Quality of Life in Long-Term Survivors of Adult-Onset Cancers

Carolyn Cook Gotay, Miles Y. Muraoka*

The long-term survival of cancer patients has risen dramatically during the last few decades, yet little is known about the quality of life experienced by these survivors. This paper reviews research on the quality of life in long-term cancer survivors to identify quality-of-life concerns in this population, to provide a critical evaluation of the literature, and to suggest areas for future research. Searches of computerized literature databases were conducted to identify all studies of quality of life in cancer survivors that were published in English language journals during the period from January 1, 1980, through February 12, 1998, and that were based on responses from individuals who have survived 5 or more years after the diagnosis of adult-onset cancers. Thirty-four papers were identified. Most studies utilized self-report questionnaires to measure quality of life. Although methodologies and cancer patient populations varied greatly, most studies showed that many survivors continue to experience negative effects of cancer and/or treatment on their daily lives well beyond the completion of therapy. Sexual functioning and/or satisfaction and psychological functioning were found to be concerns for many survivors. Several reports documented positive coping strategies and enhanced quality of life in long-term cancer survivors, supporting the need to measure positive aspects of quality of life as well as problems in this population. Study designs that more accurately measure quality of life among survivors of cancer by adjusting for the effects of aging and long-term therapy and the impact of second cancers should be utilized. Additional data are needed to understand the needs of long-term survivors, especially of those in groups underrepresented in published quality-of-life studies, and to determine what kinds of support survivors want. [J Natl Cancer Inst 1998;90:656–67]

As a result of more effective treatments and approaches to early detection, the long-term survival rate of cancer patients has risen dramatically during the past few decades. Whereas the proportion of cancer patients who survived 5 or more years was only one in five in 1930 (1), this proportion increased to approximately one in two in 1997 (2). Improved survival has been found for patients with many, but not all, cancers. The mean 5-year survival rate for patients with lung cancer, the most commonly diagnosed cancer in the United States, is approximately 14% for whites, and this figure has hardly changed in the past 20 years. Nonetheless, for other cancers, including many of the most common cancers, the prognosis is much more favorable; more than 80% of patients with Hodgkin’s disease or with cancer of the breast, uterus, prostate, testis, or thyroid can expect to live at least 5 years after their diagnosis.

The same treatments that have enabled long-term survival, however, can also cause potentially debilitating deficits, ranging from disruptions in day-to-day activities to late effects such as second primary cancers. While numerous long-term physical effects of cancer have been documented, the impact of such sequelae on patients’ quality of life (QOL) is much less well understood. Although a growing number of studies have documented the considerable impact of cancer diagnosis and treatment on QOL in newly diagnosed cancer patients (3–7) and short-term survivors (8–12), less attention has focused on QOL in long-term survivors, partly because of the recency of the rise in survival rates.

It is possible that long-term effects may differ from those experienced around diagnosis and treatment. New issues may present that were not of concern earlier on. For example, the possibility of being denied insurance coverage because of a cancer history may not emerge until a survivor looks for a new job years after diagnosis. Some of the late physical effects of cancer treatment, such as those that occur because of the cardiotoxic effects of some chemotherapeutic agents, are just being identified (13), and how these sequelae may affect the patient’s QOL is not known. In addition, the impact of persistent effects of cancer treatment (such as an amputation or functional change like incontinence) on QOL is not clear: Survivors may learn to live with and adjust to their limitations, they may continue to experience problems to the same degree as during short-term survival, or they may have decreased tolerance of disability with the passage of time (i.e., an enhanced QOL, an unchanged QOL, or a worsened QOL, respectively). At the present time, reports are starting to appear in the literature (14) that will ultimately enable researchers to distinguish among these possible scenarios.

This paper provides a review of published studies of QOL in...
long-term cancer survivors. The purposes of the review are 1) to identify QOL concerns in this population, 2) to provide a critical evaluation of the literature, and 3) to suggest areas where additional research is needed.

Methods

MEDLINE® (National Library of Medicine, Bethesda, MD), CANCERLIT® (National Cancer Institute, Bethesda), Cumulative Index to Nursing and Allied Health Literature (CINAHL®) (Cinal Information Systems, Glendale, CA), and PsycLIT® (American Psychological Association, Washington, DC) databases were used to identify relevant publications, as were the references of said papers. Key words included “long-term survivor(s),” “survivor(s),” “cancer,” “QOL,” and “quality of life.” We also looked at dimensions that are often included as components of QOL, including psychosocial adjustment, physical limitations, and psychiatric status of cancer survivors. Additional selection criteria included 1) papers published in English, 2) publication date of January 1, 1980, through February 12, 1998, 3) studies based on cancer survivors who were disease free, and those who had a cancer recurrence. These studies have been included and noted accordingly. We did not include studies of QOL in patients with metastatic disease. A number of studies included survivors of 5 or more years after diagnosis along with respondents who were closer to their time of diagnosis. If results for the long-term survivors were reported separately or if time since diagnosis was statistically controlled through univariate or multivariate analyses, we have included these reports; in most of these studies, however, this was not the case.

Results

Based on the above criteria, a total of 34 publications was found (Table 1). These papers have been grouped according to their primary focus: 1) cancer survivors treated with bone marrow transplantation, 2) survivors of head and neck cancer, 3) survivors of breast cancer, 4) survivors of other cancers, and 5) QOL questionnaire development.

QOL in Long-Term Survivors Treated With Bone Marrow Transplantation

Haberman et al. (15) conducted a qualitative analysis of the responses to a mailed questionnaire in a sample of 125 survivors of various cancers (50 of whom had acute leukemia) who had had a bone marrow transplant 6–18 years earlier. Questions were designed to identify areas of concern, such as adjustment to daily activities, management of life changes, and comparison of current QOL relative to that prior to the transplant. On the basis of an analysis of themes emerging from the questions, Haberman et al. (15) concluded, “. . . most long-term survivors, despite the persistence of lingering side effects, perceive themselves as cured and well, leading full and meaningful lives” (p. 1545).

In a related study based on the same cohort of survivors, Bush et al. (16) reported QOL scores on standardized questionnaires. The results showed that 93 (74%) of the 125 survivors reported their current QOL as being the same or better than prior to the transplant, 110 (88%) reported that the benefits of their transplant outweighed negative side effects, and 100 (80%) rated their current QOL and physical health status as good to excellent; only six (5%) survivors rated their current QOL and health status as poor. In addition, although many survivors reported a moderate incidence of fatigue, pain, sleep difficulties, and emotional, sexual, and cognitive dysfunction, the level of distress associated with these sequelae was low.

The QOL of short-term (12–30 months after bone marrow transplantation; n = 29), mid-term (31–48 months after bone marrow transplantation; n = 30), and long-term (≥5 years after bone marrow transplantation; n = 31) survivors of bone marrow transplantation was examined by Fromm et al. (21). All 90 participants had been treated for hematologic cancers; 27 had been treated for non-Hodgkin’s lymphomas, and 25 had been treated for acute leukemia. QOL was assessed by a semistructured telephone interview, and standardized QOL measures were completed and returned by mail. This report focused on how respondents defined QOL, rather than indicating whether the patients were experiencing a satisfactory QOL. The results of a one-way analysis of variance showed that the numbers of positive and negative sequelae, derived from the interview, were not statistically significantly different among the three groups, although long-term survivors reported fewer positive sequelae than participants in the other two groups. Pearson product-moment correlations revealed that, for all participants, the number of positive sequelae did not correlate statistically significantly with any of the standardized instruments; the number of negative sequelae, however, was statistically significantly correlated with all but one of the standardized measures.

Lesko et al. (29) compared the psychosocial adjustment of 70 acute leukemia survivors treated with either bone marrow transplantation (n = 21) or conventional chemotherapy (n = 49) (mean survival times of 8.4 and 5 years after diagnosis, respectively). They performed a multivariate analysis of covariance, with current age, years after diagnosis, and years after completion of treatment as covariates. The results of their analysis showed that there were no statistically significant differences in long-term psychosocial distress and social adjustment between the two treatment groups, after the groups were equated with respect to the covariates.

Wellisch et al. (33) also compared the QOL of bone marrow transplantation-treated (n = 11) and chemotherapy-treated (n = 19) acute leukemia survivors (mean of 5 years and 6.5 years after diagnosis, respectively). In multivariate analyses that controlled for other variables (e.g., treatment regimen, sex, and age), they found that months since diagnosis was a statistically significant predictor of positive functioning, as measured by the psychological and physical subscale scores of the Cancer Rehabilitation Evaluation System (34) as well as the Brief Symptom Inventory (30) phobic anxiety subscale. These results suggest that QOL is better among survivors who had survived longer.

QOL in Long-Term Survivors of Head and Neck Cancer

Bjordal and colleagues published three reports (36–38) examining components of QOL in a single cohort of 204 long-term survivors (7–11 years since treatment) of head and neck cancers. The survivors received either conventional (2 Gy, 5 days per week; n = 103) or hypofractionated (2.35 Gy, 4 days per week; n = 101) radiation therapy in the context of a randomized clinical trial. Bjordal et al. (36) assessed the QOL in long-term survivors, who completed and returned a 71-item questionnaire through the mail. Their results indicated that treatment factors affected QOL: Survivors who received hypofractionated radiation therapy reported QOL equal to or better than the QOL of those receiving the conventional treatment. In their second study, Bjordal and Kaasa (37) examined the levels of psycho-
Table 1. Methods used in long-term survivor quality-of-life studies*

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of cancer/treatments</th>
<th>No. of survivors</th>
<th>Time since diagnosis</th>
<th>Instruments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haberman et al. (15) and Bush et al. (16)</td>
<td>Various cancers/BMT</td>
<td>125</td>
<td>Range = 6–18 y Mean = 10 y</td>
<td>European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (EORTC QLQ-30) (17); Profile of Mood States (POMS) (18); Demands of BMT Recovery Inventory (19); Ware Health Perception Questionnaire (20)</td>
</tr>
<tr>
<td>Fromm et al. (21)</td>
<td>Various cancers/BMT</td>
<td>31</td>
<td>Range = 5–10 y</td>
<td>Functional Living Index—Cancer (22); Positive and Negative Affect Scale (23); POMS (18); two subscales from Psychological Adjustment to Illness Scale (24); five subscales from Sickness Impact Profile (25); Rosenberg Self-Esteem Scale (26); Global QOL Rating Scale (27); 10-Step Health Ladder (28)</td>
</tr>
<tr>
<td>Lesko et al. (29)</td>
<td>Acute leukemia/BMT and chemotherapy</td>
<td>70</td>
<td>Mean = 8.4 y (BMT) and 5 y (chemotherapy)</td>
<td>Brief Symptom Inventory (30); Impact of Events Scale (31); Social Adjustment Scale (32)</td>
</tr>
<tr>
<td>Wellisch et al. (33)</td>
<td>Acute leukemia/BMT and chemotherapy</td>
<td>30</td>
<td>Mean = 5 y (BMT) and 6.5 y (chemotherapy)</td>
<td>Cancer Rehabilitation Evaluation System (34); Center for Epidemiological Studies Depression Scale (35); Brief Symptom Inventory (30)</td>
</tr>
<tr>
<td>Bjordal et al. (36–38)</td>
<td>Head and neck cancer/ conventional or hypofractionated radiation therapy</td>
<td>204</td>
<td>Range = 7–11 y</td>
<td>EORTC QLQ-30 (17); EORTC Head/Neck Specific Module (39); General Health Questionnaire (40); two items adapted from Social Indicators of Well-being (41)</td>
</tr>
<tr>
<td>Meyer and Aspegren (42)</td>
<td>Breast cancer/modified mastectomy or breast-conserving surgery</td>
<td>58</td>
<td>≥5 y</td>
<td>Clinical interview; depression scale (43); anxiety/phobia scale (44)</td>
</tr>
<tr>
<td>Onme-Ponten et al. (45)</td>
<td>Breast cancer/ mastectomy or breast-conserving surgery</td>
<td>66</td>
<td>Range = 5–8 y Median = 6 y</td>
<td>Social Adjustment Scale (46); author-developed interview</td>
</tr>
<tr>
<td>Halttunen et al. (47)</td>
<td>Breast cancer/ mastectomy</td>
<td>22</td>
<td>≥8 y</td>
<td>Beck Depression Inventory (48); Semantic Differential of Psychosocial Behavior Patterns (49); Attitude to Illness Scale and interview (author-developed)</td>
</tr>
<tr>
<td>Sorensen (50)</td>
<td>Breast cancer/ mastectomy</td>
<td>32</td>
<td>Range = 5–26 y</td>
<td>Clinical interview, standardized instruments (not specified)</td>
</tr>
<tr>
<td>Vinokur et al. (51)</td>
<td>Breast cancer/ mastectomy</td>
<td>95</td>
<td>≥5 y</td>
<td>Author-developed questionnaire packet, based on standardized scales including Hopkins Symptom Checklist (52); Bradburn’s Positive Affect Scale (53); Rosenberg’s Self-Esteem Scale (26); and Rotter’s Internal–External Scale (54)</td>
</tr>
<tr>
<td>Saleeba et al. (55)</td>
<td>Breast cancer/ mastectomy</td>
<td>52</td>
<td>Range = 5–18 y Mean = 8.5 y</td>
<td>Beck Depression Inventory (56); Spielberger State–Trait Anxiety Scale (57)</td>
</tr>
<tr>
<td>Dorval et al. (58)</td>
<td>Breast cancer/ mastectomy</td>
<td>124</td>
<td>Range = 8–9 y Mean = 8.8 y</td>
<td>Medical Outcomes Study (MOS) (59); Psychiatric Symptom Index (60); MOS Social Support Survey (61); Life Experiences Survey (62)</td>
</tr>
<tr>
<td>Carter (63)</td>
<td>Breast cancer/ radical and modified radical mastectomy</td>
<td>25</td>
<td>Range = 5–26 y Mean = 10 y</td>
<td>Semistructured interview</td>
</tr>
<tr>
<td>Fredette (64)</td>
<td>Breast cancer/ radical and modified radical mastectomy</td>
<td>14</td>
<td>Range = 8–30 y Mean = 13.7 y</td>
<td>Semistructured interview</td>
</tr>
<tr>
<td>Wyatt et al. (65)</td>
<td>Breast cancer/ mastectomy</td>
<td>11</td>
<td>Range = 5–14 y Mean = 10 y</td>
<td>Semistructured interview</td>
</tr>
<tr>
<td>Baba et al. (66)</td>
<td>Esophageal cancer/ esophagectomy</td>
<td>43</td>
<td>≥10 y</td>
<td>Author-developed questionnaire</td>
</tr>
<tr>
<td>McLarty et al. (67)</td>
<td>Esophageal cancer/ esophagectomy</td>
<td>64</td>
<td>Range = 5–23.2 y Median = 10.2 y</td>
<td>MOS 36-Item Short-Form (MOS SF-36) (68)</td>
</tr>
<tr>
<td>Fobair et al. (69)</td>
<td>Hodgkin’s disease/ chemotherapy and radiation therapy</td>
<td>330</td>
<td>Range = 1–21 y Median = 9 y</td>
<td>Center for Epidemiological Studies Depression Scale (35); author-developed questionnaire</td>
</tr>
</tbody>
</table>
logical distress of the survivors and found that 64 (31%) of the 204 survivors would be likely to meet the criteria of *The Diagnostic and Statistical Manual of Mental Disorders* (3rd ed.) (94) for psychiatric disorders. In addition, survivors who reported low physical (n = 32), role (n = 63), social (n = 46), or cognitive (n = 29) functioning or those with high pain (n = 29) or fatigue (n = 40) scores were more psychologically disturbed, as indicated by the higher General Health Questionnaire (20-item version) scores (40). Many survivors experienced treatment-related side effects, including mouth dryness (n = 58 [28%]) and/or lowered mucus production (n = 58 [28%]). Although 42 patients had experienced a recurrence of disease (n = 23) or second primary cancer (n = 19), there were no significant bivariate correlations between either of these factors and psychological distress scores. Finally, Bjordal et al. (38) mailed a two-item questionnaire to the same cohort of survivors and to age-, sex-, marital status-, and education-matched control subjects (n = 766). The two questions were adapted from (41). One question assessed the respondents’ satisfaction with life, and the other measured physical energy. The mean satisfaction with life score reported by survivors was 2.92 (on a 7-point scale) (95% confidence interval [CI] = 2.46–3.39) compared with a mean of 2.72 (95% CI = 2.43–3.01) for the control group. The mean physical energy score was 3.50 (95% CI = 3.25–3.75) for the survivors and 3.47 (95% CI = 3.33–3.61) for the control group. One hundred twenty-eight (63%) survivors reported satisfaction with life compared with 626 (82%) of 766 control participants.

### Table 1—continued. Methods used in long-term survivor quality-of-life studies*

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of cancer/treatments</th>
<th>No. of survivors</th>
<th>Time since diagnosis</th>
<th>Instruments</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Tulder et al. (70)</td>
<td>Hodgkin’s disease/ mantle field irradiation</td>
<td>81</td>
<td>Range = 10–18 y Mean = 14 y</td>
<td>MOS SF-36 (68); author-developed questionnaire</td>
</tr>
<tr>
<td>Stoter et al. (71)</td>
<td>Testicular cancer/ combination chemotherapy</td>
<td>48</td>
<td>Range = 7–10 y Median = 8 y</td>
<td>Author-developed questionnaire</td>
</tr>
<tr>
<td>Herr (14)</td>
<td>Prostate cancer/surgery</td>
<td>50</td>
<td>Range = 1–5+ y</td>
<td>Author-developed questionnaire</td>
</tr>
<tr>
<td>DirkSEN (72,73)</td>
<td>Malignant melanoma/ wide excision + chemotherapy or immunotherapy</td>
<td>31</td>
<td>Range = 5–20 y Mean = 9 y</td>
<td>Search for Meaning Scale (74); Index of Well-being (75); one item to assess self-blame (author-developed)</td>
</tr>
<tr>
<td>Greaves-Otte et al. (76)</td>
<td>Various cancers/not specified</td>
<td>649</td>
<td>≥5 y Mean = 8 y</td>
<td>Dutch version of Affect Balance Scale (77); author-developed quality-of-life and demographic questionnaire</td>
</tr>
<tr>
<td>Olweny et al. (78)</td>
<td>Various cancers/not specified</td>
<td>102</td>
<td>≥5 y</td>
<td>Hospital Anxiety and Depression Scale (79); Psychological Adjustment to Illness Scale (24); Weissman Social Adjustment Scale (80); Cattell’s 16 Personality Factor Inventory (81); Bond Defense Style Questionnaire (82); Goldberg’s Clinical Interview Schedule (83)</td>
</tr>
<tr>
<td>Halstead and Fernsler (84)</td>
<td>Various cancers/ surgery, chemotherapy, radiotherapy, immunotherapy, and hormonal therapy</td>
<td>59</td>
<td>Range = 5–48 y Mean = 13 y</td>
<td>Jalowiec Coping Scale (85)</td>
</tr>
<tr>
<td>Grassi and Rosti (85)</td>
<td>Various cancers/ surgery</td>
<td>52</td>
<td>6 y</td>
<td>Symptom Check List 90—Revised (87); Mental Adjustment to Cancer Scale (88); Illness Behavior Questionnaire (89); semistructured clinical interview</td>
</tr>
<tr>
<td>Kurtz et al. (90)</td>
<td>Various cancers/not specified</td>
<td>191</td>
<td>Range = 5–10+ y</td>
<td>Long-Term Quality of Life questionnaire (90); two subscales from Cancer Rehabilitation Evaluation System (34)</td>
</tr>
<tr>
<td>Wyatt and Friedman (91)</td>
<td>Various cancers/ surgery + chemotherapy and radiation therapy</td>
<td>187</td>
<td>Range = 5–33 y Mean = 8.4 y</td>
<td>Long-Term Quality of Life questionnaire (90)</td>
</tr>
<tr>
<td>Wyatt and Friedman (92)</td>
<td>Various cancers/ surgery + chemotherapy and radiation therapy</td>
<td>188</td>
<td>Range = 5–33 y Mean = 8.4 y</td>
<td>Long-Term Quality of Life questionnaire (90)</td>
</tr>
<tr>
<td>Wyatt et al. (93)</td>
<td>Various cancers/ surgery + chemotherapy and radiation therapy</td>
<td>188</td>
<td>Range = 5–33 y Mean = 8.4 y</td>
<td>Long-Term Quality of Life questionnaire (90); Cancer Rehabilitation Evaluation System (34)</td>
</tr>
</tbody>
</table>

*BMT = bone marrow transplantation.
described their physical health status as being "strong and healthy" compared with 393 (51%) of the 766 control participants. These results suggest that survivors had significantly lower satisfaction with life and lower physical energy levels than control participants.

**QOL in Long-Term Survivors of Breast Cancer**

Two studies (42,45) compared QOL in survivors who had received different primary treatments for breast cancer. Meyer and Aspegren (42) reported on 58 long-term survivors who had received either a modified radical mastectomy (n = 30) or breast-conserving surgery (n = 28). The women took part in a structured clinical interview (conducted by the first author) and also completed a self-administered depression scale and anxiety/phobia scales. The two treatment groups were not significantly different with respect to demographic variables or histories of psychiatric disorders prior to the cancer diagnosis. In terms of QOL issues, however, results of chi-squared analyses revealed that women who had received modified mastectomy showed significantly more avoidance of activities requiring exposure of the torso (e.g., swimming), were more socially isolated, were more likely to avoid looking at themselves in a mirror, and were more likely to be on anxiolytic medications. More importantly, however, among the 58 women in both groups, 41 (71%) women feared disease recurrence, 25 (43%) had breast pain (phantom or contralateral breast pain in the case of women who had received mastectomy), 19 (33%) survivors reported a decrease in sexual desire and/or dissatisfaction with their sex lives, 17 (29%) participants reported elevated anxiety and/or mood impairment after surgery, and 16 (28%) women showed "...obvious clinical signs of mental unbalance" (p. 15) during the interview. Of these 16 women, 12 (75%) displayed "...psychiatric symptoms of such a magnitude that indication for psychiatric care was obvious" (p. 15).

Omne-Ponten et al. (45) also sought to compare the psychosocial adjustment of women who had received breast-conserving surgery (n = 26) with that of women who had received mastectomies (n = 40). A semistructured interview and standardized questionnaires were used to measure a range of social and emotional indicators. No differences according to treatment were found for global ratings or subscale scores on the psychometric instruments. Nineteen (29%) of the 66 women had very poor or suboptimal psychosocial adjustment, based on the global rating scale. Of the 43 women who were married, 10 (23%) rated their marriage as not entirely satisfactory because of sexual disturbances or inadequate emotional support; sexual disturbances were found in eight (27%) of the 30 women who were sexually active. Anxiety and/or depression was found in 10 (15%) of all participants. Fifteen women had experienced cancer recurrence; their evaluations of the health care they had received did not differ from those of women who did not have disease recurrence, but possible differences in adjustment were not reported.

Joray et al. (63–65) investigated QOL in breast cancer survivors. Halltunen et al. (47) interviewed 22 women who had survived 8 years or more since their breast cancer diagnosis. They found that 20 (91%) of these women rated their current health as very good or fairly good, and 19 (86%) reported that they were either very or fairly satisfied with their lives in general. At the same time, however, 11 (50%) women frequently or occasionally thought of disease recurrence, and 16 (73%) reported that they got depressed more easily since having been diagnosed with cancer. Although a standardized questionnaire to measure depression was administered, findings were not reported.

Sorensen (50) examined survivors’ and each of their partners’ adjustment to their breast cancer experience. Thirty-two women who were alive 5–26 years after mastectomies were administered a semistructured interview and standardized instruments. Responses to standardized questionnaires showed that the breast cancer survivors scored below clinical levels on psychological distress (i.e., were not clinically distressed). Women who were satisfied with social support were less anxious and psychologically distressed. Husbands’ perceptions of their wives’ distress were not correlated with actual distress levels. The interview elicited information, which expanded on objective test findings. The respondents reported a number of positive outcomes, including increased emotional intimacy, increased value of life, and a discovery of emotional strength and resilience. However, 12 (38%) of the 32 women reported using alcohol or prescribed medications to help them cope, 13 (41%) women reported a decrease in sexual desire and activity, and eight (25%) couples reported decreases in frequency of orgasm.

Vinokur et al. (51) compared the QOL in breast cancer survivors as a function of age and time since diagnosis. They found that younger women (i.e., <65 years old) at least 5 years after diagnosis had statistically significantly lower anxiety and depression scores and higher positive morale scores than women of the same age group who had more recent diagnoses. However, in older women (i.e., ≥65 years), no differences in anxiety, depression, and positive morale were observed between the long- and short-term survivors.

Saleeba et al. (55) compared scores on standardized measures of anxiety and depression in 52 long-term survivors of breast cancer (mean time since diagnosis, 8.5 years; range, 5–18 years) and in a control group made up of 88 women who had received breast cancer screening. Although the control group was younger and better educated, an analysis of covariance by use of education as a covariate showed that survivors had higher depression scores relative to control participants. (Age was not significantly correlated with anxiety or depression scores.) Furthermore, a greater number of survivors scored in the mildly or moderately depressed category than control women (15 [29%] versus eight [9%], respectively). Although anxiety scores did not differ between the groups, 12 (23%) of the 52 survivors scored in the mildly to moderately anxious range, compared with 10 (11%) of 88 control women.

Dorval et al. (58) examined differences between survivors of breast cancer (mean follow-up of 8.8 years after diagnosis) and control women matched for age and area of residence. QOL was assessed in terms of physical health, functional status, social functioning, and psychological distress. The results of chi-squared analyses showed that survivors who remained free of disease since the date of diagnosis had levels of QOL similar to those of control women, although the former experienced significantly more arm problems (e.g., swelling and loss of sensation) and, for those with spouses, were significantly less satisfied with their sex lives.

Three qualitative studies of breast cancer survivors (63–65)
were identified; all of these studies provided information about the process of long-term survival in breast cancer. Carter (63) used a semistructured interview to assess the QOL experiences of 25 women during the 5 or more years following their cancer diagnosis. The interview focused on the women’s responses to diagnosis and treatments, as well as changes in their lifestyle and in their interpretation of the meaning of cancer. Carter described the process that women went through, including interpreting the diagnosis, confronting mortality, reprioritizing, coming to terms, moving on, and flashing back. This process enabled the women to “. . . emerge from the cancer experience with a clearer sense of self, gratitude for life, and strength and confidence in their ability to manage life crises” (p. 354).

Similar findings were reported by Fredette (64), who interviewed 14 long-term survivors to assess their concerns and coping styles. The interview addressed various areas, such as the role of family and friends, spirituality, employment issues, and existential aspects of the cancer experience. The analysis of the responses suggested that these women used multiple coping schemes, characterized as problem-focused techniques (e.g., involvement in work, active information-seeking about breast cancer, and support of family and friends) and emotion-focused strategies (e.g., increased spirituality and having a hopeful attitude). In short, according to Fredette, “These women made adjustments to living with cancer and were able to describe positive aspects of their cancer experiences” (p. 35).

Finally, Wyatt et al. (65) identified four themes that emerged during focus group discussions of 11 long-term survivors of breast cancer. The themes were 1) integration of the disease process into current life, 2) change in relationships with others, 3) restructuring of life perspective, and 4) unresolved issues. Wyatt et al. (65) concluded that their findings “. . . offer a message of hope for patients, families, and health-care providers. Women do survive breast cancer and with many positive outcomes” (p. 445).

**QOL in Long-Term Survivors of Other Cancers**

**Esophageal cancer.** Two studies that included QOL assessment were identified. Baba et al. (66) assessed physical sequelae of 43 ten-year survivors of esophageal cancer by a mailed questionnaire. The results showed that 10 participants were unable to climb one flight of stairs without resting, and 15 survivors were not satisfied with the amount of food they could eat.

Using mailed, standardized questionnaires, McLarty et al. (67) assessed QOL in 64 long-term survivors who had undergone esophagectomy; the median survival time was 10.2 years (range, 5–23.2 years). Compared with age- and sex-matched national norms, the survivors’ scores reflected significantly poorer physical functioning but significantly better mental health. In other aspects of QOL (e.g., ability to work, social interaction, daily activities, emotional dysfunction, and health perceptions), the survivors’ scores did not differ significantly from the national norms. However, on the basis of the outpatient clinic records of the total sample of 107 five-year survivors, McLarty et al. (67) reported that many survivors continued to have complications related to the resection, such as post-prandial dumping (n = 53 [50%]), reflux symptoms (n = 64 [60%]), and dysphagia (n = 49 [46%]); only 17 (16%) respondents were totally asymptomatic.

**Hodgkin’s disease.** Fobair et al. (69) found that 330 (82%) of 403 survivors of Hodgkin’s disease (median, 9 years after treatment; range, 1–21 years) scored within the normal range on the Center for Epidemiological Studies Depression Scale (35). By use of the Kaplan–Meier projection at 5 years, these survivors had a 70% likelihood of achieving normal energy levels 5 years after completing their treatment for cancer, whereas the survivors who scored in the clinical range (n = 73) had only a 38% likelihood that their energy levels would return to normal during the same time period.

van Tulder et al. (70) examined the responses of 81 long-term survivors of Hodgkin’s disease (10–18 years since diagnosis) and 55 age-matched hospital visitors to a mailed survey consisting of a standardized QOL questionnaire and questions generated by the authors to assess financial, employment, and insurance issues. The results involving the standardized instrument showed that, relative to the control participants, the survivors had significantly poorer physical functioning, role functioning related to physical health, and general health perceptions; there were no significant differences between the two groups in social functioning or mental health. Survivors had significantly more problems related to sexual functioning: they were less interested in sex, had sex less often, and were more dissatisfied with their sexual activity. In addition, survivors had significantly more problems than the control participants in obtaining personal loans or mortgages because of medical reasons (11 [14%] of 81 versus two [4%] of 55) and obtaining life insurance (21 [26%] of 81 versus two [4%] of 55). The survivors also had significantly higher percentages of health-related unemployment (39 [48%] of 81) than the control respondents (19 [35%] of 55).

**Testicular cancer.** Stoter et al. (71) mailed a QOL questionnaire to 48 men who had been treated by an experimental chemotherapeutic protocol for advanced testicular cancer; for these men, median years after therapy was 8 years (range, 7–10 years). The results indicated that 26 (54%) men reported a decrease in physical condition, particularly related to fatigue, paresthesia, and decreased muscle strength. As expected, sexual problems affected a considerable number of survivors; of the 48 men, 19 (40%) experienced a decline in the quality of their sexual lives, 15 (31%) reported ejaculatory dysfunction, and 10 (21%) reported a decrease in sexual desire. On the other hand, six (13%) men experienced an improvement in their sexual life. Forty-three (90%) of the survivors were employed.

**Prostate cancer.** Herr (14) examined patient satisfaction with prostate surgery in a group of 50 incontinent prostate cancer survivors, all of whom had chosen surgical treatment. The results showed that the level of satisfaction with surgery varied as a function of time after treatment; 83% of the men who were 1–3 years after surgery would opt for this treatment again in spite of their incontinence, whereas only 53% of incontinent men who were 5 or more years after treatment would choose surgery again.

**Malignant melanoma.** Dirksen published two studies (72,73) based on the same cohort of 31 long-term survivors (5–20 years after diagnosis) of malignant melanoma. In the first study (72), the relationships between well-being and locus of control, social support, self-esteem, and past experiences were examined. The results showed that an internal locus of control, high self-esteem levels, treatment consisting of chemotherapy...
and vitamin A, and fewer episodes of noncancerous chronic illnesses accounted for 52% of the variance in well-being scores (i.e., scores on these variables are significant predictors of QOL scores). In the second study (73), Dirksen found that 16 of the 31 survivors attempted to identify the reason why they had contracted cancer and had evaluated the impact of the diagnosis on their lives. Analysis of open-ended questions showed that, of the 14 survivors who had reported that their QOL had changed, 13 (93%) had regarded the changes as positive. These alterations were spiritual/philosophical in nature, which can be “... summarized as changes in self-awareness, with a re-ordering of priorities, and a sense of living for today” (p. 631). Participants who did not search for meaning did not report any changes in their QOL since diagnosis.

Various cancers. Seven studies (76,78,84,86,90–92) included survivors of cancer of a variety of sites. The largest study in this category was reported by Greaves-Otte et al. (76), who conducted a mail survey of 649 long-term survivors of various types of cancers; 370 (57%) of these survivors had been diagnosed with cancer of the breast or female reproductive system. The survivors were identified through a regional cancer center. They completed and mailed back questionnaires including a standardized mood scale and additional questions about health, activities, social relationships, and psychological well-being. The results revealed that more than half of the respondents continued to have physical symptoms related to their cancer or its treatment, such as fatigue and problems with their arms, hands, and neck. Five hundred six (78%) respondents considered themselves healthy, and 130 (20%) considered themselves disabled. Employment status remained unchanged for 402 (62%) of the survivors, while 110 (17%) had retired because of physical impairments. Of 143 survivors, 100 (70%) trying to open or modify existing life, medical, or funeral insurance policies had difficulty as a result of their cancer history, mainly because of increased premiums. Survivors also had poorer emotional/psychological well-being, as evidenced by their lower score on the mood scale relative to national norms.

Olweny et al. (78) compared the QOL in 102 long-term cancer survivors with that of 95 age- and sex-matched neighborhood controls and a group of survivors of coronary bypass surgery (n = 78) who had been hospitalized at the same time as the cancer patients. Half of the survivors (n = 51) had been diagnosed with Hodgkin’s disease and 33 were survivors of testicular cancer, with the remaining 18 subjects being survivors of lymphoma, leukemia, or bone cancer. Standardized measures assessed physical functioning, psychosocial functioning, personality traits, and defense mechanisms; a clinical interview was also used. On the basis of Wilcoxon sum tests, the cancer survivors were found to be significantly more impaired than the neighborhood control group on 13 different measures of subjective well-being, including the overall clinical interview schedule score, irritability, anxiety, phobias, sexual dysfunction, work at home, and permanent relationships. The survivors also used different defense mechanisms than the control population. There were no statistically significant differences in depression between the groups. Relative to cardiac patients, cancer survivors were less irritable and anxious and used different defense mechanisms. Olweny et al. (78) concluded, “... cancer survivors enjoy a quality of life similar to their neighbours, whereas coronary bypass survivors adjust less well psychosocially” (p. 826). However, given the large number of differences between the cancer patients and the control group on well-being scores, this conclusion should be questioned.

Halstead and Fernsler (84) examined coping styles of 59 survivors of various cancers, 30 (51%) of whom had breast cancer. A standardized coping scale was administered, as was a demographic and medical background questionnaire developed by the authors. Approximately 28 (47%) survivors reported that, since the time of diagnosis, they had changed their coping styles to more positive ones (e.g., positive thinking, confronting reality, and spiritually oriented). In addition, 30 (51%) participants reported no physical, emotional, and social difficulties. However, 16 (27%) reported physical problems (e.g., sexual limitations, fatigue, and pain), 11 (19%) reported emotional problems (e.g., fear of disease recurrence), and nine (15%) had experienced social problems (e.g., divorce/separation as a result of cancer, isolation, and difficulty obtaining insurance policies).

A prospective study investigating psychiatric morbidity and psychological adjustment to cancer was reported by Grassi and Rosti (86). Participants were administered a clinical interview and a battery of standardized questionnaires within 3 months after diagnosis and again at 6 years after diagnosis. The sample consisted of 52 survivors of various cancers (38 [73%] of whom had breast cancer); 43 (83%) of the participants were women. There was an overall decrease in the prevalence of disorders [according to The Diagnostic and Statistical Manual of Mental Disorders, 3rd ed., revised (95)] from the initial assessment (n = 24 [46%]) to the follow-up (n = 19 [37%]), although there was a twofold increase in the prevalence of anxiety disorders (initial assessment—n = 4 [8%] versus follow-up—n = 8 [15%]). The scores on standardized instruments assessing interpersonal sensitivity, paranoia, psychotism, disease conviction, and anxious preoccupation also decreased. High psychological distress and poor coping resources at the time of diagnosis were statistically significantly correlated with maladjustment and psychological disturbances at follow-up.

Wyatt and colleagues published a series of papers (90–92) concerning the development of a long-term-survivor-specific QOL instrument, the Long-Term Quality of Life questionnaire (90). (See the next section regarding the psychometric properties of the questionnaire.) Kurtz et al. (90) reported preliminary results of the Long-Term Quality of Life questionnaire in a sample of 191 women who had been diagnosed at least 5 years previously with breast cancer (n = 110 [58%]), ovarian/uterine cancer (n = 28 [15%]), or other cancers (n = 52 [27%]); 32 (17%) had experienced disease recurrence. The questionnaire measures the following four components of QOL: 1) somatic concerns, 2) health habits, 3) social/emotional support, and 4) philosophical/spiritual view. In that study, subscales from the Cancer Rehabilitation Evaluation System (34) were used to assess sexual satisfaction and psychological adjustment. The results showed that the women reported little psychological distress and relative satisfaction with their sexual lives. Elevated somatic concerns were reported by women who had a recurrence of cancer, women who were longer term survivors (≥10 years after diagnosis), and women who had breast cancer. Women with more education and those who had a positive philosophical/spiritual...
attitude were more willing to give support to others. Wyatt and Friedman (91,92) reported similar results.

**Long-Term-Survivor-Specific QOL Scale**

To date, there is only one published QOL scale specifically developed for, and validated with, long-term survivors of cancer. Wyatt et al. (93) reported the psychometric properties of the Long-Term Quality of Life (LTQL) questionnaire. It should be noted that Ferrell et al. (96,97) have also developed a Quality of Life—Cancer Survivors questionnaire. However, this research fell outside the parameters of this review, since it was validated on a group of survivors at 4 months to 28 years after diagnosis and possible differences between shorter and longer term survivors were not reported.] On the basis of the same sample of the study by Wyatt and Friedman (92), Wyatt et al. (93) conducted a factor analysis, an internal consistency analysis, and determined the content, concurrent, and construct validities of the scale. The results of the factor analysis revealed a four-factor solution, which accounted for 53% of the total variance. The factors were 1) somatic concerns, 2) spiritual/philosophical views of life, 3) fitness, and 4) social support (giving and receiving). The factor analysis resulted in a reduction of 33 items, to yield a 34-item questionnaire. The internal consistency analysis resulted in Cronbach’s alphas of .87 to .92 across the four subscales. Content validity was demonstrated by the conceptual congruence between the four subscales and the four QOL domains of Ferrell et al. (96,97). However, it should be noted that the four areas are not the same and that some of the same items were correlated with different factors in the two lines of research; the model used by Ferrell et al. includes psychological, spiritual, social, and physical domains, whereas the LTQL includes social support, fitness, spiritual/philosophical concerns, and somatic concerns.

The Cancer Rehabilitation Evaluation System (34) was used to analyze concurrent validity. The total LTQL score was significantly correlated with the total Cancer Rehabilitation Evaluation System score and all of the Cancer Rehabilitation Evaluation System subscales, with the exception of the marital subscale. The validity of the construct of long-term survivorship was demonstrated by the significant correlations that were expected between demographic and cancer-related health variables and LTQL scores. For example, participants who were currently experiencing a disease recurrence had lower overall QOL but had more somatic concerns and social support than those who had not experienced a recurrence; women who had mastectomies scored lower on the somatic and fitness subscales than did women who had lumpectomies; and younger women reported lower spiritual/philosophical views of life than older women.

**Discussion**

This review identified a wide variety of studies that have measured QOL in long-term cancer survivor populations during the last decade. There is considerable diversity of methods, including both qualitative and quantitative studies. Most studies involved the use of self-report questionnaires to measure QOL. Although a variety of QOL assessment tools was used in these studies, most investigators paid careful attention to assessment issues and used measures of demonstrated validity where available, increasing confidence that the findings are replicable. A number of studies found that semistructured interviews and directed questions were more successful than self-report questionnaires in eliciting specific concerns of long-term survivors. In this still-evolving area of research, it is wise for investigators to include an opportunity for survivors to report additional concerns not covered in standardized QOL scales wherever possible.

Only one questionnaire was reported that focused specifically on QOL in long-term cancer survivors—the questionnaire used by Wyatt et al. (93). Based on its careful development and sound psychometric properties, this tool is promising for use in long-term survivor populations. The QOL domains reflected in this tool vary considerably from most commonly used cancer patient QOL questionnaires and may reflect the different priorities of long-term survivors. Because the concerns of the cancer survivors in the cohort studied by Wyatt and co-workers (90–93) appeared to differ from those of other comparable survivor groups (as discussed below), the LTQL needs to be used and tested in other patient populations. Additional QOL questionnaires, such as the one developed by Ferrell et al. (96,97) and other scales used by other studies reviewed [which include the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (17), Functional Living Index—Cancer (22), Medical Outcomes Study (59), and Cancer Rehabilitation Evaluation System (34), among others], should also be considered. Whether to use a cancer-specific QOL questionnaire or a QOL survey appropriate for the general population remains an issue. Cancer-specific QOL assessments designed for use during therapy may include treatment-specific concerns (e.g., nausea and vomiting) that are not relevant in healthy survivor populations. On the other hand, questionnaires developed for a healthy population may omit symptoms that continue to be important to cancer survivors. It is recommended that investigators consider using a generic core questionnaire in conjunction with supplementary items or scales to address specific survivor concerns.

Most studies employed a cross-sectional design, with a single measurement providing “point prevalence” estimates of the magnitude of QOL outcomes. Only Omne-Ponten et al. (45) and Grassi and Rosti (86) measured QOL in the same individuals at more than one time point, and both studies found evidence that psychosocial dysfunction decreased over time. Both studies also identified some factors that may predict problems in long-term survival; this kind of information is vitally important to identify groups at risk and target support where and when it is needed. Some studies used control groups in order to try to determine whether the QOL of cancer survivors is different from that experienced by others of the same age and sex in the general population. Olweny et al. (78) employed a particularly creative design by measuring QOL in survivors of cardiovascular disease in order to distinguish how the impact of cancer may differ from that of another potentially fatal disease.

The characteristics of the patients who participated in the studies varied a great deal, in terms of site and stage of their cancer at diagnosis and type of therapy given. While we used 5-year survival as a minimum cutoff for inclusion of published studies in this review, the reports still differed considerably in
the mean or median time since diagnosis of their survivor populations, and there is too much variability to determine if this factor systematically influenced QOL findings. In addition, 5 years after diagnosis represents different lengths of time since completion of treatment, depending on the site of disease and therapeutic regimen. Using 5 years after diagnosis as the starting point for “long-term survivorship” is meaningful, especially since cancer survival rates have traditionally been expressed in terms of “5-year survival” and because most recurrences occur within 5 years of diagnosis. Being free of disease for 5 years after diagnosis may be psychologically meaningful as well. For example, Wellisch et al. (33) speculate that “...significant anniversary-type events such as 5-year survival postdiagnosis...” (p. 151) may affect QOL. However, without more systematic study, we have no way of knowing whether, for example, 4 years or 10 years may be a more meaningful or useful demarcation for survivors.

Given all of these differences between studies, perhaps it is not surprising that the QOL reported by survivors varies a great deal as well, making it impossible at this time to come to firm conclusions about the magnitude and nature of long-term consequences for cancer survivors. It seems clear, however, that considerable numbers of survivors continue to experience negative impacts of cancer and/or treatment on their daily lives, resulting in decrements in QOL, well beyond the completion of therapy. It is likely that the amount of dysfunction varies according to site of disease and treatment. For example, the survivors treated with bone marrow transplantation appear to be among the most healthy in terms of QOL of any groups addressed in this sample. There are several reasons why this may be so. The bone marrow transplantation recipients were younger at diagnosis than most of the other samples reported here and may be more likely to have an extended multigenerational social support system. In addition, as arduous as bone marrow transplantation is at the time it is performed, the treatment does not pose visible everyday disabilities. In contrast, survivors such as those treated with radical surgery for esophageal cancer must live daily with a modified pattern of eating. Similarly, a breast cancer patient is confronted with a changed body as she dresses herself each day.

The largest numbers of studies focused on breast cancer survivors or included a high proportion of breast cancer survivors in heterogeneous samples. Almost every study documents considerable physical, psychological, and social problems among these women. The sample studied by Wyatt and co-workers (90–93) stands in contrast, since sexual and psychological issues were not major problems in these women. It is likely that aspects of sample selection such as age, treatment, socioeconomic factors, social support, services available in the community, and other factors explain the variation in findings. More research is needed to sort out the important issues that differentiate groups of survivors.

The aspects of QOL that pose the most difficulty for survivors are likely to vary by cancer site, but this literature strongly implies that sexual functioning and/or satisfaction is a common issue for many survivors, regardless of diagnosis or treatment. Psychological dysfunction is also a major problem identified in most studies. Only a handful of studies asked questions about obtaining insurance (70,76,84), but those studies that did inquire found that survivors had encountered problems in this area.

However, one of the most notable conclusions to be drawn from this review is the need to focus on positive aspects of cancer survivorship, as well as on problems. Several studies (21,63–65,73,84) documented the positive coping strategies and processes used by cancer survivors and the ways that QOL may be enhanced rather than diminished by the experience of having faced a potentially fatal disease, undergone toxic and painful treatments, and survived. Human beings have an amazing capacity to meet and to adapt to challenges they face, and cancer survivorship exemplifies the strength of the body and spirit.

Clearly, more data about all aspects of QOL are needed to provide a more comprehensive and complete perspective on the needs of long-term cancer survivors. As more people survive cancer and for longer periods of time, their needs assume increased priority in health care. The visibility and political participation of the National Coalition for Cancer Survivorship have raised the profile of survivors and the need for information about their well-being, as have activities of the National Cancer Institute, which has established an Office of Cancer Survivorship and issued in 1997 requests for administrative supplements and applications (RFA [i.e., request for application] CA97018) for research on long-term survivors. Thus, we are confident that researchers will devote considerable attention to research on long-term survivors in the future. There are several areas that we suggest are particular priorities.

1) Need to address methodological issues in long-term survivorship research. A major problem in assessing QOL in long-term survivors is distinguishing effects due to cancer from those due to aging and/or other comorbidities, since the probability of having a chronic disease or functional limitation increases with advanced age. Several of the studies reviewed here (38,55,58,67,70,78) included control groups matched for age or other factors, and such designs are recommended. However, the optimal control group is difficult to specify. For example, should cancer survivors be compared with a healthy population, or with cancer patients around the time of diagnosis, or with a group that has been treated for another serious noncancerous health condition? The answer to this question depends on the hypothesis under investigation.

2) Need to understand long-term impact of different treatments on QOL. It is important to document how varying therapeutic modalities may give rise to different long-term effects. Such information can establish if there are any residual effects of one treatment but not another and if there are treatment-related decrements in QOL that vary in the short term and long term. Such data can assist patients in treatment decision-making.

3) Need to assess QOL in survivors experiencing second cancers. Considerable evidence has demonstrated that cancer survivors are at increased risk of being diagnosed with second cancers because of long-term effects of treatment and/or host effects such as genetic susceptibility (98). Virtually nothing is known about how QOL is affected by having a second cancer or about the effects of experiencing recurrence after an extended disease-free interval.

4) Need to assess more diverse populations. It is surprising that some of the most prevalent cancers are poorly or not at all represented in this literature. For example, there is only one study based on long-term survivors of prostate cancer (14), and there are none on long-term survivors of colorectal cancer, de-
spite the considerable numbers of these survivors in the population. Given the documented short-term morbidity associated with prostate cancer treatment and its impact on QOL (14) and the increasing numbers of prostate diagnoses, there is a critical need to evaluate the long-term impact of prostate cancer and its therapy. In general, men who are long-term survivors are underrepresented in the literature to date. Their perspectives may reveal additional aspects of long-term cancer survival that are not currently evident.

Many of the studies reported to date are based on European samples; this seems to be an area of research where European researchers have taken a lead. However, as Greaves-Otte et al. (76) stated, there are many cultural differences between European countries and the United States, as well as dissimilarities in their health care systems, particularly with respect to health care insurance. Furthermore, the cultural distinctions between and within national boundaries provide an exciting opportunity to examine differences in the meaning of survivorship, as well as values and behaviors, in different groups. For example, no studies to date have examined possible differences in long-term survival in different ethnic groups.

5) Need to examine the impact of long-term survival on the family. Family issues are no less important in long-term cancer survival than in other parts of the cancer continuum. The long-term impact of survivor problems affects the whole family unit. For example, sexual problems can be fully assessed only when both survivors and their partners are included. In addition, there may well be effects on the family that are not reflected in the survivors’ evaluations of their own QOL; e.g., the whole family may have to work so hard to provide support for the survivor that the other members develop problems of their own. It is only by including family members in the research process that the full scope of survivorship issues can be identified and appropriate responses identified.

6) Need to ask survivors what they need and want. As we learn more about the challenges associated with long-term cancer survival, interventions will be needed to address the problems identified. It is possible that some problems can be prevented and others remediated with the provision of appropriate care. However, it is critical to determine the kind of support desired by long-term survivors and to identify who is most in need of and likely to benefit from such intervention (99,100).

With the increasing number of long-term cancer survivors, the need to assess their QOL is becoming more important and meaningful. Extending life is but one criterion of successful cancer therapy, and assessment of long-term psychosocial and physical effects will ultimately determine the functional effectiveness of the treatment as well as guide the development of new approaches to care.

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Note

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