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Virtual reality for psycho-education on self-stigma in depression: Design of a randomised controlled trial☆

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ABSTRACT

Background: Major Depressive Disorder (MDD) is a prevalent and disabling mental health condition. Patients with MDD often deal with self-stigma, which can lead to more depressive symptoms. Psychoeducation about depression has proven to be effective in reducing depressive symptomatology and self-stigma. Involving a significant other in psychoeducation for depression, might increase mutual understanding. Virtual reality (VR) offers the opportunity to experience the perspective of having or living with someone with a mental condition. For this study an immersive VR environment is developed. The main objective of this study is to test whether our VR psychoeducation intervention is more successful in reducing self-stigma than standard psychoeducation for MDD.
Methods: In this randomised controlled trial (RCT), 80 couples of patients and their significant other will be included and randomly assigned to one of two conditions: the VR psychoeducation intervention and standard psychoeducation. Patients will be aged 18 to 65, diagnosed with MDD. The main study parameter is self-stigma, as measured by the Internalized Stigma of Mental Illness scale. Secondary parameters include depressive symptoms, loneliness and perceived social support for the patient and burden of care and quality of life for the significant other.
Limitations: No control for nonspecific factors, limited individual adjustment, patients are not able to participate without a significant other.
Conclusions: VR might open up the opportunity to reduce self-stigma and thereby improve the efficacy of psychoeducation in MDD.

1. Background

Major Depressive Disorder (MDD) is the most prevalent psychiatric disorder with a lifetime prevalence of 19% (De Graaf et al., 2011). Depression has a major impact on daily life functioning of both the patient and their significant others and is the leading cause of disability worldwide (Lépine and Briley, 2011). Patients with depression not only suffer from the symptoms, distress, and disabilities caused by their depressive disorder, they are also hindered by self-stigma. Self-stigma refers to the loss of self-esteem and self-efficacy that occurs when people internalize the public stigma (Corrigan et al., 2005), which is characterized by a subjective perception of devaluation, marginalization, secrecy, shame, and withdrawal (Boyd et al., 2014). Self-stigma is a source of chronic stress and a major barrier to recovery for people with mental illnesses (Corrigan et al., 2005).

Patients with depression who have more severe self-stigma report a lower quality of life (Holubova et al., 2016). Even after controlling for sociodemographic and clinical background characteristics, self-stigma still contributes to depressive symptoms, with this effect being mediated by experienced loneliness (Switaj et al., 2014). Loneliness on its own, is a unique risk factor for depressive symptoms (Cacioppo et al., 2006). A concept related to loneliness is experienced social support

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(Bernardon et al., 2011). There is substantial evidence from prospective studies that people with depression who perceive their social support as poorer, have worse outcomes in terms of depressive symptoms including suicidal ideation, recovery and social functioning (Wang et al., 2018; Xie et al., 2018). Therefore, an intervention that reduces self-stigma, loneliness, and increases experienced social support is potentially powerful in decreasing depressive symptoms.

For significant others, depression can result in heavy psychosocial burden. Providing care and support to a seriously mentally ill family member, for example MDD, can result in heavy psychosocial burden and a disruptive effect on one's health and quality of life (Zauszniewski et al., 2009). Fadden and colleagues reported that the burden of spouses of patients with MDD included restrictions in social and leisure activities, a fall in family income, and a considerable strain on the marital relationship. Negative consequences for significant others of depression were misery, withdrawal, and worrying which commonly caused problems. Few significant others know how to deal with the difficult behavior of patients with depression (Fadden et al., 1987). Similar results were found in a study in which relatives of depressed persons were interviewed; many relatives expressed a feeling of not living their own life, after living with a depressed person for a long time. The depression did not only affect family dynamics, but also the relatives' social and professional lives (Stjernswärd and Östman, 2008). Therefore, it is important to include the significant other when treating patients with depression and consider the impact of the depression on them, to help creating a feeling of shared responsibility and less burden.

One way to successfully reduce self-stigma in patients with depression and involve their significant others at the same time, is to decrease negative attitudes towards depression in both patients and their significant others (Griffiths et al., 2008a). A common way to do this is by providing adequate psychoeducation to both groups. During psychoeducation, information on the causes, course and consequences of depression is discussed. Research shows that psychoeducation programs can lead to significantly improved attitudes about mental illness (Griffiths et al., 2008b; Holmes et al., 1999; Keane, 1990) and that it can improve the patients' experienced social support (Rotondi et al., 2015). It might also reduce experienced loneliness in people with mental illness (Mann et al., 2017). In general, psychoeducation for depression has proven to be effective. A systematic review based on 15 studies, that included 2139 patients with major depressive disorder, has shown that psychoeducation improves the clinical course, treatment adherence and psychosocial functioning of depressive patients (Tursi et al., 2013a). However, comparison of the studies turned out to be difficult as result of the great diversity in methodologies (face to face meetings, personalized mailings, websites), samples (individual, group, with/without relative), and content of the interventions. Furthermore, research reveals several positive effects of involving family members in psychoeducation interventions. Family psychoeducation has shown to be a useful intervention to reduce the burden of the significant others of patients with depressive disorder (Katsuki et al., 2011a), and it has been proven to be effective in the prevention of relapse in adult patients with major depression (Shimazu et al., 2011). Moreover, a cost-effectiveness analysis of family psychoeducation shows that it is also highly likely to be cost-effective (Shimodera et al., 2012). Overall, psychoeducation for depression has positive effects on both patients suffering from depression and their significant others.

Immersive virtual reality (VR), might be a powerful tool to use in psychoeducation interventions for depression. In VR, a computer-generated simulation of a real-life environment is created which a person can experience using electronic equipment, such as a head-mounted display (HMD). It enables users to feel that they are in a different environment from where they are physically (Gorini et al., 2011). A recent meta-analysis of studies on VR interventions for anxiety and depression has shown that VR-based therapies were just as effective than control conditions for anxiety and depression (Fodor et al., 2018), however, little is known about implementing VR in psychoeducation for depression. VR makes it possible to convey another person's experience or feelings to a viewer. In VR environments, viewers may strongly feel another person's emotions or situation by being in the same place, close to the character in VR. Becoming absorbed by VR can stimulate empathy, allowing people to understand others (Shin, 2018). Several studies have confirmed that VR increases empathy (Louie et al., 2018; Schutte and Stilinović, 2017), and that it can elicit a positive attitudinal change in users, because of a higher involvement in the content in VR (Bujić et al., 2020). In addition, depressive patients might take in and remember information better when provided through VR compared to psychoeducation that is provided solely in writing or verbally, since concentration problems is one of the core symptoms in MDD (Boschloo et al., 2016), and patients with MDD show evidence of impaired verbal learning (Marazziti et al., 2010). Therefore, through VR both patients and their significant others get the opportunity to identify themselves or empathize with another person with depression, which may lead to improved understanding. This makes VR a potentially powerful tool to reduce self-stigma in the patient, and for their significant others, to improve the ability to support the patient with depression.

For this study, we created a VR immersive experience with the purpose to experience a day in the life of a patient who is suffering from depression, as well as a day in the life of the partner of the patient with depression. It was generated using input from patients who actually suffered from a depression, combined with the input of clinicians with experience in diagnosing and treating patients with depression. The aim of the present randomised controlled trial (RCT) is to include this element in a novel psychoeducation model, using Immersive VR during the psychoeducation phase of the treatment as compared to psychoeducation as usual.

1.1. Study objectives and purpose

In the present RCT, the main aim is to test whether our newly developed VR psychoeducation intervention is more successful in reducing self-stigma compared to psychoeducation as usual for MDD. We hypothesize that compared to the standard psychoeducation, the VR psychoeducation will lead to a larger decrease of self-stigma for the patient.

The secondary aim is to test the effect of the VR psychoeducation intervention on depressive symptoms, experienced loneliness and social support for the patient, and perceived burden of care and quality of life of the significant other of the patient, as compared to standard psychoeducation. We hypothesize that compared to the standard psychoeducation, the VR psychoeducation intervention will lead to a larger decrease in depressive symptoms and loneliness and a larger increase in experienced social support for the patient. In addition, we expect that the VR psychoeducation will lead to a larger decrease in burden of care for significant others and a larger increase of their quality of life compared to standard psychoeducation.

2. Methods

2.1. Study design and setting

In this RCT, a VR psychoeducation intervention will be compared to a standard psychoeducation intervention for depression. The study takes place at Center for Mental Health care GGZ Delfland, the Netherlands. Four locations for outpatient mental health care from GGZ Delfland will be participating in this trial. The sample will consist of 80 couples of outpatients with a diagnosis of MDD, with their chosen significant other. After giving written informed consent, the couples will be equally randomised overtwo conditions: VR psychoeducation intervention or psychoeducation intervention as usual. A trained therapist will conduct the psychoeducation session. After the psychoeducation session, patients will start psychotherapy as usual. A trained researcher will perform the assessment of primary and secondary outcomes, this takes place before the psychoeducation session, directly after the session, after 1 week, and

at the follow up after 10 weeks. For an overview of the procedure, see Fig. 1.

2.2. Participants

2.2.1. Recruitment

We will recruit potential participants for this study through advertising in the waiting room and on the website. At the intake interview, a licensed psychologist or psychiatrist determines a principal diagnosis of depression (mild, moderate, severe), and informs patient about the VR psychoeducation study. If the patient agrees to be contacted, the therapist will inform the researcher about the potential participant. All advertising has prior approval of the medical ethical board of the Academic Medical Center.

2.2.2. Assessment of eligibility

After informed consent is obtained, trained researchers will conduct a pre-assessment interview with the Structured Clinical Interview for DSM-5 disorders (SCID-5-S), module A; section depressive disorder, to assess and confirm depressive symptoms (First et al., 2017). Possible comorbid diagnosis that were determined during the intake interview with their own therapist will be included in our study. We aim to conduct a pragmatic RCT including MDD patients without and with comorbid psychiatric disorders, as long as MDD is the primary diagnosis.

2.2.3. Sample size

Using GPower, a sample size of 36 participants per group would be required to detect a medium effect at alpha level of .05 and power of .95 in a repeated measure ANOVA with an interaction of between (PE vs. PE-VR) and within (pre, after session, 1 week, 10 weeks) factors on self-stigma. Allowing for 10% drop-out, we will include 40 patients with a depression and their chosen significant other per condition. Meta-analysis of the effect of therapeutic interventions for internalized stigma of severe mental illness showed a favourable small to medium significant effect of psychoeducation (SMD = −0.40; P = .001) (Tsang et al., 2016).

2.2.4. Inclusion criteria

Criteria for inclusion for participants are: A principal diagnosis of MDD (mild, moderate, severe) as recently stated during the intake interview by either a licensed psychologist or psychiatrist and validated with the SCID by a trained researcher, age between 18 and 65 years, willing to involve a significant other (partner, friend, family member), scheduled to start psychotherapy individually or in a group at an outpatient clinic, written informed consent by both the patient and the significant other to participate in the study.

2.2.5. Exclusion criteria

Exclusion criteria are: Severe current comorbid psychiatric disorders including schizophrenia-like disorders, bipolar disorder or addiction disorders, intellectual disability in the history, abnormal hearing or uncorrected vision. Previous therapy is no exclusion criteria, although patients that already started with psychotherapy during their current application for therapy are excluded.

2.2.6. Withdrawal

Subjects can leave the study at any time for any reason if they wish to do so, without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons. Data that has been collected until withdrawal will be included in the analysis.

2.3. Randomization

In this study, patients and their chosen significant others will be equally randomised as a couple, immediately after given informed consent and screening for eligibility. We will use the validated variable block randomization model of Castor EDC for this purpose (Arts, 2019). Trained researchers perform this action in Castor and inform the participants, local principal investigator and the VR-therapist immediately after. No one will be blinded to the interventions.

2.4. Data management

The handling of the personal data is according to the Dutch Act on Implementation of the General Data Protection Regulation (in Dutch: Uitvoeringswet AVG, UAVG). The data files will be separated from the name and date of birth data. Participants get a research code: a three-digit number (YYY) with a or b (patient, relative). The data files will be collected and stored in the online database Castor. The key with name and date of birth data is locked and saved on a local drive. Members of

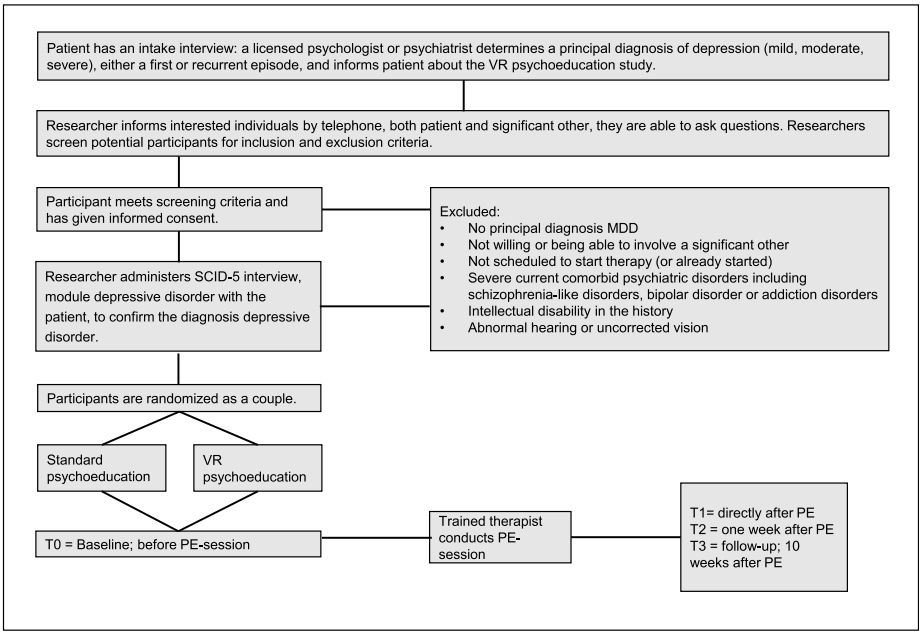

Fig. 1. Flowchart of the study.
PE = Psychoeducation.

the local study team of GGZ Delfland and the Sponsor; AMC have access to the final dataset.

2.5. The interventions

Both psychoeducation interventions; with and without the VR experience, will be provided in one session of 60 min.

2.5.1. Standard psychoeducation

The patient and the significant other will join the psychoeducation session together. The standard psychoeducation manual was designed by GGZ Delfland, based on the Dutch CBT intervention book 'Protocollaire behandelingen voor volwassenen met psychische klachten', section depressive disorder (Bockting et al., 2017) and the Minddistrict e-health intervention for depression. It consists of a verbal explanation of the symptoms, possible causes, diagnosis and treatment of depression. Instead of watching the VR depression experience video, the therapist will stimulate a discussion, about the impact of the depressive disorder on the relationship/family/daily life. Subsequently the therapist will stimulate a mutual discussion with them about the content of the psychoeducation. After the psychoeducation session both the patient and the significant other will fill in a questionnaire about their experience with the psychoeducation.

2.5.2. VR psychoeducation

Patients and significant others who receive the VR psychoeducation get the same verbal explanation as described above, followed by watching the VR depression experience videos. These consist of two 360° videos which summarize multiple fragments of a day in the life of a female depressive patient (1) from her perspective and (2) from the perspective of her male partner. The VR depression experience videos were created with input from patients who have suffered from depression and healthcare professionals with extensive experience treating patients with depression. Although the VR experience video is filmed from the perspective of a female depressive patient, we have chosen to include both female and male participants. Research has shown that there are few gender differences in experience of depression, in either duration, type or severity prior to treatment. Gender differences that were found were related to levels of arousal, anxiety symptoms, rather than depressive symptoms per se (Wilhelm et al., 2002).

The VR-experience includes getting up in the morning, having breakfast, interaction with the partner, sitting around in the afternoon not being able to undertake an activity and taking medication. All activities are experienced through the eyes of the patient whilst hearing her inner thoughts. The significant other watches the video from the patients' perspective, this takes 6 min. The patient watches along on a screen. The patient watches the VR-experience from the perspective of the partner, this takes 4 min. This experience includes mainly the same scenes; getting up in the morning, having breakfast, the evening after the partner returns from his place of work. This time, patient watches the scenes whilst hearing the inner thoughts of the partner, and the significant other of the patient watches along on a screen. For an impression of the VR experience video, see Fig. 2.

Subsequently the therapist will stimulate a mutual discussion with them about the content of the psychoeducation. After the psychoeducation session, both the patient and the significant other will fill in a questionnaire about their experience with the psychoeducation.

2.6. Study outcome measures

The primary outcome in this study is patients' self-stigma as measured by the Internalized Stigma of Mental Illness scale (ISMI) (Ritsher et al., 2003). Recent research has suggested that the 'Stigma Resistance' subscale is conceptually different to the other subscales (Sibitz et al., 2011). Therefore, we will use a summed average of the other 4 ISMI subscales as outcome measure in the analyses.

Secondary study parameters concern the following measures for the patient: depressive symptoms as measured by the Quick Inventory of Depressive Symptomatology Clinician-Rated QIDS-C (Rush et al., 2003), loneliness as measured by the short version of the Loneliness Scale from De Jong Gierveld (LS-GV) (Gierveld and Van Tilburg, 2006), and perceived social support as measured by the Multidimensional Scale of Perceived Social Support (MSPSS) (Zimet et al., 1988). From the significant other, the following measures will be obtained: burden of care as measured by the core module of the Involvement Evaluation Questionnaire (IEQ) (Van Wijngaarden et al., 2002), and quality of life as measured by the short version of the World Health Organization Quality of Life (WHOQOL-BREF) (De Vries and Van Heck, 1997) A trained researcher will administer all questionnaires by telephone.

We created a questionnaire about the participants' experience with the psychoeducation, in particular about the effect on attitudes, coping

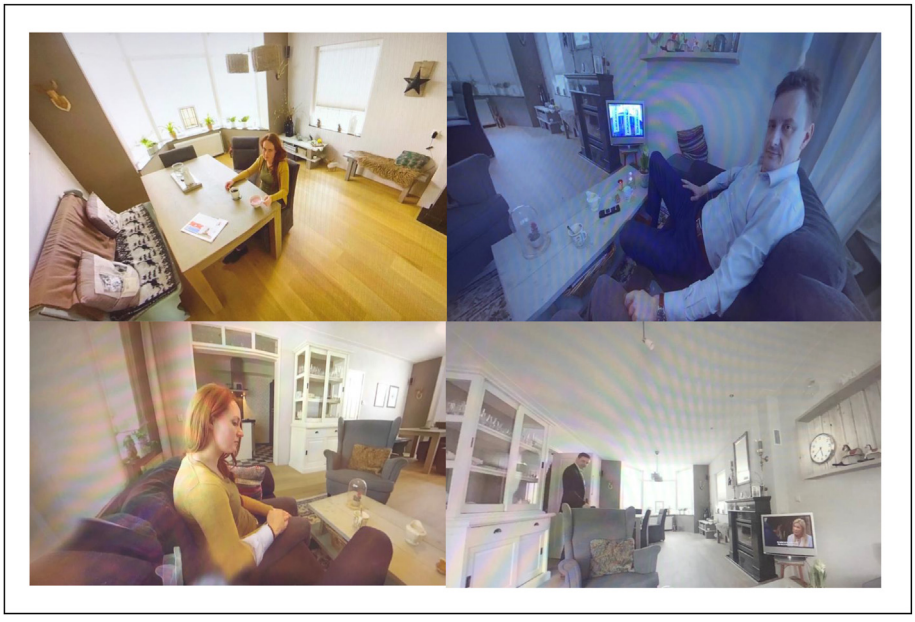

Fig. 2. VR experience video.
Left side = Photos of VR experience from perspective of the significant other, right side = Photos of VR experience from perspective of patient.

skills and on empathy for depression. This includes for instance: *'Things have changed in the way I think about depression*' and '*I notice a change in the way my significant other handles my depressive symptoms'*, '*I liked being able to empathize with the patient with depression in the VR experience video'*. Participants will rate these questions using a visual analogue scale. Besides, patients will rate their satisfaction with the session, using the Session Rating Scale (SRS) (Duncan et al., 2003) during the psychoeducation session.

Patients and significant others will be asked to fill in questionnaires at baseline (T0), directly after the psychoeducation (T1), after 1 week (T2), and at the follow up after 10 weeks (T3). For an overview of the assessments, see Table 1.

2.7. Analysis

For all analysis, alpha will be set at $P < .05$. In order to assess whether the PE and VR + PE groups are comparable on age, education level, daily living situation, diagnosis, comorbidity, use of medication, and relationship with the patient, we will perform chi square tests.

We will analyze our primary and secondary outcomes using a mixed ANOVA with group (PE vs. VR + PE) as between and time point (T0, T1, T2, T3) as within factor. Separate mixed ANOVA's will be run with self-stigma, depressive symptoms, loneliness, perceived social support, burden of care and quality of life as outcome variable.

To check whether the PE and VR + PE groups differ in their satisfaction with the session and attitudes towards depression, a *t*-test will be performed.

Within the PE + VR group, we expect that both male and female patients will sufficiently empathize with the characters in the depression experience movie. To check we included a question about the degree to which one is able to empathize with the character in the video, and will compare mean score on this question between male and female patients using a *t*-test. If the score differs between groups, we will include sex as covariate in the main analysis.

Comorbidity is assessed during the intake interview and used to describe our sample. Information about the type and length of treatment received after PE will be recorded. This information is used to describe our sample. State of the art of imputation of missings will be used.

2.8. Patient and public involvement

Patients who suffered from depression and a member of the association for depression were involved from the preparation phase of the study protocol up to and including the phase of running the trial. They contributed to different aspects of the design of the study, including the outcome measures, timeline of measurements and recruitment of the study. In addition, the VR experience videos were created with input from patients who suffered from depression.

Table 1
Overview of assessments.

	Screening	T0	T1	T2	T3
SCID-5-S	x				
ISMI		x	X	x	x
QIDS-C		x		x	x
LS-GV		x		x	x
MSPSS		x		x	x
IEQ		o		o	o
WHOQOL-BREF		o		o	o
Experience PE-session			xo	xo	
SRS			x		

*PE = Psychoeducation.
**T0 = Baseline; before PE-session, T1 = directly after PE-session, T2 = one week after PE-session, T3 = follow-up; 10 weeks after PE-session.
***x = measured with the patient, o = measured with the significant other.
****SCID-5-S = Structured Clinical Interview for DSM-5 disorders, ISMI = Internalized Stigma of Mental Illness scale, QIDS-C = Inventory of depressive symptomatology, LS-GV = Short version of the Loneliness Scale from De Jong Gierveld, MSPSS = Multidimensional Scale of Perceived Social Support, IEQ = Core module of the Involvement Evaluation Questionnaire, WHOQOL-BREF = Short version of the World Health Organization Quality of Life, SRS = Session Rating Scale.

2.9. Ethics and dissemination

The present study has been approved by the medical ethical board of the Academic Medical Center (No. 2020–202). The study was designed and conducted in accordance with the latest version of the Helsinki Declaration of 1975, as revised in 2008. Amendments will be submitted for approval to the medical ethical board. The results of the trial will be submitted for publication to peer-reviewed international scientific journals. This study will be monitored by the Amsterdam UMC Clinical Monitoring Center (CMC) according to the guidelines of the Dutch Federation of University Medical Centers. The VR experience video is for sale with the provider Vrendle.

3. Discussion

Depressive disorder is highly prevalent and has a major impact on daily life functioning of both the patient and their significant others (Lépine and Briley, 2011). Self-stigma, defined as internalization of stereotypes, diminishes self-esteem and self-efficacy, hampers recovery of depression and may as such be a target for improving the efficacy of interventions for depression (Oexle et al., 2018). Psychoeducation for depression has proven to be effective in reducing depressive symptomatology (Tursi et al., 2013b). Moreover, it can reduce the burden of care of significant others (Katsuki et al., 2011b). An effective psychoeducation intervention for depression involving both patient and their significant others, might reduce self-stigma, decrease loneliness and increase perceived social support with the patient, which might contribute to better treatment outcome. Also, it might lead to a decrease in burden of care of others and increase their quality of life.

This study has limitations that need to be acknowledged. First, in the present design, there is no control for nonspecific factors, such as the effect of extra attention, since there is no control group that will not get any psychoeducation about depression. Second, the depression experience video has only one version; therefore, it is not possible to adjust the video to the specific situation of the patient and their family member. Third, an important group of patients with depression are not able to participate, because they do not have a significant other to involve in the study.

Taken together, this trial will be the first RCT that examines the effect of VR in psychoeducation for depression. In this study, we mainly examine whether our newly developed VR psychoeducation intervention is more successful in reducing self-stigma, depressive symptoms and experienced loneliness and increasing social support with the patient, as compared to psychoeducation as usual for depression. Moreover, the effect of the VR psychoeducation intervention on perceived burden of care and quality of life as compared to psychoeducation as usual will be examined. In addition, potential pathways to reduce self-stigma and depressive symptomatology will be studied. In conclusion, VR might open up the opportunity to reduce self-stigma and thereby improve the efficacy of psychoeducation in MDD.

Authors contributions

NS drafted this paper (which was added to and revised by all other authors), wrote the treatment manual for the used intervention and was responsible for the training of psychologists. NS, MvB, AB, CB and WV were responsible for the development of the study design. All authors read and approved the final manuscript.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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