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The VRIMM study: Virtual Reality for IMMunisation pain in young children—protocol for a randomised controlled trial

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ABSTRACT

Introduction Pain caused by routine immunisations is distressing to children, their parents and those administering injections. If poorly managed, it can lead to anxiety about future medical procedures, needle phobia and avoidance of future vaccinations and other medical treatment. Several strategies, such as distraction, are used to manage the distress associated with routine immunisations. Virtual reality (VR), a technology which transports users into an immersive 'virtual world', has been used to manage pain and distress in various settings such as burns dressing changes and dental treatments. In this study, we aim to compare the effectiveness of VR to standard care in a general practice setting as a distraction technique to reduce pain and distress in 4-year-old children receiving routine immunisations.

Methods and analysis The study is a randomised controlled clinical trial comparing VR with standard care in 100 children receiving routine 4-year-old vaccination. Children attending a single general practice in metropolitan Melbourne, Australia will be allocated using blocked randomisation to either VR or standard care. Children in the intervention group will receive VR intervention prior to vaccination in addition to standard care; the control group will receive standard care. The primary outcome is the difference in the child's self-rated pain scores between the VR intervention and control groups measured using The Faces Pain Scale-Revised. Secondary outcomes include another measure of self-rated pain (the Poker Chip Tool), parent/guardian and healthcare provider ratings of pain (standard 100 mm visual analogue scales) and adverse effects.

Ethics and dissemination Ethics approval has been obtained in Australia from the Royal Australian College of General Practitioners National Research and Evaluation Ethics Committee (NREEC 18-010). Recruitment commenced in July 2019. We plan to submit study findings for publication in a peer-reviewed journal and presentation at relevant conferences.

Trial registration number ACTRN12618001363279.

Strengths and limitations of this study

- This study tests the effectiveness of virtual reality (VR) to reduce pain and distress in young children undergoing vaccinations.
- The study compares use of VR to standard care in a general practice setting with a primary patient-centred outcome—self-rated pain score.
- Blinding is not possible due to the differences between VR and standard care.
- The study is from a single metropolitan general practice in Melbourne, Australia, so may not be generalisable to other settings.

INTRODUCTION

Background and rationale

The most common source of iatrogenic pain in childhood is due to needles for routine immunisations.[1] The associated pain is distressing for children, their parents and healthcare providers.[2] One in four adults is estimated to have a fear of needles,[3] which often develops in childhood.[4] If immunisation pain and distress is poorly managed, this can result in anxiety prior to future medical procedures, and healthcare avoidance behaviour.[5] It has been reported that up to 10% of the population avoid vaccination due to needle phobia.[5]

The current Victorian immunisation schedule recommends a series of injections consistent with the Australian Immunisation Handbook, as well as annual influenza vaccination for children aged 6 months to less than 5 years of age.[6]

If all recommended vaccines are administered, a child will have received nine needles prior to their first birthday, and another five in their second year of life. As the child matures, their ability to conceptualise and react to the prospect of a painful experience increases. The 4-year-old immunisation is often challenging for all involved—the child, the parents and those administering the vaccine.

Various techniques are recommended to reduce the pain and distress associated with immunisation. These include optimising positioning and injection techniques, tactile stimulation, topical anaesthesia and various distraction techniques.[2] This study seeks to compare these standard techniques with an increasingly popular technology—virtual reality (VR)—as a distraction technique in young children undergoing vaccination.

VR is a computer system which allows users to be immersed in and explore an interactive three-dimensional environment.[7] It is often delivered by the use of a purpose-designed headset, which may be augmented by other sensory systems such as treadmills or gloves.[7] In recent years, there has been increased access to the technology, with it now being available through the purchase of an inexpensive headset and the use of a smartphone.

VR has been successfully utilised in various settings where children may experience painful procedures, including application of burns dressings,[8–13] dental treatment,[14] intravenous cannula placement[15] and medical oncology treatments.[16 17]

Although VR appears to be safe and effective for the management of pain, the mechanism is yet to be fully elucidated.[18] However, functional MRI studies have demonstrated that VR distraction for procedural pain in burns patients led to reductions in pain-related brain activity.[19] This has led to theories that suggest that a patient's attention is directed into a virtual world, leaving less attention available to process incoming signals from pain receptors.[19] Other effects on pain perception relate to emotion, concentration and memory.[20]

There has been some public discussion regarding a successful pilot study of the use of VR for children undergoing vaccination[21] however, the study is yet to be published in the peer-reviewed literature.

Objectives

Our study aims to determine the effectiveness of the use of VR to reduce the pain and distress associated with childhood vaccination in the general practice setting.

The hypothesis relating to our primary aim is that VR content delivered through a headset will reduce pain and distress associated with childhood vaccination compared with the use of standard techniques used in the primary care setting.

METHODS

Study design

This is a randomised controlled superiority trial comparing the effectiveness of VR to standard care for the pain and distress associated with vaccination of 4-year-old children in the general practice setting.

Setting

The study will be conducted in a single general practice in metropolitan Melbourne. The clinic is staffed by 19 doctors (10 full-time equivalent), and has practice nurses available from 8:30 to 20:30 during weekdays, and from 9:00 to 13:00 on Saturdays. The clinic provides routine vaccinations to approximately 120 4-year-old children per year.

Participants

Parents/guardians of children attending the clinic for their routine 4-year-old immunisations will be approached to participate in the study. In Australia, the recommended 4-year-old immunisations are included in a single combination injection, which includes diphtheria, tetanus, pertussis and poliomyelitis. In Victoria, the available vaccine brands are *Infanrix IPV* (GlaxoSmithKline) or *Quadracel* (Sanofi Pasteur Inc).[6]

Consent

Written informed consent from the child's parent/legal guardian will be undertaken prior to any study-related procedures occurring.

Recruitment

Written information and a participant information and consent form about the study will be provided by reception staff to all parents/carers who attend with their child for a planned 4-year-old vaccination.

It is routine practice for the child to be reviewed by a doctor prior to vaccine administration. During this time, the doctor will assess suitability for study participation, and—if eligible—provide a verbal explanation of the study in lay terms to each parent/carer. At this time, the parent/carer will have the opportunity to ask questions.

Once the child is moved to the procedure room, nursing staff will demonstrate the equipment and seek assent from the child, and formal written consent from the parent/guardian, which will be documented on a Participant Information and Consent Form.

Inclusion criteria

1. Children attending the general practice for their 4-year-old immunisations.
2. Judged by their treating doctor to be able to comply with the study protocol for its duration.
3. Written informed consent signed and dated by parent/legal guardian according to local regulations.

Exclusion criteria

1. Significant medical disease or condition that is likely to interfere with the child's ability to participate in the study.
2. Inability of the parent/ legal guardian to provide informed consent.
3. Known needle phobia is not an exclusion criteria.

Participant safety and criteria for withdrawal

In this study, an adverse event will be defined as any unfavourable or unintended sign or symptom temporally associated with the use of the VR equipment, whether or not considered related to the equipment.

All adverse events will be documented in the clinical research form (CRF), and serious adverse events will be reported to the overseeing ethics committee.

Withdrawals

Participants will be withdrawn from the study if:

1. Consent is withdrawn.
2. The treating doctor or nurse believes that continuation in the study is no longer in the participant's best interests (which may be as a result of an adverse event related to the VR equipment, or the rare occurrence of an allergic reaction to the vaccine).
3. The participant is unable to participate with the study protocol.

In all cases, the reason for withdrawal from the study will be documented in the relevant section of the CRF.

Randomisation and blinding

Random allocation to either VR or standard care will occur through the use of blocked randomisation, with block sizes randomly varying from four to eight. The allocation sequence was generated by a study author (SC) using computer-generated random numbers. This occurred independently of any staff involved in recruitment of patients for the study, and SC did not recruit any patients into the study. Allocation will be concealed in opaque study envelopes which will be opened once the child's parent/carer has signed the consent form.

Due to the nature of the VR intervention, it is impossible to blind patients, carers, or observers to the intervention.

Intervention

The study intervention is VR digital content delivered through a purpose-designed headset. VR hardware is a Google Pixel XL and Google Daydream VR headset. The hardware/software unit is a VR Apparatus Diversion therapy device (TGA approved Class 1 medical device (ID 156474)), manufactured by Smileyscope Pty Ltd. The device was purchased from the company at recommended retail price, and the company has no role in protocol design, patient recruitment, data analysis or decision to publish study findings.

The intervention group will receive the VR intervention prior to vaccine administration in addition to standard care, while the control group will receive standard care alone (figure 1). The VR headset plays an interactive marine adventure which begins with a relaxation sequence, and progresses to underwater scenes, including gaze-based tracking of virtual fish. The same VR intervention, which lasts for 1 min is provided to all children, with the injection provided approximately 30 s after commencement of the sequence.

Standard care within the clinic includes a range of interventions used to reduce the pain and distress of immunisations. These vary, depending on the interaction between nursing staff and children, and include distraction through conversation about age-appropriate interests such as pets, siblings, or an upcoming birthday,

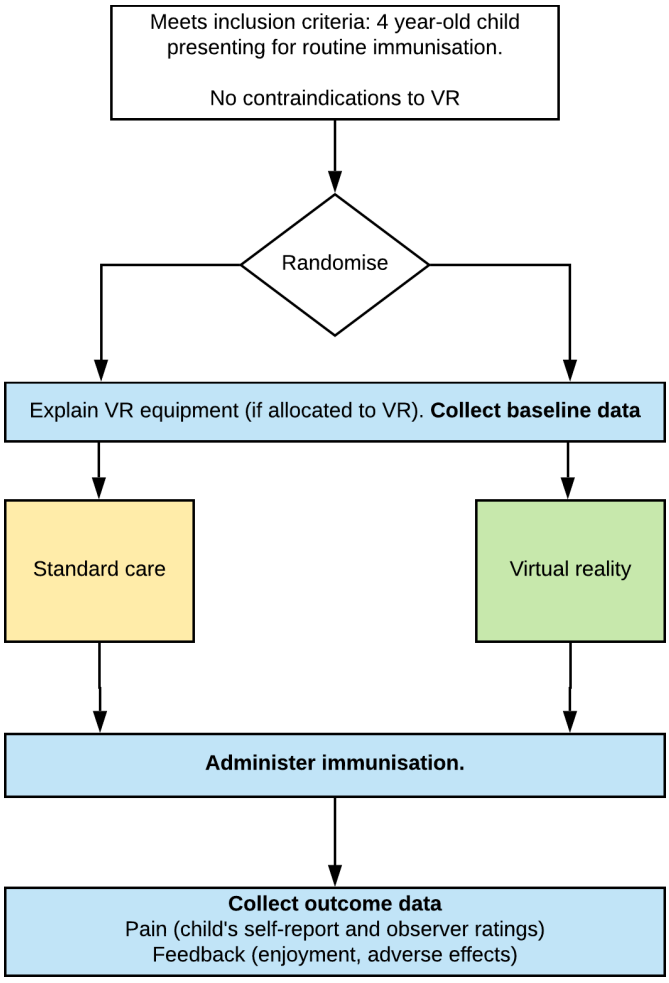

Figure 1 Study flow diagram. VR, virtual reality.

reading a book or watching a video on a parent's phone. The interventions used in the standard care group will be documented. Topical anaesthetics are not routinely offered by the clinic.

Outcome measures

The primary end-point is the difference in self-rated pain scores between the intervention and control groups. Different self-report measurement tools are recommended for different age groups, consistent with the expected verbal and emotional level attained. The Faces Pain Scale-Revised (FPS-R) is recommended for those aged 4–16,[22] and will be the primary outcome measure for the study.

To allow for the likely range of developmental abilities in normal 4-year-old children, the Poker Chip Tool[23] will be a secondary outcome measure used for self-reported pain. This tool, recommended for 3–6 year olds, quantifies pain intensity by using four objects such as counters or poker chips to represent amounts of pain. Children indicate how much hurt they have by referring to one poker chip as a little bit of hurt, two as a little more hurt, three as more yet, and four as the most hurt they could ever have.[24]

Additional secondary outcome measures include observer ratings of pain and distress by parents/guardians and healthcare providers, which will be recorded on standard 100 mm visual analogue scales (VAS), satisfaction with the intervention, and measurement of any adverse events relating to the use of the VR intervention.

Data measures

Prior to immunisation, the following data will be collected through a questionnaire administered to the parent/carer: child's age, gender, previous exposure to VR, languages spoken at home other than English, significant medical history, visual, behavioural or developmental concerns and level of apprehension towards needles (rated as low, medium or high).

During the procedure, additional data will be collected and recorded on the CRF. This will include distraction and other interventions used, needle experience (Pieces of Hurt and FPS-R), observed pain and distress (parent/carer) and observed pain and distress (healthcare provider).

Following the procedure, further information recorded will include the proceduralist's experience with vaccine administration (<10, 10–50, 51–100, >100), and the VR experience from patient and parent/carer (enjoyment, rated as low, medium or high, and any adverse effects).

Data management

Study data will be obtained by trained nursing staff, using the study CRF. The investigators are responsible for ensuring the accuracy, completeness, legibility and timeliness of the data reported. The documents/forms will be stored securely, archived and destroyed in compliance with local regulations. Study data will be stored on a password-protected file, and securely deleted in compliance with local regulations.

Ongoing surveillance and adherence to the study protocol will be monitored by the principal investigators (KE and SC). All serious adverse events and protocol violations will be submitted to the approving Human Research Ethics Committee (HREC).

Monitoring

Due to the brief nature of the intervention, a data monitoring committee was not deemed necessary, nor was it required after review by the approving HREC. No interim analysis or stopping guidelines were planned.

SAMPLE SIZE AND STATISTICAL ANALYSIS PLAN

Sample size

GraphPad Statmate (V.2.0 for Windows, GraphPad Software, San Diego, California, USA; www.graphpad.com) was used for sample size determination. Forty-two children in each arm of study would be able to demonstrate a difference of 2 in the 10-point FPS–R score, with the use of an unpaired t-test with a power of 0.8, an α of 0.05 and a SD of 3.2. The SD of 3.2 is a conservative estimate based on previous validation of the FPS-R in children aged 4–6 years in the hospital setting.[22] A difference of two points (one face) is considered the minimum clinically significant difference in the FPS-R.[25]

To allow for any attrition due to inability to comply with the VR treatment, the study sample size has been set at 100 patients in total, with recruited children randomised 1:1 to receive VR or standard care.

Statistical analysis plan

An intention-to-treat analysis will be performed. Continuous data such as the primary and secondary pain scores will be assessed to determine whether they are normally distributed. If normally distributed, results will be presented using mean and SD, and analysed using two-tailed t-tests. If not normally distributed, then the data will be presented using median and IQR, and the Mann-Whitney test will be used to determine differences between treatment groups.

Categorical data will be presented using number and percentage, and analysed using the χ^2 test or Fisher's exact test as appropriate.

Summary descriptive statistics (number and percentage) will be used for baseline demographic and clinical data. Exploratory subgroup analysis will be used to compare results between the following groups: (1) those with versus without previous exposure to VR, and (2) those with a parent-rated high level of apprehension towards needles versus those with a low or medium level of apprehension towards needles.

Outcomes and significance

Although VR has been successfully applied in other settings where children undergo painful procedures, there is no published data on its use in vaccination. The use of this technology in the General Practice setting could open the door to further studies on its use in vaccination in older age groups as well as other minor procedures.

Limitations

The intervention of VR cannot be blinded, and a certain clinician-driven or parent/guardian-driven bias may occur.

Current status of the trial

The study enrolment commenced in June 2019, with 70 children recruited by February 2020. The expected end date of recruitment to this trial is July 2020.

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Contributors SC and KE were responsible for identifying the research question and contributing to the drafting of the protocol. KE, HT, RM, LB, DR, KV, AD, SM, FB, MJW and SC have contributed to the development of the protocol and study design. SC, KE, HT and MJW were responsible for drafting this manuscript, with comments and feedback from all other authors. All authors attest to having approved the final manuscript. KE and SC take responsibility for the manuscript as a whole.

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Competing interests The VR headset was purchased using grant funding.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval This study protocol has been reviewed and approved by the Royal Australian College of General Practitioners National Research and Evaluation Ethics Committee (NREEC 18-010). Any protocol modifications will be approved by the NREEC, uploaded to the Australian New Zealand Clinical Trials Registry, and made available on request. We plan to submit study findings for publication in a peer-reviewed journal and presentation at relevant conferences. Authorship of all publications will be decided by mutual consensus of the research team.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

1 Schechter NL, Zempsky WT, Cohen LL, *et al*. Pain reduction during pediatric immunizations: evidence-based review and recommendations. *Pediatrics* 2007;119:e1184–98.
2 Taddio A, Appleton M, Bortolussi R, *et al*. Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline. *CMAJ* 2010;182:E843–55.
3 statement G. Guideline statement: management of procedure-related pain in children and adolescents. *J Paediatr Child Health* 2006;42 Suppl 1:S1–29.
4 Hamilton JG. Needle phobia: a neglected diagnosis. *J Fam Pract* 1995;41:169–75.
5 Taddio A, Chambers CT, Halperin SA, *et al*. Inadequate pain management during routine childhood immunizations: the nerve of it. *Clin Ther* 2009;31 Suppl 2:S152–67.
6 Department of Health and Human Services. Immunisation schedule Victoria and vaccine eligibility criteria, 2018. Available: www.health.vic.gov.au/public-health/immunisation/ [Accessed 26 Apr 2018].
7 What is Virtual Reality? Virtual reality Society, United Kingdom. Available: https://www.vrs.org.uk/ [Accessed 26 Apr 2018].
8 Chan EA, Chung JW, Wong TK, *et al*. Application of a virtual reality prototype for pain relief of pediatric burn in Taiwan. *J Clin Nurs* 2007;16:786–93.
9 Faber AW, Patterson DR, Bremer M. Repeated use of immersive virtual reality therapy to control pain during wound dressing changes in pediatric and adult burn patients. *J Burn Care Res* 2013;34:563–8.
10 Jeffs D, Dorman D, Brown S, *et al*. Effect of virtual reality on adolescent pain during burn wound care. *J Burn Care Res* 2014;35:395–408.
11 Khadra C, Ballard A, Déry J, *et al*. Projector-based virtual reality dome environment for procedural pain and anxiety in young children with burn injuries: a pilot study. *J Pain Res* 2018;11:343–53.
12 Kipping B, Rodger S, Miller K, *et al*. Virtual reality for acute pain reduction in adolescents undergoing burn wound care: a prospective randomized controlled trial. *Burns* 2012;38:650–7.
13 Mott J, Bucolo S, Cuttle L, *et al*. The efficacy of an augmented virtual reality system to alleviate pain in children undergoing burns dressing changes: a randomised controlled trial. *Burns* 2008;34:803–8.
14 Asl Aminabadi N, Erfanparast L, Sohrabi A, *et al*. The impact of virtual reality distraction on pain and anxiety during dental treatment in 4-6 year-old children: a randomized controlled clinical trial. *J Dent Res Dent Clin Dent Prospects* 2012;6:117–24.
15 Gold JI, Kim SH, Kant AJ, *et al*. Effectiveness of virtual reality for pediatric pain distraction during i.v. placement. *Cyberpsychol Behav* 2006;9:207–12.
16 Gershon J, Zimand E, Lemos R, *et al*. Use of virtual reality as a distractor for painful procedures in a patient with pediatric cancer: a case study. *Cyberpsychol Behav* 2003;6:657–61.
17 Nilsson S, Finnström B, Kokinsky E, *et al*. The use of virtual reality for needle-related procedural pain and distress in children and adolescents in a paediatric oncology unit. *Eur J Oncol Nurs* 2009;13:102–9.
18 Arane K, Behboudi A, Goldman RD. Virtual reality for pain and anxiety management in children. *Can Fam Physician* 2017;63:932–4.
19 Hoffman HG, Chambers GT, Meyer WJ, *et al*. Virtual reality as an adjunctive non-pharmacologic analgesic for acute burn pain during medical procedures. *Ann Behav Med* 2011;41:183–91.
20 Gold JI, Belmont KA, Thomas DA. The neurobiology of virtual reality pain attenuation. *Cyberpsychol Behav* 2007;10:536–44.
21 Mack H. Pilot study shows VR goggles reduce fear, pain in children during vaccination. Available: www.mobihealthnews.com/content/pilot-study-shows-vr-goggles-reduce-fear-pain-children-during-vaccination [Accessed 26 Apr 2018].
22 Hicks CL, von Baeyer CL, Spafford PA, *et al*. The faces pain Scale-Revised: toward a common metric in pediatric pain measurement. *Pain* 2001;93:173–83.
23 Hester NFR, Kristensen K. Measurement of pain in children: generalizability and validity of the pain ladder and the poker chip tool. In: Tyler DKE, ed. *Pediatric pain: advances in pain research and therapy*. New York: Raven Press, 1990: 79–84.
24 von Baeyer CL. Children's self-reports of pain intensity: scale selection, limitations and interpretation. *Pain Res Manag* 2006;11:157–62.
25 Tsze DS, Hirschfeld G, von Baeyer CL, *et al*. Clinically significant differences in acute pain measured on self-report pain scales in children. *Acad Emerg Med* 2015;22:415–22.