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# A mixed methods analysis of perceived cognitive impairment in hematopoietic stem cell transplant survivors

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## Abstract

**Objectives—**Hematopoietic stem cell transplant (HSCT) survivors may evidence objective cognitive impairment. However, perceived cognitive problems and their impact on quality of life are less well-understood. The purpose of this study was to explore HSCT survivors' perceptions of cognitive impairment and its impact on daily life functioning.

**Methods—**Sixty-nine autologous and allogeneic HSCT survivors 9 months to 3 years post-transplant experiencing mild survivorship problems completed a brief structured interview regarding perceived cognitive impairment since transplant. Data were coded and content analyzed. The frequency of participants reporting cognitive problems by domain and associations between reports of cognitive problems and age, depressed mood, anxiety, and health-related quality of life were examined.

**Results—**Overall, 49 of the 69 participants (71%) reported cognitive impairments after transplant – 38 in memory (55%), 29 in attention and concentration (42%), and smaller numbers in other domains. There were no significant differences in problems reported by transplant type. Of the 50 participants who worked prior to transplant, 19 (38%) did not return to work following transplant, with 12 of them citing cognitive and health problems as being the reason. There were significant associations between reports of cognitive impairment and younger age ($p$=.02), depressed mood ($p$=.02), anxiety ($p$=.002), and health-related quality of life ($p$=.008).

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**Disclosures**

The authors have no conflicts of interest to declare.

**Significance of Results—**A large proportion of survivors reported cognitive impairment following HSCT that impaired daily life functioning. Perceived cognitive impairment was associated with younger age, greater distress and reduced health-related quality of life.

### Keywords

cognitive dysfunction; cancer survivors; hematopoietic stem cell transplantation; qualitative research; quality of life; cancer-related cognitive impairment

## Introduction

Hematopoietic stem cell transplant (HSCT) is a common treatment for various hematological malignancies, including leukemia, lymphoma, and myeloma. While there is a notable increase in survival rates as a result of this treatment, HSCT can lead to multiple side effects (Copelan, 2006) that can make recovery challenging in many areas of a person's life beyond just physical well-being (Cooke, Chung, & Grant, 2011; Mosher, Redd, Rini, Burkhalter, & DuHamel, 2009; Syrjala, Langer, et al., 2004). One side effect affecting HSCT patients' daily lives concerns cognitive changes after transplant (Booth-Jones, Jacobsen, Ransom, & Soety, 2005; Harder et al., 2002; Kelly et al., 2018; Syrjala et al., 2011; Syrjala, Dikmen, Langer, Roth-Roemer, & Abrams, 2004) that may be related to high dose chemotherapy and radiation during the conditioning phase of transplant. Such changes have been found to be associated with poor quality of life up to 7 years post-transplant (Harder et al., 2002; Wu et al., 2012).

There is a growing body of research focused on cognitive impairments in HSCT patients such as problems with attention and concentration, processing speed, memory, and executive functioning. Typically, cognitive functioning is measured by neuropsychological tests (Friedman et al., 2009; Harder et al., 2002; Scherwath et al., 2013; Syrjala et al., 2011; Syrjala, Dikmen, et al., 2004). However, such tests generally do not capture what patients themselves see as problematic. Objective cognitive functioning as measured by neuropsychological tests do not always correlate with cognitive functioning measured with self-report instruments (Hutchinson, Hosking, Kichenadasse, Mattiske, & Wilson, 2012). For example, a patient may be tested as having intact executive functioning, but nevertheless, reports increased problems with organizing work tasks. Self-reported cognitive functioning is usually more closely associated with psychological distress, such as depressed mood and anxiety (Booth-Jones et al., 2005; Scherwath et al., 2013), but this does not mean that self-reported cognition is not "real." Quantitative self-report measures of cognitive problems may have limited researchers' ability to provide a detailed description of the nature of perceived cognitive problems, and how such problems affect patients' ability to return to work and perform daily life activities. Obtaining information about perceived cognitive symptoms i) can provide important complementary information about the lived experience of cognitive impairments, ii) may be an important harbinger of cognitive decline that may not yet be detectable with neuropsychological tests (Reisberg, Shulman, Torossian, Leng, & Zhu, 2010), and importantly, iii) are associated with reduced quality of life (Booth-Jones et al., 2005; Wu et al., 2012). Furthermore, studies are increasingly demonstrating associations between self-reported cognition and underlying neurological dysfunction in cancer patients

in studies that have measured brain structural networks, brain metabolism, and inflammatory immune function (Ganz et al., 2013; Zeng et al., 2017). Studies that collect qualitative data using open-ended interviews can offer researchers a method to generate narrative descriptions beyond what is obtainable from questionnaires making it possible to gather information about the effect of cognitive problems on a person's life (Patton, 2002). Few qualitative studies have examined perceived cognitive problems following HSCT. One study gathered qualitative data from support group meetings, and found that a number of survivors reported memory and concentration issues following transplant but the authors reported no specific frequencies nor detail about the nature of cognitive problems (Sherman, Cooke, & Grant, 2005). A second pilot study gathered qualitative interview data about subjective cognitive complaints experienced in daily life activities (in addition to quantitative data) from HSCT survivors and found that 6 out of 12 participants reported problems in memory and concentration at 6 months post-transplant, and 3 out of 9 reported memory problems at 12 months post-transplant. However, the authors did not describe their interview/coding procedures, nor did they describe any specific effects on daily life functioning (Harder, Duivenvoorden, van Gool, Cornelissen, & van den Bent, 2006). Given that cognitive impairment is a common concern for cancer patients (Mitchell, Delfont, Bracey, & Endacott, 2018), understanding the perceived nature of impairments is important for providing effective support and care for survivors. Hence, the objective of the present qualitative study was to specifically examine HSCT survivors' perceived experiences of cognitive impairment, and how such impairment may or may not have impacted their daily life functioning. A secondary objective was to explore the associations between perceived cognitive impairment and known correlates of cognitive impairment – age (Murman, 2015), depressed mood, anxiety, and health-related quality of life (Booth-Jones et al., 2005; Wu et al., 2012).

## Methods

### Participants and procedures

Survivors were English-speaking adults (aged 18 or older) who had an autologous or allogeneic HSCT 9 months to 3 years prior. They were identified through databases at Mount Sinai Hospital and Hackensack University Medical Center or through community recruitment (i.e., announcements in newsletters and internet sites for relevant patient populations, and through patient advocacy groups). All participants were part of a larger parent study in HSCT survivors that examined the effectiveness of an expressive helping intervention involving a combination of expressive writing and peer helping using structured writing sessions (Rini et al., 2014). All study procedures were approved by Mount Sinai's Program for the Protection of Human Subjects (GCO#06-0391) and by Hackensack University Medical Center's Institutional Review Board (#00000682). Informed consent was obtained from all participants. In order to qualify for the parent trial, participants had to have at least mild physical or psychosocial distress and survivorship problems based on published cutoffs or findings in relevant populations (87% of those screened). Detailed procedures and inclusion criteria for the parent study are described in detail elsewhere (Rini et al., 2014). Eligible participants then completed a baseline assessment consisting of a battery of questionnaires capturing information about survivorship problems after HSCT including

general distress, self-reported physical symptoms and quality of life. Half of the questionnaires were administered by phone, and the second half completed by patients on their own. Participants were randomized to one of four writing groups for four weeks. Three months after the end of the writing intervention, they completed a follow up assessment of more questionnaires. Relevant to the present study, a brief structured interview consisting of one of a number of modules focusing on different survivorship issues was also administered 3 months after the end of the intervention. Different modules were administered throughout the study's life, one of which pertains to and was designed for the present study. Hence, sixty nine consecutive participants out of the 315 participants completed the module that focused on participants' experiences of cognitive impairment since transplant, and the remaining participants completed one of the other modules.

## Measures

*Depressed mood and anxiety* were measured using subscales of the Brief Symptom Inventory (BSI) (Derogatis, 1993). The BSI is a 53-item measure of psychological distress and symptoms that is appropriate for use with medical patients and has frequently been used in HSCT patients (Çuhadar, Tanriverdi, Pehlivan, Kurnaz, & Alkan, 2016; Johnson Vickberg et al., n.d.). It is a brief version of the 90-item Symptom Checklist-90-Revised (Derogatis, 1993). The 6-item depression and 6-item anxiety subscales assess symptomatology (e.g., 'feeling no interest in things' and 'suddenly scared for no reason') over the prior 7 days on a scale ranging from 1 = *not at all* to 4 = *extremely*. The baseline (pre-intervention) administration of this measure was used for the current study.

*Health related quality of life* was measured using the Functional Assessment of Cancer Therapy Bone Marrow Transplant version 4 scale (FACT-BMT) (Cella et al., 1993; McQuellon et al., 1997). This is a commonly used and well-validated measure of the health-related quality of life of cancer patients who have undergone HSCT. It measures four primary quality of life domains using the 27 items of the general Functional Assessment of Cancer Therapy scale (FACT-G) (Cella et al., 1993) and HSCT-related concerns using the FACT-BMT which consists of 10 items (e.g., 'The effects of treatment are worse than I had imagined') (McQuellon et al., 1997). A total health-related quality of life score was used in the present study by summing all subscale and FACT-BMT scores after reverse coding negatively-valenced items. The baseline (pre-intervention) administration of this measure was used for the current study.

*Self-reported cognitive functioning* was measured using a brief version of the Functional Assessment of Cancer Therapy–Cognitive Scale (FACT-Cog) (Jacobs, Jacobsen, Booth-Jones, Wagner, & Anasetti, 2007), a self-report measure of cognitive functioning in cancer patients. We used 28 items from the 50-item scale, choosing items that had been endorsed most frequently in our earlier research with HSCT survivors or that corresponded with complaints we have observed in this population. Participants rate on a five-point Likert scale (0 = *never* to 4 = *several times a day*) the frequency with which each cognitive symptom occurred in the past 7 days. This 28-item scale demonstrated excellent internal consistency in our sample (Cronbach $\alpha = .98$). The baseline (pre-intervention) administration of this measure was used for the current study.

*Medical information* was gathered from medical chart review at baseline and self-report and included the number of days since transplant, the number of days since diagnosis, and the type of transplant.

*Sociodemographic information* was self-reported and included age, gender, race, marital status, and education level.

### Structured interviews

Participants were interviewed by telephone and asked to reflect back on their treatment experience in order to report whether (or not) they noticed changes to memory, thinking and concentration following HSCT. Participants verbally responded to the following questions:

- I want you to think back to life before your transplant compared to now. Did you notice changes to your concentration, thinking and memory?
- Did friends and family notice changes to your concentration, thinking, and memory?
- If yes: What did they notice?
- Did you work before your transplant?
- If yes:
  - Did you go back to work after the transplant?
  - What has that been like?
  - Have you noticed that certain tasks are more challenging than they were before? (Ask them to elaborate if necessary)
- If no: What has prevented you from going back to work?

If participants answered, “yes” to any question above, they were prompted to explain further what was noticed, for instance, the nature of any changes, how the changes affected their functioning, and specific examples where possible. Responses were written down verbatim by the interviewer. Sixty percent of the interviews were audio recorded as part of the parent study and were cross-checked with the written responses for accuracy.

### Qualitative content analysis

Two trained research assistants (NK and KH) coded all of the transcribed responses of the 69 participants using QSR International’s NVivo 7 software. Coders were trained by LMW (the lead author) to code each participant’s entire interview text for sentences that captured instances of impairment in predetermined cognitive domains covering basic cognitive functions through to higher level functions, and that are commonly included in studies of this nature (Poppelreuter, Weis, Mumm, Orth, & Bartsch, 2008; Reisberg et al., 2010), i.e., ‘attention and concentration,’ ‘information processing,’ ‘verbal fluency,’ ‘memory,’ ‘executive functioning,’ and a general cognitive impairment category to capture non-specific cognitive problems. Definitions of the cognitive domain coding categories are provided in Table 1. Training included studying and discussing the content of each coding category prior to coding the interviews. Inter-rater agreement between coders occurred 70% of the time

(i.e., where the same code was captured by both raters for the participant in question). Where there was disagreement between coders, they discussed the coding together with LMW until a consensus was reached. Based on these discussions, the coding categories of "information processing" and "general cognitive impairment" were collapsed into one category called "information processing" because the responses that comprised these two categories overlapped between raters. Specifically, both categories included reports of impairment to the speed, accuracy, and efficiency of processing information. Additional coding was not required for the questions regarding whether family and friends had noticed the changes and questions that pertained to work functioning.

### Quantitative data analysis

The frequency and percentage of participants who reported in the interviews of having a given cognitive problem were calculated. Chi-square tests were used to examine differences by previous exposure to active vs. neutral (control) writing conditions in the parent intervention trial. Fisher's exact tests were used to explore differences by transplant type. In order to examine associations between individuals who endorsed cognitive problems and depressed mood, anxiety, and health-related quality of life, point-biserial correlations were calculated using baseline measurements of the psychosocial outcomes in order to minimize the potentially confounding effect of the parent study's intervention trial. Point-biserial correlations were also used to explore associations with participants' responses on the FACT-Cog. All quantitative data analyses were undertaken using IBM SPSS Statistics version 24 software.

## Results

### Sample characteristics

The participant sample consisted of 69 HSCT survivors. Table 2 summarizes the demographic and clinical characteristics of the participants. The majority of HSCTs were performed for malignancies such as leukemia, lymphoma, or myeloma (95.7%).

### Interview transcriptions

Responses to the questions tended to be brief. Only 1 of the 41 interviews with audio recordings available to them had a portion of the participant's response that was not noted, and required a correction culminating in one additional code endorsement. The notes were otherwise accurate with respect to the reporting of cognitive impairments and the impact of cognitive impairments on their lives. Any differences in participants' narratives were superficial/grammatical in nature, rather than substantive.

Among participants who reported cognitive impairment, the average length of interviews was 3.43 minutes with a range of 1.45 to 12.23 minutes (SD=2.23). Among those who did not report cognitive impairment, the length of interviews was on average 1.50 minutes (SD=0.73; range .62 to 2.9).

### Perceived cognitive impairment

A chi-square test indicated that there was no association between previous exposure to neutral vs. active writing conditions in the parent trial and whether or not participants reported perceived cognitive impairment $\chi^2$ (1) = .78, $p$=.39.

Overall, forty-nine of the sixty-nine participants (71%) reported noticeable impairments in cognitive functioning after their transplant (28 autologous and 21 allogeneic participants) with no difference by type of transplant ($p$=.19) even within specific cognitive domains. Table 1 includes the frequency of participants who endorsed impairments by cognitive domain. A majority (55%; n=38) of participants reported problems in memory that, in some cases, affected interpersonal interactions and activities of daily living:

> Pt 591: "(I) can't remember things, like forgetting why I came into a room. I lose things all the time, e.g., keys…I put things in safe places, then can't remember where I put them….I'll repeat stories I've told them before. I can't remember the things they told me.'
>
> Pt 681: 'Yes, I have difficulty recalling things like names and words.'
>
> Pt 597: 'If I'm introduced to someone, I often forget their name. Short-term memory is a problem.'

Memory problems were also prospective in nature, affecting memory for future planned actions (Lezak, Howieson, Bigler, & Tranel, 2012):

> Pt 591: 'I forget appointments and need to write them down 10 times.'
>
> Pt 571: 'I need to keep lists.'
>
> Pt 431: '(I have to) write notes to myself.'

Attention and concentration problems were endorsed by 30 participants (42%). Examples of attention and concentration problems were:

> Pt 588: 'When I go to ask a question, it leaves my mind and I have to come back to it at a later time.'
>
> Pt 597: 'Sometimes when reading a novel I have to concentrate more.'
>
> Pt 606: 'I used to read all the time and now I can't focus.'

Eleven participants (16%) reported problems with verbal fluency. Examples included:

> Pt 573: 'When I'm talking, I know the words but can't think of it even though it was on the tip of my tongue. I know the English (which is my 2nd language) but it doesn't come to me like it used to. Happens in both languages (Bengali too).'
>
> Pt 592: 'Sometimes I can't think of the word I'm thinking of and have to circumvent the word to explain it. They could be simple words.'
>
> Pt 634: 'I go blank in the middle of a sentence.'

The same proportion of participants reported problems in information processing:

Pt 588: 'It's hard at first trying to get directions in my mind when I need to get to a certain point.'

Pt 661: '(My thinking) is a little slower and foggier…'

Five (7%) reported problems with executive functioning:

Pt 633: 'It's very difficult for me to multitask.'

Pt 678: '(I have) difficulty keeping track of life's little details, like coordinating mine and my children's schedules.'

### Impact of cognitive impairments on return to work

Of the fifty participants (72%) who were working before the transplant, nineteen (38%) did not return to work following transplant. Twelve of those participants (24%) had to stop working due to cognitive and health problems. Work issues included taking longer to complete tasks than before HSCT and struggling to maintain concentration, memory, and executive functioning. For example, Pt 618 reported that he could not 'remember things including names or procedures at work' and Pt 573 stated that 'writing out lesson plans was harder because (even if) I knew that I had done something before, I couldn't remember from the past what I needed to do (now).' Pt 657 had to stop working because of memory problems: 'I couldn't remember things so I couldn't go back to work.'

### Cognitive changes noticed by family and friends

In addition, 31 participants (46%) reported that friends and family members had also noticed cognitive changes after the transplant. For example, Pt 563 reported, 'It is a joke. They don't ask me time or place of where we are going because it is always wrong' and Pt 595 said, '(My husband) noticed that I couldn't remember what we'd spoken about.'

### Associations with age, depressed mood, anxiety and quality of life

Upon examination of the point biserial correlations between reporting noticeable cognitive changes and age, there was a significant negative association ($r=-.28$, $p=.02$) such that younger participants were more likely to report declines in cognition following transplant. With respect to psychosocial outcomes, there were significant correlations between reporting noticeable cognitive changes and depressed mood ($r=.29$, $p=.02$), anxiety ($r=.37$, $p=.002$), and health-related quality of life ($r=-.32$, $p=.008$).

### Associations with subjective cognitive functioning

Point biserial correlations were undertaken to measure associations between the total score of the abbreviated version of the FACT-Cog (in which a higher score means better functioning) and the qualitative reports of noticeable cognitive changes overall and reports of specific problems in different cognitive domains. Analyses indicated significant correlations with reports of noticeable cognitive changes ($r=-.40$, $p=.001$) and also with reports of memory changes ($r=-.46$, $p<.001$). There were no other significant correlations between the FACT-Cog total score and any other cognitive domain reported in the interviews.

## Discussion

The aim of this study was to characterize perceived cognitive impairments experienced by survivors in their post-HSCT life that may not be captured by formal, objective neuropsychological tests or by self-report questionnaires. Our findings illustrate that the cognitive impairments reported by participants in this study are largely consistent with the cognitive domains found to be impaired in previous HSCT research using neuropsychological tests (Friedman et al., 2009; Harder et al., 2002; Scherwath et al., 2013; Syrjala et al., 2011; Syrjala, Dikmen, et al., 2004). The current study also elaborates on those findings by providing information about how those impairments manifest and impact HSCT survivors' daily lives. Previous studies have been limited due to their focus on questionnaire responses and qualitative self-report data that have not provided details regarding the nature of perceived cognitive problems, nor how such problems affect patients' ability to return to work and perform daily life activities (Booth-Jones et al., 2005; Harder et al., 2006; Scherwath et al., 2013; Sherman et al., 2005). Open-ended reports of perceived cognitive functioning, as in the present study, can capture these abilities and describe them in the context of work and other daily life activities. Indeed, our results indicate that HSCT survivors reported impairments in all of the cognitive domains assessed, but most notably in memory, and attention and concentration, similar to previous research (Sherman et al., 2005). Importantly, even when responses on a self-reported cognition questionnaire were compared with the responses in the qualitative interview, the questionnaire was not adequate in capturing the full gamut or impact of perceived problems on specific aspects of the person's daily life functioning (e.g., in relationships or at work). In the interviews, over half of the sample described problems with memory, both retrospective and prospective, that seemed to affect their activities of daily living as well as social interactions (e.g. forgetting appointments, forgetting names, and repeating stories). A large group of participants also reported being affected by attention and concentration difficulties that impacted work productivity (e.g., writing out lesson plans is harder) and non-work time (e.g. not being able remember conversations). Participants reported difficulties in executive functioning and information processing less often. The few cases of reported verbal fluency problems were mostly related to word retrieval.

There were strong indicators that the quality of life of these people had been affected as evidenced by both the interviews and a significant association with health-related quality of life. Given growing interest in return to work as an important patient and public health outcome (Duijts, van der Beek, Boelhouwer, & Schagen, 2016), it is notable that over a third of employed participants were not able to return to work after the transplant, at least by the time this study had been conducted up to 3 years after transplant. Almost two thirds of them cited health and cognitive issues as the reason. It is difficult to determine the extent to which impairments to work performance were caused by cognitive issues; however, these findings highlight the need for more targeted research on the effects of cognitive problems on survivors' ability – or inability – to return to work, and, for those who have been able to return to work for at least some period of time, to complete work-related tasks. The inability to return to work is likely to have implications on survivors' lives, such as contributing to financial difficulties, emotional distress, and a less positive self-image (Jim, Syrjala, &

Rizzo, 2012; Khera et al., 2014; Mosher et al., 2009; Syrjala, Langer, et al., 2004). Indeed, we found that the reporting of noticeable cognitive changes after transplant was associated with depressed mood, anxiety, and health-related quality of life. While matters of self-image and financial difficulties were outside of the scope of this study, some sense of embarrassment when respondents spoke about their family reactions filtered through as well as frustration and distress caused by the cognitive changes. It is also possible that impaired cognition affects emotion regulation itself, thus contributing to distress symptoms (Richards & Gross, 2000). These findings suggest that cognitive changes following HSCT have negative effects on interpersonal and daily life functioning. Consistent with earlier research in cancer survivors (Amidi et al., 2015), younger participants were more likely to report cognitive problems following transplant suggesting that this group may be most at risk for experiencing these problems.

## Study limitations

A number of limitations ought to be considered when interpreting these findings. First, most of the sample consisted of survivors who were mostly well-educated, White, and had high income limiting its generalization to other groups. However, these numbers unfortunately reflect the lack of diversity among patients who undergo transplantation across the United States and among participants in HSCT studies in general (Bush, Donaldson, Haberman, Dacanay, & Sullivan, 2000). Second, the sample consisted of HSCT patients who reported at least mild psychological distress or other survivorship difficulty and so the findings are limited to that population. However, it is important to note that a majority of participants who screened for the study (87%) met these criteria. Third, the briefness of the interviews is a weakness in that we were unable to collect more elaborate narratives of the patients' self-reported experiences and perhaps did not gain rich insights that a more extensive interview or even focus group could have provided. Lastly, it is unclear the extent to which reported cognitive difficulties were attributable to aging and other medical and psychological conditions of the respondents.

## Clinical implications

Despite these limitations, our findings provide us with important insights into the lived experience of cognitive changes in HSCT survivors in a relatively large sample for a qualitative study. It also highlights the importance of *asking* HSCT survivors about their experiences of cognitive impairment during recovery, and that such self-report data is a necessary complement to formal neuropsychological testing. For particular cognitive skills that are rarely assessed using neuropsychological tests, such as prospective memory (i.e., the ability to remember to execute a planned action in the future), this questioning becomes all the more important. In addition, the brevity of the interviews illustrate that this line of questioning is likely to be feasible in clinical settings where time is limited. Further research continues to be needed in order to improve not only the identification and assessment of cognitive impairment in cancer survivors, but to also better understand the impact of cognitive impairments on daily life functioning. Perhaps most importantly, experiences of cognitive impairment, whether or not they are corroborated by neuropsychological tests, still warrant intervention efforts due to their significant impact on quality of life.

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## References

Amidi A, Christensen S, Mehlsen M, Jensen AB, Pedersen AD, Zachariae R. 2015; Long-term subjective cognitive functioning following adjuvant systemic treatment: 7-9 years follow-up of a nationwide cohort of women treated for primary breast cancer. British Journal of Cancer. 113(5): 794–801. [PubMed: 26171932]

Baddeley, A, Eysenck, MW, Anderson, MC. Memory. New York: Psychology Press; 2009.

Booth-Jones M, Jacobsen PB, Ransom S, Soety E. 2005; Characteristics and correlates of cognitive functioning following bone marrow transplantation. Bone Marrow Transplantation. 36(8):695–702. [PubMed: 16086044]

Bush NE, Donaldson GW, Haberman MH, Dacanay R, Sullivan KM. 2000; Conditional and unconditional estimation of multidimensional quality of life after hematopoietic stem cell transplantation: a longitudinal follow-up of 415 patients. Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 6(5A): 576–591.

Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, Brannon J. 1993; The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology. 11(3):570–579. [PubMed: 8445433]

Cooke L, Chung C, Grant M. 2011; Psychosocial care for adolescent and young adult hematopoietic cell transplant patients. Journal of Psychosocial Oncology. 29(4):394–414. [PubMed: 21966725]

Copelan EA. 2006; Hematopoietic stem-cell transplantation. The New England Journal of Medicine. 354(17):1813–1826. [PubMed: 16641398]

Çuhadar D, Tanriverdi D, Pehlivan M, Kurnaz G, Alkan S. 2016; Determination of the psychiatric symptoms and psychological resilience levels of hematopoietic stem cell transplant patients and their relatives. European Journal of Cancer Care. 25(1):112–121. [PubMed: 25040559]

Derogatis, LR. BSI Brief Symptom Inventory: Administration, Scoring, and Procedures Manual. 4th. Minneapolis, MN: National Computer Systems; 1993.

Duijts SFA, van der Beek AJ, Boelhouwer IG, Schagen SB. 2016; Cancer-related cognitive impairment and patients' ability to work. Current Opinion in Supportive and Palliative Care. 1

Friedman MA, Fernandez M, Wefel JS, Myszka KA, Champlin RE, Meyers CA. 2009; Course of cognitive decline in hematopoietic stem cell transplantation: a within-subjects design. Archives of Clinical Neuropsychology: The Official Journal of the National Academy of Neuropsychologists. 24(7):689–698. [PubMed: 19767298]

Ganz PA, Bower JE, Kwan L, Castellon SA, Silverman DH, Geist C, Cole SW. 2013; Does tumor necrosis factor-alpha (TNF-alpha) play a role in post-chemotherapy cerebral dysfunction? Brain, Behavior, and Immunity. 30(Suppl):S99–108.

Gioia GA, Isquith PK. 2004; Ecological Assessment of Executive Function in Traumatic Brain Injury. Dev Neuropsychol. 25:135–158. [PubMed: 14984332]

Harder H, Cornelissen JJ, Van Gool AR, Duivenvoorden HJ, Eijkenboom WM, van den Bent MJ. 2002; Cognitive functioning and quality of life in long-term adult survivors of bone marrow transplantation. Cancer. 95(1):183–192. [PubMed: 12115332]

Harder H, Duivenvoorden HJ, van Gool AR, Cornelissen JJ, van den Bent MJ. 2006; Neurocognitive functions and quality of life in haematological patients receiving haematopoietic stem cell grafts: a

one-year follow-up pilot study. Journal of Clinical and Experimental Neuropsychology. 28(3):283–293. [PubMed: 16618620]

Hutchinson AD, Hosking JR, Kichenadasse G, Mattiske JK, Wilson C. 2012; Objective and subjective cognitive impairment following chemotherapy for cancer: a systematic review. Cancer Treatment Reviews. 38(7):926–934. [PubMed: 22658913]

Jacobs SR, Jacobsen PB, Booth-Jones M, Wagner LI, Anasetti C. 2007; Evaluation of the functional assessment of cancer therapy cognitive scale with hematopoietic stem cell transplant patients. Journal of Pain and Symptom Management. 33(1):13–23. [PubMed: 17196903]

Jim HSL, Syrjala KL, Rizzo D. 2012; Supportive care of hematopoietic cell transplant patients. Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 18(1 Suppl):S12–6.

Johnson Vickberg SM, Duhamel KN, Smith MY, Manne SL, Winkel G, Papadopoulos EB, Redd WH. Global meaning and psychological adjustment among survivors of bone marrow transplant. Psycho Oncology. 10(1):29–39.

Kelly DL, Buchbinder D, Duarte RF, Auletta JJ, Bhatt N, Byrne M, Shaw BE. 2018; Neurocognitive Dysfunction in Hematopoietic Cell Transplant Recipients: Expert Review from the Late Effects and Quality of Life Working Committee of the Center for International Blood and Marrow Transplant Research and Complications and Quality of Life Working Party of the European Society for Blood and Marrow Transplantation. Biology of Blood and Marrow Transplantation. 24(2):228–241. [PubMed: 28939455]

Khera N, Chang Y, Hashmi S, Slack J, Beebe T, Roy V, Mikhael J. 2014; Financial Burden in Recipients of Allogeneic Hematopoietic Cell Transplantation. Biology of Blood and Marrow Transplantation. 20(9):1375–1381. [PubMed: 24867778]

Lezak, MD, Howieson, DB, Bigler, ED, Tranel, D. Neuropsychological assessment. New York: Oxford University Press; 2012.

McQuellon RP, Russell GB, Cella DF, Craven BL, Brady M, Bonomi A, Hurd DD. 1997; Quality of life measurement in bone marrow transplantation: development of the Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) scale. Bone Marrow Transplantation. 19(4):357–368. [PubMed: 9051246]

Mirsky AF, Anthony BJ, Duncan CC. et al. 1991; Analysis of the elements of attention: a neuropsychological approach. Neuropsychol Rev. 2:109–145. [PubMed: 1844706]

Mitchell KSJ, Delfont S, Bracey ML, Endacott R. 2018; Top ten concerns burdening people with cancer: Perceptions of patients with cancer and the nurses caring for them. European Journal of Oncology Nursing. 33:102–106. [PubMed: 29551171]

Mosher CE, Redd WH, Rini CM, Burkhalter JE, DuHamel KN. 2009; Physical, psychological, and social sequelae following hematopoietic stem cell transplantation: a review of the literature. Psycho Oncology. 18(2):113–127. [PubMed: 18677717]

Murman DL. 2015; The Impact of Age on Cognition. Seminars in Hearing. 36(3):111–21. [PubMed: 27516712]

Ollendick, TH, Schroeder, CS. Encyclopedia of clinical child and pediatric psychology. New York: Kluwer Academic/Plenum Publishers; 2003.

Patton, MQ. Qualitative research and evaluation methods. 3rd. Thousand Oaks, CA: Sage Publications, Inc; 2002.

Poppelreuter M, Weis J, Mumm A, Orth HB, Bartsch HH. 2008; Rehabilitation of therapy-related cognitive deficits in patients after hematopoietic stem cell transplantation. Bone Marrow Transplantation. 41(1):79–90. [PubMed: 17934527]

Reisberg B, Shulman MB, Torossian C, Leng L, Zhu W. 2010; Outcome over seven years of healthy adults with and without subjective cognitive impairment. Alzheimer's & Dementia: The Journal of the Alzheimer's Association. 6(1):11–24.

Richards JM, Gross JJ. 2000; Emotion regulation and memory: the cognitive costs of keeping one's cool. Journal of Personality and Social Psychology. 79(3):410–424. [PubMed: 10981843]

Rini C, Austin J, Wu LM, Winkel G, Valdimarsdottir H, Stanton AL, Redd WH. 2014; Harnessing benefits of helping others: A randomized controlled trial testing expressive helping to address

survivorship problems after hematopoietic stem cell transplant. Health Psychology. 33(12):1541–1551. [PubMed: 24274798]

Rosen WG. 1980; Verbal fluency in aging and dementia. J Clin Neuropsychol. 2:135–146.

Scherwath A, Schirmer L, Kruse M, Ernst G, Eder M, Dinkel A, Mehnert A. 2013; Cognitive functioning in allogeneic hematopoietic stem cell transplantation recipients and its medical correlates: A prospective multicenter study. Psycho Oncology. 22(7):1509–1516. [PubMed: 22945857]

Shao Z, Janse E, Visser K. et al. 2014; What do verbal fluency tasks measure? Predictors of verbal fluency performance in older adults. Front Psychol. 5:772. [PubMed: 25101034]

Sherman RS, Cooke E, Grant M. 2005; Dialogue Among Survivors of Hematopoietic Cell Transplantation. Journal of Psychosocial Oncology. 23(1):1–24.

Syrjala KL, Artherholt SB, Kurland BF, Langer SL, Roth-Roemer S, Elrod JB, Dikmen S. 2011Prospective Neurocognitive Function Over 5 Years After Allogeneic Hematopoietic Cell Transplantation for Cancer Survivors Compared With Matched Controls at 5 Years. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology.

Syrjala KL, Dikmen S, Langer SL, Roth-Roemer S, Abrams JR. 2004; Neuropsychologic changes from before transplantation to 1 year in patients receiving myeloablative allogeneic hematopoietic cell transplant. Blood. 104(10):3386–3392. [PubMed: 15251983]

Syrjala KL, Langer SL, Abrams JR, Storer B, Sanders JE, Flowers ME, Martin PJ. 2004; Recovery and long-term function after hematopoietic cell transplantation for leukemia or lymphoma. JAMA: The Journal of the American Medical Association. 291(19):2335–2343. [PubMed: 15150205]

Wu LM, Austin J, Hamilton JG, Valdimarsdottir H, Isola L, Rowley S, Rini C. 2012; Self-efficacy beliefs mediate the relationship between subjective cognitive functioning and physical and mental well-being after hematopoietic stem cell transplant. Psycho Oncology. 21(11):1175–1184. [PubMed: 21739524]

Zeng Y, Cheng ASK, Song T, Sheng X, Zhang Y, Liu X, Chan CCH. 2017; Subjective cognitive impairment and brain structural networks in Chinese gynaecological cancer survivors compared with age-matched controls: a cross-sectional study. BMC Cancer. 17(1):796. [PubMed: 29179739]

**Table 1**

Coding themes and number of patients endorsing problems by themes

| Coding Themes | Description/Definition | Number of Patients N (%) | | | |
|---|---|---|---|---|---|
| | | Type of transplant | | | |
| | | Autologous (*n*=43) | Allogeneic (*n*=26) | Total (*n*=69) | Fisher's Exact Test *p*-value |
| Attention & Concentration | The ability to select target information from an array for enhanced processing; the ability to maintain focus and alertness over time (Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991) | 17 (40%) | 12 (46%) | 29 (42%) | .62 |
| Information Processing | The ability to interpret sensory information and process it in an integrated way (Ollendick & Schroeder, 2003) | 7 (16%) | 2 (8%) | 9 (13%) | .47 |
| Verbal Fluency | The ability to retrieve verbal information (Rosen, 1980) and to access their mental lexicon to formulate verbal response (Shao, Janse, Visser, & Meyer, 2014) | 6 (14%) | 5 (19%) | 11 (16%) | .74 |
| Memory | Retrospective memory is the ability to remember information from the past (Baddeley, Eysenck, & Anderson, 2009); prospective memory is the ability to remember to execute a planned action in the future (Lezak et al., 2012) | 22 (51%) | 16 (62%) | 38 (55%) | .46 |
| Executive Functioning | A collection of related yet distinct abilities that provide for intentional, goal-directed, problem-solving action (Gioia & Isquith, 2004) | 1 (2%) | 4 (15%) | 5 (7%) | .06 |

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**Table 2**

Participant characteristics ($n = 69$).

| Characteristic | n | % | Mean | SD | Range |
|---|---|---|---|---|---|
| Age | | | 57.8 | 10.5 | 32–79 |
| Gender | | | | | |
| Female | 46 | 66.7 | | | |
| Male | 23 | 33.3 | | | |
| Patient race/ethnicity | | | | | |
| Black or African American | 6 | 8.7 | | | |
| White/non-Hispanic | 53 | 76.8 | | | |
| Spanish/Latino/Hispanic | 5 | 7.2 | | | |
| Asian or Pacific Islander | 5 | 7.2 | | | |
| Marital status | | | | | |
| Married/marriage-like relationship | 53 | 76.8 | | | |
| Single or never married | 4 | 5.8 | | | |
| Divorced or Separated | 6 | 8.7 | | | |
| Widowed | 6 | 8.7 | | | |
| Education level | | | | | |
| High school graduate | 8 | 11.6 | | | |
| Partial college (at least 1 year) | 14 | 20.3 | | | |
| Completed trade school | 4 | 5.8 | | | |
| College education | 23 | 33.3 | | | |
| Graduate degree | 20 | 29.0 | | | |
| Employment status | | | | | |
| Employed full-time | 16 | 23.2 | | | |
| Employed part-time | 9 | 13.0 | | | |
| Homemaker | 4 | 5.8 | | | |
| Retired | 16 | 23.2 | | | |
| Full-time student | 1 | 1.4 | | | |
| On sick leave or disability | 13 | 18.8 | | | |
| Looking for work | 1 | 1.4 | | | |

| Characteristic | n | % | Mean | SD | Range |
|---|---|---|---|---|---|
| Something else | 7 | 10.1 | | | |
| Did not report | 2 | 2.9 | | | |
| Annual household income | | | | | |
| <$35,000 | 7 | 10.1 | | | |
| $35,000 to $64,999 | 18 | 26.1 | | | |
| $65,000 to $94,999 | 12 | 17.4 | | | |
| ≥$95,000 | 26 | 37.7 | | | |
| Not reported | 6 | 8.7 | | | |
| Transplant type | | | | | |
| Autologous | 45 | 65.2 | | | |
| Allogeneic | 24 | 34.8 | | | |
| Time since diagnosis (in years) | | | 3.75 | 3.89 | 1.10–2.01 |
| Time since transplant (in years) | | | 1.41 | 0.48 | 0.68–3.12 |