze the association between the KDQOL-36 and numerous aspects of dialysis care and clinical outcomes

KDQOL-36 Questionnaire

The score algorithm allows for 0-100 scale, with higher score representing better status.

OBJECTIVE

- To identify KDQOL-36 items associated with anemia severity
- To examine the association between KDQOL-36 items and anemia by dialysis type (hemodialysis vs peritoneal dialysis) and hospitalization (hospitalization in previous 30 days vs no hospitalization in previous 30 days)

METHODS

Study Design

- This was a retrospective cross-sectional analysis of 30 491 dialysis patients from a large US dialysis organization who completed the KDQOL-36 between June 1, 2009 and June 30, 2010
- Patients were included
  - Age ≥ 18 years
  - On dialysis > 120 days
- Patients were excluded
  - A history of or current cancer diagnosis
- Hb value used in the study was the one measured within one week of KDQOL administration

Analysis

- Comparison between responders vs non-responders to KDQOL-36 to ensure no response bias and generalizability of the results
  - We compared the 30 491 patients who completed a KDQOL-36 during the observation period with 89 830 patients who did not complete the survey
- Univariate analysis
  - Raw score from 0-100 was calculated based on the scoring manual of the KDQOL v1.3
  - Raw scores of KDQOL-36 items were assessed across hemoglobin (Hb) categories including: <10 g/dL, 10-12 g/dL, > 12 g/dL
  - P values from ANOVA test across the Hb levels (< 10 g/dL, 10-12 g/dL and > 12 g/dL) are reported
- Multivariate analysis
  - We conducted two linear regressions, with hemoglobin as the outcome variable and the 36 items of the KDQOL as predictors:
    - Forced entry (FE) so that all items were entered sequentially
    - Stepwise entry (SW) with entry tolerance set at 0.15 and exit tolerance set at 0.20
    - Response to each KDQOL item question was recorded as ordinary variable. The ordinary variables were directly incorporated in the regression model because they resemble continuous variables.
  - Significance was set at p ≤ 0.05
  - The regression analyses were run on the full cohort of 30 491 patients, as well as by dialysis type (hemodialysis [HD] vs peritoneal dialysis [PD]) and hospitalization in the previous 30 days:
    - HD patients with no hospitalization in previous 30 days
    - HD patient hospitalized in previous 30 days
    - PD patient with no hospitalization in previous 30 days
    - The subgroup of PD patients hospitalized in the previous 30 days was too small to perform the analysis

RESULTS

Characteristics of Patient Responders Versus Non-Responders to the KDQOL-36 Questionnaire

	Survey completed 6/2009 - 6/2010 (n = 30 491)	Survey not yet completed by 6/2010 (n = 89 830)
Age (years), mean (SD)	61.9 (14.9)	61.6 (15.2)
Vintage (time on dialysis, years), mean (SD)	3.8 (3.6)	3.6 (3.7)
Percent of patients < 1 year	18.1	22.0
Male (%)	55.3	55.7
Race (%)		
African American	37.0	36.5
Caucasian	41.8	37.3
Hispanic	13.0	17.2
Asian/Pacific Islander	2.7	4.6
Native American/Alaskan Native	1.1	1.5
Other	2.0	2.7
Missing	2.4	0.2
Body Mass Index, mean (SD)	28.9 (7.4)	28.1 (7.2)
Hospitalized in last 30 days (%)	10.4	14.1
Hospitalized in last 90 days (%)	23.4	27.3
Hb (g/dL), mean (SD)	11.0 (1.2)	11.5 (1.3)
TSAT (%), mean (SD)	30.4 (13.8)	29.8 (13.9)
Ferritin (ng/dL), mean (SD)	576.3 (367.8)	591.3 (373.3)
Dialysis adequacy, mean (SD)	1.6 (0.3)	1.6 (0.3)
Albumin (g/dL), mean (SD)	3.9 (0.4)	3.8 (0.5)
PCR (g/kg/day), mean (SD)	1.02 (0.3)	1.0 (0.3)
PTH (pg/mL), mean (SD)	291.7 (181.2)	289.1 (184.0)
Serum calcium (mg/dL), mean (SD)	9.0 (0.6)	9.0 (0.7)
Serum phosphorous (mg/dL), mean (SD)	5.2 (1.5)	5.1 (1.6)

Hb, hemoglobin; TSAT, transferrin saturation; PCR, protein catabolic rate; PTH, parathyroid hormone; SD, standard deviation

- Patients who completed the questionnaire were:
  - Less likely to be incident patients (18.1% vs 22.0%)
  - Less likely to be Hispanic (13.0% vs 17.2%)
  - Less likely to have been hospitalized in the last 30 days (10.4% vs 14.0%)

KDQOL-36 Item Raw Score by Baseline Hemoglobin Value

	Basline Hemoglobin (g/dL)			P value
	< 10 (N = 1852)	10 - 12 (N = 13 642)	> 12 (N = 9273)	
1. General health	39.4 (23.1)	43.2 (23.4)	45.1 (23.6)	< .05
2. Moderate activities	41.1 (38.9)	44.3 (38.5)	46.2 (38.3)	< .001
3. Climbing stairs	34.8 (38.3)	36.2 (37.8)	38.5 (38.4)	< .001
4. Accomplish less: physical	29.5 (45.6)	35.5 (47.9)	37.6 (48.4)	< .001
5. Limited in kinds of activities	26.2 (44.0)	31.7 946.5)	33.6 (47.2)	< .001
6. Accomplish less: emotional	55.0 (49.8)	59.3 (49.1)	60.2 (49.0)	< .001
7. Didn't do work carefully	59.8 (49.0)	65.5 (47.5)	66.4 (47.2)	< .001
8. Pain interferes	56.7 (33.4)	62.0 (31.6)	63.7 (31.2)	< .001
9. Calm and peaceful	60.6 (27.2)	63.7 (26.5)	65.1 (26.1)	< .001
10. Energy	40.1 (27.7)	44.2 (27.4)	46.0 (27.4)	< .001
11. Downhearted and blue	70.0 (27.5)	73.0 (26.4)	73.6 (26.5)	< .001
12. Interferes with social activities	59.8 (32.1)	65.8 (30.7)	66.4 (30.6)	< .001
13. Interferes with life	37.3 (33.3)	39.0 (33.5)	39.7 (33.3)	< .001
14. Too much time dealing with kidney disease	41.1 (33.6)	44.3 (34.0)	44.9 (34.1)	< .05
15. Frustrating	47.0 (36.0)	51.1 (35.7)	51.7 (35.9)	< .001
16. Burden	54.4 (38.4)	58.8 (37.5)	59.0 (37.6)	< .001
17. Muscle soreness	64.6 (31.3)	66.7(30.2)	68.7 (29.4)	< .001
18. Chest pain	87.7 (22.5)	90.0 (19.8)	90.6 (19.3)	< .001
19. Cramps	74.5 (28.3)	71.9 (28.2)	72.2 (28.1)	< .001
20. Itchy skin	67.5 (32.2)	70.7 (30.1)	71.5 (29.8)	< .001
21. Dry skin	62.4 (32.4)	65.6 (31.1)	65.8 (31.1)	< .001
22. Shortness of breath	73.9 (30.4)	78.5 (26.9)	80.4 (26.0)	< .001
23. Faintness or dizziness	82.0 (25.4)	83.9 (23.6)	84.3 (23.0)	< .001
24. Lack of appetite	74.8 (29.2)	79.5 (26.9)	80.4 (26.4)	< .001
25. Washed out or drained	61.9 (31.3)	64.7 (29.7)	66.0 (29.1)	< .001
26. Numbness in hands or feet	70.8 (31.2)	69.7 (32.2)	71.3 (31.6)	< .001
27. Nausea or upset stomach	74.9 (29.4)	78.2 (27.5)	79.6 (26.5)	< .001
28. Access site problem	82.2 (29.4)	86.2 (24.8)	86.4 (24.5)	< .001
29. Fluid restrictions	63.7 (33.5)	64.4 (32.8)	65.3 (32.2)	< .001
30. Dietary restrictions	65.1 (32.0)	67.3 (30.4)	67.4 (30.2)	< .05
31. Work around house	61.7 (33.6)	64.6 (33.1)	66.2 (32.2)	< .001
32. ESRD affects travel	56.0 (36.5)	57.1 (36.5)	57.7 (36.2)	.289
33. Dependent on doctors/medical staff	67.4 (33.1)	70.6 (32.2)	71.1 (31.9)	< .001
34. Stress or worries	65.4 (33.1)	68.6 (31.6)	69.4 (31.3)	< .001
35. Sex life	69.5 (37.6)	70.7 (37.3)	70.7 (37.0)	.455
36. Personal appearance	73.2 (32.0)	76.8 (30.2)	77.4 (29.7)	< .001

Note: Highlighted items showed differences of >5 points change across Hb categories
Raw scores ranging from 0 to 100, with higher scores indicating better HRQOL

- It appears that scores increase for the majority of items as Hb levels increase
- In univariate analysis, items associated physical function showed differences of > 5 points change across Hb categories, specifically for Hb < 10 to ≥ 10 g/dL

Association between Hemoglobin and KDQOL-36 Items In the Whole Cohort

Item	Item Direction	Response valence	Total (N = 30 228)	
			FE beta	SW beta
1. General health	Neutral	(1 = excellent, 5 = poor)	SIG	SIG
6. Accomplish less: emotional	-	(1 = yes, 2 = no)	SIG	NS
8. Pain interferes	-	(1 = not, 6 = extremely)	NS	SIG
10. Energy	+	(1 = all time, 6 = none time)	SIG	SIG
13. Interferes with life	-	(1 = true, 6 = false)	SIG	SIG
14. Too much time dealing with kidney disease	-	(1 = true, 5 = false)	SIG	NS
17. Muscle soreness	-	(1 = no bother, 5 = bother)	SIG	SIG
19. Cramps	-	(1 = no bother, 5 = bother)	SIG	SIG
22. Shortness of breath	-	(1 = no bother, 5 = bother)	SIG	SIG
24. Lack of appetite	-	(1 = no bother, 5 = bother)	SIG	SIG
28. Access site problem	-	(1 = no bother, 5 = bother)	SIG	SIG
32. ESRD affects travel	Neutral	(1 = no bother, 5 = bother)	SIG	SIG

Note: Highlighted areas statistically significant; NS, non-significant; Hosp, hospitalization

- In multivariate analysis, about 1/3 of the items were associated with anemia severity
  - General health status, severity in pain interference, energy, severity of soreness in muscles, severity of shortness of breath, and lack of appetite, less accomplishment, too much time spent on kidney disease, severity of access site problems, and travel ability were significantly positively associated with lower Hb level
  - The association between Hb level and the degree that kidney disease interferes with life and leg cramps may be counter intuitive
- The significance and the direction of results are largely similar in the stratified multivariate analysis in the following subgroups:
  - HD patients with no hospitalization in previous 30 days
  - HD patients hospitalized in previous 30 days
  - PD patients with no hospitalization in previous 30 days

LIMITATIONS

- This is a cross-sectional analysis, and thus examines only concurrent hemoglobin values and does not take into account change in hemoglobin
- Interpretation of the findings is intended to be done at the domain level, but because the converted raw scores are used in the unvariate analysis and response scales were used in the multivariate analysis, the magnitudeof the coefficients is not clinically meaningful.
- However, the objective of this analysis is to identify the association between KDQOL-36 items and anemia severity. Follow-up study will develop an anemia specific domain based on the items identified in this analysis.

CONCLUSIONS

- KDQOL-36 was developed to evaluate the overall burden of ESRD, but specific items related to patient-reported physical function and anemia symptoms are found to be associated with Hb level
  - The statistically significant items identified above are largely consistent with existing anemia guidelines (NKDKTS, US NHLBI, NKF, RSN)[4-7]
  - Items associated with anemia severity have lower scores when Hb <10 g/dL versus Hb ≥ 10 g/dL
  - Findings are consistent with the literature including the Canadian Erythropoietin Study Group (CESG) trial used to support the PRO benefits[2] and a recent systematic review and meta-analysis[10]
- Items identified from the analysis could be used to construct an anemia-specific scale of the KDQOL-36
- Developing a domain specific to anemia may complement CMS Quality Incentive Program.

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ACKNOWLEDGMENTS

CONFLICTS OF INTEREST

- SW, MG, DH, and AA are employees of Amgen
- This study was funded by Amgen