



## Reviews

# Positive Psychological Constructs and Health Outcomes in Hematopoietic Stem Cell Transplantation Patients: A Systematic Review

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### A B S T R A C T

Positive psychological constructs (eg, optimism, positive affect) have been independently associated with superior health outcomes across many medical populations. However, there has been little synthesis of the literature examining these associations among patients with hematologic malignancies receiving hematopoietic stem cell transplantation (HSCT). To address this gap we completed a systematic review, using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, of studies examining relationships between positive psychological constructs and health-related outcomes (eg, psychiatric symptoms, function, health-related quality of life [HRQoL], or treatment compliance) after HSCT. Eighteen eligible studies (N = 4201; 47% women; mean age, 47.1) were identified. Optimism (n = 12 studies) was the most frequently studied positive construct and HRQoL (examined in n = 11 studies) the most common outcome. All 17 studies with quantitative analyses found a significant ( $P < .05$ ) association between a positive psychological construct and a health outcome; most but not all controlled for 1 or more relevant covariates. Among patients with hematologic malignancies who receive HSCT, positive psychological constructs appear to be associated with improved HRQoL and other health outcomes. Further work is warranted to more comprehensively understand the independent effects of positive psychological constructs on a variety of health outcomes and to develop interventions to promote well-being that are adapted to the needs of this population.

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## INTRODUCTION

Hematopoietic stem cell transplantation (HSCT), either from an individual's own stem cells (autologous) or those of a donor (allogeneic), is an increasingly used and potentially life-saving treatment for patients with blood or bone marrow malignancies. Approximately 8,000 allogeneic and 14,000 autologous HSCTs are performed annually in the United States, and they are associated with increased relapse-free intervals, improved 5-year survival rates, and lower long-term mortality [1]. The significant number of HSCT survivors and the projected increase in number of survivors by 2030 [2] has led to a need to better understand factors that promote recovery and health-related quality of life (HRQoL) in this growing population.

Patients' psychological factors and well-being play an important role in recovery and HRQoL after HSCT for a myriad of reasons [3]. The process of undergoing and recovering from HSCT is intense, with a lengthy hospitalization period, social isolation because of quarantine status, common and painful side effects, and secondary infections. For many patients, functional recovery after HSCT occurs slowly over several months, and full recovery may take a year or longer [4]. Even after discharge, HSCT patients undergo intensive routine follow-up care, including frequent clinic visits, active medication management, adherence to a healthy diet, and management of common complications, including graft-versus-host disease (GVHD). Such intensive management and self-care requirements during and after admission can result in substantial emotional distress and HRQoL impairments [5]. HSCT patients and their caregivers must also constantly monitor for post-transplant complications, and such vigilance and fear of cancer recurrence requires resilience and motivation [5]. Unsurprisingly, in both early and late recovery, depression and anxiety

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are prevalent in HSCT patients [6] and are associated with poorer HRQoL and long-term well-being [3,4]. Hence, many studies have focused on the negative psychological constructs as predictors of poor health outcomes after HSCT. However, although most HSCT patients are not clinically depressed and do not require evidence-based pharmacotherapy or psychotherapy, many experience substantial distress, anxiety, and difficulties with adjustment.

In contrast to psychological distress, positive psychological well-being, defined as “the positive components of psychological health (including positive constructs such as optimism, gratitude, hope, perseverance) that characterize individuals who feel good about life and function well” [7], has been prospectively and independently associated with better HRQoL and superior health outcomes in medical populations, above and beyond the adverse effects of depression and anxiety [8]. For example, in patients suffering from an acute coronary syndrome, optimism immediately after the event has been associated with better HRQoL, more physical activity, and lower rates of readmission in the subsequent 6 months, controlling for multiple relevant variables [9].

Positive psychological constructs are not merely fixed traits but are mutable and can deliberately be taught and enhanced. Interventions that aim to promote optimism, gratitude, and related positive psychological constructs in HSCT patients may have the potential to improve HRQoL and recovery. For example, positive psychology interventions that consist of systematic, simple, and enjoyable exercises (such as writing a gratitude letter, doing acts of kindness, and finding humor in everyday life) that target a variety of positive psychological constructs have been shown to significantly impact health outcomes in a variety of medical populations [8–10]. Existing literature suggests that lower levels of positive psychological well-being related constructs (including spirituality and social support) are associated with greater fatigue and lower function in HSCT patients [11], making this a potentially important target in this specific population. In the 1 previous review looking at the impact of negative or positive emotions on mortality after adult stem cell transplants, Hoodin et al. [12] found that pretransplant optimism appeared to effect survival in the short term, suggesting that this maybe an important area for further study in this population. Research examining the relationships between positive psychological constructs (eg, optimism, positive affect) and clinical outcomes in HSCT patients has grown substantially since these and broader concepts were reviewed by Hoodin and colleagues over 10 years ago. Hence, this updated and focused view is dedicated to examining relationships between positive psychological constructs and health-related outcomes in HSCT patients to assess whether such relationships exist in this important, growing, and complex population.

Accordingly, we completed a systematic review of the literature examining relationships between positive psychological constructs and health-related outcomes in HSCT patients. Specifically, we identified studies of positive psychological constructs in prospective or cross-sectional studies of adult patients with hematologic malignancies who received HSCT to understand the impact of these constructs on psychological and physical health outcomes.

## METHODS

### Overview

We conducted a systematic review to identify articles that examined the relationship between 1 or more positive psychological well-being related constructs and health outcomes. The guidelines and criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [13]

were followed and applied to ensure rigorous execution of the review and proper reporting of the data (see PRISMA checklist, Supplementary Table 1).

### Search Strategy

The systematic literature review was conducted using key words in PubMed, PsycINFO, and Scopus electronic databases. In each case, articles from database inception to the time of the search (September to November 2017) were included.

### Selection Procedure

To be included studies were required to examine a population of patients with hematologic malignancies who had received HSCT, to assess associations of positive psychological constructs and/or positive psychological interventions (see Table 1 for specific constructs and search terms) with health-related outcomes, and to use either a prospective or cross-sectional observational study design. We limited inclusion to studies published in English (not limited by country) and those focusing on adult populations (18 years or older).

Patients in identified study populations had the following hematologic malignancy diagnoses: leukemia (acute or chronic, myeloid or lymphocytic), Hodgkin lymphoma, non-Hodgkin lymphoma, diffuse large B cell lymphoma, follicular lymphoma, and multiple myeloma. Studies that examined mixed samples of cancer diagnoses (with >25% nonhematologic malignancies) were excluded.

Table 1 outlines search terms used for our queries. Existing literature on positive psychological constructs informed our choices of search terms [10,14]. In the initial round 2 study team members (H.L.A. and M.E.B.) performed searches of the electronic databases and removed duplicate articles. The nonduplicate articles were screened by titles first and then by abstracts to exclude studies that did not meet inclusion criteria. During the second round, full texts were screened for eligibility criteria by 2 study team members (H.L.A. and M.E.B.). Adjudication of articles for inclusion, including review of all included articles, was completed by the senior author (J.C.H.). Reviewers also used the reference lists of all full text manuscripts to identify other possible articles. During the search and review process we identified numerous additional constructs and interventions that were potentially related to positive psychological constructs and updated our search algorithm accordingly.

Figure 1 shows a flow diagram of the search and selection strategy. The most common reasons for full article exclusion were no discussion of positive psychology constructs, greater than 25% nonhematologic malignancy patients, reported positive psychology construct not a predictor variable, and literature review articles. Once all eligible studies were identified, relevant data were extracted separately by 2 study team members (H.L.A. and M.E.B.) and inputted into the study characteristics table; the senior author (J.C.H.) reviewed all included articles.

## RESULTS

### Study Characteristics

Study characteristics are presented in Table 2. Information from the studies were collected via the PICOS (population, intervention, comparator/comparison group, outcomes, timing and setting) framework as relevant for observational studies. The 18 included studies examined outcomes in a total of 4201 patients with individual study size ranging from 25 to 750 patients. Approximately half of patients (47%) were women, and of the studies (n = 15; 83%) that reported the age of study participants, the mean age was 47.1. Most studies (n = 14; 78%) were cross-sectional; 4 prospective studies had follow-up periods ranging from 1 to 9 years post-HSCT. Of the studies (n = 15; 83%) that reported racial composition of samples, most (79%) study participants were white. Participants had a variety of hematologic malignancy diagnoses including non-Hodgkin lymphoma, chronic myelogenous leukemia, acute lymphocytic leukemia, multiple myeloma, chronic lymphocytic leukemia, and myelodysplastic syndrome, and of the studies that reported the type of transplant, allogeneic transplants were more common (n = 11; 61%). Most studies (n = 16; 89%) occurred in the United States, with 1 study from China and another from the United Kingdom. Importantly, no studies examined associations between positive psychological interventions and health outcomes in patients with hematologic malignancies who have received HSCT.

**Table 1**  
Electronic Database Search Terms

Positive Psychological Constructs (A)	Positive Psychological Interventions (B)	Transplant Treatments (C)	Hematologic Malignancies (D)
Optimism	Positive psychology	HSCT	Hematologic malignancies
Hope	Counting your blessings	Stem cell transplant	Leukemia
Gratitude	Practicing kindness	HCT	Acute lymphocytic leukemia
Perseverance	Loving kindness	Bone marrow transplant	Acute myeloid leukemia
Vitality	Setting personal goals	Allogeneic stem cell transplant	Hodgkin lymphoma
Meaning	Expressing gratitude	Autologous stem cell transplant	Non-Hodgkin lymphoma (dif- fuse large B cell lymphoma, fol- licular lymphoma and chronic lymphocytic leukemia)
Purpose in life	Using personal strengths	Umbilical cord blood transplant	Multiple myeloma
(Subjective) well-being: hedonic* and eudaimonic†	Positive psychology intervention		Blood cancer
Satisfaction	Positive psychology therapy		Lymphoma
Contentment	Positive affect induction		
Self-acceptance	Positive psychotherapy		
Personal growth	Optimism training		
Enthusiasm			
Tranquility			
Cheerfulness			
Happiness			
Positive expectations			
Emotional well-being			
Ikigai‡			
Life enjoyment			
Positive affect			
Character strengths			

For the primary search, we combined search terms in the following manner: column A (Positive psychology well-being constructs) plus column C (transplant) and next column A plus column D (hematologic malignancies). For example, primary searches included the following: “optimism and stem cell transplant (SCT)” and “meaning and acute myeloid leukemia.” For our secondary search for articles pertaining to positive psychological *interventions*, we combined search terms in the following manner: column B (interventions) plus column C (transplant) and then column B plus column D (hematologic malignancies). A specific example of our secondary search is “positive psychology and bone marrow transplant (BMT)” or “using personal strengths and multiple myeloma.”

\* Hedonic: positive construct that focuses on happiness, pleasure attainment, and pain avoidance [54].

† Eudaimonic: positive construct that focuses on meaning and self-realization [54].

‡ Ikigai: Japanese positive construct that focuses on meaning [55].

### Positive Psychological Constructs and Study Outcome Measures

Study measures are presented in Table 2. Studies examined a wide variety of positive psychological constructs. Optimism (including dispositional optimism and optimistic expectations) was the construct studied in the largest number of studies ( $n = 12$ ; 67%). Other positive constructs examined included meaning and peace (included in spiritual well-being) measured with the Functional Assessment of Chronic Illness Therapy–Spiritual well-being [15].

A variety of HRQoL outcome measures were used by studies as follows: overall HRQoL measured with a variety of measures such as Medical Outcomes Study 36-Item Short-Form Health Survey [16], mental HRQoL measured with the Medical Outcomes Study 36-Item Short-Form Health Survey Mental Component Summary [17], bone marrow transplant-specific HRQoL measured with the Functional Assessment of Cancer Therapy–Bone Marrow Transplant–Trial Outcome Index (FACT-BMT-TOI) [18], cancer-focused quality of life measured with the FACT-G [18], and general quality of life (not disease specific) measured with the Spitzer Quality of Life Index [19]. Other psychological outcomes assessed included depressive symptoms measured with the Center for Epidemiologic Studies of Depression (CES-D) [20], post-traumatic growth measured with the Post-traumatic Growth Inventory [21], and post-traumatic stress disorder (PTSD) measured with the PTSD Checklist–Civilian [22]. Regarding medical outcomes, mortality and physical symptoms were examined. Importantly, 17 studies (94%; Table 2) that reported some quantitative assessment of predictors and outcome measures found a significant ( $P < .05$ ) association between a positive psychological construct and a health outcome.

Full details of each study and its findings are listed in Table 2. Below we summarize studies by positive psychological

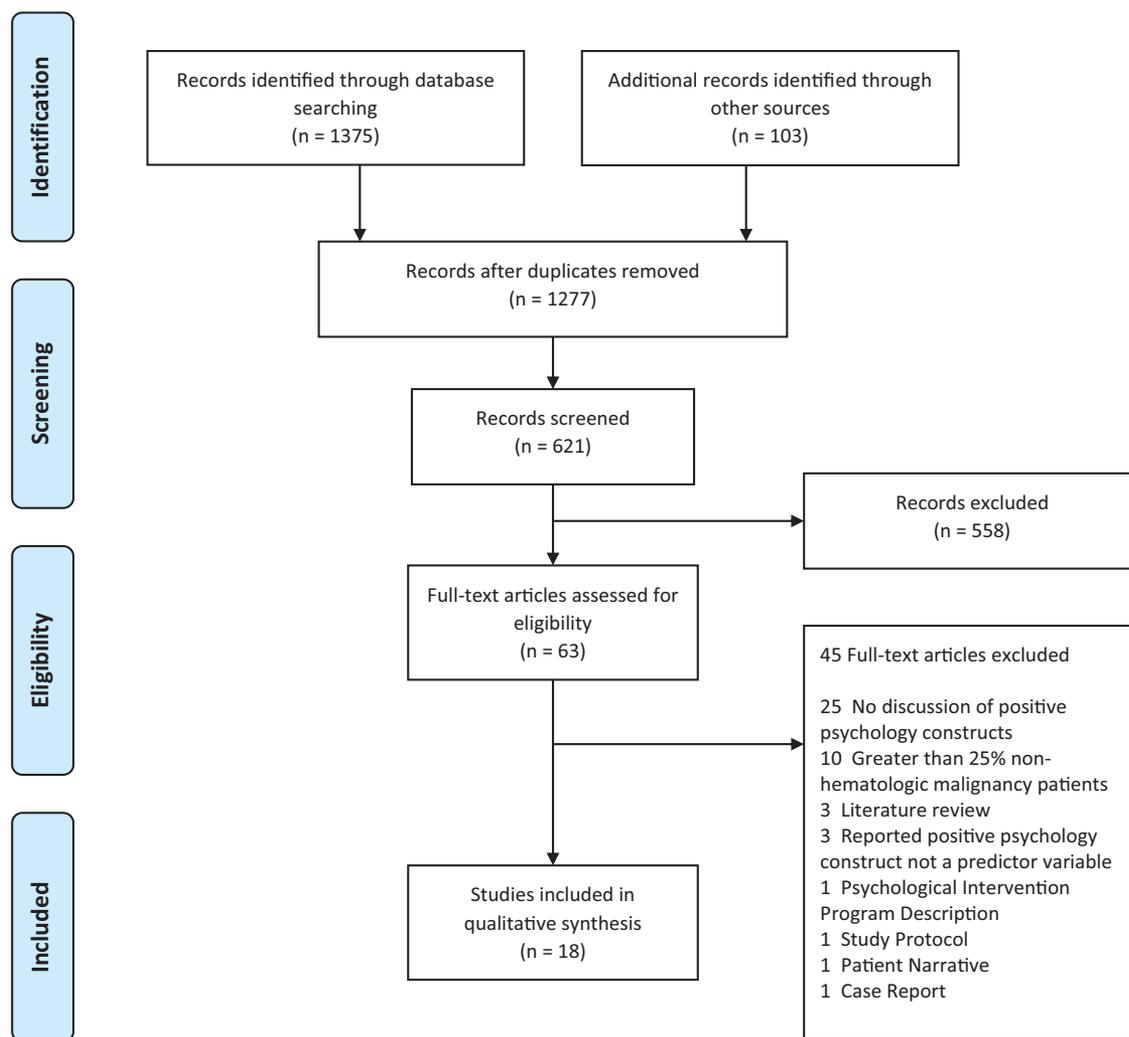
constructs (eg, optimism, other positive psychological well-being constructs) and outcome measures (eg, quality of life, other outcome measures).

### Optimism and HRQoL

Four studies examined the associations of optimism or dispositional optimism with HRQoL. Hochhausen et al. [23] examined the effects of pre–bone marrow transplant optimism on overall HRQoL, bone marrow transplant–specific HRQoL, and depressive symptoms. One year after transplant, optimism was significantly associated with all 3 outcomes (FACT-G:  $\beta = .256$ ,  $P < .05$ ; FACT-BMT-TOI:  $\beta = .272$ ,  $P < .05$ ; CES-D:  $\beta = -.235$ ,  $P < .05$ ) after controlling for age, gender, maximum grade of GVHD, and treatment arm (the primary study was a multicenter randomized control trial that examined ex-vivo T-cell depletion compared with conventional post-transplantation immunosuppressive therapy as prophylaxis for GVHD) in multivariable analyses.

In a second qualitative cross-sectional study [24] that explored the relationship between optimism and other psychosocial variables with HRQoL in 28 allogeneic and autologous HSCT patients from 1 month to 28 years post-HSCT, optimism was noted by 89% of participants as a key factor to post-HSCT adjustment and HRQoL. Additionally, in a cross-sectional study [25] of 662 survivors of hematologic cell transplant (HCT), optimism was significantly associated with patient-reported physical health ( $\beta = .16$ ,  $P < .001$ ) and mental health ( $\beta = .53$ ,  $P < .001$ ).

Finally, in a cross-sectional analysis of 52 allogeneic HSCT patients with chronic GVHD after allogeneic HSCT [26], the authors found that lower levels of spiritual well-being, which included constructs such as optimism, inner peacefulness, and meaning and purpose in life, were associated with lower levels of HRQoL ( $P < .001$ ). Of note, in this study well-being was not associated with clinician ratings of chronic GVHD severity.



**Figure 1.** Flow diagram of the literature search outlines our methodology following PRISMA guidelines. (From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. *PLoS Med.* 2009;6:e1000097.)

### Optimism and Depression/Anxiety

Two studies explored the associations of optimism with anxiety and depressive symptoms. First, in a cross-sectional study of 227 hospitalized patients with hematologic malignancy, Wang et al. [27] found that, independent of several sociodemographic variables, both optimism ( $\beta = -.479, P < .001$ ) and resilience ( $\beta = -.174, P < .05$ ) were significantly and inversely associated with depressive symptoms. Optimism alone ( $\beta = -.393, P < .001$ ) was also negatively associated with anxiety symptoms. In a secondary analysis of cross-sectional data collected from 662 long-term HSCT survivors [28], optimism was significantly associated with fewer depressive symptoms ( $B = -.74, P < .001$ ), higher mental HRQoL ( $B = .39, P < .001$ ), fewer physical symptoms ( $B = -.35, P < .001$ ), and lower physical HRQoL ( $B = -.40, P < .001$ ).

### Optimism and Other Medical Outcomes

Six studies assessed the links between optimism and a variety of medical outcomes including situational coping, survival, psychological adjustment, day to neutrophil engraftment (DTE), and post-traumatic growth. First, in a secondary analysis of 85 patients with cancer who were enrolled in a longitudinal multicenter randomized control trial of T-cell depletion for prevention of GVHD in bone marrow transplant patients,

Schoen et al. [29] found that situational avoidant coping (defined as cognitive and behavioral escape-avoidance) 1 year post-transplant was significantly and independently predicted by baseline dispositional avoidant coping ( $\beta = .393, P < .01$ ) and optimism ( $\beta = .251, P < .05$ ).

Second, among 313 patients preparing to undergo both allogeneic and autologous HSCT, those rated as having optimistic expectations (44%) had better general health perceptions (no test statistics provided;  $P = .003$ ), mental functioning ( $P < .0001$ ), social functioning ( $P = .01$ ), and a brighter outlook ( $P = .007$ ) at baseline and were also more likely to rate their health as very good or excellent (17% versus 9%;  $P = .0003$ ) [30]. Also, those with optimistic expectations had significantly lower rates of 60-day mortality (relative risk, 2.2; 95% confidence interval, 1.08 to 4.46;  $P = .03$ ) on multivariate analysis controlling for stage of disease, disease type, age, and acute GVHD. These findings held when controlling additionally for sociodemographic factors (marriage, religion), patient assessments of risk of death and likelihood of cure, patient-reported worry about relapse, and physical function.

Third, in a cross-sectional study of 54 adults undergoing either autologous or allogeneic hematologic cell transplant (HCT), Knight et al. [31] found that greater optimism was significantly associated with the favorable outcome of fewer DTEs

**Table 2**  
Study Characteristics, Outcome Measures, and Results

Authors	Sample Size	Sample Characteristics	Transplant Type	Positive Constructs (Measures Used)	Psychological Outcomes (Measures Used)	Medical Outcomes (Measures Used)	Analysis and Results
Curbow et al. (1993)	135	39.3% female 30.6 mean age 91.1% white	Autologous Allogeneic	Dispositional optimism (Life Orientation Test [56])	Personal changes (20-item nonvalidated questionnaire [11]) Psychological adjustment (nonvalidated multidimensional approach [57]) Life satisfaction (10-rungs Ladder of Life Scale [11,58]) Negative mood (Profile of Mood States [59]) Affective states (Profile of Mood States [62])	NA	Optimism and positive changes in different aspects of life ( $r = .19, P < .05$ ) Optimism and negative changes in psychological adjustment ( $r = .33, P < .001$ ) Optimism and perceived health ( $r = .25, P < .01$ ) Optimism and current and future life satisfaction ( $\beta = .18; P < .05; \beta = .19; P < .05$ )
Fromm et al. (1996)	90	42% female 38.8 mean age NR white	Autologous Allogeneic	Positive affect (Positive and Negative Affective Scale [60]) Self-esteem (Rosenberg Self-esteem scale [61])	Affective states (Profile of Mood States [62])	Quality of life (Functional Living Index-Cancer Scale [63]) Illness-related dysfunction (Sickness Impact Scale [64])	Positive affect and quality of life ( $r = .20, P < .01$ )
Vickberg et al. (2001)	85	51% female 40 mean age 63.8% white	Bone marrow transplant	Global meaning (Personal Meaning Index of Life Attitude Profile-Revised [65])	Psychological adjustment: depression and anxiety (Global Severity Index of the Brief Symptom Inventory [66]) BMT-related PTSD (PTSD Checklist-Civilian [22])	Quality of Life: mental health dimension (Medical Outcomes Study 36-Item Short-Form Health Survey [67]) Physical functioning (Medical Outcomes Study 36-Item Short-Form Health Survey [67])	Global meaning and global psychological distress (depression and anxiety; $\beta = -.41, P < .001$ ) Global meaning and BMT-related PTSD symptoms ( $\beta = -.29, P < .01$ ) Global meaning and mental HRQoL ( $\beta = .39, P < .001$ ),
Lee et al. (2003)	313	Optimistic responders: 48% female 47 median age 98% white Less optimistic responders: 48% female 46 median age 93% white	Autologous Allogeneic	Optimistic expectations (2-item nonvalidated survey [30])	NA	Quality of Life (Spitzer Quality of Life Index [19]) and Medical Outcomes Study 36-Item Short-Form Health Survey [16])	Patients with optimistic expectations (44%) had better general health perceptions (no test statistics provided; $P = .003$ ), mental functioning ( $P < .0001$ ), social functioning ( $P = .01$ ), and a brighter outlook ( $P = .007$ ) at baseline and were also more likely to rate their health as very good or excellent (17% vs. 9%; $P = .0003$ ) Patients with optimistic expectations had significantly lower rates of 60-day mortality (relative risk, 2.2; 95% confidence interval, 1.08-4.46; $P = .03$ )
Schoen et al. (2007)	85	47.1% female 35.5 mean age 91.8% white	Bone marrow transplant	Dispositional optimism (Life Orientation Test-Revised [68])	Situational avoidant coping (unvalidated version of Coping Orientation to Problems Encountered Scale [69]) Dispositional avoidant coping (unvalidated version of Coping Orientation to Problems Encountered Scale [69])	NA	Situational avoidant coping 1 year post-transplant and baseline dispositional avoidant coping ( $\beta = .393; P < .01$ ) Situational avoidant coping and optimism ( $\beta = .251; P < .05$ )
Hochhausen et al. (2007)	87	47.1% female 35 mean age 90.8% white	NA	Optimism (Life Orientation Test [56]) Self-efficacy	Depression (CES-D [20])	Overall HRQoL (FACT-G [18]) Bone marrow transplant	Optimism and overall HRQoL (FACT-G: $\beta = .256, P < .05$ ) Optimism and BMT-related quality of life (FACT-

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Table 2 (Continued)

Authors	Sample Size	Sample Characteristics	Transplant Type	Positive Constructs (Measures Used)	Psychological Outcomes (Measures Used)	Medical Outcomes (Measures Used)	Analysis and Results
Tallman et al. (2010)	25	52% female 37.2 mean age 92% white	Allogeneic	(Cancer Behavior Inventory Long Form [70]) Optimism (Life Orientation Test-Revised [68])	Post-traumatic growth (Posttraumatic Growth Inventory [21])	quality of life (FACT-BMT-TOI [18]) Long-term well-being (FACT-G [18])	BMT-TOI: $\beta = .272, P < .05$ Optimism and depression (CES-D: $\beta = -.235, P < .05$ ) Pretransplant optimism and posttraumatic growth 9 years post-transplant: personal strength ( $r = .42; P < .05$ ) and relationship with others ( $r = .46; P < .05$ )
Beeken et al. (2011)	28	53.6% female 22-71 median age 100% white	Autologous Allogeneic	Optimism (nonvalidated semi-structured interview)	NA	HRQoL (nonvalidated semi-structured interview) Post-HSCT adjustment (nonvalidated semi-structured interview)	Optimism was noted by 89% of participants as a key factor to post-HSCT adjustment and HRQoL
Harris et al. (2010)	52	44% female 41.0 mean age 90% white	Allogeneic	Spiritual well-being: optimism, inner peacefulness, meaning, purpose in life (FACT-Spiritual well-being [15])	NA	HRQoL (FACT-G [18])	Lower levels of spiritual well-being (optimism, inner peacefulness, and meaning and purpose in life) were associated with lower levels of HRQoL (mean, 54.88; standard error, 4.19; $P < .001$ )
Prince et al. (2015)	171	37.4% female 43.7 mean age 52% white	NA	Spiritual well-being: meaning and peace (FACT-Spiritual subscale [71,72])	NA	HRQoL (FACT-G [18,73])	Spiritual well-being (meaning) and HRQoL ( $\beta = 1.323, P < .01$ ) Spiritual well-being (peace) and HRQoL ( $\beta = 1.951, P < .001$ )
Kenzik et al. (2015)	662	62% female 42 mean age 92% white	NA	Optimism (Life Orientation Test [56])	Depression mental quality of life (CES-D [20])	Physical symptoms (FACT-BMT [74]) Physical HRQoL (Medical Outcomes Study 36-Item Short-Form Health Survey-Physical Component Summary [17]) Mental HRQoL (Medical Outcomes Study 36-Item Short-Form Health Survey- Mental Component Summary [17])	Optimism and physical symptoms ( $B = -.35; P < .001$ ) Optimism and physical HRQoL ( $B = -.40; P < .001$ ) Optimism and mental HRQoL ( $B = .39; P < .001$ ) Optimism and depressive symptoms ( $B = -.74; P < .001$ )
Bryant et al. (2015)	750	49.5% female 62.4 mean age 85.7% white	HSCT	Positive adaptation (Impact of Cancer Scale [75])	NA	Cancer-focused quality of life (FACT-G [18])	Positive adaptation and cancer-focused QoL (direct effect = .193; $P < .05$ )
Wang et al. (2016)	227	48.5% female 45.48 mean age 0% white	NA	Optimism (Chinese version of the Life Orientation Test-Revised [68,76]) Self-efficacy (Chinese version of the Perceived Self-efficacy and Resilience Scale [77]) Resilience (Resilience Scale-1427)	Depression (CES-D [78,79]) Anxiety (Zung self-rating anxiety scale [80])	NA	Optimism and depressive symptoms ( $\beta = -.479, P < .001$ ) Resilience and depressive symptoms ( $\beta = -.174, P < .05$ ) Optimism and anxiety symptoms ( $\beta = -.393, P < .001$ ) Resilience and anxiety symptoms ( $\beta = -.133, P > .05$ ) Self-efficacy and depressive symptoms ( $\beta = -.032, P > .05$ ) Self-efficacy and anxiety symptoms ( $\beta = -.055, P > .05$ )

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**Table 2** (Continued)

Authors	Sample Size	Sample Characteristics	Transplant Type	Positive Constructs (Measures Used)	Psychological Outcomes (Measures Used)	Medical Outcomes (Measures Used)	Analysis and Results
Knight et al. (2014)	54	48.4% female 47.03 mean age 85.94% white	Autologous Allogeneic	Optimism (Life Orientation Test [56])	NA	DTE	Optimism and DTE among autologous recipients ( $\beta = -.15, P = .01$ ) Optimism and DTE among autologous recipients (day +3) ( $\beta = -.09, P = .44$ ) Optimism and DTE among allogeneic recipients ( $\beta = -.0059, P = .97$ ) Optimism and DTE among allogeneic recipients (day +3) ( $\beta = -.0994, P = .68$ )
Campo et al. (2017)	254	57% female 53.70 mean age 84% white	Autologous Allogeneic	Personal resilience resources: optimism, self-esteem and mastery Optimism (Life Orientation Test [56]) Self-esteem (Rosenberg Self-esteem scale [61]) Optimism (Life Orientation Test [56])	Depression (Brief Symptom Inventory [66]) PTSD (Impact of Events Scale [81]) Purpose in Life (Life Engagement Test [82])	NA	Resilience resources and depressive Symptoms ( $r_{\text{baseline}} = -.65, P < .001, r_{\text{follow-up}} = -.60, P < .001$ ) Resilience resources and PTSD symptoms ( $b = -.07, P = .005$ ) Resilience resources and purpose in life ( $b = .10, P < .001$ )
Herzberg et al. (2013)	301	German-Austrian cohort: 49% female 44 mean age NR white American cohort: 56% female 53 mean age NR white	Allogeneic	Optimism (Life Orientation Test [56])	NA	HRQoL (FACT- BMT [74]) (Medical Outcomes Study 36-Item Short-Form Health Survey [67]) (Lee-chronic GVHD-symptom scale [L-cGVHD-SC] [83])	German-Austrian cohort: optimism and HRQoL (social well-being scale [ $\beta = .29, P < .001$ ] and emotional well-being scale [ $\beta = .25, P < .001$ ] of FACT-BMT) American cohort: optimism and HRQoL (emotional well-being scale [ $\beta = .24, P = .002$ ] of FACT-BMT and mental score of L-cGVHD-SC [ $\beta = -.3, P < .001$ ])
Wingard et al. (2010)	662	38% female 42.1 mean age 92% white	Autologous Allogeneic	Optimism (Life Orientation Test [56])	NA	Quality of life: self-reported physical health (Mental and Physical Component Summaries of Medical Outcomes Study 36-Item Short-Form Health Survey [67])	Optimism and self-reported mental health ( $\beta = .53, P < .001$ ) Optimism and self-reported physical health ( $\beta = .16, P < .001$ )
Leeson et al. (2015)	220	38.2% female 51 mean age 96.8% white	Autologous Allogeneic	Spirituality: meaning and peace (FACT-Spirituality [71])	Emotional well-being: depression and anxiety (Inventory of Depression and Anxiety Symptoms [84])	Fatigue (Fatigue Symptom Inventory [85]) Pain (The Brief Pain Inventory [86]) Physical well-being (FACT [87]) Functional well-being (FACT [87])	Meaning/peace and depression ( $z = -8.88, P < .001$ ) Meaning/peace and anxiety ( $z = -4.12, P < .001$ ) Meaning/peace and fatigue ( $z = -5.22, P < .001$ ) Meaning/peace and pain ( $z = -2.57, P < .001$ ) Meaning/peace and physical well-being ( $z = 5.25, P < .001$ ) Meaning/peace and functional well-being ( $z = 8.43, P < .001$ )

in autologous HCT recipients ( $\beta = -.15, P = .01$ ) as compared with allogeneic HCT recipients ( $\beta = -.0059, P = .97$ ). However, when all sample sizes were reduced to only patients who completed baseline surveys by the time of engraftment, the relationship between optimism and DTEs was not significant in both autologous ( $\beta = -.09, P = .44$ ) and allogeneic ( $\beta = -.0994, P = .68$ ) recipients. Fourth, in a cross-sectional evaluation of the influence on personality (with optimism as a personality assessment measure) on quality of life in 2 independent cohorts (German-Austrian,  $N = 208$ ; and American,  $N = 93$ ) of allogeneic HSCT recipients, Herzberg et al. [32] found that optimism was moderately associated with better scores of the social well-being ( $\beta = .29, P < .001$ ) and emotional well-being ( $\beta = .25, P < .001$ ) scales of the FACT-BMT in the German-Austrian cohort as compared with the American cohort, where optimism was moderately associated with the emotional well-being scale ( $\beta = .24, P = .002$ ) of the FACT-BMT and reduced reported symptom load in the mental score of the Lee-chronic GVHD-symptom load [L-cGVHD-SC] ( $\beta = -.3, P < .001$ ).

Additionally, in a cross-sectional study of 135 autologous and allogeneic transplant survivors, Curbow et al. [11] found that increased optimism was significantly correlated with having more positive changes in different aspects of life (such as plans for the future, relationships, leisure time, life goals;  $r = .19, P < .05$ ) and fewer negative changes ( $r = .33, P < .001$ ) in psychological adjustment. Optimism was also associated with greater perceived health ( $r = .25, P < .01$ ), current and future life satisfaction ( $\beta = .18, P < .05$ ;  $\beta = .19, P < .05$ ) independent of sociodemographic factors and illness, and lower levels of negative mood controlling for sociodemographic, illness, and psychological adjustment factors ( $\beta = -.38, P < .001$ ). Finally, in a longitudinal study [33] of 25 cancer survivors who received allogeneic HSCT from an unrelated donor that examined the effects of optimism on post-traumatic growth and long-term well-being 9 years post-transplant, pre-transplant optimism was significantly related to 2 domains of post-traumatic growth 9 years post-transplant: personal strength ( $r = .42, P < .05$ ) and relationship with others ( $r = .46, P < .05$ ), although not with overall post-traumatic growth or total well-being.

#### **Other Positive Psychological Well-Being Related Constructs and Quality of Life**

Five studies examined the association between other positive psychological well-being constructs (positive adaptation, meaning and peace as part of spiritual well-being, global meaning, and positive psychological sequelae) and quality of life. Positive adaptation was directly associated with greater cancer-focused QoL (direct effect = .193,  $P < .05$ ) in a secondary cross-sectional analysis of 750 patients with non-Hodgkin lymphoma who were at least 2 years post diagnosis [34]. Additionally, positive adaptation mediated the relationships between age, sex, race, social support, and current treatment with cancer-focused quality of life [34].

In 171 participants assessed 3 years or more after allogeneic HSCT, meaning ( $\beta = 1.323, P < .01$ ) and peace ( $\beta = 1.951, P < .001$ ) but not faith were independently associated with greater HRQoL, controlling for employment and performance status [35]. Additionally, in 220 recipients of HCT, meaning/peace as components of spiritual well-being was found to be associated with less depression ( $z = -8.88, P < .001$ ), anxiety ( $z = -4.12, P < .001$ ), pain ( $z = -2.57, P < .001$ ), and fatigue ( $z = -5.22, P < .001$ ) as well as greater physical ( $z = 5.25, P < .001$ ) and functional well-being ( $z = 8.43, P < .001$ ) [36].

Furthermore, among 85 allogeneic bone marrow transplant survivors, Johnson et al. [37] found that higher global meaning

was significantly related to lesser global psychological distress (depression and anxiety;  $\beta = -.41, P < .001$ ), fewer bone marrow transplantation-related PTSD symptoms ( $\beta = -.29, P < .01$ ), and greater mental HRQoL ( $\beta = .39, P < .001$ ), controlling for gender, physical functioning, number of days hospitalized for bone marrow transplantation, and number of rehospitalizations after initial discharge. Finally, in a cross-sectional mixed-methods study of 90 allogeneic and autologous bone marrow transplantation survivors ( $\geq 1$  year post-transplant), Fromm et al. [38] found that among 10 constructs assessed, positive affect was most strongly correlated with quality of life, but this association was not statistically significant ( $r = .20, P < .01$ ).

#### **Other Positive Psychological Well-Being Related Constructs and Depression/PTSD**

In a longitudinal study of 254 post-transplant cancer survivors 9 months to 3 years after stem cell transplantation, Campo et al. [39] found that higher personal resilience resources (optimism, self-esteem, and mastery) were significantly associated with lesser depressive symptoms ( $r_{\text{baseline}} = -.65, P < .001$ ;  $r_{\text{follow-up}} = -.60, P < .001$ ), PTSD symptoms ( $b = -.07, P = .005$ ), and greater purpose in life ( $b = .10, P < .001$ ).

#### **DISCUSSION**

To our knowledge this focused review is the first to assess the associations between positive psychological constructs and health outcomes in patients with hematologic malignancies who have received HSCT. Our systematic review yielded a variety of positive psychological constructs studied in over 4201 HSCT patients. Many prior studies of psychological factors in HSCT patients have focused on negative psychological constructs such as depression, anxiety, and PTSD symptoms as predictors of poor health outcomes after HSCT. However, positive psychological well-being is not simply the absence of negative affective states. Indeed, the benefits of positive psychological well-being on various health outcomes and the link of positive psychological constructs to superior health outcomes are independent of the effects of depression and other negative states [8,10], suggesting that it is not simply the absence of distress that drives the superior health outcomes associated with positive psychological well-being.

We found that most identified studies examined optimism and revealed significant associations between optimism and improved health outcomes, including better HRQoL and function, lower levels of depression and anxiety, and, in one study [8], reduced mortality. The strengths of these associations were small to medium in most cases. Although 1 study showed optimism was positively associated with avoidant coping [29], additional studies found that a variety of other positive psychological-related constructs, including positive adaptation, meaning and peace (as part of a spiritual well-being), and global meaning, were linked with higher cancer-focused quality of life, fewer bone marrow transplant-related PTSD diagnoses, and greater mental HRQoL. Notably, in most identified studies the observed associations between positive psychological constructs and health outcomes were independent of 1 or more medical, psychological, and/or sociodemographic variables.

Although these findings are consistent with prior studies in other chronic medical populations [9,40–43], the HSCT population is in many ways a unique population. Unlike many other cancer treatments, HSCT promises a potential cure for some patients and can lead to substantial hope [44]. However, the exhaustive preparation for the transplant, the intensive follow-up care required, and the multiple potentially life-threatening

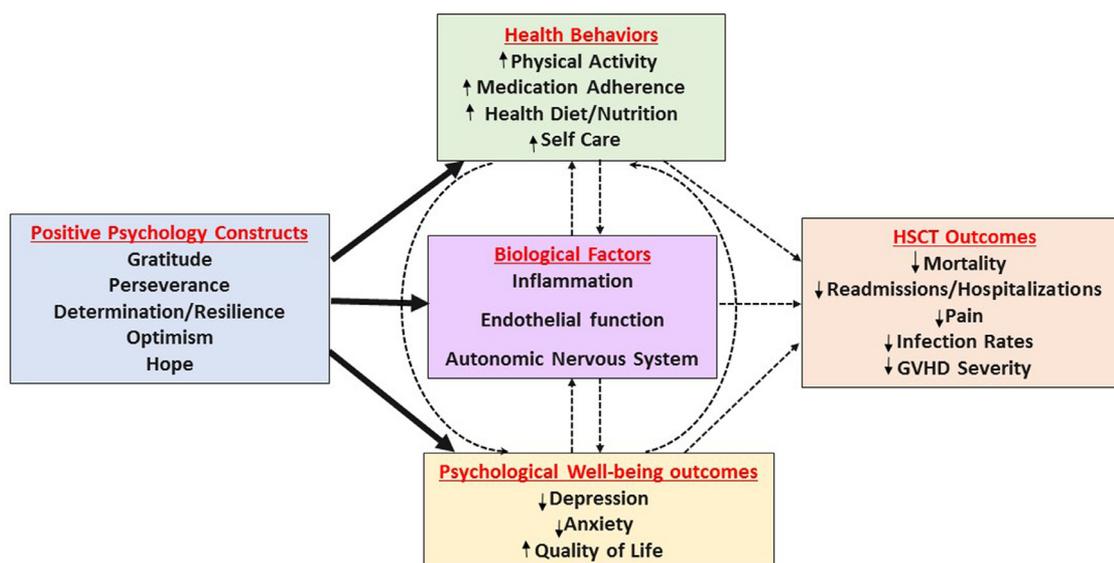
complications during recovery can undermine psychological well-being, quality of life, and overall function [4]. Additionally, considering the long recovery process after a stem cell transplant, distinct but less studied positive psychological constructs such as perseverance and determination may be especially salient for the HSCT patient population. Finally, recovery from HSCT has distinct stages that may require different psychological strengths and resources, with the acute phase (first 100 days) of recovery after HSCT differing in intensity, surveillance, and prevalence of complications compared with the different demands of longer-term recovery.

Figure 2 outlines a conceptual model with proposed mediators between positive psychological constructs and health outcomes in the HSCT population. In numerous other settings positive psychological well-being constructs have been shown to promote health behaviors [45] (eg, physical activity, medication compliance, and improved nutrition), impact biologic factors [45] (eg, reducing inflammatory markers and cytokines, improving endothelial function and autonomic system function), and reduce psychiatric symptoms [10] (eg, depression and anxiety). Decreased mortality, hospitalizations/readmissions, pain, infection rates, and GVHD severity are all potential HSCT outcomes that can be theoretically impacted by positive psychological well-being constructs. Improvements of these factors, in turn, have been linked to reduced rates of illness progression and mortality in multiple healthy and medically ill populations [8]. We therefore suggest that positive psychological well-being, mediated via changes in psychiatric symptoms, health behaviors, and biomarkers, could be linked to lower rates of mortality, hospitalizations/readmissions, pain, infection, and GVHD severity. Notably, positive psychological well-being constructs impact several other related constructs (such as self-regulation [46], motivation [47], active coping [48], resilience [10], attention, and cognitive processing [49]), even beyond this model, that could be pertinent mediators for HSCT health outcomes. Future studies with this population should consider exploring the association of dispositional optimism (widely studied) and positive affect (most malleable construct) as potential predictor variables with a variety of medical and psychological outcomes.

Importantly, although some proportion of positive psychological well-being is driven by genetics, dispositional traits, and life events, it appears that a substantial proportion of well-being is dynamic and can be modified via deliberate efforts and structured interventions [50]. Positive psychology is the scientific study and discipline of the strengths and positive emotional experiences that make life worth living [14]. Positive psychology interventions may be a novel approach to increase positive psychological well-being constructs in the HSCT population. Positive psychology interventions use simple systematic exercises (such as gratitude letters, acts of kindness, and identifying and using personal strengths) to cultivate positive thoughts and emotions [51]. Positive psychology interventions can be delivered remotely (eg, via phone), are simple for patients to complete, and require minimal provider training for implementation [14]. With effect sizes comparable with other psychological interventions, positive psychology interventions have been used successfully in over 5000 healthy subjects, in medical populations, and have been found to increase well-being, decrease negative affective states, and in some cases improve health behaviors such as diet, exercise, and medication compliance [52]. An added advantage of positive psychology interventions is that they can be applied to a wide variety of patients and not only to some patients with a specific clinical psychiatric condition such as depression [53].

Given the unique experience of undergoing HSCT, with a complex and multiphase recovery period, any intervention specific to positive psychological well-being would need to be intensively customized. An HSCT-specific positive psychology intervention that specifically targets the unique experiences of this population (such as the quarantine status during acute recovery) could be developed by an iterative process to understand the specific needs of this population via qualitative approaches involving HSCT patients and clinicians before tailoring an intervention specific to them. Such a tailored approach to well-being could have the potential to improve psychological health, HRQoL, and function in this vulnerable population.

This systematic review was limited by several important factors. There were limitations in the characteristics and quality of the identified studies. First, more than two-thirds of



**Figure 2.** Theoretical model of positive psychological well-being constructs and HSCT health outcomes. This diagram outlines a conceptual model with proposed mediators between positive psychological constructs and health outcomes in the HSCT population.

identified articles were cross-sectional, making it difficult to assess both the cause and effect relationships between positive psychological constructs and health outcomes as well as impact of early deaths and responder bias because those with higher baseline positive constructs may have been more likely to respond to surveys. In addition, most articles examined optimism, and less is known about the impact of other positive psychological constructs in HSCT patients. Although we included a broad range of health-related outcomes (including functional and HRQoL-related outcomes) and looked to include studies that examined mortality rates, remission rates, and other objective health outcomes, many studies only looked at psychological outcomes or HRQoL as outcome measures, and a significant minority of studies examined other important medical outcomes (such as infection rates, GVHD, engraftment, pain, cancer recurrence, and hospitalizations). Although most studies accounted for 1 or more covariates when examining the relationships between positive constructs and outcomes, the specific psychological, medical, and sociodemographic variables controlled in each study were inconsistent and minimal.

In addition, the small number of studies coupled with the disparity in quantitative assessments also limited our ability to conduct a more comprehensive quantitative analysis of the data such as meta-analysis. Finally, although we included all articles identified in our initial search and via reference lists of included articles, we did not complete a *de novo* search of additional new constructs. Also, because of the focused scope of this review, we did not include a wider range of potentially important and relevant constructs included in early psychological well-being research in this population such as spirituality, locus of control, self-efficacy, self-esteem, and social support. We therefore acknowledge the potential presence of additional articles identified via specific searches for those constructs that were outside the bounds of our initial comprehensive search strategy.

In conclusion, in patients with hematologic malignancies who have received a stem cell transplant, positive psychological constructs appear to be associated with improved quality of life and overall function as well as reduced rates of depression and anxiety. Additional larger observational studies in racially and ethnically diverse patient populations that are prospective in nature, control for numerous relevant covariates, and examine effects of positive psychological well-being on a wide range of medical outcomes are warranted. Furthermore, studies that aim to understand unique psychological constructs that may be especially pertinent and beneficial to this population (such as determination and perseverance) could provide additional key information relevant to this population. Studies that specifically look at several candidate mediators (eg, inflammatory markers, physical activity, and medication compliance) of the observed associations could provide useful information about mechanism. Finally, intervention studies targeting positive psychological well-being constructs in the HSCT population have not yet been completed; however, if effective, such positive psychological well-being interventions could have important effects on the quality of life and recovery of this important and growing patient population.

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#### SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at doi:10.1016/j.bbmt.2018.09.030.

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