Perceptions of Hematopoietic Stem Cell Transplantation and Coping Predict Emotional Distress During the Acute Phase After Transplantation

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Purpose/Objectives: To test whether a widely used model of adjustment to illness, the self-regulatory model, explains the patterns of distress during acute hematopoietic stem cell transplantation (HSCT). According to the model, perceptions of HSCT, coping, and coping appraisals are associated with distress.

Design: Longitudinal, correlational.

Setting: The Centre for Clinical Haematology at Nottingham City Hospital and the Department of Haematology at Royal Hallamshire Hospital in Sheffield, both in the United Kingdom.

Sample: 45 patients receiving mostly autologous transplantations for a hematologic malignancy.

Methods: Patients were assessed at baseline, on transplantation day, and two and four weeks after transplantation using three questionnaires: the short-form Depression Anxiety Stress Scales (DASS-21), Brief Coping With Problems Experienced (Brief COPE), and Brief Illness Perceptions Questionnaire (Brief IPQ) adapted for HSCT. Multilevel regression was used to analyze the clustered dataset.

Main Research Variables: Psychological distress, including depression, anxiety, stress, and overall distress (DASS-21); use of different coping styles (Brief COPE); and perceptions of HSCT and coping appraisals (Brief IPQ).

Findings: As suggested by the self-regulatory model, greater distress was associated with negative perceptions of HSCT, controlling for the effects of confounding variables. Mixed support was found for the model's predictions about the impact of coping styles on distress. Use of active and avoidant coping styles was associated with more distress during the acute phase after HSCT.

Conclusions: Negative perceptions of HSCT and coping contribute to psychological distress during the acute phase after HSCT and suggest the basis for intervention.

Implications for Nursing: Eliciting and discussing patients' negative perceptions of HSCT beforehand and supporting helpful coping may be important ways to reduce distress during HSCT.

Hematopoietic stem cell transplantation (HSCT) is a complex and intensive procedure for which its acute phase can last several weeks and involves high toxicity, prolonged isolation, and a range of debilitating side effects (e.g., fatigue, nausea) (Frödin, Börjeson, Lyth, & Lotfi, 2010; Gooley et al., 2010; Mosher et al., 2009). Patients report an overwhelming experience and loss of agency, describing the procedure as a "walk to hell and back" and "really, really hard" (Xuereb & Dunlop, 2003, p. 404). Surveys of psychiatric morbidity in patients undergoing HSCT have found that about half of patients meet clinical criteria for anxiety or depression during the first weeks, with anxiety often greatest around admission and

depression increasing thereafter (Fife et al., 2000; Lee et al., 2005; Prieto et al., 2005b; Tecchio et al., 2013). The impact of such distress on recovery from HSCT has been documented and may include reduced pain and symptom tolerance, longer hospital stay, and poorer treatment adherence, immune recovery, and survival rates (Hoodin, Uberti, Lynch, Steele, & Ratanatharathorn, 2006; Park et al., 2010; Prieto et al., 2002, 2005a; Pulgar, Garrido, Alcalá, & Reyes del Paso, 2012; Schulz-Kindermann, Hennings, Ramm, Zander, & Hasenbring, 2002).

Clinical and demographic predictors of distress during HSCT have been extensively investigated (Fife et al., 2000; Hefner et al., 2014; Prieto et al., 2005b; Schulz-Kindermann et al., 2002; Tecchio et al., 2013). However, the literature on psychological predictors of distress is less developed. From this literature, disparate factors, such as personal control and meaning making (Fife et al., 2000), sense of coherence (Pillay et al., 2015), acceptance of distress (Bauer-Wu et al., 2008), and diversion of attention from pain (Schulz-Kindermann et al., 2002), appear to be important. However, the authors argue that the absence of a unifying and well-developed psychological theory from the research has hampered the development of timely and effective psychological interventions for patients undergoing HSCT. This may partly explain the sparse and limited effectiveness of such interventions in HSCT and lack of clarity regarding what contributes to outcomes (Baliousis, Rennoldson, & Snowden, 2016; Braamse et al., 2016).

The most widely applied model of psychological adjustment to illness is the self-regulatory model (Hagger & Orbell, 2003; Leventhal et al., 1997; Ogden, 2012; Sharpe & Curran, 2006). It conceptualizes the process of psychological adjustment to illness as being comprised of three interacting components: interpretation, coping, and appraisal of coping (see Figure 1). A person's interpretation, or illness perception, includes his or her view of the severity of the consequences of the illness, duration, identity (its label and symptoms for the person), concern, level of understanding, and emotional impact. Coping describes the process of implementing strategies to reduce the psychological threat perceived by the person, and any resultant negative emotions. Two broad types of coping often associated with outcomes and distress have been used with the self-regulatory model: approach and avoidance coping (Ogden, 2012; Taylor & Stanton, 2007). Approach coping involves confronting the stressor (e.g., problem solving, planning, use of support), and avoidance reflects disengaging from it (e.g., denial, distraction) (Taylor & Stanton, 2007). Appraisal of coping forms a feedback loop, evaluating the effectiveness of the person's coping efforts (Hagger & Orbell, 2003).

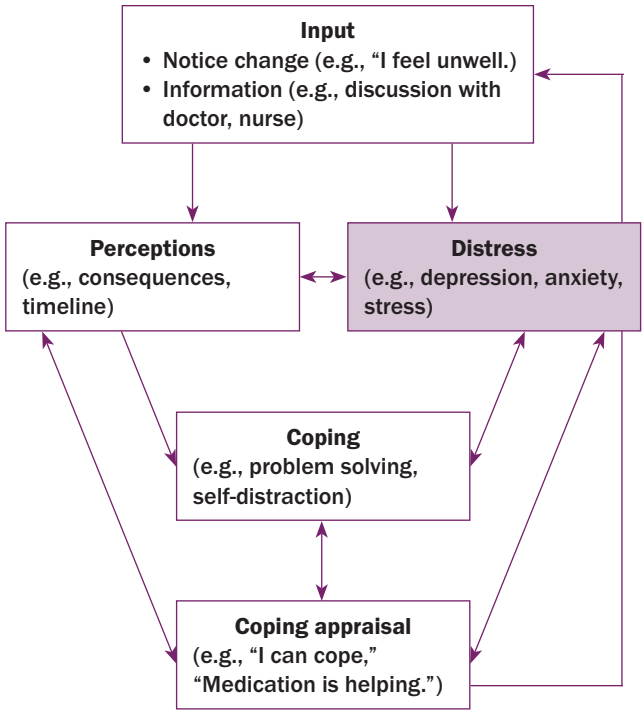


FIGURE 1. Relationships Among Perceptions, Coping, Coping Appraisals, and Distress

All three elements of the model have been extensively investigated and largely validated in other health populations. For example, more negative illness perceptions have been found to predict negative health-related outcomes, including emotional distress and poor physical functioning (Arran, Craufurd, & Simpson, 2013; Hagger & Orbell, 2003; Hall, Weinman, & Marteau, 2004; Knibb & Horton, 2008; Parry, Corbett, James, Barton, & Welfare, 2003; Petrie, Cameron, Ellis, Buick, & Weinman, 2002; Rizou, De Gucht, Papavasiliou, & Maes, 2015; Vaughan, Morrison, & Miller, 2003). Avoidant coping may be unhelpful, but engaging with the challenges of the illness and accessing social resources to support coping may be more helpful (Folkman & Moskowitz, 2004; Grant et al., 2013; Knibb & Horton, 2008; Sikkema et al., 2013; Taylor & Stanton, 2007). Positive appraisals of coping have also been found to predict greater levels of emotional well-being (Hagger & Orbell, 2003; Knibb & Horton, 2008; Rizou et al., 2015). Crucially, all three elements of the model have also been associated with physical recovery, predicting complications, treatment adherence, return to work, general physical functioning, and quality of life (Cherrington, Moser, Lennie, & Kennedy, 2004; Hagger & Orbell, 2003; Helder et al., 2002; Knowles et al., 2016; Petrie et al., 2002; Zoeckler, Kenn, Kuehl, Stenzel, & Rief, 2014). Should such findings be replicated in an HSCT population, the model, which has supported the development of effective interventions

in other health populations (Petrie, Broadbent, & Meechan, 2003; Petrie et al., 2002) may be a promising guide to effective interventions for those undergoing HSCT. Ultimately, such interventions could play an important role in alleviating some of the debilitating complications during the procedure.

Of the self-regulatory model's components, only coping has been studied in HSCT populations. However, these studies have focused on the recovery period several months after HSCT (Schoulte, Lohnberg, Tallman, & Altmaier, 2011; Wells, Booth-Jones, & Jacobsen, 2009; Wu et al., 2012); therefore, the impact of coping during the acute phase remains unclear because coping styles can have different effects at different times and circumstances (Taylor & Stanton, 2007). The self-regulatory model refers to illness, but HSCT is a medical procedure in which treatment-related toxicity poses the greatest challenge during the acute phase. Consequently, the extent to which the model may apply to HSCT requires corroboration. Therefore, the current study examined the applicability of the self-regulatory model (Hagger & Orbell, 2003; Leventhal et al., 1997; Sharpe & Curran, 2006) to acute HSCT. The authors hypothesized that more negative perceptions of HSCT would be associated with greater levels of distress; avoidance-based coping styles (e.g., disengaging, denial, self-distraction) would be associated with higher levels of distress; and approach-based coping styles (e.g., active coping, planning, seeking support) would be associated with less distress.

TABLE 1. Sample Characteristics (N = 45)

Characteristic	$\bar{X}$	SD
Age on transplantation day (years)	59.5	11.7
Years since diagnosis	2.4	3.47
Performance status (ECOG)	0.58	0.6
Length of admission (days)		
Ambulatory (n = 11)	9.4	5.27
Nonambulatory (n = 28)	21.1	5.5

Characteristic	n
Gender	
Male	31
Female	14
Marital status	
Married or cohabitating	34
Single	5
Other	6
Education	
Junior high school	19
High school	12
College	10
Not known	4
Diagnosis	
Multiple myeloma	27
Non-Hodgkin lymphoma	12
Other	6

ECOG—Eastern Cooperative Oncology Group
Note. ECOG scores range from 1–5, with greater scores indicating worse performance status (general well-being).

Methods

Participants

Participants were recruited from consecutive referrals from January to September 2015 at the Centre for Clinical Haematology at Nottingham City Hospital and the Department of Haematology at Royal Hallamshire Hospital in Sheffield, both in the United Kingdom. Inclusion criteria were receiving HSCT for hematologic malignancy, being aged 18 years or older, and having a sufficient command of the English language and the ability to participate in the study (including hearing ability for data collection via telephone). Where appropriate, patients initially attended the day ward post-transplantation, but, in practice, an admission took place for all participants during the study.

Measures

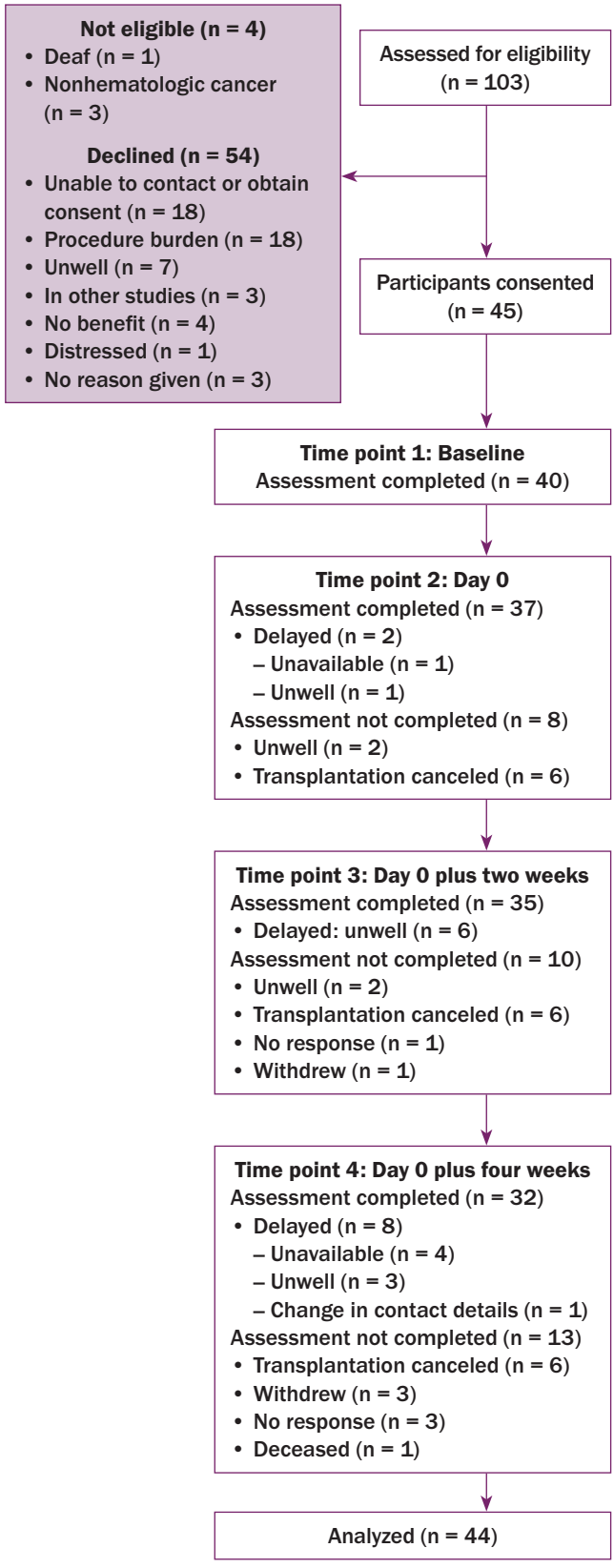
The authors used brief, well-established self-report measures. They followed standard practice by assessing HSCT perceptions and appraisal of coping of the self-regulatory model via the Brief Illness Perceptions Questionnaire (Brief IPQ) (Broadbent, Petrie, Main, & Weinman, 2006) and coping styles via the Brief Coping With Problems Experienced (Brief COPE) questionnaire (Carver, 1997; Hagger & Orbell, 2003). The authors measured the dependent variable of distress using the short-form Depression Anxiety Stress Scales (DASS-21). All measures asked about the participants' experience during the preceding week.

The authors selected the DASS-21 because of its brevity (21 items to reduce burden on participants), coverage of three constructs that may capture the complex distress patterns in HSCT (anxiety, depression, and traumatic stress) (Fife et al., 2000; Lee et al., 2005; Prieto et al., 2002, 2005b), and clinical validity in this respect (Antony, Bieling, Cox, Enns, & Swinson, 1998; Henry & Crawford, 2005). DASS-21 measures depression, anxiety, and stress (ongoing tension, worry in the context of persistent demands) and provides a total distress score from these three constructs (Antony et al., 1998; Henry & Crawford, 2005). Each subscale is comprised of seven items rated on a four-point Likert-type scale with total scores ranging from 0–21 for each (greater scores denote greater distress) (Henry & Crawford, 2005). Moderate-level cutoffs (depression 7 or greater, anxiety 5 or greater, stress 10 or greater) are representative of clinical populations (Lovibond & Lovibond, 1995; Ronk, Korman, Hooke, & Page, 2013). The instrument has good to excellent

internal consistency (Cronbach alpha values range from 0.82–0.94), good criterion validity, acceptable discriminant validity, moderate sensitivity to clinical change, and acceptable to good temporal stability (r = 0.71–0.81) in clinical samples (Antony et al., 1998; Brown, Chorpita, Korotitsch, & Barlow, 1997; Henry & Crawford, 2005; Ng et al., 2007; Page, Hooke, & Morrison, 2007).

The Brief COPE has been widely used and is relatively short but comprehensive (Carver, 1997; Carver, Scheier, & Weintraub, 1989; de Ridder, 1997). It measures several theoretically derived coping styles. Self-distraction, denial, disengagement, venting, and self-blame are generally considered avoidance-based, and active coping, support, positive reframing, planning, humor, and acceptance (versus denial) are considered approach-based; however, groupings can vary across contexts (Carver et al., 1989; Folkman & Moskowitz, 2004; Taylor & Stanton, 2007) and have not been established in HSCT. Each style is comprised of two items rated on a four-point Likert-type scale, (greater scores denoting more frequent use) (Carver, 1997). The instrument has good construct, concurrent, and predictive validity in relation to emotional well-being and adjustment in different clinical populations, including HSCT (Bautista & Erwin, 2013; Cooper, Katona, Orrell, & Livingston, 2008; Folkman & Moskowitz, 2004; Hooper, Baker, & McNutt, 2013; Knowles, Cook, & Tribbick, 2013; Meyer, 2001; Schoulte et al., 2011). Some limitations to reliability have been reported (Cronbach alpha values range from 0.5–0.9) and test-retest reliability coefficients are from 0.42–0.89 (six to eight weeks) (Carver, 1997; Carver et al., 1989). Low reliability is common among coping measures, but the Brief COPE has been found to be one of the most psychometrically robust (de Ridder, 1997; Folkman & Moskowitz, 2004). It is also designed to assess individual coping styles rather than a priori coping style groupings (Carver, 1997; Carver et al., 1989) that have not been established in HSCT.

The Brief IPQ is based on the self-regulatory model and assesses illness and coping appraisals (consequences, timeline, identity, concern, understanding, emotional impact, personal control, and treatment control). It contains eight items, with each measuring a different perception and being rated on an 11-point Likert-type scale; greater scores reflect greater endorsement (Broadbent et al., 2006). A greater summary score (range = 0–80) reflects more negative perceptions (Knowles et al., 2013; Løchting, Garratt, Storheim, Werner, & Grotle, 2013). The measure has been validated in several clinical populations (Bean, Cundy, & Petrie, 2007; Figueiras & Alves, 2007; Hagger & Orbell, 2003; Knowles et al., 2013; Løchting et al., 2013).



Note. Responses were delayed if they exceeded two days from their due date. Participants who missed a time point could complete later ones without having to be excluded altogether. Forty-four participants provided data for at least one time point (144 time points). Day 0 was the day of transplantation.

FIGURE 2. Participant Completion of Measurements

TABLE 2. Mean Distress Over Time Using Multilevel Modeling

Measure	T1		T2		T3		T4		Effect of Time							
											T2		T3		T4	
	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	Δx^2	R_1^2	ß	SE	ß	SE	ß	SE
Total distress (0–57)	9.84	10.93	9.89	6.87	15	10.5	13.6	10.2	10.6*	-	0.08	1.6	3.74*	1.48	2.74	1.47
Depression (0–21)	3.84	4.6	2.47	2.64	4.9	3.94	5.39	5.13	31.1**	15%	-0.83	0.57	1.56**	0.56	2.17**	0.78
Anxiety (0–15)	1.45	2.49	1.38	1.78	2.42	2.32	1	1.24	28.2**	< 0	0.46	0.27	1.53**	0.38	0.16	0.32
Stress (0–21)	4.55	4.94	4.58	3.41	4.64	5.09	4.8	4.34	18.2**	< 0	-0.05	0.76	0.63	0.6	0.66	0.67

* $p < 0.05$; ** $p < 0.01$

Δx^2—2log likelihood change compared to baseline; ß—fixed parameter estimate (compared to baseline); R_1^2—explained variance compared to intercepts-only model; SE—standard error; T—time point

Note. The greater the score, the greater the symptom is experienced.

Note. The random effects model for total distress did not converge (the coefficients shown are for fixed effects).

It has acceptable internal consistency for the summary score (Cronbach alpha values range from 0.58–0.82) and stability (r = 0.42–0.88 up to six weeks) (Broadbent et al., 2006; Løchting et al., 2013) and good concurrent, predictive, and discriminant validity (Bean et al., 2007; Broadbent et al., 2006; Knowles et al., 2013; Løchting et al., 2013). The authors adapted it for HSCT as the original measure refers to illness. For example, the question about consequences, "How much does your illness affect your life?" was reworded to, "How much does the transplant process affect your life?" The question about timeline, "How long do you think your illness will continue?" was reworded to, "How long do you think the transplant process will continue?" and so forth.

Design and Procedure

The authors used a longitudinal design with four time points to examine the relationships between emotional distress and psychological processes over time. A member of the clinical team invited eligible patients to take part following referral to the service. Interested patients provided informed consent after reviewing the study materials and were given the opportunity to ask questions. At time point 1, participants completed baseline questionnaires (DASS-21, Brief COPE, and Brief IPQ) on site or returned them via mail. Participants completed the same questionnaires via telephone at three additional time points: on transplantation day and two and four weeks after the transplantation. In light of HSCT's physical side effects (e.g., mucositis) (Copelan, 2006), the authors also asked participants to attribute physiologic symptoms of DASS-21 anxiety (items 2, 4, 7, and 19, referring to dry mouth, breathing difficulty, etc.) to clarify whether they reflected HSCT side effects rather than anxiety, and remove them in the case of the former. The authors recorded participant characteristics and nonconcordant events (intensive care, patient leaving isolation, psychological input) from clinical records at the end of the study. A National Research Ethics Service committee in the United Kingdom approved the study. A patient panel helped develop the study procedure.

Data Analysis

Preliminary analyses examined descriptive statistics, input errors, outliers, assumptions, and missing data (Field, 2013; Snijders & Bosker, 2012). The authors used Cronbach alpha coefficients to assess internal consistency (Field, 2013) and removed DASS-21 items that could not be differentiated from HSCT's side effects. Because the dataset was clustered within patients, data were missing, and some assumptions were violated, the authors used multilevel modeling ([MLM], developed to deal with clustered data) with nonparametric, bias-corrected bootstrapping to include all available information and improve accuracy (Snijders & Bosker, 2012). The authors examined the effect of time (categorical predictor) and participant characteristics (covariates) on distress and the effect of time on HSCT perceptions and coping styles. For the main analyses, the authors used MLM to examine the change of HSCT perceptions and coping style over time and their relationship with distress across all time points while controlling for previously significant covariates. The authors assessed model improvements (Δx^2) and explained variance (R_1^2) at each step of model development (Snijders & Bosker, 2012).

They also examined improvements by taking account of variance across participants (random effects) for significant predictors (Snijders & Bosker, 2012). MLwiN, version 2.34, was used for MLM, and SPSS®, version 22.0, was used for all other analyses. The level of significance was 0.05.

Results

Preliminary Analyses

Table 1 presents characteristics of the 45 participants recruited. The authors removed DASS-21 items 2 (dry mouth) and 7 (trembling) because they reduced reliability coefficients, and 25 participants indicated that these items reflected side effects of HSCT rather than anxiety. Cronbach alpha coefficients determining internal consistency across time were 0.72–0.95 for total distress, depression, and stress, and 0.46–0.78 for anxiety (lower at later time points). For HSCT perceptions, total Brief IPQ coefficients were 0.63–0.68, which is common for this measure (Bean et al., 2007; Løchting et al., 2013). The two coping appraisal items appeared to reduce coefficients from more than 0.7. The coefficients of acceptance, positive reframing, behavioral disengagement, denial, self-blame, self-distraction, and venting were variable across time points, with at least one coefficient being less than 0.5 (e.g., acceptance coefficients ranged from 0.23–0.81). The mean across time points was at least 0.5 for all of the scales. Other coefficients were as much as 0.94.

Of the 184 possible data points (45 participants completing questionnaires as many as four times), 144 were completed by 44 participants and were included in the final dataset (see Figure 2). The dataset provided sufficient power to detect at least medium effects in the chosen type of analysis, which would have required from 116 data points (29 participants with full datasets) to 172 data points (43 participants with full datasets), using standard power analyses for MLM (Twisk, 2006). Of the data points, completion was delayed for 22 (15%) (more than two days overdue). Regarding missing data, Little's test was significant ($x^2[127] = 163.99$, $p = 0.015$), and missing data were related to poorer baseline physical functioning (performance status) at time points 2 and 3 ($ts[3.6–7] \geq 3.4$, $ps \leq 0.03$) and greater baseline and time 2 stress at time point 3 ($t[8.9–34] \geq 2.5$, $p \leq 0.04$). Therefore, missing data could be considered mostly random for MLM

TABLE 3. Multilevel Models for Distress With Negative HSCT Perceptions and Coping Styles as Predictors

	Total Distress		Depression		Anxiety		Stress	
Scale	Δx^2	R_1^2 (%)	Δx^2	R_1^2 (%)	Δx^2	R_1^2 (%)	Δx^2	R_1^2 (%)
Negative HSCT perceptions	60.5***	34	53.8***	28	42.2***	38	36.9***	28
Consequences	24.8***	< 0	18.8***	6	6.23*	3	47.5***	< 0
Timeline	40.1***	< 0	33.1***	< 0	41.4***	< 0	33.7***	< 0
Identity	42***	< 0	25.3***	4	23.9***	< 0	28.6***	< 0
Concern	16.4***	< 0	34.9***	< 0	31.1***	< 0	35.5***	< 0
Understanding	25.6***	< 0	11.4***	7	32.1***	< 0	1.72	5
Emotional impact	71.7***	< 0	41***	35	42.9***	< 0	38***	37
Personal control	–0.35	–	0.02	–	16.2**	< 0	0.15	–
Treatment control	2.13	–	0.32	1	0.79	–	0.54	–
Coping								
Self-distraction	2.38	5	0.48	1	1.83	1	4.52*	10
Denial	28***	35	23.3***	28	27.9***	33	6.58*	16
Behavioral disengagement	29.6***	33	35***	34	24.4***	32	11.6***	10
Venting	28.8***	28	14.1**	–	19.5***	18	28***	33
Self-blame	44***	47	19.6***	28	47.1***	44	28.4***	34
Active coping	2.71	5	2.09	3	1.54	1	2.23	9
Emotional support	9.69**	6	3.5	5	3.15	2	6.01*	6
Instrumental support	12***	15	8.18**	10	7.36**	4	9.06**	16
Positive reframing	1.13	2	0.01	–	2.83	2	2.62	4
Planning	10.4**	13	3.77	5	2.5	5	29***	42
Humor	0.25	–	1.08	–	20.7***	29	0.88	–
Acceptance	0.01	–	0.001	–	0.001	–	–	–

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Δx^2—2log likelihood change compared to baseline; HSCT—hematopoietic stem cell transplantation; R_1^2—explained variance compared to intercepts-only model

Note. Random effects models did not converge for consequences (depression and anxiety), personal control (depression), treatment control (anxiety), understanding (stress), emotional impact (depression, stress), or instrumental support (total distress and depression).

TABLE 4. Multilevel Models for Distress With Negative HSCT Perceptions and Coping Styles as Predictors

	Total Distress		Depression		Anxiety		Stress	
Scale	ß	SE	ß	SE	ß	SE	ß	SE
Negative HSCT perceptions	0.37***	0.07	0.17***	0.04	0.07***	0.2	0.13***	0.04
Consequences	0.85***	0.22	0.45***	0.11	0.15*	0.06	0.29**	0.12
Timeline	1.18**	0.41	0.42*	0.19	0.26*	0.11	0.45*	–
Identity	0.75**	0.26	0.49***	0.1	0.19**	0.06	0.14	0.14
Concern	1.3***	0.28	0.5***	0.13	0.21**	0.07	0.56***	0.15
Understanding	–1.15***	0.5	–0.53***	0.19	–0.26*	0.12	–0.37	0.2
Emotional impact	1.72***	0.24	0.79***	0.11	0.3***	0.08	0.79***	–
Personal control	0.02	0.2	–0.02	0.13	0.08	0.12	0.05	0.13
Treatment control	0.11	0.36	–0.1	0.18	0.08	0.09	0.13	0.18
Coping								
Self-distraction	0.66	0.42	0.15	0.2	0.14	0.1	0.45*	0.21
Denial	3.53**	1.04	1.98***	0.36	0.46	0.28	1.16**	0.42
Behavioral disengagement	4.28**	1.47	2.64***	0.69	0.38	0.44	1.51**	0.46
Venting	2.54**	0.73	0.7*	0.33	0.56***	0.14	1.32***	0.32
Self-blame	3.44**	1.05	1.2*	0.46	0.58*	0.25	1.51***	0.34
Active coping	0.66	0.4	0.28	0.19	0.12	0.1	0.3	0.19
Emotional support	1.02*	0.4	0.44*	0.21	0.16	0.11	0.5*	0.2
Instrumental support	1.34***	0.37	0.54**	0.19	1.76**	0.29	0.63**	0.2
Positive reframing	0.42	0.39	–0.02	0.19	0.16	0.1	0.31	0.19
Planning	1.24**	0.39	0.37*	0.18	0.15	0.09	0.76**	0.25
Humor	0.2	0.4	–0.2	0.19	0.25	0.13	0.18	0.19
Acceptance	0.04	0.44	0.01	0.22	0.003	0.11	0.002	0.213

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$
ß—fixed parameter estimate; HSCT—hematopoietic stem cell transplantation; SE—standard error
Note. Random effects models did not converge for consequences (depression and anxiety), personal control (depression), treatment control (anxiety), understanding (stress), emotional impact (depression, stress), or instrumental support (total distress and depression).

(Snijders & Bosker, 2012). Of noncondordant events, one participant received psychological input (time point 3), which may have affected distress.

Effects of Time and Participant Characteristics

The authors observed a significant main effect of time for all distress scales except stress (see Table 2). This was also reflected in the proportion of patients reporting at least moderate distress, reaching 42% at any time during the acute phase (time points 2–4). Compared to baseline, total distress was significantly greater at time point 3, depression was greater at time points 3 and 4, and anxiety was greater at time point 3. As covariates, younger participants reported less depression, males reported less distress overall, and those with better baseline physical functioning reported less anxiety and stress across time points ($\Delta x^2[\Delta df = 1] \geq 4.58$, ps ≤ 0.03). No other covariates reached statistical significance ($\Delta x^2[\Delta df \leq 2] \leq 5.51$, ps ≥ 0.06). Estimation terminated (converged) when random effects were added for physical functioning (total distress), ambulatory treatment (depression), and length of admission (total distress) only (models did not improve significantly).

Psychological Processes

Overall, negative HSCT perceptions were greater at time points 3 and 4 compared to baseline ($\Delta x^2[\Delta df = 3] = 31.4$, $p < 0.001$), but the difference did not reach significance for subscales ($\Delta x^2[\Delta df = 3] \leq 6.61$, ps ≥ 0.09). More negative perceptions of HSCT and the majority of subscales measured were significantly associated with greater distress across the study period, with identity and understanding showing no relationship with stress (see Tables 3 and 4).

Of the coping styles, use of self-distraction, active coping, emotional and instrumental support, humor, and positive reframing was greater compared to baseline across time points 2–4 (time point 2 only for humor and time points 2 and 3 for reframing) ($\Delta x^2[\Delta df = 3] \geq 8.42$, ps ≤ 0.04) but not use of other styles ($\Delta x^2[\Delta df = 3] \leq 7.48$, ps ≥ 0.06). More frequent use of avoidance-based (unhelpful) styles was significantly associated with greater distress. However, more frequent use of approach-based or coping styles considered helpful was also associated with greater distress. The effects of HSCT perceptions and coping remained unchanged after controlling for age, gender, and physical functioning.

Discussion

The authors examined whether perceptions of HSCT and coping predict distress during the acute phase of HSCT in line with the self-regulatory model (Hagger & Orbell, 2003; Leventhal et al., 1997; Sharpe & Curran, 2006). The results supported the model, given that negative perceptions and coping styles predicted distress during the acute phase of HSCT. This extends the literature about this period of HSCT, which has previously focused predominantly on clinical and demographic variables (Fife et al., 2000; Prieto et al., 2005b; Schulz-Kindermann et al., 2002; Tecchio et al., 2013).

Perceptions of Hematopoietic Stem Cell Transplantation and Coping

The results support the hypothesized role of negative interpretations about HSCT in maintaining distress, including how physical symptoms are perceived. This is consistent with qualitative research findings highlighting loss of meaning and interpretations of threat in HSCT, and with the wider literature on cognition in depression, anxiety, and stress, suggesting the relevance of negative outlook, perceptions of threat, and challenge, respectively (Lazarus, 2000; Tarrier, 2006; Xuereb & Dunlop, 2003). The effect of perceived emotional impact of the procedure was particularly high, indicating that patients experiencing distress generally attributed this to HSCT and, in conjunction with other perceptions of HSCT (e.g., lengthy course), may compound distress. However, the large association between distress scales and this Brief IPQ item also suggests that the measures may overlap conceptually.

The lack of association between coping appraisals (personal and treatment control) and distress was contrary to expectations. However, these items did not appear internally consistent within the Brief IPQ. This has also been observed in other studies (Morgan, Villiers-Tuthill, Barker, & McGee, 2014), and the items have shown variable ability to predict distress (Hagger & Orbell, 2003), which may suggest a limitation to the contribution of coping appraisals (and the self-regulatory model) in some populations, including HSCT. However, the complexity of HSCT, heterogeneity of care (Copelan, 2006), and social desirability when rating helpfulness of treatment (treatment control) may have introduced complexity in these appraisals that was not possible to capture in the current research. The null results may also reflect the findings in relation to coping.

The findings indicated that several coping styles were ineffective. Although this was expected for avoidance-based styles, it was not expected for those that are considered helpful in the wider literature, such as planning and support seeking (Carver et al., 1989; Taylor & Stanton, 2007). Studies examining the post-acute period of HSCT have not observed reliable effects of these latter styles (Schoulte et al., 2011; Wells et al., 2009), but the circumstances of acute HSCT may render many coping strategies ineffective or counterproductive. For example, an adverse effect of planning has been noted in acute cancer care but not subsequent periods (Carver et al., 1993). This lack of effectiveness in acute cancer care and HSCT may be because of limited access to resources so that planning becomes ineffective. In addition, social support is believed to provide a resource for coping (Taylor & Stanton, 2007), but the acute phase of HSCT, which encompasses isolation and disabling side effects (Copelan, 2006), may render attempts to use this resource ineffective (Schulz-Kindermann et al., 2002). These observations may also explain the lack of reliable associations between distress and perceptions of personal and care control.

Distress Patterns

Results replicated the pattern of high but declining anxiety and increasing depression that has been found in other studies of response to HSCT, including the acute phase (Fife et al., 2000; Lee et al., 2005; Prieto et al., 2005b). The pattern of anxiety may reflect perceptions of uncertainty and threat at the beginning of the procedure; the increase in depression may reflect perceptions of a lengthening timeline, severe consequences, and ineffective coping; and stable stress may suggest a sustained level of challenge. However, anxiety peaked after transplantation in the current sample rather than closer to the transplantation day, as reported previously (Fife et al., 2000; Prieto et al., 2005b; Schulz-Kindermann et al., 2002; Tecchio et al., 2013). This could be because of the way in which the DASS-21 conceptualizes anxiety. Unlike measures used in the other studies, DASS-21 separates stress from anxiety and draws considerably on physical symptoms to measure the latter. Shortly following transplantation, physical symptoms may be exacerbated and patients await to find out whether engraftment has been successful, potentially contributing to the higher anxiety scores. In addition, some patients were admitted to the hospital after transplantation in an ambulatory care setting, which may also have contributed to a later increase in anxiety. Lower distress in younger individuals, men, and those with better physical functioning supports findings from previous studies (Prieto et al., 2005b; Schulz-Kindermann et al., 2002; Tecchio et al., 2013). Overall, the current findings highlighted considerable complexity in patients' psychological needs.

Knowledge Translation

- Patients are more distressed when they perceive hematopoietic stem cell transplantation (HSCT) negatively and risk becoming stuck in a vicious cycle because distress appears worse if patients attribute it to undergoing HSCT.
- Avoidant coping is associated with worse distress, but positive approach coping, which is helpful in other populations, seems to be ineffective during HSCT.
- Discussing patients' negative perceptions of HSCT and identifying effective coping approaches for patients undergoing HSCT are important.

Limitations and Strengths

The findings need to be viewed in light of some limitations. The correlational evidence was unable to establish causation. Perceptions about HSCT and coping may also interact with physical functioning in predicting distress, but such effects could not be examined. Social desirability may have resulted in more favorable reports (e.g., of coping style use). Results may not be generalizable to individuals with poorer physical functioning or greater stress because missed time points were associated with both of these. Findings may also not be generalizable to other settings, minority groups, younger individuals, allogeneic patients, or patients with rarer diagnoses than the current sample. The novel Brief IPQ adaptation requires additional validation, and the Brief COPE is not exhaustive, so the observed effects regarding coping may not apply to other styles. Statistically, lack of convergence in some random effects models, limited internal consistency of some scales, and the small sample may have introduced bias. Reliability for some Brief COPE scales, in particular, was variable and, at times, limited. However, Cronbach alpha is less suitable for small scales (such as the two-item Brief COPE scales) (Field, 2013), and such low coefficients are common in coping research even when larger groupings are used, including in HSCT (de Ridder, 1997; Folkman & Moskowitz, 2004; Schoulte et al., 2011; Wells et al., 2009). Because the Brief COPE is one of the most reliable scales in the field (de Ridder, 1997) and showed good construct validity for the purpose of the study, the scale was considered acceptable for this initial investigation in spite of these limitations. Finally, the number of tests may have inflated type I errors, particularly for coping styles in which overall analysis was not conducted. However, the findings are strengthened by a longitudinal design showing reliable and enduring effects, and a new and promising scale for HSCT perceptions. Consecutive referrals with reasons for nonparticipation, two sites, and the heterogeneity of the sample enhanced external validity. In addition, MLM with bootstrapping maximized the dataset, accounted for variability across participants, and improved statistical validity.

Implications for Nursing

The findings suggest that the high rates of distress found during HSCT may be related to negative perceptions of the treatment. In addition, active coping strategies that commonly alleviate distress during other medical procedures may not be as effective during HSCT. The authors suggest that nurses concerned with the supportive care of patients leading up to and during HSCT use these findings in three ways. First, negative perceptions of HSCT may be an indicator that a patient is at risk for developing distress during treatment and may require some psychological care. Second, such perceptions are potentially modifiable through discussion and information giving; research in other patient groups, including those with hematologic malignancies, suggests this is possible (Broadbent, Ellis, Thomas, Gamble, & Petrie, 2009; Husson et al., 2013; Keogh et al., 2011). Nurses may wish to use the framework of Leventhal's self-regulatory model or use the adapted IPQ used in this research as a guide to help them explore patients' negative perceptions of HSCT. Third, nurses should advise patients that coping strategies aimed at avoiding or controlling aversive experiences of uncontrollable side effects may be counterproductive. Psychological strategies, such as acceptance and mindfulness, may be more helpful responses to the challenges of HSCT. These methods have shown promise in the period during and following HSCT and could be feasibly integrated with standard clinical care (Bauer-Wu et al., 2008; Grossman et al., 2015).

Conclusion

Nurses should be aware that effectiveness research into pre-HSCT interventions aimed at preventing or reducing distress is in its infancy, and no approach has substantively demonstrated its effectiveness (Baliousis et al., 2016). Additional intervention research in this area may benefit from targeting illness perceptions, acceptance, and mindfulness. In light of the range of complications associated with HSCT (Copelan, 2006), addressing negative perceptions and coping in such ways could play an important role in improving quality of life and physical outcomes. The benefits of such input could be diverse in domains such as improved pain and symptom tolerance, shorter hospital stay, better treatment adherence, faster immune recovery, and lower mortality (Hagger & Orbell, 2003; Hoodin et

al., 2006; Prieto et al., 2002, 2005a; Pulgar et al., 2012; Schulz-Kindermann et al., 2002). However, replication of the current findings with larger samples and other clinical subgroups and settings remains necessary. Additional studies into the role of physical functioning on perceptions, coping and broader coping categories, distress, physical long-term outcomes, and establishing causality (e.g., via intervention) appear necessary.

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