Extended Reality Interventions for Chronic Pain

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to conduct timely, rigorous, and independent systematic reviews to support VA clinicians, program leadership, and policymakers improve the health of Veterans. ESP reviews have been used to develop evidence-informed clinical policies, practice guidelines, and performance measures; to guide implementation of programs and services that improve Veterans' health and wellbeing; and to set the direction of research to close important evidence gaps. Four ESP Centers are located across the US. Centers are led by recognized experts in evidence synthesis, often with roles as practicing VA clinicians. The Coordinating Center, located in Portland, Oregon, manages program operations, ensures methodological consistency and quality of products, engages with stakeholders, and addresses urgent evidence synthesis needs.

Nominations of review topics are solicited several times each year and submitted via the ESP website. Topics are selected based on the availability of relevant evidence and the likelihood that a review on the topic would be feasible and have broad utility across the VA system. If selected, topics are refined with input from Operational Partners (below), ESP staff, and additional subject matter experts. Draft ESP reviews undergo external peer review to ensure they are methodologically sound, unbiased, and include all important evidence on the topic. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. In seeking broad expertise and perspectives during review development, conflicting viewpoints are common and often result in productive scientific discourse that improves the relevance and rigor of the review. The ESP works to balance divergent views and to manage or mitigate potential conflicts of interest.

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Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

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Technical Expert Panel

To ensure robust, scientifically relevant work, the technical expert panel (TEP) guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members included:

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Disclosures

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The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. The final research questions, methodology, and/or conclusions may not necessarily represent the views of contributing operational and content experts. No investigators have affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

Executive Summary

KEY FINDINGS

- **Chronic low back pain:** Virtual reality (VR) pain psychology and coping skills interventions may result in greater improvement in pain-related functioning and pain intensity as compared to VR sham or usual care, but the evidence for adverse events is very uncertain; the effects of augmented reality (AR) physical activity on pain-related functioning, pain intensity, and adverse events are also very uncertain.
- **Chronic neck pain:** VR physical activity may result in little to no difference in pain-related functioning at 3-6 weeks and the evidence is very uncertain at 3-4 months; for pain intensity, VR physical activity may result in greater improvement at 3-6 weeks but little to no difference at 3-4 months; only 1 study evaluated AR physical activity and no trials reported on adverse events.
- **Fibromyalgia:** The effects of AR physical activity on pain-related functioning and pain intensity are very uncertain; the effect of AR-enhanced cognitive behavioral therapy on pain-related functioning is very uncertain; no trial evaluated VR interventions, and none reported on adverse events.
- **Chronic knee pain:** VR physical activity may result in better pain-related functioning and less pain at 7 weeks, but the single trial did not address adverse events; the effects of AR interventions on pain-related functioning, pain intensity, and adverse events are very uncertain.
- **Post-surgical pain and rehabilitation:** The effects of VR and AR interventions (primarily involving physical activity) on pain-related functioning, pain intensity, and adverse events are very uncertain.
- **Current evidence gaps:** Methodological concerns include small study sizes, lack of studies examining certain pain conditions, and lack of reporting on adverse events; these generally reflect the early state of the science in this field.
- **Future research** should evaluate mechanisms of XR therapies, assess patient experiences and technology acceptance, apply implementation frameworks, and include more diverse participant populations.

More than a quarter of United States (US) Veterans have chronic pain and 12% reported that their pain caused frequent functional limitations in daily life or work activities. Non-drug therapies (*eg*, exercise and psychological interventions) are first-line treatments for common pain conditions due to their known benefits and low risks, particularly as compared to opioids and invasive procedures. Accordingly, Veterans Health Administration (VHA) initiatives have emphasized use of non-drug therapies to improve chronic pain management and decrease inappropriate opioid prescribing. Effects of non-drug therapies may vary across common pain conditions and patient characteristics; for example, while targeted exercise is generally effective for chronic low back pain, integration of psychotherapy techniques with exercise may be needed for maximal benefit in those with high fear of movement (*ie*, kinesiophobia). Outcomes of non-drug therapies may also be different depending on whether these are being used to treat established chronic pain (*eg*, chronic low back pain) or to prevent the development of persistent or chronic symptoms from acute pain (*eg*, post-surgical pain

management and rehabilitation). Additionally, non-drug treatments often require long-term adherence to yield maximum benefit, making patient engagement a key factor in effectiveness over time.

Extended reality (XR) is a spectrum of digital technologies that can be used to deliver different types of interventions for pain, such as teaching pain management skills or guiding and engagement in physical activity. Virtual reality (VR) entails the highest level of immersion in an interactive, fully digital environment, while augmented reality (AR) provides partially immersive user experiences by adding digital elements to real-world environments (usually visually) or by translating user activities into the digital world. Interventions using Microsoft Kinect or Nintendo Wii gaming systems are examples of AR physical activity programs. With the increased availability of low-cost XR devices and widespread popularity of these technologies, interest in a broad range of XR clinical applications has also grown.

Although XR interventions have been implemented in clinical settings for a range of health conditions, including acute and chronic pain treatment, the ways in which XR contributes to therapeutic effects remain unclear and likely vary by type of intervention (*eg*, building mindfulness skills vs performing targeted exercises). Some have also proposed that XR technology can specifically facilitate embodiment (the perception of one's body as comprising both digital and real-world elements), a potentially important mechanism for addressing conditions like phantom limb pain. The use of XR to decrease acute pain through distraction is also well documented (*eg*, during dental treatments), and for chronic pain, distraction may enable participation in recommended exercises, leading to better engagement and adherence. As the field continues to expand and diverse XR interventions are being developed, understanding the current evidence for XR pain therapies is critically needed to guide future implementation efforts and further research to address knowledge gaps.

CURRENT REVIEW

The VHA's XR Network is a nationwide resource hub for dissemination and pilot testing of XR technologies across VHA facilities. Current pilots of XR interventions for pain are occurring in post-operative care, Community Living Centers, and various outpatient settings. To inform future research on XR interventions for pain and implementation of XR treatments at VA facilities, the VHA XR Network, in collaboration with VA Health Systems Research (HSR) and VA National Pain Management, Opioid Safety, and Prescription Drug Monitoring Program (PMOP) Office, requested this evidence review on the benefits and harms of XR interventions for chronic pain.

In this systematic review, we present findings by pain condition, beginning with chronic low back pain and chronic neck pain, followed by other conditions. Within each condition, we provide results separately for VR and AR interventions, and then by types of XR interventions (see below). We conducted quantitative meta-analyses where feasible and qualitative summaries otherwise.

The a priori protocol for this review was registered in PROSPERO (CRD42023439903). We searched MEDLINE, Embase, CINHAL, PsycINFO, and Scopus databases (until May 2023) using key words and subject headings for VR and AR, exergaming, pain, and a variety of pain conditions (*eg*, neuralgia and fibromyalgia). We also hand-searched relevant systematic reviews identified via the database searches, and clinical trial registries for recently completed and ongoing trials (until August 2023).

Eligible studies evaluated XR interventions to treat (Key Question [KQ] 1) or prevent (KQ2) chronic pain in adults and addressed at least 1 primary outcome of interest (*ie*, pain-related functioning or interference, pain intensity or severity, pain catastrophizing, pain global change, quality of life, and/or

adverse events). Additionally, eligible studies for KQ1 must be randomized controlled trials (RCTs), and KQ2 studies had ≥3 months of follow-up. Risk of bias (RoB) assessments were conducted independently by 2 researchers and discrepancies resolved by consensus or with a third reviewer.

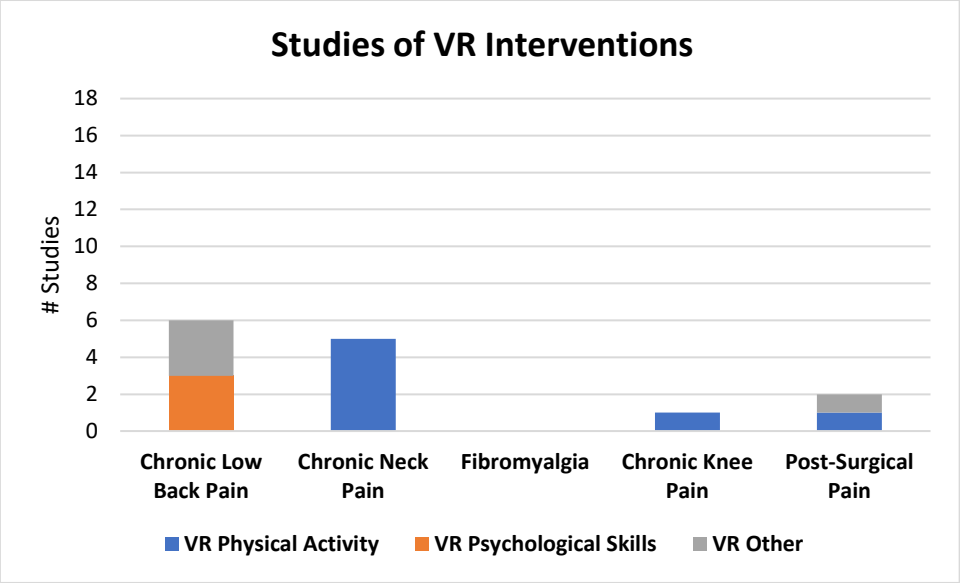
Data abstraction elements included participant characteristics and inclusion/exclusion criteria, intervention characteristics (technology and devices used, content and goals of intervention), study design and settings, and findings for outcomes of interest. Based on intervention content and goals, we classified XR intervention type into 4 categories: 1) pain psychology and coping skills, 2) guide and engage in physical activity, 3) embodiment only, or 4) distraction only.

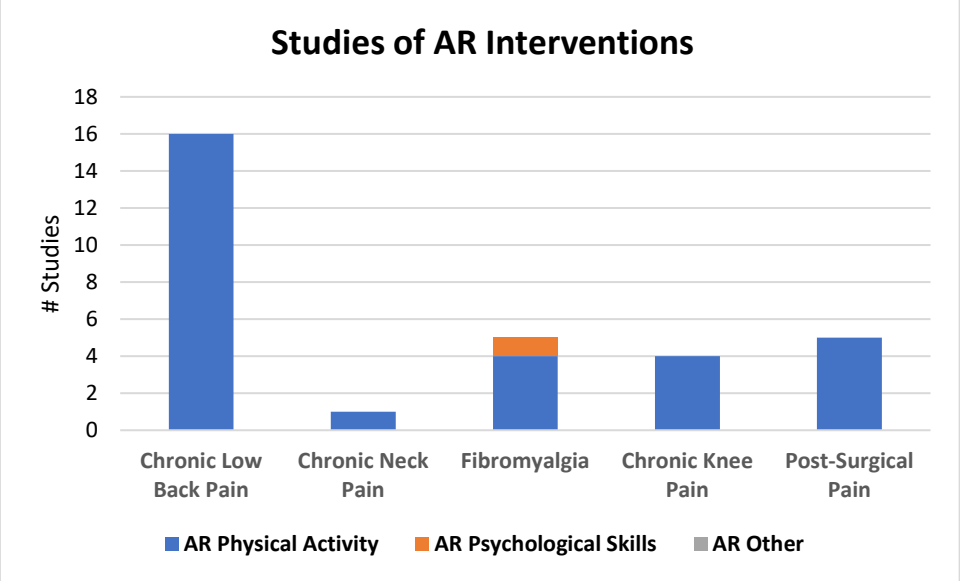
For synthesis of findings, we first grouped studies by pain condition (*eg*, chronic back pain, chronic knee pain) and then by intervention characteristics (*ie*, first separating VR and AR interventions, and then by intervention types as noted above). We conducted random effects meta-analyses when there were ≥3 sufficiently similar eligible studies (*ie*, for participant population, intervention and comparator characteristics, and reported outcomes). Otherwise, we provided narrative syntheses of study characteristics and findings. We focused on between-group comparisons of the mean change in continuous outcomes (*ie*, difference in mean change scores [Diff Δ]), preferentially as standardized effect sizes (Diff Δ/standard deviation [SD] of change). For outcome measures where lower scores are better (*eg*, pain intensity or severity), a negative value for Diff Δ generally indicates that there were greater improvements in the XR intervention group. We evaluated heterogeneity using visual inspection, τ^2, and 95% prediction intervals (PI).

We assessed certainty of evidence (COE) for the top 3 prioritized outcomes: pain-related functioning or interference, pain intensity or severity, and adverse events. Before data analysis and synthesis of eligible study findings, we engaged operational partners and Technical Expert Panel members in outcome prioritization. We rated COE separately for different XR intervention types (and comparators) for chronic low back pain, chronic neck pain, fibromyalgia, chronic knee pain, and post-surgical pain and rehabilitation. We used Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology to rate overall COE as high, moderate, low, or very low.

We identified 71 eligible articles reporting 60 unique primary studies—49 studies (58 articles) that addressed KQ1 and 11 studies (13 articles) for KQ2. Most studies assessed pain-related functioning (k = 43) and/or pain intensity (k = 53). In contrast, few reported on adverse events (k = 15), and of these, most did not systematically assess adverse effects for all study arms. Half of the studies were very small (k = 30 with total $n \leq 50$), and only 4 studies had total $n > 100$. Most studies were conducted outside of the US (k = 54), and most included young and middle-aged adults (k = 46). All studies were rated high or some concerns for RoB, with half being high RoB (k = 30). We also identified 47 ongoing or recently completed studies.

Figure. Studies Evaluating Various XR Intervention Types for Pain Conditions





KQ1: What Are the Benefits and Harms of VR and AR Interventions for Treatment of Chronic Pain?

Of studies evaluating XR interventions for treatment of chronic pain (KQ1), most addressed low back pain ($k = 22$), and fewer examined chronic neck pain ($k = 6$), fibromyalgia ($k = 5$), and chronic knee pain ($k = 5$). There were also a variety of other chronic pain conditions with only a single eligible study (*eg*, headache or phantom limb pain). Most KQ1 studies evaluated AR interventions ($k = 32$), and physical activity was the most common type of XR intervention ($k = 36$; see Figure above).

For chronic low back pain, most studies evaluated AR physical activity ($k = 16$) compared with non-AR physical activity, medications, or usual care. In pooled analyses for pain intensity at 2-8 weeks for AR physical activity versus any active comparator, the standardized between-group difference in mean change scores (stand. Diff Δ) was -0.7 (95% CI [-1.2, -0.2]) but the PI was quite large (-2.1, 0.7).

Overall, the evidence is very uncertain on the effects of AR physical activity on pain intensity and pain-related functioning, compared with either non-AR physical activity or medications; no trials evaluated adverse events for these comparisons. AR physical activity may result in better pain-related functioning (*eg*, Diff Δ -0.4 on Roland-Morris Disability Questionnaire) when compared with usual care, but the evidence is very uncertain for pain intensity and adverse events. The remaining studies on low back pain evaluated VR psychological skills ($k = 3$) or VR embodiment ($k = 3$). Compared with VR control or usual care, VR psychological skills may result in better pain-related functioning and reduced pain intensity (*eg*, Diff Δ -0.7 on Defense and Veterans Pain Rating Scale [DVPRS] overall interference, and -0.5 on DVPRS pain intensity), but the evidence on adverse events is very uncertain. The evidence is also very uncertain on the effects of VR embodiment, compared with either conventional therapy or VR control, on pain-related functioning and pain intensity; none of these trials evaluated adverse events.

Six trials evaluated XR physical activity (5 VR, 1 AR) for chronic neck pain, all compared with non-XR physical activity. Interventions lasted 3-6 weeks and follow-up range was 3 weeks to 4 months. VR interventions showed little to no difference in pain-related functioning at 3-6 weeks (pooled stand. Diff Δ -0.2 [-0.5, 0.2]), and the evidence is very uncertain at 3-4 months. VR interventions may result in greater decreases in pain intensity at 3-6 weeks (pooled stand. Diff Δ -0.5 [-0.8, -0.1]) but little to no difference at 3-4 months (pooled stand. Diff Δ -0.2 [-0.9, 0.5]). The single AR study showed that AR physical activity may lead to improved pain-related functioning and decreased pain intensity at 4-9 weeks (*eg*, Diff Δ -5.6 on the Neck Disability Index and -18.8 on the Visual Analogue Scale [VAS] 0-100). No study on chronic neck pain reported on adverse events.

Five studies examined XR interventions for fibromyalgia, and all used AR interventions. Four trials evaluated AR physical activity lasting 7-24 weeks, compared with either non-AR physical activity or usual care. The evidence is very uncertain on the effects of AR physical activity on pain-related functioning and pain intensity. The fifth study compared AR-enhanced cognitive behavioral therapy with usual care; the evidence is also very uncertain on the effects of AR psychological skills on pain-related functioning and pain intensity. No study on fibromyalgia reported on adverse events.

Five trials evaluated XR interventions for chronic knee pain due to osteoarthritis, and all compared XR physical activity programs (1 VR, 4 AR) with conventional exercises and rehabilitation. The single trial on VR physical activity showed greater improvement in pain-related functioning and pain intensity in the VR group (*eg*, Diff Δ -5.1 on the Western Ontario and McMaster Universities Arthritis Index [WOMAC] and -1.1 on VAS 0-10 at 7 weeks). This trial did not address adverse events. The evidence is very uncertain on the effects of AR physical activity on pain-related functioning, pain intensity, and adverse events. All 4 AR studies evaluated pain-related functioning and pain intensity; generally, all study groups improved over time. Only 1 AR study evaluated adverse events, reporting no events detected in either group during the 4-week intervention.

KQ2: What are the Benefits and Harms of VR and AR Interventions for Prevention of Chronic Pain?

Eleven studies examined XR interventions for the prevention of chronic pain (KQ2), with 7 of these addressing post-surgical pain and rehabilitation. Nearly all post-surgical studies involved XR physical activity interventions ($k = 6$; see Figure above). The remaining 4 studies included 2 RCTs on AR physical activity interventions for post-stroke pain and rehabilitation, 1 RCT on AR physical activity for flight-associated neck pain (both acute and chronic), and 1 cohort study on VR psychological skills

intervention for pain from work-related injuries. Most evaluated AR ($k = 7$) while the rest addressed VR interventions (4); most were physical activity interventions ($k = 9$).

Seven trials evaluated XR interventions for post-surgical pain management and rehabilitation, primarily after knee replacement surgery (1 trial also included participants who had hip replacement surgery). Two studies used brief VR interventions (1 distraction, 1 physical activity) in the immediate post-operative period while participants were still hospitalized. The evidence is very uncertain on the effects of these VR interventions on pain-related functioning and pain intensity; neither trial provided information on adverse events. The remaining 5 studies all compared AR physical activity with standard rehabilitation and varied widely in treatment duration (2 weeks to 4 months). The evidence is also very uncertain on the effects of AR physical activity on pain-related functioning, pain intensity, and adverse events.

Evidence Gaps & Future Research

The evidence on XR interventions for chronic pain is limited by serious methodological concerns (half of eligible studies were rated high for RoB) and by the small size of most study samples. Due to concerns regarding the limits of randomization to achieve balance in very small trials (with respect to baseline measures and unmeasured confounding), we elected to calculate the between-group differences in change scores (Diff Δ), instead of directly comparing follow-up scores. Although we undertook this strategy to provide the most informative interpretation of study findings, this approach cannot eliminate risks of bias that would be successfully addressed by randomization in sufficiently large trials Additionally, few studies addressed adverse events and side effects, or provided information on baseline comorbidities that may impact ability to use or tolerate XR devices. Of the 47 ongoing or recently completed trials on XR interventions for chronic pain, most were small ($n < 100$) and specified outcomes in the protocol did not generally include adverse events. The preponderance of small pilot studies using convenience samples is consistent with the early state of the science in the emerging field of XR for pain care.

To identify the highest-value contributions of XR to pain care, future research is needed to clarify how VR and AR may improve pain outcomes, including the *mechanisms* by which XR technologies may enhance the benefits of specific types of pain therapies. Often, included studies were not designed to address this question because XR interventions were not compared with analogous *non*-XR intervention types. One commonly proposed mechanism for XR benefits is increased patient engagement with varying intervention types. To understand whether patient engagement is affected positively or negatively by different forms of XR technology, it would be important to evaluate patient engagement (including adherence and patient experience) in comparing XR interventions with the analogous *non*-XR interventions. Current evidence also does not address XR technology acceptance across diverse patient populations or evaluate how this may impact intervention effects. Future work will need to evaluate acceptance of XR technology among diverse populations, investigate associated intervention engagement and adherence, and examine outcomes and implementation resources for populations (such as older adults) that have high prevalence of chronic pain conditions but may face greater barriers—internal or external—to technology adoption.

Included studies rarely evaluated adverse events using rigorous methods that allowed for direct comparisons between XR and non-XR interventions. This is a critical gap because adverse events are an important component of the patient experience and often impact whether someone will start or continue an intervention. At a minimum, adverse events should be assessed systematically, reported for

each arm, and involve participant interviews with open-ended questions and/or checklists. In addition to information on whether the adverse event led to discontinuation of the treatment, studies should report the rates of serious adverse events (usually defined as events that are life-threatening, requiring hospitalization, or resulting in persistent disability). Accurate observation of serious adverse event rates will likely require substantially larger studies. It will also be important to examine whether adverse events for XR interventions vary for different subgroups of patients, such as by sex or gender.

Furthermore, intervention dose and duration varied widely across included studies. Minimal effective dose and duration are likely to vary by intervention type and mechanism. Overall, XR interventions lasted from several weeks to several months. Future studies on XR psychological skills interventions should consider applying methods developed for analogous non-XR interventions to provide critical information on minimum effective dose and duration, and the impact of participant adherence on these values.

Limited understanding of XR's impacts on pain therapy mechanisms and intervention adherence also makes it difficult to differentiate when XR is a key active component of the therapeutic intervention versus enhancing the effects of an existing therapy (*eg*, by increasing engagement). This distinction between core intervention components and modifiable peripheral components is fundamental to implementation science, making implementation science frameworks potentially helpful even in this early phase of XR pain research. Intentionally designing hybrid implementation-effectiveness studies as part of the research continuum may help clarify XR contributions earlier.

Use of XR interventions in clinical settings is also particularly dependent on implementation contexts, making implementation research key to effective rollout for XR interventions with demonstrated benefits. Clinicians often have a wide range of interest and experience in using XR technologies as well, and substantial facility investment may be required for clinician training. Integrating an implementation science lens during development phases and beyond could speed the translation of XR technologies to the end user. Although cost considerations were beyond the scope of this review, an evaluation of resources needed for XR treatments for pain should consider both the cost of treatments themselves (particularly as compared with non-XR versions of therapies) and what is needed for successful implementation (*eg*, staff training materials and time, logistical support for distributing XR devices to patients).

In summary, XR technology has considerable potential as part of a comprehensive plan for pain treatment. Given the possibilities for home use and remote monitoring, and the increasing affordability of some XR technologies, XR interventions may be an important way to address common patient barriers to access and use of non-drug therapies for pain. But it remains unclear how and under which circumstances XR adds the most benefit and the least risks for pain treatments. Evaluating benefits and risks in generalizable ways will require larger studies that include more diverse populations (particularly those who may experience more barriers to technology use, such as older adults and rural populations*)*, compare XR interventions to analogous non-XR intervention types, investigate mechanisms and added value of XR technology, and generate further evidence on participant experiences—including adverse events, attitudes toward XR, and barriers and facilitators of access and use.

CONCLUSIONS

Evidence on benefits and harms of XR interventions to treat or prevent chronic pain is limited due to methodological concerns, small study size, and lack of reporting on adverse events. XR physical activity interventions may have benefits for some conditions (*eg*, chronic neck pain) but the evidence is very uncertain for others (*eg*, chronic low back pain and post-surgical pain and rehabilitation). XR psychological skills interventions may also have some benefit for chronic low back pain, but studies did not compare to analogous non-XR treatments. Future work is needed to better understand how and by what mechanisms XR interventions may impact pain outcomes, particularly in more diverse populations and settings. Larger studies and application of implementation frameworks are important next steps for advancing this field.