Conjoint Associate Professor Jed Duff

Chief Investigator / Project Supervisor

School of Nursing and Midwifery | Faculty of Health and Medicine

M:+61 407 063 138 |Email: j2.duff@qut.edu.au

Study protocol for the Research Project:

The Effectiveness of Using Virtual Reality Technology for Surgery-related Anxiety among Adults

Document Version [number]; dated [dd/mm/yy]

STUDY DESIGN

A type 1 hybrid effectiveness-implementation design will be used in this study. The study will assess the effectiveness of Oculus Quest Virtual Reality (VR) Headset fitted with a smartphone on perioperative anxiety among adults undergoing elective surgery (Aim 1); while the implementation is observed and information gathered on the potential barriers and facilitators to its widespread uptake (Aim 2). This selected type of design is appropriate in order to provide a pathway for the rapid transfer of knowledge from research to implementation if the intervention is effective (Curran, Bauer, Mittman, Pyne, & Stetler, 2012).

RESEARCH AIMS

The aims of this study are:

1- To evaluate the effectiveness of using VR technology for perioperative anxiety among adults undergoing elective surgery.

2- To identify the potential barriers and facilitators to the widespread implementation of VR for perioperative anxiety

STUDY SETTING

This study will be conducted in the surgical unit at King Abudulaziz University Hospital, Jeddah city, Western region, Saudi Arabia. The King Abudulaziz University Hospital is the largest tertiary care hospital in the western region. The facilities have the most advanced technology infrastructure, and they are staffed with about 4,000 healthcare providers and administrators (King Abdulaziz University Hospital, 2015). The bed capacity is 1,067. The department of operation room consists of 25 operating rooms distributed as follows; 16 major operating theaters in the main operating rooms (OR); 2 operating theaters in the emergency department; 2 theaters in the labor delivery; 4 theaters for one day surgery; and one burn unit operating room. The OR department is serving most surgical specialties ,including general surgery, neurosurgery, cardiac surgery, thoracic surgery, ophthalmic, ears nose and throat (ENT), plastic, pediatric, vascular ,and robotic surgery (King Abdulaziz University Hospital, 2015).

3.1 AIM ONE

Evaluate the effectiveness of using VR technology for perioperative anxiety among adults undergoing elective surgery.

DESIGN

A two-group parallel Randomised Controlled Trial (RCT) with allocation ratio 1:1 will be conducted in accordance with the CONSORT guidelines (Schulz, Altman, & Moher, 2010); 150 patients undergoing elective surgery will be randomised to the control (standard preoperative care) or the intervention (routine preoperative care with VR) group.

HYPOTHESIS

Compared with standard care, the VR intervention delivered during the preoperative period will significantly reduce perioperative anxiety in adult elective surgical patients by 20 points on a 100-point Visual analog scale for anxiety (VAS-A).

RECRUITMENT

The PhD candidate will consult the hospital's admission team, who will review the surgical list and identify potential participants. The potential participants will be asked by the preoperative clinic nurse to take part in the study during their preoperative visit. They will be provided with a participant information statement and consent form. The consent form will have two agreement statements: the first statement regarding participating in the quantitative study, the second statement regarding participating in the qualitative study (interviews). Potential participants will be instructed to return their signed consent prior to their day of surgery if they are interested in participating in the study.

INCLUSION AND EXCLUSION CRITERIA

Patients will be eligible for inclusion if they are 18 years old and over; scheduled for elective surgery; able to understand Arabic and follow instructions. Patients will be excluded if they scheduled to undergoing dental surgery; have mental illness; visual or hearing problems; history of seizures or motion sickness; an inability to complete a self-reported questionnaire, or cognitive impairment.

SECREEING

Patients who meet the above inclusion criteria will be screened for their anxiety level using a validated tool which is The Amsterdam Preoperative Anxiety and Information score (APAIS) (Boker et al., 2002; Laufenberg-Feldmann & Kappis, 2013). The PhD candidate will apply the Amsterdam Preoperative Anxiety and Information score (APAIS) on the day of their surgery in the preoperative holding area. Patients with moderate to high level of preoperative anxiety - defined as a preoperative anxiety score ≥11 (Song et al., 2019) - will be included.

The APAIS is a rapid and clinically practical assessment tool developed by Nelly Moerman and previously validated against other scales to evaluate patients' preoperative anxiety with good sensitivity and strong specificity for clinically significant anxiety (Boker et al., 2002; Laufenberg-Feldmann & Kappis, 2013). It consists of six questions in total. Each question is rated on a five-point Likert scale from 1: ''not at all'' to 5: ''extremely''. The sum of scores from questions 1, 2, 4, and 5

show the anxiety level. The sum of scores from questions 3 and 6 show the level of information required by each individual regarding the anesthesia and surgical procedure. A patient with a score of 11 or more (scoring range from 4 to 20) on the anxiety scale experiences moderate to severe anxiety requiring further intervention (Berth, Petrowski, & Balck, 2007; Boker et al., 2002; Laufenberg-Feldmann & Kappis, 2013). On the need for information scale, patients scoring 2 – 4 are categorised as having little and no need for information, patients scoring 5 – 7 are categorised as having an average need for information and the patients scoring 8 – 10 are considered as having high need for information(Berth et al., 2007; Laufenberg-Feldmann & Kappis, 2013).

Amsterdam Preoperative Anxiety and Information score (APAIS)(Berth et al., 2007):

Questions:	1	2	3	4	5
1- I am worried about the anesthetic	□	□	□	□	□
2- The anesthetic is on my mind continually	□	□	□	□	□
3-I would like to know as much as possible about the anesthetic	□	□	□	□	□
4- I am worried about the procedure	□	□	□	□	□
5-The procedure is on my mind continually	□	□	□	□	□
6- I would like to know as much as possible about the procedure	□	□	□	□	□

1:Not at all, .2:Somewhat, 3:Moderate, 4: Moderately high, 5:Extremely

RANDOMISATION

Participants will be randomly allocated to intervention or control via block randomisation on a 1:1 ratio (control: intervention) using a computerised random number sequence created by an independent statistician. In addition, randomisation will be stratified by surgery type (i.e., general surgery, neurosurgery, cardiac surgery, thoracic surgery, and orthopedic surgery).

ALLOCATION CONCEALMENT

Sealed opaque envelopes organised in numbered sequential order will be used to conceal the treatment allocation. Following screening, potential participants with moderate to high levels of

anxiety will be allocated to the treatment group (either intervention or control) contained in the next envelope.

INTERVENTION AND CONTROL

The control group will receive standard preoperative care only, while the intervention group will receive standard preoperative care plus VR. Standard preoperative care will include the preparation of the preoperative surgical site, preoperative bathing, preoperative hair removal, wearing theater gown, remove all jewelry, correct patient ID bracelet, and complete patient preoperative checklist and health record.

VIRTUAL REALITY INTERVENTION

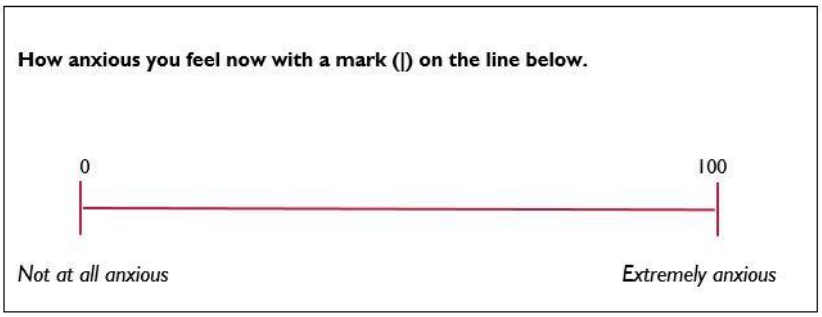
The participants will be given VR for 5 to 10 minutes, which has been suggested in the literature to be an effective time frame to apply VR without adverse side effects (Chow et al., 2016; Lawson, 2014). Exposure to VR should not last longer than 30 minutes to avoid VR adverse effects (Lawson, 2014). Sickness in virtual environments has been found to increase after ten minutes with head-mounted displays in simulator studies (Min, Chung, Min, & Sakamoto, 2004; Moss et al., 2011). The potential participants will be seated in a quiet environment and will be watching a natural scene with natural sound in the preoperative holding area. This area has been selected because evidence suggests that preoperative anxiety levels among adult surgical patients peaks in the preoperative holding area (Pokharel, Bhattarai, Tripathi, Khatiwada, & Subedi, 2011). The participant's face and forehead will be cleaned using skin-friendly antibacterial cleaning wipes before using the VR device. Disposable Hygiene Covers will also be used to protect the VR device.

PRIMARY OUTCOME

Perioperative anxiety as measured by the visual analog scale for anxiety (VAS-A).

The visual analog scale for anxiety (VAS-A) is valid, reliable, and frequently used for evaluation of perioperative anxiety that allows detection of high anxiety levels in the various surgical group

(Kindler, Harms, Amsler, Ihde-Scholl, & Scheidegger, 2000). The VAS-A consists of a 100 mm horizontal line that represents two behavioral extremes at either end of the continuum (i.e., 'not at all anxious' = 0, whereas 'extremely anxious' = 100). Potential participants will be asked to rate their level of anxiety on the VAS-A tool at three-time points in the study. On admission to the preoperative area **(T1),** immediately before surgery **(T2)**, and one hour after surgery **(T3).** Scores on the VAS-A of 25 or higher are said to reflect significant levels of anxiety (Kindler et al., 2000). The primary outcome will be collected by a Research Assistant at the research site, King Abdulaziz University Hospital.



Visual analog scale for anxiety (VAS-A)

SECONDARY OUTCOMES

1. **Stress** level as measured by:

A) Cortisol levels measured using Salivette® Cortisol.

Saliva cortisol levels are widely used as a biomarker for psychological stress and associated mental or physical diseases (Hellhammer, Wüst, & Kudielka, 2009; Reinhardt, Schmahl, Wüst, & Bohus, 2012). The Salivette® Cortisol is specially designed to achieve reliable analytical values from small volumes and very low cortisol samples (Sarested AG &Co). Saliva samples will be collected from participants at three-time points; on admission to the preoperative area **(T1)** and immediately before surgery **(T2)** and one hour after surgery **(T3)**. The samples will be collected by a Research Assistant at the research

site, King Abdulaziz University Hospital. The Samples will be collected, labelled, and sent to pathology by a researcher.

B) Heart rate (HR) as measured using Polar continuing heart rate sensor.

Increase HR is considered a physiological reaction to stressful situations. This reaction occurs as a result of the fight-or-flight response to a stressful situation, which is controlled by the autonomic nervous system (Gilbert & Gilbert, 2003). The participants will wear the Polar sensor (Figure 2) on their arm, and the HR will be analysed at three-time points. On admission to the preoperative area **(T1),** immediately before surgery **(T2)** and one hour after surgery **(T3)**.The HR will be measured by a Research Assistant at the research site, King Abdulaziz University Hospital.

2- **Postoperative pain** as measured by the visual analog scale for pain (VAS-P).

The visual analog scale for pain (VAS-P) is valid, reliable and commonly used to measure subjective pain (Hawker, Mian, Kendzerska, & French, 2011). The VAS-P consists of a 100 mm horizontal line that represents two behavioral extremes at either end of the continuum (i.e., 'no pain' = 0, whereas 'worst pain' = 100). The participants will be asked to rate their pain on the VAS-P tool at two-time points; on admission to the preoperative area **(T1)**, and one hour after surgery **(T3)**. This outcome will be collected by a research assistant at the research site, King Abdulaziz University Hospital.

3- **Patient satisfaction** as measured by the Leiden Perioperative Patient Satisfaction questionnaire (LPPSq).

The Leiden Perioperative Patient Satisfaction questionnaire (LPPSq) is a valid and reliable tool used to assess and measure different aspects of patient satisfaction with perioperative care (Caljouw, Van Beuzekom, & Boer, 2008). This questionnaire consists of 39 questions which are divided over six dimensions; (1) information provision (four questions), (2) discomfort and needs (seven questions), (3) fear and concern (seven questions), (4) professional competence (four questions), (5) staff -patient relationship (14 questions), and (6) service quality (three questions). Patient satisfaction with

perioperative care will be expressed by the mean satisfaction scores and the percentage of the maximum possible scores for each dimension (Caljouw et al., 2008). The participants will be asked to complete the questionnaire 24 hours after surgery before they are discharged **(T4).** This outcome will be collected by a research assistant at the research site, King Abdulaziz University Hospital.

4- **Hospital Length of Stay (LOS)** as measured from the date of admission to discharge from hospital.

The hospital length of stay is a proven recovery time indicator that can be used as a valid measure of robust outcomes in a variety of surgical fields and medical conditions (Laderman & Mate, 2016). The LOS will be measured in days that recorded on patients' discharge summary by subtracting the date of admission to hospital from the date of discharge from hospital (Abdelhak, Grostick, & Hanken, 2014). This outcome will be collected by a research assistant at the research site, King Abdulaziz University Hospital.

5- **Adverse effect of VR intervention at any time point** as measured by the Virtual Reality Symptom Questionnaire (VRSQ)

The Virtual Reality Symptom Questionnaire (VRSQ) is a valid and reliable measure used to evaluate the possible occurrence of symptoms of cybersickness, a type of motion sickness caused by exposure to VR (Sevinc & Berkman, 2020). This questionnaire assesses eight general physical side effects, (1) general discomfort, (2) fatigue, (3) boredom, (4) drowsiness, (5) headache, (6) dizziness, (7) concentration difficulties, and (8) nausea. It also assesses five visual effects (1) tired eyes, (2) aching eyes, (3) eyestrain, (4) blurred vision, and (5) difficulties focusing on a seven-point range from 0 to 6, with 0 indicating that the symptom is not present and 6 that the symptom is severe. The potential participants in the intervention group will be asked to complete the questionnaire immediately before surgery **(T2)**. This outcome will be collected by the PhD candidate.

Summary of Outcomes variables and Measures:

Variable	Scales/ Questionnaires/instruments
Primary outcome	
Perioperative anxiety	Visual Analog Scale for Anxiety (VAS-A)
Secondary outcomes	
1. Stress level	Saliva cortisol test Mean Heart rate
2. Postoperative pain	Visual Analog Scale for pain (VAS-P)
3. Patient satisfaction	Leiden Perioperative Patient Satisfaction Questionnaire (LPPSQ)
4. Hospital Length of Stay (LOS)	Date of admission to the hospital from the date of discharge
5. Adverse effect of VR intervention	The Virtual Reality Symptom Questionnaire (VRSQ)

STUDY PERIOD							
	Pre-admission	Preoperative phase			Postoperative phase		Discharge
TIMEPOINT**	$-t_1$	t_0	t_1	t_2	t_3	t_4	t_5
ENROLMENT:							
Eligibility	X						
Informed consent	X						
screen: using APAIS		X					
Allocation		X					
INTERVENTIONS:							
VR exposure				X			
ASSESSMENTS:							
Primary outcome: Perioperative anxiety			X	X	X		
Secondary outcomes: Stress level			X	X	X		
Postoperative pain			X		X		
Patient satisfaction						X	
Length of hospital stay							X
Virtual reality adverse effect				X			

**-t_1: pre-admission; t0: on admission; t1: on admission to preoperative area; t2: immediately before surgery (holding area); t3: one-hour post-surgery; t4: after 24 hours post-surgery and before discharge; t5: discharge.

OTHER DATA

Participant's socio-demographic data and surgery data will be collected, including age, gender, marital status, education level, occupation, and type of surgery, type and dose of anaesthetic and previous surgeries. This data will be collected from the participant's health record by the PhD candidate.

BLINDING

The Research Assistant involved in outcome data collection will be blinded to the group allocation, as will the statistician who will conduct the analysis. Clinicians (nurses, doctors, and other health providers) will not be told who is participating in the study nor their group allocation; however, it is acknowledged that it is not possible to prevent participants from sharing this information with them.

SAMPLE SIZE

Based on the previous study of Bekelis et al. (2017), a sample of 150 participants (75 per group) will give the study 80% power to detect a moderate effect size of 0.5 standard deviations between groups in the primary outcome variable, with a type 1 error rate of 5%. This calculation assumes a dropout rate of 15%.

STATISTICAL PLAN

Characteristics of groups will be summarised using counts and percentages for categorical variables and means and standard deviations for continuous variables. The primary outcome will be compared between groups at each follow-up time points using a linear mixed effects regression model, with fixed effects including treatment arm time (categorical), the interaction between treatment and time, and the baseline value of the outcome variable. Differences in mean VAS anxiety scores

between groups at each time point will be presented together with 95% confidence intervals and p-value. Continuous secondary outcomes with repeated measurements will be compared using the same model. Hospital length of stay will be compared using the rank-sum test. Patient satisfaction and the VRSQ will be compared between groups using an independent sample t-test.

3.2 AIM TWO

Identify the potential barriers and facilitators to the widespread implementation of VR for perioperative anxiety

THEORETICAL FRAMEWORK

The interview schedule and analysis will be informed by the Consolidated Framework for Implementation Research (CFIR), which is a highly organised explanatory framework that identifies factors that potentially influence implementation success (Damschroder et al., 2009). The CFIR is well suited to facilitate the rapid-cycle evaluation of the implementation of complex health care delivery interventions, as it provides a comprehensive framework for systematically identifying variables that may occur in various, multi-level contexts to affect implementation (Keith, Crosson, O'Malley, Cromp, & Taylor, 2017). The CFIR is organised across five domains; each of these could affect the implementation of an intervention. Firstly, the characteristics of the intervention, which are the features of an intervention that might influence implementation. There are eight constructs included in this domain. Secondly, the inner setting, which includes the implementing organization features that might influence implementation. There are 12 constructs included in this domain. Thirdly, the outer setting, which includes the external context or environment features that might influence implementation. There are four constructs included in this domain. Fourthly, characteristics of the Individuals involved in implementation that might influence implementation. There are five constructs included in this domain. Finally, the implementation process, which includes strategies that might influence implementation. Eight constructs are included in this domain (Damschroder & Lowery, 2013). See CFIR website http://cfirwiki.net/guide/app/index.html#/

PARTICIPANTS AND RECRUITMENT

Semi-structured interviews will be conducted with 20 stakeholders or until data saturation is reached. Saturation is reached by sampling to the point when redundancy or repetition of the data in a particular sample yields no new information (Crabtree, Miller, Crabtree, & Miller, 1999; Francis, Tatam, & Groves, 2010). Purposive maximum variation sampling will be used to capture a wide range of stakeholders' perspectives relating to the intervention. The semi-structured interviews will be conducted with a variety of stakeholders, including department heads, medical staff, nurses, administrative staff, and patients. Patients who signed the consent form agreeing to be interviewed will be followed up by the PhD candidate. Consecutive patients will be interviewed on a first come first-served basis before they are discharged. Other stakeholders will be contacted via email by the clinical research coordinator of the hospital on behaving the PhD candidate. The main principle underpinning participant selection for an interview will be that they experienced VR either as a clinician, administrator, or patient.

DATA COLLECTION AND ANALYSIS

All interviews will be conducted face-to-face by the PhD candidate at any time point from the beginning of the study to the end (estimated study period is four months). The potential participants will choose the location and time of the interview. The interviews will be audio-recorded and transcribed verbatim. The interviews will be structured around the five CFIR domains and included questions guides drawn from online CFIR http://cfirwiki.net/guide/app/guide.html as a start point for the PhD candidate to commence the interviews.

The following is a sample of semi-structured interview questions by stakeholder group:

Stakeholder Group	Question	CFIR Domain(s)	Constructs
Department Heads	How well do you think the VR will meet the needs of the individuals served by your department?	Outer setting	Patient Needs & Resources
Medical Staff	How complicated is the virtual reality?	Characteristics of the intervention	Complexity
Nurses	How confident are you that you will be able to successfully implement the VR?	Characteristics of individuals	Self-efficacy
Administrative Staff	What is the general level of receptivity in your organization to implementing the VR?	Inner setting	Implementation Climate
Department Heads	What are influential individuals saying about the VR? -Who are these influential individuals? -To what extent will they influence others' use of the VR the success of the implementation?	Process	Opinion leaders

The transcribed interviews will be analyzed using qualitative content analysis techniques, inspired by a deductive directed approach. This approach is recommended for CFIR (Keith et al., 2017). Data

analysis will begin simultaneously with data collection to guide the PhD candidate to modify the interview's questions. The analysis will be performed by two researchers independently by using the CFIR NVivo template - pre-populated with construct codes. Firstly, reading all transcripts to obtain a general overview to develop initial coding nodes and subnodes based on the domains and constructs of the CFIR framework (Damschroder et al., 2009). Secondly, units of analysis, such as sentences or longer semantic units, will be deductively coded into the nodes and subnodes. Thirdly, the coded text will then be subjected to a rating process following the recommended method by CFIR author (Damschroder et al., 2009). In the rating process, a deliberated consensus process will be used to assign a rating to each construct obtained from each interviewer. The ratings reflect the positive or negative influence and the magnitude or strength of each construct. To organize and manage a large amount of data, the software program NVivo version 12 will be used.

QUALITATIVE RIGOR

To enhance trustworthiness, credibility, transferability, dependability, and confirmability will be assessed. Credibility will be ensured by peer debriefing and support, which will occur by regular meetings with the research team to share study processes and findings to identify biases also to support each other. Transferability will be ensured by using a thick description, which provides a comprehensive explanation of the study context, including the cultural and social contexts during data collection. Dependability and conformability will be ensured by maintaining the audit trail, which includes audio recordings, transcripts of interviews, and documents for data analysis (Cypress, 2017; Moser & Korstjens, 2018).

3.3 ETHICAL CONSIDERATIONS

ETHICAL CONDUCT

Before the commencement of this study, approval of the study will be obtained from:

1. Ethical Committee at the University of Newcastle
2. Independent Ethical Committee (IEC) at King Abdulaziz University Hospital
3. Saudi Food and Drug Authority (SFDA).

RISK AND BENEFITS

There are possible risks associated with participating in this study include discomfort, headache, stomach awareness, nausea, vomiting, pallor, sweating, fatigue, drowsiness, disorientation, and apathy (Hicks & Durbin, 2011).; however, if the intervention is effective, people in the intervention group may experience reduced perioperative anxiety.

The participants will be monitored by the researcher continuously to assess for side effects. If a side effect occurs, the Virtual Reality session will be ceased immediately and treating doctor will be consulted.

PARTICIPANT RIGHTS

Potential participants will be told that involvement in the study is entirely their choice and their decision will not affect their relationship with their healthcare team or impact on their care. Participants will be given the option to withdraw from the study at any time without explanation and have their data destroyed.

PRIVACY

Each consenting patient will be assigned a participant ID number which will be used on all study documents. The spreadsheet linking the study number with the participant's personal identifying information will be kept separate from all other documents. Participants will not be individually identifiable in the reporting of the data.

DATA STORAGE

Electronic data will be kept on the password-protected in both the King Abdulaziz University Hospital research server and the University of Newcastle research server. Hard copy data will be stored in a locked cabinet in the office of the Chief Investigator. Only the named researchers will have access to the identifiable research data. The data will be kept for at least 15 years at the University of Newcastle before being destroyed as per policy and protocol (The University of Newcastle, 2020).