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Feasibility and preliminary efficacy of an intervention combining hypnosis and virtual nature exposure in patients following hematopoietic cell transplantation

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Abstract

Introduction. Hematopoietic cell transplantation (HCT) is associated with physical symptoms, psychological distress, and cognitive fatigue. Hypnosis has demonstrated benefits in oncology but typically requires cognitive resources underlying active mental imagery. Virtual reality (VR) could reduce this cognitive load by providing structured visual inputs. This study evaluated the feasibility and preliminary efficacy of an intervention combining hypnosis with virtual nature exposure in patients undergoing HCT.

Methods. A randomized longitudinal feasibility trial was conducted. Participants in the experimental group used an application offering virtual nature environments and hypnosis for two weeks. Feasibility outcomes included recruitment, attrition, usability, cybersickness, and qualitative user experience interviews. Main outcome of interest for preliminary efficacy was quality of life. Immediate pre-post session effects on pain, anxiety, and relaxation were examined using visual numeric scales. **Results.** Forty participants were enrolled. Application use averaged 2.8 sessions over two weeks, and cybersickness was minimal. Qualitative feedback indicated positive user experience, with perceived benefits for anxiety. Immediate effects included significant reductions in fatigue and anxiety and increase in relaxation and amusement after the first session. However, no significant group effect was observed for outcomes at 1 and 3 months.

Conclusion. The intervention appears feasible for patients undergoing HCT, with promising immediate psychological effects. Further studies with optimized implementation and larger samples are required to evaluate clinical efficacy.

Ethics. This project was approved by the Research Ethics Committee of Hôpital Maisonneuve-Rosemont (Project no MP-2023-3251). Procedure of this study has been preregistered on ClinicalTrials.gov (Registration number: NCT06817759), on Open Science Framework (<https://doi.org/10.17605/OSF.IO/Z67YA>), and published (Laurin et al., 2026). Raw anonymized data are available on OSF.

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Keywords

Hematology, hematopoietic cell transplantation, virtual reality, hypnosis, feasibility study

Introduction

Hematopoietic cell transplantation (HCT) is increasingly used for hematologic diseases, particularly for hematologic cancers and represents an effective therapeutic option [1]. HCT comprises several phases: After confirmation of eligibility, patients receive a conditioning regimen and have autologous or allogeneic cells infused [2]. HCT is associated with significant physical symptom burden (e.g., organ toxicity, severe mucositis causing pain, infections, graft-versus-host disease for allogeneic transplant) [3–7] and psychological distress [8]. Furthermore, these difficulties are exacerbated by protective isolation prescribed because of immunodeficiency, limiting social contact [9]. Finally, HCT can induce cognitive fatigue during hospitalization, persisting in a substantial proportion of survivors [10,11].

Improving HCT patients' well-being represents an important clinical challenge. Among existing interventions, hypnosis has been shown to be effective in oncology for reducing pain, fatigue, anxiodepressive symptoms, and improving quality of life (QoL) [12–14]. Hypnosis is defined as “a state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion” [15]. However, the effectiveness of hypnosis varies considerably across individuals, largely depending on hypnotisability, which refers to a stable trait reflecting one's capacity to enter in a hypnotic state, respond to suggestions, and engage in suggestion-related imagery [16]. Given the cognitive fatigue commonly observed in patients undergoing HCT, these individual differences may be further amplified, potentially limiting accessibility of hypnosis in this population. It has been hypothesized that virtual reality (VR) may partly respond to this limitation by providing externally generated sensory immersion engaging attention resources required without relying on self-generated imagery, potentially making hypnotic suggestion accessible for individuals with lower hypnotisability [17,18]. VR refers to immersion, via a mediating device, in an environment that simulates elements of reality and bringing a sense of presence [19]. It has been shown to be efficient in decreasing anxiety, pain and stress in oncology [20]. Beyond their independent efficacy, VR and hypnosis share a common attentional pathway that may justify their combination. Both modalities rely on capture and narrowing of attention: hypnosis operates through focused top-down attentional absorption [21], while immersive VR engages overlapping attentional systems through bottom-up sensory immersion [22]. Trait absorption, predicting both hypnotisability and VR presence, supports this mechanistic overlap [23]. Selecting an appropriate VR scenario therefore becomes a key consideration. Exposure to nature has demonstrated beneficial effects on multiple psychosocial outcomes across diverse contexts (better physical and psychological health, reduced stress, improved mood, less negative emotions and fatigue)

[24]. When direct nature exposure is impossible (such as in HCT context), VR may serve as an effective alternative [25]. These benefits of exposure to nature can be explained by Attention Restoration Theory [24,26,27]. According to the theory, natural environments promote the recovery of psychological resources through their ability to capture attention. This elicits a “soft fascination” effortlessly and involuntarily to provide a sense of being away, allowing individuals to restore their attentional capacities [26]. This attentional profile is close to the attentional loosening required at the onset of hypnotic induction [28].

The combination of virtual reality and hypnosis (VRH) has been shown to be effective in different clinical contexts such as burn care, perioperative settings, and oncology-related procedures [18,29]. However, the population of patients undergoing HCT is understudied [30]. Given the unique clinical and psychological burden of this population, there is a crucial need to develop tailored interventions. This development should be methodologically sound by using models like ORBIT [31] which provides a processual methodological framework guiding both development and optimization of interventions to ensure feasibility and effectiveness. In this context, a user-experience study was conducted to test the acceptability of the intervention in 10 patients with multiple myeloma following autologous or allogeneic HCT (Phase I) [32]. Results showed that the intervention is well-received by participants and provided early-stage evidence on the acceptability of the intervention, while also offering adaptation pathways and recommendations to ensure the tool is suitable for clinical care. Considering those elements, the present randomized controlled feasibility trial was developed as a Phase II study. It aimed to further explore feasibility of an intervention combining virtual nature exposure and hypnosis and to evaluate its preliminary efficacy in reducing symptoms of anxiety, depression, pain, and fatigue, and impact on quality of life (QoL) among HCT recipients.

Methods

Study design and ethics

This study referred to a Phase IIb feasibility pilot study according to the ORBIT model [31]. This was a parallel group randomized, controlled, longitudinal, and bicentric study led at Hôpital Maisonneuve-Rosemont and Hôpital du Sacré-Cœur, both in Montréal, Québec, Canada.

This project was approved by the Research Ethics Committee of Hôpital Maisonneuve-Rosemont for a multicentric study including Hôpital Sacré-Cœur (Project no MP12-2023-3251). Procedure of this study

has been preregistered on ClinicalTrials.gov (Registration number: NCT06817759), on Open Science Framework (<https://doi.org/10.17605/OSF.IO/Z67YA>), and published [33].

Participants

Inclusion criteria were to be 18 years old or older, having a hematological disease for which an HCT was considered and being able to follow a conversation in French. Exclusion criteria were conditions impairing communication or inability to consent due to a sensory deficit (deafness, blindness) or cognitive impairment (confusion, dementia, uncontrolled psychiatric disorder), having head wounds that keep from using a headset and an history of seizures induced by flashing lights.

Procedure and intervention

After being informed of the presence of a potentially eligible patient by the transplant ward head nurse, the investigator (AL) proceeded to randomization to the intervention or the passive control group, using a computer-generated sequence created via the web-based tool Research Randomizer (<https://www.randomizer.org/>). Participants in the control group received standard care. No allocation concealment was performed as the experimental group received the intervention and the control group did not.

Participants were recruited during the week following graft infusion. At the first meeting, participants were verbally informed of the purpose of this research and design of the study. If interested, they were provided with a written consent form and informed they could exercise their right to withdraw from the study at any time, to access and rectify their collected data, and to oppose to the statistical analysis of their data.

Participants in the experimental group were offered a first accompanied session during which they were provided a demonstration of headset utilization and of the application delivering the intervention. Technical data sheets were then provided. The application comprised a large bank of landscapes they could visit and four hypnosis exercises that combined virtual nature exposure and hypnosis. After this first session, participants were asked to use the application autonomously for two weeks, at least 3 times and as often as desired. Hypnosis scripts are described in Supplementary Material 1.

Measures took place in both groups: one week after HCT (Day +7, T0), one month after HCT (Day +28, T1), and three months after HCT (Day +100, T2). In the experimental group, immediate efficacy measures were performed before and after each utilization.

Interviews were conducted online after data collection. Participants remaining in the experimental group were contacted by AL and invited to participate in an interview aimed at discussing how they felt during participation. Among contacted participants, four didn't answer when phoned and two refused (one without giving any reason and the other no longer interested in participating).

A graphical representation of the procedure is displayed in Figure 1 and a detailed description of protocol deviations is reported on Open Science Framework (OSF).

Measures

Feasibility and usability outcomes

Feasibility outcomes included dropout rates, reasons for study withdrawal, frequency of the application utilization, and overall satisfaction. The occurrence of cybersickness after utilization was recorded with the Simulator Sickness Questionnaire [34].

Semi-structured interviews were conducted online by DO (Ph.D., researcher in psychology and clinical psychologist, trained in qualitative research, male) and AL (MSc., student in psychology, trainee in qualitative research, female) to explore participants' experience regarding the intervention and their recommendations for development of future interventions and studies.

Preliminary efficacy

Consent, questionnaire data and sociodemographic information were collected on a tablet using the software REDCap. Sociodemographic and clinical data included sex, age, marital status, education, profession, transplant conditioning regimen, diagnosis, and type of transplant.

The immediate effects of the intervention were assessed in the experimental group before and after each utilization with numeric visual scales evaluating anxiety, fatigue, pain (from 0 to 10), relaxation and amusement (from 1 to 10).

QoL was assessed by the Functional Assessment of Cancer Therapy - Bone Marrow Transplantation (FACT-BMT) [35,36] ($\alpha = .92$). The FACT-BMT describes physical ($\alpha = .85$), social/family ($\alpha = .72$) (excluding the item relative to sexual life), emotional ($\alpha = .79$), and functional well-being ($\alpha = .85$), and evaluates symptoms associated with transplantation ($\alpha = .78$). Higher scores reflect better perceived QoL (score range: 0-148).

Anxiodepressive symptoms were measured with the Hospital Anxiety and Depression Scale (HADS) [37,38] ($\alpha = .78$). This measure comprises two subscales evaluating depressive and anxiety symptoms. Higher scores indicate more severe symptoms (score range: 0-21).

Pain experience was assessed with the Brief Pain Inventory - Short Form (BPI-SF) [39,40] ($\alpha = .90$). This questionnaire explores multiple dimensions of pain (sensory, emotional, functional), the worst, least, and average pain during the past days, and disruption caused by pain in daily activities. Higher scores indicate greater level of pain (score range: 0-40 for severity, 0-70 for interference).

Fatigue was evaluated with the Multidimensional Fatigue Inventory - 10 Items [41,42] ($\alpha = .93$). This instrument assesses physical, emotional, and cognitive dimension of fatigue through 10 items. Higher total score corresponds to greater level of perceived fatigue (score range: 10-50).

Power analysis and data analysis

The sample size for a repeated measures MANOVA (two groups, three measurement time points) was determined using an a priori power analysis with G*Power 3.1.9.7 software. The calculation was based on quality of life (assessed using the FACT-BMT) as primary outcome. A medium effect size $f = 0.25$ (as recommended [43]), an α level of .05, and a statistical power ($1-\beta$) of .95 were considered. This yielded a required sample size of 54 participants. Accounting for an estimated 5% attrition at each time point, the planned total sample size was 64 participants.

Quantitative variables were summarized as means and standard deviations (Mean $\pm$ SD) and categorical variables as frequency and percentages.

Paired samples Wilcoxon rank tests were applied for immediate pre-post utilization comparisons. A PERMANOVA was applied to test the efficacy of the intervention on preliminary efficacy variables as a non-parametric alternative to MANOVA. The dependent variables were the differences in the scores of QoL scores, anxiodepressive symptoms, pain, and fatigue between T0 and T1, and the independent variable was the group. The test was conducted controlling for age, sex, and type of transplant. The significance threshold was set at $\alpha = .05$ and 95% confidence intervals were considered. The code and extensive results are presented in Supplementary Material 3.

Statistical analyses were performed using jamovi 2.3.18 and R 4.5.3 software, using the *vegan* package.

Regarding qualitative data, a deductive approach was used to identify themes emerging from the interviews. First, interviews recordings were transcribed using Wispr Flow software. Then, transcriptions

were reread and anonymized by OD (BSc., student in psychology, trainee in qualitative research, female). Audio recordings were deleted after transcription. AL and OD proceeded independently to the thematic analysis, and their finding were confirmed by VF (Ph.D., postdoctoral researcher in health psychology trained in qualitative research, male). The deductive approach was a theory-driven approach since it involved identifying themes from the interview guide (see Supplementary Material 2).

Results

Participants' characteristics

Recruitment took place between January 2025 and November 2025. A CONSORT flowchart of inclusion is presented in Figure 2 [43]. Before obtaining informed consent, 72 patients were identified as potentially eligible for the study. After consideration, 7 patients were considered ineligible and 5 were unavailable, leaving 60 potential patients for the study. After consideration, 17 patients refused to participate, one was not included due to technical issues with the application, one because of organizational difficulties, and one deceased before inclusion. The remaining 40 participants were randomly assigned to the experimental (n=20) or control group (n=20) and provided data at T0. Between T0 and T1, 19 participants dropped out (9 in the experimental group, 10 in the control group) and one was not considered because of technical issues. Finally, 6 participants did not complete the questionnaire at T2.

Forty participants were enrolled, and their characteristics are presented in Table 1. Average age of participants was of 50 ± 15.7 years (range: 21-71); 19 were women and 21 were men. Regarding medical data, 12 participants had acute leukemia, 12 had lymphoma, 5 had myeloma, and 11 had other hematological diseases (myelodysplastic syndrome, chronic myelomonocytic leukemia, aplastic anemia, myeloproliferative neoplasm, immune deficiency). Patients received allogeneic (n=31) or autologous HCT (n=9).

No significant difference was observed in the repartition of those variables according to the group (experimental, control) (all $p > .05$).

Feasibility and usability results

Participants in the experimental group used the application 2.80 ± 1.96 (Min = 1; Max = 7; Mode = 1) times during the two weeks of autonomous utilization, with low symptoms of cybersickness after the first utilization (0.24 ± 0.39).

Interviews were led on 8 participants (Table 2). According to the interview guide, qualitative data addressed three themes: variables influencing utilization, satisfaction and users' experience, and recommendations. Excerpt of participants' discourses illustrating themes are presented in Table 3.

Theme 1: Variables influencing utilization. When asked about the variables that could impair autonomous utilization of the intervention, participants considered that age could restraint autonomous use of the device and the application. Another element to be considered is physical condition of patients. For instance, time of treatment seemed important given that the first week after conditioning chemotherapy is not suitable given physical and cognitive fatigue and physical symptoms such as pain.

Theme 2: Satisfaction and users' experience. Positive aspects included quality of the pictures and their combination with sounds of nature, the sense of space, and simplicity of utilization. Participants reported a positive experience except for one participant who indicated that proposed landscapes were disappointing. Regarding the material, participants reported a few negative elements (smell of disinfectant applied on the headset, discomfort related to wearing glasses, occasional lag between movement of the controller and its representation in the application). Despite reporting some minor side effects (nausea or dizziness during the first minutes of utilization, fatigue related to the duration of the session), participants outlined a perceived efficacy to decrease anxiety, social isolation, pain, and itching.

Theme 3: Recommendations. Recommendations were formulated by users. Regarding the device and application, participants suggested to implement an additional tool that could hinder ambient noise in their hospital room or making menus more ergonomic, appealing for a relative simplification. Participants reported they would appreciate enrichment of proposed landscapes. For the implementation, participants suggested to proceed to an extended explanation session, giving more information on headset, the code of conduct in case of technical issues or difficulties in the utilization, underlining that the presence of the research assistant at the first session was helpful.

Preliminary efficacy

Immediate pre-post comparisons after the first utilization revealed a significant diminution of fatigue ($W = 50.00, p = .02, d = 0.707$), anxiety ($W = 15.50, p = .031, d = 0.692$) and increased relaxation ($W = 9.00, p = .020, d = -0.778$) and amusement ($W = 0.00, p = .004, d = -1.465$). No statistical difference was observed for pain ($W = 15.50, p = .339, d = 0.267$). After two, three, or four utilizations, no significant changes were observed for fatigue or anxiety. An improvement of pain score was observed after two utilizations ($W = 28.00, p = .020, d = 1.00$) but not after three or four. Relaxation and amusement still increased significantly

after two (respectively: $W = 0.00$, $p = .034$, $d = -1.00$; $W = 0.00$, $p = .009$, $d = -1.00$) and three utilizations (respectively: $W = 0.00$, $p = .034$, $d = -1.00$; $W = 0.00$, $p = .022$, $d = -1.00$) but not after four (see Supplementary Material 5 for spaghetti plots).

Baseline score for outcomes of interest did not differ significantly between the two groups, except for depressive symptoms on HADS subscale ($T(38) = 2.20$; $p = .034$) with scores being lower in the experimental group (respectively, 6.05 ± 3.15 and 8.5 ± 3.86) (Table 4).

The PERMANOVA test was conducted on scores of differences between T0 and T1 to examine the effect of group while controlling for age, sex, and transplant status. After adjustment for covariates, the effect of group did not reach statistical significance ($F(1,17) = 2.28$, $R^2 = 0.10$, $p = .121$). Neither age ($F(1,17) = 1.53$, $R^2 = 0.07$, $p = .200$), sex ($F(1,17) = 0.26$, $R^2 = 0.01$, $p = .764$), nor type of transplant ($F(1,17) = 1.26$, $R^2 = 0.11$, $p = .285$) were significantly associated with the multivariate outcome. The overall model explained 29.1% of the total variance. Given the attrition rate, no analysis was conducted regarding T2.

Discussion

This study examined the feasibility and preliminary efficacy of an intervention combining hypnosis and virtual nature exposure in patients undergoing HCT. Our findings show that this intervention is feasible, although a non-negligible proportion of eligible patients declined participation or dropped out. Participants in the experimental group used the intervention a limited number of times over the two-week period of autonomous utilization. Reported cybersickness symptoms were very low. Qualitative findings suggest overall positive user experience, with perceived benefits for anxiety, isolation, and pain, despite minor technical and physical inconveniences. Participants formulated recommendations that should be considered in further development, with an emphasis on the fact that utilization should be accompanied. Small to moderate within-subject effects were found for several immediate outcomes of the VRH intervention in the experimental group. Small effects were also observed for some clinical outcomes comparing T0 to T1 across groups. These preliminary findings provide evidence to conduct future RCTs assessing efficacy following the recommendations of ORBIT Phase III study.

Studies evaluating VRH in context of HCT remain very limited, which restricts comparisons with the existing literature [45]. In the present study, reasons for declining participation included lack of interest, concurrent enrolment in other studies, a perceived lack of need for this type of intervention, fatigue and headaches, and the anticipated complexity of the intervention. These reasons are broadly consistent with those reported in other studies in oncology patients [46]. However, concerns related to anxiety about VR

and a perceived loss of control were not reported by participants in our study. This could be explained by the fact that participants were trained to use the intervention during the first session and that the research team was available in case of technical difficulties.

Our findings show an overall positive user experience, also consistent with VR studies conducted in oncology [50]. However, some minor points (technical aspects, content of the intervention, or ergonomic elements) that may impact engagement and adherence to the intervention should be considered in the development of future interventions [51]. Participants recommended better attenuation of ambient noise, supporting the idea that the hospital environment can interfere with relaxation and immersion [52]. They also highlighted the usefulness of having a research assistant present during sessions and emphasized the need for more explicit guidance regarding headset use, troubleshooting procedures in case of technical difficulty, consistent with other feasibility studies reporting a preference for supervised sessions [50].

Patients with hematologic diseases undergoing HCT represent a highly vulnerable population, and rigorous evaluation of adverse effects related to immersive technologies is essential before broader implementation [47]. In that sense, the low level of cybersickness constitutes an encouraging indicator of the safety and tolerability of the intervention, which is consistent with evidence reporting that nature-based VR content is associated with lower cybersickness [48,49]. On the pre-post measures, we observed immediate effects on fatigue, anxiety, and relaxation, which is consistent with the oncology VR literature showing that VR interventions tend to produce primarily short-term effects on stress and affect [53]. In hematology, a study conducted prior to bone marrow biopsy similarly reported an immediate benefit of VRH on patient's concerns and anxiety that did not persist after the procedure, highlighting the acute potential of VR-based interventions [54]. Regarding preliminary efficacy findings, our results are also in line with the literature. Indeed, because VR interventions are short in duration and aiming at increasing relaxation, they may not impact multidimensional variables such as QoL [55,56].

Recommendations for future studies and interventions

Given the pilot nature of this study, we recommend recruiting more participants in future studies to investigate the efficacy of such an intervention. Referring to the literature and the present results, an attrition rate should be anticipated given the longitudinal design of these studies [57]. Moreover, participants attrition during follow-up is expected after HCT, where maintaining regular follow-ups after transplantation and hospital discharge represents a major challenge [58]. Thus, a solid methodology of recruitment aiming at limiting attrition and missing data should thus be implemented. For example, recruitment and investigation should follow medical timepoints narrowly as HCT process is associated with

relatively frequent medical visits (pre-conditioning time, one month and three months after transplant) [59].

Regarding implementation of the intervention, it is crucial to consider the prevalence and dynamic of variables of interest. Indeed, longitudinal evidence suggests that anxiety and depression may be higher between hospital admission and the first week after transplant and then decrease afterward [60]. Thus, implementing the intervention earlier in the HCT trajectory would be more relevant to target periods of heightened emotional distress. Moreover, given that exposure to nature is described as dose-dependent, with observable benefits emerging from approximately 30 minutes per week [61], it appears essential to ensure that patients are effectively exposed at least weekly.

Given that participants explicitly asked for an extended explanation session at the first use, we highly recommend implementing a first educational session aimed at familiarizing with the intervention or the presence of a research team member during sessions in case of technical or practical difficulties. In line with the Technology Acceptance Model [62], perceived ease of use of a technology is a central determinant of technology acceptance, particularly in non-familiar individuals or for recent or innovative technologies. In that sense, implementing a demonstration, supervised sessions, or a written guide addressing common technical issues are solutions that should be considered in the future.

Limitations, perspectives, and recommendations

Our study has several limitations that should be acknowledged. The exploratory nature of this study led to numerous deviations from the pre-registered protocol (see OSF for details). In that sense, the present results and follow-up studies should help develop standardized intervention guides. Baseline scores of depression symptoms were also different between the two groups and could have impacted the results. The utilization rate was also relatively low in the intervention group. Thus, future studies should prioritize supervised sessions scheduled as appointments to enhance motivation and ensure a more homogeneous exposure across participants. They should also include more frequent and closely spaced assessments of outcomes of interest, ideally incorporating an immediate post-intervention evaluation to better capture the effects of the intervention. Finally, our studied population is characterized by the heterogeneity of its clinical profiles. Further studies should control diagnosis and type of transplant. Finally, retention strategies focused on integrating follow-up assessments into routine clinical visits should be implemented to reduce participants' burden and limit attrition.

Conclusion

362 This study constitutes a Phase IIb ORBIT feasibility trial supporting the development of an innovative non-
363 invasive intervention combining hypnosis and virtual nature exposure. It highlights the potential of this
364 intervention to be a suitable solution for patients undergoing HCT given its immediate effects on fatigue
365 and anxiety with absence of significant cybersickness. Importantly, it brings recommendations from
366 participants for a better implementation that should consider medical timepoints and accompaniment in
367 utilization. Further steps should include those recommendations in an efficacy trial in this population. In
368 the long term, those studies should bring an innovation solution to help mitigate psychological impact of
369 HCT in hematological context.

370 **Authors contributions**

371 The authors refer to CRediT (Contributor Roles Taxonomy).

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Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. JSB has served on advisory boards for Janssen, GSK and Sanofi.

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Open science statement

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References

1. Singh, A. K. & McGuirk, J. P. Allogeneic Stem Cell Transplantation: A Historical and Scientific Overview. *Cancer Research* **76**, 6445–6451 (2016).
2. Giralt, S. & Bishop, M. R. Principles and Overview of Allogeneic Hematopoietic Stem Cell Transplantation. *Cancer Treat Res* **144**, 1–21 (2009).
3. Braamse, A. M. J. *et al.* Predictors of health-related quality of life in patients treated with auto- and allo-SCT for hematological malignancies. *Bone Marrow Transplant* **47**, 757–769 (2012).
4. Fenech, A. L. *et al.* Post-Traumatic Stress Symptoms in Hematopoietic Stem Cell Transplant Recipients. *Transplant Cell Ther* **27**, 341.e1–341.e6 (2021).
5. Amonoo, H. L. *et al.* Positive psychological experiences in allogeneic hematopoietic stem cell transplantation. *Psychooncology* **28**, 1633–1639 (2019).
6. Xu, P. *et al.* Symptom clusters and sentinel symptoms during post-transplant recovery in recipients of allogeneic hematopoietic stem cell transplantation: A cross-sectional study. *Asia Pac J Oncol Nurs* **12**, 100782 (2025).
7. Ma, J. D., El-Jawahri, A. R., LeBlanc, T. W. & Roeland, E. J. Pain Syndromes and Management in Adult Hematopoietic Stem Cell Transplantation. *Hematology/Oncology Clinics of North America* **32**, 551–567 (2018).
8. Mosher, C. E., Redd, W. H., Rini, C. M., Burkhalter, J. E. & DuHamel, K. N. Physical, psychological, and social sequelae following hematopoietic stem cell transplantation: a review of the literature. *Psycho-Oncology* **18**, 113–127 (2009).

9. Amonoo, H. L. *et al.* Sharing and caring: The impact of social support on quality of life and health outcomes in hematopoietic stem cell transplantation. *Cancer* **127**, (2021).
10. Boberg, E. *et al.* Mental fatigue after allogeneic hematopoietic stem cell transplantation is associated with cognitive dysfunction, but not central nervous system inflammation. *Haematologica* **105**, e310–e314 (2020).
11. Hacker, E. D. *et al.* Persistent Fatigue in Hematopoietic Stem Cell Transplantation Survivors. *Cancer nursing* **40**, (2017).
12. Rosendahl, J., Alldredge, C. T. & Haddenhorst, A. Meta-analytic evidence on the efficacy of hypnosis for mental and somatic health issues: a 20-year perspective. *Front Psychol* **14**, 1330238 (2024).
13. Montgomery, G. H. *et al.* Mediators of a brief hypnosis intervention to control side effects in breast surgery patients: response expectancies and emotional distress. *Journal of consulting and clinical psychology* **78**, (2010).
14. Chen, P.-Y., Liu, Y.-M. & Chen, M.-L. The Effect of Hypnosis on Anxiety in Patients With Cancer: A Meta-Analysis. *Worldviews Evid Based Nurs* **14**, 223–236 (2017).
15. Elkins, G. R., Barabasz, A. F., Council, J. R. & Spiegel, D. Advancing Research and Practice: The Revised APA Division 30 Definition of Hypnosis. *American Journal of Clinical Hypnosis* **57**, 378–385 (2015).
16. Sadler, P. & Woody, E. Z. Does the More Vivid Imagery of High Hypnotizables Depend on Greater Cognitive Effort? A Test of Dissociation and Social-Cognitive Theories of Hypnosis: Pamela Sadler und Erik Z. Woody. *International Journal of Clinical and Experimental Hypnosis* **54**, 372–391 (2006).

- 451 17. Askay, S. W., Patterson, D. R. & Sharar, S. R. Virtual reality hypnosis. *Contemporary*
452 *Hypnosis* **26**, 40–47 (2009).
- 453 18. Rousseaux, F. *et al.* Hypnosis Associated with 3D Immersive Virtual Reality Technology
454 in the Management of Pain: A Review of the Literature. *Journal of Pain Research* **13**,
455 1129–1138 (2020).
- 456 19. Sanchez-Vives, M. V. & Slater, M. From presence to consciousness through virtual
457 reality. *Nat Rev Neurosci* **6**, 332–339 (2005).
- 458 20. Alvarado-Omenat, J. J. *et al.* Effectiveness of virtual reality in cancer patients
459 undergoing chemotherapy. Systematic review. *Int J Cancer* **156**, 1419–1428 (2025).
- 460 21. Jiang, H., White, M. P., Greicius, M. D., Waelde, L. C. & Spiegel, D. Brain Activity and
461 Functional Connectivity Associated with Hypnosis. *Cereb Cortex* **27**, 4083–4093 (2017).
- 462 22. Grassini, S., Segurini, G. V. & Koivisto, M. Watching Nature Videos Promotes
463 Physiological Restoration: Evidence From the Modulation of Alpha Waves in
464 Electroencephalography. *Front. Psychol.* **13**, (2022).
- 465 23. Weber, S., Weibel, D. & Mast, F. W. How to Get There When You Are There Already?
466 Defining Presence in Virtual Reality and the Importance of Perceived Realism. *Front.*
467 *Psychol.* **12**, (2021).
- 468 24. Twohig-Bennett, C. & Jones, A. The health benefits of the great outdoors: A systematic
469 review and meta-analysis of greenspace exposure and health outcomes.
470 *Environmental Research* **166**, 628–637 (2018).
- 471 25. Spano, G. *et al.* Virtual nature, psychological and psychophysiological outcomes: A
472 systematic review. *Journal of Environmental Psychology* **89**, 102044 (2023).

26. Kaplan, S. The restorative benefits of nature: Toward an integrative framework. *Journal of Environmental Psychology* **15**, 169–182 (1995).
27. Ohly, H. *et al.* Attention Restoration Theory: A systematic review of the attention restoration potential of exposure to natural environments. *Journal of Toxicology and Environmental Health, Part B* **19**, 305–343 (2016).
28. Chirico, A. *et al.* Effectiveness of Immersive Videos in Inducing Awe: An Experimental Study. *Sci Rep* **7**, 1218 (2017).
29. Enea, V., Dafinoiu, I., Opreș, D. & David, D. Effects of Hypnotic Analgesia and Virtual Reality on the Reduction of Experimental Pain Among High and Low Hypnotizables. *International Journal of Clinical and Experimental Hypnosis* **62**, 360–377 (2014).
30. Amonoo, H. L. *et al.* A novel psychosocial virtual reality intervention (BMT-VR) for patients undergoing hematopoietic stem cell transplantation: Pilot randomized clinical trial design and methods. *Contemp Clin Trials* **142**, 107550 (2024).
31. Czajkowski, S. M. *et al.* From ideas to efficacy: The ORBIT model for developing behavioral treatments for chronic diseases. *Health Psychol* **34**, 971–982 (2015).
32. Véronneau, J. *et al.* Combining Virtual Reality and Hypnosis? A User Experience Study in Patients with Multiple Myeloma Following Stem Cell Transplantation. *Journal of Patient Experience* **12**, 1–9 (2025).
33. Laurin, A. *et al.* Using virtual reality hypnosis during stem cell transplant for patients in hematology: A protocol for a feasibility randomized study. *PLOS ONE* **21**, e0338617 (2026).

- 494 34. Kennedy, R. S., Lane, N. E., Berbaum, K. S. & Lilienthal, M. G. Simulator Sickness
495 Questionnaire: An Enhanced Method for Quantifying Simulator Sickness. *The*
496 *International Journal of Aviation Psychology* **3**, 203–220 (1993).
- 497 35. Cella, D. F. et al. The Functional Assessment of Cancer Therapy scale: development
498 and validation of the general measure. *J Clin Oncol* **11**, 570–579 (1993).
- 499 36. McQuellon, R. P. et al. Quality of life and psychological distress of bone marrow
500 transplant recipients: the ‘time trajectory’ to recovery over the first year. *Bone marrow*
501 *transplantation* **21**, (1998).
- 502 37. Razavi, Darius., Delvaux, N., Farvacques, C. & Robaye, E. Validation de la version
503 française du HADS dans une population de patients cancéreux hospitalisés. [Validation
504 of the French version of the Hospital Anxiety and Depression Scale (HADS) in a
505 population of hospitalized cancer patients.]. *Revue de Psychologie Appliquée* **39**, 295–
506 307 (1989).
- 507 38. Zigmond, A. S. & Snaith, R. P. The hospital anxiety and depression scale. *Acta Psychiatr*
508 *Scand* **67**, 361–370 (1983).
- 509 39. Cleeland, C. S. & Ryan, K. M. Pain assessment: global use of the Brief Pain Inventory.
510 *Ann Acad Med Singap* **23**, 129–138 (1994).
- 511 40. Poundja, J., Fikretoglu, D., Guay, S. & Brunet, A. Validation of the French Version of the
512 Brief Pain Inventory in Canadian Veterans Suffering from Traumatic Stress. *Journal of*
513 *Pain and Symptom Management* **33**, 720–726 (2007).

41. Baussard, L., Carayol, M., Porro, B., Baguet, F. & Cousson-Gelie, F. Fatigue in cancer patients: Development and validation of a short form of the Multidimensional Fatigue Inventory (MFI-10). *European Journal of Oncology Nursing* **36**, 62–67 (2018).
42. Smets, E. M., Garssen, B., Bonke, B. & De Haes, J. C. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J Psychosom Res* **39**, 315–325 (1995).
43. Cohen, J. *A Power Primer*. (American Psychological Association, Washington, DC, US, 2016). doi:10.1037/14805-018.
44. Hopewell, S. *et al.* CONSORT 2025 statement: updated guideline for reporting randomised trials. *BMJ* **389**, e081123 (2025).
45. Terzulli, C. *et al.* Virtual reality hypnosis diminishes experimental cold pain and alters autonomic responses. *Front. Pain Res.* **4**, (2023).
46. White, M. P. *et al.* A prescription for “nature” – the potential of using virtual nature in therapeutics. *Neuropsychiatric Disease and Treatment* **14**, 3001–3013 (2018).
47. Bruno, R. R. *et al.* Virtual and augmented reality in critical care medicine: the patient’s, clinician’s, and researcher’s perspective. *Critical Care* **26**, 326 (2022).
48. Saredakis, D. *et al.* Factors Associated With Virtual Reality Sickness in Head-Mounted Displays: A Systematic Review and Meta-Analysis. *Front Hum Neurosci* **14**, 96 (2020).
49. Schaumburg, M. *et al.* Immersive virtual reality for older adults: Challenges and solutions in basic research and clinical applications. *Ageing Research Reviews* **109**, 102771 (2025).

- 535 50. Janssen, A. *et al.* Experiences of Patients Undergoing Chemotherapy With Virtual
536 Reality: Mixed Methods Feasibility Study. *JMIR Serious Games* **10**, e29579 (2022).
- 537 51. Finkler, W. *et al.* Virtual nature and well-being: Exploring the potential of 360° VR. *Appl*
538 *Psychol Health Well Being* **17**, e70008 (2025).
- 539 52. Dong, J. & Guo, J. Effects of Comprehensive Noise Reduction Management Combined
540 with Reality Therapy on Anxiety and Depression in Hospitalised Patients with Breast
541 Cancer. *Noise Health* **25**, 211–219 (2023).
- 542 53. Stansel, C. C. *et al.* Effects of Virtual Reality on Pain, Stress, and Affect in an Outpatient
543 Chemotherapy Infusion Clinic: A Randomized Controlled Trial. *Clin J Oncol Nurs* **29**, 65–
544 71 (2025).
- 545 54. Levy Yurkovski, I. *et al.* Virtual reality and hypnosis for symptom alleviation before bone
546 marrow procedure. *Sci Rep* **15**, 38795 (2025).
- 547 55. Wu, Y. *et al.* Effectiveness of Virtual Reality in Symptom Management of Cancer
548 Patients: A Systematic Review and Meta-Analysis. *Journal of Pain and Symptom*
549 *Management* **65**, e467–e482 (2023).
- 550 56. Zeng, Y., Zhang, J.-E., Cheng, A. S. K., Cheng, H. & Wefel, J. S. Meta-Analysis of the
551 Efficacy of Virtual Reality–Based Interventions in Cancer-Related Symptom
552 Management. *Integr Cancer Ther* **18**, 1534735419871108 (2019).
- 553 57. Kang, H. Sample size determination and power analysis using the G*Power software. *J*
554 *Educ Eval Health Prof* **18**, 17 (2021).

555 58. Shaw, B. E. *et al.* National Institutes of Health Hematopoietic Cell Transplantation Late
556 Effects Initiative: Consensus Recommendations for Research Methodology and Study
557 Design. *Biol Blood Marrow Transplant* **23**, 10–23 (2017).

558 59. El-Jawahri, A. *et al.* Effect of Inpatient Palliative Care During Hematopoietic Stem-Cell
559 Transplant on Psychological Distress 6 Months After Transplant: Results of a
560 Randomized Clinical Trial. *J Clin Oncol* **35**, 3714–3721 (2017).

561 60. Seo, H.-J. *et al.* Anxiety and Depression of the Patients with Hematological
562 Malignancies during Hospitalization for Hematopoietic Stem Cell Transplantation.
563 *Psychiatry Investig* **16**, 751–758 (2019).

564 61. Shanahan, D. F. *et al.* Health Benefits from Nature Experiences Depend on Dose. *Sci*
565 *Rep* **6**, 28551 (2016).

566 62. Davis, F. D. & Venkatesh, V. A critical assessment of potential measurement biases in
567 the technology acceptance model: three experiments. *International Journal of Human-*
568 *Computer Studies* **45**, 19–45 (1996).

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570 **Tables and figures**

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Figure 1. Graphical representation of the procedure

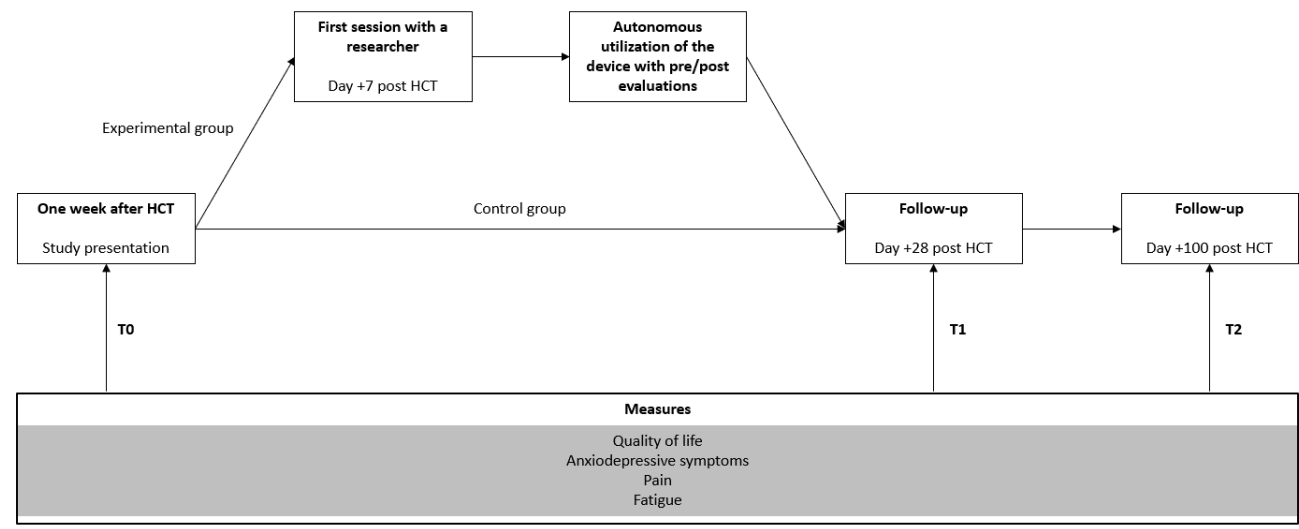
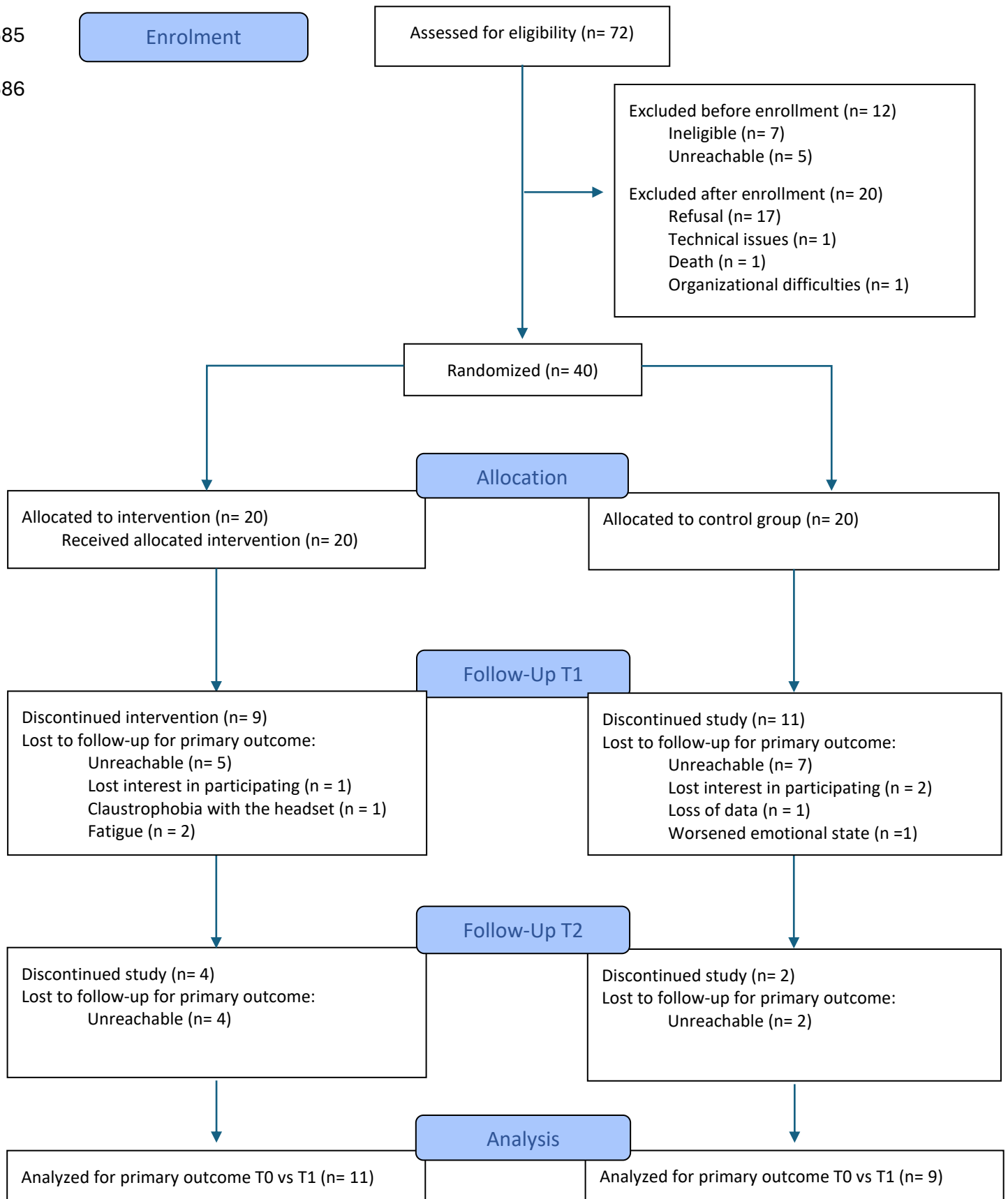


Figure 2. Flowchart of participation



587 **Table 1. Participant characteristics considering group**

Variable		Experimental	Control	Total	X ² (p)	T (p)
Age		48.6±14.8	51.3±16.8	-	-	0.529 (.600)
Sex	Female	8	11	19	0.902 (.342)	-
	Male	12	9	21	0.00 (1.00)	-
Marital status	In a relationship	14	14	28		-
	Single	6	6	12		-
Professional status	Retired	7	3	10	5.78 (.216)	-
	Unable to work	6	4	10		-
	Temporary work incapacity	7	2	9		-
	Full-time employee	3	6	9		-
Diagnosis	Unemployed	1	1	2		-
	Acute leukemia	7	5	13	0.958 (.812)	-
	Lymphoma	5	7	13		-
	Myeloma	2	3	5		-
Type of transplant	Other diseases	6	5	11		-
	Allogeneic	18	13	31	3.58 (.058)	-
	Autologous	2	7	9		-
Conditioning regimen	Myeloablative	15	13	28	1.48 (.478)	-
	Reduced intensity	3	6	9		-
	Nonmyeloablative	2	1	3		-

588

589 **Table 2. Interview participants characteristics**

590

ID	Age	Sex	Marital status	Educational level	Professional status	Diagnosis	Transplant type
P6	48	Male	Single	Highschool	Unable to work	Lymphoma	Allogeneic transplant
P12	29	Female	Single	University	Unable to work	Lymphoma	Allogeneic transplant
P15	48	Female	In a relationship	University	Temporary sick leave	Other diseases	Allogeneic transplant
P18	32	Female	In a relationship	University	Temporary sick leave	Myeloma	Autologous transplant
P29	33	Male	In a relationship	Highschool	Temporary sick leave	Other diseases	Allogeneic transplant
P36	55	Male	In a relationship	University	Unemployed	Leukemia	Allogeneic transplant
P40	52	Male	In a relationship	College	Full-time	Other diseases	Allogeneic transplant
P44	44	Female	Single	College	Temporary sick leave	Leukemia	Allogeneic transplant

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592

Theme	Subtheme	Representative quote (free translation from French)
Variables of utilisation	Age	P10: "It seems to me that she explained it to me once. After that, I remembered it. Maybe for older people it could help them. But for millennials and younger, in any case, it's perfect. There's no problem." P25: "For sure, I think an older person with cognitive problems, say memory issues, might find it a bit more difficult, but I think there are ways to make it work."
	Physical condition	P7: "It still takes a minimum of energy to do it. When you're really coming off heavy chemo, the first week after chemo, I'd say you don't have the energy to do much. Not even to do that." P32: "Certainly not during chemotherapy, that's for sure. After my chemotherapy, I had so much, listen, I couldn't even swallow my saliva anymore, I couldn't swallow my pills or water, my concentration was on just one thing: my saliva. It's definitely not during chemotherapy." P35: "Because there are certain periods, like the one I experienced, when your mouth feels like it's on fire and you can't stand it anymore. I think getting into hypnosis becomes complicated, because the pain prevents you from concentrating."
	Interest	P10: "I found that I didn't even have time to look at everything." P32: "I did another stay, I went back to the hospital recently from the 2nd to the 11th. [...] I would have liked to have it there."
	User experience	P16: "If you tell me I'm going to see a forest, I expected a greener forest. But I still remember, I think there are like seven... if I counted correctly, there are about seven different landscapes shown. There were three or four that looked like... not that they were on fire, but like they had been through a fire." P25: "Yes. For me it was the first time I used something like that, and it was quite impressive." P32: "But from what I saw, and all the little Quebec touches, I loved it." P32: "The strong points are definitely the music, the relaxation it provided." P35: "For my part, I find the idea brilliant. It's definitely acceptable. I think the concept is really good."
	Satisfaction: material	P32: "The headset was really special; it was my first experience with a virtual headset. And I know it's something very costly and expensive. It was very good." P35: "One of the problems I mentioned is that unfortunately with my glasses, it didn't work very well. I had pressure on my nose. [...] It's not a problem with the application, it's more with the conceptual design of the headset." P39: "What I noticed is that probably the headset, from being cleaned so often, I personally thought there was an odor. [...] But I noticed it at the beginning and then I forgot about it."
Satisfaction: intervention		P10: "First of all, I think anything involving hypnosis exercises or simply meditation and relaxation with a virtual reality headset during hospitalization, whether during the transplant or recovery afterward, is like a gem."

	P16: "Yes, yes, I'm really in favor of things that can help people who are, not imprisoned, but kind of stuck in this ordeal, let's say. [...] I'm really happy to be able to participate in this."
	P16: "[...] I think I liked the VR experience better, in the sense beyond the exercise itself. [...] For me, that aspect of being by the sea was really more beneficial."
	P35: "I think the product could be interesting for any hospitalized person [...] I can see that the product could also be interesting for other people who are hospitalized for a month, even in shared rooms, to help them refocus, concentrate, and get through it."
Landscapes choice	P39: "What I noticed is that what made me feel good were the landscapes, that we could move around everywhere."
Entertainment	P39: "What I found very positive in the images was the escape, the entertainment."
Usability	P10: "Yes, totally, because it's not complicated. If it's something people appreciate, it's simple, even if you feel unwell, really unwell and sick. Putting on a headset and lying down... there's nothing complicated about it. It doesn't hurt. In my case, I didn't get tired."
	P16: "I don't really have a reference point, but I still found it user-friendly. It was quite easy."
Perceived efficacy	P7: "Psychologically, it's a huge benefit because when we're in a situation like that, we're vulnerable."
	P10: "I know it's a branch of cancer that requires fairly invasive and intense treatments that demand a lot of strength and resilience, both physical and psychological. I think the virtual reality headset really helps in both spheres."
	P11: "It allowed you to escape, to focus on something else. It allowed you to calm down."
	P16: "When I visited the beaches, I remember finding it quite relaxing."
	P35: "I think it depends on the kind of pain you have, the level and the intensity. It's still my opinion, but I think there are pains like that. I have a bit of itching. It's nothing abnormal, but maybe, in an ideal world, we could focus on self-hypnosis. Maybe that would help me calm down."
Cybersickness	P25: "No, maybe just the very first time, but what I told you was more dizziness than nausea."
	P39: "No, never. It happened once, I remember it was when I moved my head. I said to myself, 'I want to see over there.' When I moved my head, I felt a little 'whoa.' But not enough to cause nausea."
Recommendations	P7: "I don't know if there are headsets that eliminate outside noise. I don't know if the technology allows for noise attenuation."
	P16: "As I said, I think it could be implemented, but maybe it should just be explained a little more. [...] I think maybe either the person bringing the headset should explain it a bit, or it could be good to have a video explaining the purpose of it."
	P32: "However, maybe before, just a bit before chemotherapy, present the program earlier. I think we were introduced to it after chemotherapy, but presenting the program earlier in the process."
	P39: "It would also be nice to explore other countries. That would make it feel even more like traveling."

595 **Table 4. Mean scores for each variable of interest**

	Group	HADS-A	HADS-D	BPI experience	FACT PWB	FACT SWB	FACT EWB	FACT FWB	FACT BMT	MFI
N	Experimental	20	20	20	20	20	20	20	20	20
	Control	20	20	19	20	20	20	20	20	20
Missing	Experimental	0	0	0	0	0	0	0	0	0
	Control	0	0	1	0	0	0	0	0	0
Mean	Experimental	5.10	6.05	28.1	14.4	20.3	17.8	15.9	23.4	29.5
	Control	5.55	8.50	30.1	14.7	20.1	18.4	14.1	20.9	28.6
Median	Experimental	5.00	6.00	21.0	12.0	21.0	18.0	15.5	23.0	29.5
	Control	5.00	8.50	31.0	14.5	20.0	19.0	14.0	20.0	29.5
Standard deviation	Experimental	3.09	3.15	20.4	6.13	3.06	4.21	6.41	6.64	10.3
	Control	3.44	3.86	23.3	7.16	3.25	4.73	6.52	6.45	9.91
Minimum	Experimental	1.00	1.00	7.00	6.00	14.0	9.00	6.00	10.0	12.0
	Control	1.00	3.00	0.00	5.00	14.0	7.00	0.00	9.00	11.0
Maximum	Experimental	11.0	12.0	67.0	26.0	24.0	24.0	27.0	36.0	50.0
	Control	15.0	15.0	66.0	27.0	24.0	24.0	26.0	34.0	44.0

596

597 **Supplementary material 1. Hypnosis scripts**

598 Script 1 — Forest Setting

599 *Phase 1 — Induction*

600 You may settle in comfortably and make yourself at ease!

601 Good! I invite you to take a deep breath in, and then to breathe out deeply, very deeply!

602 Excellent!

603 Now, you can allow your body to relax, let go, with each breath in, breath out.

604 Allow yourself to be guided by each breath in, each breath out, as though you were drifting deeply into a
605 state of relaxation, a state of deep, profound ease. You may even let your imagination picture oxygen
606 bubbles gently floating around you. You can breathe in... breathe out. The intention is simply to allow this
607 relaxation to settle in as comfortably as possible. Very good!

608 With each breath in... breath out, your body relaxes more deeply, as though you allow your body to rest
609 right there, in the chair or on the bed... in a comfortable way.

610 As you allow yourself to drift more deeply into this state of deep... very deep relaxation, surrounded by
611 that pleasant, comfortable oxygen, your body enters a pleasant ease, resting comfortably in the chair. You
612 may allow yourself to forget about this body, to let it remain quietly relaxed. Make no effort to relax, do
613 nothing. It is not useful to spend energy on this — save it for later... excellent! And if you notice any
614 discomfort, simply acknowledge it but do nothing to change it. Let relaxation do that for you, let relaxation
615 make you comfortable.

616 And your imagination can drift even more deeply into this state of ease, of comfort... with every breath in,
617 breath out. You may simply allow yourself to enter as deeply as possible into this experience of relaxation.
618 And in a few moments, simply let your imagination settle pleasantly in a place of comfort, of ease.

619 *Phase 2 — Forest Imagery*

620 You may settle in comfortably in the forest.

621 You can simply look around you, look at the sky, the landscapes, the trees... look at the place you are in!
622 Look to the right, to the left... Excellent!

623 And this body continues to relax as the eyes can look, the ears can hear. Perhaps simply hear the sound of
624 the wind [add wind sound] ... through the trees, around you, comfortably, to be pleasantly immersed in
625 this experience, relaxed... And by listening carefully, [add birdsong] allow yourself to be soothed by the
626 birdsong, simply connecting to these sounds that bring calm, always relaxed, always at ease.

627 And as you are in this place, simply notice how your body can connect to this relaxation, how deeply the
628 body can feel settled, feeling connected to nature, doing nothing, simply being immersed in these
629 sounds..., in these images..., it is even possible that some people can also sense the temperature of the
630 place you are in — with a great deal of imagination one can simply become even more immersed in
631 oneself, in this temperature.

632 There are some people... I do not know whether you are one of them... who can smell the scent of pine,
633 the fragrance of flowers... of this calm and tranquil forest.

634 Contemplate nature, the calm, what relaxes you. Excellent!

635 As you are immersed in this experience, you can let this body rest, as though it too could find itself in the
636 heart of nature, as though it could relax, unwind, comfortably... as though there were a connection
637 between what the mind sees and thinks, and the way the body responds. Excellent!

638 And now I invite your body to repair its discomforts... During this time, do nothing... simply let go, let the
639 experience guide you in this moment of ease, of relaxation, of comfort. Very good!

640 And perhaps this experience, this place brings you back to another experience you have already lived... in
641 the heart of nature, without any effort... you can simply reconnect to certain pleasant moments of your
642 life, certain positive, comfortable memories... to perhaps recall moments of ease, of joy, of comfort, as
643 you wish.

644 And so that you may enjoy this moment and so that the body feels what the mind is offering it, I will simply
645 remain silent for 3 minutes, so that you can simply live this experience as you wish, comfortably.

646 Very good!

647 Allow yourself to be guided by these relaxing images. Observe how this calm relaxes you. A little like being
648 by a fire [add fire sound]... in a clearing... Relaxed.

649 *Phase 3 — Anchoring*

650 Excellent! If you wish... during this experience... it is possible for you to record the benefits of this journey
651 into nature, the benefits for the body that relaxes, that unwinds. You can even record this sensation. To
652 do this, you can make a simple gesture: touch the thumb and index finger of one hand, right or left — it is
653 your choice.

654 Touching the thumb and index finger of one of your hands, right or left, is a way of recording your body as
655 relaxed, at ease, comfortable. As though you are anchoring this experience inside your body, comfortably.

656 The body is more comfortable, the mind is more free, it enjoys the present moment, it relaxes. And the
657 next time you make this gesture... touching the thumb and index finger of that hand... it will be a signal
658 for you to return — even without the images offered to you today — to the comfort you are experiencing
659 right now. Very good!

660 The next time you make this gesture, when you touch the thumb and index finger of that hand, it will be
661 a signal for you to simply find this feeling of comfort in your body... And you will be able to reproduce this
662 pleasant sensation at any time, whenever you wish. Very good!

663 *Phase 4 — Re-alerting*

664 Gradually... now... you can simply prepare to leave this experience... to move away from this place.
665 Perhaps gradually, you hear

666 You can also allow yourself to be gradually guided by this music, which is beginning to bring you energy,
667 progressively restoring vitality.

668 And I now invite you to focus on your breathing

669 Take a deep breath in. You can simply return to this experience of breathing. See this oxygen circulating
670 around you.

671 As this oxygen circulates comfortably around you, you can start to feel more and more energy returning
672 to the body. This oxygen brings you all the energy necessary for you to regain movement.

673 And do not be surprised... that even as energy returns... you will keep this comfort in your body, relaxed,
674 pleasant. And, guided by this music and these oxygen bubbles, you will gradually begin to rise back towards
675 your waking state of awareness, to emerge in a few moments from this experience, full of energy, the
676 body comfortable and the mind clear.

677 And simply, at your own pace, you can begin to take deep breaths in, deep breaths out... There you are...
678 to regain all the necessary and sufficient energy. And when you wish, when you have regained a
679 comfortable body and can once again feel the contact of your feet on the floor, the support of the chair...
680 you will regain all the sensations of the room, the temperature, the sounds of the room...

681 As soon as you regain all these sensations and are ready to emerge from this experience, simply let me
682 know by raising your hand, at your own pace.

683 Excellent. Thank you very much.

684

685 Script 2 — Sea/Beach Setting

686 *Phase 1 — Induction*

687 Are you sitting comfortably? Are you at ease?

688 Good! I am going to ask you simply to take a deep breath in, and then to breathe out deeply, very deeply!

689 Excellent!

690 Now! I invite you to let your body relax, let go in this chair, with each breath in, breath out.

691 Allow yourself to be guided by each breath in, each breath out, as though you were drifting deeply into a
692 state of relaxation, a state of deep, profound ease. You may even let your imagination picture oxygen
693 bubbles gently floating around you. You can breathe in... . breathe out. The intention is simply to allow
694 this relaxation to settle in as comfortably as possible. Very good!

695 With each breath in... breath out, your body relaxes more deeply, as though you allow your body to rest
696 right there, in the chair or on the bed... in a comfortable way.

697 As you allow yourself to drift more deeply into this state of deep... very deep relaxation, surrounded by
698 that pleasant, comfortable oxygen, your body enters a pleasant ease, resting comfortably in the chair. You
699 may allow yourself to forget about this body, to let it remain quietly relaxed. Make no effort to relax, do
700 nothing. It is not useful to spend energy on this — save it for later... excellent! And if you notice any
701 discomfort, simply acknowledge it but do nothing to change it. Let relaxation do that for you, let relaxation
702 make you comfortable.

703 And your imagination can drift even more deeply into this state of ease, of comfort... with every breath in,
704 breath out. You may simply allow yourself to enter as deeply as possible into this experience of relaxation.
705 And in a few moments, simply let your imagination settle pleasantly in a place of comfort, of ease.

706 *Phase 2 — Seaside Imagery*

707 You may settle in comfortably at the beach.

708 You can simply look around you, see the place you are in, look to the right, look to the left, [add wind
709 sound] simply hear the pleasant sound of the wind,

710 Perhaps simply hear the ocean [add ocean sound]... and the waves around you, comfortably, to be
711 completely immersed in this pleasant, relaxing experience... And this body continues to relax as the eyes

712 can look, the ears can hear, perhaps even [add birdsong] the birdsong, simply connecting to these sounds
713 that bring ease, calm, always relaxed, always at ease.

714 And as you are in this place, simply notice how your body can connect to this relaxation, how deeply the
715 body can feel settled, feeling present before the sea, doing nothing, simply being immersed in these
716 sounds..., in these images..., it is even possible that some people can also feel the coolness of the breeze,
717 the temperature of the place you are in — with a great deal of imagination one can simply become even
718 more immersed in oneself, in this temperature.

719 There are some people... I do not know whether you are one of them... who can smell the scents, the salty
720 air of this place, at the water's edge... of this beach... or perhaps another beach

721 To contemplate nature even further, the calm, what relaxes you. Excellent!

722 As you are immersed in this experience, you can let this body rest, as though it too could find itself on this
723 beach, as though it could relax, unwind, comfortably... as though there were a connection between what
724 the mind sees and thinks, and the way the body responds. Excellent!

725 And now I invite your body to repair the discomforts in this body... During this time, do nothing... simply
726 let go, let the experience guide you in this moment of ease, of relaxation, of comfort. Very good!

727 And perhaps this experience, this place brings you back to another experience you have already lived... at
728 the beach, without any effort... you can simply reconnect to certain pleasant moments of your life, certain
729 positive, comfortable memories... to perhaps recall moments of ease, of joy, of comfort, as you wish.

730 And so that you may enjoy this moment and so that the body feels what the mind is offering it, I will simply
731 remain silent for 3 minutes, so that you can simply live this experience as you wish, comfortably.

732 Very good!

733 Allow yourself to be guided by these relaxing images. Observe how this setting sun relaxes you. A little like
734 being by a fire [add fire sound, lower ocean sound]... on the beach... Relaxed.

735 *Phase 3 — Anchoring*

736 Excellent! If you wish... during this experience... it is possible for you to record the benefits of this journey
737 to the beach, the benefits for the body that relaxes, that unwinds. You can even record this sensation. To
738 do this, you can make a simple gesture: touch the thumb and index finger of one hand, right or left — it is
739 your choice.

740 Touching the thumb and index finger of one of your hands, right or left, is a way of recording your body as
741 relaxed, at ease, comfortable. As though you are anchoring this experience inside your body, comfortably.

742 The body is more comfortable, the mind is more free, it enjoys the present moment, it relaxes. And the
743 next time you make this gesture... touching the thumb and index finger of that hand... it will be a signal
744 for you to return — even without the images offered to you today — to the comfort you are experiencing
745 right now. Very good!

746 The next time you make this gesture, when you touch the thumb and index finger of that hand, it will be
747 a signal for you to simply find this feeling of comfort in your body... And you will be able to reproduce this
748 pleasant sensation at any time, whenever you wish. Very good!

749 *Phase 4 — Re-alerting*

750 Gradually... now... you can simply prepare to leave this experience... to move away from this beach.
751 Perhaps gradually, you hear

752 You can also allow yourself to be gradually guided by this music, which is beginning to bring you energy,
753 progressively restoring vitality.

754 And I now invite you to focus on your breathing

755 Take a deep breath in. You can simply return to this experience of breathing. See this oxygen circulating
756 around you.

757 As this oxygen circulates comfortably around you, you can start to feel more and more energy returning
758 to the body. This oxygen brings you all the energy necessary for you to regain movement.

759 And do not be surprised... that even as energy returns... you will keep this comfort in your body, relaxed,
760 pleasant. And, guided by this music and these oxygen bubbles, you will gradually begin to rise back towards
761 your waking state of awareness, to emerge in a few moments from this experience, full of energy, the
762 body comfortable and the mind clear.

763 And simply, at your own pace, you can begin to take deep breaths in, deep breaths out... There you are...
764 to regain all the necessary and sufficient energy. And when you wish, when you have regained a
765 comfortable body and can once again feel the contact of your feet on the floor, the support of the chair...
766 you will regain all the sensations of the room, the temperature, the sounds of the room...

767 As soon as you regain all these sensations and are ready to emerge from this experience, simply let me
768 know by raising your hand, at your own pace.

769 Excellent. Thank you very much.

770 **Supplementary material 2. Interview guide**

771 1. Relevance and Acceptability of the Program

- 772 • Is the RVH program suitable for supporting a patient with a hematological disease?
- 773 • Is the RVH program suitable for supporting a patient undergoing a stem cell transplant?
- 774 • Can the RVH program be implemented in a hematology clinic?
- 775 • Do you have any other comments regarding the relevance and acceptability of the RVH?

776

777 2. Use of the RVH

- 778 • Overall, the RVH program...
- 779 • Are you satisfied with the VR experience?
- 780 • Are you satisfied with this system?
- 781 • Was watching this film through VR an enjoyable and satisfying experience?
- 782 • Did watching this film through VR provide you with useful information?
- 783 • Was listening to the story an enjoyable and satisfying experience?
- 784 • Did listening to the story provide you with useful information?
- 785 • Do you feel that this system (VR) was created by an expert?
- 786 • Was the presentation of the exercise through VR appropriate?
- 787 • Do you have any other comments to expand on your viewpoint regarding the use of the RVH?

788

789 3. Expected effects

- 790 • Will the RVH help improve patients' quality of life?
- 791 • Will the RVH help reduce distress?
- 792 • Will the RVH help reduce anxiety?
- 793 • Will the RVH help improve mood?
- 794 • Will the RVH help reduce pain?
- 795 • Will the RVH help reduce fatigue?
- 796 • Will the RVH help reduce nausea?
- 797 • Will the RVH help reduce other treatment side effects? If so, which ones?

798 • Do you have any other comments to expand on your viewpoint regarding the expected effects of
799 the RVH?

800 User experience

801 • Could you elaborate on your experience testing this RVH prototype?

802 • What are the strengths of the RVH prototype?

803 • What are the weaknesses of the RVH prototype?

804

805 4. Recommendations

806 What are your recommendations for improving this RVH prototype for administration to patients

807 undergoing a transplant?

808

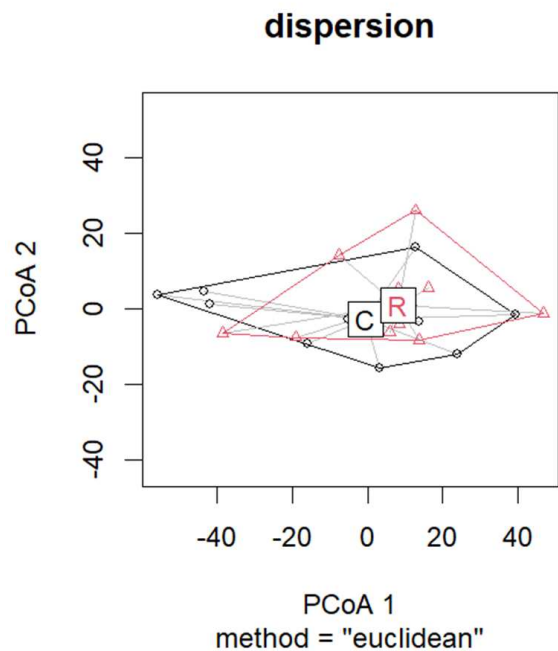
809 **Supplementary material 3. Code and extensive results for the PERMANOVA**

```

810 > library(readxl)
811 > data <- read_excel("source document")
812 > names(data) [1] "ID"      "group"   "sex"     "age"     "transplant" "D_HADSa" [7] "D_HADSd"
813 "D_HADSt"    "D_BPlseverity" "D_BPlinterf" "D_BPllexpe" "D_FACTpwb" [13] "D_FACTswb" "D_FACTewb"
814 "D_FACTfwb"  "D_FACTbmt"    "D_FACTglobal" "D_MFI"
815 > data$group <- as.factor(data$group)
816 > data$sex <- as.factor(data$sex)
817 > data$transplant <- as.factor(data$transplant)
818 > data$age <- as.numeric(data$age)
819 > vars_sel <- c("D_HADSa", "D_HADSd", "D_BPllexpe", "D_FACTpwb", "D_FACTswb", "D_FACTewb", "D_FACTfwb",
820 "D_FACTbmt", "D_MFI")
821 > > data_subset <- data[, c("group", "sex", "age", "transplant", vars_sel)]
822 > > complete_cases <- complete.cases(data_subset)
823 > data_clean <- data_subset[complete_cases, ]
824 > > dist_matrix <- vegdist(data_clean[, vars_sel], method = "euclidean")
825 > > permanova_result <- adonis2(+ dist_matrix ~ age + sex + transplant + group,+ data = data_clean,+
826 permutations = 999,+ by = "margin"+ )
827 > > print(permanova_result)
828 Permutation test for adonis under reduced model
829 Marginal effects of terms
830 Permutation: free
831 Number of permutations: 999
832 adonis2(formula = dist_matrix ~ age + sex + transplant + group, data = data_clean, permutations = 999, by =
833 "margin")
834
835          Df SumOfSqs    R2    F Pr(>F)
836 age          1 1218.4 0.06797 1.5340 0.200
837 sex          1  205.7 0.01148 0.2590 0.764
838 transplant  2 1997.8 0.11144 1.2575 0.285
839 group       1 1808.5 0.10088 2.2768 0.121
840 Residual    16 12709.0 0.70895

```

```
840      Total  21 17926.4 1.00000
841  >> dispersion <- betadisper(dist_matrix, data_clean$group)
842  >> anova(dispersion)
843  Analysis of Variance Table
844  Response: Distances
845      Df Sum Sq Mean Sq F value Pr(>F)
846  Groups  1 338.5  338.45  1.5517 0.2273
847  Residuals 20 4362.3  218.12
848  > permutest(dispersion, permutations = 999)
849  Permutation test for homogeneity of multivariate dispersions
850  Permutation: free
851  Number of permutations: 999
852  Response: Distances
853      Df Sum Sq Mean Sq  F N.Perm Pr(>F)
854  Groups  1 338.5  338.45 1.5517  999 0.236
855  Residuals 20 4362.3  218.12
856  >> plot(dispersion)
```



857

858 **Supplementary material 4. CONSORT checklist**

Section / Topic	No	CONSORT 2025 checklist item description	Reported on page no.
Title and abstract			
Title and structured abstract	1a	Identification as a randomised trial	1
	1b	Structured summary of the trial design, methods, results, and conclusions	3
Open science			
Trial registration	2	Name of trial registry, identifying number (with URL) and date of registration	3
Protocol and statistical analysis plan	3	Where the trial protocol and statistical analysis plan can be accessed	3
Data sharing	4	Where and how the individual de-identified participant data (including data dictionary), statistical code and any other materials can be accessed	3
Funding and conflicts of interest	5a	Sources of funding and other support (e.g., supply of drugs), and role of funders in the design, conduct, analysis and reporting of the trial	16
	5b	Financial and other conflicts of interest of the manuscript authors	16
Introduction			
Background and rationale	6	Scientific background and rationale	4-5
Objectives	7	Specific objectives related to benefits and harms	5
Methods			
Patient and public involvement	8	Details of patient or public involvement in the design, conduct and reporting of the trial	-
Trial design	9	Description of trial design including type of trial (e.g., parallel group, crossover), allocation ratio, and framework (e.g., superiority, equivalence, non-inferiority, exploratory)	5
Changes to trial protocol	10	Important changes to the trial after it commenced including any outcomes or analyses that were not prespecified, with reason	5
Trial setting	11	Settings (e.g., community, hospital) and locations (e.g., countries, sites) where the trial was conducted	5
Eligibility criteria	12a	Eligibility criteria for participants	6
	12b	If applicable, eligibility criteria for sites and for individuals delivering the interventions (e.g., surgeons, physiotherapists)	-
Intervention and comparator	13	Intervention and comparator with sufficient details to allow replication. If relevant, where additional materials describing the intervention and comparator (e.g., intervention manual) can be accessed	6 + Protocolv

Outcomes	14	Pre-specified primary and secondary outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (e.g., median, proportion), and time point for each outcome	7
Harms	15	How harms were defined and assessed (e.g., systematically, non-systematically)	7
Sample size	16a	How sample size was determined, including all assumptions supporting the sample size calculation	8
	16b	Explanation of any interim analyses and stopping guidelines	-
Randomisation:			
Sequence generation	17a	Who generated the random allocation sequence and the method used	6
	17b	Type of randomisation and details of any restriction (e.g., stratification, blocking and block size)	6
Allocation concealment mechanism	18	Mechanism used to implement the random allocation sequence (e.g., central computer/telephone; sequentially numbered, opaque, sealed containers), describing any steps to conceal the sequence until interventions were assigned	6
Implementation	19	Whether the personnel who enrolled and those who assigned participants to the interventions had access to the random allocation sequence	6
Blinding	20a	Who was blinded after assignment to interventions (e.g., participants, care providers, outcome assessors, data analysts)	-
	20b	If blinded, how blinding was achieved and description of the similarity of interventions	-
Statistical methods	21a	Statistical methods used to compare groups for primary and secondary outcomes, including harms	8-9
	21b	Definition of who is included in each analysis (e.g., all randomised participants), and in which group	8-9
	21c	How missing data were handled in the analysis	-
	21d	Methods for any additional analyses (e.g., subgroup and sensitivity analyses), distinguishing prespecified from post-hoc	-
Results			
Participant flow, including flow diagram	22a	For each group, the numbers of participants who were randomly assigned, received intended intervention, and were analysed for the primary outcome	Flowchart
	22b	For each group, losses and exclusions after randomisation, together with reasons	Flowchart
Recruitment	23a	Dates defining the periods of recruitment and follow-up for outcomes of benefits and harms	9
	23b	If relevant, why the trial ended or was stopped	9
Intervention and comparator delivery	24a	Intervention and comparator as they were actually administered (e.g., where appropriate, who delivered the intervention/comparator, how participants adhered, whether they were delivered as intended [fidelity])	Flowchart 9
	24b	Concomitant care received during the trial for each group	-
Baseline data	25	A table showing baseline demographic and clinical characteristics for each group	Table 1

Numbers analysed, outcomes and estimation	26	For each primary and secondary outcome, by group: - the number of participants included in the analysis - the number of participants with available data at the outcome time point - result for each group, and the estimated effect size and its precision (such as 95% confidence interval) - for binary outcomes, presentation of both absolute and relative effect size	Table 4
Harms	27	All harms or unintended events in each group	-
Ancillary analyses	28	Any other analyses performed, including subgroup and sensitivity analyses, distinguishing pre-specified from post-hoc	-
Discussion			
Interpretation	29	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	11-12
Limitations	30	Trial limitations, addressing sources of potential bias, imprecision, generalisability, and, if relevant, multiplicity of analyses	13

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Supplementarymaterial4.CONSORTchecklist.docx](#)
- [Supplementarymaterial1.Hypnosisscripts.docx](#)
- [Supplementarymaterial5.Spaghettiplots.docx](#)
- [Supplementarymaterial2.Interviewguide.docx](#)
- [Supplementarymaterial3.CodeandextensiveresultsforthePERMANOVA.docx](#)