Clinical Trial Protocol

This document contains a hypothetical clinical trial study protocol that I have written using principles of experimental design. The study protocol contains important context and specific parameters for executing the hypothetical clinical trial contained in the Clinical Trial Simultation.ipynb notebook. I have thought carefully about the study design elements including how to design a control group as similar as possible to the experimental group and how to execute randomisation and blinding procedures to prevent revealing group allocation.

General Information

Title of the study: Evaluating the effectiveness of virtual reality (VR) therapies compared to the standard of care (SOC) for patients with chronic back pain.

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Background

Chronic back pain is a prevalent and debilitating condition that significantly impacts the quality of life for many individuals and costs the UK economy £10 billion every year (Maniadakis and Gray, 2000). To solve this problem researchers have developed an immersive hypnotherapy treatment delivered in Virtual Reality (VR), VR hypnotherapy is a hypnotic induction and analgesic suggestion delivered by customised VR software. The 7-minute self-care programme is voiced by hypnotherapist Ursula who guides patients through an experience that begins and ends in a virtual room. During the session a beautiful kaleidoscope graphic is revealed while the therapist coaches' patients to reflect on how they are feeling (developing somatic awareness) and how they might care for their needs. The aim of the study is to test whether the hypnotic VR therapy works to reduce pain intensity scores.

Potential risks and benefits:

It is hoped that the VR therapy will enable people to experience relief from chronic pain. There are no notable risks of taking part.

Aim(s) of the study:

To evaluate the effectiveness of a hypnotic VR therapy compared to standard of care (SOC) in reducing pain intensity levels for patients with chronic back pain.

Who can participate?

Adults 18+ with a confirmed diagnosis of non-specific chronic back pain for at least 3 months.

What does the study involve?

Participants are randomly allocated to the VR therapy group, or the VR documentary group. The VR treatment comprises about six 7-minute VR sessions, whilst the VR documentary group comprises six 7-minute nature documentaries. Both groups will continue with their standard of care treatments throughout the study which may be any combination of prescription pain relief, physiotherapy and talking therapies. Baseline assessments are conducted at the start of the study and after 6 (post-treatment) and 24 weeks (follow-up) to understand the long-term effects of VR. The primary outcome is self-reported pain intensity levels using the McGill pain Questionnaire (MPQ).

Study Design:

- Randomised controlled trial
- Double-blind (participants and outcome assessors blinded to treatment allocation)
- Two parallel arms:
    1. VR therapy group (experimental)
    2. VR documentary group (control)

Treatment Arms:

1. VR Therapy Group:
    - Intervention: Participate in a 7-minute 'self-care' VR session designed by a hypnotherapist, once per week for 6 weeks
    - Continued existing treatment plans as per standard care
2. **VR Documentary Group (Control):**
    - Intervention: Watch a 7-minute nature documentary in VR, once per week for 6 weeks
    - Continued existing treatment plans as per standard care

Duration, assessments and follow up:

- Pain and quality of life assessments at baseline, 6 weeks (post-treatment), and 24 weeks (follow-up)

Randomisation and blinding procedures

Participant recruitment and randomisation will be operated by an independent researcher who has no other touch points in the study. Participants will be allocated to the VR therapy or VR documentary group using a random number generator and will receive their group allocation in a sealed envelope. A team of study coordinators will be responsible for setting up the intervention delivery of each session.

Separately, the team of assessors will be blinded to the group allocation and will have no access to information that could reveal participant group assignment. They will conduct all outcome assessments (pain, quality of life) at baseline, 6 weeks, and 24 weeks.

Participants will be instructed not to disclose their group assignment or provide information about the intervention they received to each other, the study co-ordinators or the team of assessors.

Eligibility

Inclusion criteria:

1. Adults aged 18 years or older.
2. Diagnosis of non-specific chronic back pain for at least 3 months, confirmed by a General Practitioner or Electronic Health Records (EHR).
3. Ability to understand and comply with study procedures, including the use of virtual reality equipment.
4. Willingness to provide informed consent.

Exclusion criteria (if applicable):

1. Unable to attempt a McGill Pain Questionnaire (MPQ) the primary outcome measure at baseline
2. Photosensitive epilepsy
3. Significant visual, auditory, or balance impairment (e.g. severe motion sickness, vertigo)
4. Insufficient comprehension of English
5. Current or recent (within the past 6 months) substance abuse or dependence.
6. Participation in another interventional clinical trial that could confound the study results.
7. Inability to attend study visits or comply with study procedures.
8. Specific back pain conditions or causes that may require different treatment approaches, such as:
    1. Acute back pain (less than 3 months duration)
    2. Spinal cord compression or cauda equina syndrome
    3. Unstable spinal fractures
    4. Active spinal infection or malignancy
9. Planned or scheduled back surgery during the study period
10. Significant cognitive impairment or psychiatric conditions that may impact the ability to understand and follow study procedures (e.g., dementia, severe intellectual disability, active psychosis).
11. Current active suicidal plans

Strategies for recruitment

- **GP Practice Networks**: Collaborate with general practitioners (GPs) and use EHR systems to find eligible patients. Automated alerts can be set up to notify GPs when their patients qualify for a trial.

Study Procedures

- Schedule of assessments and procedures

    - Baseline assessment (0 weeks)
    - Post-treatment assessment (6 weeks)
    - Follow-up assessment (24 weeks)
- Description of assessments and outcome measures
    - Primary outcome measure: Pain levels measured using the McGill Pain Questionnaire (MPQ)
    - Secondary outcome measure: Quality of life measured using the five-level EQ-5D

Statistical Considerations

- A minimum of 40 patients per group (VR therapy and VR documentary) is required to achieve a power of 80.3% for detecting a clinically significant difference in the primary outcome measure.
- Per-protocol (PP) analysis: A secondary analysis will include only participants who completed the full course of treatment and did not have major protocol deviations.
- Primary outcome (pain levels):
    - Mixed-effects model for repeated measures (MMRM) analysis to compare the change in MPQ scores from baseline to 6 weeks and 24 weeks between the two groups.