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SafeSpace: Co-design and evaluation of a unique virtual reality intervention, incorporating compassionate mind training, to support people undergoing cancer treatment.

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Title Page

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Article Summary

Strengths and Limitations of this study

- First study in an oncology setting exploring use of VR to deliver a psychological support intervention.
- The SafeSpace intervention is novel, incorporating virtual reality and compassionate mind training to provide a low-cost and flexible resource to support people to relax, reduce their stress and cope with cancer treatments.
- An experience based co-design approach was used to develop and evaluate the intervention, working with people affected by cancer.
- Acceptability and feasibility were tested in the oncology setting. Within the evaluation phase, the potential impact of the intervention on psychological, physiological well-being and quality of life was assessed.
- Mixed-methods approach: qualitative techniques employed to capture experience of intervention use.
- The intervention consisted of three short sessions per participant. As compassionate mind training is relatively new and has had very limited use in cancer care, participants only received a small dose. This may have limited the overall effect of the intervention.
- This was an acceptability and feasibility project so sample size was small which limits the inferences that can be drawn from this study.

Abstract:

Objectives: The SafeSpace study co-designed and tested a virtual reality intervention, incorporating relaxation and compassionate mind-training to determine acceptability/feasibility in an oncology setting and evaluate impact on physical/psychological well-being and quality-of-life.

Design: A two-phase study. Phase 1 determined key characteristics using an Experienced-based Co-Design approach. Phase 2 evaluated the intervention using various measures and qualitative interviews. Descriptive statistics were used to analyse measures data and framework analysis was used to analyse interviews.

Setting: A specialist cancer centre in London, UK.

Participants: 18 in phase 1; 21 in phase 2. Participants were in cancer treatment, recovery or palliative care.

Primary and secondary outcome: Primary outcome was acceptability of the intervention, assessed by >60% uptake of three sessions. Secondary outcomes were impact on psychological well-being using: EQ-5D/QLQ-C30, Profile of Mood Scale (POMS), Warwick and Edinburgh Mental Well-being scale (WEMWBS), Depression and Anxiety Severity Scale 21 (DASS21), Self-Compassion Scale (SCS), Acceptance and Action Questionnaire (AAQII), and a locally developed questionnaire to capture self-compassion post-use. Physiological impact was assessed by change in heart rate (HR)/heart rate variability (HRV) and electrodermal activity (EDA).

Results: Twenty participants (mean age=48.7 years; SD=16.87); 65% (n=13) completed three sessions. Mental well-being improved following each use and from baseline to after session 3 (VR 1- z= 2.846, p = < 0.01; VR 2 -z = 2.501, p = <0.01; VR 3 - z = 2.492, p = <0.01). There was statistically significant difference in mean scores for EDA at mid- and post-session compared to pre-session (F (1.658, 4.973) = 13.364, p < 0.05). There was statistically significant reduction in stress levels from baseline to post-session 3. Participants found the intervention acceptable and highlighted areas for development.

Conclusion: The intervention is acceptable, and has shown positive effects on mental well-being/stress in the oncology setting. Larger studies are needed to confirm findings.

Word count: 300

Background:

The number of people living with cancer is expected to double to four million over the next 20 years. (1). Treatment involves surgery, radiotherapy, chemotherapy or other, alone or in combination. Many are unpleasant and lead to lack of compliance/adherence to recommended regimens (2). People affected by cancer (PABC) commonly experience poor psychological wellbeing and poor quality of life (QoL) (3, 4, 5). Some become isolated from friends/family, or are unable to continue working, causing financial difficulties and further isolation (2). At least one in four – around 500,000 people in the UK – face poor health or disability after treatment (1).

Virtual Reality

Healthcare has seen a growth in technology to provide support (6). Virtual reality (VR) in particular has been used in various applications including pain management, multiple sclerosis (7, 8, 9) and treatment of psychological conditions, such as phobias and anxiety (10, 11, 12). Within cancer care, VR has been used to manage pain, anxiety, and symptom distress. However, current literature regarding its effectiveness is equivocal. In a review of 19 studies (13), of those which reported on pain (n=6), half found that VR had a statistically significant positive effect in cancer patients. This was substantiated by other work (14) which reported decreased pain and state anxiety levels post-VR use by women with severe/chronic pain following breast cancer treatment. In contrast, a recent meta-analysis of cancer-related symptom management (15) showed the only statistically significant effect was reduced fatigue levels. Other studies (16, 17) reported positive results as a distraction technique during chemotherapy administration. These were small samples (n=16; n=20 respectively) of women with breast cancer. Subsequent studies of larger, more diverse cohorts reported significant impact on reducing perception of time when receiving chemotherapy, validating the distractive nature of VR (18, 19).

Compassion Focused Therapy

Compassion can be defined as 'the sensitivity to suffering in self and others, with a deep commitment to try to relieve it', and compassion-focused therapy (CFT) is an integrated, multimodal treatment approach that draws from sociology, psychology, and neuroscience (20). Central to CFT is compassionate mind-training (CMT), which helps people develop self-compassion (21). CFT and CMT have been shown to reduce suffering and improve QoL in a range of health problems such as anxiety/depression, eating disorders, phobias and pain management (22, 23, 24, 25) and are becoming more mainstream and acceptable (26, 27).

Whilst the application of VR within cancer is accepted, its use to deliver psychological therapies, such as CMT, remains unexplored. Little is known about how these treatment approaches might be combined, and whether there is any synergistic effect. The aim of this study was to co-design a low-cost VR intervention with PABC enabling rapid access to safe, calm and soothing environments accompanied by guided CMT exercises, and assess acceptability in the oncology setting.

Methods:

A pilot/proof of concept two-phased study using mixed-methods and an experience based co-design (EBCD) approach. EBCD is a method of participatory research that embeds experience of service

users and staff into service design (28). Phase 1: development of the intervention by co-designing and refining a number of continuously improved prototypes with PABC. Intervention delivery and evaluation model were also established. Phase 2: formal acceptability and evaluation of the intervention, with PABC, using the range of psychological, physiological, and QoL measures agreed in Phase 1.

Instruments for psychological assessment:

Demographic data collected included age, gender, diagnosis, cancer group, cancer stage and aim of treatment.

The POMS

The POMS (29) examines six mood subscales: tension-anxiety, depression, anger-hostility, vigour, fatigue, and confusion. Total mood disturbance score is computed by adding the five negative subscale scores and subtracting the vigour score. Higher total mood score indicate greater degree of mood disturbance (30). The POMS subscales and total score have demonstrated sound internal consistency reliability ($\alpha \geq 0.84$) (31).

The WEMWBS

The WEMWBS (32) is a 14-item scale of mental well-being covering subjective well-being and psychological functioning. It is scored by summing responses to each item on a 1-5 Likert scale. The minimum scale score is 14; maximum is 70. It has been validated in the UK in ages 16+ (33). A non-validated, adapted version, AWEMWBS, was used immediately after each intervention use.

The AAQII

The AAQII is a seven-item measure of psychological inflexibility, or experiential avoidance. Items are scored on a Likert scale of 1 (never true) to 7 (always true) and are summed up. Higher scores equal greater levels of psychological inflexibility, with proven reliability and validity (34).

The SCS

The SCS (35) is a 26-item instrument that measures self-compassion through three hypothesized dimensions with their negative counterparts: self-kindness versus self-judgment, common humanity versus isolation, and mindfulness versus over-identification, according to a 5-point scale (1= Almost Never; 5= Almost Always). Subscale scores are computed by calculating the mean of subscale item responses. To compute the total score, the Self-Kindness, Common Humanity, and Mindfulness are summed with reverse scores of the Self-judgment, Isolation, and Over-identification subscales. Higher scores indicate greater self-compassion. In the original version, the total score showed excellent internal consistency ($\alpha = .92$) and so did the six subscales (range: .75 - .81) (36).

The DASS21

The DASS 21 (37) is a 21-item instrument that assesses depression, anxiety and stress. Each seven-item scale has four responses ranging from 0 (did not apply to me at all) to 3 (applied to me much/most of the time). A higher score indicates higher levels of depression, anxiety and stress. The DASS-21 has excellent internal consistency (38), and construct validity (38, 39).

The EQ5D-3L

The EQ5D (40) is designed to measure generic health outcome and comprises two parts: the EQ5D-3L self-classifier, a self-reported description of health problems according to five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), and the EQ-VAS, a self-rated health status using a visual analogue scale to record perception of current overall health; the scale is graduated from 0 (the worst imaginable health state) to 100 (the best imaginable state). It has been shown to be reliable and valid in cancer populations (41).

The QLQ-C30

The QLQ-C30 (42) is used to measure general aspects of HRQOL in cancer patients. EORTC QLQ-C30, Version 3, incorporates five functional scales on physical (PF), role (RF), cognitive (CF), emotional (EF) and social (SF) functioning, three symptom scales on fatigue (FA), pain (PA) and nausea and vomiting (NV), single items assessing dyspnoea (DY), insomnia (SL), loss of appetite (AP), constipation (CO) and diarrhoea (DI), one item assessing perceived financial impact (FI) and global health status/QoL scale (Global QoL). Each item is scored in one of four categories 1) 'Not at all', 2) 'A little', 3) 'Quite a bit' 4) 'Very much', with the exception of 'Global QoL'. It has been shown to be reliable and valid in cancer populations (43, 44, 45).

Locally-developed questionnaire

The locally-developed questionnaire specifically targeted self-compassion after intervention use. It comprised 12 questions such as: 'To what extent did the virtual reality help you have insight into your current situation?' and 'To what extent did the virtual reality make you feel encouraged about the future?' Scored using a 7-item Likert scale ranging from not at all (1) to very much (7), the tool had excellent internal consistency (α = 9.44) (46); a higher score indicated that the intervention had a more positive impact.

Physiological assessment:

Physiological assessment was made using heart rate (HR), heart rate variability (HRV) and electrodermal activity (EDA) (47).

Procedure:

Potential participants were identified by clinical teams, and a diverse convenience sample undergoing a range of cancer treatments across tumour types from one specialist centre recruited. Inclusion criteria were: 1) having a diagnosis of cancer; 2) age over 18 years; 3) ability to provide written consent. Exclusion criteria were people: 1) considered too unwell; 2) in who use of VR is not recommended e.g. registered blind or known psychological disorder. Exclusion criteria were assessed by self-report or in consultation with clinical staff. All procedures were in accordance with the Declaration of Helsinki (1964) and later amendments or comparable ethical standards. Ethical approval was acquired from a UK Research Ethics Committee (South Central – Oxford B REC 18/SC/0346) and Health Research Authority (IRAS ID – 241770). Patient and Public involvement was sought for study design. Eligible participants received written information prior to giving consent.

Phase 1 - Intervention Development

Five workshops, conducted over six months, were facilitated by a research team including experts in VR and CMT, using an EBCD approach. All were digitally recorded and, along with observations collected by two researchers, transcribed and analysed using thematic analysis.

Initial design workshop - Seven participants took part, which started with individuals telling their story, challenges along their pathway and what was important to include. Participants were able to try a range of equipment and experiences in a VR demonstration. They were encouraged to share, critique and propose ideas, using the design studio method (48). Analysis of data identified a number of 'touch points', these being what was emotionally most important to participants, which were used to inform the first iteration of the intervention.

User-testing workshops - Three user-testing workshops took place in which three/four participants each were invited to try the subsequently developed prototype; a total of 11 participants took part in one or more. Participants were asked about their experience particularly focusing on quality and content of the intervention. Further 'touch points' informed the design of the next iteration, which was refined until the co-design team were satisfied it had been developed to acceptable quality.

Findings from Phase 1:

Over the course of the user-testing workshops, the intervention became more refined and focused on detail within, such as recognition of what constitutes a 'safe space', voice quality (e.g. pace/tone), and guidance versus instruction. The key features underpinning design of the final specification included: *1) being given permission to 'step out' of current situation; 2) importance of voice; 3) need for sign-posting/on-boarding information; 4) being able to explore; 5) being guided versus being instructed.* The final iteration consisted of three short sessions of VR/CMT, with CMT language developing progressively with each use, from simple, soothing rhythm breathing to a CMT self-compassion exercise. A choice of three environments was given; a beach as a 360-degree video, and animated mountain and forest scenes. Professional voiceover actors provided a choice of female or male audio. It was agreed that the intervention should be offered at any stage of treatment, and acknowledged that three sessions may not be sufficient to administer a meaningful 'dose' of CMT, but would be enough to generate preliminary data.

Evaluation workshop - A final workshop was held with five participants, who had taken part in either design or testing, to establish an evaluation model. A range of demographic, psychological and physiological measures were reviewed and agreed to be collected at baseline, and pre- and post-each intervention use (see Table 1). The final intervention was delivered on a head-mounted, stand-alone device; this was considered inexpensive and practical.

Table 1: Schedule for study procedure

Measure		Baseline	Pre each intervention	Post each intervention
Name/age/gender/dx/tx etc	Demographic information	X		
EQ-5D	HRQoL	X	X	
QLQ C30	HRQoL	X		X
Action and Acceptance Questionnaire II - AAQII	Psychological flexibility	X		
Depression, Anxiety and Stress Scale 21 – DASS21	Anxiety/depression/stress	X		X
Profile of Mood State - POMS	Mood	X	X	X
Warwick Edinburgh Mental Well-being Scale - WEMWBS	Mental well-being	X	X	
Self-compassion Scale - SCS	Self-compassion	X		X
Adapted Warwick Edinburgh Mental Well-being Scale - AWEMWBS	Mental well-being immediate time-point			X
Locally developed questionnaire	Self-compassioin			X
Heart rate/heart rate variation/electrodermal activity	Physiological	Monitored continuously before, during and after intervention		

Phase 2 – Evaluation/acceptability of intervention

The final intervention was evaluated and tested for acceptability. A further twenty-one people were recruited. Four study visits were organised, coinciding with planned appointments, spaced at least a week apart. At initial visit, written consent was obtained and demographic data collected. Participants completed the baseline set of questionnaires relating to psychological state and QoL. The study then proceeded as per table 1. Telephone interviews were conducted once the participant had completed intervention use.

Results:

Quantitative

Summary measures for participant characteristics, VR use data variables and questionnaire scores were presented as means and standard deviations for continuous (approximate) normally distributed variables and frequencies and percentages for categorical variables. Shapiro-Wilk test was used to confirm normal distribution of continuous summary scales (all p values >0.05). Friedman's test for repeated measures was performed to assess there was a statistically significant difference in scores between baseline, VR1, VR2 and VR3. Wilcoxon signed ranks test was used to

compare baseline and VR3 session scores. ANOVA were performed to assess changes in EDA, HR and HRV within each session. All p values were two-sided throughout; significance was set at the 5% level. IBM SPSS version 25 was used to analyse the data. Missing data was addressed, see suppl Table 1.

Participants

Seven males and 14 females consented to take part. One participant was subsequently lost to follow-up. Mean age was 48.7 years (SD=16.87; range: 22-77). Mean time elapsed since diagnosis was 37.08 months (SD= 45.00; range: 2-149). 16 participants (80%) were in active treatment. They had various tumour types with gynaecological cancer being most common (N=4; 20%) (See table 2).

Table 2: Tumour type

Tumour Type	N	%
Lower GI	2	10
Haematological	1	5
Gynaecological	4	20
Head and Neck	3	15
Breast	3	15
Genitourinary (GU)	3	15
Other	4	20

Acceptability/Feasibility Data

In total, 49 sessions of VR were delivered and completed. Acceptability of the intervention was deemed satisfactory as > 60% (N=13; 65%) of participants completed all three sessions. Reasons for not completing included: insufficient time within duration of the study, deterioration in clinical condition leading to changes in treatment, or transfer of care. There were 12 occasions (24% of total number of sessions delivered) when participants experienced a problem e.g. with equipment (see Table 3).

Table 3: Acceptability and feasability data

	VR1		VR2		VR3	
	n	%	n	%	n	%
No. that took part in VR:	20	100	16	80	13	65
No. that did not take part in VR:			4	20	7	35
Reasons for not completing VR:						
Insufficient time			1	25	3	43
Deterioration in condition					1	14
Discontinuation of treatment at site			1	25	1	14
Adverse effect from VR					1	14
Unknown			2	50	1	14
Voice:						
Male	12	60	8	50	6	46
Female	8	40	8	50	7	54
Chosen VR environment:						
Beach	12	60	5	31	8	61
Mountain	6	30	8	50	5	39
Forest	2	10	3	19	0	0
Private room:						
Yes	11	55	9	56	8	61
No	9	45	7	44	5	39
Did the participant change the environment whilst using VR?	2	10	0	0	1	8
Yes	18	90	16	100	12	92
No						
Did the participant experience external noise?						
Yes	9	45	6	37.5	5	38
No	11	55	10	62.5	8	62
Total time in VR (minutes):						
Mean	10.8		10.44		10.00	
SD	1.852		2.502		1.633	
Range	7-15		7-16		8-14	
Did the participant experience any problems with the equipment?	12		13		12	
No	8		3		1	
Yes:	5		0		1	
Minor	2		3		0	
Additional intervention	1		0		0	
Unresolvable						
Did the participant experience an adverse event?						
Yes	1	5	2	12.5	0	0
No	19	95	14	87.5	13	100

Adverse Events

Three minor adverse events (AE) were recorded by two participants who experienced mild nausea and dizziness whilst using the intervention. In both, this resolved spontaneously. The third was in one of the same participants but occurred 48 hours after completing VR2. They reported nausea and

dizziness for 48 hours resolving with bed-rest. In light of this, they were advised not to undergo the third session.

Descriptive Statistics

Descriptive statistics were computed for all questionnaire scores within respective domains and are presented as frequencies and standard deviations (See Suppl. Table 2). Friedman and Wilcoxon signed ranks tests were performed to compare potential changes in variables between baseline and VR1, VR2 and VR3 sessions. Missing data for each variable is shown in Suppl. table 3.

Multi-variate Analyses

Quality of Life

There were no statistically significant changes in QoL in either the EQ5D-3L or the QLQ-C30 responses (see Suppl. Table 4).

Psychological Measures

Total mood scores (POMS) were compared pre- and post-intervention. There was a statistically significant increase in total scores after the first session (VR 1) ($z = -2.136$, [b] $p = 0.03$) suggesting there was an improvement in mood. There was improvement in scores post-second session (VR2) but this was not statistically significant (see Suppl. Table 5). Mental well-being (WEMWBS) scores showed statistically significant changes to mental well-being from pre- to post-VR session (VR 1 $z = -2.846$[b] $p = < 0.01$; VR 2 $z = -2.501$[b] $p = <0.01$; VR 3 $z = -2.492$, [8] $p = <0.01$). There was a consistent beneficial effect maintained throughout all sessions and a statistically significant increase in WEMWBS scores from baseline to VR 3 ($x^2 = 12.905$, $df = 3$, $p = 0.005$) (see Suppl. Table 4 & 5).

There was a statistically significant reduction in stress levels as measured by the DASS21 from baseline to post-session 3 ($z = -2.138$[b], $p = 0.03$) (see Suppl. Table 5). While there was a positive and beneficial trend observed from baseline to post-session 3 (VR3) for DASS21 sub-scores for depression and anxiety, psychological flexibility (AAQII), self-compassion sub-domains self-kindness, self-judgement, and isolation and over-identification, as well as the locally developed questionnaire scores, none reached statistical significance (see Suppl. Tables 4 & 5).

Physiological measures

ANOVA were conducted to compare EDA, HR and HRV within each session. A decrease in mean EDA for each of the three sessions was recorded, dropping from pre-intervention level and maintained following removal of headset; this was significant for the first session. Using ANOVA with repeated measures and a Greenhouse-Geisser correction, mean scores for EDA were statistically significantly different at mid- and post-session compared to pre-session levels (F (1.658, 4.973) = 13.364, $p < 0.05$). Similarly, the only statistically significant change in HR was in the second session with a decrease from pre- to mid-session followed by a return to pre-session levels at post-session (F (1.424, 4.271) = 13.364, $p < 0.05$) (see Suppl. Tables 5a & 5b). No change was observed in HRV.

Qualitative

Participants were invited to participate in a short semi-structured telephone interview to acquire a deeper understanding of their experience of use; 11 consented to take part. Interviews were audio-recorded and transcribed. Feedback was also given following each individual use of the intervention; this was summarised and recorded manually by the researcher and analysed alongside interview data using framework analysis (49). The framework was informed by analysis of the first two transcripts which were coded independently by three researchers and themes discussed and agreed. The subsequent interview transcripts and participant comments were analysed using the agreed framework. Three themes emerged: *1) Practical issues; 2) Immersion; 3) Impact of intervention.*

Practical Issues:

Participants reported equipment as comfortable and relatively straightforward to use. Clear guidance was considered important, and a designated room suggested for the future.

> *'…putting the headset on isn't really a problem … we're all going to have to get used to some kind of virtual reality at some point … hadn't tried it before but it was very interesting.' 012*

The importance of tailoring to the individual was highlighted:

> *'I find breathing exercises really frustrating … I have tumours in my lungs, the amount I can inhale, the amount of time I can hold for is less than for other people. So someone will say hold it this many beeps and then you can't . . . you feel like you failed at it and you check out ...' 019*

Immersion:

This relates to quality of VR imagery, ability to explore, and impact of voices used in the audio. Lack of quality was seen as negatively impacting immersion and improvement suggested for the future with a preference for 'real' environments rather than animated:

> *'The beach was definitely more...realistic, you felt more sort of immersed in . . . compared with the other two.' 026*

Whilst there was positive reaction to the professional voices, some participants described becoming disengaged:

> *'…I had the final session with the lady [voice], and she was excellent . . . it was very believable. She really did explain it, she was really part of it, and all that. Whereas, I felt with him [male voice], more like that he was reading a script.' 027*

Not all participants liked the compassion therapy aspect of the intervention:

> *'… the compassionate mind therapy, I couldn't see the point of at all . . . you are in a compassion rich environment with the Nurses, the Doctors, friends and family. And the last thing you, sort of, need is another dose of compassion . . . ' 027*

There was mixed reaction to external noise; some found it detracted from the quality of experience but others found it reassuring as it gave awareness of what was going on around them:

> *'…the noise cancelling was pretty good but I did still hear, if I focused properly, the pump beeping if something went wrong . . . it was sort of the right balance between not being completely disconnected if something happened. I think, anymore and I would have felt too isolated.' 026*

Impact of intervention:

The intervention was seen as having immediate and lasting effects, with some recognising the ability to replicate the 'safe space' for themselves:

> *'The breathing techniques, I started to employ when I was having a scan even though the scan was very short. I thought that was quite useful for that. I hadn't really thought of that before but I found it actually quite calming.' 017*

For others, the impact was short-lived but still considered useful:

> *'I don't think it will have a lasting impact...It definitely made the rest of the day easier . . . . But the next day, the day after, I didn't still have that same sense of calm, it was just kind of immediately after… ' 019*

Participants' past experience of non-medical support measures emerged as relevant to receptiveness and engagement with the overall VR/CMT experience:

> *'But I've also been on some of these yoga type things where you just try and relax and get into the mood and all that kind of thing. And I thought it was quite useful for that. You know, the talking was the same.' 012*

Participants also gave valuable feedback regarding the research process and informing a larger study, with particular reference to burden of questionnaires:

> *'I think some of them were a little bit repetitive, I though the one with all the options about being angry, sad, that one went on for ages. I don't think that really needs to be that long.' 017*

Discussion:

The aim of the study was to co-design a low-cost VR intervention enabling rapid access to safe, calm and soothing environments accompanied by quality-controlled and guided CMT exercises, and assess acceptability/feasibility in an oncology setting. The intervention was found to be acceptable with nearly two-thirds of participants completing three sessions, meeting the defined end-point. This was supported by findings from interview data, confirming participants were positive, and supporting need for such interventions to help PABC deal with the psychological impact of cancer /treatment, and consistent with wider literature in which new technologies were found to be favourable regardless of age, background or gender (16, 50). Also consistent, it was found to be acceptable and safe to use across a number of settings including inpatient, outpatient and day-care (16, 17, 18, 50, 51, 52).

The final version of the intervention consisted of three short, separate sessions of VR/CMT. It is difficult to determine whether VR or CMT had more effect as arguably patients only received a relatively small dose of CMT. This was substantiated in interview findings which highlighted that most participants were unaware of any progression and/or did not relate to the CMT exercises. Participants thought the intervention should be longer, and incorporate more sessions, to have lasting effect. Other research in people having chemotherapy (19) argues that VR may not be effective for all as those with greater symptom distress had more accurate perception of time, suggesting they were not able to block out negative external cues. In order to effect significant change on individual levels of self-compassion, more and longer sessions may be required (53). A future multi-arm RCT may explore which aspect (VR/CMT/ both) has most, if any, effect.

Throughout both phases, participants expressed that they liked being able to step out of their situation and into a 'safe space', and some positively described re-imagining the VR environment when they felt stressed. This happened quickly; for some, it was after the first session. Consistent with other work (18, 19), participants reported time passed quickly whilst using the intervention suggesting distractive qualities which may be helpful during lengthy or perceived unpleasant procedures. Presence causes the user to suspend disbelief and believe they are in the virtual environment, reacting as if they are in the real world (54). This varied between participants, as the quality of imagery and content of audio were reported by some as detracting from the immersive experience. It is generally acknowledged that presence is dependent on either the characteristics of the user and the media employed (55), and relates to willingness to suspend disbelief. Our findings support this; those who had engaged with psychological therapies previously reported they were less concerned with the quality of imagery. Arguably, this study engaged a convenience sample who may have been more willing. Moving forward, using tools to evaluate the degree of presence and perhaps time perception may be valuable.

A key challenge is identifying who might benefit most from VR, alongside who is not appropriate, to ensure safety. Research (16, 17, 18) has highlighted benefits in chemotherapy populations in particular, with reduction of fatigue, anxiety, symptom distress and perception of time. Contrary to this, in our study both participants who experienced AEs were undergoing chemotherapy. However, effects were mild and could not definitively be attributed to the intervention. For one, the effect was so mild that it was not mentioned at the time, and the other was disappointed not to continue,

seeing the benefit of the VR experience outweighing effect of the AE. Clinical guidance surrounding patient monitoring during use is recommended.

Interesting findings in terms of *secondary* aims emerged; in particular, improvements in mental well-being and stress. Surprisingly, and consistent with other research (56) we did not see a statistically significant reduction in anxiety levels as reported in other VR studies in this setting (14, 17). This could be due to use of different measures. Standardisation may help to make future findings more generalisable/comparable.

A strength is the mixed-methods approach: qualitative techniques were employed to capture experience of intervention use. The majority of studies use tools to capture symptom change (14, 19, 51) with only one (57) using open-ended questions in their methodology. Further commonalities included issues surrounding appropriate usage space, and the negative effect of external noise. Developing the intervention for home use may improve quality and impact of experience. The sample size was small (n=21), but deemed appropriate by the EBCD group and local statisticians to assess acceptability, and included a diverse mix of demographics, tumour/treatment type. It is acknowledged that a larger sample would be needed moving forward. Even though the EBCD group designed the evaluation and chose measures, interview data highlighted that the quantity were burdensome and repetitive. Consequently, participants described being unable to give full attention and findings may not be a true reflection of feelings. Two non-validated tools were used to capture mental wellbeing and participant self-compassion, and as such may lack consistency and sensitivity.

8. Conclusion

A VR/CMT intervention is acceptable to PABC, and is recognized as offering a novel approach to addressing unmet psychological needs at various stages of the cancer pathway. Whilst feasible/safe to deliver in the oncology setting, developing a flexible approach in which users can access the intervention independently e.g. in their own homes, may increase uptake/impact and allow more autonomy.

Future research should focus on conducting larger scale RCT's in which length or frequency of VR and amount of CMT given would be increased, alongside a bigger sample and a control to increase generalizability of findings. Careful consideration is required when selecting evaluative measures.

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Appendix

Supplementary tables

Supplementary Table 1: Missing data management

Questionnaire	Variable measured	Missing Data	Statistical test
EQ-5D – 3D	QoL	No computation if values missing as single scores	
QLQ-C30	QoL	Values computed if < or = 10% data missing. Calculated mean for subscore	
DASS-21	Depression, Anxiety, Stress		Friedman (missing listwise)
AAQ II	Psychological flexibility		Friedman (missing listwise)
POMs	Mood state		Friedman (missing listwise)
SCS	Self-compassion		Friedman (missing listwise)
WEBWBS/Ad WEMWBS	Mental well-being		Friedman (missing listwise)
Locally developed Q	Self-compassion after intervention use		Friedman (missing listwise)

Supplementary Table 2: Descriptive Statistics Questionnaire Domain Scores

QUESTIONNAIRES & DOMAINS	N	Mean	Std. Dev.	Min	Max
EQ-5D-5L					
MOBILITY					
B_EQ5DM	12	1.33	.49	1	2
VR1_EQ5DM	12	1.33	.49	1	2
VR2_EQ5DM	12	1.33	.49	1	2
VR3_EQ5DM	12	1.33	.49	1	2
SELF-CARE					
B_EQ5DSC	12	1.25	.45	1	2
VR1_EQ5DSC	12	1.25	.45	1	2
VR2_EQ5DSC	12	1.17	.39	1	2
VR3_EQ5DSC	12	1.17	.39	1	2
USUAL ACTIVITIES					
B_EQ5DUA	12	1.58	.52	1	2
VR1_EQ5DUA	12	1.58	.52	1	2
VR2_EQ5DUA	12	1.42	.52	1	2
VR3_EQ5DUA	12	1.42	.52	1	2
PAIN & DISCOMFORT					
B_EQ5DPD	12	1.50	.67	1	3
VR1_EQ5DPD	12	1.58	.67	1	3
VR2_EQ5DPD	12	1.33	.49	1	2
VR3_EQ5DPD	12	1.67	.65	1	3
ANXIETY & DEPRESSION					
B_EQ5DAD	12	1.42	.52	1	2
VR1_EQ5DAD	12	1.42	.52	1	2
VR2_EQ5DAD	12	1.42	.52	1	2
VR3_EQ5DAD	12	1.42	.67	1	3
BAROMETER / VAS					
B_BAROMETER	12	71.83	15.30	50	100
VR1_BAROMETER	12	71.00	15.09	50	100
VR2_BAROMETER	12	72.17	16.68	40	100
VR3_BAROMETER	12	67.50	20.62	29	100
QLQ C30 – EORTC QoL					
GLOBAL HEALTH SCORE					
BQLQC30GHS	11	-43.18	25.77	-83.33	-8.33
VR1QLQC30GHS	11	-43.94	22.39	-83.33	-8.33
VR2QLQC30GHS	11	-48.48	23.51	-83.33	-16.67
VR3QLQC30GHS	11	-48.48	23.81	-83.33	-16.67
FUNCTIONAL SCALE					
BQLQC30FS	11	7.07	24.05	-42.22	33.33
VR1QLQC30FS	11	4.44	23.83	-42.22	33.33
VR2QLQC30FS	11	7.47	24.10	-44.44	33.33
VR3QLQC30FS	11	7.27	24.93	-46.67	33.33
SYMPTOM SCORE					
BQLQC30SS	11	10.02	21.13	-35.90	30.77
VR1QLQC30SS	11	8.39	20.13	-35.90	30.77
VR2QLQC30SS	11	10.26	21.54	-43.59	33.33
VRQLQC30SS	11	10.02	21.62	-43.59	33.33
DASS21 – DEPRESSION, ANXIETY, STRESS 21					
DEPRESSION					
BDASDEP	11	9.09	9.01	0	28
VR1DASDEP	11	8.91	9.05	0	28
VR2DASDEP	11	8.73	8.40	0	24
VR3DASDEP	11	6.91	7.34	0	18
ANXIETY					
BDASANX	10	8.00	8.79	0	30

VR1DASANX	10	6.60	5.82	0	16
VR2DASANX	10	7.40	6.33	0	18
VR3DASANX	10	4.60	3.53	0	10
STRESS					
BDASSTRS	19	13.37	8.11	0	28
BDASDEP	19	7.68	8.41	0	28
BDASANX	18	7.89	7.62	0	30
VR3DASSTRS	13	8.15	7.89	0	24
VR3DASDEP	12	6.67	7.05	0	18
VR3DASANX	11	4.36	3.44	0	10
AAQ – ACTION & ACCEPTANCE QUESTIONNAIRE					
BTOTAAQ	12	18.75	9.30	7	41
VR1TAAQ	12	19.25	8.85	7	39
VR2TAAQ	12	21.08	10.80	7	43
VR3TAAQ	12	18.08	9.06	7	39
POMS – PROFILE OF MOOD STATE					
VR1PREPOM	19	20.42	5.79	12	36
VR2PREPOMS	16	21.50	7.14	9	39
VR3PREPOMS	13	23.62	6.97	17	36
VR1POSTPOM	18	23.06	6.91	8	36
VR2POSTPOM	13	22.38	4.25	16	31
VR3POSTPOM	13	23.31	6.74	17	39
SCS – SELF-COMPASSION SCALE					
SELF-KINDNESS					
BSCSSK	10	3.14	.811	2.00	4.40
VR1SCSSK	10	3.14	.79	2.00	4.20
VR2SCSSK	10	3.26	.92	1.8	5.0
VR3SCSSK	10	3.30	1.13	1.8	5.0
SELF-JUDGEMENT					
BSCSSJ	10	3.48	1.05	1.40	4.80
VR1SCSSJ	10	3.48	1.05	1.40	4.80
VR2SCSSJ	10	3.34	1.30	1.0	5.0
VR3SCSSJ	10	3.50	1.14	1.6	5.0
COMMON HUMANITY					
BSCSCH	10	3.13	.68	2.25	4.25
VR1SCSCH	10	3.23	.79	2.25	4.75
VR2SCSCH	10	2.90	1.12	1.25	4.50
VR3SCSCH	10	3.15	1.04	1.50	5.00
ISOLATION					
BSCSISO	10	3.30	1.14	1.75	5.00
VR1SCSISO	10	3.38	1.13	1.75	5.00
VR2SCSISO	10	3.43	1.13	1.75	5.00
VR3SCSISO	10	3.58	1.24	1.50	5.00
MINDFULNESS					
BSCSM	10	4.10	.74	3	5
VR1SSCSM	10	4.05	.64	2.75	5.00
VR2SSCSM	10	3.73	.76	2.75	5.00
VR3SSCSM	10	3.75	.82	2.75	5.00
OVER-IDENTIFIED					
BSCSOI	10	3.30	1.12	1.50	5.00
VR1SCSOI	10	3.35	1.14	1.50	5.00
VR2SCSOI	10	3.70	1.26	1.50	5.00
VR3SCSOI	10	3.58	1.24	1.50	5.00
LDL – LOCALLY DEVELOPED QUESTIONS					
VR1LDQTS	12	51.08	15.92	33	80
VR2LDQTS	12	50.67	14.75	36	77
VR3LDQTS	12	50.50	17.42	14	77
WEMWBS WARWICK-EDINBURGH MENTAL WELL-BEING SCALE					

BWEMTS	19	48.74	8.92	34	67
VR1TWEWM	19	48.58	9.17	34	67
VR2WEMWTS	15	48.13	9.48	37	70
VR3WEMWTS	13	49.46	10.44	39	70
AWEMWBS – ADAPTED WARWICK-EDINBURGH METAL WELL-BEING SCALE					
VR1TAWEM	18	53.00	8.24	36	70
2AWEMTS	14	54.43	12.64	37	85
VR3AWEMTS	13	52.69	8.98	39	70
BWEMTS	12	45.92	7.76	34	58
VR1TAWEM	12	51.67	8.66	36	70
2AWEMTS	12	54.00	13.52	37	85
VR3AWEMTS	12	52.83	9.36	39	70

Supplementary table 3: Number of missing variables (number of participants)

	Baseline	VR1	VR1	VR2	VR2	VR3	VR3
Measure		Pre intervention	Post intervention	Pre intervention	Post intervention	Pre intervention	Post intervention
EQ-5D	0	0	N/A	0	N/A	0	N/A
QLQ C30	0	0	N/A	2(2)	N/A	0	N/A
Action and Acceptance Questionnaire II - AAQII	0	0	N/A	4(2)	N/A	0	N/A
Depression, Anxiety and Stress Scale 21 – DASS21	7(3)	8(2)	N/A	2(2)	N/A	14(2)	N/A
Profile of Mood State - POMS	6 (2)	8(3)	5(3)	9(3)	6(2)	1	2(2)
Warwick Edinburgh Mental Well-being Scale - WEMWBS	1	2(1)		0	N/A	0	
Self-compassion Scale - SCS	23 (1)	2(1)	N/A	0	N/A	0	N/A
Adapted Warwick Edinburgh Mental Well-being Scale - AWEMWBS	N/A	N/A	0	N/A	0	N/A	1
Locally developed questionnaire	N/A	N/A	0	N/A	1	N/A	0

Supplementary Table 4: Multivariate analyses comparing baseline, VR1, VR2 and VR3 session scores

Friedman Test for EQ-5D-5L, QLQ C30 EORTC, DASS21, AAQ, SCS, LDQ, WEMWBS, AWEMWBS and Heart Rate Variation

Ranks							
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**
B_EQ5DM	2.50	B_EQ5DSC	2.58	B_EQ5DUA	2.67	B_EQ5DPD	2.46
VR1_EQ5DM	2.50	VR1_EQ5DSC	2.58	VR1_EQ5DUA	2.67	VR1_EQ5DPD	2.63
VR2_EQ5DM	2.50	VR2_EQ5DSC	2.42	VR2_EQ5DUA	2.33	VR2_EQ5DPD	2.13
VR3_EQ5DM	2.50	VR3_EQ5DSC	2.42	VR3_EQ5DUA	2.33	VR3_EQ5DPD	2.79
N	12	**N**	12	**N**	12	**N**	12
Chi-Square	.000	**Chi-Square**	2.000	**Chi-Square**	6.000	**Chi-Square**	5.526
df	3	**df**	3	**df**	3	**df**	3
Asymp. Sign.	1.000	**Asymp. Sign.**	.572	**Asymp. Sign.**	.112	**Asymp. Sign.**	.137
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**		**M Rank**	
B_EQ5DAD	2.50	B_BAROMETER	2.63	BQLQC30GHS		2.82	
VR1_EQ5DAD	2.50	VR1_BAROMETER	2.42	VR1QLQC30GHS		2.82	
VR2_EQ5DAD	2.50	VR2_BAROMETER	2.67	VR2QLQC30GHS		2.27	
VR3_EQ5DAD	2.50	VR3_BAROMETER	2.29	VR3QLQC30GHS		2.09	
N	12	**N**	12	**N**		11	
Chi-Square	.000	**Chi-Square**	.880	**Chi-Square**		4.935	
df	3	**df**	3	**df**		3	
Asymp. Sign.	1.000	**Asymp. Sign.**	.830	**Asymp. Sign.**		.177	
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**		**M Rank**	
BQLQC30FS	2.41	BQLQC30SS	2.64	BDASDEP		2.59	
VR1QLQC30FS	2.18	VR1QLQC30SS	2.00	VR1DASDEP		2.45	
VR2QLQC30FS	2.64	VR2QLQC30SS	2.77	VR2DASDEP		2.59	
VR3QLQC30FS	2.77	VRQLQC30SS	2.59	VR3DASDEP		2.36	
N	11	**N**	11	**N**		11	
Chi-Square	1.709	**Chi-Square**	3.000	**Chi-Square**		.365	
df	3	**df**	3	**df**		3	
Asymp. Sign.	.635	**Asymp. Sign.**	.392	**Asymp. Sign.**		.947	
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**		**M Rank**	
BDASANX	2.75	BDASSTRS	2.96	BTOTAAQ		2.38	
VR1DASANX	2.50	VR1DASSTRS	2.92	VR1TAAQ		2.63	
VR2DASANX	2.80	VR2DASSTRS	2.38	VR2TAAQ		3.04	
VR3DASANX	1.95	VR3DASSTRS	1.75	VR3TAAQ		1.96	
N	10	**N**	12	**N**		12	
Chi-Square	4.789	**Chi-Square**	8.656	**Chi-Square**		5.742	
df	3	**df**	3	**df**		3	
Asymp. Sign.	.188	**Asymp. Sign.**	.034	**Asymp. Sign.**		.125	
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**		**M Rank**	
BSCSSK	2.50	BSCSSJ	2.25	BSCSCH		2.25	
VR1SCSSK	2.45	VR1SCSSJ	2.25	VR1SCSCH		2.65	
VR2SCSSK	2.30	VR2SCSSJ	2.60	VR2SCSCH		2.40	
VR3SCSSK	2.75	VR3SCSSJ	2.90	VR3SCSCH		2.70	
N	10	**N**	10	**N**		10	
Chi-Square	.733	**Chi-Square**	2.133	**Chi-Square**		.976	
df	3	**df**	3	**df**		3	
Asymp. Sign.	.866	**Asymp. Sign.**	.545	**Asymp. Sign.**		.807	
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**		**M Rank**	
BSCSISO	2.20	BSCSM	2.90	BSCSOI		2.05	
VR1SCSISO	2.40	VR1SSCSM	2.90	VR1SCSOI		2.25	
VR2SCSISO	2.75	VR2SSCSM	2.05	VR2SCSOI		2.95	
VR3SCSISO	2.65	VR3SSCSM	2.15	VR3SCSOI		2.75	
N	10	**N**	10	**N**		10	
Chi-Square	2.018	**Chi-Square**	5.230	**Chi-Square**		4.417	
df	3	**df**	3	**df**		3	

Asymp. Sign.	.569	Asymp. Sign.	.156	Asymp. Sign.	.220
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**
VR1LDQTS	2.13	BWEMTS	1.38	VR1 HRV Pre	2.00
VR2LDQTS	1.83	VR1TAWEM	2.75	VR1 HRV Mid	2.00
VR3LDQTS	2.04	2AWEMTS	2.83	VR1 HRV Post	2.00
VR1LDQTS	2.13	VR3AWEMTS	3.04	VR1 HRV Pre	2.00
N	12	**N**	12	**N**	3
Chi-Square	.565	**Chi-Square**	12.905	**Chi-Square**	.000
df	2	**df**	3	**df**	2
Asymp. Sign.	.754	**Asymp. Sign.**	.005	**Asymp. Sign.**	1.000

Supplementary Table 5: Multi-variate analyses comparing baseline to VR3 session scores

Wilcoxon Signed Ranks Test for DASS21, AAQ, WEMWBS & AWEMWBS, POMS and SSC

DASS21		N	Mean Rank	Sum of Ranks
VR3DASSTRS - BDASSTRS	Negative Ranks	9[a]	6.33	57.00
	Positive Ranks	2[b]	4.50	9.00
	Ties	2[c]		
	Total	13		
VR3DASDEP - BDASDEP	Negative Ranks	5[d]	5.20	26.00
	Positive Ranks	4[e]	4.75	19.00
	Ties	3[f]		
	Total	12		
VR3DASANX - BDASANX	Negative Ranks	5[g]	3.00	15.00
	Positive Ranks	0[h]	.00	.00
	Ties	6[i]		
	Total	11		
		Test statistics		
	VR3DASSTRS - BDASSTRS	VR3DASDEP - BDASDEP	VR3DASANX – BDASANX	
Z	-2.138[b]	-.418[b]		-2.032[b]
Asymp. Sig. (2-tailed)	.033	.676		.042
AAQ		**N**	**Mean Rank**	**Sum of Ranks**
VR1POSTPOM - VR1PREPOM	Negative Ranks	2[a]	7.50	15.00
	Positive Ranks	11[b]	6.91	76.00
	Ties	5[c]		
	Total	18		
VR2POSTPOM - VR2PREPOMS	Negative Ranks	6[d]	4.17	25.00
	Positive Ranks	4[e]	7.50	30.00
	Ties	3[f]		
	Total	13		
VR3POSTPOM - VR3PREPOMS	Negative Ranks	4[g]	3.00	12.00
	Positive Ranks	2[h]	4.50	9.00
	Ties	7[i]		
	Total	13		
		Test statistics		
	VR1POSTPOM - VR1PREPOM	VR2POSTPOM - VR2PREPOMS	VR3POSTPOM – VR3PREPOMS	
Z	-2.136[b]	-.255[b]		-.315[c]
Asymp. Sig. (2-tailed)	.033	.799		.752
WEMWBS & AWEMWBS		**N**	**Mean Rank**	**Sum of Ranks**
VR1TAWEM - VR1TWEWM	Negative Ranks	2[d]	5.00	10.00
	Positive Ranks	13[e]	8.46	110.00
	Ties	3[f]		
	Total	18		
2AWEMTS - VR2WEMWTS	Negative Ranks	2[g]	1.50	3.00
	Positive Ranks	8[h]	6.50	52.00
	Ties	4[i]		
	Total	14		
VR3AWEMTS - VR3WEMWTS	Negative Ranks	1[j]	1.50	1.50
	Positive Ranks	8[k]	5.44	43.50
	Ties	4[l]		
	Total	13		
		Test statistics		
	VR1TAWEM - VR1TWEWM	2AWEMTS - VR2WEMWTS	VR3AWEMTS – VR3WEMWTS	
Z	-2.846[b]	-2.501[b]		-2.492[b]
Asymp. Sig. (2-tailed)	.004	.012		.013

POMS		N	Mean Rank	Sum of Ranks
VR1POSTPOM - VR1PREPOM	Negative Ranks	2[a]	7.50	15.00
	Positive Ranks	11[b]	6.91	76.00
	Ties	5[c]		
	Total	18		
VR2POSTPOM - VR2PREPOMS	Negative Ranks	6[d]	4.17	25.00
	Positive Ranks	4[e]	7.50	30.00
	Ties	3[f]		
	Total	13		
VR3POSTPOM - VR3PREPOMS	Negative Ranks	4[g]	3.00	12.00
	Positive Ranks	2[h]	4.50	9.00
	Ties	7[i]		
	Total	13		

	Test statistics		
	VR1POSTPOM - VR1PREPOM	VR2POSTPOM - VR2PREPOMS	VR3POSTPOM – VR3PREPOMS
Z	-2.136[b]	-.255[b]	-.315[c]
Asymp. Sig. (2-tailed)	.033	.799	.752

SSC	VR3SCSSK - BSCSSK	VR3SCSSJ - BSCSSJ	VR3SCSCH - BSCSCH	VR3SCSISO - BSCSISO	VR3SSCSM - BSCSM	VR3SCSOI - BSCSOI
Z	-1.011[b]	-.978[b]	-.224[c]	-1.261[b]	-1.605[c]	-1.430[b]
Asymp. Sig. (2-tailed)	.312	.328	.823	.207	.108	.153

Supplementary Tables 5a & 5b: Multi-variate analyses comparing VR session scores

ANOVA for Electrodermal Activity (EDA) and Heart Rate

Suppl Table 5a Physiology Data – Electrodermal Activity (EDA) – VR 1 – Pre/Mid/Post

DESCRIPTIVE STATISTICS

	Mean	Std. Deviation	N
VR1 EDA PRE	11.50	3.416	4
VR1 EDA MID	8.75	2.217	4
VR1 EDA POST	8.25	2.062	4

TESTS OF WITHIN-SUBJECTS EFFECTS

SOURCE		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
EDA1	Sphericity Assumed	24.500	2	12.250	13.364	.006	.817
	Greenhouse-Geisser	24.500	1.658	14.781	13.364	.011	.817
	Huynh-Feldt	24.500	2.000	12.250	13.364	.006	.817
	Lower-bound	24.500	1.000	24.500	13.364	.035	.817
ERROR(EDA1)	Sphericity Assumed	5.500	6	.917			
	Greenhouse-Geisser	5.500	4.973	1.106			
	Huynh-Feldt	5.500	6.000	.917			
	Lower-bound	5.500	3.000	1.833			

Suppl Table 5b Physiology Data – Heart Rate – VR 2 – Pre/Mid/Post

DESCRIPTIVE STATISTICS

	Mean	Std. Deviation	N
VR2 HR PRE	75.75	6.185	4
VR2 HR MID	73.75	6.850	4
VR2 HR POST	75.00	6.683	4

TESTS OF WITHIN-SUBJECTS EFFECTS

SOURCE		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
HR2	Sphericity Assumed	8.167	2	4.083	13.364	.006	.817
	Greenhouse-Geisser	8.167	1.424	5.737	13.364	.017	.817
	Huynh-Feldt	8.167	2.000	4.083	13.364	.006	.817
	Lower-bound	8.167	1.000	8.167	13.364	.035	.817
ERROR(HR2)	Sphericity Assumed	1.833	6	.306			
	Greenhouse-Geisser	1.833	4.271	.429			
	Huynh-Feldt	1.833	6.000	.306			
	Lower-bound	1.833	3.000	.611			

Standards for Reporting Qualitative Research (SRQR)*

http://www.equator-network.org/reporting-guidelines/srqr/

	Page/line no(s).
Title and abstract	
Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	Co-design approach highlighted
Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	Page 4, as per publication format
Introduction	
Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	Page 5, para 1, 2 and 3
Purpose or research question - Purpose of the study and specific objectives or questions	Page 5, para 4
Methods	
Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	• Abstract, page 4 • Page 5, para 5: Methods • Page 7, last line • Page 10: Qualitative • Rationale: Page 5, para 5
Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	• Page 7, para 5: procedure • Page 7: Phase 1- intervention development
Context - Setting/site and salient contextual factors; rationale**	Page 7, para5: Procedure
Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	• Abstract, page 4 • Page 5: Compassion focused therapy • Page 7: Procedure • Rationale: Page 7 - procedure
Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	Page 7: procedure

Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	• Abstract, page 4 • Methods, page 5 • Page 6, para 2: Instruments for psychological assessment • Page 8, para 1 • Page 8, Findings from Phase 1 • Page 8, Phase 2: Evaluation/Acceptability
Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	Page 10: Qualitative section
Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	• Page 8: Initial design workshop • Page 8: User testing workshops • Page 10: Qualitative section • Table 4
Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	• Page 8: Initial design workshop • Page 10: Qualitative section
Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	• Page 7: Phase 1 interviews • Page 10: Qualitative section
Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	Page 10: Qualitative section

Results/findings

Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	Page 8: Initial design/user testing workshop/findings
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Page 10-12: Qualitative quotes

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	• Page 13: Discussion, para 1 and 2 • Page 14, para 1 and 2
Limitations - Trustworthiness and limitations of findings	Article summary page 3 Page 14, para 2

Other

Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	None declared
Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	Funding acknowledged Page 14, last line. Not involved in data collecting, interpretation or reporting.

*The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

Reference:
O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. **Standards for reporting qualitative research: a synthesis of recommendations.** *Academic Medicine*, Vol. 89, No. 9 / Sept 2014
DOI: 10.1097/ACM.0000000000000388

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1 and 4
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 5
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4 abstract
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5 and 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Page 7 and table 1
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6 and 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*Page 6 and 7*
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	Page 5 and 6, Page 14
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 9 and 10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 9 and 10
		(*b*) Describe any methods used to examine subgroups and interactions	Page 9 and 10
		(*c*) Explain how missing data were addressed	Page 9 and appendix suppl table 1
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A

		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Page 8, 9, 10 and table 3
		(b) Give reasons for non-participation at each stage	Page 9 and table 3
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Page 9, Tables 1, 2, 3
		(b) Indicate number of participants with missing data for each variable of interest	Page 9, Supp table 3
		(c) Summarise follow-up time (eg, average and total amount)	Page 8
Outcome data	15*	Report numbers of outcome events or summary measures over time	Page 9 and 10, Supp Tables 2, 4, 5
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 8
		(*b*) Report category boundaries when continuous variables were categorized	Page 8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Qual page 10-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 9, table 3, sup table 2, 4, 5
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 13 and 14
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Acknowledged page 14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

SafeSpace: What is the feasibility and acceptability of a co-designed virtual reality intervention, incorporating compassionate mind training, to support people undergoing cancer treatment in a clinical setting?

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Title Page

Title: SafeSpace: What is the feasibility and acceptability of a co-designed virtual reality intervention , incorporating compassionate mind training, to support people undergoing cancer treatment in a clinical setting?

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Word count: 5443

Article Summary

Strengths and Limitations of this study

- First study in an oncology setting exploring use of VR to deliver a psychological support intervention.
- Acceptability and feasibility were tested in the oncology setting. Within the evaluation phase, the potential impact of the intervention on psychological, physiological well-being and quality of life was assessed.
- Mixed-methods study: intervention developed using an experience-based co-design approach working with people affected by cancer, alongside qualitative techniques to capture experience of intervention use.
- The intervention consisted of three short sessions per participant. As compassionate mind training is relatively new and has had very limited use in cancer care, participants only received a small dose. This may have limited the overall effect of the intervention.
- This was an acceptability and feasibility project so sample size was small which limits the inferences that can be drawn from this study.

Abstract:

Objectives: The SafeSpace study co-designed and tested a virtual reality intervention, incorporating relaxation and compassionate mind-training to determine acceptability/feasibility in an oncology setting and evaluate impact on physical/psychological well-being and quality-of-life.

Design: A two-phase study. Phase 1 determined key characteristics using an Experienced-based Co-Design approach. Phase 2 evaluated the intervention using various measures and qualitative interviews. Descriptive statistics were used to analyse measures data and framework analysis was used to analyse interviews.

Setting: A specialist cancer centre, UK.

Participants: 18 in phase 1; 21 in phase 2. Participants were in cancer treatment, recovery or palliative care.

Primary and secondary outcome: Primary outcome: acceptability of the intervention, assessed by >60% uptake of three sessions. Secondary outcomes: impact on psychological well-being using: EQ-5D/QLQ-C30, Profile of Mood Scale (POMS), Warwick and Edinburgh Mental Well-being scale (WEMWBS), Depression and Anxiety Severity Scale 21 (DASS21), Self-Compassion Scale (SCS), Acceptance and Action Questionnaire (AAQII), and a locally developed questionnaire to capture self-compassion post-use. Physiological impact was assessed by change in heart rate (HR)/heart rate variability (HRV) and electrodermal activity (EDA).

Results: Twenty participants (mean age=48.7 years; SD=16.87); 65% (n=13) completed three sessions. Mental well-being improved following each use and from baseline to after session 3 (VR 1-z= 2.846, p = < 0.01; VR 2 -z = 2.501, p = <0.01; VR 3 - z = 2.492, p = <0.01). There was statistically significant difference in mean scores for EDA at mid- and post-session compared to pre-session (F (1.658, 4.973) = 13.364, p < 0.05). There was statistically significant reduction in stress levels from baseline to post-session 3. Participants found the intervention acceptable and highlighted areas for development.

Conclusion: The intervention is acceptable and feasible, and has shown positive effects on mental well-being/stress in the oncology setting. Larger studies are needed to confirm findings.

Word count: 298

Background:

The number of people living with cancer is expected to double to four million over the next 20 years. (1). Treatment involves surgery, radiotherapy, chemotherapy or other, alone or in combination. Many treatments have unpleasant side-effects and consequently people may not comply with recommended regimens (2). People affected by cancer (PABC) commonly experience poor psychological wellbeing and poor quality of life (QoL) (3, 4 , 5). Some become isolated from friends/family, or are unable to continue working, causing financial difficulties and further isolation (2). At least one in four – around 500,000 people in the UK – face poor health or disability after treatment (1).

Virtual Reality

Virtual reality (VR) is the computer-generated simulation of a three-dimensional image or environment that can be interacted with, or explored, in a way that seems real, by an individual using 3-D glasses, a headset with integrated screen, or gloves with integrated sensors. Healthcare has seen a growth in technologies such as VR to provide support (6). Recently, it has become more affordable and seen a dramatic improvement in user experience (7). It has previously been used in various applications including pain management, multiple sclerosis (8, 9, 10) and treatment of psychological conditions, such as phobias and anxiety (11, 12, 13). Within cancer care, VR has been used to manage pain, anxiety, and symptom distress. However, current literature regarding its effectiveness is equivocal. In a review of 19 studies (14), of those which reported on pain (n=6), half found that VR had a statistically significant positive effect in cancer patients. This was substantiated by other work (15) which reported decreased pain and state anxiety levels post-VR use by women with severe/chronic pain following breast cancer treatment. In contrast, a recent meta-analysis of cancer-related symptom management (16) showed the only statistically significant effect was reduced fatigue levels. Other studies (17, 18) using VR reported positive results as a distraction technique during chemotherapy administration. These were small samples (n=16; n=20 respectively) of women with breast cancer. Subsequent studies of larger, more diverse cohorts reported significant impact on reducing perception of time when receiving chemotherapy, validating the distractive nature of VR (19, 20).

Compassion Focused Therapy

Compassion can be defined as 'the sensitivity to suffering in self and others, with a deep commitment to try to relieve it'. Compassion-focused therapy (CFT) is an integrated, multimodal treatment approach that draws from sociology, psychology, and neuroscience (21). Central to CFT is compassionate mind-training (CMT) which was originally developed for people who find self-warmth and self-acceptance difficult (22; 23). It teaches the skill and practice of training the mind, by inviting people to develop their own images of warmth through practices such as slow and deeper breathing, compassionate voice tones, imagery, and facial expressions (24), and helps people develop self-compassion (22). CMT can be delivered on a one to one or group basis (25; 23). Studies examining other psychological interventions such as Cognitive Behavioural Therapy in a cancer population have shown favourable effects (26), however, this requires specialist training, supervision and certification needs (27), and appropriate training can be complex and costly (28, 29). CMT can be self-administered and once learned, can be recalled in multiple environments including at home (21). CFT and CMT have

been shown to reduce suffering and improve QoL in a range of health problems such as anxiety/depression, eating disorders, phobias and pain management (30, 31, 32, 33) and are becoming more mainstream and acceptable (34, 35).

Whilst effectiveness is equivocal, the application of VR within cancer as a distraction technique is accepted. However, its use to deliver psychological therapies, such as CMT, remains unexplored. Little is known about how these treatment approaches might be combined, whether there is any synergistic effect, and if such an intervention is acceptable and feasible in the clinical environment.

Aim:

To co-design a VR intervention, incorporating CMT, and assess its acceptability and feasibility to support people undergoing cancer treatment in a clinical setting.

Primary outcome: acceptability of the intervention, assessed by >60% uptake of three sessions.

Secondary outcomes: impact on psychological well-being using EQ-5D/QLQ-C30, Profile of Mood Scale (POMS), Warwick and Edinburgh Mental Well-being scale (WEMWBS), Depression and Anxiety Severity Scale 21 (DASS21), Self-Compassion Scale (SCS), Acceptance and Action Questionnaire (AAQII), and a locally developed questionnaire to capture self-compassion post-use. Physiological impact was assessed by change in heart rate (HR)/heart rate variability (HRV) and electrodermal activity (EDA).

Methods:

This was a two-phased study using mixed-methods and an experience-based co-design (EBCD) approach. Due to the originality of the intervention, not previously implemented in this setting and population, this research is deemed an acceptability and feasibility study. EBCD is a method of participatory research that embeds experience of service users and staff into service design (36). Phase 1: development of the intervention by co-designing and refining a number of continuously improved prototypes with PABC. Intervention delivery and evaluation model were also established. Phase 2: formal acceptability/feasibility and evaluation of the intervention, with PABC, using the range of psychological, physiological, and QoL measures agreed in Phase 1, and further explored through qualitative feedback Please see supplementary file flowchart 1 for EBCD process.

Sample:
A convenience sample was used to recruit participants to both phases of the study. Two separate groups of participants were recruited to either phase; phase 1 participants were no longer in treatment or follow-up; phase 2 participants were either receiving treatment or were in treatment follow-up.

Instruments for psychological assessment:
Demographic data collected included age, gender, diagnosis, cancer group, cancer stage and aim of treatment.

The POMS

The POMS (37) examines six mood subscales: tension-anxiety, depression, anger-hostility, vigour, fatigue, and confusion. Total mood disturbance score is computed by adding the five negative subscale scores and subtracting the vigour score. Higher total mood score indicate greater degree of mood disturbance (38). The POMS subscales and total score have demonstrated sound internal consistency reliability ($\alpha \geq 0.84$) (39).

The WEMWBS

The WEMWBS (40) is a 14-item scale of mental well-being covering subjective well-being and psychological functioning. It is scored by summing responses to each item on a 1-5 Likert scale. The minimum scale score is 14; maximum is 70. It has been validated in the UK in ages 16+ (41). A non-validated, adapted version, AWEMWBS, was used immediately after each intervention use. The WEMWBS asks participants to describe their experience over the last two weeks. The adapted version asks the participant to describe how they are feeling immediately after the intervention.

The AAQII

The AAQII is a seven-item measure of psychological inflexibility, or experiential avoidance. Items are scored on a Likert scale of 1 (never true) to 7 (always true) and are summed up. Higher scores equal greater levels of psychological inflexibility, with proven reliability and validity (42).

The SCS

The SCS (43) is a 26-item instrument that measures self-compassion through three hypothesized dimensions with their negative counterparts: self-kindness versus self-judgment, common humanity versus isolation, and mindfulness versus over-identification, according to a 5-point scale (1= Almost Never; 5= Almost Always). Subscale scores are computed by calculating the mean of subscale item responses. To compute the total score, the Self-Kindness, Common Humanity, and Mindfulness are summed with reverse scores of the Self-judgment, Isolation, and Over-identification subscales. Higher scores indicate greater self-compassion. In the original version, the total score showed excellent internal consistency ($\alpha = .92$) and so did the six subscales (range: .75 - .81) (44).

The DASS21

The DASS 21 (45) is a 21-item instrument that assesses depression, anxiety and stress. Each seven-item scale has four responses ranging from 0 (did not apply to me at all) to 3 (applied to me much/most of the time). A higher score indicates higher levels of depression, anxiety and stress. The DASS-21 has excellent internal consistency (46), and construct validity (46, 47).

The EQ5D-3L

The EQ5D (48) is designed to measure generic health outcome and comprises two parts: the EQ5D-3L self-classifier, a self-reported description of health problems according to five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), and the EQ-VAS, a self-rated health status using a visual analogue scale to record perception of current overall health; the scale is graduated from 0 (the worst imaginable health state) to 100 (the best imaginable state). It has been shown to be reliable and valid in cancer populations (49).

The QLQ-C30

The QLQ-C30 (50) is used to measure general aspects of HRQOL in cancer patients. EORTC QLQ-C30, Version 3, incorporates five functional scales on physical (PF), role (RF), cognitive (CF), emotional (EF) and social (SF) functioning, three symptom scales on fatigue (FA), pain (PA) and nausea and vomiting (NV), single items assessing dyspnoea (DY), insomnia (SL), loss of appetite (AP), constipation (CO) and diarrhoea (DI), one item assessing perceived financial impact (FI) and global health status/QoL scale (Global QoL). Each item is scored in one of four categories 1) 'Not at all', 2) 'A little', 3) 'Quite a bit' 4) 'Very much', with the exception of 'Global QoL'. It has been shown to be reliable and valid in cancer populations (51, 52, 53).

Locally-developed questionnaire

The locally-developed questionnaire specifically targeted self-compassion after intervention use. It comprised 12 questions such as: 'To what extent did the virtual reality help you have insight into your current situation?' and 'To what extent did the virtual reality make you feel encouraged about the future?' Scored using a 7-item Likert scale ranging from not at all (1) to very much (7), the tool had excellent internal consistency ($\alpha = 9.44$) (54); a higher score indicated that the intervention had a more positive impact.

Physiological assessment:

Physiological assessment was made using heart rate (HR), heart rate variability (HRV) and electrodermal activity (EDA) (55).

Procedure:

Potential participants were identified by clinical teams, and a diverse convenience sample undergoing a range of cancer treatments across tumour types from one specialist centre recruited. Inclusion criteria were: 1) having a diagnosis of cancer; 2) age over 18 years; 3) ability to provide written consent. Exclusion criteria were people: 1) considered too unwell; 2) in who use of VR is not recommended e.g., registered blind, motion sickness (56), seizure disorder or known psychiatric conditions such as schizophrenia or personality disorder (57). Exclusion criteria were assessed by medical records, self-report and in consultation with clinical staff. All procedures were in accordance with the Declaration of Helsinki (1964) and later amendments or comparable ethical standards. Procedure included two phases with two different groups of participants; phase 1 aimed to inform development of the intervention through a series of workshops with patients with previous experience of cancer and treatment. Phase 2 involved the application and evaluation of the intervention in the clinical setting with patients currently in treatment or follow-up, to assess acceptability and feasibility through intervention uptake and user experience. The study was reviewed by a statistician; Phase 1 is purely qualitative. Phase 2 statistical considerations are referred to in the descriptive statistics section.

Ethical approval:

Ethical approval was acquired from a UK Research Ethics Committee (South Central – Oxford B REC 18/SC/0346) and Health Research Authority (IRAS ID – 241770). Patient and Public involvement was

sought for study design. Eligible participants received written information and gave informed consent before taking part.

Patient and Public Involvement:

Patient and public involvement (PPI) was sought, and we recruited two representatives to be members of the study team who further informed the research question and study processes. Both had personal experience of cancer and treatment and previous experience of PPI work as part of a research study. By nature, the experience-based co-design method involved patients in the intervention and evaluation design. The evaluation measures used were selected in collaboration with the patient participants who attended the evaluation workshop, and their burden considered. PPI representatives were not directly involved in participant recruitment. A lay summary of results will be shared with participants via email.

Results/findings:

Phase 1 - Intervention Development

Eleven participants in total took part, please see supplementary table 1. Five workshops, conducted over six months, were facilitated by a research team including experts in VR and CMT, using an EBCD approach. All were digitally recorded and, along with observations collected by two researchers, transcribed and analysed using thematic analysis.

Initial design workshop - Seven participants took part, which started with individuals telling their story, challenges along their pathway and what was important to include. Participants were able to try a range of equipment and experiences in a VR demonstration. They were encouraged to share, critique and propose ideas, using the design studio method (58). Analysis of data identified a number of 'touch points', these being what was emotionally most important to participants, which were used to inform the first iteration of the intervention.

User-testing workshops - Three user-testing workshops took place in which three/four participants each were invited to try the subsequently developed prototype; a total of 11 participants took part in one or more. Participants were asked about their experience particularly focusing on quality and content of the intervention. Further 'touch points' informed the design of the next iteration, which was refined until the co-design team were satisfied it had been developed to acceptable quality.

Findings from Phase 1:

Over the course of the user-testing workshops, the intervention became more refined and focused on detail within, such as recognition of what constitutes a 'safe space', voice quality (e.g. pace/tone), and guidance versus instruction. The themes that emerged which underpinned design of the final specification included: *1) being given permission to 'step out' of current situation; 2) importance of voice; 3) need for sign-posting/on-boarding information; 4) being able to explore; 5) being guided versus being instructed.* The final iteration consisted of three short sessions of VR/CMT. VR 1 allowed participants to get used to being in a VR environment. VR 2 introduced a soothing breathing exercise, and VR 3 introduced a CMT self-compassion exercise. CMT language developing progressively with

each use. A choice of three environments was given: a beach as a 360-degree video, and animated mountain and forest scenes. Professional voiceover actors provided a choice of female or male audio (table 1). It was agreed that the intervention should be offered at any stage of treatment and acknowledged that three sessions may not be sufficient to administer a meaningful 'dose' of CMT, but would be enough to generate preliminary data.

Table 1: Final intervention content

All sessions approx. 10 minutes long		
VR1	VR2	VR3
Choice of male or female voice	Choice of male or female voice	Choice of male or female voice
Choice of a VR beach, mountain, or forest scene	Choice of a VR beach, mountain, or forest scene	Choice of a beach, mountain, or forest scene
Adapting to wearing VR headset and being in a VR environment	Simple soothing/breathing exercise, introduction to CMT	Simple CMT exercise

Evaluation workshop - A final workshop was held with five participants, who had taken part in either design or testing, to establish an evaluation model. A range of demographic, psychological and physiological measures were reviewed and agreed to be collected at baseline, and pre- and post- each intervention use (see Table 2). The final intervention was delivered on a head-mounted, stand-alone device; this was considered inexpensive and practical.

Table 2: Schedule for study procedure

Measure		Baseline	Pre each intervention	Post each intervention
Name/age/gender/dx/tx etc	Demographic information	X		
EQ-5D	HRQoL	X	X	
QLQ C30	HRQoL	X		X
Action and Acceptance Questionnaire II - AAQII	Psychological flexibility	X		
Depression, Anxiety and Stress Scale 21 – DASS21	Anxiety/depression/stress	X		X
Profile of Mood State - POMS	Mood	X	X	X
Warwick Edinburgh Mental Well-being Scale - WEMWBS	Mental well-being	X	X	

Self-compassion Scale - SCS	Self-compassion	X		X
Adapted Warwick Edinburgh Mental Well-being Scale - AWEMWBS	Mental well-being immediate time-point			X
Locally developed questionnaire	Self-compassioin			X
Heart rate/heart rate variation/electrodermal activity	Physiological	Monitored continuously before, during and after intervention		

Phase 2 – Evaluation/acceptability of intervention

The final intervention was evaluated and tested for acceptability/feasibility. A further twenty-one people were recruited. Four study visits were organised, coinciding with planned appointments, spaced at least a week apart. At initial visit, written consent was obtained and demographic data collected. Participants completed the baseline set of questionnaires relating to psychological state and QoL. The study then proceeded as per table 2. Telephone interviews were conducted once the participant had completed intervention use.

Quantitative

Summary measures for participant characteristics, VR use data variables and questionnaire scores were presented as means and standard deviations for continuous (approximate), normally distributed variables and frequencies. Categorical variables were reported as percentages. Shapiro-Wilk test was used to confirm normal distribution of continuous summary scales (all p values >0.05). Friedman's test for repeated measures was performed to assess whether there was a statistically significant difference in scores between baseline, VR1, VR2 and VR3. Wilcoxon signed ranks test was used to compare baseline and VR3 session scores. ANOVA was performed to assess changes in EDA, HR and HRV within each session. All p values were two-sided throughout; significance was set at the 5% level. IBM SPSS version 25 was used to analyse the data. Missing data were addressed (see suppl Table 2).

Participants

Seven males and 14 females consented to take part. One participant was subsequently lost to follow-up. Mean age was 48.7 years (SD=16.87; range: 22-77). Mean time elapsed since diagnosis was 37.08 months (SD= 45.00; range: 2-149). 16 participants (80%) were in active treatment. They had various tumour types with gynaecological cancer being most common (N=4; 20%) (See table 3).

Table 3: Tumour type

Tumour Type	N	%
Lower GI	2	10
Haematological	1	5
Gynaecological	4	20
Head and Neck	3	15

Breast	3	15
Genitourinary (GU)	3	15
Other	4	20

Acceptability/Feasibility Data

In total, 49 sessions of VR were delivered and completed. Acceptability of the intervention was deemed satisfactory as >60% (N=13; 65%) of participants completed all three sessions. This was agreed by discussion with the statistician, based on evidence which reported attrition levels between 16.9% to 26.0% (59) and reporting drop-out rates of up to 41.4% (60). In addition, dropout rates were reportedly lower among studies that did not include some form of between-session intervention which was the case in the current study (59). Thus, 60% was deemed a safe option for acceptability purposes; and further agreed within the Evaluation Workshop.

Reasons for not completing and further details are displayed in Table 4.

Table 4: Acceptability and feasibility data

	VR1		**VR2**		**VR3**	
	n	%	n	%	n	%
No. that took part in VR:	20	100	16	80	13	65
No. that did not take part in VR:			4	20	7	35
Reasons for not completing VR:						
Insufficient time			1	25	3	43
Deterioration in condition					1	14
Discontinuation of treatment at site			1	25	1	14
Adverse effect from VR					1	14
Unknown			2	50	1	14
Voice:						
Male	12	60	8	50	6	46
Female	8	40	8	50	7	54
Chosen VR environment:						
Beach	12	60	5	31	8	61
Mountain	6	30	8	50	5	39
Forest	2	10	3	19	0	0
Private room:						
Yes	11	55	9	56	8	61
No	9	45	7	44	5	39
Did the participant change the environment whilst using VR?						
Yes	2	10	0	0	1	8
No	18	90	16	100	12	92
Did the participant experience external noise?						
Yes	9	45	6	37.5	5	38
No	11	55	10	62.5	8	62
Total time in VR (minutes):						
Mean	10.8		10.44		10.00	
SD	1.852		2.502		1.633	
Range	7-15		7-16		8-14	

Did the participant experience any problems with the equipment?	12		13		12	
No	8		3		1	
Yes:	5		0		1	
Minor	2		3		0	
Additional intervention	1		0		0	
Unresolvable						
Did the participant experience an adverse event?						
Yes	1	5	2	12.5	0	0
No	19	95	14	87.5	13	100

Adverse Events

Three minor adverse events (AE) were recorded by two participants who experienced mild nausea and dizziness whilst using the intervention. In both, this resolved spontaneously. The third was in one of the same participants but occurred 48 hours after completing VR2. They reported nausea and dizziness for 48 hours resolving with bed-rest. In light of this, they were advised not to undergo the third session.

Descriptive Statistics

Descriptive statistics were computed for all questionnaire scores within respective domains and are presented as frequencies and standard deviations (See Suppl. Table 3). Friedman and Wilcoxon signed ranks tests were performed to compare potential changes in variables between baseline and VR1, VR2 and VR3 sessions. Missing data for each variable is shown in Suppl. Table 4. Two-sided 95% confidence intervals for the exact percentage can be calculated with maximum +/-23% with a sample size of 20. The proposed sample size of 20 was chosen during the EBCD process mainly for pragmatic reasons and was determined by available resources. A sample size of between 24 and 50 has previously been recommended for pilot and feasibility studies (61).

Multi-variate Analyses

Quality of Life

There were no statistically significant changes in QoL in either the EQ5D-3L or the QLQ-C30 responses (see Suppl. Table 5).

Psychological Measures

Total mood scores (POMS) were compared pre- and post-intervention. There was a statistically significant increase in total scores after the first session (VR 1) (z= -2.136, [b] p=0.03) suggesting there was an improvement in mood. There was improvement in scores post-second session (VR2) but this was not statistically significant (see Suppl. Table 6). Mental well-being (WEMWBS) scores showed statistically significant changes to mental well-being from pre- to post-VR session (VR 1 z= -2.846[b] p=<0.01; VR 2 z= -2.501[b] p=<0.01; VR 3 z= -2.492, [8] p=<0.01). There was a consistent beneficial effect maintained throughout all sessions and a statistically significant increase in WEMWBS scores from baseline to VR 3 (x^2=12.905, *df*=3, p=0.005) (see Suppl. Table 5 & 6).

There was a statistically significant reduction in stress levels as measured by the DASS21 from baseline to post-session 3 (z= -2.138[b], p=0.03) (see Suppl. Table 6). While there was a positive and beneficial trendfrom baseline to post-session 3 (VR3) in most of the sub scores, none reached statistical significance (see Suppl. Tables 5 & 6).

Physiological measures

ANOVA were conducted to compare EDA, HR and HRV within each session. A decrease in mean EDA for each of the three sessions was recorded, dropping from pre-intervention level and maintained following removal of headset; this was significant for the first session. Using ANOVA with repeated measures and a Greenhouse-Geisser correction, mean scores for EDA were statistically significantly different at mid- and post-session compared to pre-session levels (F(1.658, 4.973)=13.364, p<0.05). Similarly, the only statistically significant change in HR was in the second session with a decrease from pre- to mid-session followed by a return to pre-session levels at post-session (F(1.424, 4.271)=13.364, p<0.05) (see Suppl. Tables 6a & 6b). No change was observed in HRV.

Qualitative findings

As an acceptability/feasibility study, qualitative feedback was sought to support quantitative results (62). Participants were invited to a semi-structured telephone interview to acquire a deeper understanding of their experience of the intervention use. Eleven participants consented to take part, demographic data is shown in table 5. Interviews were audio-recorded and transcribed. Feedback was also given following each individual use of the intervention; this was summarised and recorded manually by the researcher and analysed alongside interview data using framework analysis (63). The framework was informed by analysis of the first two transcripts which were coded independently by three researchers and themes discussed and agreed. The subsequent interview transcripts and participant comments were analysed using the agreed framework. Three themes emerged: *1) Practical issues; 2) Immersion; 3) Impact of intervention.*

Table 5: Demographic information of interview participants

Age	Gender	Diagnosis
Mean = 55.5,	Female: n=6, 55%	Urology: n=3, 27.3%
Range 24-77 years	Male: N=4, 45%	Gynaecology: n=3, 27.3%
		Sarcoma: n=2, 18.1%
		Bowel: n=1, 9.1%
		Lung: n=1, 9.1%
		Other: n=1, 9.1%

Practical Issues:

Participants reported equipment as comfortable and relatively straightforward to use. Clear guidance was considered important, and a designated room suggested for the future.

> *'…putting the headset on isn't really a problem … we're all going to have to get used to some kind of virtual reality at some point … hadn't tried it before but it was very interesting.' 012*

The importance of tailoring to the individual was highlighted:

> *'I find breathing exercises really frustrating … I have tumours in my lungs, the amount I can inhale, the amount of time I can hold for is less than for other people. So, someone will say hold it this many beeps and then you can't . . . you feel like you failed at it and you check out …' 019*

Immersion:

This relates to quality of VR imagery, ability to explore, and impact of voices used in the audio. Lack of quality was seen as negatively impacting immersion and improvement suggested for the future with a preference for 'real' environments rather than animated:

> *'The beach was definitely more…realistic, you felt more sort of immersed in . . . compared with the other two.' 026*

Whilst there was positive reaction to the professional voices, some participants described becoming disengaged:

> *'…I had the final session with the lady [voice], and she was excellent . . . it was very believable. She really did explain it, she was really part of it, and all that. Whereas, I felt with him [male voice], more like that he was reading a script.' 027*

Not all participants liked the compassion therapy aspect of the intervention:

> *'… the compassionate mind therapy, I couldn't see the point of at all . . . you are in a compassion rich environment …. Nurses, the Doctors, friends and family. .. the last thing you .. need is another dose of compassion . . . ' 027*

There was mixed reaction to external noise; some found it detracted from the quality of experience but others found it reassuring as it gave awareness of what was going on around them:

> *'…the noise cancelling was pretty good but I did still hear, if I focused properly, the pump beeping if something went wrong . . . it was sort of the right balance between not being completely disconnected if something happened. I think, anymore and I would have felt too isolated.' 026*

Impact of intervention:

The intervention was seen as having immediate and lasting effects, with some recognising the ability to replicate the 'safe space' for themselves:

> *'The breathing techniques, I started to employ when I was having a scan even though the scan was very short. I thought that was quite useful for that. I hadn't really thought of that before but I found it actually quite calming.' 017*

For others, the impact was short-lived but still considered useful:

> *'I don't think it will have a lasting impact...It definitely made the rest of the day easier . . . . But the next day, the day after, I didn't still have that same sense of calm, it was just kind of immediately after… ' 019*

Participants' past experience of non-medical support measures emerged as relevant to receptiveness and engagement with the overall VR/CMT experience:

> *'But I've also been on some of these yoga type things where you just try and relax and get into the mood and all that kind of thing. .. I thought it was quite useful for that. .. the talking was the same.' 012*

Participants also gave valuable feedback regarding the research process and informing a larger study, with particular reference to burden of questionnaires:

> *'I think some of them were a little bit repetitive, I though the one with all the options about being angry, sad, … went on for ages. I don't think that really needs to be that long.' 017*

Discussion:

The aim of the study was to co-design a low-cost VR intervention enabling rapid access to safe, calm and soothing environments accompanied by quality controlled and guided CMT exercises and assess acceptability/feasibility in an oncology setting. The intervention was found to be acceptable with nearly two-thirds of participants completing three sessions, meeting the defined end-point. This was supported by findings from interview data, confirming participants were positive, and supporting need for such interventions to help PABC deal with the psychological impact of cancer /treatment. This is consistent with wider literature in which new technologies were also found to be favourable, in their case, regardless of age, background or gender (17, 64). Also consistent, it was found to be acceptable and safe to use across several settings including inpatient, outpatient and day-care (17, 18, 19, 64, 65, 66). Whilst a positive trend was observed in some psychological domains, the overall effectiveness of the intervention remains unclear.

The final version of the intervention consisted of three short, separate sessions of VR/CMT. It is difficult to determine whether VR or CMT had more effect as arguably patients only received a relatively small dose of CMT. This was substantiated in interview findings which highlighted that most participants were unaware of any progression and/or did not relate to the CMT exercises. Participants thought the intervention should be longer, and incorporate more sessions, to have lasting effect. Other research in people having chemotherapy (20) argues that VR may not be effective for all as those with greater symptom distress had more accurate perception of time, suggesting they were not able to block out negative external cues. In order to effect significant change on individual levels of self-compassion, more and longer sessions may be required (67). A future multi-arm RCT may explore which aspect (VR/CMT/ both) has most, if any, effect. Acceptability and feasibility data also showed the beach scene to be the most popular, and the forest scene the least. This is echoed in other work that cites a tree environment as gloomy (68) and highlights the importance of choice.

Throughout both phases, participants expressed that they liked being able to step out of their situation into a 'safe space', and some positively described re-imagining the VR environment when they felt stressed. This happened quickly; for some, it was after the first session. Consistent with other work (19, 20), participants reported time passed quickly whilst using the intervention suggesting distractive qualities which may be helpful during lengthy or perceived unpleasant procedures. 'Presence' within the context of VR has been defined as the "sense of being there", or as the "feeling of being in a world that exists outside the self" and causes the user to suspend disbelief and believe they are in the virtual environment, reacting as if they are in the real world (69). This varied between participants, as the quality of imagery and content of audio were reported by some as detracting from the immersive experience. It is generally acknowledged that presence is dependent on either the characteristics of the user and the media employed (70),and relates to willingness to suspend disbelief. Our findings support this; those who had engaged with psychological therapies previously reported they were less concerned with the quality of imagery. Arguably, this study engaged an unusual convenience sample with a mean time since diagnosis of 3 years, of which 80% were still in treatment who potentially may have been more exposed to such therapies over time. Moving forward, using tools to evaluate the degree of presence, such as the Presence Questionnaire PQ (71) and perhaps time perception may be valuable.

A key challenge is identifying who might benefit most from VR, alongside who is not appropriate, to ensure safety. Research (17 18, 19) has highlighted benefits in chemotherapy populations in particular, with reduction of fatigue, anxiety, symptom distress and perception of time. Contrary to this, in our study both participants who experienced AEs were undergoing chemotherapy. However, effects were mild and could not definitively be attributed to the intervention. For one, the effect was so mild that it was not mentioned at the time, and the other was disappointed not to continue, seeing the benefit of the VR experience outweighing effect of the AE. Clinical guidance surrounding patient monitoring during use is recommended.

Interesting findings in terms of *secondary* aims emerged; in particular, improvements in mental well-being and stress. Surprisingly, and consistent with other research (72) we did not see a statistically significant reduction in anxiety levels as reported in other VR studies in this setting (15, 18). This needs to be treated with caution as this could be due to use of different measures. Standardisation may help to make future findings more generalisable/comparable.

A strength is the mixed-methods approach: qualitative techniques were employed to capture experience of intervention use. The majority of studies use tools to capture symptom change (1520, 66) with only one (73) using open-ended questions in their methodology. Further commonalities included issues surrounding appropriate usage space, and the negative effect of external noise. Developing the intervention for home use may improve quality and impact of experience.

The study has several limitations. The sample size was small (n=21) and the study is potentially underpowered, with a high attrition rate. However, this number of participants was deemed appropriate by the EBCD group (who developed the evaluation model) and local statisticians, to assess the intervention for acceptability, and included a diverse mix of demographics, tumour/treatment type. The small sample did not allow for adjustment of confounding variables in the quantitative analysis so that any notable differences in baseline characteristics or response to the intervention in the study population could be identified. It is acknowledged that a larger sample would be needed moving forward. Reasons for attrition are noted and may provide intelligence for any future pilot or larger study. Furthermore, even though the EBCD group designed the evaluation model and chose measures, interview data highlighted that the quantity were burdensome and repetitive. Consequently, participants described being unable to give full attention and findings may not be a true reflection of feelings. Two non-validated tools were used to capture mental wellbeing and participant self-compassion, and as such may lack consistency and sensitivity.

Conclusion

A VR/CMT intervention is acceptable to PABC and is recognized as offering a novel approach to addressing unmet psychological needs at various stages of the cancer pathway. Whilst feasible/safe to deliver in the oncology setting, developing a flexible approach in which users can access the intervention independently e.g. in their own homes, may increase uptake/impact and allow more autonomy. Future research should focus on conducting larger scale RCT's in which length or frequency of VR and amount of CMT given would be increased, alongside a bigger sample and a control to increase generalizability of findings. Careful consideration is required when selecting evaluative measures

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Data availability statement:
All data are deidentified participant data. All data are securely stored at the host organisation and can be made available upon request to the first author.

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STUDY SET-UP – Supplementary flowchart 1

Appendix

Supplementary tables

Study no	Gender	Age years	Diagnosis	Design workshop	User testing workshop 1	User testing workshop 2	User testing Workshop 3	Evaluation workshop
1	Male	54	Ca prostate	Yes	Yes	No	Yes	Yes
2	Male	66	Melanoma	Yes	No	No	No	No
3	Female	72	Ca cervix	Yes	No	Yes	No	No
4	Female	67	Medullary ca	Yes	No	No	Yes	Yes
5	Female	74	Ca lung	Yes	Yes	No	No	Yes
6	Male	74	Neuroendocrine tumour	Yes	Yes	No	No	No
7	Male	69	Ca prostate	Yes	No	Yes	Yes	Yes
8	Male	71	Ca nasopharynx	No	No	Yes	No	No
9	Female	51	Ca thyroid	No	No	Yes	No	Yes
10	Female	37	Scc tongue	No	No	No	No	No
11	Female	62	Ca breast	No	No	No	Yes	No

Supplementary table 1: Phase 1 participant demographic data

Supplementary Table 2: Missing data management

Questionnaire	Variable measured	Missing Data	Statistical test
EQ-5D – 3D	QoL	No computation if values missing as single scores	
QLQ-C30	QoL	Values computed if < or = 10% data missing. Calculated mean for subscore	
DASS-21	Depression, Anxiety, Stress		Friedman (missing listwise)
AAQ II	Psychological flexibility		Friedman (missing listwise)
POMs	Mood state		Friedman (missing listwise)
SCS	Self-compassion		Friedman (missing listwise)
WEBWBS/Ad WEMWBS	Mental well-being		Friedman (missing listwise)
Locally developed Q	Self-compassion after intervention use		Friedman (missing listwise)

Supplementary Table 3: Descriptive Statistics Questionnaire Domain Scores

QUESTIONNAIRES & DOMAINS	N	Mean	Std. Dev.	Min	Max
EQ-5D-5L					
MOBILITY					
B_EQ5DM	12	1.33	.49	1	2
VR1_EQ5DM	12	1.33	.49	1	2
VR2_EQ5DM	12	1.33	.49	1	2
VR3_EQ5DM	12	1.33	.49	1	2
SELF-CARE					
B_EQ5DSC	12	1.25	.45	1	2
VR1_EQ5DSC	12	1.25	.45	1	2
VR2_EQ5DSC	12	1.17	.39	1	2
VR3_EQ5DSC	12	1.17	.39	1	2
USUAL ACTIVITIES					
B_EQ5DUA	12	1.58	.52	1	2
VR1_EQ5DUA	12	1.58	.52	1	2
VR2_EQ5DUA	12	1.42	.52	1	2
VR3_EQ5DUA	12	1.42	.52	1	2
PAIN & DISCOMFORT					
B_EQ5DPD	12	1.50	.67	1	3
VR1_EQ5DPD	12	1.58	.67	1	3
VR2_EQ5DPD	12	1.33	.49	1	2
VR3_EQ5DPD	12	1.67	.65	1	3
ANXIETY & DEPRESSION					
B_EQ5DAD	12	1.42	.52	1	2
VR1_EQ5DAD	12	1.42	.52	1	2
VR2_EQ5DAD	12	1.42	.52	1	2
VR3_EQ5DAD	12	1.42	.67	1	3
BAROMETER / VAS					
B_BAROMETER	12	71.83	15.30	50	100
VR1_BAROMETER	12	71.00	15.09	50	100
VR2_BAROMETER	12	72.17	16.68	40	100
VR3_BAROMETER	12	67.50	20.62	29	100
QLQ C30 – EORTC QoL					
GLOBAL HEALTH SCORE					
BQLQC30GHS	11	-43.18	25.77	-83.33	-8.33
VR1QLQC30GHS	11	-43.94	22.39	-83.33	-8.33
VR2QLQC30GHS	11	-48.48	23.51	-83.33	-16.67
VR3QLQC30GHS	11	-48.48	23.81	-83.33	-16.67
FUNCTIONAL SCALE					
BQLQC30FS	11	7.07	24.05	-42.22	33.33
VR1QLQC30FS	11	4.44	23.83	-42.22	33.33
VR2QLQC30FS	11	7.47	24.10	-44.44	33.33
VR3QLQC30FS	11	7.27	24.93	-46.67	33.33
SYMPTOM SCORE					
BQLQC30SS	11	10.02	21.13	-35.90	30.77
VR1QLQC30SS	11	8.39	20.13	-35.90	30.77
VR2QLQC30SS	11	10.26	21.54	-43.59	33.33
VRQLQC30SS	11	10.02	21.62	-43.59	33.33
DASS21 – DEPRESSION, ANXIETY, STRESS 21					
DEPRESSION					
BDASDEP	11	9.09	9.01	0	28
VR1DASDEP	11	8.91	9.05	0	28
VR2DASDEP	11	8.73	8.40	0	24
VR3DASDEP	11	6.91	7.34	0	18
ANXIETY					
BDASANX	10	8.00	8.79	0	30

VR1DASANX	10	6.60	5.82	0	16
VR2DASANX	10	7.40	6.33	0	18
VR3DASANX	10	4.60	3.53	0	10
STRESS					
BDASSTRS	19	13.37	8.11	0	28
BDASDEP	19	7.68	8.41	0	28
BDASANX	18	7.89	7.62	0	30
VR3DASSTRS	13	8.15	7.89	0	24
VR3DASDEP	12	6.67	7.05	0	18
VR3DASANX	11	4.36	3.44	0	10
AAQ – ACTION & ACCEPTANCE QUESTIONNAIRE					
BTOTAAQ	12	18.75	9.30	7	41
VR1TAAQ	12	19.25	8.85	7	39
VR2TAAQ	12	21.08	10.80	7	43
VR3TAAQ	12	18.08	9.06	7	39
POMS – PROFILE OF MOOD STATE					
VR1PREPOM	19	20.42	5.79	12	36
VR2PREPOMS	16	21.50	7.14	9	39
VR3PREPOMS	13	23.62	6.97	17	36
VR1POSTPOM	18	23.06	6.91	8	36
VR2POSTPOM	13	22.38	4.25	16	31
VR3POSTPOM	13	23.31	6.74	17	39
SCS – SELF-COMPASSION SCALE					
SELF-KINDNESS					
BSCSSK	10	3.14	.811	2.00	4.40
VR1SCSSK	10	3.14	.79	2.00	4.20
VR2SCSSK	10	3.26	.92	1.8	5.0
VR3SCSSK	10	3.30	1.13	1.8	5.0
SELF-JUDGEMENT					
BSCSSJ	10	3.48	1.05	1.40	4.80
VR1SCSSJ	10	3.48	1.05	1.40	4.80
VR2SCSSJ	10	3.34	1.30	1.0	5.0
VR3SCSSJ	10	3.50	1.14	1.6	5.0
COMMON HUMANITY					
BSCSCH	10	3.13	.68	2.25	4.25
VR1SCSCH	10	3.23	.79	2.25	4.75
VR2SCSCH	10	2.90	1.12	1.25	4.50
VR3SCSCH	10	3.15	1.04	1.50	5.00
ISOLATION					
BSCSISO	10	3.30	1.14	1.75	5.00
VR1SCSISO	10	3.38	1.13	1.75	5.00
VR2SCSISO	10	3.43	1.13	1.75	5.00
VR3SCSISO	10	3.58	1.24	1.50	5.00
MINDFULNESS					
BSCSM	10	4.10	.74	3	5
VR1SSCSM	10	4.05	.64	2.75	5.00
VR2SSCSM	10	3.73	.76	2.75	5.00
VR3SSCSM	10	3.75	.82	2.75	5.00
OVER-IDENTIFIED					
BSCSOI	10	3.30	1.12	1.50	5.00
VR1SCSOI	10	3.35	1.14	1.50	5.00
VR2SCSOI	10	3.70	1.26	1.50	5.00
VR3SCSOI	10	3.58	1.24	1.50	5.00
LDL – LOCALLY DEVELOPED QUESTIONS					
VR1LDQTS	12	51.08	15.92	33	80
VR2LDQTS	12	50.67	14.75	36	77
VR3LDQTS	12	50.50	17.42	14	77
WEMWBS WARWICK-EDINBURGH MENTAL WELL-BEING SCALE					

BWEMTS	19	48.74	8.92	34	67
VR1TWEWM	19	48.58	9.17	34	67
VR2WEMWTS	15	48.13	9.48	37	70
VR3WEMWTS	13	49.46	10.44	39	70
AWEMWBS – ADAPTED WARWICK-EDINBURGH METAL WELL-BEING SCALE					
VR1TAWEM	18	53.00	8.24	36	70
2AWEMTS	14	54.43	12.64	37	85
VR3AWEMTS	13	52.69	8.98	39	70
BWEMTS	12	45.92	7.76	34	58
VR1TAWEM	12	51.67	8.66	36	70
2AWEMTS	12	54.00	13.52	37	85
VR3AWEMTS	12	52.83	9.36	39	70

Supplementary table 4: Number of missing variables (number of participants)

	Baseline	VR1	VR1	VR2	VR2	VR3	VR3
Measure		Pre intervention	Post intervention	Pre intervention	Post intervention	Pre intervention	Post intervention
EQ-5D	0	0	N/A	0	N/A	0	N/A
QLQ C30	0	0	N/A	2(2)	N/A	0	N/A
Action and Acceptance Questionnaire II - AAQII	0	0	N/A	4(2)	N/A	0	N/A
Depression, Anxiety and Stress Scale 21 – DASS21	7(3)	8(2)	N/A	2(2)	N/A	14(2)	N/A
Profile of Mood State - POMS	6 (2)	8(3)	5(3)	9(3)	6(2)	1	2(2)
Warwick Edinburgh Mental Well-being Scale - WEMWBS	1	2(1)		0	N/A	0	
Self-compassion Scale - SCS	23 (1)	2(1)	N/A	0	N/A	0	N/A
Adapted Warwick Edinburgh Mental Well-being Scale - AWEMWBS	N/A	N/A	0	N/A	0	N/A	1
Locally developed questionnaire	N/A	N/A	0	N/A	1	N/A	0

Supplementary Table 5: Multivariate analyses comparing baseline, VR1, VR2 and VR3 session scores

Friedman Test for EQ-5D-5L, QLQ C30 EORTC, DASS21, AAQ, SCS, LDQ, WEMWBS, AWEMWBS and Heart Rate Variation

Ranks							
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**
B_EQ5DM	2.50	B_EQ5DSC	2.58	B_EQ5DUA	2.67	B_EQ5DPD	2.46
VR1_EQ5DM	2.50	VR1_EQ5DSC	2.58	VR1_EQ5DUA	2.67	VR1_EQ5DPD	2.63
VR2_EQ5DM	2.50	VR2_EQ5DSC	2.42	VR2_EQ5DUA	2.33	VR2_EQ5DPD	2.13
VR3_EQ5DM	2.50	VR3_EQ5DSC	2.42	VR3_EQ5DUA	2.33	VR3_EQ5DPD	2.79
N	12	**N**	12	**N**	12	**N**	12
Chi-Square	.000	**Chi-Square**	2.000	**Chi-Square**	6.000	**Chi-Square**	5.526
df	3	**df**	3	**df**	3	**df**	3
Asymp. Sign.	1.000	**Asymp. Sign.**	.572	**Asymp. Sign.**	.112	**Asymp. Sign.**	.137
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
B_EQ5DAD	2.50	B_BAROMETER	2.63	BQLQC30GHS	2.82		
VR1_EQ5DAD	2.50	VR1_BAROMETER	2.42	VR1QLQC30GHS	2.82		
VR2_EQ5DAD	2.50	VR2_BAROMETER	2.67	VR2QLQC30GHS	2.27		
VR3_EQ5DAD	2.50	VR3_BAROMETER	2.29	VR3QLQC30GHS	2.09		
N	12	**N**	12	**N**	11		
Chi-Square	.000	**Chi-Square**	.880	**Chi-Square**	4.935		
df	3	**df**	3	**df**	3		
Asymp. Sign.	1.000	**Asymp. Sign.**	.830	**Asymp. Sign.**	.177		
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
BQLQC30FS	2.41	BQLQC30SS	2.64	BDASDEP	2.59		
VR1QLQC30FS	2.18	VR1QLQC30SS	2.00	VR1DASDEP	2.45		
VR2QLQC30FS	2.64	VR2QLQC30SS	2.77	VR2DASDEP	2.59		
VR3QLQC30FS	2.77	VRQLQC30SS	2.59	VR3DASDEP	2.36		
N	11	**N**	11	**N**	11		
Chi-Square	1.709	**Chi-Square**	3.000	**Chi-Square**	.365		
df	3	**df**	3	**df**	3		
Asymp. Sign.	.635	**Asymp. Sign.**	.392	**Asymp. Sign.**	.947		
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
BDASANX	2.75	BDASSTRS	2.96	BTOTAAQ	2.38		
VR1DASANX	2.50	VR1DASSTRS	2.92	VR1TAAQ	2.63		
VR2DASANX	2.80	VR2DASSTRS	2.38	VR2TAAQ	3.04		
VR3DASANX	1.95	VR3DASSTRS	1.75	VR3TAAQ	1.96		
N	10	**N**	12	**N**	12		
Chi-Square	4.789	**Chi-Square**	8.656	**Chi-Square**	5.742		
df	3	**df**	3	**df**	3		
Asymp. Sign.	.188	**Asymp. Sign.**	.034	**Asymp. Sign.**	.125		
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
BSCSSK	2.50	BSCSSJ	2.25	BSCSCH	2.25		
VR1SCSSK	2.45	VR1SCSSJ	2.25	VR1SCSCH	2.65		
VR2SCSSK	2.30	VR2SCSSJ	2.60	VR2SCSCH	2.40		
VR3SCSSK	2.75	VR3SCSSJ	2.90	VR3SCSCH	2.70		
N	10	**N**	10	**N**	10		
Chi-Square	.733	**Chi-Square**	2.133	**Chi-Square**	.976		
df	3	**df**	3	**df**	3		
Asymp. Sign.	.866	**Asymp. Sign.**	.545	**Asymp. Sign.**	.807		
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
BSCSISO	2.20	BSCSM	2.90	BSCSOI	2.05		
VR1SCSISO	2.40	VR1SSCSM	2.90	VR1SCSOI	2.25		
VR2SCSISO	2.75	VR2SSCSM	2.05	VR2SCSOI	2.95		
VR3SCSISO	2.65	VR3SSCSM	2.15	VR3SCSOI	2.75		
N	10	**N**	10	**N**	10		
Chi-Square	2.018	**Chi-Square**	5.230	**Chi-Square**	4.417		
df	3	**df**	3	**df**	3		

Asymp. Sign.	.569	Asymp. Sign.	.156	Asymp. Sign.	.220
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**
VR1LDQTS	2.13	BWEMTS	1.38	VR1 HRV Pre	2.00
VR2LDQTS	1.83	VR1TAWEM	2.75	VR1 HRV Mid	2.00
VR3LDQTS	2.04	2AWEMTS	2.83	VR1 HRV Post	2.00
VR1LDQTS	2.13	VR3AWEMTS	3.04	VR1 HRV Pre	2.00
N	12	**N**	12	**N**	3
Chi-Square	.565	**Chi-Square**	12.905	**Chi-Square**	.000
df	2	**df**	3	**df**	2
Asymp. Sign.	.754	**Asymp. Sign.**	.005	**Asymp. Sign.**	1.000

Supplementary Table 6: Multi-variate analyses comparing baseline to VR3 session scores

Wilcoxon Signed Ranks Test for DASS21, AAQ, WEMWBS & AWEMWBS, POMS and SSC

DASS21		N	Mean Rank	Sum of Ranks
VR3DASSTRS - BDASSTRS	Negative Ranks	9[a]	6.33	57.00
	Positive Ranks	2[b]	4.50	9.00
	Ties	2[c]		
	Total	13		
VR3DASDEP - BDASDEP	Negative Ranks	5[d]	5.20	26.00
	Positive Ranks	4[e]	4.75	19.00
	Ties	3[f]		
	Total	12		
VR3DASANX - BDASANX	Negative Ranks	5[g]	3.00	15.00
	Positive Ranks	0[h]	.00	.00
	Ties	6[i]		
	Total	11		
	Test statistics			
	VR3DASSTRS - BDASSTRS	VR3DASDEP - BDASDEP	VR3DASANX – BDASANX	
Z	-2.138[b]	-.418[b]		-2.032[b]
Asymp. Sig. (2-tailed)	.033	.676		.042
AAQ		N	Mean Rank	Sum of Ranks
VR1POSTPOM - VR1PREPOM	Negative Ranks	2[a]	7.50	15.00
	Positive Ranks	11[b]	6.91	76.00
	Ties	5[c]		
	Total	18		
VR2POSTPOM - VR2PREPOMS	Negative Ranks	6[d]	4.17	25.00
	Positive Ranks	4[e]	7.50	30.00
	Ties	3[f]		
	Total	13		
VR3POSTPOM - VR3PREPOMS	Negative Ranks	4[g]	3.00	12.00
	Positive Ranks	2[h]	4.50	9.00
	Ties	7[i]		
	Total	13		
	Test statistics			
	VR1POSTPOM - VR1PREPOM	VR2POSTPOM - VR2PREPOMS	VR3POSTPOM – VR3PREPOMS	
Z	-2.136[b]	-.255[b]		-.315[c]
Asymp. Sig. (2-tailed)	.033	.799		.752
WEMWBS & AWEMWBS		N	Mean Rank	Sum of Ranks
VR1TAWEM - VR1TWEWM	Negative Ranks	2[d]	5.00	10.00
	Positive Ranks	13[e]	8.46	110.00
	Ties	3[f]		
	Total	18		
2AWEMTS - VR2WEMWTS	Negative Ranks	2[g]	1.50	3.00
	Positive Ranks	8[h]	6.50	52.00
	Ties	4[i]		
	Total	14		
VR3AWEMTS - VR3WEMWTS	Negative Ranks	1[j]	1.50	1.50
	Positive Ranks	8[k]	5.44	43.50
	Ties	4[l]		
	Total	13		
	Test statistics			
	VR1TAWEM - VR1TWEWM	2AWEMTS - VR2WEMWTS	VR3AWEMTS – VR3WEMWTS	
Z	-2.846[b]	-2.501[b]		-2.492[b]
Asymp. Sig. (2-tailed)	.004	.012		.013

POMS		N	Mean Rank	Sum of Ranks
VR1POSTPOM - VR1PREPOM	Negative Ranks	2[a]	7.50	15.00
	Positive Ranks	11[b]	6.91	76.00
	Ties	5[c]		
	Total	18		
VR2POSTPOM - VR2PREPOMS	Negative Ranks	6[d]	4.17	25.00
	Positive Ranks	4[e]	7.50	30.00
	Ties	3[f]		
	Total	13		
VR3POSTPOM - VR3PREPOMS	Negative Ranks	4[g]	3.00	12.00
	Positive Ranks	2[h]	4.50	9.00
	Ties	7[i]		
	Total	13		

	Test statistics		
	VR1POSTPOM - VR1PREPOM	VR2POSTPOM - VR2PREPOMS	VR3POSTPOM – VR3PREPOMS
Z	-2.136[b]	-.255[b]	-.315[c]
Asymp. Sig. (2-tailed)	.033	.799	.752

SSC	VR3SCSSK - BSCSSK	VR3SCSSJ - BSCSSJ	VR3SCSCH - BSCSCH	VR3SCSISO - BSCSISO	VR3SSCSM - BSCSM	VR3SCSOI - BSCSOI
Z	-1.011[b]	-.978[b]	-.224[c]	-1.261[b]	-1.605[c]	-1.430[b]
Asymp. Sig. (2-tailed)	.312	.328	.823	.207	.108	.153

Supplementary Tables 6a & 6b: Multi-variate analyses comparing VR session scores

ANOVA for Electrodermal Activity (EDA) and Heart Rate

Suppl Table 6a Physiology Data – Electrodermal Activity (EDA) – VR 1 – Pre/Mid/Post

DESCRIPTIVE STATISTICS

	Mean	Std. Deviation	N
VR1 EDA PRE	11.50	3.416	4
VR1 EDA MID	8.75	2.217	4
VR1 EDA POST	8.25	2.062	4

TESTS OF WITHIN-SUBJECTS EFFECTS

SOURCE		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
EDA1	Sphericity Assumed	24.500	2	12.250	13.364	.006	.817
	Greenhouse-Geisser	24.500	1.658	14.781	13.364	.011	.817
	Huynh-Feldt	24.500	2.000	12.250	13.364	.006	.817
	Lower-bound	24.500	1.000	24.500	13.364	.035	.817
ERROR(EDA1)	Sphericity Assumed	5.500	6	.917			
	Greenhouse-Geisser	5.500	4.973	1.106			
	Huynh-Feldt	5.500	6.000	.917			
	Lower-bound	5.500	3.000	1.833			

Suppl Table 6b Physiology Data – Heart Rate – VR 2 – Pre/Mid/Post

DESCRIPTIVE STATISTICS

	Mean	Std. Deviation	N
VR2 HR PRE	75.75	6.185	4
VR2 HR MID	73.75	6.850	4
VR2 HR POST	75.00	6.683	4

TESTS OF WITHIN-SUBJECTS EFFECTS

SOURCE		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
HR2	Sphericity Assumed	8.167	2	4.083	13.364	.006	.817
	Greenhouse-Geisser	8.167	1.424	5.737	13.364	.017	.817
	Huynh-Feldt	8.167	2.000	4.083	13.364	.006	.817
	Lower-bound	8.167	1.000	8.167	13.364	.035	.817
ERROR(HR2)	Sphericity Assumed	1.833	6	.306			
	Greenhouse-Geisser	1.833	4.271	.429			
	Huynh-Feldt	1.833	6.000	.306			
	Lower-bound	1.833	3.000	.611			

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	4/5
	2b	Specific objectives or research questions for pilot trial	6
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	8
	4c	How participants were identified and consented	8 and 14
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	9 and 10
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	12
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N/A
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	18
Sample size	7a	Rationale for numbers in the pilot trial	13
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	N/A
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	N/A
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	N/A

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	N/A
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	N/A
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	12, 14,
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	Suppl flowchart 1. Suppl table 1. Table 2, 3, on page 12
	13b	For each group, losses and exclusions after randomisation, together with reasons	11, 12 acceptability and feasibility data
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9, 10
	14b	Why the pilot trial ended or was stopped	11, Phase 2 – Evaluation/Acceptability of intervention
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Phase 1 – Suppl table 1. Phase 2 – Page 12, table 3
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	Primary outcome: 12, Under 'Acceptability/ feasibility data.' Secondary

			outcome: 11, under heading 'Participants', and 13-14, under heading 'Descriptive Statistics.'
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	13-13 under heading 'Descriptive Statistics.'
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	12, Table 4: Reasons for not completing. Qualitative findings, 14 - 16.
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	13, under heading 'Adverse Events.'
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	18
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	17
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	17
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	17, 18
Other information			

Registration	23	Registration number for pilot trial and name of trial registry	N/A
Protocol	24	Where the pilot trial protocol can be accessed, if available	N/A
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	19
	26	Ethical approval or approval by research review committee, confirmed with reference number	8

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.

*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

BMJ Open

SafeSpace: What is the feasibility and acceptability of a co-designed virtual reality intervention, incorporating compassionate mind training, to support people undergoing cancer treatment in a clinical setting?

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Title Page

Title: SafeSpace: What is the feasibility and acceptability of a co-designed virtual reality intervention, incorporating compassionate mind training, to support people undergoing cancer treatment in a clinical setting?

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Article Summary

Strengths and Limitations of this study

- First study in an oncology setting exploring use of VR to deliver a psychological support intervention.
- Acceptability and feasibility were tested in the oncology setting. Within the evaluation phase, the potential impact of the intervention on psychological, physiological well-being and quality of life was assessed.
- Mixed-methods study: intervention developed using an experience-based co-design approach working with people affected by cancer, alongside qualitative techniques to capture experience of intervention use.
- The intervention consisted of three short sessions per participant. As compassionate mind training is relatively new and has had very limited use in cancer care, participants only received a small dose. This may have limited the overall effect of the intervention.
- This was an acceptability and feasibility project so sample size was small which limits the inferences that can be drawn from this study.

Abstract:

Objectives: The SafeSpace study co-designed and tested a virtual reality intervention, incorporating relaxation and compassionate mind-training to determine acceptability/feasibility in an oncology setting and evaluate impact on physical/psychological well-being and quality-of-life.

Design: A two-phase study. Phase 1 determined key characteristics using an Experienced-based Co-Design approach. Phase 2 evaluated the intervention using various measures and qualitative interviews in a mixed-methods approach. Descriptive statistics were used to analyse measures data, and framework analysis to analyse interviews.

Setting: A specialist cancer centre, UK.

Participants: 18 in phase 1; 21 in phase 2. Participants were in cancer treatment, recovery or palliative care.

Primary and secondary outcome: Primary outcome: acceptability of the intervention, assessed by >60% uptake of three sessions. Secondary outcomes: impact on psychological well-being using: EQ-5D/QLQ-C30, Profile of Mood Scale (POMS), Warwick and Edinburgh Mental Well-being scale (WEMWBS), Depression and Anxiety Severity Scale 21 (DASS21), Self-Compassion Scale (SCS), Acceptance and Action Questionnaire (AAQII), and a locally developed questionnaire to capture self-compassion post-use. Physiological impact was assessed by change in heart rate (HR)/heart rate variability (HRV) and electrodermal activity (EDA).

Results: Twenty participants (mean age=48.7 years; SD=16.87); 65% (n=13) completed three sessions. Mental well-being improved following each use and from baseline to after session 3 (VR 1- z= 2.846, p = < 0.01; VR 2 -z = 2.501, p = <0.01; VR 3 - z = 2.492, p = <0.01). There was statistically significant difference in mean scores for EDA at mid- and post-session compared to pre-session (F (1.658, 4.973) = 13.364, p < 0.05). There was statistically significant reduction in stress levels from baseline to post-session 3. Participants found the intervention acceptable and highlighted areas for development.

Conclusion: The intervention is acceptable and feasible and has shown positive effects on mental well-being/stress in the oncology setting. Larger studies are needed to confirm findings.

Word count: 300

Background:

The number of people living with cancer is expected to double to four million over the next 20 years. (1). Treatment involves surgery, radiotherapy, chemotherapy or other, alone or in combination. Many treatments have unpleasant side-effects and consequently people may not comply with recommended regimens (2). People affected by cancer (PABC) commonly experience poor psychological wellbeing and poor quality of life (QoL) (3, 4, 5). Some become isolated from friends/family, or are unable to continue working, causing financial difficulties and further isolation (2). At least one in four – around 500,000 people in the UK – face poor health or disability after treatment (1).

Virtual Reality

Virtual reality (VR) is the computer-generated simulation of a three-dimensional image or environment that can be interacted with, or explored, in a way that seems real, by an individual using 3-D glasses, a headset with integrated screen, or gloves with integrated sensors. Healthcare has seen a growth in technologies such as VR to provide support (6). Recently, it has become more affordable and seen a dramatic improvement in user experience (7). It has previously been used in various applications including pain management, multiple sclerosis (8, 9, 10) and treatment of psychological conditions, such as phobias and anxiety (11, 12, 13). Within cancer care, VR has been used to manage pain, anxiety, and symptom distress. However, current literature regarding its effectiveness is equivocal. In a review of 19 studies (14), of those which reported on pain (n=6), half found that VR had a statistically significant positive effect in cancer patients. This was substantiated by other work (15) which reported decreased pain and state anxiety levels post-VR use by women with severe/chronic pain following breast cancer treatment. In contrast, a recent meta-analysis of cancer-related symptom management (16) showed the only statistically significant effect was reduced fatigue levels. Other studies (17, 18) using VR reported positive results as a distraction technique during chemotherapy administration. These were small samples (n=16; n=20 respectively) of women with breast cancer. Subsequent studies of larger, more diverse cohorts reported significant impact on reducing perception of time when receiving chemotherapy, validating the distractive nature of VR (19, 20).

Compassion Focused Therapy

Compassion can be defined as 'the sensitivity to suffering in self and others, with a deep commitment to try to relieve it'. Compassion-focused therapy (CFT) is an integrated, multimodal treatment approach that draws from sociology, psychology, and neuroscience (21). Central to CFT is compassionate mind-training (CMT) which was originally developed for people who find self-warmth and self-acceptance difficult (22; 23). It teaches the skill and practice of training the mind, by inviting people to develop their own images of warmth through practices such as slow and deeper breathing, compassionate voice tones, imagery, and facial expressions (24), and helps people develop self-compassion (22). CMT can be delivered on a one to one or group basis (25; 23). Studies examining other psychological interventions such as Cognitive Behavioural Therapy in a cancer population have shown favourable effects (26), however, this requires specialist training, supervision and certification needs (27), and appropriate training can be complex and costly (28, 29).

CMT can be self-administered and once learned, can be recalled in multiple environments including at home (21). CFT and CMT have been shown to reduce suffering and improve QoL in a range of health problems such as anxiety/depression, eating disorders, phobias and pain management (30, 31, 32, 33) and are becoming more mainstream and acceptable (34, 35).

Whilst effectiveness is equivocal, the application of VR within cancer as a distraction technique is accepted. However, its use to deliver psychological therapies, such as CMT, remains unexplored. Little is known about how these treatment approaches might be combined, whether there is any synergistic effect, and if such an intervention is acceptable and feasible in the clinical environment.

Aim:

To co-design a VR intervention, incorporating CMT, and assess its acceptability and feasibility to support people undergoing cancer treatment in a clinical setting.

Primary outcome: acceptability of the intervention, assessed by >60% uptake of three sessions.

Secondary outcomes: impact on psychological well-being using EQ-5D/QLQ-C30, Profile of Mood Scale (POMS), Warwick and Edinburgh Mental Well-being scale (WEMWBS), Depression and Anxiety Severity Scale 21 (DASS21), Self-Compassion Scale (SCS), Acceptance and Action Questionnaire (AAQII), and a locally developed questionnaire to capture self-compassion post-use. Physiological impact was assessed by change in heart rate (HR)/heart rate variability (HRV) and electrodermal activity (EDA).

Methods:

This was a two-phased study using an experience-based co-design (EBCD) approach in phase 1, and mixed-methods in phase 2. Due to the originality of the intervention, not previously implemented in this setting and population, this research is deemed an acceptability and feasibility study. EBCD is a method of participatory research that embeds experience of service users and staff into service design (36). Phase 1: development of the intervention by co-designing and refining several continuously improved prototypes with PABC. Intervention delivery and evaluation model were also established (please see supplementary file flowchart 1 for EBCD process). Phase 2: formal acceptability/feasibility and evaluation of the intervention, with PABC, using the range of psychological, physiological, and QoL measures agreed in Phase 1, and further explored through qualitative feedback obtained during follow-up interviews. Data were triangulated to strengthen the credibility of the acceptability and feasibility findings (37) (please see supplementary flowchart 2 for data triangulation process).

Sample:

A convenience sample was used to recruit participants to both phases of the study. Two separate groups of participants were recruited to either phase; phase 1 participants were no longer in treatment or follow-up; phase 2 participants were either receiving treatment or were in treatment follow-up.

Instruments for psychological assessment:

Demographic data collected included age, gender, diagnosis, cancer group, cancer stage and aim of treatment.

The POMS

The POMS (38) examine six mood subscales: tension-anxiety, depression, anger-hostility, vigour, fatigue, and confusion. Total mood disturbance score is computed by adding the five negative subscale scores and subtracting the vigour score. Higher total mood score indicate greater degree of mood disturbance (39). The POMS subscales and total score have demonstrated sound internal consistency reliability ($\alpha \geq 0.84$) (40).

The WEMWBS

The WEMWBS (41) is a 14-item scale of mental well-being covering subjective well-being and psychological functioning. It is scored by summing responses to each item on a 1-5 Likert scale. The minimum scale score is 14; maximum is 70. It has been validated in the UK in ages 16+ (42). A non-validated, adapted version, AWEMWBS, was used immediately after each intervention use. The WEMWBS asks participants to describe their experience over the last two weeks. The adapted version asks the participant to describe how they are feeling immediately after the intervention.

The AAQII

The AAQII is a seven-item measure of psychological inflexibility, or experiential avoidance. Items are scored on a Likert scale of 1 (never true) to 7 (always true) and are summed up. Higher scores equal greater levels of psychological inflexibility, with proven reliability and validity (43).

The SCS

The SCS (44) is a 26-item instrument that measures self-compassion through three hypothesized dimensions with their negative counterparts: self-kindness versus self-judgment, common humanity versus isolation, and mindfulness versus over-identification, according to a 5-point scale (1= Almost Never; 5= Almost Always). Subscale scores are computed by calculating the mean of subscale item responses. To compute the total score, the Self-Kindness, Common Humanity, and Mindfulness are summed with reverse scores of the Self-judgment, Isolation, and Over-identification subscales. Higher scores indicate greater self-compassion. In the original version, the total score showed excellent internal consistency ($\alpha = .92$) and so did the six subscales (range: .75 - .81) (45).

The DASS-21

The DASS-21 (46) is a 21-item instrument that assesses depression, anxiety and stress. Each seven-item scale has four responses ranging from 0 (did not apply to me at all) to 3 (applied to me much/most of the time). A higher score indicates higher levels of depression, anxiety and stress. The DASS-21 has excellent internal consistency (47), and construct validity (47, 48).

The EQ5D-3L

The EQ5D (49) is designed to measure generic health outcome and comprises two parts: the EQ5D-3L self-classifier, a self-reported description of health problems according to five dimensions

(mobility, self-care, usual activities, pain/discomfort and anxiety/depression), and the EQ-VAS, a self-rated health status using a visual analogue scale to record perception of current overall health; the scale is graduated from 0 (the worst imaginable health state) to 100 (the best imaginable state). It has been shown to be reliable and valid in cancer populations (50).

The QLQ-C30

The QLQ-C30 (51) is used to measure general aspects of HRQOL in cancer patients. EORTC QLQ-C30, Version 3, incorporates five functional scales on physical (PF), role (RF), cognitive (CF), emotional (EF) and social (SF) functioning, three symptom scales on fatigue (FA), pain (PA) and nausea and vomiting (NV), single items assessing dyspnoea (DY), insomnia (SL), loss of appetite (AP), constipation (CO) and diarrhoea (DI), one item assessing perceived financial impact (FI) and global health status/QoL scale (Global QoL). Each item is scored in one of four categories 1) 'Not at all', 2) 'A little', 3) 'Quite a bit' 4) 'Very much', with the exception of 'Global QoL'. It has been shown to be reliable and valid in cancer populations (52, 53, 54).

Locally-developed questionnaire

The locally-developed questionnaire specifically targeted self-compassion after intervention use. It comprised 12 questions such as: 'To what extent did the virtual reality help you have insight into your current situation?' and 'To what extent did the virtual reality make you feel encouraged about the future?' Scored using a 7-item Likert scale ranging from not at all (1) to very much (7), the tool had excellent internal consistency (α = 9.44) (55); a higher score indicated that the intervention had a more positive impact.

Physiological assessment:

Physiological assessment was made using heart rate (HR), heart rate variability (HRV) and electrodermal activity (EDA) (56).

Procedure:

Potential participants were identified by clinical teams, and a diverse convenience sample undergoing a range of cancer treatments across tumour types from one specialist centre recruited. Inclusion criteria were: 1) having a diagnosis of cancer; 2) age over 18 years; 3) ability to provide written consent. Exclusion criteria were people: 1) considered too unwell; 2) in who use of VR is not recommended e.g., registered blind, motion sickness (57), seizure disorder or known psychiatric conditions such as schizophrenia or personality disorder (58). Exclusion criteria were assessed by medical records, self-report and in consultation with clinical staff. All procedures were in accordance with the Declaration of Helsinki (1964) and later amendments or comparable ethical standards. Procedure included two phases with two different groups of participants; phase 1 aimed to inform development of the intervention through a series of workshops with patients with previous experience of cancer and treatment. Phase 2 involved the application and evaluation of the intervention in the clinical setting with patients currently in treatment or follow-up, to assess acceptability and feasibility through intervention uptake and user experience. The study was reviewed by a statistician; Phase 1 is purely qualitative. Phase 2 statistical considerations are referred to in the descriptive statistics section.

Ethical approval:

Ethical approval was acquired from a UK Research Ethics Committee (South Central – Oxford B REC 18/SC/0346) and Health Research Authority (IRAS ID – 241770). Patient and Public involvement was sought for study design. Eligible participants received written information and gave informed consent before taking part.

Patient and Public Involvement:

Patient and public involvement (PPI) was sought, and we recruited two representatives to be members of the study team who further informed the research question and study processes. Both had personal experience of cancer and treatment and previous experience of PPI work as part of a research study. By nature, the experience-based co-design method involved patients in the intervention and evaluation design. The evaluation measures used were selected in collaboration with the patient participants who attended the evaluation workshop, and their burden considered. PPI representatives were not directly involved in participant recruitment. A lay summary of results will be shared with participants via email.

Results/findings:

Phase 1 - Intervention Development

Eleven participants in total took part, please see supplementary table 1. Five workshops, conducted over six months, were facilitated by a research team including experts in VR and CMT, using an EBCD approach. All were digitally recorded and, along with observations collected by two researchers, transcribed and analysed using thematic analysis.

Initial design workshop - Seven participants took part, which started with individuals telling their story, challenges along their pathway and what was important to include. Participants were able to try a range of equipment and experiences in a VR demonstration. They were encouraged to share, critique and propose ideas, using the design studio method (59). Analysis of data identified a number of 'touch points', these being what was emotionally most important to participants, which were used to inform the first iteration of the intervention.

User-testing workshops - Three user-testing workshops took place in which three/four participants each were invited to try the subsequently developed prototype; a total of 11 participants took part in one or more. Participants were asked about their experience particularly focusing on quality and content of the intervention. Further 'touch points' informed the design of the next iteration, which was refined until the co-design team were satisfied it had been developed to acceptable quality.

Findings from Phase 1:

Over the course of the user-testing workshops, the intervention became more refined and focused on detail within, such as recognition of what constitutes a 'safe space', voice quality (e.g. pace/tone), and guidance versus instruction. The themes that emerged which underpinned design of the final specification included: *1) being given permission to 'step out' of current situation; 2)*

importance of voice; 3) need for sign-posting/on-boarding information; 4) being able to explore; 5) being guided versus being instructed. The final iteration consisted of three short sessions of VR/CMT. VR 1 allowed participants to get used to being in a VR environment. VR 2 introduced a soothing breathing exercise, and VR 3 introduced a CMT self-compassion exercise. CMT language developing progressively with each use. A choice of three environments was given: a beach as a 360-degree video, and animated mountain and forest scenes. Professional voiceover actors provided a choice of female or male audio (table 1). It was agreed that the intervention should be offered at any stage of treatment and acknowledged that three sessions may not be sufficient to administer a meaningful 'dose' of CMT but would be enough to generate preliminary data.

Table 1: Final intervention content

All sessions approx. 10 minutes long		
VR1	VR2	VR3
Choice of male or female voice	Choice of male or female voice	Choice of male or female voice
Choice of a VR beach, mountain, or forest scene	Choice of a VR beach, mountain, or forest scene	Choice of a beach, mountain, or forest scene
Adapting to wearing VR headset and being in a VR environment	Simple soothing/breathing exercise, introduction to CMT	Simple CMT exercise

Evaluation workshop - A final workshop was held with five participants, who had taken part in either design or testing, to establish an evaluation model. A range of demographic, psychological and physiological measures were reviewed and agreed to be collected at baseline, and pre- and post-each intervention use (see Table 2). The final intervention was delivered on a head-mounted, stand-alone device; this was considered inexpensive and practical.

Table 2: Schedule for study procedure

Measure		Baseline	Pre each intervention	Post each intervention
Name/age/gender/dx/tx etc	Demographic information	X		
EQ-5D	HRQoL	X	X	
QLQ C30	HRQoL	X		X
Action and Acceptance Questionnaire II - AAQII	Psychological flexibility	X		
Depression, Anxiety and Stress Scale 21 – DASS21	Anxiety/depression/stress	X		X

Profile of Mood State - POMS	Mood	X	X	X
Warwick Edinburgh Mental Well-being Scale - WEMWBS	Mental well-being	X	X	
Self-compassion Scale - SCS	Self-compassion	X		X
Adapted Warwick Edinburgh Mental Well-being Scale - AWEMWBS	Mental well-being immediate time-point			X
Locally developed questionnaire	Self-compassioin			X
Heart rate/heart rate variation/electrodermal activity	Physiological	Monitored continuously before, during and after intervention		

Phase 2 – Evaluation/acceptability of intervention

The final intervention was evaluated and tested for acceptability/feasibility. A further twenty-one people were recruited. Four study visits were organised, coinciding with planned appointments, spaced at least a week apart. At initial visit, written consent was obtained and demographic data collected. Participants completed the baseline set of questionnaires relating to psychological state and QoL. The study then proceeded as per table 2. Telephone interviews were conducted once the participant had completed intervention use.

Quantitative

Summary measures for participant characteristics, VR use data variables and questionnaire scores were presented as means and standard deviations for continuous (approximate), normally distributed variables and frequencies. Categorical variables were reported as percentages. Shapiro-Wilk test was used to confirm normal distribution of continuous summary scales (all p values >0.05). Friedman's test for repeated measures was performed to assess whether there was a statistically significant difference in scores between baseline, VR1, VR2 and VR3. Wilcoxon signed ranks test was used to compare baseline and VR3 session scores. ANOVA was performed to assess changes in EDA, HR and HRV within each session. All p values were two-sided throughout; significance was set at the 5% level. IBM SPSS version 25 was used to analyse the data. Missing data were addressed (see supplementary Table 2).

Participants

Seven males and 14 females consented to take part. One participant was subsequently lost to follow-up. Mean age was 48.7 years (SD=16.87; range: 22-77). Mean time elapsed since diagnosis was 37.08 months (SD= 45.00; range: 2-149). 16 participants (80%) were in active treatment. They had various tumour types with gynaecological cancer being most common (N=4; 20%) (See table 3).

Table 3: Tumour type

Tumour Type	N	%
Lower GI	2	10
Haematological	1	5
Gynaecological	4	20
Head and Neck	3	15
Breast	3	15
Genitourinary (GU)	3	15
Other	4	20

Acceptability/Feasibility Data

In total, 49 sessions of VR were delivered and completed. Acceptability of the intervention was deemed satisfactory as >60% (N=13; 65%) of participants completed all three sessions. This was agreed by discussion with the statistician, based on evidence which reported attrition levels between 16.9% to 26.0% (60) and reporting drop-out rates of up to 41.4% (61). In addition, dropout rates were reportedly lower among studies that did not include some form of between-session intervention which was the case in the current study (60). Thus, 60% was deemed a safe option for acceptability purposes; and further agreed within the Evaluation Workshop.

Reasons for not completing and further details are displayed in Table 4.

Table 4: Acceptability and feasibility data

	VR1		VR2		VR3	
	n	%	n	%	n	%
No. that took part in VR:	20	100	16	80	13	65
No. that did not take part in VR:			4	20	7	35
Reasons for not completing VR:						
Insufficient time			1	25	3	43
Deterioration in condition					1	14
Discontinuation of treatment at site			1	25	1	14
Adverse effect from VR					1	14
Unknown			2	50	1	14
Voice:						
Male	12	60	8	50	6	46
Female	8	40	8	50	7	54
Chosen VR environment:						
Beach	12	60	5	31	8	61
Mountain	6	30	8	50	5	39
Forest	2	10	3	19	0	0
Private room:						
Yes	11	55	9	56	8	61
No	9	45	7	44	5	39
Did the participant change the environment whilst using VR?						
Yes	2	10	0	0	1	8
No	18	90	16	100	12	92

Did the participant experience external noise?						
Yes	9	45	6	37.5	5	38
No	11	55	10	62.5	8	62
Total time in VR (minutes):						
Mean	10.8		10.44		10.00	
SD	1.852		2.502		1.633	
Range	7-15		7-16		8-14	
Did the participant experience any problems with the equipment?	12		13		12	
No	8		3		1	
Yes:	5		0		1	
Minor	2		3		0	
Additional intervention	1		0		0	
Unresolvable						
Did the participant experience an adverse event?						
Yes	1	5	2	12.5	0	0
No	19	95	14	87.5	13	100

Adverse Events

Three minor adverse events (AE) were recorded by two participants who experienced mild nausea and dizziness whilst using the intervention. In both, this resolved spontaneously. The third was in one of the same participants but occurred 48 hours after completing VR2. They reported nausea and dizziness for 48 hours resolving with bed-rest. Considering this, they were advised not to undergo the third session.

Descriptive Statistics

Descriptive statistics were computed for all questionnaire scores within respective domains and are presented as frequencies and standard deviations (see supplementary table 3). Friedman and Wilcoxon signed ranks tests were performed to compare potential changes in variables between baseline and VR1, VR2 and VR3 sessions. Missing data for each variable is shown in supplementary table 4. Two-sided 95% confidence intervals for the exact percentage can be calculated with maximum +/-23% with a sample size of 20. The proposed sample size of 20 was chosen during the EBCD process mainly for pragmatic reasons and was determined by available resources. A sample size of between 24 and 50 has previously been recommended for pilot and feasibility studies (62).

Multi-variate Analyses

Quality of Life

There were no statistically significant changes in QoL in either the EQ5D-3L or the QLQ-C30 responses (see supplementary table 5).

Psychological Measures

Total mood scores (POMS) were compared pre- and post-intervention. There was a statistically significant increase in total scores after the first session (VR 1) (z= -2.136, [b] p=0.03) suggesting there

was an improvement in mood. There was improvement in scores post-second session (VR2) but this was not statistically significant (see supplementary table 6). Mental well-being (WEMWBS) scores showed statistically significant changes to mental well-being from pre- to post-VR session (VR 1 z= -2.846[b] p=<0.01; VR 2 z= -2.501[b] p=<0.01; VR 3 z= -2.492, [8] p=<0.01). There was a consistent beneficial effect maintained throughout all sessions and a statistically significant increase in WEMWBS scores from baseline to VR 3 (x^2=12.905, *df*=3, p=0.005) (see supplementary table 5 & 6).

There was a statistically significant reduction in stress levels as measured by the DASS21 from baseline to post-session 3 (z= -2.138[b], p=0.03) (see supplementary table 6). While there was a positive and beneficial trend- from baseline to post-session 3 (VR3) in most of the sub scores, none reached statistical significance (see supplementary tables 5 & 6).

Physiological measures

ANOVA were conducted to compare EDA, HR and HRV within each session. A decrease in mean EDA for each of the three sessions was recorded, dropping from pre-intervention level and maintained following removal of headset; this was significant for the first session. Using ANOVA with repeated measures and a Greenhouse-Geisser correction, mean scores for EDA were statistically significantly different at mid- and post-session compared to pre-session levels (F(1.658, 4.973)=13.364, p<0.05). Similarly, the only statistically significant change in HR was in the second session with a decrease from pre- to mid-session followed by a return to pre-session levels at post-session (F(1.424, 4.271)=13.364, p<0.05) (see supplementary tables 6a & 6b). No change was observed in HRV.

Qualitative findings

As an acceptability/feasibility study, qualitative feedback was sought to support quantitative results and gather the reality of the intervention use in a real-world setting (63). Participants were invited to a semi-structured telephone interview to acquire a deeper understanding of their experience; eleven participants consented. Demographic data is shown in table 5. Interviews were audio-recorded and transcribed. Feedback was also given following each individual use of the intervention; this was summarised and recorded manually by the researcher and analysed alongside interview data using framework analysis (64). The framework was informed by analysis of the first two transcripts which were coded independently by three researchers and themes discussed and agreed. The subsequent interview transcripts and participant comments were analysed using the agreed framework. Three themes emerged: *1) Practical issues; 2) Immersion; 3) Impact of intervention.*

Table 5: Demographic information of interview participants

Age	Gender	Diagnosis
Mean = 55.5,	Female: n=6, 55%	Urology: n=3, 27.3%
Range 24-77 years	Male: N=5, 45%	Gynaecology: n=3, 27.3%
		Sarcoma: n=2, 18.1%

		Bowel: n=1, 9.1%
		Lung: n=1, 9.1%
		Other: n=1, 9.1%

Practical Issues:

Participants reported equipment as comfortable and relatively straightforward to use. Clear guidance was considered important, and a designated room suggested for the future.

> *'…putting the headset on isn't really a problem … we're all going to have to get used to some kind of virtual reality at some point … hadn't tried it before but it was very interesting.' 012*

The importance of tailoring to the individual was highlighted:

> *'I find breathing exercises really frustrating … I have tumours in my lungs, the amount I can inhale, the amount of time I can hold for is less than for other people. So, someone will say hold it this many beeps and then you can't . . . you feel like you failed at it and you check out ...' 019*

Immersion:

This relates to quality of VR imagery, ability to explore, and impact of voices used in the audio. Lack of quality was seen as negatively impacting immersion and improvement suggested for the future with a preference for 'real' environments rather than animated:

> *'The beach was definitely more...realistic, you felt more sort of immersed in . . . compared with the other two.' 026*

Whilst there was positive reaction to the professional voices, some participants described becoming disengaged:

> *'…I had the final session with the lady [voice], and she was excellent . . . it was very believable. She really did explain it, she was really part of it, and all that. Whereas, I felt with him [male voice], more like that he was reading a script.' 027*

Not all participants liked the compassion therapy aspect of the intervention:

> *'… the compassionate mind therapy, I couldn't see the point of at all . . . you are in a compassion rich environment …. Nurses, the Doctors, friends and family. .. the last thing you .. need is another dose of compassion . . . ' 027*

There was mixed reaction to external noise; some found it detracted from the quality of experience but others found it reassuring as it gave awareness of what was going on around them:

> *'…the noise cancelling was pretty good but I did still hear, if I focused properly, the pump beeping if something went wrong . . . it was sort of the right balance between not being*

completely disconnected if something happened. I think, anymore and I would have felt too isolated.' 026

Impact of intervention:

The intervention was seen as having immediate and lasting effects, with some recognising the ability to replicate the 'safe space' for themselves:

'The breathing techniques, I started to employ when I was having a scan even though the scan was very short. I thought that was quite useful for that. I hadn't really thought of that before but I found it actually quite calming.' 017

For others, the impact was short-lived but still considered useful:

'I don't think it will have a lasting impact...It definitely made the rest of the day easier . . . . But the next day, the day after, I didn't still have that same sense of calm, it was just kind of immediately after… ' 019

Participants' past experience of non-medical support measures emerged as relevant to receptiveness and engagement with the overall VR/CMT experience:

'But I've also been on some of these yoga type things where you just try and relax and get into the mood and all that kind of thing. .. I thought it was quite useful for that. .. the talking was the same.' 012

Participants also gave valuable feedback regarding the research process and informing a larger study, with particular reference to burden of questionnaires:

'I think some of them were a little bit repetitive, I though the one with all the options about being angry, sad, … went on for ages. I don't think that really needs to be that long.' 017

Qualitative findings supported the quantitative results and indicated that the intervention was acceptable and had a beneficial effect on mental well-being, anxiety, and stress (see supplementary table 7 for an example of data synthesis).

Discussion:

The aim of the study was to co-design a low-cost VR intervention enabling rapid access to safe, calm, and soothing environments accompanied by quality controlled and guided CMT exercises and assess acceptability/feasibility in an oncology setting. The intervention was found to be acceptable with nearly two-thirds of participants completing three sessions, meeting the defined end-point. This was supported by findings from interview data, confirming participants were positive, and supporting need for such interventions to help PABC deal with the psychological impact of cancer /treatment. This is consistent with wider literature in which new technologies were also found to be favourable, in their case, regardless of age, background or gender (17, 65). Also consistent, it was found to be acceptable and safe to use across several settings including inpatient, outpatient and day-care (17, 18, 19, 65, 66, 67). Whilst a positive trend was observed in some psychological domains, the overall effectiveness of the intervention remains unclear.

The final version of the intervention consisted of three short, separate sessions of VR/CMT. It is difficult to determine whether VR or CMT had more effect as arguably patients only received a relatively small dose of CMT. This was substantiated in interview findings which highlighted that most participants were unaware of any progression and/or did not relate to the CMT exercises. Participants thought the intervention should be longer, and incorporate more sessions, to have lasting effect. Other research in people having chemotherapy (20) argues that VR may not be effective for all as those with greater symptom distress had more accurate perception of time, suggesting they were not able to block out negative external cues. In order to effect significant change on individual levels of self-compassion, more and longer sessions may be required (68). A future multi-arm RCT may explore which aspect (VR/CMT/ both) has most, if any, effect. Acceptability and feasibility data also showed the beach scene to be the most popular, and the forest scene the least. This is echoed in other work that cites a tree environment as gloomy (69) and highlights the importance of choice.

Throughout both phases, participants expressed that they liked being able to step out of their situation into a ‘safe space’, and some positively described re-imagining the VR environment when they felt stressed. This happened quickly; for some, it was after the first session. Consistent with other work (19, 20), participants reported time passed quickly whilst using the intervention suggesting distractive qualities which may be helpful during lengthy or perceived unpleasant procedures. ‘Presence’ within the context of VR has been defined as the “sense of being there”, or as the “feeling of being in a world that exists outside the self” and causes the user to suspend disbelief and believe they are in the virtual environment, reacting as if they are in the real world (70). This varied between participants, as the quality of imagery and content of audio were reported by some as detracting from the immersive experience. It is generally acknowledged that presence is dependent on either the characteristics of the user and the media employed (71), and relates to willingness to suspend disbelief. Our findings support this; those who had engaged with psychological therapies previously reported they were less concerned with the quality of imagery. Arguably, this study engaged an unusual convenience sample with a mean time since diagnosis of 3 years, of which 80% were still in treatment who potentially may have been more exposed to such therapies over time. Moving forward, using tools to evaluate the degree of presence, such as the Presence Questionnaire PQ (72) and perhaps time perception may be valuable.

A key challenge is identifying who might benefit most from VR, alongside who is not appropriate, to ensure safety. Research (17 18, 19) has highlighted benefits in chemotherapy populations in particular, with reduction of fatigue, anxiety, symptom distress and perception of time. Contrary to this, in our study both participants who experienced AEs were undergoing chemotherapy. However, effects were mild and could not definitively be attributed to the intervention. For one, the effect was so mild that it was not mentioned at the time, and the other was disappointed not to continue, seeing the benefit of the VR experience outweighing effect of the AE. Clinical guidance surrounding patient monitoring during use is recommended.

Interesting findings in terms of *secondary* aims emerged; in particular, improvements in mental well-being and stress. Surprisingly, and consistent with other research (73) we did not see a statistically significant reduction in anxiety levels as reported in other VR studies in this setting (15, 18). This needs to be treated with caution as this could be due to use of different measures. Standardisation may help to make future findings more generalisable/comparable.

A strength is the mixed-methods approach whereby qualitative techniques were employed to capture experience of the intervention, and strengthen the rigour of the acceptability and feasibility process (37). The majority of studies use tools to capture symptom change (15, 20, 67) with only one (74) using open-ended questions in their methodology. Further commonalities included issues surrounding appropriate usage space, and the negative effect of external noise. Developing the intervention for home use may improve quality and impact of experience.

The study has several limitations. The sample size was small (n=21) and the study is potentially underpowered, with a high attrition rate. However, this number of participants was deemed appropriate by the EBCD group (who developed the evaluation model) and local statisticians, to assess the intervention for acceptability, and included a diverse mix of demographics, tumour/treatment type. The small sample did not allow for adjustment of confounding variables in the quantitative analysis so that any notable differences in baseline characteristics or response to the intervention in the study population could be identified. It is acknowledged that a larger sample would be needed moving forward. Reasons for attrition are noted and may provide intelligence for any future pilot or larger study. Furthermore, even though the EBCD group designed the evaluation model and chose measures, interview data highlighted that the quantity were burdensome and repetitive. Consequently, participants described being unable to give full attention and findings may not be a true reflection of feelings. Two non-validated tools were used to capture mental wellbeing and participant self-compassion, and as such may lack consistency and sensitivity.

Conclusion

A VR/CMT intervention is acceptable to PABC and is recognized as offering a novel approach to addressing unmet psychological needs at various stages of the cancer pathway. Whilst feasible/safe to deliver in the oncology setting, developing a flexible approach in which users can access the intervention independently e.g. in their own homes, may increase uptake/impact and allow more autonomy. Future research should focus on conducting larger scale RCT's in which length or frequency of VR and amount of CMT given would be increased, alongside a bigger sample and a control to increase generalizability of findings. Careful consideration is required when selecting evaluative measures

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Data availability statement:
All data are deidentified participant data. All data are securely stored at the host organisation and can be made available upon request to the first author.

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Appendix

Supplementary tables

Study no	Gender	Age years	Diagnosis	Design workshop	User testing workshop 1	User testing workshop 2	User testing Workshop 3	Evaluation workshop
1	Male	54	Ca prostate	Yes	Yes	No	Yes	Yes
2	Male	66	Melanoma	Yes	No	No	No	No
3	Female	72	Ca cervix	Yes	No	Yes	No	No
4	Female	67	Medullary ca	Yes	No	No	Yes	Yes
5	Female	74	Ca lung	Yes	Yes	No	No	Yes
6	Male	74	Neuroendocrine tumour	Yes	Yes	No	No	No
7	Male	69	Ca prostate	Yes	No	Yes	Yes	Yes
8	Male	71	Ca nasopharynx	No	No	Yes	No	No
9	Female	51	Ca thyroid	No	No	Yes	No	Yes
10	Female	37	Scc tongue	No	No	No	No	No
11	Female	62	Ca breast	No	No	No	Yes	No

Supplementary table 1: Phase 1 participant demographic data

Supplementary Table 2: Missing data management

Questionnaire	Variable measured	Missing Data	Statistical test
EQ-5D – 3D	QoL	No computation if values missing as single scores	
QLQ-C30	QoL	Values computed if < or = 10% data missing. Calculated mean for subscore	
DASS-21	Depression, Anxiety, Stress		Friedman (missing listwise)
AAQ II	Psychological flexibility		Friedman (missing listwise)
POMs	Mood state		Friedman (missing listwise)
SCS	Self-compassion		Friedman (missing listwise)
WEBWBS/Ad WEMWBS	Mental well-being		Friedman (missing listwise)
Locally developed Q	Self-compassion after intervention use		Friedman (missing listwise)

Supplementary Table 3: Descriptive Statistics Questionnaire Domain Scores

QUESTIONNAIRES & DOMAINS	N	Mean	Std. Dev.	Min	Max
EQ-5D-5L					
MOBILITY					
B_EQ5DM	12	1.33	.49	1	2
VR1_EQ5DM	12	1.33	.49	1	2
VR2_EQ5DM	12	1.33	.49	1	2
VR3_EQ5DM	12	1.33	.49	1	2
SELF-CARE					
B_EQ5DSC	12	1.25	.45	1	2
VR1_EQ5DSC	12	1.25	.45	1	2
VR2_EQ5DSC	12	1.17	.39	1	2
VR3_EQ5DSC	12	1.17	.39	1	2
USUAL ACTIVITIES					
B_EQ5DUA	12	1.58	.52	1	2
VR1_EQ5DUA	12	1.58	.52	1	2
VR2_EQ5DUA	12	1.42	.52	1	2
VR3_EQ5DUA	12	1.42	.52	1	2
PAIN & DISCOMFORT					
B_EQ5DPD	12	1.50	.67	1	3
VR1_EQ5DPD	12	1.58	.67	1	3
VR2_EQ5DPD	12	1.33	.49	1	2
VR3_EQ5DPD	12	1.67	.65	1	3
ANXIETY & DEPRESSION					
B_EQ5DAD	12	1.42	.52	1	2
VR1_EQ5DAD	12	1.42	.52	1	2
VR2_EQ5DAD	12	1.42	.52	1	2
VR3_EQ5DAD	12	1.42	.67	1	3
BAROMETER / VAS					
B_BAROMETER	12	71.83	15.30	50	100
VR1_BAROMETER	12	71.00	15.09	50	100
VR2_BAROMETER	12	72.17	16.68	40	100
VR3_BAROMETER	12	67.50	20.62	29	100
QLQ C30 – EORTC QoL					
GLOBAL HEALTH SCORE					
BQLQC30GHS	11	-43.18	25.77	-83.33	-8.33
VR1QLQC30GHS	11	-43.94	22.39	-83.33	-8.33
VR2QLQC30GHS	11	-48.48	23.51	-83.33	-16.67
VR3QLQC30GHS	11	-48.48	23.81	-83.33	-16.67
FUNCTIONAL SCALE					
BQLQC30FS	11	7.07	24.05	-42.22	33.33
VR1QLQC30FS	11	4.44	23.83	-42.22	33.33
VR2QLQC30FS	11	7.47	24.10	-44.44	33.33
VR3QLQC30FS	11	7.27	24.93	-46.67	33.33
SYMPTOM SCORE					
BQLQC30SS	11	10.02	21.13	-35.90	30.77
VR1QLQC30SS	11	8.39	20.13	-35.90	30.77
VR2QLQC30SS	11	10.26	21.54	-43.59	33.33
VRQLQC30SS	11	10.02	21.62	-43.59	33.33
DASS21 – DEPRESSION, ANXIETY, STRESS 21					
DEPRESSION					
BDASDEP	11	9.09	9.01	0	28
VR1DASDEP	11	8.91	9.05	0	28
VR2DASDEP	11	8.73	8.40	0	24

VR3DASDEP	11	6.91	7.34	0	18
ANXIETY					
BDASANX	10	8.00	8.79	0	30
VR1DASANX	10	6.60	5.82	0	16
VR2DASANX	10	7.40	6.33	0	18
VR3DASANX	10	4.60	3.53	0	10
STRESS					
BDASSTRS	19	13.37	8.11	0	28
BDASDEP	19	7.68	8.41	0	28
BDASANX	18	7.89	7.62	0	30
VR3DASSTRS	13	8.15	7.89	0	24
VR3DASDEP	12	6.67	7.05	0	18
VR3DASANX	11	4.36	3.44	0	10
AAQ – ACTION & ACCEPTANCE QUESTIONNAIRE					
BTOTAAQ	12	18.75	9.30	7	41
VR1TAAQ	12	19.25	8.85	7	39
VR2TAAQ	12	21.08	10.80	7	43
VR3TAAQ	12	18.08	9.06	7	39
POMS – PROFILE OF MOOD STATE					
VR1PREPOM	19	20.42	5.79	12	36
VR2PREPOMS	16	21.50	7.14	9	39
VR3PREPOMS	13	23.62	6.97	17	36
VR1POSTPOM	18	23.06	6.91	8	36
VR2POSTPOM	13	22.38	4.25	16	31
VR3POSTPOM	13	23.31	6.74	17	39
SCS – SELF-COMPASSION SCALE					
SELF-KINDNESS					
BSCSSK	10	3.14	.811	2.00	4.40
VR1SCSSK	10	3.14	.79	2.00	4.20
VR2SCSSK	10	3.26	.92	1.8	5.0
VR3SCSSK	10	3.30	1.13	1.8	5.0
SELF-JUDGEMENT					
BSCSSJ	10	3.48	1.05	1.40	4.80
VR1SCSSJ	10	3.48	1.05	1.40	4.80
VR2SCSSJ	10	3.34	1.30	1.0	5.0
VR3SCSSJ	10	3.50	1.14	1.6	5.0
COMMON HUMANITY					
BSCSCH	10	3.13	.68	2.25	4.25
VR1SCSCH	10	3.23	.79	2.25	4.75
VR2SCSCH	10	2.90	1.12	1.25	4.50
VR3SCSCH	10	3.15	1.04	1.50	5.00
ISOLATION					
BSCSISO	10	3.30	1.14	1.75	5.00
VR1SCSISO	10	3.38	1.13	1.75	5.00
VR2SCSISO	10	3.43	1.13	1.75	5.00
VR3SCSISO	10	3.58	1.24	1.50	5.00
MINDFULNESS					
BSCSM	10	4.10	.74	3	5
VR1SSCSM	10	4.05	.64	2.75	5.00
VR2SSCSM	10	3.73	.76	2.75	5.00
VR3SSCSM	10	3.75	.82	2.75	5.00
OVER-IDENTIFIED					
BSCSOI	10	3.30	1.12	1.50	5.00
VR1SCSOI	10	3.35	1.14	1.50	5.00
VR2SCSOI	10	3.70	1.26	1.50	5.00

VR3SCSOI	10	3.58	1.24	1.50	5.00
LDL – LOCALLY DEVELOPED QUESTIONS					
VR1LDQTS	12	51.08	15.92	33	80
VR2LDQTS	12	50.67	14.75	36	77
VR3LDQTS	12	50.50	17.42	14	77
WEMWBS WARWICK-EDINBURGH MENTAL WELL-BEING SCALE					
BWEMTS	19	48.74	8.92	34	67
VR1TWEWM	19	48.58	9.17	34	67
VR2WEMWTS	15	48.13	9.48	37	70
VR3WEMWTS	13	49.46	10.44	39	70
AWEMWBS – ADAPTED WARWICK-EDINBURGH METAL WELL-BEING SCALE					
VR1TAWEM	18	53.00	8.24	36	70
2AWEMTS	14	54.43	12.64	37	85
VR3AWEMTS	13	52.69	8.98	39	70
BWEMTS	12	45.92	7.76	34	58
VR1TAWEM	12	51.67	8.66	36	70
2AWEMTS	12	54.00	13.52	37	85
VR3AWEMTS	12	52.83	9.36	39	70

Supplementary table 4: Number of missing variables (number of participants)

	Baseline	VR1	VR1	VR2	VR2	VR3	VR3
Measure		Pre intervention	Post intervention	Pre intervention	Post intervention	Pre intervention	Post intervention
EQ-5D	0	0	N/A	0	N/A	0	N/A
QLQ C30	0	0	N/A	2(2)	N/A	0	N/A
Action and Acceptance Questionnaire II - AAQII	0	0	N/A	4(2)	N/A	0	N/A
Depression, Anxiety and Stress Scale 21 – DASS21	7(3)	8(2)	N/A	2(2)	N/A	14(2)	N/A
Profile of Mood State - POMS	6 (2)	8(3)	5(3)	9(3)	6(2)	1	2(2)
Warwick Edinburgh Mental Well-being Scale - WEMWBS	1	2(1)		0	N/A	0	
Self-compassion Scale - SCS	23 (1)	2(1)	N/A	0	N/A	0	N/A
Adapted Warwick Edinburgh Mental Well-being Scale - AWEMWBS	N/A	N/A	0	N/A	0	N/A	1
Locally developed questionnaire	N/A	N/A	0	N/A	1	N/A	0

Supplementary Table 5: Multivariate analyses comparing baseline, VR1, VR2 and VR3 session scores

Friedman Test for EQ-5D-5L, QLQ C30 EORTC, DASS21, AAQ, SCS, LDQ, WEMWBS, AWEMWBS and Heart Rate Variation

Ranks							
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**
B_EQ5DM	2.50	B_EQ5DSC	2.58	B_EQ5DUA	2.67	B_EQ5DPD	2.46
VR1_EQ5DM	2.50	VR1_EQ5DSC	2.58	VR1_EQ5DUA	2.67	VR1_EQ5DPD	2.63
VR2_EQ5DM	2.50	VR2_EQ5DSC	2.42	VR2_EQ5DUA	2.33	VR2_EQ5DPD	2.13
VR3_EQ5DM	2.50	VR3_EQ5DSC	2.42	VR3_EQ5DUA	2.33	VR3_EQ5DPD	2.79
N	12	**N**	12	**N**	12	**N**	12
Chi-Square	.000	**Chi-Square**	2.000	**Chi-Square**	6.000	**Chi-Square**	5.526
df	3	**df**	3	**df**	3	**df**	3
Asymp. Sign.	1.000	**Asymp. Sign.**	.572	**Asymp. Sign.**	.112	**Asymp. Sign.**	.137
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
B_EQ5DAD	2.50	B_BAROMETER	2.63	BQLQC30GHS	2.82		
VR1_EQ5DAD	2.50	VR1_BAROMETER	2.42	VR1QLQC30GHS	2.82		
VR2_EQ5DAD	2.50	VR2_BAROMETER	2.67	VR2QLQC30GHS	2.27		
VR3_EQ5DAD	2.50	VR3_BAROMETER	2.29	VR3QLQC30GHS	2.09		
N	12	**N**	12	**N**	11		
Chi-Square	.000	**Chi-Square**	.880	**Chi-Square**	4.935		
df	3	**df**	3	**df**	3		
Asymp. Sign.	1.000	**Asymp. Sign.**	.830	**Asymp. Sign.**	.177		
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
BQLQC30FS	2.41	BQLQC30SS	2.64	BDASDEP	2.59		
VR1QLQC30FS	2.18	VR1QLQC30SS	2.00	VR1DASDEP	2.45		
VR2QLQC30FS	2.64	VR2QLQC30SS	2.77	VR2DASDEP	2.59		
VR3QLQC30FS	2.77	VRQLQC30SS	2.59	VR3DASDEP	2.36		
N	11	**N**	11	**N**	11		
Chi-Square	1.709	**Chi-Square**	3.000	**Chi-Square**	.365		
df	3	**df**	3	**df**	3		
Asymp. Sign.	.635	**Asymp. Sign.**	.392	**Asymp. Sign.**	.947		
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
BDASANX	2.75	BDASSTRS	2.96	BTOTAAQ	2.38		
VR1DASANX	2.50	VR1DASSTRS	2.92	VR1TAAQ	2.63		
VR2DASANX	2.80	VR2DASSTRS	2.38	VR2TAAQ	3.04		
VR3DASANX	1.95	VR3DASSTRS	1.75	VR3TAAQ	1.96		
N	10	**N**	12	**N**	12		
Chi-Square	4.789	**Chi-Square**	8.656	**Chi-Square**	5.742		
df	3	**df**	3	**df**	3		
Asymp. Sign.	.188	**Asymp. Sign.**	.034	**Asymp. Sign.**	.125		
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
BSCSSK	2.50	BSCSSJ	2.25	BSCSCH	2.25		
VR1SCSSK	2.45	VR1SCSSJ	2.25	VR1SCSCH	2.65		
VR2SCSSK	2.30	VR2SCSSJ	2.60	VR2SCSCH	2.40		
VR3SCSSK	2.75	VR3SCSSJ	2.90	VR3SCSCH	2.70		
N	10	**N**	10	**N**	10		
Chi-Square	.733	**Chi-Square**	2.133	**Chi-Square**	.976		
df	3	**df**	3	**df**	3		
Asymp. Sign.	.866	**Asymp. Sign.**	.545	**Asymp. Sign.**	.807		
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**		
BSCSISO	2.20	BSCSM	2.90	BSCSOI	2.05		

VR1SCSISO	2.40	VR1SSCSM	2.90	VR1SCSOI	2.25
VR2SCSISO	2.75	VR2SSCSM	2.05	VR2SCSOI	2.95
VR3SCSISO	2.65	VR3SSCSM	2.15	VR3SCSOI	2.75
N	10	**N**	10	**N**	10
Chi-Square	2.018	**Chi-Square**	5.230	**Chi-Square**	4.417
df	3	**df**	3	**df**	3
Asymp. Sign.	.569	**Asymp. Sign.**	.156	**Asymp. Sign.**	.220
Domain	**M Rank**	**Domain**	**M Rank**	**Domain**	**M Rank**
VR1LDQTS	2.13	BWEMTS	1.38	VR1 HRV Pre	2.00
VR2LDQTS	1.83	VR1TAWEM	2.75	VR1 HRV Mid	2.00
VR3LDQTS	2.04	2AWEMTS	2.83	VR1 HRV Post	2.00
VR1LDQTS	2.13	VR3AWEMTS	3.04	VR1 HRV Pre	2.00
N	12	**N**	12	**N**	3
Chi-Square	.565	**Chi-Square**	12.905	**Chi-Square**	.000
df	2	**df**	3	**df**	2
Asymp. Sign.	.754	**Asymp. Sign.**	.005	**Asymp. Sign.**	1.000

Supplementary Table 6: Multi-variate analyses comparing baseline to VR3 session scores

Wilcoxon Signed Ranks Test for DASS21, AAQ, WEMWBS & AWEMWBS, POMS and SSC

DASS21		N	Mean Rank	Sum of Ranks
VR3DASSTRS - BDASSTRS	Negative Ranks	9[a]	6.33	57.00
	Positive Ranks	2[b]	4.50	9.00
	Ties	2[c]		
	Total	13		
VR3DASDEP - BDASDEP	Negative Ranks	5[d]	5.20	26.00
	Positive Ranks	4[e]	4.75	19.00
	Ties	3[f]		
	Total	12		
VR3DASANX - BDASANX	Negative Ranks	5[g]	3.00	15.00
	Positive Ranks	0[h]	.00	.00
	Ties	6[i]		
	Total	11		
	Test statistics			
	VR3DASSTRS - BDASSTRS	VR3DASDEP - BDASDEP	VR3DASANX – BDASANX	
Z	-2.138[b]	-.418[b]	-2.032[b]	
Asymp. Sig. (2-tailed)	.033	.676	.042	
AAQ		N	Mean Rank	Sum of Ranks
VR1POSTPOM - VR1PREPOM	Negative Ranks	2[a]	7.50	15.00
	Positive Ranks	11[b]	6.91	76.00
	Ties	5[c]		
	Total	18		
VR2POSTPOM - VR2PREPOMS	Negative Ranks	6[d]	4.17	25.00
	Positive Ranks	4[e]	7.50	30.00
	Ties	3[f]		
	Total	13		
VR3POSTPOM - VR3PREPOMS	Negative Ranks	4[g]	3.00	12.00
	Positive Ranks	2[h]	4.50	9.00
	Ties	7[i]		
	Total	13		
	Test statistics			
	VR1POSTPOM - VR1PREPOM	VR2POSTPOM - VR2PREPOMS	VR3POSTPOM – VR3PREPOMS	
Z	-2.136[b]	-.255[b]	-.315[c]	
Asymp. Sig. (2-tailed)	.033	.799	.752	
WEMWBS & AWEMWBS		N	Mean Rank	Sum of Ranks
VR1TAWEM - VR1TWEWM	Negative Ranks	2[d]	5.00	10.00
	Positive Ranks	13[e]	8.46	110.00
	Ties	3[f]		
	Total	18		
2AWEMTS - VR2WEMWTS	Negative Ranks	2[g]	1.50	3.00
	Positive Ranks	8[h]	6.50	52.00

	Ties	4[i]		
	Total	14		
VR3AWEMTS - VR3WEMWTS	Negative Ranks	1[j]	1.50	1.50
	Positive Ranks	8[k]	5.44	43.50
	Ties	4[l]		
	Total	13		
	Test statistics			
	VR1TAWEM - VR1TWEWM	2AWEMTS - VR2WEMWTS	VR3AWEMTS – VR3WEMWTS	
Z	-2.846[b]	-2.501[b]	-2.492[b]	
Asymp. Sig. (2-tailed)	.004	.012	.013	
POMS		N	Mean Rank	Sum of Ranks
VR1POSTPOM - VR1PREPOM	Negative Ranks	2[a]	7.50	15.00
	Positive Ranks	11[b]	6.91	76.00
	Ties	5[c]		
	Total	18		
VR2POSTPOM - VR2PREPOMS	Negative Ranks	6[d]	4.17	25.00
	Positive Ranks	4[e]	7.50	30.00
	Ties	3[f]		
	Total	13		
VR3POSTPOM - VR3PREPOMS	Negative Ranks	4[g]	3.00	12.00
	Positive Ranks	2[h]	4.50	9.00
	Ties	7[i]		
	Total	13		
	Test statistics			
	VR1POSTPOM - VR1PREPOM	VR2POSTPOM - VR2PREPOMS	VR3POSTPOM – VR3PREPOMS	
Z	-2.136[b]	-.255[b]	-.315[c]	
Asymp. Sig. (2-tailed)	.033	.799	.752	

SSC	VR3SCSSK - BSCSSK	VR3SCSSJ - BSCSSJ	VR3SCSCH - BSCSCH	VR3SCSISO - BSCSISO	VR3SSCSM - BSCSM	VR3SCSOI - BSCSOI
Z	-1.011[b]	-.978[b]	-.224[c]	-1.261[b]	-1.605[c]	-1.430[b]
Asymp. Sig. (2-tailed)	.312	.328	.823	.207	.108	.153

Supplementary Tables 6a & 6b: Multi-variate analyses comparing VR session scores

ANOVA for Electrodermal Activity (EDA) and Heart Rate

Supplementary Table 6a Physiology Data – Electrodermal Activity (EDA) – VR 1 – Pre/Mid/Post

DESCRIPTIVE STATISTICS

	Mean	Std. Deviation	N
VR1 EDA PRE	11.50	3.416	4
VR1 EDA MID	8.75	2.217	4
VR1 EDA POST	8.25	2.062	4

TESTS OF WITHIN-SUBJECTS EFFECTS

SOURCE		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
EDA1	Sphericity Assumed	24.500	2	12.250	13.364	.006	.817
	Greenhouse-Geisser	24.500	1.658	14.781	13.364	.011	.817
	Huynh-Feldt	24.500	2.000	12.250	13.364	.006	.817
	Lower-bound	24.500	1.000	24.500	13.364	.035	.817
ERROR(EDA1)	Sphericity Assumed	5.500	6	.917			
	Greenhouse-Geisser	5.500	4.973	1.106			
	Huynh-Feldt	5.500	6.000	.917			
	Lower-bound	5.500	3.000	1.833			

Supplementary Table 6b Physiology Data – Heart Rate – VR 2 – Pre/Mid/Post

Descriptive Statistics							
	Mean	Std. Deviation	N				
VR2 HR Pre	75.75	6.185	4				
VR2 HR Mid	73.75	6.850	4				
VR2 HR Post	75.00	6.683	4				

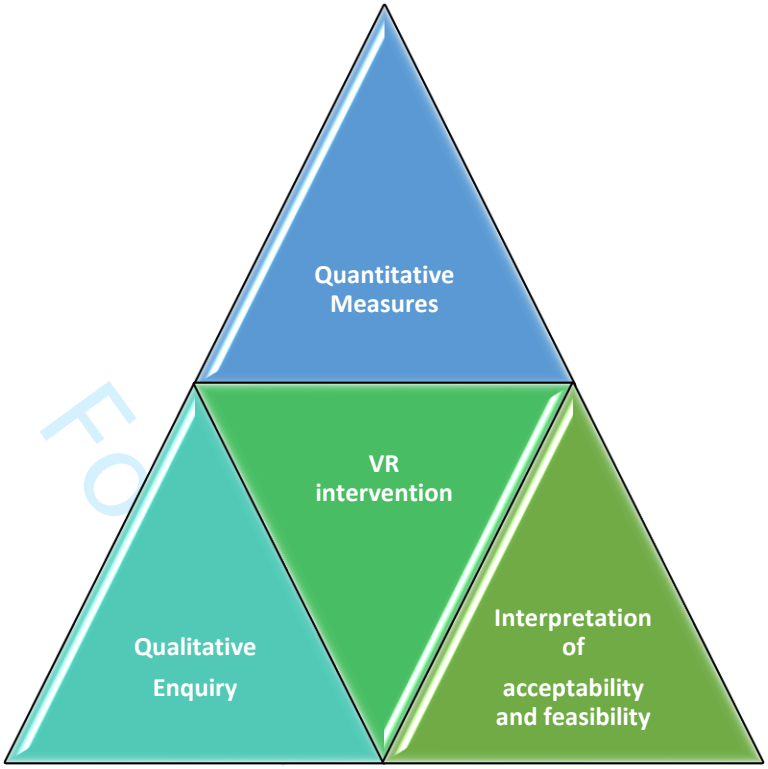
Tests of Within-Subjects Effects							
Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
HR2	Sphericity Assumed	8.167	2	4.083	13.364	.006	.817
	Greenhouse-Geisser	8.167	1.424	5.737	13.364	.017	.817
	Huynh-Feldt	8.167	2.000	4.083	13.364	.006	.817
	Lower-bound	8.167	1.000	8.167	13.364	.035	.817
Error(HR2)	Sphericity Assumed	1.833	6	.306			
	Greenhouse-Geisser	1.833	4.271	.429			
	Huynh-Feldt	1.833	6.000	.306			
	Lower-bound	1.833	3.000	.611			

	Qualitative	Quantitative
Stress	'… it takes you away from that situation, even if it's only for a few minutes, and it helps to calm when you're feeling anxious, as I think most patients are when they undergo cancer treatment.' Participant 013	DASS-21: Statistically significant reduction in stress levels as measured by the DASS21 from baseline to post-session 3 (z= -2.138[b], p=0.03)
Mental well-being	'Very relaxed, very safe for the first one on the beach. It was 11/10. I truly enjoyed even though I was having treatment I enjoyed it. . . Participant 031	WEMWBS: Statistically significant changes to mental well-being from pre- to post-VR session (VR 1 z= -2.846[b] p=<0.01; VR 2 z= -2.501[b] p=<0.01; VR 3 z= -2.492, [8] p=<0.01)
Mood	'…did make me relax and gave me a break from the hustle and bustle of being in a hospital, so, it definitely, I definitely felt sort of calmer after using it…and more relaxed, a bit sort of more optimistic, that was the case.' Participant 026	POMS: Statistically significant increase in total scores after the first session (VR 1) (z= -2.136, [b] p=0.03)
Acceptability	' I think that if it was something that I was putting on my head every single day or every other day I think that the positive effect would probably increase even more so.' Participant 017 'But I def think if I had the VR just like, at night, all the lights are off, I'd do VR for like 10 mins, then I'd be able to visualise the place I'd been like, the beach or whatever, and drift off. Participant 019	65%; 60% was deemed a safe option for acceptability purposes

Supplementary table 7 – Data synthesis

STUDY SET-UP – Supplementary flowchart 1

Supplementary flowchart 2 – Data triangulation



CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	4/5
	2b	Specific objectives or research questions for pilot trial	6
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	8
	4c	How participants were identified and consented	8 and 14
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	9 and 10
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	12
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N/A
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	18
Sample size	7a	Rationale for numbers in the pilot trial	13
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	N/A
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	N/A
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	N/A

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	N/A
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	N/A
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	12, 14,
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	Suppl flowchart 1. Suppl table 1. Table 2, 3, on page 12
	13b	For each group, losses and exclusions after randomisation, together with reasons	11, 12 acceptability and feasibility data
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9, 10
	14b	Why the pilot trial ended or was stopped	11, Phase 2 – Evaluation/Acceptability of intervention
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Phase 1 – Suppl table 1. Phase 2 – Page 12, table 3
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	Primary outcome: 12, Under 'Acceptability/ feasibility data.' Secondary

			outcome: 11, under heading 'Participants', and 13-14, under heading 'Descriptive Statistics.'
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	13-13 under heading 'Descriptive Statistics.'
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	12, Table 4: Reasons for not completing. Qualitative findings, 14 - 16.
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	13, under heading 'Adverse Events.'
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	18
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	17
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	17
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	17, 18
Other information			

Registration	23	Registration number for pilot trial and name of trial registry	N/A
Protocol	24	Where the pilot trial protocol can be accessed, if available	N/A
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	19
	26	Ethical approval or approval by research review committee, confirmed with reference number	8

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.

*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.