

Health & Research Journal

Vol 9, No 4 (2023)

Volume 9 Issue 4 October - December 2023



Volume 9 Issue 4 October - December 2023

EDITORIAL

PATIENT SAFETY AND QUALITY OF HEALTH CARE PROVIDED

RESEARCH ARTICLES

WHAT IS STRESS IN EPILEPSY? A CONTENT ANALYSIS AND AN OPEN LETTER TO THE WORLD HEALTH ORGANIZATION (WHO): HIGHLY TIME TO DEFINE STRESS

THE EFFICACY OF A SPECIFICALLY DESIGNED PRINTED MATERIAL ON SATISFACTION FROM INFORMATION PROVISION AND QUALITY OF LIFE OF HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS: A RANDOMIZED CONTROLLED TRIAL

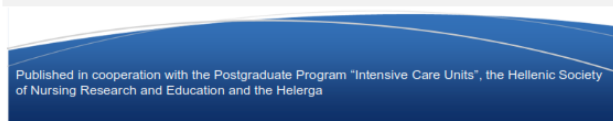
THE INFLUENCE OF CANNED LAUGHTER IN THE SENSE OF HUMOR OF HEALTHY GREEK ADULTS. A PILOT STUDY WITH DEBATABLE RESULTS.

A STUDY OF THE BIOPSYCHOSOCIAL REHABILITATION OF PATIENTS WITH MYOCARDIAL INFARCTION SIX MONTHS AFTER THEIR DISCHARGE FROM THE CARDIAC CARE UNIT

HIGH-VS MEDIUM-FREQUENCY NEUROMUSCULAR ELECTRICAL STIMULATION PROTOCOLS ON MUSCLE MASS IN INTENSIVE CARE UNIT PATIENTS, A PILOT STUDY

SYSTEMIC REVIEW

FREQUENCY OF NURSING STUDENT MEDICATION ERRORS: A SYSTEMATIC REVIEW



Published in cooperation with the Postgraduate Program "Intensive Care Units", the Hellenic Society of Nursing Research and Education and the Helergo

The efficacy of a specifically designed printed material on satisfaction from information provision and Quality of Life of hematopoietic stem cell transplantation patients: A randomized controlled trial

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doi: [10.12681/healthresj.33968](https://doi.org/10.12681/healthresj.33968)

To cite this article:

Kiropoulou, A., Katsareli, M., Zyga, S., Nanas, S., & Vasileiadis, I. (2023). The efficacy of a specifically designed printed material on satisfaction from information provision and Quality of Life of hematopoietic stem cell transplantation patients: A randomized controlled trial. *Health & Research Journal*, 9(4), 186-200. <https://doi.org/10.12681/healthresj.33968>

RESEARCH ARTICLE

THE EFFICACY OF A SPECIFICALLY DESIGNED PRINTED MATERIAL ON SATISFACTION FROM INFORMATION PROVISION AND QUALITY OF LIFE OF HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Background: Patients with hematological malignancies who undergo hematopoietic stem cell transplantation (HSCT) face complex challenges and need appropriate information to help them cope with the physical and psychological demands of their treatment and experience greater health related quality of life (HRQoL). This study investigated the impact of a specially designed booklet about HSCT, on patients' satisfaction from information, overall emotional distress and HRQoL.

Method and Material: A total of 127 HSCT patients were randomly assigned to receive standard verbal information (control group, n=63) or the additional printed information (intervention group, n=64). Patients' satisfaction was assessed at two time-points; at admission to the transplant unit and at discharge. Emotional distress and HRQoL were also evaluated at 3 and 6 months post-HSCT. Intention-to-treat analysis was performed.

Results: Patients' characteristics were similar in the two arms. The experimental group reported highest levels of satisfaction when compared with patients attending standard verbal approach ($p<0.004$). No significant differences between groups were noted, regarding patients' desired attitude about the amount of perceived information. Overall, 65% of patients wanted all the available information. Most participants considered that the booklet was easy to read and helpful in recalling medical instructions. High levels of satisfaction were strongly correlated with reduction in anxiety levels and improvement in overall HRQoL, at discharge from the transplant unit.

Conclusion: Our results demonstrate printed materials can be a beneficial and practical method for patients to gain comprehensible information for HSCT. However, further well-designed, longitudinal multicenter randomized trials are needed to confirm our findings.

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

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Cite as: Kiropoulou, A., Katsareli, M., Zyga, S., Nanas, S., Vasileiadis, I. (2023). The efficacy of a specifically designed printed material on satisfaction from information provision and quality of life of hematopoietic stem cell transplantation patients: A randomized controlled trial. *Health and Research Journal*, 9(4), 186-200. <https://ejournals.epublishing.ekt.gr/index.php/HealthRes/>

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a complex procedure and one of the most aggressive treatments for hematological disorders, that requires high doses of chemotherapy, and in some cases radiation, to eradicate the disease.^{1,2} HSCT patients accept significant risks in return for the possibility of cure and face numerous physical, mental and emotional challenges across the HSCT trajectory.¹ Psychosocial distress often results from regimen-related toxicities, long periods of isolation, lengthy in-hospital stays, a range of symptoms induced by graft versus host disease (GvHD) and long lasting complications.² High rates of anxiety and depression are evident amongst hematological cancer patients undergoing HSCT and may be minimized by ensuring that patients are adequately prepared for such threatening procedures. This presupposes that patients are provided with tailored information and are sufficiently involved in decision making.³⁻⁵

Although little work has been done with patients diagnosed with hematological cancers, research with other cancer patient groups (solid tumors), suggests clinicians should be able to identify the amount and type of information patients wish to receive and to recognize their preferences for the extent of their involvement in decision making. The provision of relevant, up to date and understandable information is seen as an important dimension of quality in patient-centered cancer care. There is now clear evidence to suggest that the need for detailed information is especially elevated among cancer patients and their families. The majority of cancer patients (>80%) want as much information as possible about their disease, treatment and rehabilitation.⁶⁻⁸

However, the general pattern that emerges from the literature is that large numbers of patients with cancer often report poor understanding and recall of what doctors tell them and, in addition, often express dissatisfaction with the quantity (defined as the amount of received information) and quality (defined as the usefulness of the received information) of information they receive about aspects of their disease and treatment. Poorly informed patients are less likely to comply with treatment and adhere to medical advice, or participate in the medical decision-making process. They are also more likely to experience a high degree

of uncertainty and anxiety, or seek scientifically unacceptable therapies.^{5,8,9}

The goal of providing sufficient information is to prepare patients for their treatment, to increase adherence and abilities to cope with the illness, as well as to promote recovery. Adequate information can reduce patients' psychological burden and improve their health related quality of life (HRQoL) and satisfaction with care. It has been shown that in order to be effective, preparatory information should be clear and easy to comprehend, responsive to patients' needs and preferences and in accordance with their cognitive coping style.⁹⁻¹³

There are a number of existing approaches to providing information to cancer patients. These include patient-clinician interaction, written/printed leaflets, audio-visual materials, telephone helplines, and more recently, websites accessed via the Internet.^{1,14-17} Recent reviews of randomized controlled clinical trials (RCTs) have evaluated the impact of information-giving interventions and demonstrated that in the main, these methods are effective, when enhancing understanding, knowledge and recall, and promoting satisfaction with communication. However, some information sources often are not tailored to the individual needs of cancer patients. The appropriate satisfaction of information provision preferences has been associated with positive health outcomes. With regard to anxiety and depression, the evidence is equivocal, because a number of studies have shown positive effects, whereas others have shown no benefit. Much less is known about the impact of information-giving tools on overall HRQoL. Concerning the efficacy of information interventions specifically for hematological cancer patients undergoing HSCT, there has been limited published research.^{1,2,17-22}

We hypothesized that a patient-centered information intervention, performed as a face-to-face discussion supplemented with written material about HSCT, would increase satisfaction levels from information provision (primary outcomes), improve HRQoL and reduce levels of psychological distress (secondary outcomes), in an assessment up to six months after transplantation. In a RCT we investigated the efficacy of an information booklet, especially designed for Greek hematological cancer patients undergoing HSCT.

MATERIALS AND METHODS

Study design

A prospective non-blinded, one single center RCT was conducted at the Department of Hematology and Lymphomas and Blood and Marrow Transplantation (BMT) Unit of Evangelismos Hospital in Athens, between January 2018 and September 2020.

Patient eligibility

Patients were eligible to participate if they had: a confirmed diagnosis of hematological malignancy (myeloma, lymphoma, leukemia), scheduled to be treated with HSCT for the first time; were aged 18 years or older and were able to provide informed consent. Non-Greek patients were excluded, as were those who were illiterate or had vision impairments that could affect their ability to read. Also exclusion criteria comprised pre-existing major psychiatric problems, therapy with CAR-T cells and relapse or reoccurrence of major disease, requiring supplementary transfusion of hematopoietic stem cells. Patients received follow-up care after HSCT at the hospital where they had been transplanted. Eligible patients were identified by the clinical trial nurse.

Recruitment and consent procedure

Patients were recruited from the inpatient BMT Unit of the hospital. The clinical trial nurse approached patients shortly after their admission to the BMT Unit and invited them in-person to participate in the study. An information sheet and a consent form were provided to patients, explaining the nature and the purpose of the study, outlining of their right to withdraw at any time and guaranteeing their privacy and anonymity. Patients who indicated an interest in participating, were asked to sign the consent form before randomization. Identifiable data was anonymized via a Unique Participant Number (UPN), given automatically at admission time through the electronic record system.

Randomization and blinding

Randomization was performed by the transplant coordinator nurse, in order to prevent selection bias from the clinical trial nurse, using a random digit generator and sealed envelopes. Health care providers and the clinical trial nurse were blinded to the allocation sequence. However, neither participants nor the

research team could be blinded to the intervention applied. Patients were informed about their assignment exactly after they signed the informed consent. A research assistant, not involved in the intervention delivery, carried out all data analysis.

Sample size

A priori power analyses indicated a required sample size of N=128 patients at baseline (64 per arm), with an anticipated dropout rate of 10% from baseline up to 6 months. The sample size was determined to achieve 80% power, at a 0.05 significance level.

The Information procedure

Each patient allocated to the experimental group attended an information session given by the clinical trial nurse, during which patients were given a booklet about HSCT, especially designed for the current study. The average time for the completion of the presentation was approximately 30 minutes. Afterwards patients were encouraged to ask questions and express concerns. The research protocol prescribed that the nurse would not provide any additional information other than that included in the booklet. Questions that could not be addressed by the nurse were referred back to the treating hematologists. At the end of the session, patients were given the booklet to read again whenever necessary.

The booklet used in the intervention was entitled 'Stem cell transplantation - an information guide for patients' and it consisted of 32 pages, altogether with illustrations. The content was designed to outline both the procedures and the sensations the patient would experience, as well as to present practical instructions on diet, precautions and self-care, pointing out that booklets cannot substitute the discussion with the doctor or the register nurse. Its sections were headed: *'Introduction: general information about blood and blood marrow'*, *'General information about HSCT: the major types of transplantation and sources of transplants'*, *'Detailed information about your stay at the BMT unit (your room, the recommended precautions to prevent infections, your daily program of care, your caregivers' role, the appropriate diet to follow)'*, *'Detailed information about HSCT (conditioning treatment, stem cell infusion, side-effects, duration of hospitalization)'*, *'Information and useful advice about your discharge from the BMT unit and the immediate post-transplant period'*

(medication compliance, coming back safely to daily life, recognizing the symptoms you must immediately report to the healthcare team, next follow-up appointment with your doctor)' and 'Information to keep in mind (contact list, important highlights about medicine, diet and hygiene)'. The information tool was pilot tested on 6 randomly selected patients (they were excluded from the final sample), who gave feedback on content and structure. Their feedback was evaluated and incorporated, if recommended changes reflected the views of the majority.

In the control condition of the study, patients received the routine verbal information about HSCT, provided during the treatment consultation by the medical hematologist and it was supplemented with a brief written material, explaining the treatment process and its consequences, accompanied with a consent form, necessary to be signed by all recipients before transplantation.

Data collection

Medical records and hospital charts were consulted to retrieve clinical and basic sociodemographic data (sex, age). Clinical data included transplant details, information about diagnosis, length of stay at the BMT unit, Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI), the Karnofsky Performance Scale Index (used to classify patients as to their functional impairment). Additional sociodemographic data (marital status, educational level, occupation, place of residence) were elicited from patients, using a study-specific questionnaire. Data of non-consenters was also recorded to allow for possible consent bias to be examined.

Study measures

Data collection was carried out at four measuring time-points: the day of admission to the BMT unit (T1, baseline), day of discharge (T2), 3 months (T3) and 6 months post-HSCT (T4). Validated and self-report questionnaires were used to collect data according to the objectives set at the current study. The internal consistency of the (sub)scales of all questionnaires was satisfied (Cronbach's alpha >0.70). Mean time taken to complete all questionnaires was about 10-15 minutes.

Information Satisfaction Questionnaire (ISQ)

A one A4-page questionnaire, freely available on [www.cancer-](http://www.cancer-net.co.uk)

[net.co.uk](http://www.cancer-net.co.uk) was used to measure patients' satisfaction to information provided. The questionnaire was completed at baseline and T2 time. It incorporated five categories of information: explanation of the illness (diagnosis); types of treatment available (options and benefits); information on side effects (early and late side effects of HSCT); advices on lifestyle (diet, medicine, support, social life, sexual issues) and other practical daily issues (follow-up plans). The score for each section was rated on a 5-point Likert scale, from 0 (very unsatisfied) to 4 (very satisfied). An additional question was also included to give patients the opportunity to provide a score for satisfaction with the overall information provided. The total score ranged from 0 to 24. A cut-off score ≥ 15 indicated patients' better satisfaction with the information they received. Finally, patients' perceptions about the amount of information they desired to receive were also measured with a single item, where three possible answers to choose were described: 'I would like all available information and be involved in decision about my illness'; 'I would only like positive information about my illness' and 'I would only like limited information and would prefer the doctor to make decisions on my behalf'.²³

Hospital Anxiety and Depression Scale (HADS)

This self-report questionnaire was used to measure psychological distress and consisted of 14 items rated on a 4-point likert scale (range 0-3), 7 items for anxiety (HADS-A) and 7 for depression (HADS-D). The score ranged from 0 to 21, with higher scores indicating higher levels of anxiety or depression. A cutoff score ≥ 8 was used to determine symptoms of anxiety or depression.²⁴

Functional Assessment of Cancer Therapy–Bone Marrow Transplant (FACT-BMT)

The FACT-BMT (Version 4) questionnaire was used to assess patients' HRQoL. The 50-item FACT-BMT evaluated the effects of cancer therapy in the five major areas of: physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), functional well-being (FWB) and BMT related concerns (BMTs). Responses were assessed on a 5-point Likert scale ranging from 'not at all' to 'very much,' with higher scores representing higher levels of HRQoL. Raw scores were linearly transformed to values between 0 and 100.²⁵

Patients completed the HADS and FACT-BMT questionnaires, both used to assess the secondary outcomes, at all four time-points (baseline, at discharge time, 3 and 6 months post-HSCT).

The booklet evaluation

At T2 time, the intervention group patients also completed a short questionnaire to evaluate the usage and properties of the booklet administered. Patients were asked about the number of times they read all (or part) of the booklet and whether they would recommend it to other patients. In addition, four 5-point items, from 1 (not at all) to 5 (very much), asked patients to indicate how useful, easy to read and understandable the booklet was and whether it helped them to better recall medical instructions and advice. Finally, patients rated their overall satisfaction on a 5-point scale item from 1 (very dissatisfied) to 5 (very satisfied), with higher scores indicating higher satisfaction. All items scored from 1 to 25. Score ≥ 18 indicated satisfactory acceptance of the booklet.

Statistical analysis

All continuous variables were tested for normality with the Kolmogorov-Smirnov test. Patients groups were compared with Chi-square, independent sample t-test and Mann-Whitney test, where appropriate. Spearman's correlation coefficient (ρ) was used to test the relationship of two variables non-normally distributed. A mixed Analysis of variance (ANOVA) with repeated measures was performed in order to estimate if there was an interaction 'within-subjects' factor (4 time-points) and 'between-subjects' factor (type of information) on the dependent variables (anxiety, depression and HRQoL). Post-hoc comparisons were performed with Bonferroni test. The level of significance was set at $p < 0.05$. SPSS Statistics version 26 software was used for data analysis.

RESULTS

A total of 157 subjects who were scheduled to undergo autologous or allogeneic HSCT, were invited to participate in the study. Of these, 30 did not meet eligibility criteria. The flow chart of the study is shown in Figure 1. The remaining 127 eligible patients were randomized to the experimental group ($n=64$) or the control group ($n=63$) and the response rate was 72.4% at all four

time-points. An intention to treat approach (ITT) was used for the analysis. No significant differences were revealed at baseline between responders and non-responders to the study, neither between the two intervention groups, for any of the sociodemographic and clinical characteristics. The average age of the patients was 49.2 years ($SD=12.1$) and 52% ($n=67$) were males. Leukemia was the most common diagnosis. Although 37.8% of patients ($n=48$) had one or more comorbidities, almost all participants (98%) were able to carry on normal activity with no obvious evidence of disease, according to Karnofsky performance status scale (Table 1).

Primary outcome measures – satisfaction from information provision

No reliable differences emerged between information groups at baseline phase according to ISQ questionnaire. However, statistically significant differences emerged on overall satisfaction levels between groups at T2 time-point ($p < 0.004$). Participants that received both verbal and written information rated higher their satisfaction, in comparison to the control group patients ($Md=19$, $IQR=16-22$ vs $Md=18$, $IQR=16-18$). Moreover, statistically significant differences were also demonstrated for the intervention group patients between time-points (T1 vs T2). The ISQ medians indicated that experimental group patients reported significant highest levels of satisfaction at discharge time in comparison to baseline assessment ($Md=19$, $IQR=16-22$ vs $Md=16$, $IQR=14-19$, $p < 0.001$), (Figure 2). The dimensions of information referred to 'the possible side-effects of the HSCT' and to 'patients' future situation when they leave the hospital', gathered the lowest score between all answers. No significant differences were noted regarding patients' desired attitude about the amount of perceived information. Overall, the majority of participants (65%) wanted all the available information and taking part in decision making.

Secondary outcome measures

Clinically significant anxiety symptoms were observed prior to transplant, while depressive symptoms were absent. No reliable differences emerged between groups in the HADS and FACT-BMT questionnaires, at baseline evaluation. A mixed ANOVA

analysis with repeated measures determined that mean HADS-A score differed significantly over time [$F(2.05,255.64)=113.78$, $p<0.001$]. Moreover, there was a significant interaction between 'information condition' and 'time' [$F(2.05,255.64)=7.39$, $p=0.001$]. The mean scores of anxiety levels for both groups decreased over time, but the reduction was greater for those that followed written plus verbal information versus only verbal, 3 and 6 months post-HSCT. In addition, there was a significant main effect of time on HADS-D scores [$F(2.39,298.49)=38.39$, $p<0.001$] and a significant interaction between 'groups' and 'time' [$F(2.39,298.49)=3.23$, $p=0.032$]. A significant increase in depression levels was observed at T2 and T3 time-points and returned to baseline levels 6 months post-HSCT, for both groups. However, patients at the intervention group experienced significantly lower levels of depression at T2 time-point, compared with control group patients (Figure 3). In what concerns the FACT-BMT subscales, experimental group patients experienced a statistically significant improvement in emotional functioning (EWB) over time, compared with control group patients ($p<0.05$). The EWB was the only subscale that indicated a significant interaction between 'information condition' and 'time' [$F(2.46,306.95)=3.98$, $p=0.013$]. Patients for both groups experienced worse overall HRQoL at discharge time, but improved over time. The FACT-BMT Total score was significant higher for the intervention group patients (Table 2).

Correlations were estimated for the intervention group, taking into account ISQ total score at T2 time-point. Results indicated that there was a statistically significant negative, very strong relationship between the ISQ total score and anxiety levels ($\rho=-0.895$, $p=0.01$) and a significant but weak correlation between the ISQ total score and depression levels ($\rho=-0.360$, $p=0.01$), at discharge from the BMT unit. Moreover, there was a statistically significant, positive and strong relationship between satisfaction and overall HRQoL and also the EWB subscale of the FACT-BMT questionnaire ($\rho=0.697$, $p=0.01$ and $\rho=0.699$, $p=0.01$, respectively).

Booklet evaluation

Of the 64 experimental group patients all but one (98.4%) read the booklet and 42% read it an average of more than once. The

majority of patients (87%) rated the booklet as easy to read and 75% reported that it helped them to recall medical instructions and advice. Patients also rated the booklet as helpful to manage with the HSCT experience and they would recommend it to other patients. However, 41% of patients were not highly satisfied overall with the booklet.

DISCUSSION

To our knowledge, the current single-center RCT is the first to evaluate the impact of a specifically designed printed material about the HSCT therapy, aimed at improving satisfaction, psychological distress and overall HRQoL, in Greek patients with hematological malignancies, treated with autologous and allogeneic stem cell transplantation. A central finding of our work was that the majority of participants preferred shared decision-making and wanted to receive all the available information. Moreover, patients attending the written information session, in addition to the standard verbal explanations, reported significantly higher rates of satisfaction with the information, than those allocated to the control group, at discharge time-point (T2). The dimensions of information referred to 'the possible side-effects of the HSCT' and to 'patients' recovery far away from the hospital', gathered the lowest score in the ISQ questionnaire. Importantly, increased satisfaction was associated with a reduction in anxiety and depression levels and an improvement in HRQoL across time, assessed with the HADS and FACT-BMT scales, respectively. Finally, the booklet was widely accepted for its usefulness and usability. It seemed to have adequately provided the information the majority of the HSCT patients needed, to help them recall and understand medical advice.

Our results are consistent with the findings of other studies that revealed that face-to-face discussions to communicate all desired elements about cancer to patients and survivors may not be adequate, if used individually. Information provided by verbal explanations only is likely to be forgotten easily, especially when the content of information was complex and the amount of data was large.^{16,26} Recent results showed that when information is offered both verbally and in a more personal manner, supplemented with other materials, tends to be more helpful.^{17,19,27-29}

Iconomou et al. were the first to highlight the importance of informational resources for cancer patients in Greece, a few years ago. They conducted a RCT and investigated the impact of a booklet about chemotherapy on patient satisfaction, quality of life and emotional distress as well. Patients provided with the booklet, in addition to verbal instructions, reported significantly higher rates of satisfaction and this data is in accordance with our results. In contrast, the intervention produced no benefits in terms of anxiety, depression and HRQoL.¹⁷ Moreover, a recent study in Japan showed that the degree of cancer survivors' satisfaction was significantly higher when both verbal and written forms of information were provided.²⁷

Much of the current research among cancer patients indicated that new reliable information sources are available in everyday oncology setting, which are an important determinant of patient satisfaction and affect overall HRQoL.^{1,4,16} However, there are few RCT's in recent bibliography that have previously evaluated patient-centered information interventions and have proved to exert beneficial effect on a number of outcomes for HSCT patients. Our results are in line with those of a multicenter study of 458 HSCT survivors, 1-5 years post transplantation, that revealed a significant decrease in distress scores and an improvement in mental domain of quality of life, among patients randomized to the Survivorship Care Plan (SCP) study arm. The SCP was a printed tool used to facilitate long-term care for cancer survivors.¹⁹ Our conclusions can be further confirmed with data published by Cioce et al. who conducted a RCT and demonstrated that educational interventions a week before transplant hospitalization, improved significantly patients' knowledge of different aspects of allogeneic HSCT, reduced psychological distress and increased levels of HRQoL. They compared a standard approach with therapeutic patient education (TPE). Verbal instructions and personalized printed informative material were accompanied by audio-videos presentations and complemented by multidisciplinary and interactive educational teaching tools.²⁸ Moreover, our findings are partly in accordance with the data previous research has demonstrated on the effectiveness of information interventions based on web technologies. Syrlala et al. examined the efficacy of an online program named INSPIRE

(Internet-based Survivorship Program with Information and Resources), alone or in combination with Problem Solving Treatment (PST) telehealth calls, for providing information to 755 adult survivors, 3-18 years after HSCT. Those allocated to the intervention group (INSPIRE + PST) reported improved distress, but not depressive symptoms, at a 6-month assessment. However, there was a lack of intervention efficacy for physical dysfunction.²² Horne et al. developed and evaluated a specifically designed website named ALLINEX (ALLograft Information Exchange) for adult allogeneic HSCT, with the aim to provide open access to information about different aspects of HSCT, as an adjunct to standard care. ALLINEX evaluation demonstrated acceptable usability, but its reported impact on patient self-management was low.¹⁸ Nevertheless, despite the benefits mentioned so far, some studies concluded to contradictory results and revealed no significant effects of information interventions proposed, on HSCT patients' overall satisfaction and psychological distress.^{2,20}

Concerning HSCT patients' attitude in decision-making, a cross-sectional study confirmed our results and revealed that most patients wanted to be fully informed and actively involved in treatment decisions.⁵

The studies mentioned so far differed substantially with our trial and several factors may explain this differentiation. The first explanation concerns the design and the nature of the intervention options analyzed. Strategies to provide information have changed over time and a lot of new sources have been available in the health care system. This can be explained by the fact that a number of shortcomings may result from traditional approaches to providing information to patients, centered on their limited ability to meet patient preferences and literacy levels. New generation web-based technologies (tools) for health information provision offer an innovative and pragmatic solution for overcoming these limitations, by providing a platform for interactive information seeking. A second factor explaining the different uptake of our intervention in comparison with the other RCTs, can be the heterogeneity in the study populations. Patients were not all at a similar time-point when follow-up assessment was held. In our study, participants were under the active care of the transplant center at the whole duration of the

follow-up period and this might have impacted positively patient-reported outcomes assessed (better satisfaction related to less anxiety and depression and better emotional well-being). In some other studies the sample was composed only of survivors and the mean time since the transplantation was at least one year. As a result, participants had less contact with their health care providers and that could have influenced the recall effect of information received. Moreover, the low uptake of some information interventions could be probably related to the time of offering the information. In some cases, emotional concerns might occur at the time chosen to apply the intervention, but also in an earlier stage of the treatment or controversially, in a later stage. For example, the low levels of distress could be observed already at baseline assessment, so a significant reduction over time should not be expected.

Limitations

Some limitations of our study must be acknowledged. First, this study included a heterogeneous group of patients in terms of diagnosis. Secondly, the sample was small, since HSCT is a rare treatment and therefore the number of eligible patients available to take part in the study was limited and probably inadequate to detect safe differences between groups. Moreover, patients were recruited from a single transplant center and thus the responders might not be representative of hematological cancer patients, generally in Greece. A multicenter trial may highlight different needs among a more sociodemographically diverse group of patients. Furthermore, the use of different instruments in comparison to other trials, highlights the risk in drawing insecure results. However, the fact that we included inpatients and also outpatients strengthened our attempt to obtain a more precise insight into the course of satisfaction from information, from the admission time to the BMT unit to the survivorship care.

CONCLUSIONS

HSCT patients provided with the information booklet reported significantly higher rates of overall satisfaction, than those allocated to the control group. In addition, the intervention produced significant benefits in terms of anxiety, depression and

HRQoL. Our results may contribute to the improvement of patient tailored information provision and shared-decision making in clinical practice and clearly demonstrate that printed materials can be relatively a simple, beneficial, practical and inexpensive method to offer sufficient information to HSCT patients. However, further well-designed longitudinal multicenter trials are needed to clarify and optimize the efficacy of informational programs and particular attention should be paid to methodology applied.

Institutional Review Board Statement: The study was approved by the Medical Ethical Committee of Evangelismos Hospital (approval number: 355/26-10-2016) and was conducted according to the guidelines of the Declaration of Helsinki.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Acknowledgements: Our sincere thanks go to the patients who participated in the study and to the BMT units that hosted and made this study possible. This work has been partly supported by the Special Account for Research Funding (E.L.K.E) of NKUA.

Conflicts of Interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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ANNEX

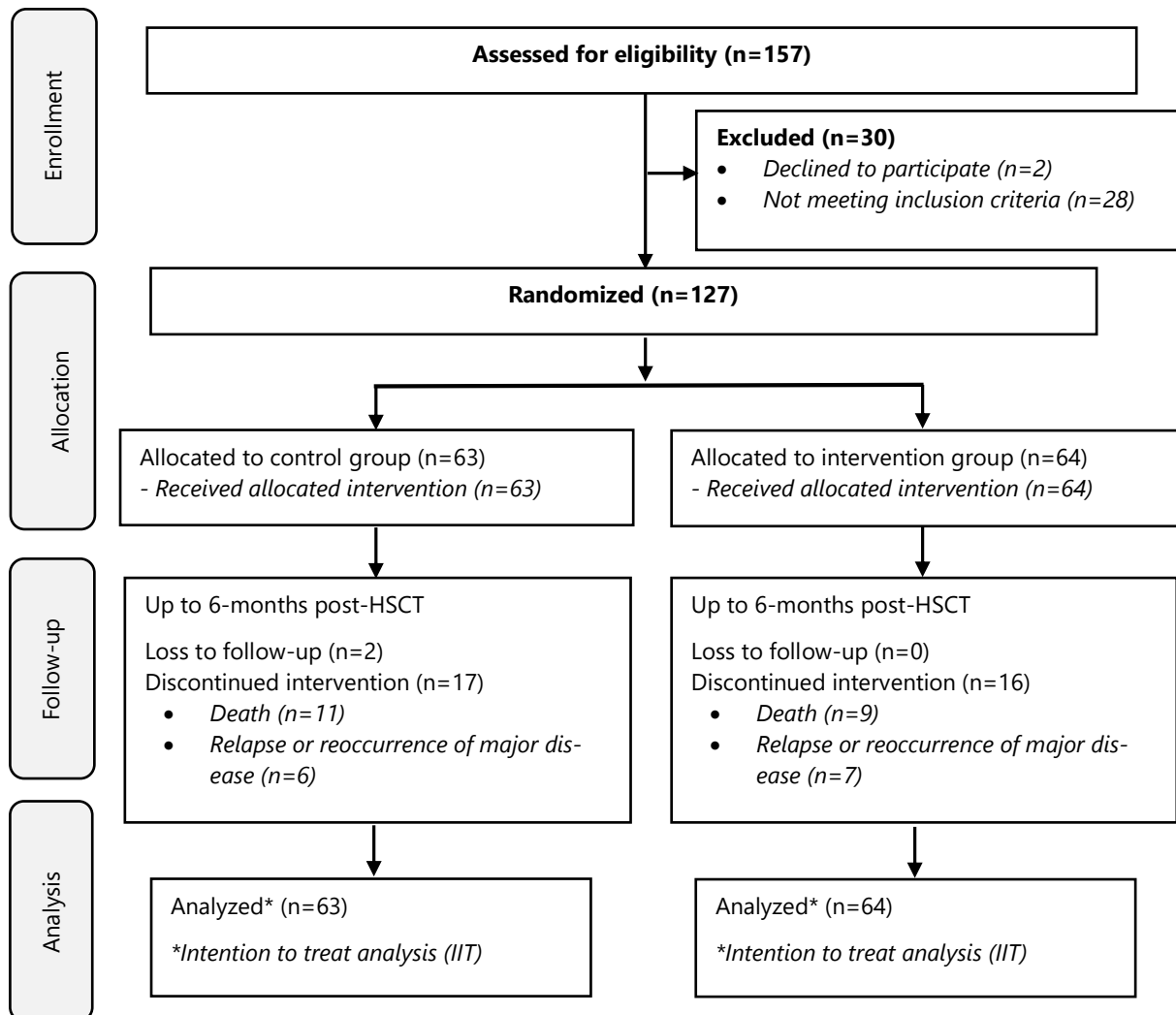
Figure 1. Flow chart describing the process of the randomized clinical trial.

Table 1. Socio-demographic and clinical characteristics of respondents (n=127) who completed baseline questionnaires and significances in comparisons between groups.

	Total (N=127)	CG ⁸ (N=63)	IG ⁹ (N=64)	p [§]
	N (%)	N (%)	N (%)	
Sex				
Male	67 (52.8)	35 (55.6)	32 (50.0)	0.531*
Age (years), mean (SD)	49.2 (12.1)	48.9 (12.8)	49.5 (11.3)	0.799 ⁺
Diagnosis				
Leukemia (AML ¹ , ALL ² , CML ³)	51 (40.2)	30 (47.6)	21 (32.9)	0.423**
Hodgkin / Non-Hodgkin lymphoma (B-NHL, T-NHL)	30 (23.5)	12 (19.0)	18 (28.2)	
Plasma cell disorders	18 (14.2)	9 (14.3)	9 (14.1)	
MDS, MPN, MDS/MPN ⁴	26 (20.4)	12 (19.0)	14 (21.8)	
Other	2 (1.6)	0 (0.0)	2 (3.1)	
Time since first diagnosis				
< 2 years	106 (83.5)	52 (82.5)	54 (84.4)	0.781*
> 2 years	21 (16.5)	11 (17.5)	10 (15.6)	
Donor type				
Allogeneic	81 (63.8)	43 (68.3)	38 (59.4)	0.298*
Autologous	46 (36.2)	20 (31.7)	26 (40.6)	
Stem Cell Source				
Peripheral Blood	114 (89.8)	54 (85.7)	60 (93.8)	0.301**
Blood Marrow	9 (7.1)	6 (9.5)	3 (4.7)	
Umbilical Cord Blood	4 (3.1)	3 (4.8)	1 (1.6)	
Comorbidities (HCT-CI⁵)				
Yes	48 (37.8)	18 (28.6)	30 (46.9)	0.123**
Karnofsky performance scale				
0 – 40 (unable to care for self)	0 (0.0)	0 (0.0)	0 (0.0)	1.000**
50 – 70 (unable to work, able to care basic needs)	3 (2.4)	1 (1.6)	2 (3.1)	
80 – 100 (normal activity, no special care needed)	124 (97.6)	62 (98.4)	62 (96.9)	
BMT⁶ unit stay (days), median (IQR⁷)	42 (36-59)	45 (36-60)	41.5 (36-55.5)	0.550 ⁺⁺

Notes: ¹AML: Acute Myelogenous Leukemia. ²ALL: Acute Lymphocytic Leukemia. ³CML: Chronic Myelogenous Leukemia.

⁴MDS/MPN: Myelodysplastic/Myeloproliferative Syndrome.

⁵HCT-CI: Hematopoietic Cell Transplantation Comorbidity Index. ⁶BMT: Blood Marrow Transplantation.

⁷IQR: interquartile range. ⁸CG: Control Group. ⁹IG: Intervention Group.

[§]Significance level at 0.05. *Pearson's chi-square test. **Fisher's exact test.

⁺Independent samples test. ⁺⁺Independent-Samples Mann-Whitney U Test.

Figure 2. A) Comparisons of Satisfaction from information provision between control (n=63) and experimental (n=64) group of HSCT patients, measured with the Information Satisfaction Questionnaire (ISQ), at 2 time-points (T1= at admission to the BMT unit and T2= the day of discharge), *p-values calculated using Independent-samples Mann-Whitney test. **B)** Pairwise comparisons at ISQ Total Score over time, **p-values calculated with Related-samples Wilcoxon Signed Rank test, [Box plot, median (25th -75th percentiles)].

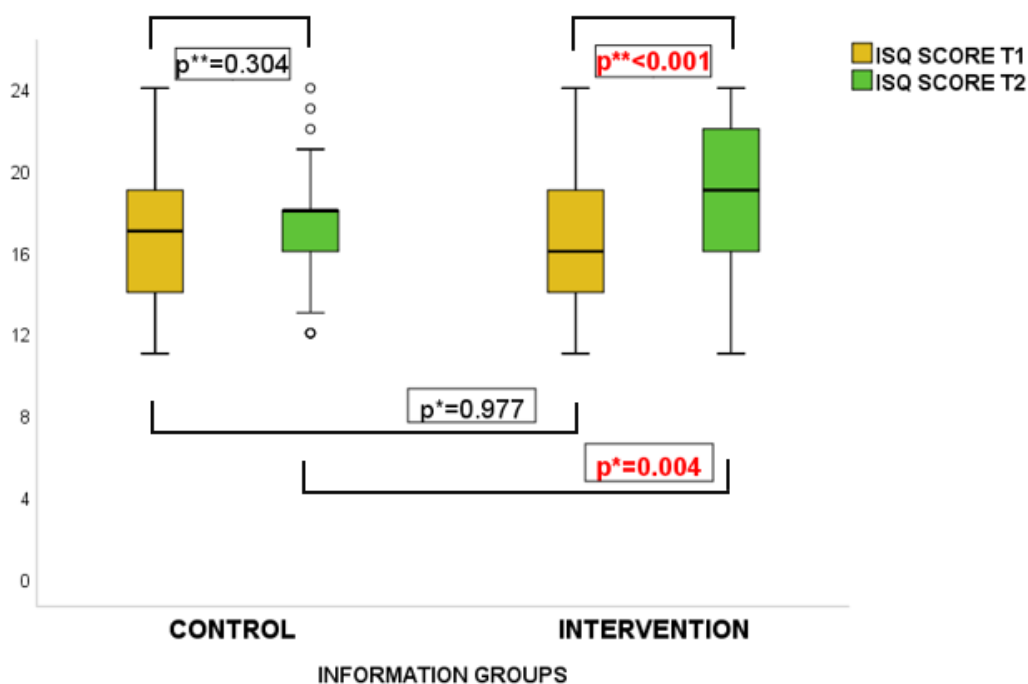
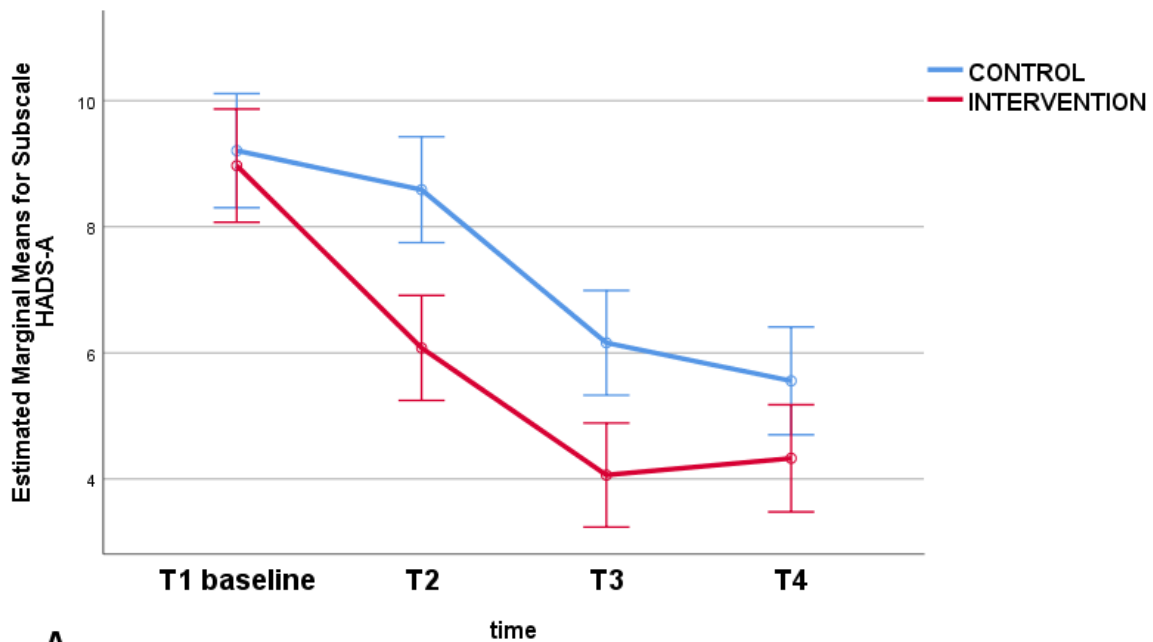
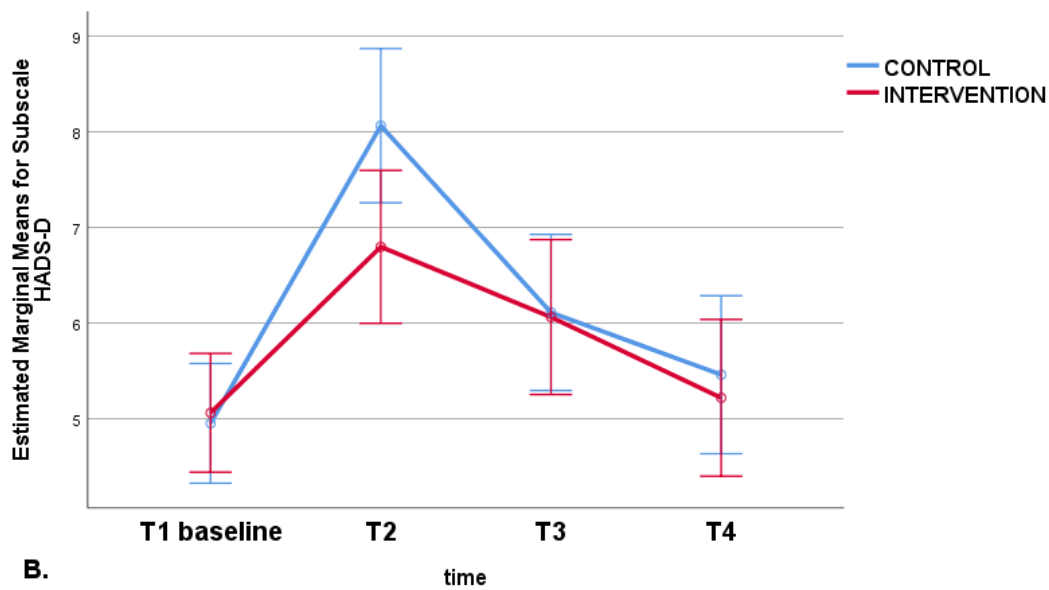


Figure 3. Anxiety (HADS-A) and Depression (HADS-D) estimated means for the four phases (T1= baseline-at admission to the BMT unit, T2= the day of discharge, T3= 3 months post-HSCT and T4= 6 months post-HSCT), after mixed ANOVA with repeated measures analysis.



A.

Error bars: 95% CI



B.

Error bars: 95% CI

Table 2. Comparisons between control (n=63) and intervention (n=64) groups for the FACT-BMT subscales, for each time-point (T1= baseline, T2= discharge from the BMT unit, T3= 3 months post-HSCT, T4= 6 months post-HSCT) and FACT-BMT changes over time.

Group	T1	T2	T3	T4	Pairwise Comparisons**
PWB^a					T1 vs T2 (p<0.001) T1 vs T3 (p=0.002) T2 vs T3,T4 (p<0.001) T3 vs T4 (p=0.008)
Control	22.2 (3.5) ^{\$}	16.4 (5.2)	19.5 (6.1)	20.6 (6.5)	T1 vs T2 (p<0.001) T2 vs T3,T4 (p<0.001)
Intervention	21.3 (5.1)	16.6 (6.0)	19.5 (6.4)	21.1 (6.8)	T1 vs T2 (p<0.001) T2 vs T3,T4 (p<0.001)
p*	0.555 ⁺⁺	0.877 ⁺⁺	0.908 ⁺⁺	0.580 ⁺⁺	T3 vs T4 (p<0.001)
SWB^b					none
Control	20.7 (3.2)	20.3 (3.3)	20.8 (3.3)	20.8 (3.6)	
Intervention	21.8 (3.9)	22.7 (3.6)	22.0 (3.7)	21.9 (3.7)	T1 vs T2 (p=0.035)
p	0.094 ⁺	0.001⁺	0.049⁺	0.140 ⁺⁺	
EWB^c					T1 vs T4 (p=0.001) T2 vs T4 (p=0.001) T3 vs T4 (p=0.002)
Control	17.5 (5.2)	17.8 (5.1)	18.6 (3.9)	19.9 (4.2)	T1 vs T3,T4 (p<0.001) T2 vs T3 (p=0.026) T3 vs T4 (p=0.025)
Intervention	18.8 (4.3)	20.4 (5.4)	22.0 (2.1)	20.9 (3.8)	
p	0.183 ⁺⁺	<0.001⁺⁺	<0.001⁺⁺	0.026⁺⁺	
FWB^d					T1 vs T2 (p<0.001) T2 vs T3 (p=0.004) T2 vs T4 (p<0.001)
Control	16.1 (3.1)	14.1 (4.1)	15.8 (4.9)	16.2 (5.3)	T3 vs T4 (p=0.001)
Intervention	17.1 (4.8)	15.9 (4.4)	15.8 (4.8)	16.8 (5.1)	
p	0.187 ⁺⁺	0.036⁺⁺	0.845 ⁺⁺	0.746 ⁺⁺	
BMTs^e					T1 vs T2,T3 (p<0.001) T2 vs T3 (p=0.011) T2 vs T4 (p=0.001)
Control	26.9 (3.2)	23.71 (4.4)	24.9 (5.1)	25.7 (5.9)	T1 vs T2 & T2 vs T3,T4 & T3 vs T4 (p<0.001)
Intervention	26.5 (5.6)	22.2 (3.6)	25.4 (6.3)	26.9 (6.6)	
p	0.954 ⁺⁺	0.214 ⁺	0.409 ⁺⁺	0.130 ⁺⁺	
FACT-BMT Total^f					T1 vs T2 & T2 vs T3,T4 & T3 vs T4 (p<0.001) for both groups
Control	103.6 (13.8)	91.8 (15.9)	99.7 (19.9)	103.4 (23.4)	
Intervention	105.6 (18.4)	97.8 (16.1)	104.7 (18.7)	107.7 (20.3)	
p	0.501 ⁺	0.037⁺	0.156 ⁺⁺	0.396 ⁺⁺	

Notes: ^aPWB: Physical Well-being. ^bSWB: Social/Family Well-being. ^cEWB: Emotional Well-being. ^dFWB: Functional Well-being.

^eBMTs: BMT subscale. ^fFACT-BMT Total: PWB+SWB+EWB+F WB+BMTs. ^{\$} Mean (SD).

* p-values calculated using: ⁺Independent-Samples t-test & ⁺⁺Independent-Samples Mann-Whitney U Test.

** Pairwise comparisons calculated using Wilcoxon Signed Ranks test, at repeated measures of analysis of variance (ANOVA). Significant level at 0.05.