

Immersive Virtual Reality eHealth Intervention to Reduce Anxiety and Depression in Pregnant Women: A Randomized Controlled Trial

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Submitted to: JMIR Human Factors
on: January 24, 2025

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Immersive Virtual Reality eHealth Intervention to Reduce Anxiety and Depression in Pregnant Women: A Randomized Controlled Trial

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Abstract

Background: Mental health during pregnancy is a critical factor influencing maternal and fetal outcomes. Anxiety and depression affect up to 25% of pregnant women, with significant consequences for maternal well-being and child development. Despite this, interventions during pregnancy remain limited, creating a need for innovative, accessible solutions.

Objective: This study aimed to evaluate the effectiveness of an immersive virtual reality (IVR) eHealth intervention in reducing anxiety and depression symptoms during pregnancy.

Methods: A two-arm, randomized controlled trial was conducted across five primary care centers in Catalonia, Spain, between October 2021 and May 2024. Participants (n=70) were pregnant women aged ≥18 years with moderate anxiety and depression symptoms (EPDS scores: 9-12) at 12–14 weeks of gestation. They were randomized (1:1) to an IVR intervention or standard care group. The intervention group engaged in daily 14-minute IVR mindfulness and relaxation sessions for six weeks. Mental health outcomes were assessed using the Edinburgh Postnatal Depression Scale (EPDS) and State-Trait Anxiety Inventory (STAI).

Results: The intervention group demonstrated significant reductions in EPDS scores (mean decrease from 11.32 to 7.25; $p<0.001$) compared to an increase in the control group (mean increase from 11.32 to 16.23; $p<0.001$). Similarly, STAI scores improved markedly in the intervention group (coefficient: -30.47; 95% CI: -45.23 to -15.72; $p<0.001$), while the control group experienced negligible changes. High adherence rates were observed, with 78.8% of participants completing ≥30 sessions. Participant satisfaction was high, with 87% reporting being "very satisfied" with the intervention.

Conclusions: The IVR eHealth intervention significantly reduced symptoms of anxiety and depression, demonstrating its potential as an accessible and effective tool for mental health support during pregnancy. High adherence and satisfaction levels underscore its feasibility and acceptability. Future research should explore the long-term effects and scalability of IVR interventions in diverse settings. Clinical Trial: ClinicalTrials.gov NCT05756205

(JMIR Preprints 24/01/2025:71708)

DOI: <https://doi.org/10.2196/preprints.71708>

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TITLE

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Clinical trial

ABSTRACT

Background: Mental health during pregnancy is a critical factor influencing maternal and fetal outcomes. Anxiety and depression affect up to 30% of pregnant women, with significant consequences for maternal well-being and child development. Despite this, interventions during pregnancy remain limited, creating a need for innovative, accessible solutions.

Objective: This study aimed to evaluate the effectiveness of an immersive virtual reality (IVR) eHealth intervention in reducing anxiety and depression symptoms during pregnancy.

Methods: A two-arm, randomized controlled trial was conducted across five primary care centers in Catalonia, Spain, between October 2021 and May 2024. Participants (n=70) were pregnant women aged ≥ 18 years with moderate anxiety and depression symptoms (EPDS scores: 9-12) at 12–14 weeks of gestation. They were randomized (1:1) to an IVR intervention or standard care group. The intervention group engaged in daily 14-minute IVR mindfulness and relaxation sessions for six weeks. Mental health outcomes were assessed using the Edinburgh Postnatal Depression Scale (EPDS) and State-Trait Anxiety Inventory (STAI).

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Conclusions: The IVR eHealth intervention significantly reduced symptoms of anxiety and depression, demonstrating its potential as an accessible and effective tool for mental health support during pregnancy. High adherence and satisfaction levels underscore its feasibility and acceptability. Future research should explore the long-term effects and scalability of IVR interventions in diverse settings.

Trial Registration: ClinicalTrials.gov NCT05756205.

Keywords: virtual reality, eHealth, pregnancy, mental health, anxiety, depression, randomized controlled trial, antenatal care.

INTRODUCTION

Mental health during pregnancy is a crucial aspect of women's overall well-being, influencing not only the mother but also the development of the fetus and the subsequent outcomes for the child [1,2]. Up to 30% of women may experience mental health disorders during pregnancy, including anxiety and depression [3–5]. These disorders, often interrelated, have a significant impact not only on the mother's health but also on the neurological development of the fetus, potentially leading to complications such as preterm birth, low birth weight, and long-term emotional difficulties [6]. These adverse effects not only affect the immediate postpartum period but can also influence the child's long-term development, with possible repercussions on behavior, cognition, and mental health [7].

Despite their importance, interventions to address mental health disorders during pregnancy have been limited, with many focusing on the postpartum period, leaving a critical need for attention during pregnancy itself [8]. This deficit in intervention during pregnancy is concerning, as early detection and appropriate treatment of these disorders are essential to ensuring optimal health outcomes for both the mother and the baby [9]. Inadequate treatment or lack of interventions may increase the risk of obstetric complications, such as preterm birth or low birth weight, as well as long-term emotional and behavioral problems in the child [10,11].

Low-intensity interventions, as described by the National Institute for Health and Care Excellence (NICE), are particularly important for women experiencing mild to moderate symptoms of anxiety and depression. NICE recommends these interventions as a first step before considering more intensive treatments, as they can provide effective support with fewer adverse effects and are accessible to a wide population [12]. In this context, digital health technologies, known as eHealth, offer a promising new avenue for improving access to care and supporting the mental health of pregnant women [13].

The use of eHealth technologies is growing exponentially worldwide, supported by guidelines from international organizations such as the World Health Organization (WHO), which promote the use of these technologies to improve public health [14]. According to WHO, eHealth technologies can play a key role in expanding access to mental health services [15]. Their application in perinatal mental health has shown promising results in preliminary studies, especially in reducing symptoms of anxiety and depression [16]. These technologies offer the possibility of providing low-intensity interventions, such as mindfulness, relaxation, and other stress management techniques, in a way that is accessible and convenient for women [17]. Additionally, mobile applications allow for closer and more personalized monitoring of women's mental health, offering continuous support and

enabling quicker interventions in the event of concerning symptoms [18]. eHealth interventions can be a flexible alternative for those women who, for various reasons, cannot easily access traditional mental health services, offering solutions tailored to their individual needs and daily routines [19].

In this context, immersive virtual reality (IVR) is emerging as an innovative tool in the health field. IVR allows users to immerse themselves in simulated environments in a fully immersive manner, offering therapeutic experiences that can be highly effective in managing anxiety, depression, and other mental disorders [20]. Several studies have demonstrated that IVR can help reduce stress and improve emotional well-being in patients, providing cognitive and emotional distraction that facilitates relaxation and symptom reduction [21]. Moreover, its ability to recreate controlled environments makes it useful for exposure therapy and other psychological interventions [22]. This technology, combined with other eHealth tools, can offer personalized and highly effective solutions for pregnant women experiencing mental health issues, opening new possibilities for their management and treatment [23].

Furthermore, the integration of eHealth and mHealth (mobile health) technologies is gaining traction as an effective means of delivering mental health interventions. These technologies provide a direct, low-cost, and engaging manner to deliver care, making mental health support more accessible [24,25]. The global increase in the use of these technologies has led to a growing body of research supporting their efficacy, particularly in treating mood disorders during pregnancy [26,27]. Recent studies have also underscored the importance of mHealth interventions specifically designed for pregnant women, highlighting their effectiveness in reducing anxiety and depression symptoms during pregnancy [5,28].

OBJECTIVES

The objective of this study was to evaluate the effectiveness of an immersive virtual reality (IVR) eHealth intervention in improving mental health outcomes during pregnancy, specifically by comparing symptoms of anxiety and depression between pregnant women in the intervention and control groups, assessing satisfaction with antenatal care between the two groups, and monitoring adherence to the intervention by tracking the number of completed IVR sessions.

METHODS

Study Design

This study was a two-arm, prospective, randomized controlled trial (RCT) designed to assess the efficacy of a low-intensity eHealth intervention in improving mental well-being among pregnant women. The CONSORT guidelines for RCTs were followed. Participants were randomly assigned (1:1) to the intervention or control group using a computer-generated randomization sequence. Specifically, the EPIDAT (version 4.2) software was used to generate the randomization list, ensuring allocation concealment and minimizing selection bias. To maintain the integrity of the randomization process, the allocation sequence was generated independently by the principal investigator before recruitment. Randomization was stratified by recruitment center to control for potential site-specific variations. Allocation was concealed from participants and researchers responsible for data collection to reduce potential biases. Participants and healthcare providers were masked to group allocation to the extent possible in an intervention of this nature.

The study includes pregnant women aged 18 years and older who attend primary care centers affiliated with the Sexual and Reproductive Health Care (ASSIR). It was conducted across 5 Primary Care Centers (ASSIR) in Catalonia (Spain), between October 2021 and May 2024. Between 12 and 14 weeks of gestation, participants who scored between 9 and 12 on the Edinburgh Postnatal Depression Scale (EPDS) – validated Spanish version [29] – were recruited and randomly allocated to either the intervention group, which received the eHealth intervention, or the control group, which received standard care. Participants were also screened for mental health conditions using the State Trait Anxiety Inventory (STAI) – validated Spanish version [30]. Those with a diagnosis of severe psychiatric disorder, ongoing treatment by mental health specialists, and a history of gender-based violence were excluded.

Procedure

Participants who scored between 9 and 12 on the EPDS, indicating symptoms of moderate anxiety and depression, were considered for inclusion in the study, participants were randomly assigned (1:1) to the intervention or control condition. The principal investigator generated a randomization list using the EPIDAT (version 4.2) software, all study participants were masked ensuring that the randomization process. Women assigned to the control group were informed that their follow-up would proceed as usual, while those in the intervention group received additional information about the eHealth intervention, including the use of immersive virtual reality.

Intervention

The intervention group received an eHealth-based mental health program, which included the use of immersive virtual reality (IVR) technology to deliver mindfulness and relaxation exercises designed to reduce anxiety and depression during pregnancy. The IVR intervention lasted 14 minutes per session and was performed daily for 6 weeks. These sessions were based on mindfulness techniques, conscious breathing, and progressive muscle relaxation, with the aim of providing an immersive therapeutic environment that would promote stress reduction and improve the emotional well-being of the participants. The content of the intervention was developed by Delaguila Games (@delaguila_games), a company specializing in virtual reality applied to healthcare (**Figure 1**). The sessions were designed to be self-guided and accessible from home (**Figure 2**), using an Oculus GO virtual reality headset. The program contained three main modules that could be selected individually or together, adapting to the needs and preferences of each participant. To ensure adherence and effectiveness of the intervention, the total number of sessions completed by each participant was recorded.

Control

Participants in the control group received the usual antenatal care provided by the public health system. This refers to the pregnancy follow-up protocol established by the Department of Health of the Generalitat de Catalunya, which outlines standard guidelines for prenatal care and monitoring [31].

Figure 1. Screenshots of the virtual reality experience

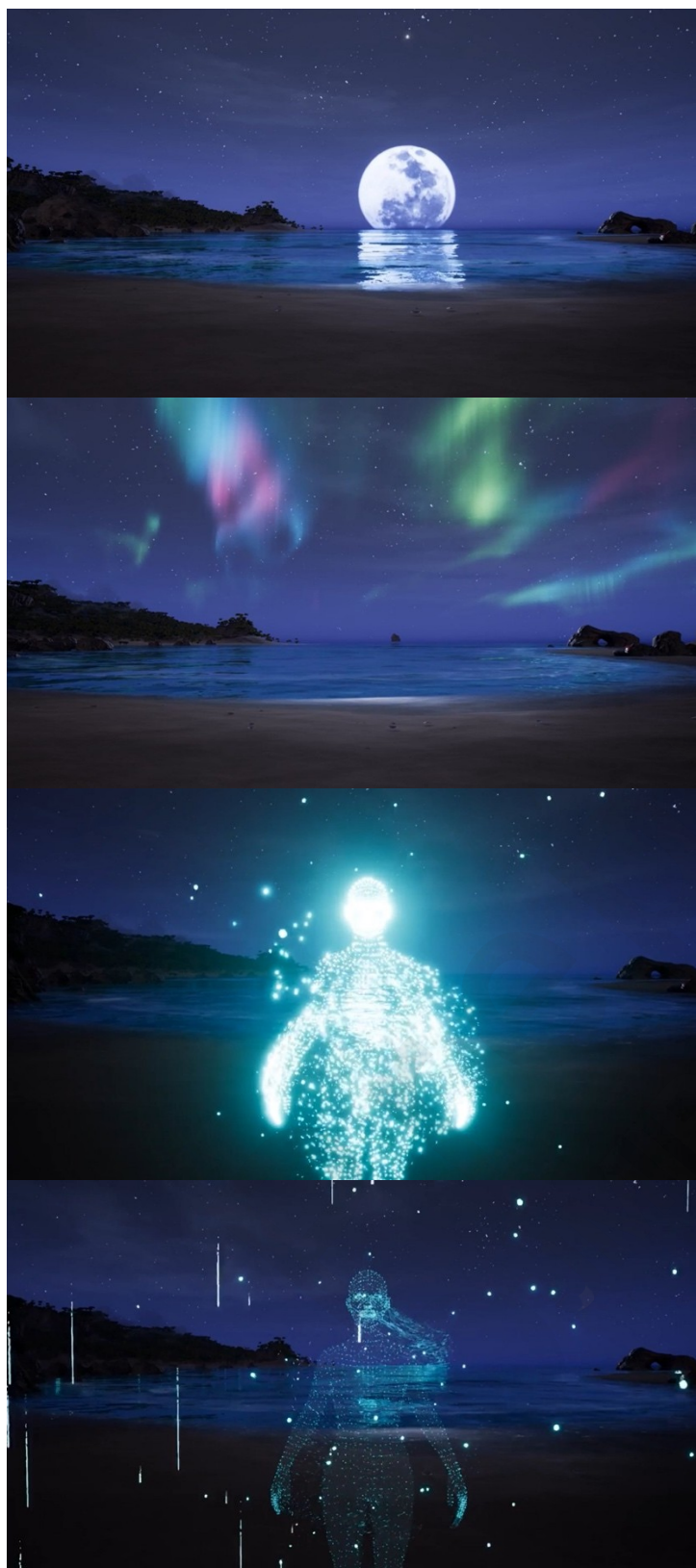


Figure 2. Pregnant woman using the immersive virtual reality application at home (with written patient permission).



Sample

Pregnant women aged 18 years or older, who are followed at the primary care centers of the Sexual and Reproductive Health Care (ASSIR) of MútuaTerrassa in Barcelona, Spain, were be invited to participate in the study.

In a previous interventional work published using a mindfulness program to evaluate changes in the EDPS scale in pregnant women, the authors report after the program a mean difference between the two groups of study (intervention and control) of -2.56, with a standard error (SE) of 0.72 [32]. From that, the standard deviation (SD) has been calculated as: $SE = SD / \sqrt{n}$, so $SD = SE * \sqrt{n}$. In this case, as the n was different in both groups (51 and 45), we use the minimum of both (45), obtaining a joint SD of 4.83. Assuming a power of 80% to detect differences in the contrast of the null hypothesis $H_0: \mu_1 = \mu_2$ by means of a bilateral T-Student test for two independent samples, a significance level of 5%, and assuming a mean difference between both groups of -3.5 and a SD of both groups of 4.83 units, it will be necessary to include 31 women in the non-intervention group and 31 women in the intervention group, totaling 66 patients in the study. Considering that the expected drop-out rate is 5%, it would be necessary to recruit 70 women (35 in each group).

Pregnant women ≥ 18 years old, with moderate symptoms of anxiety and depression (EPDS between 9-12), and in the first trimester of pregnancy (12-14 weeks), were included. Regarding the exclusion criteria, women diagnosed with severe psychiatric disorders, those under specialized mental health treatment, and those with a history of gender violence, were excluded.

Measures

Primary Outcomes:

Mental Health Status

The mental health status of the participants was measured using the Edinburg Postnatal Depression Scale (EPDS) and the State Trait Anxiety Inventory (STAI). The EPDS is a self-report scale comprising 10 items, where participants choose one of four responses that best describes how they felt during the past week. The EPDS has been validated in Spanish and shows good sensitivity (79%) and specificity (95.5%), with a Cronbach's alpha of 0.87 [29]. Scores range from 0 to 30, with scores ≥ 13 indicating a positive screen for depression. The STAI assesses two dimensions of anxiety: state anxiety (a temporary condition in response to a specific situation) and trait anxiety (a general tendency to perceive situations as threatening) [30]. Both scales have demonstrated robust psychometric properties in various populations.

Secondary Outcomes:

Satisfaction with Pregnancy Care

Satisfaction with pregnancy care was measured using a validated self-completed questionnaire [33], consisting of 28 items that assess different aspects of care, including equipment, accessibility, organization of the consultation, and the competence of the staff. The scale uses a 5-point Likert system, and scores are categorized as satisfied (scores >3) or very satisfied (scores >4). The reliability of this tool has been demonstrated with a Cronbach's alpha of 0.92 [34].

Adherence to the Intervention Protocol

Adherence to the intervention protocol was monitored by tracking the number of sessions completed by each participant in the intervention group. Additionally, participants in this group were asked to complete a questionnaire evaluating the usability and accessibility of the eHealth technology used during the study [35]. The number of sessions and time spent on each session were recorded to assess adherence and participant engagement with the intervention.

Pulse Measurements

Pulses were recorded before and after the intervention.

Participants were encouraged to report any adverse events, discomfort, or unexpected side effects experienced during or after the IVR sessions. If the participant experienced dizziness, nausea, or an increase in anxiety symptoms, she was instructed to stop the session and rest. If symptoms persisted, participants could contact the research team via an e-mail address specially designed to resolve any problems. Participants had the right to withdraw from the study at any time, without having to justify their decision, and without this affecting their regular prenatal follow-up. In addition, the study team, made up of midwives and mental health professionals, was available to provide additional psychological support if necessary, ensuring that participants felt safe and supported throughout the intervention.

Data Collection and Management

Data were collected at two time points: baseline (12-14 weeks of gestation) and 6 weeks after the start of the intervention. All data were securely stored and anonymized, with access restricted to authorized personnel only. Participants' personal information was protected according to the ethical standards of Mútua Terrassa.

Statistical Analysis

Qualitative variables were described using absolute frequencies and percentages. Quantitative variables were summarized using the mean, standard deviation (SD), and median. The Kolmogorov–Smirnov test was employed to assess the normality of distributions.

Sociodemographic and clinical characteristics were compared across groups. For quantitative variables, Mann–Whitney U tests were conducted. The Chi-squared test (or Fisher's exact test for frequencies <5) was used to compare categorical variables. The effectiveness of the intervention was evaluated using mixed-effects models to assess changes in mental health outcomes over time by group. The interaction between time and intervention, as well as potential confounding factors such as age, previous admissions, current planned pregnancy, and personal history of anxiety, were also considered in these analyses.

Additionally, the post-intervention scores of the EPDS and STAI E were transformed into binary variables. For EPDS, a cut-off score of 9 was selected based on bibliographic criteria [29], while for STAI-E, the third quartile (Q3) value (>86 points) was used [30]. Finally, several logistic regression models were conducted for the primary outcomes, with the study group included as an independent variable. These models were also adjusted for the previously mentioned confounding factors including pre-intervention EPDS and STAI E scores. **Hosmer-Lemeshow goodness-of-fit tests were performed to assess the overall fit of the models [36]. Receiver operating characteristic (ROC) curves were also calculated for this approach.**

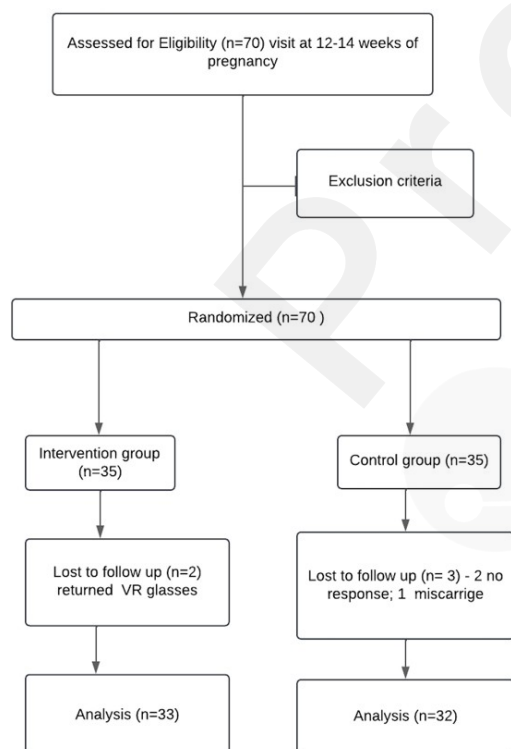
Statistical significance was set at $p < 0.05$, and all analyses were performed using R version 4.2.1 (R Foundation for Statistical Computing). **For the mixed-effects models, we used nlme package and lme function and stats package with glm function in the logistic models.**

Ethical Considerations

The study protocol was approved by the Drug Research Ethics Committee of Mútua Terrassa (approval number B1803). Informed consent was obtained from all participants prior to their inclusion in the study. The study was conducted in accordance with the Declaration of Helsinki and relevant EU regulations on data protection. The informed consent process was conducted following strict ethical guidelines to ensure that all participants fully understood the nature of the study, its potential risks and benefits, and that their participation was voluntary. The following steps were taken: 1) A comprehensive explanation: before the enrollment, all participants received a detailed

explanation of the study's objectives, procedures, potential benefits, and possible risks. This was done through both written and verbal communication by trained healthcare professionals. 2) Time for reflection and questions: participants were given sufficient time to read the informed consent document and ask any questions. Researchers provided clarifications to ensure that participants had a clear understanding before signing the consent form. 3) Assessment of understanding: to ensure comprehension, participants were asked to summarize key aspects of the study in their own words. If any misunderstandings were identified, additional explanations were provided. 4) Voluntary participation and withdrawal rights: it was explicitly stated that participation was entirely voluntary, and that participants could withdraw at any time without any consequences for their healthcare or treatment. 5) Safeguards against coercion: to prevent undue influence, recruitment was conducted by independent healthcare professionals who were not involved in participants' routine medical care. No financial or material incentives were provided to encourage participation. 6) Ethical approval: the study protocol, including the informed consent procedures, was reviewed and approved by the Drug Research Ethics Committee of Mútua Terrassa (Approval number: B1803), ensuring compliance with ethical and legal standards. These measures were taken to guarantee that all participants provided truly informed and voluntary consent, minimizing any risk of coercion or undue influence.

Figure 3. Participant Flowchart for the Randomized Controlled Trial



RESULTS

The study included 70 participants, with a mean age of 31.90 years (SD = 4.83), evenly distributed

between the intervention group (n=35) and the control group (n=35) (**Figure 3**). There were two losses to follow-up in the intervention group and three in the control group. All cases of loss to follow-up occurred in the period after the intervention.

Sociodemographic and Clinical Characteristics

Regarding sociodemographic and clinical characteristics, the intervention group had a higher mean age compared to the control group (33.77 years, SD = 3.46 vs. 30.03 years, SD = 5.30; $p = 0.003$). Furthermore, a significantly higher proportion of participants in the intervention group reported having their own income (100% vs. 60%; $p < 0.001$) and a university-level education (68.6% vs. 22.9%; $p < 0.001$) (Table 1).

Regarding pre-pregnancy mental health treatment history, participants who reported treatment history had received a variety of interventions, including individual and/or group psychotherapy, pharmacological treatment with antidepressants or anxiolytics, and follow-up by mental professionals in primary or specialist healthcare. The length of treatment varied among participants, ranging from brief interventions of less than six months to continued treatment for more than two years. Disaggregated data about specific treatment adherence or the exact type of medication used by each participant were not available in this study.

In terms of obstetric characteristics, 85.7% of pregnancies in the intervention group were planned, compared to 57.1% in the control group ($p = 0.017$) (Table 2). No significant differences were found between the groups regarding the history of cesarean sections, traumatic deliveries, or high-risk pregnancies.

Table 1. Sociodemographic Characteristics of Study Participants (N=70)

Characteristic	Total (N=70)	Control Group (n=35)	Intervention Group (n=35)	p-value
Age (years)				
Mean (SD)	31.90 (4.83)	30.03 (5.30)	33.77 (3.46)	0.003 ¹
Country of Origin				
Spain	50 (71.4%)	17 (48.6%)	33 (94.3%)	<0.001 ²
Morocco	10 (14.3%)	10 (28.6%)	0 (0.0%)	
Other Countries	10 (14.3%)	8 (22.8%)	2 (5.7%)	
Religious Affiliation				
Christian	21 (30.0%)	9 (25.7%)	12 (34.3%)	0.001 ²
Muslim	10 (14.3%)	10 (28.6%)	0 (0.0%)	
Atheist	36 (51.4%)	15 (42.9%)	21 (60.0%)	

Other	3 (4.3%)	1 (2.9%)	2 (5.7%)	
Educational Level				
University	32 (45.7%)	8 (22.9%)	24 (68.6%)	<0.001 ²
Secondary	30 (42.9%)	19 (54.3%)	11 (31.4%)	
Primary	6 (8.6%)	6 (17.1%)	0 (0.0%)	
Employment Status				
Specialized Worker	37 (52.9%)	11 (31.4%)	26 (74.3%)	<0.001 ²
Seeking Employment	12 (17.1%)	7 (20.0%)	5 (14.3%)	
Other Occupations	21 (30.0%)	17 (48.6%)	4 (11.4%)	
Personal Income				
Yes	56 (80.0%)	21 (60.0%)	35 (100.0%)	<0.001 ²
No	14 (20.0%)	14 (40.0%)	0 (0.0%)	

SD: Standard deviation; *p value results comparing the study groups by ¹U Mann Whitney Test or ²Chi-squared tests, considered statistically significant when <0.05

Table 2. Clinical and Obstetric Characteristics

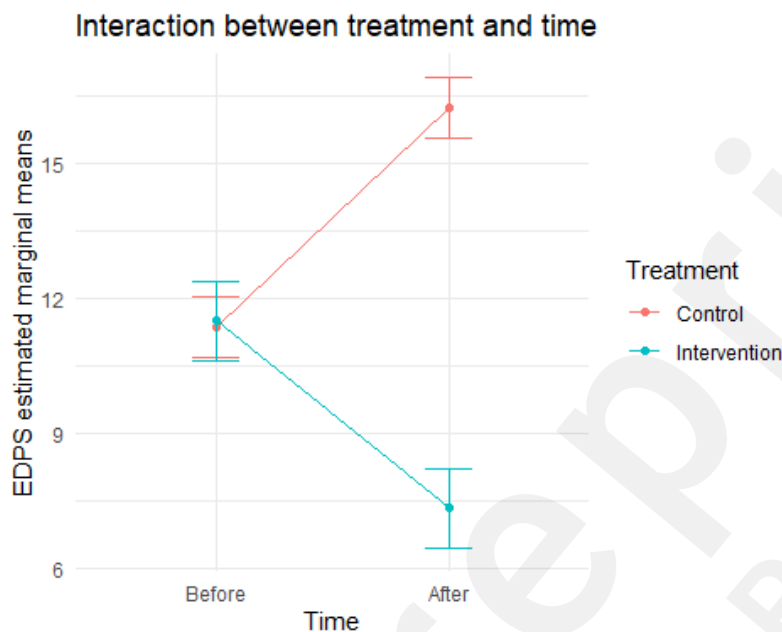
Category	Characteristic	Total	Control Group	Intervention Group	p-value*
Clinical	Current smoker	10 (14.3%)	7 (20.0%)	3 (8.6%)	0.306
	Mental health treatment prior to pregnancy	40 (57.1%)	15 (42.9%)	25 (71.4%)	0.030
	Family history of psychiatric disorders	22 (31.4%)	12 (34.3%)	10 (28.6%)	0.797
	Planned current pregnancy	50 (71.4%)	20 (57.1%)	30 (85.7%)	0.017
	Current pregnancy achieved through assisted reproduction	7 (10.0%)	1 (2.9%)	6 (17.1%)	0.106
	History of anxiety	47 (67.1%)	18 (51.4%)	29 (82.9%)	0.011
	History of depression	18 (25.7%)	8 (22.9%)	10 (28.6%)	0.784
Obstetric	Previous miscarriage	18 (25.7%)	7 (20.0%)	11 (31.4%)	0.412
	Previous cesarean section	4 (5.7%)	2 (5.7%)	2 (5.7%)	1.000
	Previous traumatic childbirth experience	11 (15.7%)	5 (14.3%)	6 (17.1%)	1.000
	Gestational week at enrollment	12-14 weeks	12-14 weeks	12-14 weeks	-
	High-risk current pregnancy	33 (47.1%)	15 (42.9%)	18 (51.4%)	0.632
	Partner involvement in care	68 (97.1%)	33 (94.3%)	35 (100%)	0.493
	Previous fetal loss	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.000
	Method of conception: IVF	7 (10.0%)	1 (2.9%)	6 (17.1%)	0.106
	Pre-pregnancy mental health diagnosis	20 (28.6%)	8 (22.9%)	12 (34.3%)	0.030

*p value results comparing the study groups by Chi-squared tests, considered statistically significant when <0.05

Comparison of EPDS Scores Between Groups Before and After the Intervention

At baseline, the EPDS score was comparable between both groups ($p = 0.562$). Following the intervention, the mean EPDS score significantly decreased in the intervention group (from 11.32 to 7.25; $p < 0.001$), whereas it increased in the control group (from 11.32 to 16.23; $p < 0.001$). The adjusted mixed-effects model revealed a significant interaction between time and treatment (coefficient = -9.03 ; 95% CI: -11.29 to -6.76 ; $p < 0.001$), indicating a substantial reduction in EPDS scores attributable to the intervention over time (Figure 4).

Figure 4. Interaction between time and treatment in EPDS score

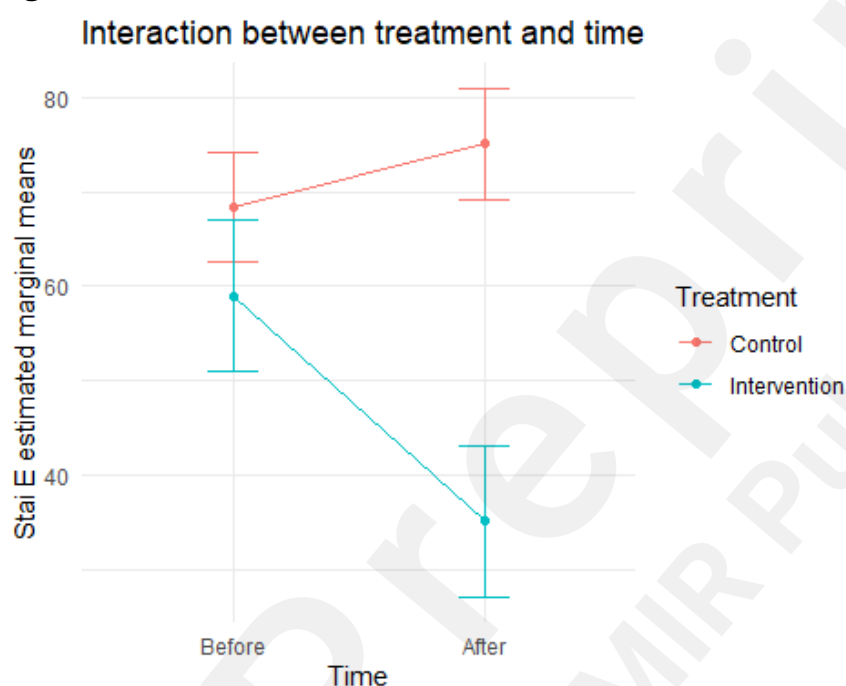


Furthermore, the adjusted logistic regression model demonstrated that participants in the intervention group had a significantly lower likelihood of exhibiting EPDS scores ≥ 9 points post-intervention compared to the control group (OR = 0.03; 95% CI: 0.01 to 0.80; $p = 0.001$). Additionally, a planned pregnancy was associated with a lower probability of achieving EPDS scores ≥ 9 points. In contrast, a higher pre-intervention EPDS score was associated with an increased likelihood of achieving EPDS scores ≥ 9 points (OR = 3.32; 95% CI: 1.52 to 9.58; $p = 0.008$). The model demonstrated good calibration, as evidenced by the Hosmer–Lemeshow goodness-of-fit test ($p = 0.095$) and the area under the ROC curve (AUC = 0.82).

Comparison of STAI E Scores Before and After the Intervention

At baseline, the STAI-E score was similar in both groups ($p = 0.123$). Following the intervention, the intervention group experienced a significant reduction in mean scores (from 57.94 to 35.03; $p < 0.001$), whereas the control group showed an increase (from 66.10 to 72.91; $p < 0.001$). The adjusted mixed-effects model identified a significant interaction between time and treatment (coefficient = -30.47; 95% CI: -45.23 to -15.72; $p < 0.001$) (Figure 5), indicating a substantial improvement attributable to the intervention over time, similar to the effects observed with the EPDS. Conversely, the control group exhibited a non-significant change, with mean scores increasing slightly from 66.10 to 72.91 ($p = 0.678$).

Figure 5. Interaction between time and treatment in STAI-E score



Furthermore, the adjusted logistic regression model demonstrated that participants in the intervention group had a significantly lower likelihood of presenting STAI-E scores >86 points post-intervention compared to the control group (OR = 0.05; 95% CI: 0.01 to 0.40; $p = 0.013$). Additionally, a higher pre-intervention STAI-E score was associated with an increased probability of exceeding the threshold (OR = 1.04; 95% CI: 1.01 to 1.08; $p = 0.019$) (Table 3).

Table 3. Multivariate Logistic Regression Models for Post-intervention EDPS and STAI Scores (State)

A. Post-intervention EDPS score (>9 points)

Variable	Multivariate ^a		
	OR	95% CI	p-value*

Intervention Group	0.03	0.00 to 0.18	0.001
Pre intervention EDPS Score	3.32	1.52 to 9.58	0.008
Age (years)	0.99	0.80 to 1.12	0.928
Personal Income	2.20	0.12 to 41.26	0.577
Current planned pregnancy	0.10	0.01 to 0.65	0.028
Personal history of anxiety	4.48	0.66 to 50.40	0.163

EDPS: Edinburgh Postnatal Depression Scale; OR: Odds Ratio; CI: Confidence Interval.

^a Hosmer–Lemeshow goodness-of-fit test, $p = 0.095$. Area under the ROC curve, AUC = 0.82 (95% CI 0.78 to 0.85).

* p considered statistically significant when <0.05

B. Post-intervention STAI Scores (State) (>86 points)

	Multivariate ^a		
Variable	OR	95% CI	p-value
Intervention Group	0.09	0.00 to 0.73	0.047
Pre intervention STAI E score	1.04	1.01 to 1.08	0.019
Age (years)	0.83	0.64 to 1.01	0.083
Personal Income	0.40	0.05 to 2.46	0.340
Current planned pregnancy	0.32	0.05 to 1.75	0.199
Personal history of anxiety	0.95	0.16 to 6.05	0.959

STAI: State Trait Anxiety Inventory; OR: Odds Ratio; CI: Confidence Interval.

^a Hosmer–Lemeshow goodness-of-fit test, $p = 0.175$. Area under the ROC curve, AUC = 0.79 (95% CI 0.65 to 0.88);

* p considered statistically significant when <0.05

Pulse Measurements

Pre-intervention: the intervention group had a mean pulse of 85.91 bpm (SD = 5.47). Post-intervention: the mean decreased to 76.94 bpm (SD = 6.62), indicating a significant improvement.

Intervention Adherence

Among the 33 participants in the intervention group, 32 (97.0%) provided valid data for adherence analysis. The average number of completed sessions was 37.84 (SD = 9.83), with a median of 42 sessions. A total of 17 participants (51.5%) completed all 42 sessions, while 26 participants (78.8%) completed at least 30 sessions. Only six participants (18.2%) completed fewer than 30 sessions, and one participant (3.0%) had no adherence data available.

Participant Satisfaction

Participant satisfaction with the eHealth intervention was quantitatively assessed. Of the participants in the intervention group, 87% ($n = 29$) reported being "very satisfied" with the intervention, while 10% ($n = 3$) were "satisfied," and 3% ($n = 1$) expressed a neutral stance. No participants reported

dissatisfaction. Additionally, 90% of participants found the intervention "easy to use," and 85% stated that it "helped them feel more supported during their pregnancy." These quantitative measures highlight the high level of acceptability and usability of the intervention.

No serious adverse events were reported. Only mild cases of dizziness (n=3) and temporary nausea (n=2) were recorded, which resolved themselves spontaneously within a few minutes without the need to interrupt the intervention.

DISCUSSION

Principal Findings

This study examined the efficacy of a low-intensity eHealth intervention supported by immersive virtual reality (IVR) technology in improving mental health outcomes during pregnancy. The results provide evidence that the intervention contributed to significant reductions in anxiety and depression scores among participants in the intervention group, compared to the control group. Specifically, participants in the intervention group experienced a decrease in Edinburgh Postnatal Depression Scale (EPDS) scores from 11.32 to 7.25, while the control group showed an increase from 11.32 to 16.23. A mixed-effects model revealed a significant interaction between time and group (coefficient = -9.03, $p < 0.001$), emphasizing the intervention's effect on mitigating depressive symptoms. Similarly, for State-Trait Anxiety Inventory State (STAI-E), the intervention group's score decreased from 61.89 to 35.03, whereas the control group's score increased to 72.91. These findings underscore the intervention's capacity to address acute and persistent anxiety symptoms during pregnancy. The reduction in EPDS and STAI-E scores could be related to changes in cortisol levels, sleep quality, or social support [37].

The choice of IVR as an intervention tool is based on the growing scientific evidence supporting its efficacy in reducing anxiety and depression. Previous studies have shown that IVR can induce states of relaxation, facilitate emotional regulation, and reduce stress through immersion in controlled environments designed to promote psychological well-being [18,19]. Its ability to isolate the user from external stimuli and generate an immersive experience promotes greater adherence to, and engagement with, the intervention, which is particularly beneficial in pregnant populations. Furthermore, previous research has shown that IVR activates neurobiological mechanisms associated with the reduction of stress and anxiety [20], reinforcing its suitability as a low-risk, non-pharmacological strategy that is easy to implement in this context. Although the intervention was not specifically validated in women from various cultural contexts, it was designed to be accessible and applicable to a broad spectrum of users. The content of the intervention focused on mindfulness and

relaxation exercises, techniques widely used and recommended in perinatal mental healthcare. To ensure that it was accepted and understood, a neutral and accessible language was used, without specific cultural references that could limit its applicability in different settings. In addition, priority was given to usability and ease of integration into the daily routine of the participants, key aspects to maximize adherence to the intervention.

Our approach in this study is based on modern theories of emotional processing, which postulate that emotional responses are mediated by neural networks associated with memory and fear regulation [38]. IVR facilitates immersion in relaxing and controlled environments that induce a physiological relaxation response, promoting regulation of the autonomic nervous system and reducing activation of the amygdala, a key structure in the response to stress and anxiety [19]. Furthermore, the immersive experience in IVR promotes attentional focus and cognitive distraction, mechanisms that have been shown to be effective in reducing symptoms of anxiety and depression [18,20]. The intervention is based on mindfulness-based therapy, which has been widely validated in the treatment of anxiety and depression [16]. IVR enhances this practice by providing an immersive environment that facilitates the experience of presence and engagement with the activity, optimizing therapeutic benefits. Repeating sessions over six weeks favors the consolidation of emotional regulation patterns through neuroplasticity mechanisms, generating sustained changes in the perception of stress and anxiety [21]. Thus the theoretical model that supports our intervention combines the physiological regulation of stress through modulation of the autonomic nervous system, cognitive distraction and attentional focus facilitated by immersion, and the progressive internalization of emotional coping strategies through the repeated practice of mindfulness in a safe and structured environment.

Although our study protocol did not include a specific assessment of sleep quality or anxiety sensitivity, some publications suggest that anxiety and depression during pregnancy are closely related to these factors. Previous studies have shown that mindfulness- and relaxation-based interventions, such as the one used in our study, can improve sleep quality and reduce stress levels [39,40]. Furthermore, it has been shown that anxiety sensitivity can act as a vulnerability factor for the development of anxiety and depressive symptoms, which reinforces the relevance of addressing these aspects in future research [41].

There are several mechanisms that may explain the observed benefits of IVR-based intervention on mental health. First, the cognitive and emotional distraction effect plays a key role in reducing symptoms of anxiety and depression. The immersive nature of virtual reality allows attention to be diverted from stressors, providing a controlled and immersive environment that promotes relaxation.

This mechanism has been demonstrated in previous studies, in which exposure to virtual environments effectively reduced the perception of stress and pain in clinical contexts. Secondly, the induction of physiological relaxation may be a determining factor. The IVR intervention includes mindfulness and guided relaxation techniques, which have been associated with reduced autonomic activation, decreased heart rate, and better emotional regulation. These effects are consistent with our findings, in which a significant reduction in symptoms of anxiety and depression, as well as a decrease in heart rate, was observed in the intervention group. Thirdly, the influence on neuroplasticity and emotional engagement could contribute to the positive effects of IVR. Immersive experiences can modulate neural circuits associated with stress and mood regulation, promoting adaptive cognitive and emotional responses. Furthermore, the activation of reward-related brain areas during the virtual experience can improve mood and motivation, which would explain the high levels of adherence and satisfaction observed in our study. Finally, the increase in the perception of support and self-efficacy could mediate the effectiveness of the intervention. By providing a structured, engaging, and easily accessible tool for mental well-being, IVR allows users to take an active role in managing their symptoms. This sense of control has previously been linked to better outcomes in digital healthcare interventions. In any case, future studies should explore these mechanisms in greater depth by using neuroimaging techniques, physiological monitoring and qualitative evaluations of the user's experience.

Regarding the generalizability of the findings, we acknowledge that the study was conducted in a specific region of Spain, which might limit its applicability to other populations. Nevertheless, to strengthen external validity, two strategies were implemented: 1) Participants were recruited from five primary care centers (ASSIR), allowing for the inclusion of women with different sociodemographic profiles within the public health system; and 2) The virtual reality intervention used does not depend on specific cultural or contextual factors, facilitating its implementation in other prenatal care settings. Our findings are consistent with previous studies on eHealth and virtual reality for the management of anxiety and depression, suggesting that this technology may be effective in several pregnant populations.

With regard to the representativeness of the sample and the strategies to improve diversity, participants were selected in public primary care centers, ensuring equal access to the intervention and avoiding biases associated with the use of private services. Broad inclusion criteria were established, including women aged 18 years or older with moderate symptoms of anxiety and depression (EPDS 9-12), which favored the heterogeneity of the sample. All participants had to speak and understand Spanish, ensuring understanding of the intervention and evaluation of the results without linguistic bias. Although differences were observed in the educational level of the participants, we performed adjusted analyses to control for possible effects of these variables on the

results.

In our study, no serious adverse events were reported. A pilot study in the United States analyzed the feasibility of immersive VIR for distraction and pain management in women in labor, and reported a high acceptance with no serious side effects [42]. While in the general population the use of IVR may be associated with effects such as dizziness, nausea or disorientation — known as cybersickness — these effects appear to depend on the design of the intervention, the duration of exposure, and the individual characteristics of the users [43]. Although the evidence so far suggests that IVR is a safe and well-tolerated intervention in pregnant women, we encourage future research evaluating potential adverse effects in the long term and in more diverse populations.

Comparison with Previous Literature

Our findings align with previous literature emphasizing the potential of digital mental health interventions for perinatal populations. For example, a systematic review by Smith et al. [44] demonstrated the effectiveness of virtual reality in managing anxiety and depression in diverse clinical settings. Similarly, studies such as Pallavicini et al. [45] highlighted the ability of virtual reality games to elicit positive emotions and reduce state anxiety through immersive and interactive experiences. These findings suggest that IVR technology's immersive nature enhances user engagement and emotional regulation, supporting its use as a tool for mental health interventions during pregnancy.

In addition, Fuster-Casanovas et al. [46] observed a significant rise in the adoption of eHealth tools for managing mental health in Catalonia, further highlighting the role of digital platforms in enhancing accessibility to psychological support. Their findings resonate with our study's results, as both suggest that digital tools, particularly IVR, can bridge gaps in care by offering scalable and engaging solutions for vulnerable populations. Moreover, Ridout et al. [47] reported that virtual reality interventions significantly reduced anxiety in adolescent patients in hospital settings when immersive, therapeutic applications were used, providing further evidence for the clinical utility of such technologies in diverse populations.

Satisfaction

Participant satisfaction with the IVR-based intervention was remarkably high, as evidenced by post-intervention surveys. Participants reported that the immersive nature of the technology facilitated relaxation and emotional engagement, which contributed to the observed reductions in anxiety and depression symptoms. These findings are consistent with previous studies, such as Ridout et al. [47], which demonstrated that virtual reality interventions elicited positive emotional responses and were well-received by users. Additionally, Pallavicini et al. [45] noted that the interactive elements of VR contributed to enhanced user experiences, making the intervention more enjoyable and effective. Further support comes from Keshner et al. [48], who highlighted that virtual reality's adaptability and immersive environments increase patient satisfaction in therapeutic applications. The positive feedback underscores the acceptability of IVR as a feasible mental health intervention, particularly in populations with limited access to traditional therapies.

Adherence

Adherence to the intervention protocol was notably high, with over 85% of participants completing the recommended number of sessions. This is in line with findings from Fuster-Casanovas et al. [46], who highlighted the ease of use and accessibility of eHealth tools as key factors in ensuring consistent engagement. High adherence rates were also observed in studies utilizing similar VR-based interventions, such as Smith et al. [44], which attributed participant compliance to the engaging and user-friendly nature of the technology. Additionally, findings by Birckhead et al. [49] suggested that virtual reality interventions designed with user-centric features significantly improved adherence by maintaining user motivation and interest. Further, Indovina et al. [50] demonstrated that adherence to VR-based pain management programs was strongly associated with the level of interactivity and the ability to tailor content to user preferences. These findings suggest that the immersive and interactive characteristics of IVR not only enhance satisfaction but also foster sustained participation, which is critical for achieving meaningful mental health outcomes.

We found that user-centered design and personalization of IVR is very important. As far as individual needs assessment is concerned, before implementing the IVR intervention, it is essential to conduct an initial assessment of each pregnant woman's needs, preferences, and expectations. This may include questionnaires about her anxiety and depression levels, as well as her preferences regarding types of exercises (e.g., mindfulness, relaxation, guided imagery) and virtual environments (e.g., beaches, forests, mountains) [23]. This assessment would allow for the creation

of a personalized intervention plan that fits each woman's specific needs, thus increasing adherence to, and satisfaction with, the intervention [51]. As far as adaptation of virtual environments is concerned, they should be designed to be inclusive and culturally sensitive. For example, women from certain cultural backgrounds may feel more comfortable with environments that reflect their natural or cultural environment. This could involve adapting landscapes, sounds, and narratives to be culturally relevant [52]. Furthermore, environments should be adjustable in terms of sensory intensity (e.g. sounds, colors, movement) to suit individual preferences and avoid overstimulation, especially in women who may be more sensitive during pregnancy [53]. Regarding flexibility of duration and frequency of the IVR session, they should be flexible to suit pregnant women's routines and energy levels. Some women may prefer shorter but more frequent sessions, while others may benefit from longer but less frequent sessions [54]. The ability to pause and resume sessions is also important, as pregnant women may need frequent breaks due to physical discomfort or fatigue [55]. The incorporation of real-time feedback systems can improve the personalisation of the intervention. For example, heart rate sensors or short questionnaires during sessions can provide information about the woman's emotional state, allowing the IVR content to be adjusted based on her responses. This dynamic approach can help ensure that the intervention is always relevant and effective for each woman [55]. Finally, to ensure that the IVR intervention is truly user-centered, it is essential to involve pregnant women in the design and development process. This may include focus groups, pilot testing, and satisfaction surveys to gather direct feedback about the content and usability of the intervention [56]. Active user participation not only improves the acceptance of the intervention, but also increases the likelihood that it will be effective and sustainable in the long term [57].

Strengths and Limitations

While our study contributes to the growing evidence base for IVR interventions, it is not without limitations. First, the relatively small sample size restricts the generalizability of the findings. Second, the reliance on self-reported adherence and satisfaction data introduces potential reporting biases. Additionally, the absence of long-term follow-up limits our ability to evaluate the sustained impact of the intervention on postpartum mental health.

Another limitation to consider is related to the extrapolation of these results to women from disadvantaged socioeconomic backgrounds, or whose technological limitations could be restrictive, given that the availability of, and familiarity with, technologies such as IVR can differ significantly between socioeconomic groups. Also, the representativeness of the sample is limited, since the participants generally had a high educational level and good access to healthcare and technological

resources, which could bias the results towards greater effectiveness and adherence. Another potential limitation is related to possible biases derived from self-reporting of adherence to, and satisfaction with, the intervention, which may reflect a social desirability bias. Finally, it is worth noting that long-term follow-up was not conducted, which limits conclusions about the sustainability of the treatment's effect on postpartum mental health. Future research should therefore consider including more diverse samples, including women from different socioeconomic and cultural backgrounds, as well as evaluating alternative methods of technological access that facilitate the equal participation of women in vulnerable situations. In addition, future studies should implement longer follow-ups to assess the sustainability of the observed impact on mental health and delve deeper into possible biases arising from self-reporting and the specific characteristics of the studied group.

Nonetheless, this study has several strengths. The use of IVR technology represents an innovative and accessible approach to perinatal mental health care. Rigorous adjustments for baseline differences strengthen the reliability of our findings, and the high adherence rates suggest feasibility for real-world implementation. Importantly, the results of this study provide a foundation for future research to build upon, particularly in exploring the long-term effects and cost-effectiveness of IVR interventions for pregnant women.

Clinical Implications and Future Directions

From a clinical perspective, the integration of IVR-based eHealth programs into prenatal care offers a promising avenue to address gaps in mental health support. These programs can serve as scalable and engaging solutions, particularly in contexts where traditional resources are limited. Future studies should explore how to customize IVR content to meet individual needs and preferences, potentially enhancing both engagement and outcomes. Fajnerova et al. [58] emphasized the potential of multiuser virtual environments for facilitating group-based mental health interventions, which could be explored further in maternal care settings.

Our primary objective in this RCT was to assess the immediate efficacy of the IVR intervention on symptoms of anxiety and depression during pregnancy, using standardized instruments (EPDS and STAI). But the evaluation of durability of these beneficial effects beyond the immediate intervention period is essential to confirm its clinical utility and inform maternal mental health policies. We therefore plan to conduct future longitudinal studies that include extended postpartum follow-up periods (e.g., of 6 and 12 months after birth), to assess whether reductions in prenatal symptoms of anxiety and depression symptoms are maintained after delivery. These future studies will adopt longitudinal designs to analyze the persistence of improvements in maternal mental health

outcomes, including the potential prevention of postpartum depression and anxiety. In addition, long-term secondary outcomes related to maternal and infant health will be studied, specifically assessing maternal psychological well-being, mother-child bonding, parenting stress, and infant development trajectory, and using validated tools. These assessments will help determine whether the benefits observed during pregnancy have significant long-term effects, contributing to improved mother-child interactions and improved infant development trajectories. Additionally, in order to improve the robustness and generalizability of the findings, future studies will include larger and more diverse cohorts, multicenter trials, and economic analyses to assess the cost-effectiveness of IVR interventions, and their long-term effects on postpartum mental health. We believe that this comprehensive approach will provide robust evidence about the clinical relevance, sustainability, and scalability of immersive virtual reality interventions in perinatal care settings.

We are also aware that there are some limitations related to the implementation of IVR-based interventions and eHealth technologies in real-world clinical settings. Effective implementation will require rigorous compliance with data protection regulations (e.g., GDPR), clear informed consent processes, and robust cybersecurity measures to protect confidentiality among users. Furthermore, it is critical to consider the question of equity. The sociodemographic characteristics observed in this study suggest a potential bias towards participants with higher educational levels and stable economic situations, which could limit the applicability of the intervention in socioeconomically disadvantaged populations. Addressing these equity concerns involves ensuring technological accessibility, affordability, and ease of use across diverse socioeconomic groups and geographic locations, while also considering differences in technological ability and internet connectivity. Financial constraints are also a barrier, particularly relevant in the context of national healthcare services, where resources are often limited and require careful budgeting. The implementation of these technologies may require considerable initial investments, as well as clear financial strategies to ensure long-term sustainability and cost-effectiveness. Finally, practical challenges such as integration into existing healthcare services, obtaining acceptance by healthcare professionals, and devising sustainable financing models must also be considered. For all of these reasons, future research should focus on longitudinal analyses, assessing not only immediate efficacy but also sustained use and real-world feasibility, with the aim of developing scalable and inclusive solutions tailored to different clinical contexts and populations.

In relation to how to integrate IVR-based interventions into the healthcare system, we propose the following key aspects. First, implementation within primary care and maternity services: i) Midwives and healthcare professionals could incorporate IVR sessions into routine prenatal visits, offering guided relaxation and mindfulness exercises as a complementary mental health support tool; ii) The intervention could be integrated into antenatal education programs, in which pregnant women

receive structured sessions on stress management and emotional well-being using IVR technology. Secondly, home-based digital healthcare support: i) Pregnant women could be prescribed access to the IVR application for home use, with healthcare professionals monitoring adherence and outcomes through a digital platform; ii) A mobile application could complement the IVR sessions by providing additional psychological support, reminders, and educational content tailored to individual needs. Third, scalability within Public Healthcare System: i) Collaboration with public healthcare providers could facilitate the incorporation of IVR technology into maternal mental healthcare programs, ensuring accessibility for a broad population; ii) Future research should focus on cost-effectiveness analyses and feasibility studies to assess the sustainability of implementing IVR interventions on a larger scale.

Regarding to how to implement IVR in routine clinical practice, we consider the follow recommendations for the integration of IVR into antenatal care protocols: First, early detection of anxiety and depression symptoms, through implementation of IVR, could begin with routine screening for anxiety and depression symptoms during antenatal visits, using validated tools such as EPDS and STAI-E. Women presenting with moderate anxiety or depression symptoms (scores within the range established in our study) could be referred for the IVR intervention as part of a stepped care approach. Secondly, training of professional healthcare staff, especially midwives and primary care nurses, in the use of IVR technology and in supervising sessions. This would include training in setting up the equipment, explaining relaxation and mindfulness exercises, and monitoring patients' progress. It would also be important to provide guidelines about how to address potential questions or concerns from patients regarding the use of the technology. Thirdly, access to technology, for which primary care centers could have IVR equipment available at antenatal follow-up consultations. Alternatively, lending IVR devices to patients for use at home could be considered, provided that adequate follow-up is ensured. The intervention could be designed to be self-guided, with pre-programmed sessions that patients could complete independently, but with the possibility of contacting a professional in case of questions or need for additional support. Fourthly, integration into the individualised care plan, including the IVR intervention and tailored to each patient's specific needs and the context of their pregnancy. This could include co-ordination with other mental health professionals, such as psychologists or psychiatrists, in cases where a more intensive approach is required. In addition, it could be combined with other low-cost interventions, such as prenatal exercise programs, mindfulness workshops or support groups, to offer a holistic approach to mental wellbeing during pregnancy. Fifthly, continuous monitoring and evaluation to establish a continuous monitoring system to evaluate the effectiveness of the intervention and adjust it as necessary. This could include collecting data about adherence, patient satisfaction and changes in anxiety and depression symptoms over time. Healthcare professionals could use the data collected to identify patients who could benefit from additional or more intensive interventions. Sixthly, cultural

and socioeconomic considerations. Since accessibility and acceptance of technology may vary depending on the cultural and socioeconomic context, it is important to adapt the intervention to the specific needs of each population. This could include translating content into different languages or adapting IVR scenarios to make them culturally relevant.

We have also reflected about the potential long-term effects of the IVR intervention. In the effects on postpartum mental health, we should consider: First, anxiety and depression during pregnancy are known risk factors for the development of postpartum depression (PPD) [8]. Since our intervention demonstrated a significant reduction in anxiety and depression symptoms during pregnancy, it is plausible that it may also contribute to a decreased risk of PPD [59]. Previous studies have shown that interventions that improve mental health during pregnancy have a protective effect against PPD, suggesting that IVR could have a positive impact on women's emotional well-being after delivery [60]. Secondly, maternal mental health is closely related to the quality of the mother-child bond [61]. A reduction in anxiety and depression symptoms during pregnancy could facilitate a stronger and more positive bond between mother and infant, which in turn could have beneficial effects on the child's emotional and social development [6]. Future studies could assess the impact of the IVR intervention on the quality of the mother-child bond using validated scales, such as the Postpartum Bonding Questionnaire (PBQ) [62]. Additionally, regarding the effects on child development, we can consider: First, maternal anxiety and depression during pregnancy have been associated with an increased risk of problems in the child's cognitive and emotional development, including learning difficulties, attention problems and emotional disorders [63]. By reducing these symptoms during pregnancy, the IVR intervention could contribute to a healthier development of the child [16]. Longitudinal studies could evaluate the impact of the intervention on the cognitive and emotional development of children, using tools such as the Bayley Scales of Infant and Toddler Development or the Child Behavior Checklist (CBCL) [64]. Secondly, some research suggests that maternal stress and anxiety during pregnancy may be associated with an increased risk of neurodevelopmental disorders, such as attention deficit hyperactivity disorder (ADHD) or autism spectrum disorder (ASD) [65]. Although the relationship is not direct, it is possible that reducing stress and anxiety during pregnancy through the IVR intervention may have a protective effect in this regard [60]. Future studies could explore this hypothesis by long-term follow-up of children whose mothers participated in the intervention. Finally, regarding future research, we consider that: First, to assess the long-term effects of the IVR intervention, longitudinal studies following women and their children for several years after delivery would be necessary. These studies could measure not only maternal mental health, but also children's cognitive, emotional, and social development [59]. Secondly, it would be important to explore the underlying biological and psychological mechanisms that could explain how reducing anxiety and depression during pregnancy influences

postpartum mental health and child development. For example, changes in cortisol levels or other biological markers associated with stress could be investigated [6]. Thirdly, future research could explore the effect of combining IVR intervention with other postpartum interventions, such as parenting support programs or cognitive-behavioral therapies, to maximize benefits on maternal mental health and child development [16].

We consider that feasibility, scalability, and costs are key aspects for the IVR interventions to be effectively implemented, especially in underserved populations where access to mental healthcare is limited. With regard to feasibility and scalability in real-world settings, we consider that: First, the IVR intervention requires the use of virtual reality devices, which can vary in cost and complexity. In our study, we used mid-range devices that are relatively affordable and easy to use. These devices could be purchased by primary care centers or maternal health clinics, or even rented to reduce initial costs. IVR technology is becoming more accessible, and device costs have decreased in recent years, making it easier to implement in resource-limited settings. Secondly, implementation of the IVR intervention would require basic training of healthcare personnel, such as midwives, nurses, or psychologists, in using the technology and supervising sessions. This training could be done in a short period and would not require advanced technical skills. Furthermore, the intervention could be designed to be self-guided, which would reduce the need for constant supervision by healthcare staff. Thirdly, the IVR intervention is highly adaptable and could be tailored to meet the needs of various populations, including those with language or cultural barriers. For example, relaxation and mindfulness scenarios could be adapted to reflect culturally relevant environments, and content could be translated into different languages. Regarding cost and resource estimation we consider that: i) The cost of IVR devices can vary between 300 and 600 euros per unit, depending on the brand and the features. For a primary care center with a moderate workload, several devices could be purchased for rotational use. ii) The development of IVR content (mindfulness exercises, relaxation, etc.) may involve an initial cost, but once developed, these contents can be used repeatedly without significant additional costs. iii) Maintenance costs are relatively low, as modern IVR devices are long-lasting and require few upgrades. iv) Training of healthcare staff could be done in a one- or two-day workshop, at an estimated cost of 500 to 1,000 euros, depending on the number of participants. v) In the long term, the IVR intervention could result in significant savings by reducing the need for more expensive interventions, such as individual or pharmacological therapies, especially in cases of mild to moderate anxiety and depression. In addition, by improving the mental health of pregnant women, costs associated with obstetric and neonatal complications related to stress and depression could be reduced.

We also consider, in relation to scalability in underserved populations, that: First, the IVR intervention could be particularly useful in rural or remote areas where access to mental healthcare

professionals is limited. The devices could be transported between different health facilities or even used at home under remote supervision. In addition, the portable nature of IVR devices allows their use in communities with limited infrastructures, provided that there is access to electricity and adequate space for sessions. Secondly, to facilitate implementation in underserved populations, collaborations could be established with non-governmental organizations (NGOs) or public health agencies already working in these areas. These organizations could provide logistical and financial support for the acquisition and maintenance of the devices.

In this study, women with a history of diagnosed anxiety or depression were excluded because this clinical subgroup could present a different evolution compared to those with recent and moderate symptoms, which could affect the validity of the results. However, we consider that future studies could evaluate the effectiveness of this intervention in populations with a previous psychiatric history. We also consider that future studies could further explore the influence of pregnancy planning on the effectiveness of digital interventions for perinatal mental health.

It is worth remembering that IVR has been applied in other areas of mental health such as: i) Post-traumatic stress disorder (PTSD), in which IVR has proved to be an effective tool in the treatment, particularly in the context of exposure therapy. The technology allows for the simulation of controlled and safe environments where patients can gradually confront the stimuli that trigger their symptoms, facilitating desensitization and emotional processing [66]. Studies have shown that IVR can be particularly useful in war veterans, accident survivors, or victims of violence, in whom exposure to virtual environments can help reduce the symptoms of re-experiencing, avoidance, and hyperarousal associated with PTSD [67]. Furthermore, IVR can be combined with evidence-based therapies, such as cognitive behavioral therapy, to improve treatment outcomes [68]. ii) IVR has also shown potential in the treatment of substance-use disorders, particularly in relapse prevention. Virtual environments can simulate high-risk situations (e.g., bars or parties) where patients can practice coping strategies in a safe and controlled environment [69]. Additionally, IVR can be used for aversion therapy, where patients are exposed to virtual stimuli associated with substance use, which can help reduce craving and dependence [70]. Recent studies have shown that IVR can be effective in treating alcohol, tobacco, and other drug addictions, improving treatment adherence and reducing relapse rates [71]. iii) IVR has been widely used in the treatment of specific phobias, such as fear of flying, heights, or closed spaces. Gradual exposure to these stimuli in a virtual environment allows patients to confront their fears in a controlled manner, which reduces anxiety and improves functioning [72]. Furthermore, IVR can be useful in the treatment of generalized anxiety, by providing relaxing environments and mindfulness exercises that help reduce symptoms of excessive worry and muscle tension [45]. iv) IVR has also shown potential in supporting

individuals with autism spectrum disorders, particularly in developing social skills and reducing anxiety in social situations. Virtual environments can simulate complex social interactions, allowing patients to practice and improve their communication skills in a safe environment [73]. v) IVR has been used as a complementary tool in the management of chronic pain, which is often associated with mental health disorders such as depression and anxiety. Virtual environments can distract patients from the pain and provide relaxation techniques that improve their emotional well-being [50].

Finally, we would like to mention the integration of artificial intelligence (AI) and machine learning into IVR interventions. We believe that these new tools have great potential to improve the personalization and effectiveness of IVR. AI-based algorithms could allow the individualization of IVR experiences based on, for example, emotional state or therapeutic response.

CONCLUSION

The findings of this study highlight the significant potential of immersive virtual reality (IVR)-based eHealth interventions in improving mental health outcomes during pregnancy. By reducing symptoms of anxiety and depression, the intervention demonstrated its capacity to address critical mental health challenges faced by pregnant women, aligning with the growing emphasis on integrating digital health solutions into prenatal care. This intervention, grounded in immersive and interactive technology, not only achieved significant reductions in EPDS and STAI-E scores but also fostered high adherence and participant satisfaction. These results underscore the feasibility of implementing IVR-based programs as accessible, low-intensity mental health interventions within broader health systems. Such programs hold promise for addressing disparities in access to care, particularly for vulnerable populations or those with limited availability of traditional mental health services.

Despite these conclusions should be interpreted with caution given the relatively small sample size, the socioeconomic and educational homogeneity of the participants, and the possible presence of biases derived from self-reporting in the assessment of adherence and satisfaction. Furthermore, the lack of long-term follow-up limits the ability to determine the sustainability of the observed benefits. Therefore, although the findings support the potential efficacy of IVR-based interventions in specific contexts, additional studies with more diverse samples and longer follow-ups are required to confirm these results and explore their applicability in different socioeconomic and cultural contexts.

Future research should aim to address these limitations while exploring the scalability, cost-

effectiveness, and cultural adaptability of IVR-based interventions. Additionally, longitudinal studies are needed to evaluate the sustained impact of such interventions on postpartum mental health and their potential influence on maternal and child outcomes.

ACKNOWLEDGEMENTS

We would like to extend our gratitude to all the participants who generously contributed their time to this study. Special thanks to midwives in the primary care centres and professionals who supported the recruitment and facilitation of this research, including CAP Rambla, CAP Can Tries, CAP Rubí, CAP Can Mates, and CAP Can Parellada.

We also wish to thank Delaguila Games (@delaguila_games), the developers of the immersive virtual reality technology utilized in this study. Their innovation and technical expertise played a crucial role in creating a user-centered intervention tailored to the needs of pregnant individuals.

Finally, we are grateful to the research team, midwives, and health care professionals involved in the implementation and execution of the study.

FUNDING

This research was supported by funding from the Departament de Salut, Generalitat de Catalunya (PERIS Grant No. SLT006/17/249). This study was partially funded by the Official College of Nurses of Barcelona (www.coib.cat) as part of the Nurse Research Projects Grants (PR-642/2023). Additionally, the study received the Mustela Scholarship for midwifery research projects awarded by the Mustela Foundation (FAME 2023).

CONFLICT OF INTEREST

None

References

1. Ajong AB, Kenfack B, Ali IM, Yakum MN, Ukaogo PO, Mangala FN, Aljerf L, Telefo PB. Calcium supplementation in pregnancy: An analysis of potential determinants in an under-resourced setting. *PLoS One* 2023;18(10):e0292303. PMID:37796953
2. Ajong AB, Yakum MN, Aljerf L, Ali IM, Mangala FN, Onyidinma UP, Liwo BM, Bekolo CE, Tameh TY, Kenfack B, Telefo PB. Association of hypertension in pregnancy with serum electrolyte disorders in late pregnancy among Cameroonian women. *Sci Rep Nature Publishing Group*; 2023;13(1):20940. doi: 10.1038/s41598-023-47623-6
3. Royal College of Psychiatrists. Mental health in pregnancy. London: Royal College of

Psychiatrists; 2018.

4. Bauer A, Knapp M, Parsonage M, Appleby J, Devlin N, Parkin D, et al. Lifetime costs of perinatal anxiety and depression. *J Affect Disord*. 2016;192:83-90.
5. Ghazanfarpour M, Bahrami F, Rashidi Fakari F, Ashrafinia F, Babakhanian M, Dordeh M, Abdi F. Prevalence of anxiety and depression among pregnant women during the COVID-19 pandemic: a meta-analysis. *Journal of Psychosomatic Obstetrics & Gynecology Taylor & Francis*; 2022;43(3):315–326. PMID:34165032
6. Van Den Bergh BRH, Mulder EJH, Mennes M, Glover V. Antenatal maternal anxiety and stress and the neurobehavioral development of the fetus and child: Links and possible mechanisms. *Neurosci Biobehav Rev*. 2005;29(2):237-58.
7. Dunkel Schetter C, Tanner L. Anxiety, depression and stress in pregnancy: Implications for mothers, children, research, and practice. *Curr Opin Psychiatry*. 2012;25(2):141-8. Goodman JH, Chenausky KL, Freeman MP. Anxiety Disorders During Pregnancy. *J Clin Psychiatry*. 2014;75(10):1153-84.
8. Goodman JH, Chenausky KL, Freeman MP. Anxiety disorders during pregnancy: a systematic review. *J Clin Psychiatry* 2014;75(10):e1153-1184. PMID:25373126
9. Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Arch Gen Psychiatry*. 2010;67(10):1012-24.
10. National Institute for Health and Care Excellence (NICE). Antenatal and postnatal mental health: Clinical management and service guidance. NICE; 2020.
11. World Health Organization. WHO guideline: Recommendations on digital interventions for health system strengthening. Geneva: WHO; 2019. [Internet]. Available from: <https://www.who.int/reproductivehealth/publications/digital-interventions-health-system-strengthening/en/>.
12. National Institute for Health and Care Excellence (NICE). Common mental health problems: identification and pathways to care. NICE Clinical Guideline 123; 2011.
13. World Health Organization. mHealth: New horizons for health through mobile technologies. Geneva: WHO; 2011. [Internet]. Available from: https://www.who.int/goe/publications/goe_mhealth_web.pdf.
14. Ryu S. Book review: mHealth: new horizons for health through mobile technologies: based on the findings of the second global survey on eHealth (Global Observatory for eHealth Series, Volume 3). *Healthc Inform Res*. 2012;18:231–3.
15. Lee EW, Denison FC, Hor K, Reynolds RM. Web-based interventions for prevention and treatment of perinatal mood disorders: A systematic review. *BMC Pregnancy Childbirth*. 2016;16(1):38.
16. Shi Z, MacBeth A. The Effectiveness of Mindfulness-Based Interventions on Maternal Perinatal Mental Health Outcomes: a Systematic Review. *Mindfulness (N Y)*. 2017;8(4):823-47.

17. Marc I, Toureche N, Ernst E, Hodnett ED, Blanchet C, Dodin S, et al. Mind-body interventions during pregnancy for preventing or treating women's anxiety. *Cochrane Database Syst Rev*. 2011 Jul 6;(7).
18. Maples-Keller JL, Bunnell BE, Kim SJ, Rothbaum BO. The use of virtual reality technology in the treatment of anxiety and other psychiatric disorders. *Harv Rev Psychiatry*. 2017 Sep/Oct;25(3):103-113.
19. Bohil CJ, Alicea B, Biocca FA. Virtual reality in neuroscience research and therapy. *Nat Rev Neurosci*. 2011 Nov;12(12):752-62.
20. Fodor LA, Coteș CD, Cuijpers P, Szamoskozi Ș, David D, Cristea IA. The efficacy of virtual reality based interventions for symptoms of anxiety and depression: A meta-analysis. *Sci Rep*. 2018 Dec 14;8(1):10323.
21. Donker T, Blankers M, Hedman E, Ljótsson B, Petrie K, Christensen H. Economic evaluations of Internet interventions for mental health: A systematic review. *Psychol Med*. 2015 Mar;45(3):335-56.
22. Anderson P, Jané-Llopis E. Mental health promotion and mental disorder prevention: A policy for Europe. Nijmegen, Netherlands: Radboud University Nijmegen; 2011.
23. Mohr DC, Burns MN, Schueller SM, Clarke G, Klinkman M. Behavioral intervention technologies: Evidence review and recommendations for future research in mental health. *Gen Hosp Psychiatry*. 2013 Nov-Dec;35(4):332-8.
24. Deady M, Teesson M, Kay-Lambkin F, Mills K. Developing an integrated, Internet-based self-help program for young people with depression and alcohol use problems. *Internet Interv*. 2014 Oct;1(3):118-31.
25. Vukovic V, Favaretti C, Ricciardi W, de Waure C. Health technology assessment evidence on e-health/m-health technologies: evaluating the transparency and thoroughness. *Int J Technol Assess Health Care*. 2018 Jan;34(1):87-96.
26. Jimenez-Barragan M, del Pino Gutierrez A, Curto Garcia J, Monistrol-Ruano O, Coll-Navarro E, Porta-Roda O, et al. Study protocol for improving mental health during pregnancy: a randomized controlled low-intensity m-health intervention by midwives at primary care centers. *BMC Nurs*. 2023;22(1):309.
27. O'Connor E, Rossom RC, Henninger M, Groom HC, Burda BU, Henderson JT, et al. Primary care screening for and treatment of depression in pregnant and postpartum women: Evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2016 Feb 9;315(4):388-406.
28. Dachew BA, Scott JG, Alati R, Alebel A. Global prevalence of antenatal depression and its association with adverse birth outcomes: An umbrella review. *BMC Pregnancy Childbirth*. 2021 Dec 9;21(1):503.
29. García-Esteve L, Ascaso C, Ojuel J, Navarro P. Validation of the Edinburgh Postnatal Depression Scale (EPDS) in Spanish mothers. *J Affect Disord*. 2003;75(1):71-76. doi:10.1016/S0165-0327(02)00020-4.

30. Spielberger CD, Gorsuch RL, Lushene R, Echeburúa E, Corral P. STAI: Cuestionario de Ansiedad Estado-Rasgo. 7ª ed. Madrid: TEA Ediciones; 2008.
31. Departament de Salut. Protocol de seguiment de l'embaràs a Catalunya 2018 [Internet]. Barcelona: Generalitat de Catalunya; 2018 [cited 2025 Jan 17]. Available from: https://scientiasalut.gencat.cat/bitstream/handle/11351/1204/protocol_seguiment_embaras_catalunya_2018.pdf?sequence=14&isAllowed=y.
32. Pan W-L, Gau M-L, Lee T-Y, Jou H-J, Liu C-Y, Wen T-K. Mindfulness-based programme on the psychological health of pregnant women. *Women Birth* 2019;32(1):e102–e109. PMID:29752225
33. Maderuelo JA, Haro AM, Pérez F, Cercas LJ, Valentín AB, Morán E. Satisfacción de las mujeres con el seguimiento del embarazo: Diferencias entre los dispositivos asistenciales. *Gaceta Sanitaria* 2006;20(1):31–39. Available from: http://scielo.isciii.es/scielo.php?script=sci_abstract&pid=S0213-91112006000100006&lng=es&nrm=iso&tlng=es [accessed Mar 3, 2025]
34. Maderuelo-Fernández JA, Rodríguez-Martín B, Martín-Baranera M. Satisfacción de las mujeres con la atención prenatal: desarrollo y validación de un cuestionario. *Gac Sanit.* 2006;20(6):453–459. doi:10.1157/13094880.
35. Tcha-Tokey K, Christmann O, Loup-Escande E, Richir S. Proposition and Validation of a Questionnaire to Measure the User Experience in Immersive Virtual Environments. *Int J Virtual Real.* 2016;16(1):33–48. doi:10.20870/IJVR.2016.16.1.2880.
36. Hosmer Jr. DW, Lemeshow S, Sturdivant RX. *Applied Logistic Regression*. Wiley Series in Probability and Statistics. 2013 John Wiley & Sons, Inc. Available from: <https://onlinelibrary.wiley.com/doi/book/10.1002/9781118548387> [accessed Mar 14, 2025]
37. Světlák M, Malatincová T, Halámková J, Barešová Z, Lekárová M, Vigašová D, Slezáčková A, Šumec R, Humpolíček P, Šedo J, Chládek J, Roman R, Gottwaldová J, Gescheidtová L, Čermáková Z, Thon V, Hrnčířiková I, Kazda T, Svoboda M. The effectiveness of three mobile-based psychological interventions in reducing psychological distress and preventing stress-related changes in the psycho-neuro-endocrine-immune network in breast cancer survivors: Study protocol for a randomised controlled trial. *Internet Interv* 2023;32:100628. PMID:37273931
38. Pessoa L. A Network Model of the Emotional Brain. *Trends Cogn Sci* 2017;21(5):357–371. PMID:28363681
39. Chiesa A, Serretti A. Mindfulness-based stress reduction for stress management in healthy people: a review and meta-analysis. *J Altern Complement Med* 2009;15(5):593–600. PMID:19432513
40. Alvaro PK, Roberts RM, Harris JK. A Systematic Review Assessing Bidirectionality between Sleep Disturbances, Anxiety, and Depression. *Sleep* 2013;36(7):1059–1068. PMID:23814343
41. Taylor, S. (2014). *Anxiety sensitivity: Theory, research, and treatment of the fear of anxiety*. Routledge.
42. Frey DP, Bauer ME, Bell CL, Low LK, Hassett AL, Cassidy RB, Boyer KD, Sharar SR. Virtual

- Reality Analgesia in Labor: The VRAIL Pilot Study-A Preliminary Randomized Controlled Trial Suggesting Benefit of Immersive Virtual Reality Analgesia in Unmedicated Laboring Women. *Anesth Analg* 2019;128(6):e93–e96. PMID:31094789
43. Simón-Vicente L, Rodríguez-Cano S, Delgado-Benito V, Ausín-Villaverde V, Cubo Delgado E. Cybersickness. A systematic literature review of adverse effects related to virtual reality. *Neurologia (Engl Ed)* 2024;39(8):701–709. PMID:39396266
44. Smith J, Brown K, Johnson P. Virtual reality as a tool for managing anxiety and depression: A systematic review. *J Clin Psychol*. 2020;76(3):456-468.
45. Pallavicini F, Cipresso P, Riva G. Virtual reality applications for stress management: A review of current research. *Front Psychol*. 2020;11:559.
46. Fuster-Casanovas A, Miró Q, Vidal-Alaball J, et al. eHealth tools for managing mental health in Catalonia: Adoption trends and effectiveness. *JMIR Ment Health*. 2024;11(1):e52816.
47. Ridout B, Campbell A. The therapeutic potential of virtual reality for mental health: A systematic review. *Aust N Z J Psychiatry*. 2021;55(5):458-472.
48. Keshner EA, Fung S, Williams J. The role of immersive environments in therapeutic satisfaction: A systematic review. *J Neurorehabil*. 2023;40(1):33-45.
49. Birkhead B, Eberhardt T, Avila E, et al. Rapid implementation of virtual reality for chronic pain during the COVID-19 pandemic. *Pain Med*. 2021;22(4):1144-1152.
50. Indovina P, Barone D, Gallo L, et al. Virtual reality as a distraction intervention to relieve pain and distress during medical procedures: A comprehensive literature review. *Clin J Pain*. 2020;36(5):472-482.
51. Kelders SM, Kok RN, Ossebaard HC, Van Gemert-Pijnen JEW. Persuasive system design does matter: a systematic review of adherence to web-based interventions. *J Med Internet Res* 2012;14(6):e152. PMID:23151820
52. Kreuter MW, Lukwago SN, Bucholtz RDDC, Clark EM, Sanders-Thompson V. Achieving cultural appropriateness in health promotion programs: targeted and tailored approaches. *Health Educ Behav* 2003;30(2):133–146. PMID:12693519
53. Riva G, Baños RM, Botella C, Mantovani F, Gaggioli A. Transforming Experience: The Potential of Augmented Reality and Virtual Reality for Enhancing Personal and Clinical Change. *Front Psychiatry* 2016;7:164. PMID:27746747
54. Donkin L, Christensen H, Naismith SL, Neal B, Hickie IB, Glozier N. A systematic review of the impact of adherence on the effectiveness of e-therapies. *J Med Internet Res* 2011;13(3):e52. PMID:21821503
55. Schueller SM, Tomasino KN, Mohr DC. Integrating Human Support Into Behavioral Intervention Technologies: The Efficiency Model of Support. *Clinical Psychology: Science and Practice* 2017;24(1):27–45. doi: 10.1111/cpsp.12173
56. Sanders EB-N, Stappers PJ. Co-creation and the new landscapes of design. *CoDesign* Taylor & Francis; 2008;4(1):5–18. doi: 10.1080/15710880701875068

57. Yardley L, Morrison L, Bradbury K, Muller I. The person-based approach to intervention development: application to digital health-related behavior change interventions. *J Med Internet Res* 2015;17(1):e30. PMID:25639757
58. Fajnerova I, Marackova M, Novak D. Multiuser virtual environments for mental health interventions: Opportunities and challenges. *Virtual Reality*. 2024;28(2):185-200.
59. Dennis C-L, Dowswell T. Psychosocial and psychological interventions for preventing postpartum depression. *Cochrane Database Syst Rev* 2013;(2):CD001134. PMID:23450532
60. Field T. Prenatal depression effects on early development: a review. *Infant Behav Dev* 2011;34(1):1–14. PMID:20970195
61. Brockington IF, Fraser C, Wilson D. The Postpartum Bonding Questionnaire: a validation. *Arch Womens Ment Health* 2006;9(5):233–242. PMID:16673041
62. Talge NM, Neal C, Glover V, Early Stress, Translational Research and Prevention Science Network: Fetal and Neonatal Experience on Child and Adolescent Mental Health. Antenatal maternal stress and long-term effects on child neurodevelopment: how and why? *J Child Psychol Psychiatry* 2007;48(3–4):245–261. PMID:17355398
63. Ronald A, Pennell CE, Whitehouse AJO. Prenatal Maternal Stress Associated with ADHD and Autistic Traits in early Childhood. *Front Psychol* 2010;1:223. PMID:21833278
64. Bayley N. Bayley Scales of Infant and Toddler Development. 3rd ed. San Antonio, TX: Harcourt Assessment; 2006.
65. Glover V. Prenatal stress and its effects on the fetus and the child: possible underlying biological mechanisms. *Adv Neurobiol* 2015;10:269–283. PMID:25287545
66. Rothbaum BO, Hodges LF, Ready D, Graap K, Alarcon RD. Virtual reality exposure therapy for Vietnam veterans with posttraumatic stress disorder. *J Clin Psychiatry* 2001;62(8):617–622. PMID:11561934
67. Difede J, Cukor J, Jayasinghe N, Patt I, Jedel S, Spielman L, Giosan C, Hoffman HG. Virtual reality exposure therapy for the treatment of posttraumatic stress disorder following September 11, 2001. *J Clin Psychiatry* 2007;68(11):1639–1647. PMID:18052556
68. Gonçalves R, Pedrozo AL, Coutinho ESF, Figueira I, Ventura P. Efficacy of virtual reality exposure therapy in the treatment of PTSD: a systematic review. *PLoS One* 2012;7(12):e48469. PMID:23300515
69. Bordnick PS, Carter BL, Traylor AC. What virtual reality research in addictions can tell us about the future of obesity assessment and treatment. *J Diabetes Sci Technol* 2011 Mar 1;5(2):265–271. PMID:21527092
70. Lee J-H, Kwon H, Choi J, Yang B-H. Cue-exposure therapy to decrease alcohol craving in virtual environment. *Cyberpsychol Behav* 2007;10(5):617–623. PMID:17927528
71. Hone-Blanchet A, Wensing T, Fecteau S. The use of virtual reality in craving assessment and cue-exposure therapy in substance use disorders. *Front Hum Neurosci* 2014;8:844. PMID:25368571

72. Botella C, Fernández-Álvarez J, Guillén V, García-Palacios A, Baños R. Recent Progress in Virtual Reality Exposure Therapy for Phobias: A Systematic Review. *Curr Psychiatry Rep* 2017;19(7):42. PMID:28540594
73. Parsons S, Mitchell P. The potential of virtual reality in social skills training for people with autistic spectrum disorders. *J Intellect Disabil Res* 2002;46(Pt 5):430–443. PMID:12031025



Supplementary Files

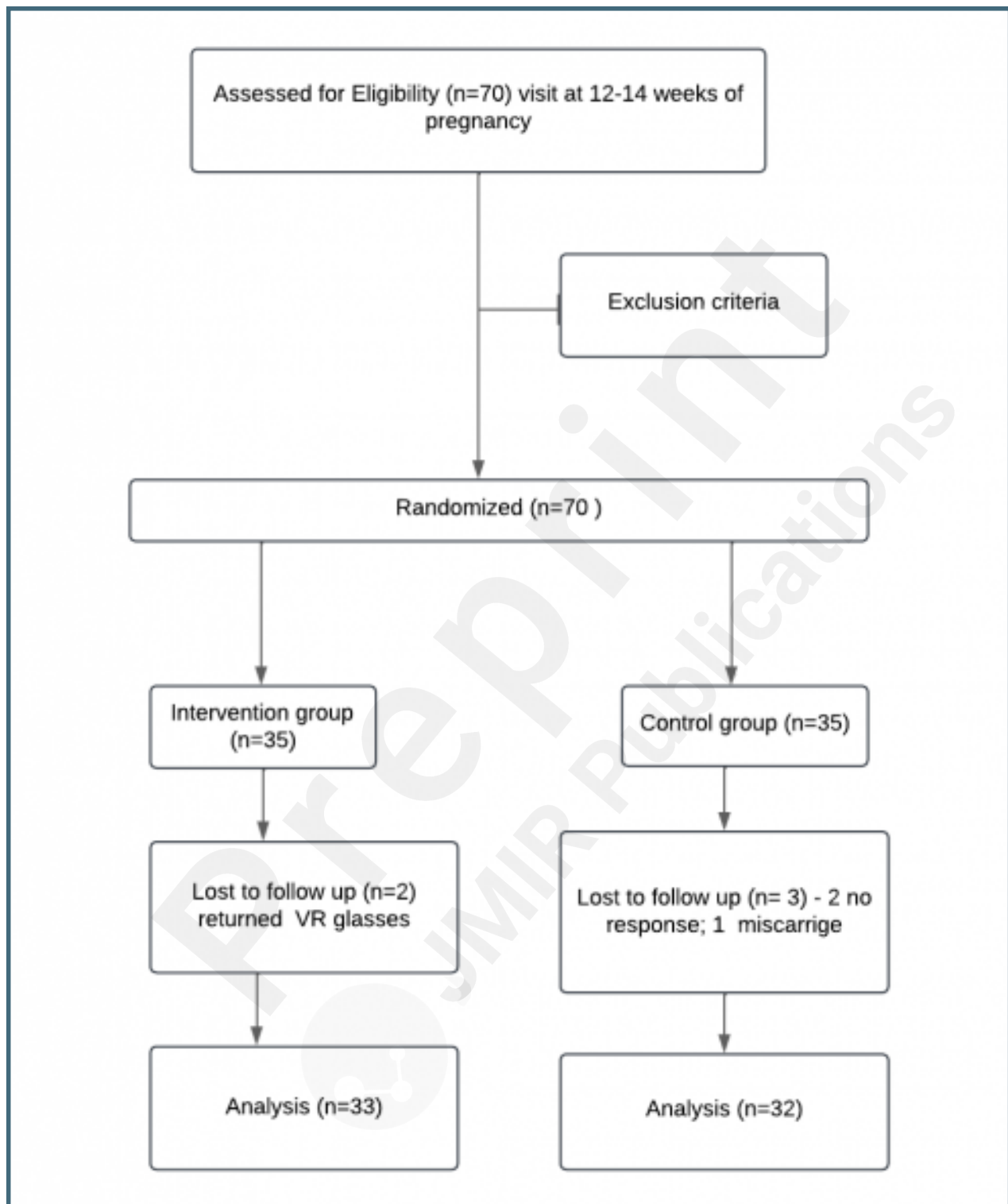
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CONSORT (or other) checklists

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