RelieVRx® Clinical Resource Library

This guide is intended to help product evaluation teams make informed coverage decisions about RelieVRx.

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Product Basics

RelieVRx is an FDA-authorized first-in-class virtual reality (VR)-based behavioral treatment for moderate to severe chronic lower back pain (CLBP), a condition with significant unmet need.[1]

The RelieVRx program is a prescription-use immersive virtual reality system intended to provide adjunctive treatment based on cognitive behavioral therapy skills and other evidence-based behavioral methods for patients (age 18 and older) with a diagnosis of CLBP (defined as moderate to severe pain lasting longer than three months). The device is intended for in-home use for the reduction of pain and pain interference associated with CLBP.[2]

RelieVRx is a self-administered behavioral program of 56 sequential sessions averaging 6 minutes each (range 2-13 minutes). RelieVRx delivers multimodal content based on cognitive behavioral therapy (CBT) skills and other evidence-based behavioral methods encompassing pain education, breathing techniques, pain distraction, and mindfulness. Together, these elements train the patient's brain (e.g., executive, emotional, and multisensory pathways) to experience pain differently.

RelieVRx is intended for independent use in the home under the prescribing clinician's supervision, minimizing access barriers that contribute to underutilization of guideline-recommended behavioral treatment for CLBP.[3-8] Clinical studies have demonstrated the program's ability to yield lasting effects on the severity of various pain indicators.[9-15] Thus, RelieVRx offers an effective and engaging non-pharmacological behavioral therapy option that patients with CLBP can complete in the comfort of their home.

The FDA designated RelieVRx a "breakthrough device" prior to granting it, in November 2021, authorization as a Class II medical device via the De Novo pathway.[16-17]

RelieVRx is commercially available to patients in the US, billable under HCPCS code E1905 and recognized by the Centers for Medicare & Medicaid Services (CMS) as durable medical equipment (DME). Commercial payers are reviewing the evidence to establish coverage policies.[18]

FDA Authorization

→ ***DE NOVO DECISION SUMMARY***

→ ***RECLASSIFICATION ORDER LETTER***

In November 2021, RelieVRx received market authorization as a Class II medical device via the De Novo regulatory pathway.[17]

This pathway is for the classification and authorization of certain low- to moderate-risk medical devices that do not have a predicate device on the market. The FDA review evaluated the device's safety and effectiveness, which involved assessing the device's intended use, technology, and potential risks.

The FDA's authorization established a new device classification, which other manufacturers can use as a predicate for future 510(k) submissions, demonstrating how AppliedVR is paving the way for future VR therapeutic devices entering the field.

Five special controls—concerning clinical performance; biocompatibility; software verification; electromagnetic compatibility and electrical, mechanical, and thermal safety; and product labeling—apply to the authorization.[19]

RelieVRx has been designated a breakthrough device by the FDA, meaning it is a medical device deemed to provide for more effective treatment of an irreversibly debilitating condition. The FDA's Breakthrough Device Program is intended to provide patients and providers with timely access to medical devices like RelieVRx while meeting the FDA's rigorous standards for safety and effectiveness.[16]

Commercialization and Reimbursement

AppliedVR worked with CMS to include RelieVRx in the existing benefit category for DME, the first immersive VR therapeutic to follow this strategy to tap into existing payment authority.

In March of 2023, CMS granted a unique Healthcare Common Procedure Coding System (HCPCS) Level II code, E1905, "Virtual reality cognitive behavioral therapy device (CBT), including pre-programmed therapy software" for RelieVRx.[18] In addition, CMS published a fee schedule, paving the way for reimbursement and adoption of this novel approach to CLBP management.[18]

This groundbreaking coding decision positions the RelieVRx program as the first immersive therapeutic to be integrated into an existing benefit category. The decision fulfills all 5 of CMS's requirements for DME categorization and allows a clearer path to Medicare coverage eligibility, thereby facilitating wider commercial

coverage. The official DME determination from CMS clarified their reasoning: "The medical software and the device on which it is housed are so integral to each other that we consider them to be one whole device, not software and a separate device."[20]

The following billing codes may be useful in identifying appropriate patients and facilitating transactions around RelieVRx:

HCPCS Code[18]

E1905 (Virtual reality cognitive behavioral therapy device [CBT], including pre-programmed therapy software)

ICD-10-CM Diagnosis Codes[21]

M54.50 (Low back pain, unspecified)

M54.51 (Vertebrogenic low back pain)

M54.59 (Other low back pain)

RelieVRx is covered on the Federal Supply Schedule for Veterans Affairs and by Highmark.[22-23]

CLBP: Clinical Issues and Gaps

CLBP is a prevalent, complex, and expensive condition that carries a significant health economic burden in the US.

Recognized as a national public health problem, the pain experience has profound physical, emotional and societal costs.[24] Chronic pain is estimated to impact 50 million US adults with 19.6 million experiencing daily debilitating pain interfering with daily life or work activities.[25] Meanwhile, a recent study found that 39% of US adults had experienced back pain in the previous 3 months.[26] The national cost is high, estimated to be between $560 and $635 billion annually in 2010.[27] The efficacy of a multimodal, multidisciplinary approach to pain management including addressing the biopsychosocial (biological, psychological, and social) effects on patients has been shown to reduce pain intensity, improve quality of life, and increase functioning.[28-34] A 2023 editorial in the *Lancet Rheumatology* asserted that the burden of low back pain increased during the COVID-19 pandemic, especially for the economically disadvantaged.[35]

With current pain management, patients cycle through treatments (e.g., opioids and other drug classes, surgeries) with suboptimal efficacy and risks of serious adverse events, searching for relief.[36] Patients with back pain use resources at a high rate, making almost twice as many yearly doctor visits as those without back pain.[37]

Support for Behavioral Therapy

RelieVRx incorporates proven techniques of behavioral treatment into an accessible and engaging program with proven clinical benefits.

Pain management best practices[3] and national and global clinical treatment guidelines[4-8] recommend non-pharmacologic and patient-centric biopsychosocial approaches that include behavioral treatment.

The behavioral therapy techniques recommended as first-line treatment for CLBP introduce significant access barriers. Strict reliance on skilled therapists that are in short supply, travel burdens, long treatment duration, inadequate insurance coverage, and high costs all contribute to a lack of treatment accessibility and patient engagement.[38] These proven therapeutic interventions are incorporated into the RelieVRx program, making these efficacious methods accessible and engaging.

Support for VR-Based Delivery

→ ***PROOF OF CONCEPT RCT***

→ ***PIVOTAL STUDY PROTOCOL***

→ ***PERSPECTIVES ON WHY/HOW VR WORKS***

RelieVRx uses immersive VR, an emerging behavioral therapy tool that improved CLBP outcomes in a randomized controlled trial.

VR has been used for decades in the healthcare setting. These uses were limited to research or inpatient use due to cost and operating challenges.[39] More recently, VR headset technology has evolved to be relatively affordable and effective, and it is now a very promising tool for therapeutic delivery in multiple settings, including

the home. VR broadly engages multiple learning systems in the brain in synchrony, thus having the unique potential to increase the effectiveness and speed of therapeutic change.[40] Indeed, the isolated effects of VR-based CBT with RelieVRx vs audio-only CBT have been demonstrated in a randomized, controlled proof of concept study.[41] Three systematic reviews further attest to the efficacy of VR-based interventions in the treatment of chronic pain and CLBP.[42-44]

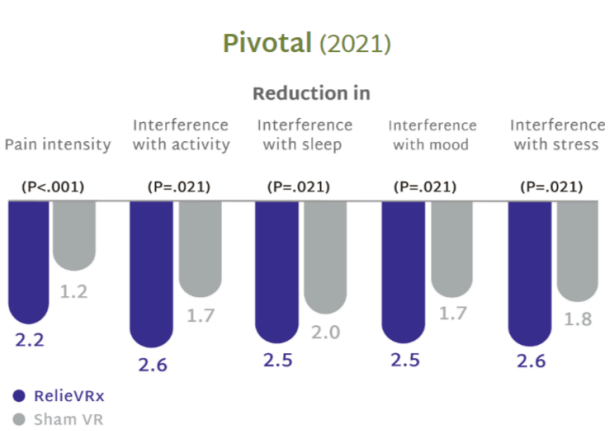
Clinical Impact of RelieVRx

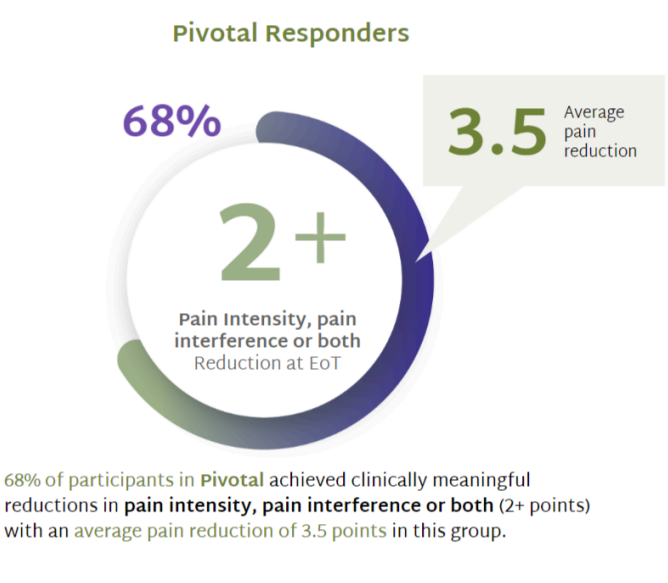
Two randomized controlled trials in over 1200 patients have demonstrated the lasting efficacy of RelieVRx in CLBP.

Two randomized, controlled trials were designed to compare skills-based VR-delivered therapy with an active sham control in adults with moderate to severe CLBP.[9-10]

→ ***8-WEEK PIVOTAL STUDY***

The pivotal study was conducted in a sample that was homogeneous (female: 76%, non-white: 9%, high school or less: 8%) and clinically moderate (baseline pain intensity = 5.1/10, baseline pain interference = 4.8/10, disability = within normal range, sleep disturbance = mild). Clinically meaningful reductions (≥2 points[45-46]) in pain intensity (2.2) and pain interference (2.6) were observed for the RelieVRx program that were significantly larger than for sham.[9]

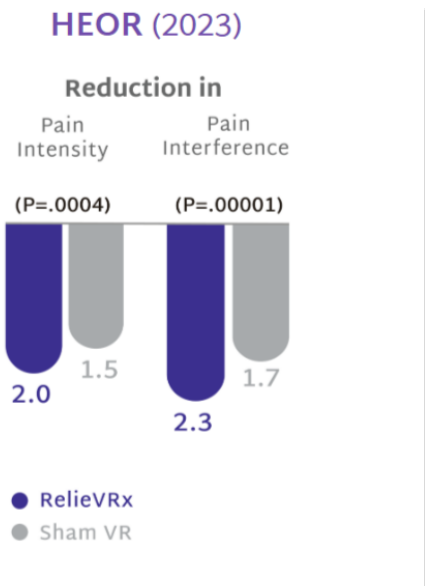


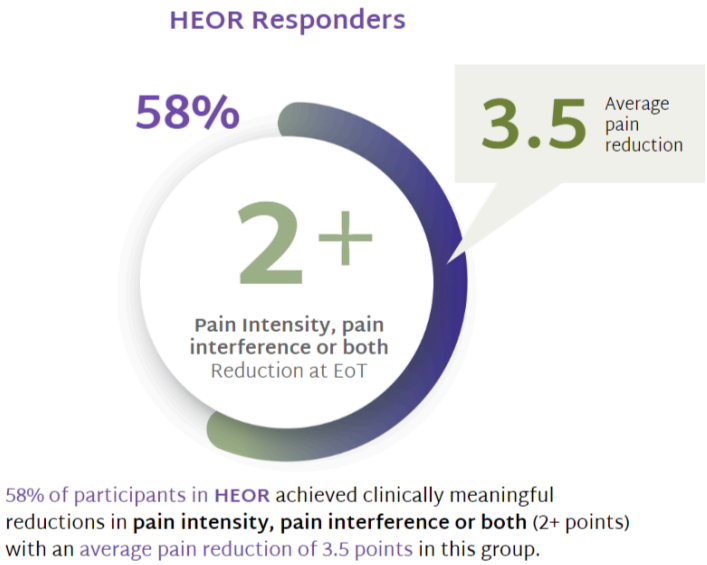


The trial protocol for this study is also available for review.[38]

→ *8-WEEK HEOR STUDY*

In the health economics and outcomes research (HEOR) study, Maddox et al. conducted a similar trial in 1093 adults with CLBP that was demographically diverse (female: 72%, non-white: 32%, high school or less: 20%) and clinically severe (baseline pain intensity = 6.6/10; baseline pain interference = 6.2/10, disability = severe/completely disabled; sleep disturbance = moderate/severe). Clinically meaningful reductions in pain intensity (2.0) and pain interference (2.3) were observed for the RelieVRx program that were significantly larger than for sham.[10]





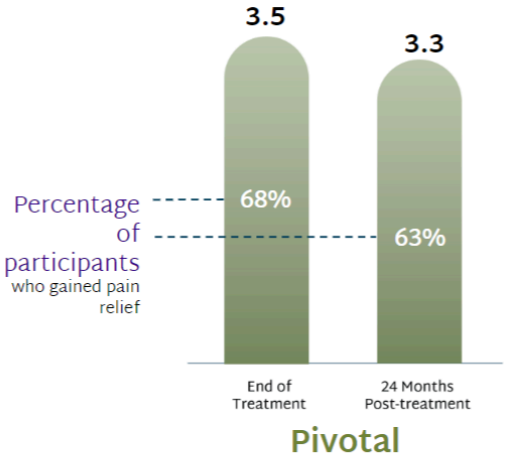
Across both studies, therapeutic program engagement was high, ranging from 4.7 - 5.4 sessions per week, and device usability received an A+ rating based on the System Usability Scale.[9-10]

LONG-TERM FOLLOW-UP

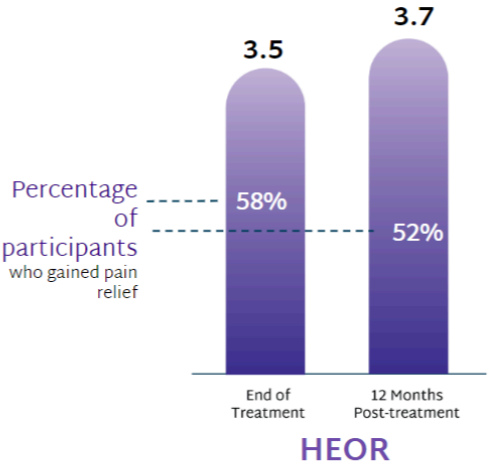
→ Pivotal: 24-month follow-up

→ HEOR: 12-month follow-up submitted for publication to *PAIN Reports*

Participants from both studies have been followed post-treatment to record the durability of treatment benefits. For pivotal trial participants, the average reduction in pain intensity at 24 months post treatment was 1.2 and average reduction in pain interference was 2.2, indicating durability of treatment benefits with some attenuation over time as expected.[11] Meanwhile, pain reductions in the HEOR group have thus far been durable at 12 months post-treatment (pain intensity reduction = 1.7, pain interference reduction = 1.9), again with some expected attenuation.[12]



At 24-months post, 63% of participants in **Pivotal** achieved clinically meaningful reductions in **pain intensity, pain interference,** or **both** (2+ points) with an average pain reduction of 3.3 points in this group.



At 12-months post, 52% of participants in **HEOR** achieved clinically meaningful reductions in **pain intensity, pain interference,** or **both** (2+ points) with an average pain reduction of 3.7 points in this group.

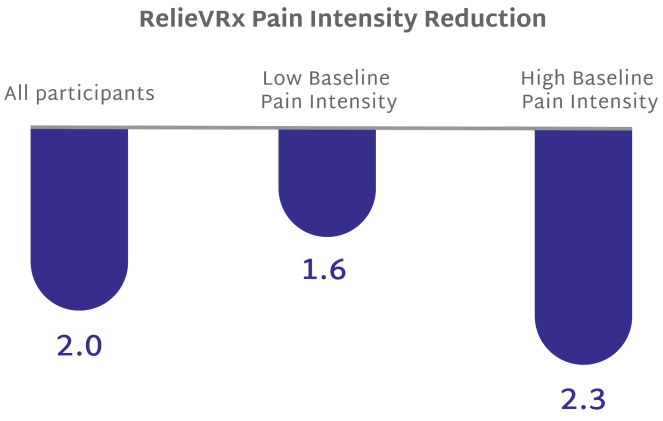
Additional follow-up studies for the pivotal trial (at 3, 6, and 18 months) have been published.[13-15]

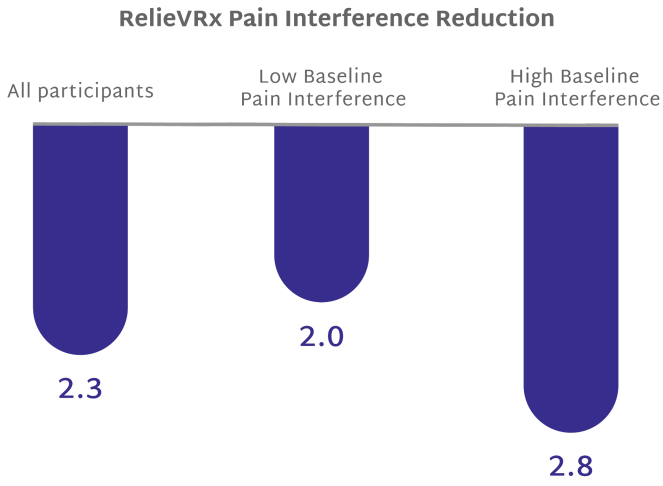
SECONDARY ANALYSES

→ Sociodemographic Predictors

Secondary analyses were performed on the HEOR trial given the large sample size. Clinical effectiveness, therapeutic program engagement, and VR device usability of RelieVRx were examined across a number of sociodemographic factors. Investigators found that clinical effectiveness, therapeutic program engagement, and VR device usability of RelieVRx was generally unaffected by age (<65 vs 65+), gender (male vs female), race/ethnicity (white vs black vs other), and socioeconomic status (low vs high), with a few exceptions. These included age difference for therapeutic program engagement, with >65 having slightly higher engagement and race/ethnicity difference for device usability, with non-white

slightly lower than white, though still an A+ rating.[47] These results are important to mitigate uncertainty about differences in engagement and usability in underrepresented populations and the subsequent clinical benefits. Second, demographic and baseline factors for which the RelieVRx program was especially advantageous were identified. Higher baseline pain intensity ratings were associated with larger reductions in pain intensity, and higher baseline pain interference ratings were associated with larger reductions in pain interference following RelieVRx therapy.[48]





Technical Considerations

RelieVRx is designed according to the highest standards of advanced technology.

RelieVRx is an FDA-authorized Class II medical device. As such, it has undergone rigorous electromagnetic compatibility testing and meets the International

Electrotechnical Commission's 60601-1-11 safety standard for medical devices in the home. Clinical performance has been tested under the labeled conditions for use to validate the model of behavioral therapy as implemented by the device and to evaluate all adverse events. The patient-contacting components of the device have been deemed biocompatible. Software verification, validation, and hazard analysis have been performed.[19]

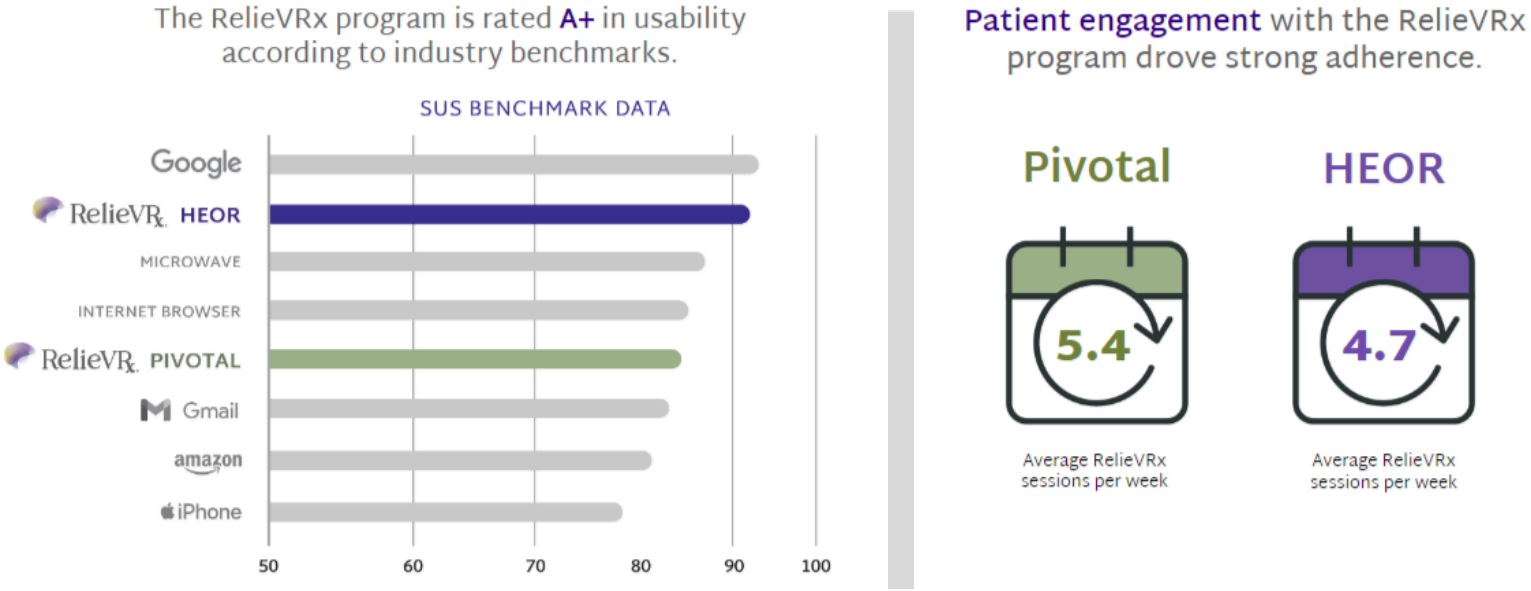
Product Usability and Engagement

The RelieVRx program is easy to use and engaging and leads to high patient satisfaction.

In the pivotal trial, it was rated significantly higher than ShamVR for satisfaction, likelihood to recommend to others, and likelihood to continue using the device after the 56-session treatment phase if it was made available. Treatment engagement and usability were high in both groups, with no significant differences found. RelieVRx participants completed a mean of 43.3 sessions (SD 15.9; ShamVR 48.1, SD 24.8), and they gave RelieVRx a usability rating of 84.33 (ShamVR 81.16) on the validated 100-point System Usability Scale (SUS).[9]

In the HEOR trial, RelieVRx was studied in a large sample of diverse participants with a range of clinical severity and depressive symptoms to better represent real-world patients. A secondary analysis of trial participants suggests that RelieVRx may help transcend pain care disparities via in-home treatment. The clinical effectiveness, therapeutic program engagement, and VR device usability of

RelieVRx are unaffected by key sociodemographic factors often associated with reduced patient engagement and clinical effectiveness.[47]



Additionally, the AVR Pathway® patient support program is available to answer non-medical questions and provide technical support. (The patient's clinical team will be their first resource for medical questions.)

Data Privacy and Governance

AppliedVR is committed to maintaining the highest levels of data security for patients using the RelieVRx program and their providers.

AppliedVR is HITRUST certified.[49] Independent review and security certification is the gold standard for healthcare information security, and HITRUST is recognized by healthcare organizations for its security framework to ensure compliance. Its

comprehensive security and privacy framework is used by healthcare organizations to comply with HIPAA, GDPR, PCI-DSS, and other regulations. Requests to view the RelieVRx HITRUST certification may be submitted to: security@appliedvr.io.

No personal health information is stored on the device, and data is only used and shared as permitted by applicable law.

Product Authorization and Distribution

RelieVRx is available by prescription only.

Indication for Use

The RelieVRx program is a prescription-use immersive virtual reality system intended to provide adjunctive treatment based on cognitive behavioral therapy skills and other evidence-based behavioral methods for patients (age 18 and older) with a diagnosis of chronic lower back pain (defined as moderate to severe pain lasting longer than three months). The device is intended for in-home use for the reduction of pain and pain interference associated with chronic lower back pain.

Contraindications

There are no known contraindications.

Connecting patients to therapy:

Prescription

Provider submits RelieVRx Enrollment Form via fax and reviews program education and expectations with patient.

Device Fulfillment

The RelieVRx device is shipped directly to member's home with **easy-to-follow instructions.**

RelieVRx Therapy

Member engages in the **56-session** treatment Weekly support communications drive adherence and mitigate obstacles.

Device Return

After treatment completion, the device is returned using the **prepaid shipping label** included in the initial shipment box.

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