THE EFFECTS OF VIRTUAL REALITY ON PAIN AND ANXIETY IN PEDIATRIC ONCOLOGY PATIENTS

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ABSTRACT: Pediatric patients undergoing cancer treatments often experience excessive pain and anxiety during medical procedures, especially those involving the insertion of needles. These feelings are usually associated with dangerous consequences such as attempts to escape and the avoidance of health care. Therefore, it is essential to improve the management of discomfort and fear to ensure appropriate care for the patients. In recent years, many studies and numerous randomized trials have been focusing on the effects of virtual reality (VR) during distressing procedures and rehabilitation sessions, and it has been reported that VR is a successful form of distraction from both pain and anxiety. This innovative form of non-pharmacological analgesic therapy has also been used together with opioids (standard care), such as morphine, while performing unpleasant therapies, successfully reducing the feelings of distress and fear compared to the patients treated with the standard medications. This manuscript aims to analyze the most recent literature in VR for the management of pain and anxiety during cancer-related treatments in pediatric patients. The use of VR during medical procedures offers patients relaxing and pleasant scenarios. VR represents a promising strategy to alleviate the suffering and stress of pediatric patients, ensuring better patient management.

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Impact statement: The effectiveness of Virtual Reality (VR) has proven to be promising as a potential novel form of palliative pain and anxiety management for pediatric oncology patients.

Key words: virtual reality; cancer pain; palliative care; opioids; analgesics; pediatric patients; oncology; rehabilitation; non-pharmacological.

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INTRODUCTION
Cancer is a primary cause of death among children and teenagers. Globally, it has been estimated that almost 400,000 children and adolescents of 0-19 years develop cancer yearly (1).

Since pain and anxiety are significant symptoms experienced during cancer treatment, palliative care is considered an essential component of comprehensive oncology therapy. It has been demonstrated that patients receiving palliative treatment along...
with standard cancer care, improved the management of their symptoms, their quality of life, and this latter effect has been showed to improve also for the caregivers and their families (2). According to the World Health Organization (WHO), pain in children is a public health concern of high significance in most parts of the world, especially in low-income countries. Numerous data suggest that these nations offer inadequate and frequently non-existent pain treatments to patients, who are subject to unnecessary agony (3). The perception of children’s pain has evolved through time, and now people value pain alleviation highly. Pain used to be extensively disregarded, and commonly ignored, and it was believed that children rapidly forgot about unpleasant disregarded, and commonly ignored, and it was believed that children rapidly forgot about unpleasant experiences. Since the 1970s, pain started to be the subject of many studies, resulting in the urgency for pediatric pain research (4).

At this time, the standard strategy for the management of pain and anxiety in cancer patients is pharmacological. The WHO guidelines to manage cancer pain usually recommend paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), steroids and opioids (3). Opioids (morphine-like drugs) are used worldwide to alleviate painful symptoms. Most industrialized countries have widespread access to opioids in healthcare settings, although availability may be limited in developing nations. Opioids are administered either parenterally or orally, and the dosage is often based on the body weight of the child (5).

However, these medications are well known for their significant side effects including nausea, constipation, and hallucination (6). Therefore, to reduce these eventual risks during pain management, it is important to find efficacious nonpharmacological strategies. Recently, virtual reality (VR) has been used to distract children during painful procedures, emerging as a novel non-pharmacological therapy for pain and anxiety (7). This innovative technology has been successfully appreciated by patients in the pediatric unit, as it appeals to various age groups, and sometimes it may be adapted to mobile phones, thus, providing a more economic option. It has been shown that VR has the potential to keep patients distracted during painful procedures by keeping them active. For instance, using a VR headset, playing games or observing different scenarios during the procedure, will lead them to experience less pain and anxiety (8).

VR can be used during various medical procedures, helping the child to perceive the therapy as a safe environment (9).

Studies have shown that regional cerebral blood flow related to the processing of a painful event is decreased when a person is distracted (10). Similar to this, when the attention of the person is diverted by a task, there is less activation in the brain regions connected to pain, such as the thalamus, insula, and anterior cingulate cortex, which results in proportionately lower pain levels (11). In this manuscript, we will review the most recent literature on the effects of VR on pain and anxiety for pediatric oncology patients.

**VIRTUAL REALITY: HOW DOES IT WORK?**

Virtual Reality can be best described as the simulation of a three-dimensional environment generated by a computer (10). VR systems can be classified into three categories: Immersive VR, Semi-immersive VR, and Non-immersive VR. Immersive VR relies on the full immersion of a person in a computer-generated world, instead of the actual one. This level of immersion is only achievable with a head-mounted display that excludes the view of the real world, and with headphones, that block the sounds of the surrounding environment (11).

Semi-immersive VR involves the utilization of a large screen for projecting the virtual environment (VE). Advanced interface devices, such as cyber-gloves, haptic feedback devices, or infrared cameras, are employed to facilitate user interaction with the VE. Notably, users can concurrently perceive the real world, resulting in a state of partial immersion and a heightened sense of presence (12).

Lastly, the non-immersive form is distinguished by a computer screen where the user can interact with the real world while also connected to the virtual one (11).

VR has proven to work as an efficient distraction tool from pain. Studies have shown that regional cerebral blood flow related to processing a painful event is decreased when a person is distracted (13). Similar to this, when the attention of the person is diverted by a task, there is less activation in the brain regions connected to pain, such as the thalamus,
insula, and anterior cingulate cortex, which results in proportionately lower pain levels (14).

Various studies have been conducted in recent years to address the expanding field of Virtual Reality (VR) interventions, investigating their efficacy as palliative care for pain and anxiety management, along with their role in rehabilitation (VRR) (Table 1).

### VR IN PAIN MANAGEMENT

Cancer therapy represents a very unpleasant experience for pediatric patients. Indeed, pediatric cancer patients often undergo treatments, such as chemotherapy, radiation therapy, surgery, and procedures involving the use of needles. These approaches can result in a status of anxiety and pain and make the management of these patients quite difficult (13).

Many studies have been using the following methods to measure pain intensity in the patients: Numerical Rating Scale (NRS), Visual Analogue Scale (VAS), Wong-Baker FACES pain scale and Faces Pain Scale-Revised (FPS-R) (14, 15, 16).

NRS is an 11-, 21-, or 101-point numeric rating scale. Patients are asked to express a numeric value within a specific numeric range to quantify their pain. Depending on the number of points that are present on the scale, the numeric range is from 0 to 10, or 0 to 20 or 0 to 100 where zero corresponds to “no pain” while the maximum range values represent “the worst pain” (15, 17). Instead, in VAS, patients indicate the intensity of their pain on a line whose extreme limits represent the absence of pain and the worst possible pain. The addition of a numerical scale or terms describing pain as “mild,” “moderate,” and “severe” in VAS defines the “Graphical Rating Scale” (GRS) (15). However, pain measurement methods involving the graphic representation of pain using drawn faces, such as Wong-Baker FACES and Faces Pain Scale-Revised, are highly preferred for younger children, compared with the usage of numerical scales (16). The Wong-Baker FACES is a scale that is based on the use of six drawings of faces with an expression ranging from absence of pain (smiling face) to maximum pain (crying face) with associated numerical scores from 0 to 5. The child is asked to indicate the face that is most representative to identify his or her level of pain (16). The Faces Pain Scale Revised also uses 6 drawn faces to represent pain, but unlike the Wong-Baker FACE, these drawings do not express too much emotion, since there are no significantly smiling or crying faces (16).

The measurement scales mentioned above are widely used to assess pain in the pediatric field (18). Since pain associated with painful procedures during cancer treatments negatively affects the emotional status and well-being of the child, it is crucial to develop approaches to reduce needle-induced anxiety and pain in pediatric patients (13, 19, 20). The use of VR is well known to improve the emotional and psychological status of cancer patients, acting as a distractor and pain reliever during painful procedures (11).

Several studies proved through various pain measurement scales, such as VAS, Wong-Baker faces and NRS, that VR exhibited a beneficial effect in reducing pain in pediatric oncology patients (21, 22, 23) and in distracting these patients during numerous medical procedures involving needles, including port access with a Huber needle, peripheral intravenous cannulation, and venipuncture (21, 24, 25). Indeed, VR can simultaneously engage several senses in patients. While using VR, patients focus their attention on pleasant stimuli determined by the virtual environment, thus distracting themselves from painful perceptions (26).

Immersive and non-immersive VR results in different outcomes in reducing pain in pediatric patients with solid or hematologic tumors (27). Although non-immersive VR is well accepted by children during procedures involving the use of needles, Nilsson et al. observed few statistically significant differences when comparing various quantitative pain assessments in pediatric oncology patients undergoing non-immersive type VR compared to control patients (28).

In contrast, the use of immersive VR exhibits a relevant beneficial effect on pain in pediatric cancer patients undergoing painful medical procedures (27). In detail, Atzori et al. proved that the use of immersive VR in venipuncture procedures led to a significant reduction in pain sensory perception and time spent by pediatric patients thinking about pain (25).

Examples of scenarios observed during immersive VR by pediatric cancer patients undergoing painful procedures include swimming with marine animals (Ocean Rift), discovering a forest through the eyes of an animal (In the Eyes of the Animal), throwing snowballs at animals or snowmen (SnowWorld) (21, 25); riding a rollercoaster that increases...
Table 1. Summary of Studies Conducted for Virtual Reality (VR) in Pain and Anxiety Management and Rehabilitation (VRR). A comprehensive overview of the aforementioned studies conducted in the field of research for Virtual Reality (VR) as palliative care for pain and anxiety management as well as rehabilitation (VRR). This table summarizes key findings from various studies exploring the effectiveness of VR in alleviating pain and anxiety, and enhancing rehabilitation outcomes for pediatric oncology patients. The studies cover diverse aspects. Each entry provides valuable insights into the evolving landscape of VR applications in the multifaceted care of pediatric patients undergoing cancer treatments.

<table>
<thead>
<tr>
<th>STUDY</th>
<th>PAIN OR ANXIETY MANAGEMENT OR REHABILITATION (VRR)</th>
<th>AUTHORS</th>
<th>METHODOLOGY</th>
<th>KEY FINDINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects of virtual reality on pain, fear and anxiety during blood draw in children aged 5-12 years old: A randomized controlled study</td>
<td>VR in Pain and Anxiety Management</td>
<td>Özalp et al. (2020)</td>
<td>CONSORT checklist, Child Fear Scale, Children's Anxiety Meter, Wong-Baker FACES pain rating scale</td>
<td>Virtual reality significantly reduces pain, fear, and anxiety during blood draw in children</td>
</tr>
<tr>
<td>A Pilot Randomized Controlled Trial of Virtual Reality Distraction to Reduce Procedural Pain During Subcutaneous Port Access in Children and Adolescents</td>
<td>VR in Pain Management</td>
<td>Hundert et al. (2021)</td>
<td>NRS, VAS, Wong-Baker FACES pain rating scale, FPS-R</td>
<td>VR exhibits a beneficial effect in reducing pain in pediatric oncology patients</td>
</tr>
<tr>
<td>Virtual Reality Intervention Targeting Pain and Anxiety Among Pediatric Cancer Patients Undergoing Peripheral Intravenous Cannulation: A Randomized Controlled Trial</td>
<td>VR in Pain Management</td>
<td>Wong et al. (2021)</td>
<td>NRS, VAS, Wong-Baker FACES pain rating scale, self-report scales of Anxiety</td>
<td>VR intervention significantly reduced pain and anxiety levels among pediatric cancer patients undergoing peripheral intravenous cannulation</td>
</tr>
<tr>
<td>Virtual Reality Analgesia During Venipuncture in Pediatric Patients With Onco-Hematological Diseases</td>
<td>VR in Pain Management</td>
<td>Atzori et al. (2018)</td>
<td>VAS</td>
<td>The use of VR during venipuncture in pediatric patients with onco-hematological diseases was associated with an analgesic effect, contributing to reduced pain during the procedure</td>
</tr>
<tr>
<td>Effects of Virtual Reality on Pain During Venous Port Access in Pediatric Oncology Patients: A Randomized Controlled Study</td>
<td>VR in Pain Management</td>
<td>Semerci et al. (2021)</td>
<td>Wong-Baker FACES Pain Rating Scale</td>
<td>VR effectively reduces pain during venous port access in pediatric oncology patients</td>
</tr>
<tr>
<td>The effect of virtual reality on pain, fear, and anxiety during access of a port with huber needle in pediatric hematology-oncology patients: Randomized controlled trial</td>
<td>VR in Pain and Anxiety Management</td>
<td>Gerçeker et al. (2020)</td>
<td>Child Fear Scale, Children's Anxiety Meter, Wong-Baker Faces Pain Rating Scale</td>
<td>VR diminishes procedure-related pain, fear and anxiety in children aged 5-12 years old during blood draw</td>
</tr>
<tr>
<td>Effects of virtual reality therapy on perceived pain intensity, anxiety, catastrophizing and self-efficacy among adolescents with cancer.</td>
<td>VR in Pain and Anxiety Management</td>
<td>Sharifpour et al. (2021)</td>
<td>MPQ, PASS, PCS, PSEQ</td>
<td>VR was effective in reducing pain anxiety, pain intensity and pain catastrophizing. VR increases pain self-efficacy</td>
</tr>
</tbody>
</table>
and slows down the speed (29), and other videos from AAA VR Cinema v.1.6.1 application (30).

Some studies aimed to compare the effectiveness of immersive VR with non-immersive VR in relieving pain in pediatric oncology patients and found no significant difference in outcomes between the two types of VR (27). In a recent study conducted by Hundert et al., values obtained from pain measurement using the NRS scale revealed a greater reduction in pain intensity in patients undergoing immersive VR than those undergoing non-immersive VR, during subcutaneous port access. Nevertheless, this difference was not statistically significant (23).

Thus, VR represents an effective distraction method to reduce pain in pediatric cancer patients. Based on registers for ongoing clinical trials, ISRCTN and clinicaltrials.gov, there seem to be several clinical trials to evaluate the effect of VR on pain in pediatric cancer patients (NCT05042479; NCT05275881; NCT02995434; NCT04092803; NCT03888690; NCT04138095; NCT04931745; NCT04853303) (27) (Table 2) and further studies are needed to clarify the mechanisms underlying the analgesic effect of VR (26).

**VR IN ANXIETY MANAGEMENT**

Anxiety has often been described as the “psychologic equivalent of physical pain” and in some cases, it can appear in the form of phobias (31). Cancer patients may experience anxiety due to many different reasons, including the reaction to the diagnosis of the disease, critical pain, and long-term treatments (32). Anxiety has multiple negative effects on the therapies of oncology patients, slowing down the healing process (33).

For instance, chemotherapy’s physical and psychological side effects cause patients to fear the chemotherapy and sometimes even reject or resist receiving anti-cancer treatment (34).
Pharmacological and nonpharmacological techniques can both be used to treat anxiety in cancer patients (6). However, the use of pharmacological medications (e.g., benzodiazepine) to treat anxiety can have negative side effects, such as the development of tolerance, dependency, and drug interactions. Because of this, nonpharmacological methods for treating anxiety were seen to be safer (35). Studies on VR technology have shown that feelings such as anxiety and fear can be decreased through immersion into a relaxing and engaging environment (20, 23, 36).

At this point, various VR applications can be used. The reaction of each child to VR may differ. Some kids prefer soothing, musical films while others enjoy moving, fascinating videos.

To assess the anxiety in children during medical procedures, many studies have used the “Children's Anxiety Meter” (CAM) (Figure 1). CAM is displayed as a thermometer with a bulb at the bottom and horizontal lines spaced out along the top. To measure the anxiety state, children are asked to mark how they are feeling at that specific moment, and scores can be between 0 (very low anxiety) and 10 (very high anxiety) (7).

### Table 2. A Comprehensive List of Clinical Trials for Virtual Reality (VR) utilized as palliative care for pediatric oncology patients taken from clinicaltrials.gov as of February 2024. Based on the various filters applied (“Virtual reality pain, anxiety pediatric oncology”, childbirth-17, all sexes, not yet recruiting, recruiting, completed, enrolled by invitation, clinical trial), there are four clinical trials worldwide which seek or have sought to better understand the effects of VR as a method of distraction for pediatric oncology patients. There have been four completed clinical trials. These results do not include Scopus.gov clinical trial results, thus eliminating grant clinical trials. Source: clinicaltrials.gov.

<table>
<thead>
<tr>
<th>STUDY TITLE</th>
<th>NCT NUMBER</th>
<th>STATUS</th>
<th>AGE</th>
<th>CONDITIONS</th>
<th>INTERVENTIONS</th>
<th>LOCATION</th>
<th>LAST UPDATE POSTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virtual Reality on Pain, Fear, and Emotional Appearance During Phlebotomy in Pediatric Hematology and Oncology Patients</td>
<td>NCT05675358</td>
<td>Completed</td>
<td>4-12 years (Child)</td>
<td>Virtual Reality Pain, Acute Pediatric Cancer</td>
<td>Behavioral: Virtual Reality</td>
<td>Izmir, Turkey</td>
<td>2023-01-09</td>
</tr>
<tr>
<td>Impact of Virtual Reality on Peri-interventional Pain, Anxiety and Distress in a Pediatric Oncology Outpatient Clinic</td>
<td>NCT06235723</td>
<td>Completed</td>
<td>6-18 years (Child, Adult)</td>
<td>Pediatric Cancer Procedural Anxiety Procedural Pain</td>
<td>Device: Virtual Reality</td>
<td>Hanover, Lower Saxony, Germany</td>
<td>2024-02-01</td>
</tr>
<tr>
<td>The Effect of Biofeedback-Based Virtual Reality Game on Children</td>
<td>NCT05585840</td>
<td>Completed</td>
<td>6–12 years (Child)</td>
<td>Pediatric Cancer</td>
<td>Device: Biofeedback-based virtual reality game</td>
<td>Istanbul, Turkey</td>
<td>2022-10-19</td>
</tr>
<tr>
<td>Distracting Through Procedural Pain and Distress</td>
<td>NCT04892160</td>
<td>Completed</td>
<td>8–25 years (Child, Adult)</td>
<td>Chronic Illness, Hematologic Malignancy, Bone Marrow Transplant Infection Oncology, Sickle Cell Disease</td>
<td>Other: Guided Imagery, Other: Virtual Reality</td>
<td>Milwaukee, Wisconsin, United States</td>
<td>2021-05-19</td>
</tr>
</tbody>
</table>
VR IN REHABILITATION (VRR)

Virtual reality rehabilitation (VRR) is an innovative approach that involves interactive computer-generated environments to simulate real-world experiences and promote physical and cognitive rehabilitation in a safe and engaging manner (36). Unlike virtual reality (VR) intervention, or therapy, which focuses primarily on distracting patients from pain and anxiety during medical procedures, VRR aims to improve patients’ physical and cognitive abilities and promote recovery and rehabilitation (37). For pediatric oncology patients, who often experience a wide range of physical and cognitive challenges during and after treatment, including muscle weakness, balance impairments, and cognitive deficits, VRR offers a tailored approach that allows them to perform specific tasks designed to meet their unique needs and abilities (37).

Despite the studied benefits of traditional rehabilitation for cancer patients and survivors, a minority of cancer survivors are referred to rehabilitation programs (36). A 20-year follow-up study conducted by Stensvold et al. in Norway found that among the pediatric brain cancer survivors, 86% had an unmet rehabilitation need (38). This lack of access and information may be due to various factors, including the incapability of cancer care systems to deliver early detection of impairing symptoms, inadequate traditional training programs, transportation issues, and limited knowledge (39, 40, 41).

Virtual reality rehabilitation (VRR) offers a promising solution to these issues. VRR has been shown to improve adherence rates and training intensity due to its entertaining nature, which can lead to greater patient engagement and motivation (42). VRR also offers a safe and engaging environment for pediatric oncology patients to perform rehabilitation exercises and activities, which may help reduce anxiety, pain, and stress. Research studies have shown that VRR can be effective in improving physical function, reducing pain, and enhancing emotional well-being in pediatric oncology patients (37).

For example, a recent study conducted by Nuara et al. demonstrated that VRR was associated with significant improvements in upper extremity function and quality of life in pediatric cancer patients undergoing chemotherapy (41). Another study by Tanner et al. found that VRR was effective in reducing pain and anxiety in pediatric oncology patients undergoing bone marrow aspiration and biopsy procedures (37).

VRR offers a promising approach to improve outcomes in pediatric oncology patients. Despite the potential benefits, there is a need for greater awareness and access to VRR for patients. Health professionals and cancer care systems should consider incorporating VRR into rehabilitation programs to improve outcomes and quality of life for pediatric oncology patients.

**VR SIDE EFFECTS AND LIMITATIONS**

Despite the benefits of utilizing VR technology as non-pharmacological palliative care, there are potential side effects and limitations that must be considered for pediatric oncology patients.

One of the potential side effects of VR is motion sickness, which can cause nausea and discomfort in some patients (43). This can be especially problematic for younger patients who may not be able...
to articulate their discomfort as well as adults. Therefore, it is recommended that children have a limit for screen time between 5 to 10 minutes to avoid “simulator sickness” (44). Prolonged use of VR headsets can also cause eye strain, headaches, and fatigue in some patients, which could exacerbate existing symptoms and negatively impact patient engagement (45). Additionally, the various types of VR and intervention scenarios presented to the children expose them to intense or frightening VR experiences which could potentially lead to negative behavioral changes, including increased aggression, nightmares, or anxiety (46).

Some VR simulations expose the patient and family to a specific medical procedure, which increases the patient’s procedural knowledge but at the same time may cause additional stress, anxiety and fear (47). Physical limitations of VR technology exist despite offering a safe virtual environment. Although VR provides a promising tool to influence psychological and physiological functions, the headsets, or head-mounted displays (HMD) utilized may be too heavy or too large for pediatric patients (48). Therefore, alternative strategies, such as lighter and more comfortable headsets, or the use of other devices, such as smartphones, need to be explored to overcome the physical limitations of VR technology and enhance the patient’s experience since active interaction, navigation and immersion are key characteristics of VR systems (49, 50).

Another limitation of VR technology is while there are some VR experiences specifically designed for pediatric oncology patients, there is still a limited amount of content available, which could limit the usefulness of the technology for some patients (51). Finally, it is important to note that VR technology is not a replacement for human interaction and emotional support that patients may need from healthcare providers, family, and friends (43). VR therapy can complement traditional care approaches, but it cannot replace them entirely. Children may still experience acute distress reactions based on the separation from parents, unfamiliar environments, medical equipment and negative experiences with previous medical procedures (47). Furthermore, preschool and elementary school-age children may have difficulty differentiating virtual experiences from real ones thus leading to potential false memories since they are still developing the ability to distinguish between reality and fantasy (44).

While VR technology can provide significant benefits to pediatric oncology patients, there are potential side effects and limitations that must be considered when using this technology. By carefully assessing patients and developing an individualized treatment plan, healthcare providers can help maximize the benefits of VR therapy while minimizing its potential risks.

CONCLUSION AND FUTURE DIRECTIONS

Although VR is based on the principle of distraction and has proven to be effective, there still remain drawbacks and limitations to its application in the medical field for palliative care. VR provides non-invasive real perceptual stimuli such as visual images, spatial sounds, tactile and olfactory feedback (48). Nonetheless, further research must be conducted to determine the safety of VR technology. Along with VR, Augmented Reality (AR) is also at the forefront these types of technologies in medical applications (52). AR differs from VR in which it utilizes elements of VR and superimposes them in the real-world environment (52). The preliminary evidence and use of these digital technologies has proven to be beneficial in diagnostics, surgical procedures and rehabilitation. Further research must be performed to assess the short and long-term impact on clinical practices and patients’ lives.

It is worth noting that not all studies have standardized criteria for what VR technology entails. VR technology encompasses studies that utilize VR video, VR games, and iPad videos (53), therefore it must be specified which VR type and scenario are used. This will allow researchers to better understand which VR type is more beneficial to reduce anxiety, pain and fear for a given pediatric patient.

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Conflict of interests
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Availability of data and materials
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Authors’ contributions
CN, SB, EA and AC: worked on the conception of the work; CN, SB, EA and AC: worked on drafting and revising it critically for important intellectual content; AC and AG: provided approval for publication of content; CN, SB, EA, AC and AG: agree to be accountable for all aspects of the work.

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N/A.

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Publications ethics

Plagiarism
The article provides a comprehensive review of the latest studies in the field, with accurate citations.

Data falsification and fabrication
The writing and contents of the article are entirely original and were developed entirely by the authors.

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