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SYSTEMATIC REVIEW

THE EFFICACY OF INFORMATION INTERVENTIONS FOR PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION: A SYSTEMATIC REVIEW OF RANDOMIZED TRIALS

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Abstract

Background: The provision of information to patients is one of the most important factors of supportive cancer care. We conducted a systematic review to detect information-giving interventions and their impact on quality of life, psychological distress and satisfaction of hematopoietic stem cell transplant (HSCT) patients.

Methods: Randomized controlled trials (RCTs) from 2010 to 2021 in Pubmed, CINAHL, Cochrane Library and Scopus databases were reviewed.

Results: Eight RCTs with total of 1550 HSCT patients enrolled were identified. Most studies indicated that groups exposed to interventions displayed higher rates of satisfaction. However, the minority of the studies produced significant benefits in terms of distress and quality of life. RCTs were heterogeneous regarding sample size, diagnosis, transplant type and follow-up duration.

Conclusion: Additional research is needed to make definitive conclusions. More longitudinal multicenter studies with consistency in the methodological approach, assessment and interpretation are necessary.

Keywords: Hematopoietic stem cell transplantation, quality of life, information provision, information needs, satisfaction.

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INTRODUCTION

Hematopoietic stem cell transplantation (HSCT), commonly referred to as blood and marrow transplantation (BMT), is an effective treatment performed for many life-threatening diseases, especially hematological malignancies, with the potential for long-term survival and recovery. However, it may result in significant morbidity and mortality and serious short and long-term outcomes that affect patient's health related quality of life (HRQoL).¹⁻³ HSCT is a complex procedure wherein patients face numerous physical, psychosocial, emotional, mental, spiritual and behavioral challenges across the HSCT trajectory and represent one of the most critically ill cancer populations.⁴⁻⁶

Given the complexity and risk of HSCT, adequate counselling of patients before, during and in the years after the treatment is pertinent.⁷ According to international standards and national regulations, obtaining informed consent from hematopoietic stem cell recipients is an obligatory step in the transplantation process. Extensive medical and psychosocial information is required to be clearly communicated to patients and their families during the pre-transplant preparation.^{8,9}

Information-seeking behaviors must be taken into account on the way information is presented. Some patients want all available information, however, some others want to be protected from having information that is too detailed or threatening. On the other hand, some patients want to be informed but as they may have severe anxiety due to an often unpleasant diagnosis, it is unrealistic to expect them to easily understand and recall all the information provided.^{2,10-12} Therefore, to overcome this difficulty, the transplant team and especially clinicians develop communication methods often based on personal experiences. They invite individuals, alone or with their caregivers, to attend a counselling meeting, where adequate information on disease status, prognosis, potential benefits, drawbacks and expectations of the HSCT treatment are explained. Possible acute or long-term side effects, adverse events and their impact on HRQoL are extensively mentioned and discussed.^{8,13,14}

Tailoring information to the unique circumstances, preferences, coping styles and needs of individual patients may contribute to reducing patients' worries and anxiety levels, increasing their

empowerment and autonomy in relevant decision making processes, enhancing their self-management and sense of responsibility for their own health. Providing personalized and comprehensive information may also increase patients' psychological wellbeing and satisfaction with care, improve medication adherence and help them prevent treatment-related complications.¹⁵⁻¹⁸

In an attempt to address patients' requirements, a variety of procedures have been proposed to facilitate the passage of information from health professionals and other information sources to cancer patients and their families. These include information techniques using, either alone or in addition to others, verbal face-to-face contact, printed tools, telephone help-lines, audio-visual materials including animations or graphs, web-based (eHealth) and mobile information apps. Obtaining information is also achieved through educational interventions.¹⁹⁻²⁶ While there are a number of tools that may be harnessed to improve patients' understanding of their diagnosis and treatment, the use of such strategies should be patient-centered to ensure the type and amount of information provided by health care professionals addresses the needs and preferences of the patient.^{15,27-29}

Clinical guidelines recommend that HSCT recipients are continually informed during the transplantation journey and encouraged to ask questions after the information session has been completed. Verification of their understanding throughout the educational procedure is also important.⁹

Providing timely, efficient and accurate information to HSCT patients is a challenge in clinical practice. Although several efforts have been well received, little attention has been given to the effectiveness of the methods employed for HSCT recipients and survivors. The primary aim of the current review was to detect different information approaches implemented in HSCT patients and then evaluate their effectiveness on aspects of HRQoL and investigate which of the methods seem to benefit them more.

MATERIAL AND METHODS

Searching strategy

A systematic literature search was conducted using the PubMed (Medline), CINAHL (with full text), Cochrane Library and Scopus

electronic databases, to screen and identify all eligible studies published between January 2010 and March 2021. The research designs chosen for review were experimental reports (randomized studies). Clinical trials added to Cochrane Library CENTRAL (ClinicalTrials.gov) were not included since access to full-text was not available. The EBSCOhost and HEALink research platforms were used. The objectives of the literature search were specified using the PICOs criteria, including details on population, intervention, comparator and outcome (Table 1). Controlled vocabularies such as Medical Subject Headings (MeSH terms), keywords and relative synonyms were utilized in the search. Boolean Operators (AND, OR), truncation, field tags and filters were also applied. The reference lists of selected articles and existing reviews and bibliographies from recent systematic reviews in related areas were also manually searched. Letters to the editors and editorials, opinion papers, study protocols and case reports were excluded. Grey matter such as unpublished material (e.g. PhD thesis and conference abstracts) relevant to the question were not examined.

The author and a trained research assistant identified potentially relevant articles by reviewing the titles and abstracts retrieved from the referred four databases. Duplicate articles and abstracts were excluded. Articles identified as potentially relevant were retrieved in full text. Based on the inclusion criteria, several articles were excluded at different phases of this review.

Screening

Randomized studies were included if they met the following inclusion criteria: (1) human adults over 18 years old, (2) patients with a confirmed diagnosis of hematologic malignancy who were scheduled to undergo autologous or allogeneic HSCT, once or more times, (3) survivors of stem cell transplant were also included (survivors were defined as people who had completed the transplant process with curative intent), (4) studies with a sample consisting >20% of patients with hematologic malignancy undergoing HSCT were included (this means studies with a mixed sample with different types of cancers e.g. breast cancer, lung cancer, etc., were included only if more than 20% of the total sample were diagnosed with any hematological malignancy and received the transplantation as treatment), (5) search

restricted to articles published only in English.

The predefined exclusion criteria for title/abstract screening were: (1) studies irrelevant to the subject of the study, (2) pediatric and adolescent population, (3) solely one sex sample (males or females), (4) studies reporting data from health care providers, caregivers or families, and hematopoietic stem cell donors, (5) patients with other types of cancer (e.g. solid tumors) or patients transplanted for non-malignant conditions and (6) terminal phase of the disease or palliative care provided.

Assessment of quality of trials

Two reviewers independently assessed the quality of the included trials with the PEDro scale. The PEDro scale is based on the Delphi list developed by Verhagen and colleagues and assists readers to quickly assess whether a clinical trial presents reliable and meaningful results for use in clinical practice. Items are scored as either present (1) or absent (0) and a score out of 10 is obtained by summation. The higher score indicates greater methodological quality.³⁰

RESULTS

Study selection

The Preferred Reporting Items for Systematic review and Meta-Analyses (PRISMA) flowchart gives a summary of the search strategy and the selection process of the articles included in this review, as shown in Figure 1. The initial search without filters yielded 2392 abstracts. Following the application of search filters, 1594 abstracts remained. After screening, using the exclusion and inclusion criteria, 86 articles were full-text assessed for eligibility. The material of the present study was primary based on nine articles that were further reviewed to ensure consistency with the search aim.³¹⁻³⁹

In one of these studies, the participants were all diagnosed with blood cancer, however the HSCT therapy was applied to almost one quarter (22.6%, n=42) of the total sample. This percentage was congruent with the predefined inclusion criteria, so the study was included in the final results.³⁸ In one other study, the total sample of the participants was consisted of breast (n=43.2%), gastrointestinal (29.7%) and hematologic cancer patients (n=27%) that were scheduled to receive their first course

of chemotherapy. Although the proportion of hematologic cancer patients was acceptable, it was not clear mentioned that infusion of healthy stem cells was also applied as a potential therapy. So the study was excluded from the final analysis.³⁹

As a result, a total of eight randomized trials were finally identified.³¹⁻³⁸ All research studies explored the methods used to provide information to patients undergoing HSCT. The included studies were conducted in USA and Canada (n=2), UK (n=1), Asia (n=1) and Europe (n=4). Almost all studies included patients treated at a single center^{31,33-35,37,38} except of two RCTs. In the one, potentially eligible patients were from seventeen US transplant centers (a multicenter trial)³² and in the other, were from the hematology departments at two participating hospitals in the Netherlands.³⁶

Sample features

A total number of 1550 patients (HSCT recipients or survivors) were included of which 743 received an intervention and 807 served as controls. Sample sizes in the eight studies included ranged from 30 to 755. Six of the studies provided full details for participants' and transplant characteristics for both the experimental and the control group^{31-34,36,38} while in the other two studies there was missing data for the control arm.^{35,37} According to the available data, the majority of the participants were over 45 years old, 53% male and 47% female. In terms of the transplant type, there were references for 885 and 433 patients receiving allogeneic and autologous transplantation, respectively. In terms of the diagnosis, patients were mainly treated for acute myeloid leukemia (n=390), Hodgkin/Non-Hodgkin lymphoma (n=349) and multiple myeloma/plasma cells diseases (n=305).

Intervention

In the context of these eight studies, a number of interventions were performed, using several methods to provide information and improve knowledge of HSCT recipients and survivors on different aspects of transplantation. In general, information was provided with the following attitudes used individually or combined: verbal instructions, printed materials such as booklets,

guides or brochures, audiovisual methods (e.g. animations), internet-based programs, telehealth calls, face-to-face counseling. All intervention procedures are summarized in Table 2.

Specifically, one trial applied a Therapeutic Patient Education approach (TPE), a week before hospitalization for transplantation, during which verbal instructions were provided, videos were projected and printed informative material was handed out to explain areas related to nursing care (main complications, hand hygiene, protective isolation and prohibitions), psychological and nutritional health related to the transplant.³¹

One multicenter study used an individualized Survivorship Care Plan (SCP) in a printed form that provided HSCT survivors with information on the potential HSCT-related late complications and recommendations regarding preventive care.³²

In five of the eight studies, information interventions were mainly based on specially designed websites.^{33,35-38} One of these studies proposed a website named as ALLINEX (Allograft Information Exchange) conducted for allogeneic HSCT-patients and was applied as an adjunct to standard practice.³⁵ One other study that provided web-based communication, added a new function called "Psychosocial support" and "support" was defined as including information, advice and guidance for conditions where individuals perceive themselves to be in need of some sort of help.³⁷ Finally, in three of these five studies, internet-based interventions were supplemented by methods such as: a telehealth-delivered problem solving treatment to HSCT survivors named as INSPIRE intervention (Internet-based Survivorship Program with Information and Resources)³³, face-to-face counselling and booklets (named as stepped care, conducted for autologous HSCT-patients and initiated after a 6-week buffer period)³⁶ and e-mail contact with a therapist.³⁸

To conclude, one RCT used audiovisual methods for providing information to stem cell recipients in addition to standard information. At this study patients were exposed to an informational animation in pre-transplant preparation.³⁴

Information interventions were mostly provided either by a clinician or a nurse, a transplant coordinator, a dietician, a psychologist or other qualified staff, but mostly by a multidisciplinary team.

Comparator

In most of the studies, control group received standard approach in information provision. Although the definition of standard approach is not standardized, it includes the routine procedures that each center used. These included standard verbal communication^{31,34,36,37} or printed informative materials (booklets or informative letters).^{31,32,34,35} To eliminate ethical problems, in some studies the control group had delayed access to the interventions, after participants completed the outcome assessment.^{33,38}

Risk of bias

Eight studies were included in the current review. The total PEDro scores ranged from 4 points to 9 points (Table 3). Quality and findings of the studies were inconsistent. The eligibility criteria were specified for all the included RCTs and in all studies participants were randomly allocated in treatment groups. Allocation concealment was clearly referred in six studies.^{31-33,36-38} Due to the nature of the information intervention, blinding procedures were difficult to implement for both participants and therapists; there were blind assessors in only one study.³⁶ Measures of at least one key outcome were obtained from more than 85% of the participants initially allocated to groups for all studies, except one.³⁵ All but one of the eight RCTs reported an intention-to-treat analysis.³³ Between-group statistical comparisons were implemented in six trials.^{31-34,36,38} Point estimates and variability for treatment effects were reported in all studies, except one.³⁷

Outcome measures

Five of the eight studies evaluated the impact of information methods on psychological distress, including anxiety and depression, with Hospital Anxiety and Depression Scale (HADS),³⁶ Cancer and Treatment Distress (CTxD),^{32,33} Symptom Checklist-90-R (SCL-90-R),^{31,33} Spielberger State-Trait Anxiety Inventory (STAI-state), Patient Health Questionnaire (PHQ-9)³⁶ and Brief Symptom Inventory (BSI).³⁸ Five of the eight studies measured the effect of the interventions on quality of life (QoL) emphasizing on the dimensions of physical, emotional, mental and role functioning. QoL was evaluated with European Organization for

Research and Treatment of Cancer Quality of Life (EORTC QLQ-C30),³⁶ Short Form Health Survey (SF-12, SF-36),^{32,33} Fatigue Symptom Inventory (FSI),³³ Cancer Linear Analogue Scale (CLAS)³¹ and Mental Adjustment to Cancer (MAC).³⁸

Other outcomes of the studies were patients' satisfaction with the models proposed and the level of knowledge achieved on various aspects of the transplant procedure and the survivorship care, measured with feedback questionnaires, scales^{32,34,35,38} or an empirical hermeneutic approach.³⁷ An overview of the outcome measures is presented in Table 4.

*Line space please***Distress and anxiety**

The results of the effect of information interventions on psychological distress in HSCT patients emerged from five studies.^{31-33,36,38} In three of them, patients randomized into the intervention groups reported a significantly greater reduction in distress symptoms than those of the control groups.³¹⁻³³ Two out of these three studies conducted information procedures that were based on printed material.^{31,32} Only one study implemented an online program to provide information to patients which was performed in addition to telehealth calls.³³ However, in the other two RCTs, information interventions were not found superior to standard care applied in control arms.^{36,38}

Depression

Four of the eight studies included in the current review, assessed the efficacy of information interventions in depression.^{31,33,36,38} However, only one of these four RCTs reported that depressive symptoms were reduced in the group exposed to a therapeutic patient education intervention aiming to improve participants' knowledge on various aspects of transplantation.³¹ No effect on depression was observed in the other studies.^{33,36,38}

*Line space***Quality of Life**

Quality of life was assessed in five RCTs. Three of the studies indicated statistically significant improvements in QoL scores for the intervention groups^{31,32,38} but for two studies no significant changes in QoL scale were found.^{33,36} In two RCTs there was an increase in mental health domain of QoL^{32,38} and in one there

was an overall improvement in QoL 14 days after transplantation.³¹ All studies used different measures to evaluate QoL.

Satisfaction

Patients' satisfaction with the information procedures was assessed in five RCTs.^{32,34,35,37,38} Regarding the utilization of the suggested methods in the intervention groups, evaluation demonstrated that all informative programs were useful and helpful for patients and satisfaction levels were higher than in control groups. In one of these five studies, despite there was no significant difference between groups with regard to overall satisfaction, analysis showed a greater satisfaction with the written consent form in the study group compared with the control group. The participants in this study were HSCT recipients and not survivors.³⁴

DISCUSSION

The present systematic literature review was conducted to detect methods used to facilitate the passage of information from health professionals to hematologic cancer patients undergoing HSCT and then evaluate their effectiveness on psychological wellbeing, QoL and levels of patients' satisfaction with information provided. Eight studies were included, according to the predefined inclusion criteria.

The estimated quality of the included trials, according to PEDro scale, ranged from fair (score 4-5 at two studies) to good (score 6-8 at five studies) and one study was reported as of high quality. Although quality scores seem to be acceptable, due to the nature of the studies, most of them had a difficulty to implement "blinding" processes appropriately.

Moreover, there are some methodological issues that impede drawing strong conclusions on the impact that the proposed information interventions had on patients' QoL, psychological distress and level of satisfaction. It has to be noted that outcome measures used were different for almost all studies. Most instruments have been validated in cancer survivors in general, but not among HCT recipients, and it is possible that they did not adequately measure the underlying outcomes in our patient population. This makes it difficult and unsafe to compare the results of different studies.

In the experimental conditions included in our review, HSCT patients rated the information attitudes positive, felt satisfied with the overall received information and found it helpful.^{32,34,35,37,38} However, only three intervention studies observed positive relations with QoL^{31,32,38} and distress or anxiety³¹⁻³³ and only one with depression.³¹ These findings are confirmed for the most part by RCTs for cancer patients, published between 2001 and 2008. A Greek study of 145 cancer patients who were randomized to receive or not receive a booklet about chemotherapy, showed that patients provided with the information booklet reported significantly higher rates of satisfaction with information than the control group, felt better and more informed, and perceived the information received as being clearer and more detailed. However, no significant benefits in anxiety, depression and QoL occurred.⁴⁰ Another study randomized non-small cell lung cancer patients to receive oral information only or oral plus written information describing the disease and its associated surgery and outcomes. The QoL scores for each dimension (anxiety, depressed mood, positive well-being, self-control, general health and vitality) were not statistically different between both groups at each time of analysis.⁴¹ In a Swedish study, 210 consecutive cancer patients were randomized to one of three information conditions before the start of curative radiation treatment: a) standard information plus group and repeated individual information, b) standard information plus brochure, and c) standard information only. Patients receiving standard information plus group and repeated individual information were significantly more satisfied with the information than were patients in the remaining two groups. However, there were no differences with respect to anxiety, depression, subjective distress and QoL.⁴² These three RCTs described above, referred to a period not included in the current review and evaluated a diverse cancer population, without a reference to hematologic malignancies.

Regarding the type of information preferred from the HSCT patients, according to satisfaction levels reported, the studies reviewed illustrated that enhanced and structured informative interventions overweight standard approach.^{32,34,35,37,38} A wide range of strategies were implemented: three of the five RCTs have chosen to study the effectiveness of web-based methods

for information provision,^{35,37,38} while others have studied the impact of printed materials³² or informational animations in addition to standard verbal and written information.³⁴ All of the studies have shown a positive effect of all information strategies on participants' satisfaction. On the one hand, website seemed easy to use for patients that were confident in using computers. On the other hand, the provision of additional written information was a cost-effective method, caused minimal disruption in a busy clinic and had a benefit on knowledge, recall and symptom management, while a visual method contributed to better understanding and decreased perception difficulties arising from language and intellectual differences. Taking notice of these findings, it is difficult to draw conclusions which method is superior. Therefore, more extensive research is needed to evaluate other sources of information, bearing in mind that openness in communication and the imparting of sufficient and appropriate information to patients constitute a part of comprehensive cancer care.

Other factors that may have influenced the effects of informative methods on QoL, psychological well-being and satisfaction reported in this review are: the timing offering the information intervention, patients' current health status and the assessment location. For example, providing HSCT patients with structured information after allowing for their initial physical recovery, which means about six weeks after transplantation,³⁶ may not have been appropriate. Emotional problems may occur at that point in time, but also in an earlier stage of the treatment process or, conversely, in a later stage. The timing of offering the intervention should be flexible, fitting patients' needs. Moreover, the outcome assessment was held in different environments; either at the transplant unit or at a local hospital for follow-up care after transplantation or at home. Different conditions and circumstances can probably influence patients' behavior and perceptions and should be kept in mind when an intervention is designed.

It is notable, that in the studies included in the review the follow-up period ranged from about one month to 42 weeks after transplantation. Half of the studies were designed to examine long-term (above three months) follow up.^{32,33,35,36} Unlike communication satisfaction, it is perhaps unreasonable to expect

benefits on emotional distress and QoL over the short-term but rather over the medium and longer terms. Further trials with repeated measures over longer follow-ups are needed before definitive results will be made available.

In summarizing, the current review suggests that structured and personalized informative procedures can have positive effects on QoL, psychological distress and HSCT patients' satisfaction. However, it demonstrates that the research published so far on this topic has limitations with respect to: a) the small number of studies and participants; HSCT is a rare treatment and therefore the research field is limited and so is the number of eligible patients available to take part in the studies; b) the significant heterogeneity with respect to diagnosis, transplant type, stem cell source, conditioning regimen, and supportive care; The pre-transplant treatment and disease course could differ significantly based on diagnosis, responses to initial treatment approaches, and other risk characteristics, with some patients undergoing HSCT as part of first-line therapy, whereas others received transplants in second or later remissions.

CONCLUSION

Concluding and keeping in mind that the majority of cancer patients want as much information as possible, delivering the best information to HSCT patients who undergo an increasingly complex treatment would be worthy of further study. It would have been useful if we had more well-designed longitudinal multicenter studies, with carefully selected target populations and with consistency in the methodological approach, assessment and interpretation.

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ANNEX

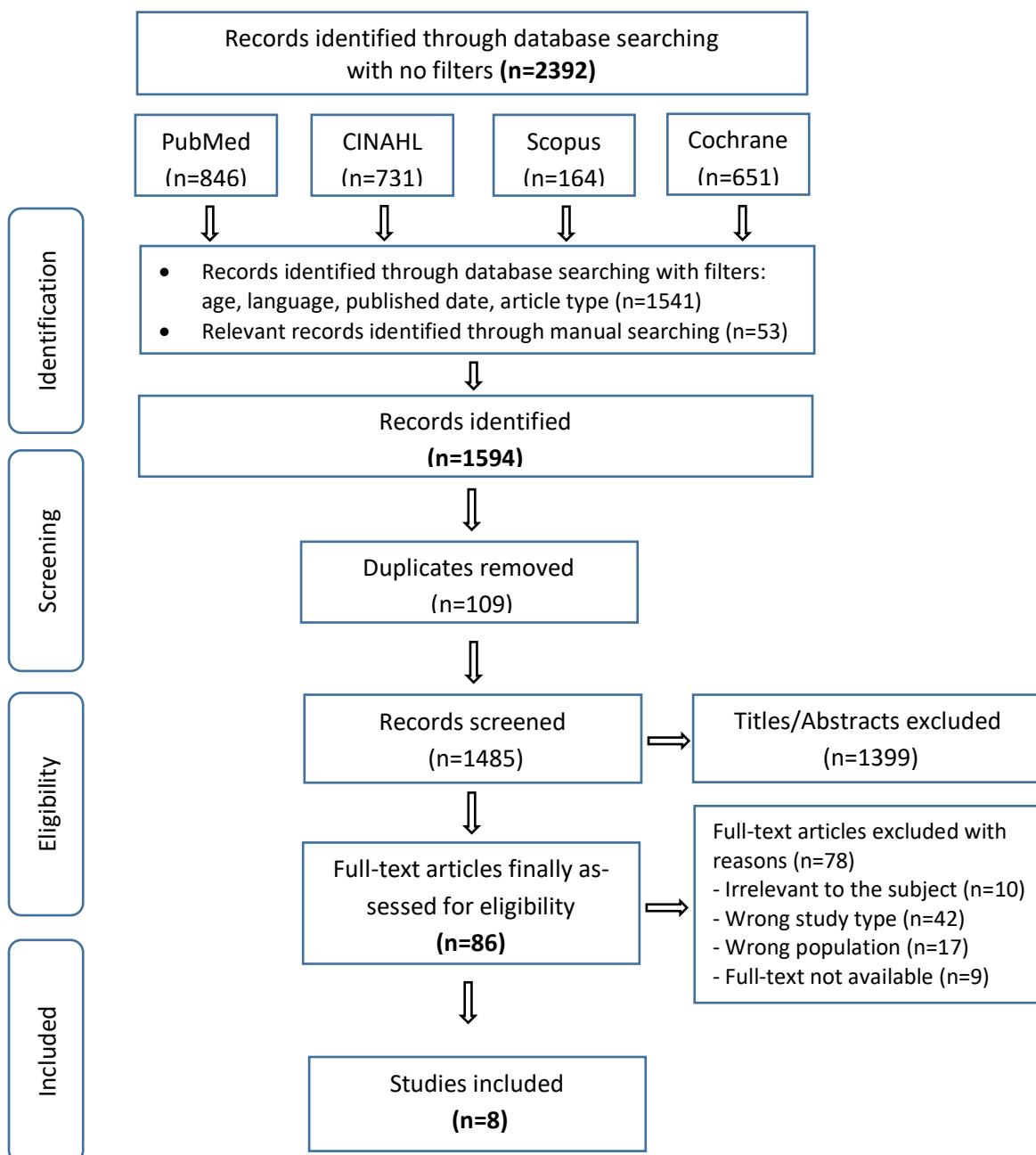
FIGURE 1. PRISMA flow diagram illustrating the inclusion and exclusion process of the literature.

TABLE 1. PICO criteria.

Population		Adults, Aged 18+ With a diagnosis of Hematologic neoplasm* OR Hematologic malignancy* OR Bone marrow transplant OR Hematopoietic stem cell transplant
Intervention	AND	Information provision OR Access to information OR Information needs OR Information seeking behavior OR Information resources
Comparison	AND	Compared with usual information practice
Outcome	AND	Effective on quality of life OR Health related quality of life (HRQoL) OR Wellness OR Patient satisfaction

TABLE 2. Characteristics of the studies investigating methods of information provision in hematologic malignancies undergoing stem cell transplant.

Study (Year, coun- try)	Sample	Intervention	Comparison	Outcomes	Type of Study
Cioce M. et al (2020) Italy^{31*}	36 Allogeneic HSCT ¹ patients	TPE (Therapeutic Patient Education) = included 60-minutes interviews, a week before transplant hospitalization. Verbal instructions, videos & printed material were used. Follow-up: till discharge after HSCT.	Standard approach & printed informative material about transplant procedure.	The exposed group had statistically better scores on HRQoL ³ 14 days after transplantation and anxiety and depression were better controlled both at hospitalization and discharge. Patients' knowledge also improved.	One center RCT ²
Majhail NS. et al (2019) USA³²	458 HSCT survivors (1-5 years after transplant)	An informative letter plus printed Survivorship Care Plan (SCP). A 6-month assessment.	Standard care= only an informative letter.	Significantly lower distress scores at 6-months for the intervention group. SCP improved mental domain of HRQoL.	Multicenter RCT
Syrjala KL. et al (2018) USA or Can- ada³³	755 HSCT adult survivors (3-18 years after transplant)	Group 1= met impaired symptom criteria → - INSPIRE + PST (Internet-based Survivorship Program with Information and REsources plus Problem Solving Treatment calls), - INSPIRE access alone Group 2= no impaired scores → INSPIRE alone A 6-month follow-up.	Control group= delayed INSPIRE access after 6-month assessment.	Participants randomized to INSPIRE + PST demonstrated improvement in distress, compared to controls. No differences in depressive symptoms and physical functioning.	RCT at a single transplant center
Sariturk C. et al (2017) Turkey³⁴	82 recipients of HSCT	A 10-min audiovisual information plus standard verbal and written information in the pre-transplant period.	Standard verbal and written information (lasted 30 minutes).	No significant difference between groups with regard to overall satisfaction with the information provided. Satisfaction with the written informed consent form was greater in the intervention group.	Prospective randomized single-center study
Horne B. et al (2016) UK³⁵	52 Allogeneic HSCT adult survivors	A specifically designed Website (ALLINEX=ALlograft Information Exchange) as an adjunct to standard care. A 12-week follow up.	Standard care only (an information booklet was given prior HSCT).	No results mentioned for the control group. Most participants stated ALLINEX as useful (63%), helpful (84%) and with acceptable usability.	One center Randomized pilot study (in Phase 4 of the project)

Braamse AM.J. et al (2016) Netherlands³⁶	95 Autologous HSCT adult patients with hematological malignancies.	Stepped care treatment initiated 6 weeks after HSCT: 1) Watchful waiting, 2) Internet-based self-help program or a booklet-based intervention for patients without access to internet, 3) individual face-to-face counseling. Follow-up up to 42 weeks after HSCT.	Care as usual= emotional support provided regularly during follow-up visits.	No statistically significant difference between groups on distress and HRQoL domain physical functioning.	Two-armed RCT, in two hospitals
Högberg KM. et al (2015) Sweden³⁷	30 patients with hematological malignancies. No clear reference to the number of HSCT patients.	Web-based communication= to the existing national case management system "My care contacts", the new function "Psychosocial support" was added (=it included advice, guidance, information) A 2-month follow-up.	Standard care= psychosocial support from physician, nurse, counselor, chaplain, dietitian, physiotherapist.	The hermeneutical approach of the Web-based communication for support, indicated that patients had the opportunity to communicate on more equal terms with the nurse, have control over the content and time dimensions, feel safe.	One center pilot RCT
David N. et al (2013) German³⁸	186 hematologic cancer patients of which n=42 (22.6%) were treated with HSCT.	Internet-based program for coping with cancer plus e-mail contact with a therapist= an interactive self-help program for individual use. A 4 week follow-up.	Waiting list group	Patient satisfaction with the intervention program was high. The intervention group scored significantly higher on the Mental adjustment to cancer scale (the "fighting spirit" domain). No effect on distress.	One center RCT

1. HSCT= hematopoietic stem cell transplant, 2. RCT=Randomized controlled trial 3. HRQoL= Health Related Quality of Life
*31-38= numbers according Reference list.

TABLE 3. PEDro Scale for rating quality of randomized controlled included studies.

Study (Author, Year)	PEDRO criteria* (1= "Present", 0="Absent")											Quality (Total of "Present")
	1\$	2	3	4	5	6	7	8	9	10	11	
Cioce M. et al (2020),^{31**}	1	1	1	1	0	1	0	1	1	1	1	8/10
Majhail NS. et al (2019),³²	1	1	1	1	1	1	0	1	1	1	1	9/10
Syrjala KL. et al (2018),³³	1	1	1	1	0	0	0	1	0	1	1	6/10
Sariturk C et al (2017),³⁴	1	1	0	1	0	1	0	1	1	1	1	7/10
Horne B. et al (2016),³⁵	1	1	0	1	0	1	0	0	1	0	1	5/10
Braamse AM.J. et al (2015),³⁶	1	1	1	1	0	0	1	1	1	1	1	8/10
Högberg KM. et al (2015),³⁷	1	1	1	0	0	0	0	1	1	0	0	4/10
David N. et al (2013),³⁸	1	1	1	1	0	0	0	1	1	1	1	7/10

* 1\$. Eligibility criteria were specified (*not included in the total score*), 2. Subjects were randomly allocated to groups, 3. Allocation was concealed, 4. The groups were similar at baseline regarding the most important prognostic indicators, 5. There was blinding of all subjects, 6. There was blinding of all therapists who administer the therapy, 7. There was blinding of all assessors who measured at least one key outcome, 8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups, 9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, were this was not the case, data for at least one key outcome was analyzed by intention to treat, 10. The results of between-group statistical comparisons are reported for at least one key outcome, 11. The study provides both point measures and measures of variability for at least one key outcome.

**31-38= numbers according to References list.

TABLE 4. Overview of outcome measures.

Outcomes	Nº of studies	Measures
Distress Anxiety Depression	5	<ul style="list-style-type: none"> - CTXD (Cancer and Treatment Distress) - HADS (Hospital Anxiety and Depression Scale) - SCL-90-R (Symptom Checklist-90-R) - STAI-state (Spielberger State-Trait Anxiety Inventory) - BSI (Brief Symptom Inventory) - PHQ-9 (Patient Health Questionnaire)
Quality of Life	5	<ul style="list-style-type: none"> - SF-12 (Short Form 12 Health Survey) - SF-36 (Short Form 36 Health Survey) - EORTC QLQ-C30 (European Organization for Research and Treatment of Cancer Quality of Life) - CLAS (Cancer Linear Analogue Scale) - FSI (Fatigue Symptom Inventory) - MAC (Mental Adjustment to Cancer)
Satisfaction	5	<ul style="list-style-type: none"> - Satisfaction score with information provided (questionnaire) - CSQ-8 (Client Satisfaction Questionnaire) - Health Care Utilization - CSI (Confidence in Survivorship Information) - PAUT (Patient Acceptance and Use of Technology) - SUS (System Usability Scale) - Feedback questionnaires - Hermeneutics (interpretation according to Gadamer)
Problem solving	1	<ul style="list-style-type: none"> - SPSI-R (Social Problem Solving Inventory-Revised)
Self-efficacy	1	<ul style="list-style-type: none"> - DGSS (Dutch General Self-efficacy Scale)