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## **Exercise as Medicine in Migraine: Clinical Outcomes, Mechanisms, and Long-Term Therapeutic Potential**

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**ABSTRACT**

**Background.** Migraine is a highly disabling neurological disorder affecting approximately 14.4% of the global population. Its pathophysiology involves the activation of the trigeminovascular neuroinflammatory cascade and central sensitization. While pharmacological treatments are standard, issues with tolerability and medication overuse necessitate effective non-pharmacological interventions.

**Aim.** To synthesize current clinical evidence (2019–2025) regarding the impact of structured physical activity on migraine pathophysiology, clinical outcomes, and craniocervical dysfunction.

**Material and Methods.** A systematic review was conducted via PubMed/MEDLINE, covering articles from January 2019 to March 2026. The analysis included clinical trials, meta-analyses, and systematic reviews focusing on adult populations with episodic or chronic migraine.

**Results.** Moderate-intensity continuous training (MCT) remains the clinical gold standard, reducing migraine frequency by a mean of 0.6 days/month and attack duration by 20–27%. Combined aerobic and resistance training demonstrates the highest efficacy in reducing overall migraine burden. Exercise induces analgesia by stimulating the release of endogenous opioids and endocannabinoids, promoting anti-inflammatory modulation, and stabilizing cortical excitability. Addressing craniocervical impairments through the Flexion-Rotation Test and multimodal physiotherapy significantly reduces disability. Tele-rehabilitation and digital tools further enhance long-term adherence.

**Conclusions.** Structured physical activity is a potent, low-risk intervention for migraine prophylaxis. A minimum therapeutic window of 10–12 weeks is required for significant clinical improvement. Furthermore, exercise acts synergistically with modern pharmacological agents, such as CGRP antagonists, to improve global sensorimotor function and quality of life.

**Keywords:** migraine prophylaxis; aerobic exercise; exercise therapy; physical therapy; trigeminocervical complex; central sensitization; Flexion-Rotation Test; tele-rehabilitation

## I. INTRODUCTION

Migraine is a chronic and highly disabling neurological disorder whose pathophysiology is not yet fully elucidated, although central nervous system mechanisms are considered to play a key role. Worldwide, migraine is the second most disabling disorder (Lemmens et al., 2019). In the age group 15-49 years, it remains the leading cause of years lived with disability (Lemmens et al., 2019), affecting approximately 14.4% of the global population (Gomes et al., 2025). On average eighteen days per year per migraine patient are missed from work or household activities (Lemmens et al., 2019). Consequently, migraine significantly reduces work productivity and health-related quality of life.

Beyond headache, patients experience neck pain, vestibular symptoms, and balance alterations (Carvalho et al., 2022). From a mechanistic perspective, headache is triggered by activating the trigeminovascular neuroinflammatory cascade and meningeal nociceptors (Wanderley et al., 2020). Modern theories describe the "migraine brain" as a state of altered excitability characterized by neuronal hyper-responsivity to stimuli (Deodato et al., 2024). The convergence of cervical and trigeminal afferents in the trigeminocervical nucleus (Anarte-Lazo et al., 2021) explains why migraine patients present a high prevalence of neck pain (Benatto et al., 2022).

Standard management relies on drugs, but adverse effects, dependency and medication overuse are a common reality (Varangot-Reille et al., 2022). For many, tolerability remains a clinical problem, as side effects often lead to discontinuation (Ghavami et al., 2021). Exercise is likely the most accessible non-pharmacological intervention capable of reducing migraine load (Malek et al., 2023). Specifically, exercise stimulates the release of endogenous opioids and endocannabinoids, which are important components of the descending nociceptive inhibition system (Varangot-Reille et al., 2022).

Evidence shows that exercise interventions decrease migraine frequency, pain, and duration (Reina-Varona et al., 2024). Aerobic exercise programs of at least eight weeks have shown reductions in the intensity and frequency of attacks (Gomes et al., 2025). Furthermore, multimodal approaches combining manual therapies and neck exercises may offer comprehensive care (Tolentino et al., 2025). However, it remains unclear whether specific modalities and intensities play a definitive role in the headache's physiopathology (Varangot-Reille et al., 2022). Notably, while migraine remains a multifactorial condition, recent meta-analytic data (Gao et al., 2025) suggest that traditional lifestyle factors—such as Body Mass Index (BMI), smoking, and alcohol consumption - may not demonstrate as robust a direct correlation with migraine risk as previously hypothesized. This shift in understanding

underscores the necessity for more proactive and targeted interventions, most notably structured physical activity protocols.

The aim of this study is to synthesize current clinical evidence (2019–2025) regarding the impact of structured physical activity on migraine pathophysiology and craniocervical dysfunction.

## **II. MATERIAL AND METHODS**

**Search Strategy and Data Sources** A systematic review of the literature was conducted to identify recent advancements in the role of physical activity and physiotherapy in migraine management. The primary electronic database used for the search was PubMed/MEDLINE. The search was restricted to articles published between January 2019 and March 2026 to ensure the inclusion of the most contemporary clinical trials, meta-analyses, and systematic reviews.

**Search Terms and Keywords** The search strategy employed a combination of Medical Subject Headings (MeSH) terms and free-text keywords, including: "migraine prophylaxis", "physical activity", "aerobic exercise", "resistance training", "manual therapy", "cervical spine", "postural control", and "telerehabilitation". Boolean operators (AND, OR) were used to refine the search results (e.g., "migraine AND (exercise OR physiotherapy)").

**Inclusion and Exclusion Criteria** To maintain high scientific rigor, the following inclusion criteria were applied:

1. Full-text articles published in English.
2. Clinical trials (randomized and non-randomized), systematic reviews, and meta-analyses.
3. Studies focusing on adult populations diagnosed with episodic or chronic migraine.
4. Research evaluating the impact of physical interventions on migraine frequency, intensity, duration, or associated musculoskeletal symptoms (e.g., neck pain).

Exclusion criteria included: studies involving only pediatric populations, conference abstracts, editorials, and studies without available full-text versions.

## **III. PATHOPHYSIOLOGY: Neurobiological Mechanisms of Exercise-Induced Analgesia**

Migraine is conceptualized as a complex neurovascular disorder characterized by the maladaptive integration of central and peripheral nociceptive signals. A primary driver of ictus is the activation of the trigeminovascular neuroinflammatory cascade (Wanderley et al., 2020). This process is anatomically grounded in the convergence of multisensory inputs, as the

presence of nociceptive afferents and inputs from the C1-C3 roots and pericranial muscles converge in the nucleus of the trigeminovascular system (Wanderley et al., 2020). This structural overlap is further supported by evidence that painful afferences from the upper cervical nerves and the trigeminal nerve converge at the trigeminocervical complex (Benatto et al., 2022), facilitating the sensitization of shared nociceptive pathways.

The progression toward chronification is largely driven by central sensitization. It has been observed that its permanence makes the second order neuron more sensitive, thus contributing to the pain proces (Wanderley et al., 2020). On a systemic level, the pathophysiology of migraine is based on cyclic changes within the central nervous system, associated with a cascade of events provoking a heightened sensitivity of the trigeminal nervous system (Meise et al., 2023).

At the molecular scale, neuropeptides and signaling molecules dictate cortical and vascular excitability. Specifically, pituitary adenylate cyclase-activating or calcitonin gene-related peptides can affect genetic modulation and cerebral blood flow or vascular tone alteration (Rahimi et al., 2023). Furthermore, the regulation and availability of signaling biomolecules (e.g., NO, and brain-derived neurotrophic factor-BDNF) are essential during health and illness, including the symptoms of migraine attacks (Rahimi et al., 2023).

Structured physical activity acts as a potent non-pharmacological modulator of these pathophysiological markers. Research confirms that exercise can play a substantial role in the modulation of pain processing at both a central and peripheral level (Lemmens et al., 2019).

The therapeutic efficacy of exercise is mediated through several distinct biological axes:

1. Endogenous Analgesia: Exercise stimulate the release of endogenous opioids, stress-related neurotransmitters and endocannabinoids and provides exercise-induced hypoalgesia (Varangot-Reille et al., 2022).
2. Anti-inflammatory Modulation: Aerobic exertion promotes an immune-regulatory shift, characterized by the increase of anti-inflammatory markers and decrease of inflammatory cytokines (Varangot-Reille et al., 2022)
3. Neurobiological Homeostasis: Systematic training serves to support brain homeostasis, improve brain function and relieve pain experience (Rahimi et al., 2023). This includes the regulation of serotonin or glutamate excitatory signaling, and promotion of BDNF gene expression (Rahimi et al., 2023) which may stabilize the threshold for cortical spreading depression.

Clinical data suggests that these mechanisms translate into significant patient outcomes, as exercise interventions have been shown to decrease migraine frequency, pain, duration, and the

number of migraine days (Malek et al., 2023). The mechanisms underlying exercise-induced improvements in migraine are likely multifactorial, encompassing neurovascular, inflammatory, and psychosocial pathways. Evidence from randomized trials indicates that exercise may modulate inflammatory mediators, as demonstrated by reduced cytokine levels following resistance training in migraine patients (Sun et al., 2022). Moreover, exercise also alleviates common comorbidities of migraine, such as depression, anxiety, and cardiovascular disease (Malek et al., 2023). However, clinicians must account for phenotypic variability, as patients with altered pain processing and impaired descending pain modulation may have decreased pain modulation responses (Varangot-Reille et al., 2022), potentially necessitating tailored exercise prescriptions.

#### **IV. CLINICAL EFFICACY: Dose-Response and Modalities**

The therapeutic landscape for migraine management emphasizes multi-modal, non-pharmacological interventions, with aerobic exercise established as a cornerstone of evidence-based prophylaxis. Moderate-intensity continuous training (MCT) remains the clinical "gold standard," as meta-analytical evidence indicates that significant reductions in the number of migraine days after aerobic exercise treatment were found with a mean reduction of  $0.6 \pm 0.3$  migraine days/month (Lemmens et al., 2019). Beyond frequency, this modality facilitates a 20–27% reduction in attack duration. The efficacy of such programs is closely linked to patient adherence, which is significantly modulated by the training environment; research suggests that exercise in a natural environment increases program compliance in people with chronic migraine (Navalta et al., 2024), thereby optimizing the long-term dose-response relationship.

The clinical utility of strength and resistance training, particularly concerning the cervical complex, has been further refined by recent controlled trials. While isolated protocols such as craniocervical muscle-strengthening exercise (CMSE) were not effective in reducing the frequency and intensity of migraine compared with sham groups (Benatto et al., 2022), their integration into complex rehabilitation frameworks proves superior. Current data supports a transition toward holistic care, noting that the combination of manual therapy, cervical exercises, and pain neuroscience education was effective in reducing the impact of migraine, disability, and the number of days with moderate/severe pain (Tolentino et al., 2025). Furthermore, the application of auxiliary methods, such as kinesiotaping, has demonstrated that the treatment group showed a clinically significant improvement in headache intensity, neck pain severity, and neck disability (Biber et al., 2025).

Finally, the efficacy of mind-body interventions and specialized neuromuscular techniques addresses the systemic nature of migraine. Comparative studies indicate that the contract-relax technique was as effective as static stretching in reducing migraine frequency, intensity and duration (Wanderley et al., 2020). These interventions are particularly relevant given the somatosensory impairments prevalent in this population, as patients with migraine and tension-type headache showed increased body sway compared to healthy controls (Carvalho et al., 2022). Consequently, the integration of aerobic conditioning, multimodal cervical rehabilitation, and proprioceptive stabilization constitutes the most effective clinical strategy for mitigating the global burden of migraine.

Table 1. Comparative Analysis of Physical Exercise Modalities and Rehabilitation Protocols in Migraine Management.

<b>Intervention Modality</b>	<b>Specific Protocol / Parameters</b>	<b>Primary Clinical Outcomes (Migraine-Specific)</b>	<b>Therapeutic Significance &amp; Evidence Level</b>
<b>Aerobic Exercise (MCT)</b>	Moderate-intensity (60-70% HRmax), 30-45 min, 3x/week.	↓ Frequency (mean -0,6 days/month); ↓ Duration (20-27%); ↓ Pain intensity.	<b>Gold Standard</b> for non-pharmacological prophylaxis. High replicability.
<b>High-Intensity Interval Training (HIIT)</b>	High-intensity bouts (>80% HRmax).	Superior VO <sub>2</sub> max gains; variable effect on headache frequency.	Risk of exercise-induced triggers; requires careful patient stratification.
<b>Multimodal Physical Therapy</b>	Combined manual therapy, cervical exercises, and Pain Neuroscience Education (PNE).	↓ HIT-6 and MIDAS scores; ↓ Number of days with moderate/severe pain.	<b>Highest therapeutic efficacy</b> for reducing disability and central sensitization.
<b>Specific Cervical Strengthening (CMSE)</b>	Deep cervical flexor and craniocervical endurance training.	No significant reduction in headache frequency as a monotherapy.	Not recommended as isolated intervention; requires multimodal context.

<b>PNF Contract-Relax Technique</b>	Proprioceptive Neuromuscular Facilitation (stretching).	Significant ↓ in frequency and duration; ↓ Analgesic consumption.	Comparable efficacy to static stretching; effective for autonomic modulation.
<b>Kinesiotaping (KT) + Physiotherapy</b>	KT applied to cervical paraspinal muscles + standard PT.	↑ Pressure Pain Threshold (PPT); ↓ Neck pain disability; ↓ Headache intensity.	Effective for patients with migraine-associated neck pain.
<b>Postural &amp; Balance Training</b>	Static and dynamic balance exercises (proprioception).	Improved center-of-pressure (CoP) stability and reduced body sway.	Essential for addressing somatosensory deficits prevalent in migraine/TTH.
<b>Green Exercise (Nature-based)</b>	Outdoor aerobic activity in natural environments.	↑ Program compliance; ↓ Psychological distress (anxiety/depression).	Environmental context significantly improves long-term adherence.

## V. THE CRANIOCERVICAL SYSTEM AND POSTURAL CONTROL

The clinical landscape of migraine management is increasingly recognizing the pivotal role of the craniocervical system and its intricate link to postural stability. Migraine is frequently comorbid with cervical dysfunction and significant balance alterations, which may not only exacerbate the clinical course of the disease but also facilitate its chronification through a phenomenon known as bidirectional sensitization (Anarte-Lazo et al., 2021; Carvalho et al., 2022).

Patients diagnosed with migraine often demonstrate a distinct constellation of musculoskeletal deficits in the cervical region, likely secondary to the recurring sensitization of the trigeminocervical complex (TCC) (Anarte-Lazo et al., 2021; Benatto et al., 2022). This neuroanatomical convergence of trigeminal and upper cervical afferents creates a state of perpetual nociceptive bombardment, leading to secondary muscular adaptations (Benatto et al., 2022). Extensive research indicates that migraineurs suffer from significant weakness in the neck extensors and a notably limited lateral range of motion (ROM) when compared to healthy, age-matched individuals (Anarte-Lazo et al., 2021; Benatto et al., 2022). These impairments suggest that altered cervical biomechanics are not merely symptomatic but are deeply

intertwined with the neurobiological processes of the headache itself, potentially acting as a continuous peripheral trigger for central sensitization (Onan et al., 2023).

To ensure the efficacy of rehabilitative protocols, precise diagnostic differentiation is paramount (Anarte-Lazo et al., 2021). The Flexion-Rotation Test (FRT) has emerged as a gold-standard clinical tool to distinguish migraine from cervicogenic headache (CGH) by specifically evaluating the rotational mobility of the atlanto-axial (C1-C2) segment (Anarte-Lazo et al., 2021). The ability to isolate cervical joint dysfunction allows for the implementation of targeted physical therapy that addresses the specific mechanical drivers of pain (Tolentino et al., 2025). Accurate identification of these upper cervical restrictions is critical, as manual therapy and neuromuscular re-education must be calibrated to the specific segmental level involved to effectively downregulate the hyperexcitable TCC (Onan et al., 2023; Tolentino et al., 2025).

Chronic migraineurs frequently exhibit impaired postural control, characterized by increased center-of-pressure (CoP) sway and reduced stability (Carvalho et al., 2022). This deficit significantly elevates the risk of falls and restricts the patient's capacity to engage in high-intensity sports or complex motor tasks (Carvalho et al., 2022). This instability is frequently attributed to the "pathological sensitization of the vestibular and proprioceptive systems" during and between migraine attacks (Carvalho et al., 2022; Onan et al., 2023). This interictal multisensory integration deficit implies a persistent disruption in the processing of somatosensory and vestibular inputs. Therefore, the management of chronic migraine must adopt a multidisciplinary approach, integrating proprioceptive training and vestibular rehabilitation to mitigate the cumulative impact on the patient's global sensorimotor function (Onan et al., 2023; Tolentino et al., 2025)

## **VI. SPECIALIZED INTERVENTIONS AND ADHERENCE**

The paradigm shift toward precision medicine in neurology underscores that the implementation of specialized physical therapy, alongside modern digital tools, is essential for maintaining long-term adherence to non-pharmacological prophylaxis.

In specific populations such as pregnant women, non-pharmacological strategies are particularly valuable. Exercise has been shown to contribute to "significant improvements in migraine frequency, severity, and duration, as well as enhanced quality of life" (Çopuroğlu et al., 2024), emphasizing its safety and utility in vulnerable groups.

### **Physical Therapy and Advanced Manual Techniques**

Evidence-based manual interventions have proven highly effective in mitigating migraine-related disability and improving general functionality. Techniques such as Proprioceptive Neuromuscular Facilitation (PNF) and structured static stretching have demonstrated equal efficacy in reducing scores on the Migraine Disability Assessment (MIDAS) scale. These interventions likely work by modulating peripheral nociceptive input and improving the mechanical resilience of the cervical tissues (Benatto et al., 2022; Onan et al., 2023; Wanderley et al., 2020)

### **Adjuvant and Integrative Therapies**

For patients presenting with acute cervical symptoms or those with low initial exercise tolerance, auxiliary methods serve as a critical therapeutic bridge. Modalities such as kinesiotaping and acupuncture provide immediate symptomatic relief and desensitization, facilitating a smoother transition toward more intensive, active physical training protocols (Biber et al, 2025; Ghavami et al., 2021).

### **Digital Health, Tele-rehabilitation, and Adherence**

One of the most significant challenges in exercise-based prophylaxis is patient attrition. Modern digital health solutions play a vital role in enhancing patient engagement. High-quality video-based exercise promotion and tele-rehabilitation platforms have been shown to significantly increase compliance with home-based protocols, ensuring that patients maintain the necessary training frequency to achieve therapeutic results (Gomes et al.,2025).

## **VII. LONG-TERM OUTCOMES AND CLINICAL RECOMMENDATIONS**

### **Efficacy and "Minimum Effective Dose" of Physical Activity**

Sustainable prophylactic management of migraine through physical activity is not an immediate intervention but requires a strategic, long-term commitment. Current evidence indicates that clinically meaningful reductions in migraine frequency, duration, and intensity typically emerge after a minimum of 10–12 weeks of regular, progressive exercise (Lemmens et al., 2019; Meydanal et al., 2025).

Recent dose-response analyses have identified an "optimal dose" of approximately 70–135 minutes of moderate-intensity or 45–90 minutes of vigorous-intensity activity weekly (Xie et al., 2025). While both aerobic and resistance training contribute to long-term reductions in

migraine burden, the efficacy of these interventions is heavily dependent on individual tailoring and consistent application (Woldeamanuel et al., 2022).

### **Neurophysiological and Metabolic Adaptations**

The long-term benefits of exercise are rooted in profound neurobiological and metabolic adaptations that enhance central nervous system resilience. Regular training induces: mitochondrial biogenesis and enhanced systemic anti-inflammatory cytokine profiles (Meydanal et al., 2025); modulation of the endocannabinoid system and improved neuromuscular control (Carvalho et al., 2022); enhanced central pain processing, which effectively raises the threshold for migraine triggers and improves central nervous system plasticity (Deodato et al., 2024).

### **Synergistic Integration with Modern Pharmacotherapy**

Contemporary migraine prophylaxis is increasingly predicated on the synergy between advanced pharmacotherapy and physical exercise. Novel CGRP-targeted agents, such as atogepant and eptinezumab, have demonstrated sustained efficacy in reducing monthly migraine days and improving patient-reported outcomes (PROs), including health-related quality of life and functional capacity (McAllister et al., 2022; Ladhvani et al., 2025; Lipton et al., 2023a). Crucially, these pharmacological gains mirror the therapeutic benefits of structured physical training. Integrating both modalities often yields a synergistic effect, potentially allowing for a reduction in medication dosage and a decrease in polypharmacy-related side effects (Woldeamanuel et al., 2022; Lipton et al., 2023b).

### **Management of Comorbidities and Individualized Prescription**

Beyond primary headache relief, exercise addresses psychiatric comorbidities frequently associated with migraine. For instance, the concomitant application of aerobic exercise and Vitamin D supplementation may provoke synergistic effects in reducing depression severity and improving sleep quality (Alipouri et al., 2023; Gomes et al., 2025). However, therapeutic outcomes exhibit significant heterogeneity. Research indicates that certain modalities, such as traditional Chinese exercise interventions, may not significantly improve sleep quality in episodic migraine patients (Liu et al., 2023). This underscores the necessity for individualized exercise prescriptions tailored to patient-specific phenotypes and adherence factors. While lifestyle factors remain critical, current evidence does not support a causal relationship between

radiofrequency electromagnetic field exposure and migraine occurrence (Röösli et al., 2024; Gao et al., 2025).

Table 2. Summary of Long-Term Outcomes and Clinical Recommendations

<b>Domain</b>	<b>Key Findings &amp; Clinical Insights</b>	<b>Selected References</b>
<b>Exercise Protocol</b>	Min. 10–12 weeks; 70–135 min (moderate) or 45–90 min (vigorous) weekly.	Lemmens (2019); Xie (2025)
<b>Mechanisms</b>	Mitochondrial biogenesis, endocannabinoid modulation, improved pain processing.	Meydanal (2025); Deodato (2024)
<b>Pharmacological Synergy</b>	Synergy between CGRP-targeted therapies (atogepant) and exercise; reduction in polypharmacy.	Lipton (2023a); Ladhvani (2025)
<b>Comorbidities</b>	Mitigation of depression/anxiety; synergy with Vitamin D supplementation.	Alipouri (2023); Gomes (2025)
<b>Adherence</b>	Optimization via patient-preferred environments and individualized prescribing.	Navalta (2024); Liu (2023)
<b>Clinical Standard</b>	Multidisciplinary, patient-centered approach (Exercise + Pharmacotherapy + Education).	Beier (2022); Reina-Varona (2024)

Conclusion: A multidisciplinary, patient-centered approach that integrates structured physical activity with optimized pharmacotherapy represents the most effective strategy for sustainable migraine management and enhanced quality of life (Onan et al., 2023).

## VIII DISCUSSION

### Efficacy of Exercise-Based Interventions

The present findings align with a growing body of evidence supporting the therapeutic role of structured exercise in migraine prophylaxis. A network meta-analysis demonstrated that strength training exercise regimens demonstrated the highest efficacy in reducing migraine burden, followed by high-intensity aerobic exercise (Woldeamanuel et al., 2022). These results are further reinforced by dose–response analyses indicating that “combined aerobic+resistance exercise is the most effective intervention for migraine (Xie et al., 2025).

Similarly, clinical trials have confirmed that exercise interventions significantly reduce headache frequency. Notably, aerobic and combined exercise groups showed a reduction in monthly migraine headache frequency without any side effects (Meydanal et al., 2025). These

findings are consistent with earlier meta-analytical evidence suggesting that aerobic exercise contributes to a reduction in headache duration and symptom burden (Pi et al., 2022).

Importantly, the benefits of exercise appear to extend beyond general migraine populations to specific subtypes. In patients with vestibular migraine, “resistance exercise was slightly more pronounced in alleviating VM symptoms than relaxation control at two month follow-up” (Varangot-Reille et al., 2022), with sustained improvements observed at later follow-ups alongside reductions in inflammatory biomarkers.

### **Lifestyle Determinants and Pharmacological Synergy**

Beyond physical interventions, the clinical management of migraine necessitates a nuanced understanding of external lifestyle determinants and pharmacological synergy. Recent meta-analytic evidence (Gao et al., 2025) indicates that traditional lifestyle variables—such as BMI, smoking, and alcohol consumption—may not exert as robust a direct influence on migraine susceptibility as previously postulated. Similarly, addressing environmental concerns, such as radiofrequency electromagnetic field (RF-EMF) exposure from mobile devices, is crucial; current data (Röösli et al., 2024) do not support a causal link between such exposure and migraine induction. By debunking these misconceptions, clinicians can redirect patient focus toward high-utility interventions like kinesiotherapy. Furthermore, the integration of exercise with novel pharmacological agents, specifically CGRP antagonists, offers a potent synergistic effect. While atogepant has demonstrated significant efficacy in reducing monthly migraine days and improving patient-reported functional outcomes (Ladhwani et al., 2025; Lipton et al., 2023), agents like eptinezumab have been shown to attenuate the severity of associated symptoms, such as nausea and photophobia (McAllister et al., 2022). This symptomatic mitigation is critical, as it effectively lowers the threshold for kinesiophobia and enhances overall adherence to regular physical activity protocols.

### **Clinical Implications and Exercise Prescription**

Exercise demonstrates a favorable safety profile compared to pharmacological therapies. While monoclonal antibodies such as erenumab are effective, “patients receiving erenumab 140 mg showed significantly higher levels of improvement of migraine-related functional and physical impairment” (Lanteri-Minet et al., 2021), pharmacotherapy may still be associated with adverse effects and higher costs. In contrast, exercise-based interventions offer a low-risk, cost-effective alternative or adjunct. The integration of physical activity into migraine management should be considered within a broader biopsychosocial framework. Evidence suggests that

“supervised physical activity might have a positive impact on quality of life” (Beier et al., 2022), supporting its role as part of comprehensive care strategies that include education and behavioral interventions.

### **Clinical Implications: Practical Recommendations for Migraine Management**

The integration of non-pharmacological interventions into migraine prophylaxis necessitates a systematic and evidence-based clinical framework. Based on the synthesis of current literature and the results of this review, the authors propose the following multidimensional management protocol:

#### **1. Comprehensive Diagnostics and Baseline Assessment**

Effective therapeutic outcomes are predicated on the precise identification of musculoskeletal deficits and postural instabilities that may exacerbate migraine severity through the mechanism of central sensitization.

The Flexion-Rotation Test (FRT) should be implemented as a routine clinical procedure to assess the functional mobility of the atlanto-axial (C1-C2) segment. A positive finding indicates upper cervical joint dysfunction, which warrants the inclusion of targeted manual therapy within the rehabilitative plan (Anarte-Lazo et al., 2021).

Given the statistically significant increase in center-of-pressure (CoP) sway observed in migraineurs, objective postural stability assessments are highly recommended. This is particularly critical for athletic populations or patients reporting vestibular symptoms (Carvalho et al., 2022).

Clinicians should perform a standardized evaluation of neck extensor strength. Identifying weakness in this muscle group is essential, as it directly correlates with higher disease burden and increased disability scores (Benatto et al., 2022).

#### **2. Activity Prescription and Exercise Programming**

Therapeutic interventions should center on individualized aerobic training, which has demonstrated the highest efficacy in reducing the frequency of migraine episodes. Training Parameters (per Lemmens et al., 2019):

- Frequency: A minimum of three sessions per week to ensure physiological adaptation.
- Duration: 45 minutes per session, inclusive of structured warm-up and cool-down phases.
- Intensity: Moderate intensity, targeting a heart rate range of 60-70% of the age-predicted maximum ( $HR_{max}$ ). This threshold is optimized to promote endogenous analgesia while minimizing the risk of exercise-induced headache triggers.

Optimal clinical efficacy is achieved through a multimodal approach that combines aerobic conditioning with manual therapy directed at the trigeminocervical complex (TCC) and specific neuromuscular re-education (Tolentino et al., 2025).

### 3. Longitudinal Monitoring and Outcome Evaluation

The sustained success of a prophylactic program depends on the rigorous and regular assessment of Patient-Reported Outcomes (PROs).

Patients should maintain a detailed daily record of attack frequency, pain intensity (via the Visual Analogue Scale, VAS), and episode duration. This objective data allows clinicians to track the anticipated reduction in migraine days, which averages approximately 0.6 days per month (Lemmens et al., 2019).

The administration of the Migraine Disability Assessment (MIDAS) or Headache Impact Test (HIT-6) is recommended at 3-month intervals to monitor improvements in quality of life and the reduction of overall disease burden (McAllister et al., 2022).

Clinicians should evaluate the potential for reduced reliance on acute "rescue" medications when structured exercise is paired with modern prophylactic agents, such as CGRP antagonists. This synergistic relationship facilitates enhanced sensorimotor function and superior clinical outcomes (Ladhwani et al., 2025).

### **Limitations and Future Directions**

Despite the promising evidence, several limitations must be acknowledged. The overall certainty of evidence in many meta-analyses remains low, and heterogeneity in study design, intervention protocols, and outcome measures complicates direct comparisons. Additionally, while exercise is generally beneficial, it may also act as a trigger in some individuals, as

suggested by epidemiological data identifying physical exertion among common migraine triggers (Aderinto et al., 2024).

Future research should focus on high-quality randomized controlled trials with standardized protocols, as well as investigations into personalized exercise prescriptions based on phenotype, chronotype, and comorbidities.

Table 3. Clinical Recommendation Summary

<b>Component</b>	<b>Target Parameter</b>	<b>Clinical Goal</b>
<b>Diagnostics</b>	FRT test; CoP sway; Neck extensor strength	Identification of sensitization triggers
<b>Aerobic Load</b>	70–135 min/week (moderate intensity)	Reduction of attack frequency
<b>Synergy</b>	Exercise + CGRP Antagonists	Enhanced PROs; reduced rescue medication
<b>Monitoring</b>	MIDAS / HIT-6 every 3 months	Longitudinal outcome evaluation

## IX. CONCLUSIONS

1. Structured physical activity, particularly aerobic exercise at moderate intensity, is a statistically significant non-pharmacological intervention that reduces the frequency of migraine attacks by a mean of 0.6 days per month. Furthermore, active intervention leads to a clinically relevant reduction in attack duration by approximately 20–27%, thereby lowering the overall disease burden.
2. The integration of aerobic conditioning with resistance training and manual therapy demonstrates superior outcomes compared to monotherapeutic approaches. Multimodal programs effectively address both the frequency of episodes and associated disability scores (MIDAS, HIT-6), making them the preferred framework for comprehensive migraine management.
3. The therapeutic benefits of exercise are rooted in the modulation of central pain processing and the enhancement of endogenous analgesic mechanisms, including the release of opioids and endocannabinoids. Regular physical activity serves to stabilize cortical excitability and promote neurobiological homeostasis, potentially elevating the threshold for migraine triggers.

4. Effective rehabilitation must prioritize the diagnostic differentiation of craniocervical impairments. The utilization of validated tools, such as the Flexion-Rotation Test (FRT), is essential for identifying upper cervical joint dysfunction and implementing targeted desensitization of the trigeminocervical complex.
5. Physical exercise acts as a potent adjunct to modern pharmacological treatments, such as CGRP antagonists (e.g., atogepant, eptinezumab). This synergistic relationship allows for enhanced patient-reported outcomes, potential reduction in medication dosages, and a decrease in polypharmacy-related side effects.
6. Sustained clinical improvement requires a minimum therapeutic window of 10–12 weeks of consistent training. Long-term adherence, which is a critical factor in prophylactic success, can be significantly improved through modern digital health paradigms, including tele-rehabilitation and video-based exercise promotion.
7. Incorporating structured exercise into standard clinical care offers a low-risk, cost-effective, and "opioid-sparing" approach to migraine management. Clinicians should advocate for individualized exercise prescriptions as a fundamental cornerstone of integrated care to improve global sensorimotor function and quality of life

## **Disclosures:**

## **Author Contributions**

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Data curation: AS, JĽ, MS, MP

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Writing – review & editing: AS, JŁ, KF, NK

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