

CADTH Horizon Scan

# An Overview of Clinical Applications of Virtual and Augmented Reality

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## Key Messages

- This Horizon Scan summarizes the available information regarding virtual reality (VR) and augmented reality (AR) interventions for various clinical applications. While the technologies are not new, the use of VR and AR as clinical interventions in health care is still emerging in Canadian health care systems.
- VR interventions have been studied in various clinical applications, including acute and chronic pain, stroke, traumatic brain injury, cerebral palsy, Parkinson disease, autism spectrum disorder, anxiety and depression, mental health in older adults, and attention-deficit/hyperactivity disorder (ADHD). Limited information on AR interventions was identified in this Horizon Scan.
- There is a wide range of VR and AR hardware and software available that varies in cost and complexity. Much of this hardware and software is commercially available; however, some have been developed specifically for clinical use.
- There are several VR interventions for various clinical indications cleared by the FDA and available in the US.
- Many factors should be taken into account when considering implementing a VR or AR intervention, including those related to safety, privacy, and access. It will be essential to ensure equitable access to VR and AR interventions so that their introduction does not exacerbate health inequities.

## Purpose

The purpose of this Horizon Scan is to present health care stakeholders in Canada with an overview of information related to VR and AR for various clinical applications, a description of some of the published studies, and a summary of some important considerations associated with the potential implementation of the technologies should emerging evidence demonstrate value. This report is not a systematic review and does not involve critical appraisal or include a detailed summary of study findings. It is not intended to provide recommendations for or against using the technology.

## Methods

### Literature Search Strategy

A limited literature search was conducted by an information specialist on critical resources, including MEDLINE, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, and a focused internet search. The search strategy comprised controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The search concepts were augmented reality, clinical applications, and pediatrics. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was completed on September 20, 2022 and limited to English-language documents published since January 1, 2017.

## Study Selection

One author screened the literature search results and reviewed the full text of all potentially relevant studies. Studies were considered for inclusion if the intervention was VR, AR, or mixed reality and the technology was used as a health intervention with the goal to have an impact on health outcomes. Studies in which the technology user was the health care provider (e.g., the technology was used for provider training or to assist with surgical procedures) were excluded.

## Peer Review

One clinical expert reviewed a draft version of this bulletin. Expert comments and feedback were considered in the final report.

## Background

Extended reality is an umbrella term that covers VR, AR, and mixed reality.<sup>1</sup> VR is a digital environment made up entirely of computer-generated content in which people can interact with their surroundings in real-time.<sup>2</sup> The level of immersion the user experiences in the virtual world can vary depending on the VR system used.<sup>3</sup> Nonimmersive VR involves screens to reproduce images of the virtual world.<sup>3</sup> Immersive VR systems provide a complete simulated experience through head-mounted displays and audio and haptic devices.<sup>3</sup> AR integrates virtual elements with reality by superimposing digital elements onto the real world as seen on a screen.<sup>1,4</sup> Unlike VR, which replaces the real-world environment with a virtual world, AR augments a user's perception of the real world without entirely obscuring it.<sup>4</sup> Mixed reality is a hybrid of virtual and real-world settings that creates an immersive environment where users can engage with virtual items as if they were in the real world.<sup>2</sup> Mixed reality is more immersive than AR and involves wearable hardware that enables interaction between the real and virtual worlds.<sup>2</sup>

Extended reality technologies have been used in health care for over a decade. For example, the first VR clinic opened in Korea in 2005 for people with schizophrenia, social phobia, and alcohol use disorder.<sup>5</sup> Initially, the cost of these technologies was prohibitive; however, the development of smartphone technology and the emergence of more affordable devices such as head-mounted displays have made the use of extended reality in health care more feasible.<sup>5,6</sup> There has been growing interest in these technologies leading to studies in a wide range of health care applications.<sup>2,4</sup> These include biomedical engineering, virtual training for surgeries and medical devices, medical education, telemedicine, telehealth, telerehabilitation, and telemonitoring, as part of diagnosis or treatment for various clinical indications.<sup>2,4</sup>

The current standard of care for multiple disease areas, such as acute and chronic pain and ADHD, includes using medications.<sup>6,7</sup> However, these medications may be associated with serious side effects and are not always effective.<sup>6,7</sup> There is interest in investigating alternative therapies, including VR,- or AR-based interventions. Additionally, VR-based interventions could provide cost savings or be more feasible than alternative options in some cases. For example, it may be more viable and less costly to use VR-based exposure therapy for flight anxiety rather than purchasing a plane ticket.<sup>8</sup> The use of VR in patient care offers many potential advantages, including creating environments that meet specific patient needs, facilitating real-time feedback, providing an entertaining tool that may increase patient motivation,

providing experiences that are fully controlled and may be better suited for repeated practice, and creating experiences which may be impossible in the real world.<sup>3,9,10</sup> There are also potential challenges to the use of extended reality technologies for health care applications, including costs (e.g., hardware, software development), technical issues (e.g., computational limitations, tracking issues, battery consumption), privacy and security concerns (e.g., hacking, data collection), and safety (e.g., side effects, addiction).<sup>4</sup> An additional challenge to be considered is the ability of health care providers and patients to use these technologies effectively. Training for health care providers and patients on these technologies may be required.

This Horizon Scan aims to provide an overview of emerging clinical applications of extended reality technologies, focusing on applications in which the technology is used as a health intervention and aims to affect the health outcomes of the user (e.g., VR distraction therapy). While there is also a range of technologies being developed to be used by and for health care providers (e.g., AR-assisted surgical procedures), these are not the focus of and are not included in this report.

## The Technologies

Extended Reality technologies used in clinical applications include hardware and software that are commercially available and developed explicitly for use in health care.

Devices used for AR can include smartphones, tablets, specialized glasses, and headsets.<sup>4,11</sup> Smartphones and tablets can combine virtual elements with the real world as seen through cameras.<sup>11</sup> AR glasses and headsets are semitransparent and overlay virtual information onto the real-world.<sup>11</sup> One example is the Microsoft HoloLens which is an AR/mixed reality headset that includes a self-contained computer with tracking sensors, 3-D mapping capabilities, a camera, speakers, and WiFi connectivity.<sup>4</sup>

Devices like computers and video game systems can be used for nonimmersive VR. In nonimmersive VR, the virtual environment is displayed on a screen. Patients can interact with the environment using various devices such as a keyboard and mouse, controllers, and motion-tracking systems.<sup>12</sup> Video game systems that have been used in research into clinical applications of nonimmersive VR include Nintendo Wii, PlayStation EyeToy, and Xbox Kinect.<sup>12</sup>

Immersive VR can involve surround-screen, projection-based, head-mounted, or boom-mounted displays.<sup>10</sup> Surround-screen projection-based displays (e.g., Cave Automatic Virtual Environment) typically have several projection walls and motion trackers that track users' head and body movements.<sup>10</sup> These displays allow multiple users to simultaneously experience the virtual world in the same physical environment.<sup>10</sup> VR head-mounted displays are small monitors that are worn on the head or built-in as part of a helmet and positioned so that they take up the entire field of view or ensure that the display is always within the field of view of the user.<sup>13</sup> There are multiple commercially available head-mounted displays, including Oculus Rift, HTC VIVE, and Samsung Gear.<sup>4,10</sup> head-mounted displays can be combined with other devices such as joysticks, haptic gloves, and motion sensors.<sup>3,10</sup> Some head-mounted displays require a computer or video game system, whereas others are standalone devices.<sup>2</sup> Boom-mounted displays are a variation of head-mounted displays in which the display is suspended from an articulated arm and held to the user's face with handles.<sup>10</sup>

VR software content can include virtual experiences, simulations, and games.<sup>14</sup> In VR software used in VR exposure therapy, patients are exposed to their source of fear or anxiety in a controlled virtual environment.<sup>14</sup> VR software that has been used in distraction therapy for pain includes VR experiences such as a rollercoaster ride, swimming underwater, travelling around the world, and enjoying nature.<sup>15</sup> VR programs studied that involved people with autism spectrum disorder include simulations that aim to teach various skills such as driving, interviewing, supermarket shopping, and emotion recognition.<sup>10,16</sup> Some VR interventions involve commercially available games, whereas others use games developed specifically for health applications.<sup>14</sup> Health games can be designed to address limitations in physical or mental functions, build specific skills, or promote positive behaviours.<sup>14</sup> Health games often involve puzzles, graded difficulty, matching patterns, repetitive exercises, exploring an environment, or a pleasant and distracting experience.<sup>14</sup> An example of a health game is SnowWorld, the first immersive VR game designed to reduce pain in patients who have suffered burns.<sup>14,17</sup> In this game, patients are tasked with throwing snowballs at snowmen and penguins.<sup>14</sup> Additionally, AR and VR software can be used to retrain people in activities of daily living such as self-care, work, or leisure.

There are also VR systems developed for clinical use that include both hardware and software. An example of a VR system explicitly developed for clinical use is Immersive Rehabilitation Exercise (IREX), an upper and lower-extremity exercise system for rehabilitation.<sup>18</sup> IREX consists of a camera connected to a computer that places a full body image of the patient onto the screen within a VR game.<sup>18</sup> IREX has various software applications in which people can enter multiple virtual environments and engage in physical activities that target different body functions.<sup>18</sup> Another example of a VR system developed for use in health care is BikeAround which is intended for use by older adults experiencing physical disabilities, memory problems, or cognitive disabilities (e.g., dementia or Alzheimer disease).<sup>19</sup> BikeAround consists of an exercise bike, a computer, and a flatscreen or dome with a projector that displays images using Google Street View.<sup>19</sup> Users can select any address displayed on the screen and then ride through the virtual path.<sup>19</sup>

## Availability

At the time of writing, there are no VR or AR devices or software as medical devices intended for therapeutic use that have been authorized by Health Canada.

There are several VR systems for use in health care cleared by the FDA in the US. RelieVRx (formerly EaseVRx; AppliedVR, US) is a VR system the FDA cleared in 2021 for adjunctive treatment of chronic low back pain in adults.<sup>20,21</sup> The RelieVRx system was developed for at-home use and includes software and a VR headset, controller, and breathing amplifier attached to the headset for use in deep breathing exercises.<sup>21</sup> The VR therapy program includes pain education, diaphragmatic breathing, pain distraction, and relaxation.<sup>20</sup>

Luminopia (Luminopia Inc., US) is a VR software indicated for improvement in visual acuity in children aged 4 to 7 with amblyopia (commonly referred to as 'lazy eye') that the FDA cleared in 2021.<sup>22,23</sup> Luminopia was designed to be used with commercially available head-mounted displays in a home environment.<sup>23</sup> The therapy involves watching television shows in a VR head-mounted display in which images are presented differently to each eye.<sup>23</sup>

EYE-SYNC (NeuroSync, US), a VR system that uses eye tracking, received FDA clearance in 2021 to aid in the diagnosis of concussion.<sup>24,25</sup> EYE-SYNC includes software as well as a VR headset with an eye tracking sensor and a tablet.<sup>24,25</sup> The patient's ability to synchronize eye movement with a moving object as well as gaze fixation are assessed.<sup>25</sup>

The REAL System (Penumbra Inc., US) is a VR system designed for physical and neuro rehabilitation in a clinical environment that received FDA clearance in 2019.<sup>26,27</sup> The REAL System includes software, a VR headset, tracking sensors, and a tablet.<sup>28</sup> Patients perform rehabilitation exercises focused on upper body, lower body, or cognition in a virtual world.<sup>27</sup>

MindMotion PRO (MindMaze, Switzerland) is a VR system cleared by the FDA in 2017 that displays and tracks upper extremity rehabilitation exercises in adults.<sup>29-31</sup> MindMotion PRO is a game-based therapy that uses a combination of 3-D virtual environments as well as avatars for visual feedback.<sup>29,31</sup> The system is intended for use in a clinical setting under the supervision of a medical professional.<sup>29</sup> Additionally, MindMotion GO (MindMaze, Switzerland) is a physical rehabilitation VR system that includes exercises for the upper extremity, trunk, and lower extremity and was cleared by the FDA in 2018.<sup>31-33</sup> MindMotion GO uses software in combination with the Microsoft Kinect v2 and Leap motion controller and can be used by adults in the clinic or at home.<sup>32</sup>

YuGo System (Biogaming Ltd., Israel) is a VR physical rehabilitation software designed to be used with the Microsoft Kinect that the FDA cleared in 2016.<sup>34</sup> Patients perform exercises for the upper and lower extremities in a virtual environment, and patient movements are analyzed in real time, and feedback is provided.<sup>34</sup>

## Cost

When calculating the costs of implementing a VR or AR intervention, the costs of the hardware and software, as well as the human resources required, must be considered. The costs of VR hardware can vary considerably depending on the VR system used. For example, the estimated costs of head-mounted displays can range from US\$10 (Google Cardboard) to US\$500 (HTC Vive).<sup>2</sup> There are additional hardware costs (e.g., computer, smartphone, video game system) if the head-mounted display is not a standalone device. A standalone head-mounted display (e.g., Oculus Go, estimated cost US\$200) could reduce costs.<sup>2</sup> In contrast, projection-based VR systems (i.e., CAVE) can be much more expensive.<sup>35</sup> CAVEs require dedicated personnel for ongoing system maintenance in addition to expensive construction and equipment costs.<sup>35</sup> One estimate of the installation costs for a CAVE is €80,000 to €750,000, with estimated monthly maintenance costs of €3,000 or more.<sup>36</sup>

In contrast to VR devices, AR headsets have yet to experience widespread commercialization due to their high cost.<sup>4</sup> The estimated cost of AR headsets ranges from US\$899 (Vuzix Blade) to US\$3,000 (Microsoft HoloLens).<sup>2</sup> However, AR can also be accessed through devices like smartphones and tablets, which are less costly.

In addition to the VR and AR hardware costs, there are also software costs. These costs will range depending on whether the intervention uses software already developed for commercial or clinical use or if the intervention requires new software development. The cost of using software that has already been developed will depend on whether the software can



be purchased outright or requires a subscription. Developing and testing new clinical VR and AR software is associated with high costs.<sup>37</sup> These include costs related to hiring software developers and clinical experts, as well as the cost of running clinical trials.<sup>37</sup>

There may also be costs associated with technical support as well as training health care staff on the use of these technologies. The time required for training staff may depend on the complexity of the hardware and software required for the intervention. Training and technical support may be included in the cost of a licence for an extended reality intervention. In an economic evaluation of a VR therapy for pain, the cost of an annual licence for the VR therapy was US\$3,500. It included a VR headset, a subscription to VR software, and unlimited training and technical support.<sup>38</sup> A Canadian cost analysis study aimed to estimate the costs associated with running a 4-week home-based VR rehabilitation program for stroke survivors.<sup>39</sup> The hardware costs included a computer, screen, keyboard, mouse, internet connection, and Microsoft Kinect camera.<sup>39</sup> Additional program costs included installation/removal, technical support, software subscription, and physiotherapist time.<sup>39</sup> The study found that a program supplying all the required technology would cost between CA\$475 and CA\$482 per patient.<sup>39</sup> They also estimated that a program that only supplied a camera would cost between CA\$242 and CA\$245 per patient.<sup>39</sup> This program would require the patient to supply the other technology needed (i.e., computer, internet etc.).<sup>39</sup>

## Summary of the Evidence

### Acute and Chronic Pain

VR has been studied as a potential intervention for both acute and chronic pain. The effect of VR on acute pain has been more widely studied than the effect on chronic pain.<sup>40</sup> A scoping review of immersive VR for acute and chronic pain found that the proposed mechanism of the impact of VR was a distraction for the majority of acute pain studies. In contrast, the proposed mechanism of effect of VR for chronic pain studies was more commonly embodiment.<sup>40</sup> Embodiment refers to the sensation that 1's self is located inside a virtual body and has control over that body.<sup>41</sup> The scoping review also found that studies of the use of VR in chronic pain were more likely to develop their own VR programs rather than using commercially available programs.<sup>40</sup>

### Children

A 2022 systematic review evaluated the use of VR distraction for pain and anxiety during medical procedures in pediatric patients.<sup>15</sup> The systematic review included a total of 77 studies (59 randomized controlled trials, 6 interventional/observational studies, 3 quasi-experimental studies, 2 cross-sectional studies, 1 retrospective chart review, and 6 case reports) that evaluated VR distraction in 2,174 patients aged from 6 months to 18 years undergoing medical procedures in a variety of settings.<sup>15</sup> The medical procedures in the included studies were burn wound care procedures, postburn injury physiotherapy, dental procedures, needle-related procedures, and other procedures.<sup>15</sup> The majority of studies used a head-mounted device for VR. Additional hardware used included projector-based VR systems, VR glasses, and smartphones inserted into disposable VR headsets.<sup>15</sup> Most studies used a VR game; in the other studies, the participants experienced a VR adventure (e.g., a rollercoaster ride, swimming underwater) or selected a cartoon or movie to watch in their VR headsets.<sup>15</sup>

Overall, the results of the included studies suggested that VR distraction may effectively reduce pain and anxiety in pediatric patients undergoing medical procedures.<sup>15</sup> When compared to standard of care (e.g., topical anesthesia, parental presence, watching television, distraction by a child life specialist or nurse), the results were mixed with some included studies reporting a significant reduction in pain or procedural anxiety, stress, or fear for patients treated with VR distraction versus standard of care and other studies reporting no significant difference between groups.<sup>15</sup> For patients undergoing burn wound care, the results of the included studies suggested that VR can reduce pain when combined with standard analgesia.<sup>15</sup> The studies included in the systematic review were heterogeneous regarding the patient population, design, sample size, and type and dosage of VR intervention which may have contributed to the variability in the results. The systematic review's authors suggest that further research is needed that compares VR interventions with varying levels of immersion and interactivity to determine the most effective interventions for different patient populations.<sup>15</sup>

Research into the efficacy of VR for reducing pain in pediatric populations living with chronic pain is limited. A 2022 scoping review of immersive VR for acute and chronic pain did not identify any studies that examined the use of VR for children living with chronic pain.<sup>40</sup>

## Adults

A 2019 systematic review evaluated immersive VR for treating acute and chronic pain in adults.<sup>6</sup> Immersive VR was defined as a patient engaged in a simulated world with visual and auditory feedback and the ability to interact with the virtual environment.<sup>6</sup> The systematic review included 20 studies (14 randomized controlled trials, and 6 quasi-experimental studies).<sup>6</sup> Ten of the included studies evaluated VR for acute pain (burn pain and medical procedure-related pain) and 10 for chronic pain (musculoskeletal pain, neuropathic pain, and unspecified pain).<sup>6</sup> The VR equipment used in the studies included goggles, glasses, or another form of head-mounted device, 3-D projectors, and a 2D screen with visual cues that responded to changes in treadmill speed.<sup>6</sup>

The results of most acute pain studies suggested that VR significantly reduces the pain experienced during various medical procedures (labour contractions, episiotomy repair, periodontal procedures) and burn-related pain.<sup>6</sup> Additionally, the results of 3 out of 4 studies that evaluated acute pain after various medical procedures (episiotomy repair, dressing changes for hand injuries, cardiac procedures) suggested that the addition of VR significantly reduced pain.<sup>6</sup> The results of studies in adult participants living with chronic pain suggested that VR may reduce pain during VR exposure; however, results were mixed for the effect of VR on reducing pain after exposure.<sup>6</sup> Therefore, although VR may have the potential to reduce pain, the effect may not be long-lasting.<sup>6</sup> The authors of the systematic review suggested that the variability in the results may be explained by the different frequencies and durations of VR therapy and the various types of VR equipment used in the included studies.<sup>6</sup>

## Rehabilitation

There is research interest in VR-based interventions to improve outcomes in various fields of rehabilitation.<sup>12,16</sup> Some of these interventions include VR-based treadmill training for lower-extremity rehabilitation, reaching and grasping of virtual objects exercises for upper extremity rehabilitation, and commercially available game platforms (e.g., Nintendo Wii and Xbox Kinect) for upper and lower limb function.<sup>12</sup> Additionally, VR has been studied in cognitive rehabilitation. Cognitive rehabilitation includes various interventions to improve

individuals' psychological, social, mental, and functional cognition.<sup>16</sup> One hypothesis as to why VR rehabilitation may be helpful has to do with the virtual environment; it is experienced as a recreational context that is both rewarding and challenging.<sup>42</sup> Cognitive and motor processes are stimulated as those using them attempts to solve problems in new and engaging contexts of differing complexity.<sup>42</sup> Additionally, clinicians can select the duration and difficulty of tasks depending on patient needs.<sup>12,42</sup>

## Stroke, Traumatic Brain Injury, and Cerebral Palsy

A 2021 umbrella review aimed to summarize published meta-analyses regarding using VR interventions to improve physical and cognitive functions in people with stroke, traumatic brain injury, and cerebral palsy.<sup>12</sup> In total, 41 reviews with meta-analyses were included in the umbrella review.<sup>12</sup> Thirty-two reviews included patients with stroke, 6 reviews included children with cerebral palsy, and 3 reviews included patients with acquired brain injury (including stroke and traumatic brain injury).<sup>12</sup> A wide range of both commercially available and customized VR systems were used in the included reviews.<sup>12</sup> The technology used included video game systems (e.g., Xbox Kinect, Nintendo Wii), head-mounted displays, projectors, treadmills, data gloves, exoskeletons, motion-tracking systems, stereoscopic glasses, and more.<sup>12</sup> Control conditions included conventional therapy and passive conditions such as wait lists.<sup>12</sup>

The umbrella review mostly identified evidence rated as low or very low quality by the review authors.<sup>12</sup> However, results from evidence rated as moderate and high quality by the review authors suggested VR may improve mobility, balance, upper limb function, and body structure/function and activity of people with stroke, upper limb function of people with acquired brain injury, and ambulation function of children with cerebral palsy.<sup>12</sup>

## Parkinson Disease

A 2019 systematic review and meta-analysis aimed to summarize the evidence on VR rehabilitation training for patients with Parkinson disease.<sup>43</sup> The systematic review included a total of 16 randomized controlled trials that evaluated VR rehabilitation in 555 patients with Parkinson disease.<sup>43</sup> The experimental groups in the included studies were treated with exercise and motor rehabilitation training using VR.<sup>43</sup> The VR technology used in the studies varied, including interactive motion-sensing training and commercially available video game systems (e.g., Nintendo Wii, Xbox 360).<sup>43</sup> The control groups received conventional rehabilitation training.<sup>43</sup>

Results from the meta-analysis suggested that VR rehabilitation training significantly improved step and stride length, balance function, mobility, and quality of life versus conventional rehabilitation training in patients with Parkinson disease.<sup>43</sup> In contrast, there was no significant difference between groups in gait, activities of daily living, or cognitive function.<sup>43</sup> The authors of the systematic review warn that the results should be interpreted with caution due to the heterogeneity among the included studies in terms of treatment intensity, intervention duration, and effect size.<sup>43</sup>

## Autism Spectrum Disorders

A 2022 systematic review evaluated VR-based technologies for improving executive functioning, attention, and memory in children and adults with an autism spectrum disorder.<sup>16</sup> The systematic review included 17 studies (3 RCTs, 4 case-control studies, and 10 single-arm studies) that assessed VR-based cognitive rehabilitation in 226 people with an autism spectrum disorder.<sup>16</sup> The VR technologies used in the studies varied and included head-mounted displays, projection systems with sensors or motion-capture capabilities,

driving simulators, and VR software operating on laptops.<sup>16</sup> A range of VR programs were used in the included studies that aimed to improve cognitive outcomes such as executive functioning (e.g., finances, driving, shopping, street-crossing), attention, and memory.<sup>16</sup> Nine of the included studies reported that VR interventions resulted in statistically significant improvement in cognitive outcomes, 7 studies reported improvements in cognitive outcomes; however, no formal statistical tests were conducted, and 1 study reported no improvements in cognitive outcomes.<sup>16</sup> The systematic review authors state that some important limitations were the small sample sizes of included studies, the need for randomized controlled trials, and the need for long-term training programs and follow-up.<sup>16</sup>

## Mental Health

Extended reality technologies have been studied to diagnose and treat various mental health conditions. VR has the potential to produce scenarios that may be therapeutically beneficial but impossible to recreate in real life.<sup>37</sup> Using VR, individuals can enter simulations of difficult situations and receive immediate feedback and coaching.<sup>37</sup> Additionally, the simulations can be repeated, and the difficulty adjusted until learning is achieved.<sup>37</sup> One example of VR for mental health conditions is VR exposure therapy which can be used for people with specific phobias and post-traumatic stress disorder.<sup>44</sup> In VR exposure therapy, patients can be exposed to their feared stimulus in a safe and controlled virtual environment.<sup>44</sup> Additionally, VR-based interventions have been studied in anxiety disorders, depression, schizophrenia, psychosis, eating disorders, substance use disorders, ADHD, cognitive impairment, and dementia.<sup>37</sup>

## Anxiety and Depression

The effectiveness of VR-enhanced interventions to improve symptoms of anxiety and depression was evaluated in a 2018 systematic review and meta-analysis.<sup>8</sup> The meta-analysis included 39 randomized controlled trials of VR interventions in 1991 adults with various conditions, including specific phobias (e.g., heights, spiders), social anxiety, panic disorder, and post-traumatic stress disorder.<sup>8</sup> The VR interventions used in the included studies were VR-enhanced exposure therapy and VR-enhanced cognitive behavioural therapy.<sup>8</sup> The majority of included studies used a head-mounted display.<sup>8</sup> Control conditions included waitlist, placebo, and treatment as usual. Active comparators included interventions not employing VR (e.g., cognitive behavioural therapy, imaginal exposure, relaxation).<sup>8</sup>

The results of the meta-analysis suggested that VR-based interventions were more effective than control conditions for improving symptoms of anxiety and depression.<sup>8</sup> There were no significant differences in symptoms of anxiety or depression when VR-based interventions were compared to other active interventions.<sup>8</sup> The authors of the meta-analysis noted several limitations, including heterogeneity in the results of the included studies, evidence of publication bias, and high or uncertain risk of bias in the included studies.<sup>8</sup>

## Older Adults

The use of VR interventions for older adults with mental health conditions was assessed in a 2022 systematic review.<sup>45</sup> A total of 55 studies were included in the systematic review; 54 studies of Alzheimer dementia or mild cognitive impairment and 1 study of post-traumatic stress disorder.<sup>45</sup> The majority of included studies were cross-sectional studies.<sup>45</sup> Computers were used to display the virtual scenes in most studies; however, some included studies used VR headsets.<sup>45</sup> A range of VR environments were used in the studies, including supermarkets, kitchens, roads and cityscapes, mazes, and forests.<sup>45</sup> Results of the

included studies suggested that VR applications improved cognitive skills across a range of domains, including spatial cognition, memory, executive function, and activities of daily living.<sup>45</sup> Additionally, performance on VR tasks in the included studies was able to distinguish between healthy controls, people with mild cognitive impairment, and people with Alzheimer dementia.<sup>45</sup> Limitations noted by the systematic review authors were that the technology used in most of the included studies does not reflect recent advances in VR technology (i.e., wireless headsets) and the preliminary nature and cross-sectional design of most included studies.<sup>45</sup> Another limitation is the heterogeneity of the interventions in the studies included in the systematic review. Some studies evaluated immersive VR using a headset and others evaluated nonimmersive VR using a computer.

## Attention-Deficit/Hyperactivity Disorder

A 2022 systematic review aimed to summarize the evidence regarding the use of VR, AR, and mixed reality for diagnosing and treating ADHD in children and adolescents.<sup>7</sup> Thirty studies (22 case-control, 3 cross-sectional, 2 case studies, 2 quasi-experimental studies, 1 randomized controlled trial) with 2,378 participants were included in the systematic review.<sup>7</sup> Most of the included studies used VR, with 2 studies that used AR and 1 study that used mixed reality.<sup>7</sup> Most studies used head-mounted displays and other hardware, including 3-D glasses, computers, headsets, motion sensors, and robots.<sup>7</sup> The interventions used included a VR classroom continuous performance test, a VR classroom environment, games, web-based VR, and an AR robot.<sup>7</sup> Six of 7 included studies found VR/AR/mixed reality technologies to be helpful for the diagnosis of ADHD.<sup>7</sup> Additionally, 8 of 9 included studies found VR/AR/mixed reality technologies beneficial for managing ADHD symptoms.<sup>7</sup> Limitations of the included studies noted in the systematic review included lack of assessment and management of confounding factors, small sample sizes, and lack of control groups.<sup>7</sup>

## Safety

VR can potentially cause very rare serious side effects, such as seizures and interference with medical devices.<sup>40</sup> More commonly, the use of VR can be linked to cybersickness which can cause fatigue, malaise, dizziness, headaches, and nausea.<sup>10,40</sup> Cybersickness is a short-term effect that tends to increase during VR exposure and then slowly dissipates once the use of VR is stopped.<sup>46</sup> Some evidence has demonstrated that cybersickness can be overcome through training with a VR device – using short sessions with breaks to minimize cybersickness symptoms.<sup>47</sup> There may also be potential long-term effects associated with the use of VR such as sleep disorders and addiction.<sup>48</sup> Despite this potential to cause adverse events, several researchers have noted a lack of consistent reporting of side effects in studies of VR.<sup>37,40</sup> The increased use of standardized tools to measure side effects such as the Simulator Sickness Questionnaire or Virtual Reality Sickness Questionnaire in studies of VR has been suggested to allow for a future meta-analysis of the side effects of various forms of VR.<sup>37</sup> Methods that have the potential to prevent cybersickness include correct calibration of the VR system, adaptation and customization according to the VR users' needs, use of a more natural user interface, use of lighter head-mounted displays, and ensuring moderate usage of the VR system.<sup>9</sup>

Safety outcomes were not reported across most of the publications discussed previously. The systematic reviews related to VR for pain and anxiety during medical procedures for children, acute and chronic pain in adults, autism spectrum disorder, anxiety and depression, and mental health conditions in older adults did not report safety outcomes.<sup>6,8,15,16,45</sup> Additionally, safety outcomes were not reported in the review of VR, AR, and mixed reality for ADHD.<sup>7</sup>

In the umbrella review of VR in patients with stroke, traumatic brain injury, and cerebral palsy 10 out of the 41 included meta-analyses reported adverse events.<sup>12</sup> Six of the included meta-analyses reported no major adverse events and 6 reported a few cases of mild adverse events (transient dizziness and headache, pain, dizziness, increase in hypertonicity, loss of control, increased spasticity, back ache and fatigue).<sup>12</sup> The systematic review of VR in people with Parkinson disease included 1 trial that reported that 4 patients developed mild dizziness and 1 patient developed severe dizziness and vomiting during the intervention.<sup>43</sup>

## Additional Considerations

### Uptake

There are several factors that may encourage the use of VR and AR interventions. For instance, motivation to use the technology may be improved if the virtual environments used are enjoyable and user-friendly.<sup>9</sup> VR and AR interventions can also be individualized so that they are language- and cultural-specific.<sup>10</sup> Additionally, the virtual environments used can allow patients to experience situations that have a therapeutic benefit but are difficult or impossible to recreate in reality.<sup>7,37</sup> VR and AR interventions also have the potential to be carried out in people's homes.<sup>7</sup> This could potentially improve access to care for patients who have difficulty accessing in-person care such as those living in rural or remote locations. However, this would require investment in technologies (e.g., devices, internet) to enable VR or AR interventions in these locations.

There are also factors that could prevent the use of VR and AR interventions. Extended reality technologies such as VR have the potential to cause adverse effects such as cybersickness.<sup>40</sup> There are other potential safety concerns around the use of these technologies such as sleep disorders, visual symptoms, and addiction.<sup>48</sup> It is also possible that some patients may find extended reality devices to be uncomfortable to wear. A common limitation noted in studies of VR interventions in children with autism was intolerance of VR glasses.<sup>16</sup> Ensuring devices are comfortable to wear and accommodating to sensory processing disorders could help to encourage their use during treatment sessions.<sup>16</sup> There are also potential negative effects that long-term immersion in AR or VR environments could have on mental health. There is concern that heavy use of VR could lead to symptoms associated with depersonalization/derealization disorder (e.g., feeling that 1's self or the external world are not real).<sup>49</sup> There are also concerns that the use of VR or AR by vulnerable populations (e.g., individuals prone to psychosis, individuals with cognitive impairment) could lead to difficulties in distinguishing between real events and those that occurred in VR or AR.<sup>50</sup>

Some VR and AR interventions may involve the recording of a range of personal information including facial expressions, eye movement patterns, and body responses and reflexes.<sup>10,49</sup> There may be privacy concerns related to the collection of this data and therefore, patients should be made aware of and consent to any data collection related to VR and AR interventions.<sup>10</sup> If VR or AR interventions require patients to have access to their own devices (e.g., computer, smartphone, tablet) or internet connection this could pose a barrier to patients without access to these technologies. Additionally, many extended reality technologies are currently commercially available however, they may need to be reclassified as medical devices to ensure coverage under health insurance plans.<sup>49</sup> Otherwise only those

with the ability to pay for these technologies would have the potential to benefit from them which could exacerbate health inequities.

## Standards and Regulations

Standards and regulations related to AR and VR vary by country, profession, and in their stage of development.

Internationally, the Institute of Electrical and Electronics Engineers (IEEE) has a working group that is developing numerous standards related to AR and VR that include device taxonomy, environmental safety, immersive video file and stream formats, and immersive audio file and stream formats, among others.<sup>51</sup> Among other goals, these standards aim to establish common concepts and language related to AR and VR as well as safety standards.

From a regulation standpoint in Canada, both immersive and nonimmersive AR and VR technologies could be regulated as medical devices if they are manufactured, sold, marketed, or represented for any of the uses outlined in the definition of a device in the Food and Drugs Act.<sup>52</sup> This would include devices already on the consumer market (such as videogaming platforms or commercial AR devices) that begin to market themselves as medical devices or make claims related to their usefulness for medical treatment. AR and VR devices that meet the definition of a device would be considered active devices<sup>53</sup> and before regulation would need to be assessed to be classified based on risk class. Additionally, the software used by AR/VR devices that are regulated as medical devices may be classified according to the Software as a Medical Device (SaMD) criteria.<sup>54</sup>

## Final Remarks

Extended reality-based interventions are being studied in a variety of clinical areas including acute and chronic pain, rehabilitation, and mental health. Should emerging evidence demonstrate a clear benefit as well as a tolerable safety profile for these interventions they could have a place in augmenting or replacing other therapeutic options. There is a wide range of virtual and AR hardware and software that is commercially available as well as technologies developed specifically for clinical use. It will be important to ensure that access to AR and VR interventions is equitable so that not only those with the ability to pay stand to benefit from these interventions. The interventions used in the identified studies were heterogeneous and therefore, it will be important to determine which components of these interventions (e.g., hardware and software used, intervention duration, level of immersion) impact efficacy. Additionally, most of the identified studies focused on VR interventions and there was a lack of information on the efficacy and safety of AR interventions for patient use identified in this Horizon Scan. There are several VR interventions that have been developed and are in use for a range of therapeutic areas including neuro- and physical rehabilitation, chronic pain, and vision. Further high-quality studies investigating the efficacy and safety of VR and AR interventions as well as cost-effectiveness studies will aid in decision-making around the use of these technologies.

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