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Health-Related Quality of Life in Adults With Hodgkin's Disease

The State of the Science

KEY WORDS
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Hodgkin's disease (HD) affects younger and older adults and can disrupt developmental tasks and cause multiple medical sequelae. Since long-term survival is excellent, understanding issues related to all domains of health-related quality of life (HRQOL)—physical, psychological, social/functional, and spiritual—after completion of treatment is a critical step in designing and testing interventions to improve survivors' adjustment and return to their previous level of functioning. This article is an integrative review of empirical studies of HRQOL in HD survivors. Following Ganong's guidelines, 35 studies were identified and reviewed. Commonly reported physical consequences of HD include fatigue, anticipatory nausea and vomiting, and cognitive problems that lasted several years after treatment completion, as well as long-term life-threatening adverse effects including secondary cancers and cardiovascular and respiratory complications. Psychological consequences include emotional distress, especially depression and anxiety, and social/functional difficulty, including inability to return to work and adjustment to the workplace environment secondary to diminished capacity to complete work tasks. Within the spiritual domain, survivors reported that they had a greater appreciation for life after treatment. Development of appropriate theory-guided interventions to improve the HRQOL for HD survivors can be achieved through more rigorous study designs and standardization of HRQOL measurements.

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Hodgkin's disease (HD), a malignancy of the lymphatic system, occurs in a bimodal age distribution, with one large incidence in young adults between the ages of 15 and 40 years and another incidence in those older than 55 years. Through the advancement of diagnostic techniques and treatment modalities, HD has evolved from a condition that was once frequently fatal to one that is highly curable. In the 1940s, less than 15% of patients with HD lived 10 years after diagnosis. Major developments in therapeutic approaches throughout the 1960s and 1970s—including the use of radiation and combined radiation and chemotherapy—have dramatically improved survival. According to the Lymphoma Information Network, patients with HD diagnosed in its early stages now have a greater than 90% chance of long-term survival and patients diagnosed in the later stages of disease have an 80% or greater chance of survival.[1]

Hodgkin's disease and its treatment are not, however, without consequence to the survivor. Medical management for HD, although effective against the cancerous cells, also causes multiple sequelae, including cardiac and lung toxicity, infertility, and various secondary malignancies.[2,3] Such sequelae may affect the survivor's health-related quality of life (HRQOL) for many years after treatment is completed.[4]

The purpose of this article was to present an integrative review of empirical studies designed to examine HRQOL in adult survivors of HD, as well as to offer suggestions for further study with this population. For this review, the concept of HRQOL encompasses the impact of the diagnosis and treatment on the individual survivor's well-being in physical, psychological, social/functional, and spiritual domains.[5,6]

■ Methods

Ganong's[7] guidelines for narrative integrative literature reviews direct researchers to select hypotheses or research questions to focus the review. Researchers also must identify inclusion criteria for the research to be reviewed, examine the characteristics of the selected studies and findings, and interpret the results of the selected literature. These guidelines were followed to compile, review, and integrate the literature describing HRQOL in adult survivors of HD.

Two research questions for this integrated review were identified: (1) what is the current state of the science regarding HD survivors' HRQOL? and (2) what theoretical and methodological issues do researchers need to address when studying HRQOL in adult HD survivors?

The relevant literature from January 1984 through July 2008 was identified through electronic searches using Ovid, Cumulative Index to Nursing and Allied Health Literature, Medline, PubMed, and PsychInfo search engines. Key words for each search were *Hodgkin's disease and survivor*, *Hodgkin's disease and quality of life*, and *Hodgkin's disease and health-related quality of life*. A hand search of the references from the retrieved articles provided additional studies. Published reports of empirical studies were included in the review if the title and/or abstract included *Hodgkin's disease*, *survivor*, or *quality of life*. Studies that focused on physical symptoms and psychosocial adaptation after treatment for HD also were included. Studies of childhood survivors of HD were excluded.

The final sample encompassed 35 studies (see Table 1), 14 conducted in the United States[8–21] and 21 conducted in European countries, including the United Kingdom.[22–42] The research questions were addressed using content analysis to identify and classify study characteristics, including conceptual or theoretical framework used to guide the study, type of research design used (correlational or experimental, cross-sectional or longitudinal, prospective or retrospective, cohort or case-control), sample size, sampling strategy (probability, nonprobability), source used to recruit study participants (tumor registry, hospital records), sample demographic characteristics (gender, age), stage of cancer and years treated, number of years after diagnosis or treatment completion, when data were collected, research instruments used, method of administration of instruments, domains of HRQOL (physical, psychological, social/functional, spiritual) studied, and summary of findings. Two members of the review team examined, extracted, and analyzed relevant information from each of the 35 studies. The 2 team members reached consensus on selection of the final sample of studies based on the above characteristics.

■ Results

Conceptual or Theoretical Framework

Just 2 of the 35 studies were guided by an explicit conceptual or theoretical framework. Cameron et al[11] used classical conditioning theory[42] to examine the prevalence of persistent aversive symptoms, such as anticipatory nausea and vomiting, in HD survivors. Wettergren et al[42] cited the Wilson and Cleary's Model[43] of causal relationships between individuals' health characteristics and HRQOL outcomes.

Study Design

Thirty-four of the 35 studies (97%) were correlational,[8–38,40–42] and one was experimental.[39] Thirty of 35 studies (86%) were retrospective and cross-sectional.[8–14,16–22,24,26–28,30–38,40–42] Just 5 of the 35 studies (14%) used longitudinal, prospective designs.[15,23,25,29,39] Twenty of the 35 studies (57%) were case-control, and 15 (43%) were cohort studies.

Sample

Sample size ranged from 42 to 818 participants. In 15 (43%) studies, the sample included fewer than 100 participants. A nonprobability convenience sampling strategy was used for all studies. Participants were enrolled in the studies using hospital-based records and/or tumor registries. All but 2 of the study reports[9,11] provided information about the numbers of patients who were eligible but did not participate. Study participants ranged in age from teens to mid-80s; reports of

Table 1 • Summary of Studies Examining HRQOL in HD Survivors

Investigator	Conceptual Theoretical Framework	Country/Sample	Design	Instruments Used to Measure HRQOL	Selected Findings
Adams et al[8]	None	United States 48 HD survivors 31.9 y, median age (18–49.5 y) Median, 14.3 y postdiagnosis Stage I: 11% Stage II: 79% Stage III: 8% Stage unknown: 2% CMT: 100% Treatment: 1970–1991	Cross-sectional Correlational Cohort Retrospective	MOS SF-36 Researcher-constructed general health questionnaire	SF-36 physical health scores in HD survivors were significantly lower than in healthy adult controls, but mental scores were not significantly different. Cardiovascular abnormalities were common and strongly correlated with decreased physical functioning in survivors receiving mantle radiation.
Bloom et al[9]	None	United States 85 Men HD survivors 88 Men testicular survivors Age, 21–60 y Median, 3 y posttreatment Stage I: 11% Stage II: 35% Stage III: 46% Stage IV: 8% Chemotherapy only: 8% RT only: 37% CMT: 7% Treatment: 1981–1986	Cross-sectional Correlational Case-control Retrospective	POMS CES-D Hamilton Clinicians Rating Scale Raskin Rating Scale Social Activity Scale	Physical outcomes such as fatigue and impaired physical activity were more likely to be reported in the HD group than in the testicular group. The HD group was more likely to report an inability to work at former pace than the testicular group did.
Bloom et al[10]	None	United States 85 Men HD survivors 88 men Testicular survivors Age, 21–60 y Median, 3 y posttreatment Stage I: 11% Stage II: 35% Stage III: 46% Stage IV: 8% Chemotherapy only: 8% RT only: 37% CMT: 7% Treatment: 1981–1986	Cross-sectional Correlational Case-control Retrospective	POMS Researcher constructed	HD survivors were more likely to change jobs or stop working compared with the testicular group. Self-reported energy levels were related to reduced leisure activities but did not curtail work activities. Older age and combined modality treatment of HD were significant predictors of decreased leisure activity. Change in leisure time activities was a predictor of mood distress.
Cameron et al[11]	Classical Conditioning Theory	United States 273 HD survivors Age, 20–66 y Median, 5 y posttreatment Stage I–II: 12% Stage III–IV: 88% Chemotherapy only: 80% RT only: 4% CMT: 16% Treatment: 1966–1986	Cross-sectional Correlational Cohort Retrospective	PAIS Researcher-constructed telephone interview	Emetic potential of treatment was not a significant predictor of conditioned distress to sights or smells. Fifty-five percent of survivors reported at least one persistent response to sight, smell, or taste cues that resulted in psychological distress, nausea, or vomiting. Psychological distress and anticipatory nausea in response to smells was most likely to occur in patients less than 2 y from treatment.

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Table 1 • continued

Investigator	Conceptual Theoretical Framework	Country/Sample	Design	Instruments Used to Measure HRQOL	Selected Findings
Carpenter et al[12]	None	United States 43 HD survivors Age, 16–36 y 1–10 y posttreatment Stage I–II: 100% RT only: 100% Treatment: 1976–1987	Cross-sectional Correlational Cohort Retrospective	PAIS SCL-90R Beck Depression Scale State-Trait Anxiety Scale Kaufman Hostility Scale	Patients who had completed treatment more than 2 y ago reported having feelings of abandonment and illness uncertainty as treatments became less frequent. Interviewers rated patients as being better adjusted to career plans as they moved further away from treatment than those patients who recently completed treatment.
Cella and Tross[13]	None	United States 60 HD survivors Mean age, 31.1 y 6–24 mo posttreatment Early stages IA, IB, IIA, IIIA: 50% Late stages IIB, IIIB, IVA, IVB: 50% CMT: 100% Treatment: 1974–1986	Cross-sectional Correlational Case-control Retrospective	BSI Derogatis Sexual Functioning Inventory: drive, satisfaction, and body image Researcher-constructed problem-oriented record interview Rosenberg Self Esteem Scale Death Anxiety Scale	No differences in psychological distress were identified between survivors and the control group (patient acquaintances/friends). Survivors demonstrated greater appreciation for life than controls. Survivors reported difficulties adjusting to work and diminished work capacity. Adjustment difficulties were identified by those survivors closer to treatment completion and those with more severe disease.
Fobair et al[14]	None	United States 403 HD survivors Mean age, 36 y 1–21 y posttreatment Stage I–II: 60% Stage III–IV: 40% Chemotherapy only: 5% RT only: 38% CMT: 58% Treatment: 1965–1985	Cross-sectional Correlational Cohort Retrospective	CES-D Researcher-constructed questionnaire—sense of well-being, family relationships, and employment	Ninety percent of patients reported that treatment had adversely affected energy levels. Thirty-seven percent of the 403 patients interviewed had not recovered from adverse energy levels. Those patients who had not recovered were more likely to have late-stage disease, received CMT, were older, and were more likely to have higher depression scores. Significantly more women than men reported that activity level was more adversely affected by therapy. The median time required to resume normal activities was 8 mo and return of energy was significantly correlated with level of activity. Forty-nine percent of survivors felt that HD disrupted personal relationships resulting in divorce or separation. Interest and participation in sexual activity declined in 71% of survivors. Survivors reported employment concerns including denial of insurance, not being offered a job, termination after employment, conflicts with coworkers and supervisors, and fear of disclosure.

Table 1 • continued

Ganz et al[15]	None	United States 246 HD survivors Median age, 31.4 y 6 mo and 1–2 y posttreatment Stages IA and IIA: 100% RT only: 50% CMT: 50% Treatment: 1992–2000	Prospective Longitudinal Case-control	MOS SF-36 CARES-SF Symptom Distress Scale	There was a significantly increased difference in physical symptoms such as fatigue for those receiving CMT compared with those receiving RT alone. Both groups reported that increased sexual dysfunction was slightly worse in the CMT group. There were no significant differences between CMT- and RT-alone groups in working status by year 1 posttreatment.
Kornblith et al[16]	None	United States 273 HD survivors Mean age, 37 y Mean, 6.3 y posttreatment Stage III–IV: 100% Chemotherapy only: 80% RT only: 4% CMT: 16% Treatment: 1966–1986	Cross-sectional Correlational Cohort Retrospective	PAIS-SR POMS BSI IES Global Sexual Satisfaction Survey	HD survivors reported significantly less psychological distress than a group of mixed cancer patients did in active treatment but experienced greater distress than healthy controls did. HD survivors reported 1 or more sexual problems including decreased sexual satisfaction, interest, and activity. Forty-two percent of HD survivors had problems with denial of life and health insurance. Eleven percent of survivors perceived job discrimination in the workplace, and 36% believed that having had cancer had a negative impact on employment, income, or educational level. HD survivors complained of nausea (39%) in response to sight and smells, and 23.4% experienced medical problems as a likely consequence of HD.
Kornblith et al[17]	None	United States 93 HD survivors Median age, 35 y Mean time, 2.2 y posttreatment Stages III, IV: 100% Chemotherapy only: 100% Treatment: 1980–1987	Cross-sectional Correlational Cohort Retrospective	PAIS-SR POMS BSI IES Global Sexual Satisfaction Survey	There were no significant differences in the adaptation of physical, psychological, psychosexual, and socioeconomic domains between the 3 HD treatment arms. Twenty-five percent of HD survivors reported problems in physical, psychological, psychosexual, and socioeconomic domains.
Kornblith et al[18]	None	United States 273 HD survivors Mean age, 37 y 4–23 y posttreatment Stage III–IV: 100% Chemotherapy only: 80% RT only: 4% CMT: 16% Treatment: 1966–1986	Cross-sectional Correlational Cohort Retrospective	PAIS-SR POMS BSI SCL-90R IES Global Sexual Satisfaction Survey Researcher-constructed conditioned nausea and vomiting survey	Fifty-six percent of those HD survivors separated or divorced attributed marital status to having had cancer. Eleven percent of HD survivors attributed one or more vocational problems to having had cancer. HD survivors with psychological distress also reported problems in areas of psychosocial and sexual functioning.
Kornblith et al[19]	None	United States 273 HD survivors Mean age, 37 y Median time, 5 y posttreatment Stage III–IV: 100% Chemotherapy only: 80% RT only: 4% CMT: 16% Treatment: 1966–1986	Cross-sectional Correlational Case-control Retrospective	PAIS-SR POMS BSI IES Global Sexual Satisfaction Survey	At 5 y after treatment, 25% of HD survivors reported significantly more psychological distress, anticipatory nausea, sexual dysfunction, and greater fatigue than the leukemia survivor control group did and 3 times the rate of psychological distress than in the general population.

continues

Table 1 • continued

Investigator	Conceptual Theoretical Framework	Country/Sample	Design	Instruments Used to Measure HRQOL	Selected Findings
Ng et al[20]	None	United States 511 HD survivors Median age, 44 y Median time, 15 y posttreatment Stage unknown Chemotherapy only: 4% RT only: 61% CMT: 35% Treatment: 1969–1996	Cross-sectional Correlational Case-control Retrospective	FACIT-F	HD survivors were found to be more fatigued than were sibling controls. Higher levels of fatigue in HD survivors were associated with reports of cardiac disease, psychiatric conditions, use of tobacco, and low exercise frequency. Tobacco history use of 100 or more cigarettes was related to increased fatigue in survivors. Low exercise frequency was a predictor of fatigue for HD survivors and controls.
Zabora et al[21]	None	United States 135 HD survivors Median age, 57 y Stage unknown Treatment: 1987–1993	Cross-sectional Correlational Case-control Retrospective	BSI	HD survivors scored the highest mean on the subscale of hostility on the BSI scale. Thirty-eight percent of HD survivors scored as positive cases demonstrating distress on the BSI.
Abrahamsen et al[22]	None	Norway 459 HD survivors 2214 Population controls Age, 19–74 y Mean, 11 y postdiagnosis Stage I–II: 61% Stage III–IV 39% Chemotherapy only: 14% RT only: 38% CMT: 48% Surgery only: <1% Treatment: 1971–1991	Cross-sectional Correlational Case-control Retrospective	Researcher-constructed survey	Professional plans changed for one-third of survivors due to HD. HD survivors were twice as likely to be permanently disabled than controls. Factors such as older age, lower socioeconomic status, combined treatment, depression, anxiety, fatigue, and physical symptoms significantly predicted disability in HD survivors.
Devlen et al[23]	None	United Kingdom 120 HD and NHL survivors Mean age, 40.4 y Newly diagnosed Stage I–II: 33% Stage III–IV: 67% Chemotherapy/ RT/CMT Unknown Treatment: 1987	Prospective Longitudinal Cohort	The Wechsler Memory Scale Researcher-constructed shortened versions of present-state examination and standardized social interview schedule	More than half of those patients who experienced gastrointestinal toxicities such as nausea, vomiting, diarrhea, loss of appetite, and sore mouth also suffered from anxiety and depression. The 21 survivors who were employed before becoming ill, 24% returned work in 6–11 mo, 19% were off for 12 mo or more, and 7% retired early. Despite complaints of short-term memory impairment and cognitive difficulties experienced by one-third of survivors, formal memory scales did not support impairment.
Devlen et al[24]	None	United Kingdom 90 HD and NHL survivors Age, 17–73 y Diagnosed 6 mo to 6 y prior Stage and treatment unknown Treatment: 1981–1987	Cross-sectional Correlational Cohort Retrospective	Researcher-constructed interview	Continuing physical/psychological symptoms experienced by survivors included lack of energy, loss of libido, irritability, and tiredness. Complaints of short-term memory impairment and cognitive difficulties were experienced by one-third of survivors. A large proportion of survivors did not return to work although they were free of disease, completed treatment, and did not have depression or anxiety.

Table 1 • continued

Flechtner et al[25]	None	Europe 818 HD survivors Age not reported, 4 mo to 10 y posttreatment Stage I–II: 56% Stage III–IV: 44% CMT: 100% Treatment: 1981–1997	Longitudinal Correlational Cohort Prospective	QLQ C30 QLQ-S LSQ MFI	Thirty-five percent of survivors had difficulties with insurance or obtaining a loan felt to be related to disease status. For most, reasons for not working included attending school, being a housewife/husband, or retiring early due to disease or treatment. Marital status changed in 20.6% of which one-third perceived this as disease related. Sexual activity declined in 32% of survivors, of which 50% perceived this disease related.
Geffen et al[26]	None	Europe 44 HD and NHL survivors Median age, 51 y 2–16 y posttreatment Stage I–II: 73% Stage III–IV: 27% RT only: 14% Chemotherapy only: 54% CMT: 32% Treatment: 1987–1999	Cross-sectional Correlational Case-control Retrospective	Posttraumatic Stress Disorder (PTSD) Inventory Scale MOS SF-36	More intense PTSD symptoms were significantly higher in those diagnosed earlier in age. Eighteen percent of HD and NHL survivors were diagnosed with PTSD. QOL was negatively correlated with PTSD.
Gil-Fernandez et al[27]	None	Europe 67 HD survivors Mean age, 34 y 8 mo to 22.1 y posttreatment Stage I–II: 57% Stage III–IV: 43% Chemotherapy only: 22% RT only: 15% CMT: 63% Treatment: 1981–2003	Cross-sectional Correlational Case-control Retrospective	EORTC QLC-30 HADS	Physical and social function was significantly lower in HD patients than in healthy population controls. Scales measuring dyspnea and economical difficulties were significantly higher in HD patients than in controls. Loss of appetite, problems with diarrhea, fatigue, and depression were higher for those older than 45 y. Physical symptoms and anxiety were higher in females than in males. No differences in HD patients compared to controls in global state of health and QOL.
Greil et al[28]	None	Europe 126 HD survivors Age range at diagnosis, 6–89 y Mean, 9.1 y posttreatment Stage I–II: 68% Stage III–IV: 32% Chemotherapy only: 10% RT only: 24% CMT: 66% Treatment: 1969–1994	Cross-sectional Correlational Case-control Retrospective	EORTC QLC-30	Those HD survivors who received CMT experienced more fatigue, pain, and dyspnea than those who received radiation (RT) or chemotherapy (CT) only. Those HD survivors who received CMT reported lower physical functioning than RT alone. Self-reported global QOL did not differ between HD survivors of 2–5 y posttreatment to those 5 y or greater posttreatment.
Hjermstad et al[29]	None	Europe 476 HD survivors Median age, 46 y 5–29 y posttreatment Stage I–II: 63% Stage III–IV: 37% Chemotherapy only: 14% RT only: 31% CMT: 55% Treatment: 1971–1997	Longitudinal Case-control Prospective	FQ	HD survivors experienced moderately elevated and significant fatigue compared to reference values from the general population. Fatigue is prevalent several years after treatment for HD. Presence of B symptoms (ie, fever, night sweats, and weight loss) was the only disease characteristics significantly associated with total and chronic fatigue. More than 50% of HD survivors who reported chronic fatigue at baseline did not report fatigue 8 y later.

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Table 1 • continued

Investigator	Conceptual Theoretical Framework	Country/Sample	Design	Instruments Used to Measure HRQOL	Selected Findings
Hjermstad et al[30]	None	Europe 475 HD survivors Mean age, 46 y Median time, 16 y posttreatment Stage I–II: 63% Stage III–IV: 37% Chemotherapy only: 14% RT only: 31% CMT: 55% Treatment: 1971–1997	Cross-sectional Correlational Case-control Retrospective	FQ MOS SF-36	HD survivors with chronic fatigue report better QOL in the mental health dimension than did the control group with chronic fatigue. HD survivors demonstrated significantly more fatigue and lower QOL compared to a general population control. HD survivors scored lower than the population control did on the general health perception scale.
Joly et al[31]	None	Europe 93 HD survivors Mean age 42 Median, 10 y posttreatment Stage I–II: 67% Stage III–IV: 33% Chemotherapy only: 4% RT only: 34% CMT: 62% Treatment: 1978–1990	Cross-sectional Correlational Case Control Retrospective	Researcher-constructed survey EORTC QLQ-C30	Physical, role, cognitive, and social functioning were significantly lower in HD survivors than in healthy population controls. HD survivors had cognitive difficulties in concentration and memory. HD survivors aged 50 y or older had significantly more difficulty in physical (dyspnea), cognitive, and role function. Social parameters such as problems borrowing from banks, being childless, and experiencing fewer divorces or separations were significantly correlated with HD survivors. HD and controls were similar in the areas of work stoppage and work discrimination, although HD survivors reported less professional ambition and more importance was placed on sport or leisure projects.
Knobel et al[32]	None	Europe 92 HD survivors Mean age, 37 y Mean, 9 y posttreatment Stage I–II: 86% Stage III–IV: 14% RT only: 32% CMT: 68% RT only: 32% CMT: 68% Treatment: 1971–1991	Cross-sectional Correlational Case-control Retrospective	FQ	HD survivors with pulmonary dysfunction had more fatigue than HD survivors with normal function. HD survivors with cardiac sequelae did not report more fatigue than HD survivors without. There was no association between fatigue and thyroid dysfunction.
Loge et al[33]	None	Europe 421 HD survivors Age, 19–74 y 3–23 y posttreatment Stage I–II: 60% Stage III–IV: 40% Chemotherapy only: 15% RT only: 37% CMT: 48% Treatment: 1971–1991	Cross-sectional Correlational Cohort Retrospective	FQ HADS	Age and educational level showed significant differences in fatigue. Chronic fatigue was associated with increased levels of psychological distress. Age and educational level were associated with significant differences in levels of fatigue.

Table 1 • continued

Loge et al[34]	None	Europe 459 HD survivors Mean age, 44 y Mean, 12 y posttreatment Stage I–II: 60% Stage III–IV: 40% Chemotherapy only: 17% RT only: 38% CMT: 45% Treatment: 1971–1991	Cross-sectional Correlational Cohort Retrospective	HADS	Anxiety levels were higher among women than men. Those survivors older than 50 y experienced more depression than did those younger than 29 y. Time from diagnosis and type of treatment were significant predictors of anxiety. HD survivors 7–10 y after diagnosis were 3 times more likely to experience depression and anxiety than those participants 3–6 y after diagnosis.
Loge et al[35]	None	Europe 459 HD survivors Mean age, 44 y Mean, 12 y posttreatment Stage I–II: 61% Stage III–IV: 39% Chemotherapy only: 14% RT only: 38% CMT: 48% Treatment: 1971–1991	Cross-sectional Correlational Case-control Retrospective	MOS SF-36	HD survivors had statistically significant lower scores on HRQOL in the subdomains of general health, physical functioning, role limitations, social functioning, and vitality scales than those of the general population controls. Type of primary treatment for HD survivors did not show statistically significant differences in HRQOL.
Loge et al[36]	None	Europe 459 HD survivors Mean age, 44 y Mean, 12 y posttreatment Stage I–II: 61% Stage III–IV: 39% Chemotherapy only: 14% RT only: 38% CMT: 47% Treatment: 1971–1991	Cross-sectional Correlational Case-control Retrospective	FQ HADS	HD survivors had higher scores in total and mental fatigue than those of the general population controls, nearly 20% higher. HD survivor age and educational level were predictors of total fatigue.
Norum and Wist[37]	None	Europe 42 HD survivors Age not reported Median, 16–120 mo posttreatment Stage I–II: 62% Stage III–IV: 38% Chemotherapy only: 16% RT only: 10% CMT: 16% Treatment: 1985–1993	Cross-sectional Correlational Cohort Retrospective	IES Visual analogue scale QOL	Fifty percent of survivors reported moderate to high stress. HD survivor women reported lower distress on the intrusive and avoidance scales of the IES and higher overall QOL than men did.
Norum and Wist[38]	None	Europe 42 HD survivors Age not reported Median, 16–120 mo posttreatment Stage I–II: 62% Stage III–IV: 38% Chemotherapy only: 16% RT only: 10% CMT: 16% Treatment: 1985–1993	Cross-sectional Correlational Cohort Retrospective	EORTC QLC-30	Survivors experienced sleep disturbances related to dyspnea, fatigue, pain, financial difficulties that were correlated with reduced QOL scores. Female survivors reported lower levels of fatigue than men did. Forty-five percent of survivors reported physical condition or medical treatment as causing financial difficulties.

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Table 1 • continued

Investigator	Conceptual Theoretical Framework	Country/Sample	Design	Instruments Used to Measure HRQOL	Selected Findings
Oldervoll et al[39]	None	Europe 53 HD survivors Mean age, 41 y 5–15 y posttreatment Stage I–II: 74% Stage III–IV: 26% Chemotherapy only: 26% RT only: 37% CMT: 37% Treatment: 1987–1997	Experimental longitudinal Phase I survey Phase II pilot intervention Prospective Cohort	FQ MOS SF-36	HD survivors experienced a significant reduction in physical, mental, and total fatigue after participating in the exercise intervention. There was a significant improvement in exercise tolerance from before to after exercise intervention.
Ruffer et al[40]	None	Europe 818 HD survivors Median, 5.2 y posttreatment Stage I–II: 56% Stage III–IV: 44% CMT: 100% Treatment: 1981–1993	Cross-sectional Correlational Case-control Retrospective	EORTC QLC C-30 MFI QLQ-S LSQ	Significant increases in fatigue for HD survivors was experienced compared to general population controls. HD survivors showed significant correlation to fatigue such as age, systemic symptoms, KPS, and relapse.
Van Tulder et al[41]	None	Europe 81 HD survivors Mean age, 43 y Mean, 14 y posttreatment Stage I–II: 80% Stage III–IV: 20% RT only: 76% CMT: 24% Treatment: 1972–1979	Cross-sectional Correlational Case-control Retrospective	MOS SF-36	HD survivors reported significantly more deficits that were attributed to limitations in physical health such as a reduction of hours spent working or carrying out activities, accomplishing less at work, being limited in the type of activities involved in, and having to exert more effort in carrying out daily activities. Reports of more difficulty obtaining loans and insurance as well as incurring higher costs as compared to healthy controls.
Wettergren et al[42]	Wilson and Cleary's Model	Europe 121 HD survivors Mean age, 47 y Mean, 14 y posttreatment Stage I–II: 55% Stage III–IV: 45% Chemotherapy only: 28% RT only: 55% CMT: 17% Treatment: 1972–1991	Cross-sectional Correlational Case-control Retrospective	SEIQOL-DW	HD survivors view family, personal health, work, and relations with other people as the most important areas in life. The QOL index score did not significantly differ between HD survivors and general population controls.

Abbreviations: BSI, Brief Symptom Inventory; CARES-SF, Cancer Rehabilitation Evaluation System; CES-D, Center for Epidemiological Studies—Depression Scale; CMT, combined modality therapy; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC QLQ-S, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Survivors; FACIT-F, Functional Assessment of Chronic Illness Therapy Fatigue; FQ, Fatigue Questionnaire; HADS, Hospital Anxiety and Depression Scale; HD, Hodgkin's disease; HRQOL, Health-Related Quality of Life; IES, Impact of Events Scale; KPS, Karnofsky Performance Status; LSQ, Life Situation Questionnaire; MFI, Multidimensional Fatigue Inventory; MOS SF-36, Medical Outcomes Study Short Form 36; NHL, Non-Hodgkin's Lymphoma; PAIS, Psychosocial Adjustment to Illness Scale; PAIS-SR, Psychosocial Adjustment to Illness Scale—Self-report; POMS, Profile of Moods States; QOL, quality of life; RT, radiation therapy; SCL-90R, symptom check list; SEIQOL-DW, Schedule for the Evaluation of the Individual Quality of Life-Direct Weighting.

2 studies did not include an age range.[37,38] In 26 (74%) of the studies, 51% to 60% of the participants were male. Only 6 studies[8,12,20,21,26,28] included more female than male participants, and 3 studies[9,10,13] included only male participants. Twenty-nine (83%) studies focused on HRQOL in HD survivors who were more than 1 year but less than 35 years after treatment completion, and 6 (17%) studies focused on HRQOL of those newly diagnosed or less than 1 year after treatment completion.[13,15,23–25,27] A complete description of the diagnostic stages and treatment regimens was included in all but 4 studies.[20,21,23,24] Early-stage disease was defined as stage I–II, and late stage, as stage III–IV. In one study, further extent of disease was defined by delineating between the absence (substage A) or presence (substage B) of key prognostic indicators including fever, night sweats, or pruritus to differentiate between early- and late-stage disease.[13] Twenty-seven (77%) studies were conducted in samples with early- and late-stage disease. Study samples were treated from 1965 to 2003. Length and type of treatment were dependent on stage of disease and ranged from 3 to 18 months for the studies in this review.

Research Instruments

A total of 29 different instruments were used to measure HRQOL in adult HD survivors; the most commonly used instruments are listed in Table 2. Ten (29%) studies used researcher-constructed questionnaires,[8,10,11,13,14,18,22–24,31] and the remainder used valid and reliable standardized instruments (Table 2). The instruments were administered most frequently as questionnaires that were mailed or administered via a telephone or face-to-face interview.

Domains of HRQOL

The variables reflecting the domains of HRQOL addressed in this integrative literature review are listed in Table 3. Twenty-seven of the 35 studies (77%) addressed the physical domain using variables such as fatigue, sexuality, and cognition. Twenty-six (74%) studies addressed the psychological domain using variables such as distress, depression, and anxiety. The social/functional domain was addressed in 16 (46%) studies; variables included relationships, work, and activities of daily living. The spiritual domain was addressed in only 2 of the 35 studies (6%)[13,42] by focusing on survivors' worldview and life meaning.

Physical Domain

FATIGUE

Fatigue remains a common problem for HD survivors, even several years after the completion of treatment. Hjermstad et al[29] found that a sample of 476 HD survivors reported higher levels of fatigue than a sample drawn from a general, healthy population.

Correlates of fatigue reported by HD survivors include age, education, gender, HD stage, type of treatment, and the presence of other physical symptoms. Loge et al[36] reported that total fatigue was significantly higher among survivors 60 years or older compared to younger HD survivors. Participants with fewer years of education also reported greater fatigue than those with more years of education. Norum and Wist[38] found that men reported significantly higher levels of fatigue than women did. In addition, patients diagnosed with

Table 2 • The Most Commonly Used Instruments

Instrument	Health-Related Quality of Life Domains Measured	No. of Studies Using the Instrument	Reliability	Validity
Medical Outcomes Study Short Form 36[8,15,26,30,35,39,41]	Physical/psychological	7	Cronbach α Test-retest	Content Construct Criterion
Fatigue Questionnaire[29,30,32,33,36,39]	Physical	6	Cronbach α Test-retest	Construct Criterion
Brief Symptom Inventory[13,16–19,21]	Psychological, social/functional	6	Cronbach α Test-retest	Construct Criterion
Psychosocial Adjustment to Illness Scale—Self-report[11,12,16–19]	Psychological	6	Cronbach α	Construct Criterion
Profile of Moods States[9,10,16–19]	Psychological	6	Cronbach α	Construct Criterion
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30[25,27,28,31,38,40]	Quality of Life in Cancer Patients—Domains	6	Cronbach α Test-retest	Construct Criterion
Impact of Events Scale[16–19,37]	All domains	5	Cronbach α Test-retest	Content Construct Criterion
Hospital Anxiety and Depression Scale[27,33,34,36]	Psychological	4	Cronbach α Test-retest	Construct Criterion
Global Sexual Satisfaction Index[16–19]	Physical	4	Cronbach α Test-retest	Construct Criterion

Table 3 • The 4 Domains and Associated Variables to Measure Health-Related Quality of Life

Domain	Variable
Physical	Fatigue Anticipatory nausea and vomiting Other physical symptoms Sexuality Cognition
Psychological	Distress Anxiety Depression PTSD
Social/functional	Relationships Work Leisure Activities of daily living
Spiritual	World view Life meaning

later stages of disease and those who received combination cancer therapy (both chemotherapy and radiation therapy) experienced a greater delay in the return of their energy levels than those who were diagnosed with earlier stages of disease and those who received monotherapy.[14] Furthermore, patients who received combination therapy reported a higher level of fatigue than those who received monotherapy.[15,28] In addition, Norum and Wist[38] found that patients who received mantle radiation experienced more fatigue and dyspnea than those who did not receive radiation up to 10 years after completion of treatment.

In one study, so-called B symptoms, such as fever, night sweats, and weight loss at diagnosis, were found to be the only defining disease characteristics that were positively correlated with survivors' fatigue after treatment.[29] In other studies, survivors' reports of cardiac disease, psychiatric disease, tobacco use, and low exercise frequency were correlated with relatively high levels of fatigue after treatment.[20,40]

ANTICIPATORY NAUSEA AND VOMITING

Anticipatory nausea and vomiting are another common physical problem experienced by HD survivors.[11,12,17] According to Cameron et al,[11] this conditioned response—a feeling of distress experienced in relation to the typical sights and/or smells in the medical environment—has been reported by as many as 55% of survivors at one point in time and is most likely to occur just after diagnosis but may continue up to 2 years after treatment. Furthermore, Kornblith et al[16] reported that 39% of HD survivors continued to experience nausea for at least a year after treatment in response to sights and smells, but episodes of vomiting were a rarer occurrence.

OTHER SYMPTOMS

Hodgkin's disease survivors experience several other symptoms related to the treatment received in the years after treatment including cardiovascular and respiratory complications,[20,38] shortness of breath and tachycardia,[8] and thyroid dysfunction.[32] Nevertheless, Adams et al[8] reported that although HD survivors reported moderate to severe problems with fatigue, shortness of breath, chest pain, and dizziness several years after treatment completion, they scored their health as good as or better than that before diagnosis.

SEXUALITY

Some researchers studied survivors' sexuality. Cella and Tross[13] found significantly lowered motivation for intimacy among 60 male HD survivors compared with a healthy control group. Kornblith et al[18] noted that 37% of 273 HD survivors reported one or more sexual problems; the most common were decreased interest in sex and loss of sexual satisfaction. Fobair et al[14] found that the most common sexuality problems were infertility and decreased interest in sexual activity in a sample of 403 HD survivors. Greil et al[28] found that survivors who had received combination therapy reported more infertility problems and less sexual enjoyment than did those who had received monotherapy.

COGNITION

A few researchers have studied cognition in HD survivors. Joly et al[31] found that cognitive problems manifested as memory impairment and poor concentration even several years after treatment completion. Similarly, Devlen et al[23] reported that 47 of 120 HD survivors described having difficulty recalling simple facts, such as their telephone number, after completing treatment. These memory impairments were attributed to the older age of the samples and to depression, anxiety, and possibly minor brain damage secondary to chemotherapy or viral infection during treatment.

Psychological Domain

DISTRESS

The incidence of emotional distress among HD survivors varied across the 35 studies. Cella and Tross[13] reported that survivors did not differ significantly from case-controls with regard to emotional distress. The findings of other studies, however, revealed that emotional distress was higher in the survivors than in healthy populations.[18,19]

Correlates of emotional distress include gender, stage of HD, and marital status. Female HD survivors in one study reported lower levels of distress than their male counterparts did, manifested as symptoms associated with posttraumatic stress disorder, such as intrusive thinking and avoidance.[37] In contrast, male HD survivors in another study reported less emotional distress after treatment than females did.[27] Furthermore, HD survivors diagnosed with later stages of disease (stage IIB, IIIB, IVA, or IVB) were found to be at higher risk for emotional distress than those diagnosed with earlier stages.[13] And HD survivors who were married had lower levels of distress than those who were not married.[21]

ANXIETY AND DEPRESSION

It is estimated that up to 50% of HD patients and survivors report anxiety and/or depression during the first year after diagnosis and treatment.[24] The influence of gender on reports of anxiety and depression is unclear. Although both Zabora et al[21] and Fobair et al[14] reported no correlation between gender and depression in HD survivors, Loge et al[34] noted that anxiety was greater for women than for men. Age and educational level may be related to anxiety and depression. Kornblith et al[17] found that survivors older than 40 years had a higher incidence of depression than their younger counterparts, and both Loge et al[33] and Kornblith et al[17] found that HD survivors with limited educational backgrounds experienced higher levels of anxiety and depression than those with higher levels of education. Marital status, however, does not seem to be related to anxiety and depression. Loge et al[34] found no significant difference in anxiety and depression between HD survivors who lived alone and those who were married.

Social/Functional Domain

Although it is common for HD survivors to return to their usual level of functioning after treatment is completed, many experience changes in their ability to function in social and occupational roles.[14,18,24,41] For example, difficulty returning to work has been reported in up to 42% of HD survivors.[14] Many HD survivors who had trouble returning to work noted that they had a diminished capacity to complete work-related tasks or adjust to the work environment.[10] In addition, when compared to survivors of testicular cancer, HD patients were significantly more likely to change jobs or stop working. Flechtner et al[25] reported that the main reason for unemployment among HD survivors was early retirement due to the disease and its treatment.

Several factors associated with permanent disability after treatment have been identified, including having little education and low income, having been treated with combined chemotherapy and radiation therapy, being older than 40 years, having depression and/or anxiety, and having experienced exertional dyspnea and pain or stiffness in the shoulders secondary to mantle field radiation.[22,40] Gender also influences function. Fobair et al[14] reported that women had a greater decrease in activity tolerance after treatment for HD compared to men. Similarly, Loge et al[35] found that women survivors scored lower than men did on a measure of the functional domain of HRQOL.

In addition, stage of HD may influence functioning. Survivors who had been diagnosed with later stage HD were found to be at highest risk for functional adjustment problems, such as readapting to premorbid work schedules during the first 2 years after treatment.[13] In contrast, Devlen et al[23] found that a large proportion of survivors of both early- and late-stage HD failed to return to work and to resume normal leisure activities up to 1 year after completion of treatment. Hodgkin's disease survivors experienced a greater decrease in leisure and work activities than did those who had testicular cancer, which was attributed to limited energy and type of treatment.[10]

The physical domain symptom of fatigue has been found to affect HD survivors' ability to participate in leisure activities for many months after treatment. Devlen et al[23] noted that 48 of the 120 survivors (40%) surveyed continued to report little interest in leisure activities even 1 year after the completion of treatment.

Several researchers identified changes in marital status, with an increased incidence of divorce and separation, among HD survivors.[22,25] Approximately 20% of participants in one study reported changes in their relationships that they associated with their cancer diagnosis and treatment.[25] Participants in another study reported having fewer children after diagnosis and treatment for HD compared with healthy controls.[31]

Spiritual Domain

Only 2 of the 35 studies (6%) addressed the spiritual domain of HRQOL. In one study, survivors reported that they had a greater appreciation for life after treatment.[13] In the other study, survivors identified family, personal health, work, and relationships with close friends as the most important aspects of their lives after HD diagnosis and treatment.[42]

■ Discussion

State of the Science

This integrated review of research that had been conducted in the United States and Europe adds to our understanding of the state of the science regarding the HRQOL of HD survivors. Overall, although survival has improved for adults diagnosed with HD through advancements in curative treatments, the research revealed that the physical, psychological, social/functional, and spiritual domains of HRQOL are compromised for months or even years after completion of treatment.

Although it is encouraging to know that HD is considered a curative illness, the potential for overtreatment of young adults diagnosed with HD is a topic of discussion and concern. The long-term impact of curative treatment on the physical domain of HRQOL is especially problematic for young adult HD survivors because of factors such as age at the time of chest irradiation and the use of alkylating chemotherapy agents that increase the risk of secondary lung and other cancers and cardiac disease in long-term survivors. In 1988, clinical researchers explored treatment reductions intended to reduce life-threatening adverse events caused by radiation while maintaining cure rates. By 1991, this fifth novel treatment regimen—named Stanford V for late-stage disease—shortened treatment courses, instituted cumulative toxic dose reductions, and decreased radiation doses and volume while maintaining favorable survival outcomes for HD.[44] Consequently, current clinical trials have been designed to determine the efficacy of treatment reductions in patients with lower radiation therapy doses and less toxic chemotherapy regimens for earlier stage disease as the risk for late mortality from causes other than HD continues to threaten survivors many years later.[3] However, until more clinical data support favorable long-term HRQOL outcomes with treatment reductions in early- and late-stage disease, researchers suggest that caution be taken when considering changes in standard treatment.[45]

The literature revealed that fatigue was the most common problem in the physical domain of HRQOL. The finding that fatigue was more severe for HD survivors than for healthy controls even years after treatment completion is consistent with prior research about cancer-related fatigue. Indeed, fatigue has been reported to occur in approximately 75% of all cancer patients and can be a more common adverse effect of treatment than nausea, depression, or pain.[46] The high incidence of cancer-related fatigue has led to proposing that it be considered the sixth vital sign.[47]

Late medical complications of HD therapy such as cardiac disease and abnormal thyroid and pulmonary function may contribute to the prevalence of fatigue in HD survivors compared to other cancer survivors.[45] Whether the occurrence of fatigue in cancer survivors is associated with treatment modality, disease, or nonclinical factors such as socioeconomic status, age, or gender, patients report that this assumption profoundly alters their quality of life before and after treatment.[27,36] Increasingly, research findings support the thesis that increased physical activity ameliorates the incidence of fatigue during and after treatment and improves physical functioning and other domains of quality of life.[48,49] For example, Oldervoll et al[39] reported that fatigue and physical conditioning improved when HD survivors participated in an aerobic exercise program.

Another common physical domain problem is nausea and vomiting. Since the introduction of 5-Hydroxytryptamine$_3$ (5-HT$_3$) receptor antagonists in 1991, there has been a significant reduction in posttreatment vomiting, yet treatment-related nausea continues to be a recurrent and continuing consequence of chemotherapy and is considered far more difficult to control than treatment-associated emesis. In one study of HD survivors, 63% experienced persistent anticipatory nausea and 5% reported anticipatory vomiting, which were thought to be a response to reminders of treatment, for as long as 6 to 140 months after completion of chemotherapy. Although these reactions lessened over time, anticipatory nausea was experienced by half the patients for more than 2.5 years.[50] Promising prevention strategies for the control of anticipatory nausea and vomiting include both new guidelines for using antiemetics during treatment and behavioral therapies such as hypnosis.[51,52]

With regard to sexuality, the finding that HD survivors reported lowered motivation for intimacy, along with a decreased interest in sex and loss of sexual satisfaction, is consistent with findings from other studies reporting that older adolescents and young adults who experience distress, depression, and anxiety may experience or show difficulty in responding to intimacy and lack sexual motivation when stressed.[53] Fertility preservation may also be a concern of young adults with HD and their partners. Issues surrounding fertility and sexuality concerns should be addressed and evaluated before, during, and after treatment.[54]

Studies of the physical domain of HRQOL focused little attention on memory impairment and cognitive problems although HD survivors often report difficulties with memory, attention, and new learning after treatment. The findings of one meta-analysis of specific cognitive effects of cancer treatment in adults indicated that executive function, verbal memory, and motor function were negatively affected by systemic cancer therapies.[55] There is some evidence that chemotherapy negatively affects cognitive ability, sometimes referred to as "chemo brain" or "chemo fog."[56,57] Other factors that may influence cognitive decline include stress, depression, sleep disturbances, fatigue, or the cancer process itself with the release of toxic by-products (cytokines). Researchers have begun to report that there is a stimulation of cytokines in breast and colorectal cancers that may be implicated in deficits of cognitive function.[58] Other researchers have reported survivor complaints of cognitive problems that can negatively affect daily functioning, vocational interests, and other aspects of quality of life. Thus, a better understanding of cognitive function in HD survivors is an important area for future research.

The psychological domain of HRQOL continues to be a frequent focus of research for long-term survivors of cancer. The most common variables measured in the psychological domain in the studies in this review were depression and anxiety. The findings revealed mixed results that may be attributed to a variety of instruments used to measure psychological distress and the diverse time points for measurement, ranging from during treatment to many years after treatment completion. Developmental level at the time a young adult is diagnosed with a serious illness may have a significant influence on psychological adjustment. For example, young survivors face the disruption of developmental milestones such as establishing intimate relationships, fertility, child rearing, and financial concerns, whereas older adults are looking forward to retirement.[59,60]

Survivor responses in the functional and social domains of HRQOL were frequently investigated as well. Seven researchers[24,25,27,28,31,41,42] investigated how HD survivors perceived changes in leisure activities, finances, and employment in response to medical conditions and treatment effects. Other investigators focused specifically on how fatigue compromised energy levels and a decline in physical performance that had a negative impact on work and leisure time.[10,29,32,33,35,39,40] Although some researchers have argued that activities not directly related to health status are outside the purview of the healthcare provider, such as the measurement of job satisfaction and economic factors, the impact of treatment on the social/functional domain of HRQOL for those with cancer or chronic illness is relevant to morbidity, mortality, and long-term surveillance.[61,62] Functional status has not traditionally included measurements of work satisfaction and the financial consequences of illness, but as demonstrated in this review, these issues have become increasingly important to cancer survivors. Advances in early detection and less debilitating treatments have led to an increased presence of cancer survivors as active members in the workplace, reinforcing the need to include this essential component in the measurement of HRQOL.[63]

Only 2 studies investigating the spirituality domain of HRQOL in HD survivors were located. Religious and spiritual coping have been shown to improve other domains of HRQOL in cancer survivors. In a study of 170 patients with advanced cancer, positive religious coping was related to better existential QOL dimensions, as well as overall QOL.[64] Balboni et al[65] reported that 72% of respondents with various types of cancer indicated that they had little opportunity to discuss spiritual concerns with their healthcare provider. Further studies are needed to understand the spiritual and religious needs of cancer survivors.[66]

Theoretical and Methodological Issues

One major finding of this review is the lack of explicit theoretical frameworks used to guide the research. Only 2 (6%) groups of researchers used an explicit theoretical framework to guide the research. The other researchers typically provided extensive explanations to justify the design and use of multiple instruments in the introduction section of the article. A theoretical framework provides a structure for all aspects of a study, from selection of study variables to specification of links between variables to interpretation of results. Atheoretical studies may yield heuristically interesting results but do not contribute to advancement of knowledge because the "why" of the study results cannot be explained.

Researchers are encouraged to use existing frameworks for future studies. For example, Wilson and Cleary[62] described a theoretical framework that posits causal relationships among biological and physiological factors, symptoms, functioning, general health perceptions, and overall quality of life. Ferrans et al[67] further developed and revised this model to describe the influences of HRQOL. The Ferrans et al[67] model underscores the importance of patient values and preferences and internal factors such as developmental stage when designing interventions that are intended to change or modify behavior and improve HRQOL. Another framework that may be used to guide future research is the Roy Adaptation Model. This conceptual model depicts individuals as biopsychosocial beings who adapt physically, psychologically, functionally, and socially to ever-changing environmental stimuli.[68] Linkages can easily be made between the modes of adaptation and variables in each domain of HRQOL, as well as between environmental stimuli and variables such as age, gender, race, education, type of treatment, and stage of disease.[68]

The findings of this review uncovered numerous methodological issues that need to be resolved, including using more rigorous study designs and standardizing the measurement of each HRQOL domain. Most studies reviewed were correlational and cross-sectional; just 4 (11%) of the studies in this review used longitudinal designs. Murdaugh[69] pointed out that HRQOL is a dynamic and nonstatic construct that cannot accurately reflect the impact of illness at one point in time, highlighting the need for longitudinal, prospective study designs.

As can be seen in Table 1, more than 29 different instruments were used to measure the various domains of HRQOL. Measurement approaches used in the studies included a single instrument or a battery of different instruments. The 2 most commonly used single questionnaires measuring HRQOL domains are the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 and the Medical Outcomes Study Short Form 36 (Table 2). The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 was used exclusively in European studies (n = 6) to measure the multidimensional construct of HRQOL. This instrument is a cancer-specific measure; subscales measure physical, emotional, cognitive, and social functioning, as well as global health status.[70] Short Form 36, in contrast, is a generic measure that enables comparison across various diseases. This instrument was used in 7 studies, most of which were conducted in Europe.[8,15,26,30,35,39,41] The use of a brief, single, and concise instrument to measure HRQOL would aid in reducing respondent burden, especially given the high incidence of fatigue experienced by HD survivors. In addition, the uniform adoption of a single instrument for measuring HRQOL would allow for direct comparison of findings across studies and contribute to the advancement of knowledge.

Researchers rarely reported categorization of study participants' race, which may be related to the low incidence of HD in nonwhite persons. Yet in 2005, HD incidence rates were similar in African American and white, non-Hispanic populations.[71] Only 8 (23%) US studies in this review included descriptions of participant racial/ethnic identity. Zabora et al[21] reported that a sample of 680 African American cancer survivors, as well as those of lower socioeconomic status, experienced greater distress than did cancer survivors of other races. Addressing HRQOL in culturally diverse populations cannot be ignored, as evidence suggests that certain groups may be at risk for decreased HRQOL.

■ Conclusion

Although cure rates and survival statistics for patients with HD have improved dramatically in the last decade, curative treatments have been implicated in the multiple medical sequelae that occur after treatment, including second malignancies, cardiac and pulmonary disease, and other late effects such as infection and endocrine disorders.[45] Because HD survivors have had an excellent prognosis for disease-free survival, this population can be used as a model for investigating the HRQOL of cancer patients transitioning to survivorship. Implementation of innovative programs that will improve survivors' adjustment and gradual return to previous levels of functioning should be a priority. The results of this systematic review suggest that there is a growing body of literature that describes the HRQOL problems that occur after treatment for HD. Gaps in the literature identified through this review include the lack of longitudinal studies and explicit theoretical frameworks, inconsistent measurement of HRQOL, and exclusion of minority groups in study samples. Consensus about standardized HRQOL instruments would enable researchers to compare findings across studies. As the evidence related to HRQOL in HD survivors grows, development and testing of theory-guided interventions are needed to improve the transition from acute care and enhance the long-term goal of the highest possible HRQOL.

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