

Post-Traumatic Stress Disorder in Israeli Survivors of Childhood Cancer

Freda DeKeyser Ganz, RN, PhD, Haya Raz, RN, MA, Doron Gothelf, MD, PhD, Isaac Yaniv, MD, and Ilana Buchval, RN, MA

In 2007, almost 10,400 American children younger than 15 years were diagnosed with cancer, with approximately 1,545 dying from the disease (National Cancer Institute, 2009). In Britain, the risk of a child younger than 15 years being diagnosed with cancer is about 1 in 500 (Cancer Research UK, 2009). Significant improvements have been made in five-year relative survival from childhood cancers, improving from 58% for those treated from 1975–1977 to 80% for those treated from 1996–2003 (Jemal et al., 2008). Approximately 270,000 people are survivors of childhood cancer. This equates an estimated 1 in every 640 young adults aged 20–39 who are survivors of childhood cancer (Candlelighters Childhood Cancer Foundation, 2010). As more and more patients with childhood cancer survive to adulthood, thanks to improvements in diagnostic and therapeutic modalities, increased attention is being focused on the long-term psychological effects of the disease and its treatments (Apter, Farbstein, & Yaniv, 2003; McGrath, 2002). Some psychologists have suggested that the stress and anxiety inherent to cancer diagnoses and treatments are a traumatic event that may lead to the development of post-traumatic stress disorder (PTSD) later in life (McGrath, 2002). Therefore, as the number of cancer survivors with PTSD is expected to increase, more significance will be placed on the determination of who suffers from PTSD and what factors are associated with its development. This description is a first step toward the development of interventions that can prevent and treat PTSD in the future.

Background

According to the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.) (DSM-IV) (American Psychiatric Association, 1994), PTSD is defined as a serious mental condition that arises after an individual is confronted with a traumatic event associated with an actual death, a threatened death, or a serious injury. The event

Purpose/Objectives: To investigate the prevalence, symptom severity, and risk factors associated with post-traumatic stress disorder (PTSD) in childhood cancer survivors.

Design: Descriptive, correlational study.

Setting: Follow-up clinic in Petach Tikva, Israel.

Sample: Convenience sample of 70 adult Israeli survivors of childhood cancer.

Methods: Questionnaires (the Post-Traumatic Diagnostic Scale and the Multidimensional Scale of Perceived Social Support) were distributed to participants, and demographic and clinical data were obtained from medical records.

Main Research Variables: Post-traumatic stress, social support, and clinical and demographic data.

Findings: Twenty (29%) of the participants met the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.) criteria for PTSD; 10% experienced mild, 40% moderate, and 50% moderate to severe symptoms. Only 16% of the sample did not experience any symptoms of PTSD. A statistically significant negative relationship was found between PTSD symptom scores and the current age of the respondent ($r_s = -0.27$, $p = 0.03$) and time since medical treatment ($r_s = -0.34$, $p = 0.004$) but not any other demographic or clinical variables or social support.

Conclusions: Higher severity of PTSD symptoms was found, possibly because of local living conditions. Most clinical and demographic variables were not risk factors. This population should be studied further in an effort to prevent PTSD via early diagnosis.

Implications for Nursing: Oncology nurses should be aware of the potential risk factors (recent completion of treatment and younger current age) and the high prevalence and severity of PTSD among survivors of childhood cancer to identify patients at higher risk and develop programs that prevent, limit, and treat PTSD.

must elicit feelings of fear, helplessness, or horror. The diagnosis of PTSD is determined by evaluation of the presence of symptoms associated with the condition. The symptoms fall into three categories: re-experiencing the event (e.g., reliving the traumatic event or having intrusive memories or nightmares), avoiding stimuli

associated with the trauma (e.g., avoiding reminders of the trauma, avoiding social situations, emotional numbing, sensing a foreshortened future), and experiencing hyperarousal (e.g., irritability, hypervigilance, difficulty concentrating). To be classified as having PTSD, a person must have experienced at least one symptom of re-experiencing, three symptoms of avoidance, and two of hyperarousal for at least a period of one month after the trauma. The symptoms also must affect the person's daily functioning.

Initially, the diagnosis of PTSD was used in relation to traumatic events such as war, major accidents, and rape. More recently, PTSD has been increasingly applied to those who have survived cancer. In a systematic review of 24 studies associated with PTSD in survivors of childhood cancer and their parents, Bruce (2006) found the current prevalence of PTSD among survivors of childhood cancer to be 5%–21%, with a lifetime prevalence of 21%–35%, and reports of severe PTSD symptoms were as high as 13%. Females survivors, as well as those with a history of prior stressful life events, were consistently found to be at higher risk for developing PTSD, but type of treatment was not found to be associated with rates of PTSD symptoms (as reviewed by Bruce, 2006). Other studies evaluating risk factors such as age at diagnosis, time since end of therapy, length of therapy and its perceived difficulty, and socioeconomic status yielded conflicting results, with some studies finding no association and others finding relationships in opposite directions (Best, Streisand, Catania, & Kazak, 2001; Bruce, 2006; Erickson & Steiner, 2001; Hobbie et al., 2000; Rourke, Hobbie, Schwartz, & Kazak, 2007; Schrag, McKeown, Jackson, Cuffe, & Neuberg, 2008). Rourke et al. (2007) found no significant differences between survivors of childhood cancer with PTSD and those without PTSD on demographic, disease, or treatment variables. They concluded that beliefs about the cancer experience were more important predictors of PTSD than demographic, disease, or treatment factors. Even after a long interval from completion of treatment, Taiwanese survivors of childhood cancer were found to suffer from PTSD (Ozono et al., 2007). One study investigated Israeli long-term survivors of Hodgkin disease and non-Hodgkin lymphoma as compared to those who suffered other types of trauma (Geffen, Blaustein, Amir, & Cohen, 2003) and found that 32% of the lymphoma survivors and 25% of the control group suffered from full or partial PTSD; however, the difference was not statistically significant.

Social support has been found to be associated with PTSD among adult survivors of childhood cancer and their parents. Social support is defined as the belief that a person will receive emotional and physical help when needed from family, friends, or significant others (Hobbie, Ruccione, Harvey, & Moore, 2002; Zimet, Dahlem, Zimet, & Farley, 1988). Smith, Zimmerman, Williams,

Preisser, and Clipp (2008) found that the level of social support perceived as an adult survivor of childhood cancer was associated with PTSD symptoms. Increased risk for PTSD was found among children of parents with PTSD (Stuber et al., 1997). Decreased levels of perceived social support among parents of children with cancer have been found to increase parental risk of PTSD (Brown, Madan-Swain, & Lambert, 2003; Kazak et al., 1997). Therefore, perceived social support among survivors of childhood cancer might be associated with PTSD.

Since the establishment of the state of Israel in 1948, and especially since the outbreak of the Second Intifada (wave of Palestinian Arab violence that began in September 2000), Israelis have been under a constant threat of war and terrorism. Studies have shown that rates of PTSD in victims and observers of terrorist attacks mirror those of victims of other forms of violence. For example, in a telephone survey of New York City residents conducted five to eight weeks after the September 11 attack on the World Trade Center, Galea et al. (2002) found that 8% had symptoms of PTSD. Furthermore, the presence of PTSD was correlated with gender, proximity of residence to the site of the attack, level of social support, and number of prior stressors. Although some found significantly higher rates of PTSD three to six months after the event among those who worked closer to the attack site than in those who worked further away (Herman, Felton, & Susser, 2002; Schlenger et al., 2002). Silver, Holman, McIntosh, Poulin, and Gil-Rivas (2002), in an Internet survey conducted at different time points after the event, found that even those who lived far away were affected. Thus, given that people not directly involved in major traumatic events can acquire symptoms of PTSD, it is not surprising that a small country such as Israel, which is continually exposed to terrorist attacks, is characterized by high rates of PTSD in the general population. Evidence of this effect in Israel was found in a study by Pat-Horenczyk (2004) of more than 1,000 Israeli adolescents. The author found that 5% of the sample met the *DSM-IV* criteria for PTSD. However, 12% of the adolescents reported having no direct exposure to terrorism. She suggested that at least some of the adolescents may have reported symptoms of PTSD because of intense media exposure of the ongoing terrorist attacks that took place during that time period.

Rates of PTSD among adults in Israel have been shown to range from 7% (Hobfoll et al., 2008) to 27% (Shalev, Tuval, Frenkiel-Fishman, Hadar, & Eth, 2006). A similar range was found among youth, with levels ranging from 8%–28% (Pat-Horenczyk et al., 2007; Solomon & Lavi, 2005). One study found mean PTSD symptom severity scores among elementary school children living in a town that suffered from terrorist attacks to be mild to moderate (25 on a scale of 0–68 as

measured by the University of California, Los Angeles, Post Traumatic Stress Disorder Index) (Berger, Pat-Horenczyk, & Gelkopf, 2007).

Therefore, survivors of childhood cancer are exposed to two potential sources of stress, one in the past (cancer) and one in the present (the current stressful environment). PTSD rates in this population might, therefore, be expected to be higher than those of other populations that do not live within a stressful environment. The combined effect that living in such an environment and having a history of childhood cancer have on developing PTSD is unknown.

In summary, evidence shows that survivors of childhood cancer are at risk for developing PTSD. Increased risk might be associated with various demographic and clinical factors as well as social support. Living in a stressful environment such as Israel might further increase the likelihood of developing PTSD. However, no literature has determined whether survivors of childhood cancer living in Israel have an increased risk for developing PTSD or what the potential risk factors might be for the population.

The purpose of the current study was to investigate the prevalence, symptom severity, and risk factors (demographic, clinical, and social support) associated with PTSD in survivors of childhood cancer.

Methods

Design and Research Questions

This was a descriptive, correlational study investigating the prevalence of PTSD and PTSD symptom severity. Two research questions were designed to determine the prevalence and symptom severity of PTSD among Israeli survivors of childhood cancer, as well as whether a relationship exists between PTSD symptom severity and demographic (gender and current age) and clinical characteristics (age at diagnosis, time since completing treatment, type of cancer, and type of treatment [surgery, chemotherapy, radiation therapy, or bone marrow transplantation]) and social support.

Setting and Sample

The setting of the study was the outpatient clinic of the department of hematology and oncology of a major tertiary medical center in Petach Tikva, Israel. All patients who complete their treatment in that department are followed by the clinic. The study group consisted of a convenience sample of 70 adult (older than 18 years) survivors of childhood cancer who had completed treatment at least six months previously. Only patients aged 18 years or older with no evidence of recurring disease and who received treatment when younger than 18 (as a child) were included. All of the patients who met the inclusion criteria and attended the clinic during the data

collection period were asked to participate in the study. The study protocol was approved by the institutional ethics committee.

All patients were asked to sign an informed consent form. All patients who were approached for the study agreed to participate. Two questionnaires (the Post-Traumatic Diagnostic Scale [PDS] and the Multidimensional Scale of Perceived Social Support [(MSPSS)]) were distributed to participants and were completed during a routine clinic follow-up visit at the same institution in which the respondent received treatment. Demographic information (gender and current age) and clinical data (age at diagnosis, time since completing treatment, type of cancer, and type of treatment [surgery, chemotherapy, radiation therapy, and bone marrow transplantation]) were collected from the medical records by one of the investigators while the patients filled out the questionnaires.

Main Research Variables

The main research variables were PTSD, social support, and clinical and demographic data. Clinical and demographic data were defined earlier in this article.

PTSD was measured with the PDS (Foa, Cashman, Jaycox, & Perry, 1997), which is a self-report instrument developed for the diagnosis of PTSD according to the *DSM-IV* criteria and for the measurement of PTSD symptom severity. It consists of three sections. In the first section, respondents are asked to indicate whether they had ever experienced a traumatic event, including 10 events originally developed by Foa et al. (1997) plus two other events: a life-threatening illness and an open-ended *other* item. In the second section, respondents are asked to rate each of the 17 symptoms listed (five associated with intrusion or re-experiencing, seven with avoidance, and five with hyperarousal) on a scale of 0 (never occurred or occurred only once in the past month) to 3 (occurred five times or more in the past week). The scores on the 17 symptoms are totaled to produce a symptom severity score which ranges from 0–51; a score of less than 10 signifies mild symptom severity, 11–20 signifies moderate, 21–35 signifies moderate to severe, and greater than 36 signifies severe. The second section also includes two other items: (a) How long has the participant suffered from the symptoms (less than one month, one to three months, or more than three months)? and (b) How long after the traumatic event did the symptoms start to occur (less than six months or six months or longer)? The third section contains items that measure whether the symptoms interfere with eight aspects of daily life, such as work or relationships with friends. Respondents are considered to have PTSD if they report at least one traumatic event along with at least one symptom of re-experiencing the event, three symptoms of avoidance,

and two symptoms of hyperarousal that occurred at least once a month and interfered with some aspect of functioning. Internal consistency reliability has been found to be 0.91–0.97, and the tool was shown to have construct and criterion validity (Coffey, Dansky, Falsetti, Saladin & Brady, 1998). The questionnaire has been used successfully with other samples, such as victims of accidents, fires, assault (sexual and nonsexual), combat, life-threatening illness, and substance abuse (Ehring, Kleim, Clark, Foa, & Ehlers, 2007; Foa et al., 1997). It has been forward- and back-translated into Hebrew by native English or Hebrew speakers for use in Israel. Internal consistency reliability for the current sample was found to be 0.9.

Social support was measured with the MSPSS (Zimet et al., 1988), which consists of 12 Likert-style items that measure instrumental and emotional social support as provided by family, friends, and significant others. The scale is based on a range of 1 (not at all) to 7 (very much). A total score of 12 denotes low social support; 84, a high level. Participants were asked to respond to the questionnaire in terms of the social support that they received when they were ill. The Cronbach alpha reliability, as determined by its authors, was found to be high (0.85–0.95), with a test-retest reliability of $r = 0.85$. The questionnaire has been used successfully with other samples such as urban adolescents (Canty-Mitchell & Zimet, 2000), college students (Zimet et al., 1988), outpatient psychiatric patients (Clara, Cox, Enns, Murray, & Torgrud, 2003), and women with breast cancer (Filazoglu & Griva, 2008). The questionnaire also was found to have construct validity as determined by factor analysis in two separate studies (Bruwer, Emsley, Kidd, Lochner, & Seedat, 2008; Clara et al., 2003) and content validity (Zimet et al., 1988). Internal consistency reliability for the current sample was found to be 0.98.

Data were analyzed with SPSS® version 12. Data were coded by the researchers in a Microsoft® Excel® data file, which then was converted to SPSS. The default mode of SPSS is that analyses do not include participants who have some missing data associated with that particular analysis. Differences in PTSD symptom severity scores were analyzed with either a student's *t* test or a chi-square test among age, diagnostic, and treatment categories. The correlations of the background variables with PTSD symptoms and their significance were determined by Spearman or Pearson correlation analysis, as appropriate.

Findings

The study group consisted of 70 patients, 38 men (54%) and 32 women (46%), with a mean age of 23.4 years ($SD = 4.3$, range = 18–38). Mean age at diagnosis was 11.1 years ($SD = 5$) with a range of 1–18 years. The patients had a mean of 11.3 ($SD = 6.6$) years since last treatment, with a range of 1–27 years. The most com-

mon type of cancer was leukemia ($n = 32$, 46%), with 14 (20%) with Hodgkin disease, 8 (11%) with non-Hodgkin lymphoma, and the remaining 16 (30%) with other forms of cancer. Nearly all of the patients were treated with chemotherapy ($n = 69$), 21 received radiation therapy (30%), and six (9%) underwent bone marrow transplantation.

In terms of the prevalence and symptom severity of PTSD, all respondents reported that the life-threatening disease was a source of trauma for them. Thirty-four (49%) also reported other sources of trauma; however, none of the other sources was found to be statistically significantly related to PTSD symptom severity scores. The rates of PTSD symptom severity are shown in Table 1. Nearly all of the patients (84%) reported having at least one symptom of PTSD. Of them, 20 (29% of the total sample) met the *DSM-IV* criteria for PTSD (except for that of having the symptoms over time, not investigated in this cross-sectional study). Of the 20 participants who met the criteria for PTSD, two (10%) had mild disease, eight (40%) had moderate disease, and 10 (50%) had moderate to severe disease. None of the participants had severe PTSD. Specifically, 55 (79%) of the sample met the *DSM-IV* criteria for intrusive thoughts, 36 (51%) avoidance, and 35 (50%) hyperarousal.

Avoidance was perceived as the highest ranking symptom category and re-experiencing as the lowest among the three categories of PTSD symptoms (avoidance: $\bar{X} = 0.71$; hyperarousal: $\bar{X} = 0.63$; re-experiencing: $\bar{X} = 0.56$, all out of three). A sense of a foreshortened future was ranked as the most severe symptom ($\bar{X} = 0.96$ out of three), with distressing dreams or nightmares as the least severe ($\bar{X} = 0.41$ out of three) (see Table 2).

The symptoms persisted for more than three months in 38% of the sample ($n = 27$), with 26 (37%) reporting symptoms starting less than six months after the cancer and 30 (43%) reporting symptoms starting six months or later. The vast majority of participants responded that the cancer had generally interfered with all aspects of their lives ($n = 54$, 77%), also interfering with their sex lives ($n = 60$, 86%), work ($n = 56$, 80%), and free time ($n = 53$, 76%). The mean level of social support was high (62.3 ± 26.8), with a range of 0–84.

PTSD symptom scores were significantly related to the current age of the respondent ($r_s = -0.27$, $p = 0.03$) and time since medical treatment ($r_s = -0.34$, $p = 0.004$) but not to any other of the demographic or clinical variables or to levels of social support.

Conclusions

The findings of this study support the view that the trauma of cancer diagnosis and treatment in childhood may be associated with PTSD later in life. The factors associated with current PTSD and PTSD symptom severity found in this study were the current age of the

Table 1. Prevalence in the Past Month of Post-Traumatic Stress Disorder Symptoms in Survivors of Childhood Cancer

Symptom	Not at All or Once Only		Once Per Week or Once in a While		2–4 Times Per Week or Half the Time		5 or More Times Per Week or Almost Always	
	n	%	n	%	n	%	n	%
Re-experiencing								
Intrusive thoughts	29	41	31	44	9	13	1	1
Distressing dreams or nightmares	46	66	20	29	3	4	1	1
Acting or feeling recurrence of the event	46	66	19	27	4	6	1	1
Intense psychological distress	35	50	23	33	7	10	5	7
Physiologic reactivity	47	67	14	20	8	11	1	1
Persistent avoidance	41	59	9	13	10	14	10	14
Avoidance								
Efforts to avoid thoughts, feelings, or conversations	45	64	6	9	5	7	14	20
Inability to recall	43	61	12	17	7	10	8	11
Efforts to avoid activities, places, or people	46	66	13	19	6	9	5	7
Markedly diminished interest or estrangement from others	46	66	14	20	5	7	5	7
Restricted range of affect	51	73	9	13	5	7	5	7
Sense of a foreshortened future	31	44	19	27	12	17	8	11
Hyperarousal								
Difficulty falling asleep	46	66	12	17	9	13	3	4
Irritability or outbursts of anger	35	50	21	30	11	16	3	4
Difficulty concentrating	37	43	19	27	9	13	5	7
Hypervigilance	48	69	12	17	8	11	2	3
Exaggerated startle response	43	61	15	21	6	9	6	9

N = 70

respondent (the older the respondent, the less likely he or she was to currently have PTSD and severe PTSD symptoms) and the time since the end of medical treatment (the longer the time since completion of treatment, the lower the likelihood of PTSD and severe PTSD symptoms).

Most of the participants in this study had some symptoms of PTSD. Previous studies, conducted mainly in the United States, also reported PTSD in some survivors of childhood cancer (Hobbie et al., 2002; Kazak et al., 1999), although at lower rates (13%–21%). One possible reason for the discrepancy is the higher rate of overall stress to which Israelis are subject because of political tensions and terrorism. Bleich, Gelkopf, and Solomon (2003) found that 9% of Israeli residents met symptom criteria for PTSD, regardless of personal risk or exposure. Others (Hobfoll et al., 2008) also have commented on the marked affect of terrorism on PTSD in Israel. One possible explanation for the elevated PTSD symptoms found in Israel is what Stoppelbein, Greening, and Elkin (2006) called the perceived risk of a future threat. The authors found more severe symptoms of PTSD among children who had lost a parent than among survivors of childhood cancer. Bereaved children also showed a higher level of perceived future threat to their lives. The authors

suggested that perceptions of an impending threat may be related to PTSD symptoms. This also could apply to survivors of childhood cancer living in Israel. However, direct comparisons of the results of this study with others should be made with caution because of different methods of data collection, measurement, and times of data collection among the various studies.

The level of social support according to the MSPSS was not significantly correlated with PTSD. This result might be explained in two ways. First, the lack of significance could have been because of a ceiling effect in which a high percentage of participants reported a high level of social support with little variance within the sample. Second, the questionnaire requires that participants respond according to the level of support they received at the time of the event (i.e., as children). Only one study was found that determined that less social support was associated with increased PTSD (Smith et al., 2008). Other studies have shown that social support perceived by parents influenced the psychological well-being of the child (Wintgens, Boileau, & Robaey, 1997; Zeidner, Klingman, & Itskowitz, 1993).

Clinical variables such as diagnosis and type of treatment also were not found to be related to PTSD. This result supports those of Stuber et al. (1997), who found

that subjective emotional factors were better predictors of PTSD than objective clinical factors. However, others have found relationships between clinical factors and PTSD (Deimling, Kahana, Bowman, & Schaefer, 2002; Kazak, 1998; Schrag et al., 2008).

Previous findings have been mixed as to the relationship between age of respondent and development of PTSD. Although this study demonstrated that older respondents and those who completed treatment longer ago had lower symptom severity of PTSD, others found either a similar relationship (Bokszczanin, 2007), an opposite relationship (Erickson & Steiner, 2001; Geffen et al., 2003; Schrag et al., 2008; Stuber et al., 1997; Terr, 1991), or no relationship at all (Kazak, 1998; Stuber, Christakis, Houskamp, & Kazak, 1996). Theoretical reasons may explain the conflicting results, but perhaps differences in study design and methodology, such as use of different instruments to collect the data about PTSD, might explain the results. Perhaps the severity of PTSD symptoms decreases naturally with time so that those treated longer ago experience lower severity of PTSD symptoms.

Study Limitations

The current study was performed in a single center in Petach Tikva, Israel, with a limited convenience sample. Data collection was conducted at only one point in time. Therefore, no information can be concluded related to the development of PTSD over time, nor can the study account for new cases of PTSD. Although the noncompliance rate with follow-up is relatively low at the center (less than 30%), the authors do not know whether those who did not arrive for follow-up had different severity of PTSD symptoms than those sampled. The results of this study are based on participants' self-reports, and results might be inaccurate because of recall of information, especially related to the level of social support. This is particularly true of those who were treated at a young age. Therefore, the findings of this study must be viewed with caution.

Implications for Nursing Practice

Clinically, emphasis should be placed on continued follow-up of survivors of childhood cancer so that those at risk for developing PTSD can be identified and treated. Attempts should be made to contact those who are less inclined to participate in clinical follow-up to determine whether they are at increased risk for developing PTSD. Based on the results of this study, a special attempt should be made to identify patients at a higher risk for developing PTSD symptoms, including those who are younger and who recently underwent treatment.

Further studies are needed on larger samples in other centers in Israel and abroad to validate the findings.

Table 2. Measures of Central Tendency and Dispersion for Post-Traumatic Stress Disorder Symptoms in Survivors of Childhood Cancer

Symptom	$\bar{X}$	SD
Re-experiencing		
Intrusive thoughts	0.74	0.74
Distressing dreams or nightmares	0.41	0.65
Acting or feeling recurrence of the event	0.43	0.67
Intense psychological distress	0.74	0.91
Physiologic reactivity	0.47	0.76
Persistent avoidance	0.84	1.13
Avoidance		
Efforts to avoid thoughts, feelings, or conversations	0.83	1.23
Inability to recall	0.71	1.05
Efforts to avoid activities, places, or people	0.57	0.93
Markedly diminished interest or estrangement from others	0.56	0.91
Restricted range of affect	0.49	0.91
Sense of a foreshortened future	0.96	1.04
Hyperarousal		
Difficulty falling asleep	0.56	0.88
Irritability or outbursts of anger	0.74	0.88
Difficulty concentrating	0.74	0.94
Hypervigilance	0.49	0.81
Exaggerated startle response	0.64	0.96

N = 70

Note. Possible scores range from 0–3.

Longitudinal studies also are recommended so that changes in the adjustment to cancer survival can be better understood and treated. Longitudinal studies also can confirm whether age at diagnosis and time since diagnosis are independent risk factors for PTSD, as well as document new cases of PTSD and the development of PTSD over time. Special attention should be placed on confirming whether time since diagnosis and current age are, in fact, predictors of PTSD in other samples. Further prospective studies also might look into the effect of developmental stage on the future development of PTSD in later life.

Freda DeKeyser Ganz, RN, PhD, is head of the master's program in the School of Nursing at Hadassah Hebrew University in Jerusalem, Israel; and Haya Raz, RN, MA, is a doctoral student and staff nurse, Doron Gothelf, MD, PhD, is a psychiatrist, Isaac Yaniv, MD, is the director of the Oncology Division, and Ilana Buchval, RN, MA, is head nurse, all in the Center for Pediatric Hematology-Oncology and Feinberg Child Study Center at the Schneider Children's Medical Center of Israel in Petach Tikva and the Sackler Faculty of Medicine at Tel Aviv University in Israel. No financial relationships to disclose. Mention of specific products and opinions related to those products do not indicate or imply endorsement by the *Oncology Nursing Forum* or the Oncology Nursing Society. DeKeyser Ganz can be reached at Freda@hadassah.org.il, with copy to editor at ONFEditor@ons.org. (Submitted July 2008. Accepted for publication May 25, 2009.)

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