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COMPARATIVE EFFECTIVENESS OF PLATELET RICH PLASMA PRP STEM CELLS AND EXOSOMES IN THE TREATMENT OF SPORTS INJURIES A NARRATIVE REVIEW

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ABSTRACT

BACKGROUND

Sports related musculoskeletal injuries are among the most common conditions in orthopedics and sports medicine and affect tendons, ligaments, muscles and articular cartilage. Impaired healing driven by mechanical overload, repetitive microtrauma and insufficient recovery may lead to sustained pro inflammatory cytokine activity including IL 1β and TNF α, progressive tissue degeneration and chronic pain. The limited vascularization and cellularity of cartilage and tendons further restrict intrinsic regenerative capacity. Conventional treatments such as nonsteroidal anti inflammatory drugs, rest, ice, compression and elevation, and physical therapy primarily provide symptomatic relief and may interfere with biological processes involved in tissue repair. These limitations have stimulated increasing interest in biologic regenerative approaches, including platelet rich plasma, mesenchymal stem cells and exosome based therapies.

AIM

To comparatively evaluate platelet rich plasma, mesenchymal stem cells and mesenchymal stem cell derived exosomes as biologic regenerative therapies in sports related musculoskeletal injuries, with focus on mechanisms of action, clinical effectiveness across tissue types, safety and clinical applicability.

METHODS

A qualitative narrative review of experimental and clinical studies published between 2000 and 2024 was conducted using PubMed, Scopus and Google Scholar. Included publications addressed biological mechanisms, regenerative effects, safety aspects and clinical outcomes of platelet rich plasma, mesenchymal stem cells and exosomes in injuries of tendons, cartilage, muscles and ligaments.

RESULTS

Platelet rich plasma, mesenchymal stem cells and exosome based therapies were associated with regenerative and anti inflammatory effects across a range of musculoskeletal conditions. Platelet rich plasma was most consistently linked to angiogenesis enhancement, collagen synthesis and symptomatic improvement, although reported outcomes varied substantially due to heterogeneity in preparation and application protocols. Mesenchymal stem cell based therapies demonstrated pronounced immunomodulatory and regenerative effects, particularly in tendon and cartilage related conditions, with some studies suggesting improved outcomes under specific dosing and administration strategies. Exosome based approaches showed promising effects on tissue repair and inflammation modulation in preclinical models, representing a potential cell free alternative, but clinical evidence remains limited. Overall safety profiles were acceptable, while methodological heterogeneity and limited direct comparative data contributed to variability in reported outcomes.

CONCLUSIONS

Biologic regenerative therapies provide complementary mechanisms that may support tissue repair in sports related musculoskeletal injuries. Platelet rich plasma, mesenchymal stem cells and exosome based approaches demonstrate clinical potential and acceptable safety, but heterogeneity of protocols and the lack of long term comparative clinical data limit definitive conclusions regarding relative effectiveness. Further standardized and well designed clinical studies are required to define optimal indications and to support integration of these therapies into personalized and mechanism oriented regenerative treatment strategies.

Keywords: Platelet rich plasma; Mesenchymal stem cells; Exosomes; Sports injuries; Regenerative medicine

INTRODUCTION

Regenerative medicine has emerged as an important area of interest in the management of sports related musculoskeletal injuries, particularly in conditions where conventional therapies provide limited regenerative benefit. Platelet rich plasma and stem cell based approaches have been increasingly investigated in the treatment of tendinopathies, muscle injuries and ligament damage, with reported effects on tissue repair processes and symptom reduction [1,2]. These biologic interventions are intended to support endogenous healing mechanisms rather than solely provide symptomatic control, thereby addressing limitations associated with standard conservative treatments [3].

Mesenchymal stem cells have demonstrated immunomodulatory and proangiogenic properties in both preclinical models and clinical studies, with an overall acceptable safety profile [4]. In parallel, MSC derived exosomes have been proposed as a cell free biologic strategy capable of mediating intercellular signaling and regenerative effects through molecular cargo delivery [5,6]. Despite growing interest and encouraging preliminary findings, the clinical effectiveness and optimal application of these biologic therapies in sports medicine remain insufficiently defined, underscoring the need for well designed randomized large scale clinical trials [7,8].

RATIONALE AND NOVELTY

Sports related musculoskeletal injuries constitute a significant clinical challenge due to the limited intrinsic regenerative capacity of tissues such as tendons and articular cartilage [11,15]. Despite growing interest in biologic regenerative approaches, including platelet rich plasma, mesenchymal stem cells and MSC derived exosomes, the current evidence base remains highly heterogeneous. Substantial variability exists across studies with respect to preparation techniques, biologic composition, dosing regimens, delivery methods and patient selection criteria, which complicates interpretation of outcomes and limits reproducibility [29,30,66].

Most existing reviews address these biologic therapies in isolation or focus on specific tissue types or indications. As a result, comparative analyses that systematically examine shared and distinct biological mechanisms, safety profiles and clinical performance across PRP, MSCs and exosomes are limited [32,46,71]. This fragmentation hampers translational decision making and obscures the relative positioning of these therapies within regenerative sports medicine.

The present review seeks to address this gap by providing an integrated narrative synthesis of experimental and clinical literature published between 2000 and 2024. By evaluating PRP, MSCs and MSC derived exosomes within a unified analytical framework, the review combines mechanistic evidence with clinical findings and identifies methodological and translational barriers that currently impede standardization and broader clinical adoption.

RELEVANCE

Sports related musculoskeletal injuries remain a major burden in orthopedics and sports medicine and frequently involve tissues with restricted healing potential, including tendons and cartilage [11,15]. Although PRP, MSC based therapies and exosome based approaches are increasingly used in clinical practice, the supporting evidence is dispersed across diverse experimental models and clinical study designs, limiting coherent interpretation [29,30,66].

A structured synthesis of available data is therefore clinically relevant to clarify the potential role of biologic therapies in enhancing tissue repair, modulating inflammation and supporting functional recovery [1,2,18]. An integrative overview may also assist in identifying factors influencing therapeutic outcomes, inform optimization of preparation and delivery protocols and support the translational development of emerging approaches, particularly exosome based strategies [30,60–65,71–73]. In addition, such an analysis can help delineate priorities for future research, including the need for standardized methodologies, comparative effectiveness studies and long term safety data required to advance regenerative sports medicine [7,29,66].

AIM AND RESEARCH QUESTIONS

The aim of this review is to critically evaluate current evidence regarding platelet rich plasma, mesenchymal stem cells and exosome based therapies in sports related musculoskeletal injuries.

The following research questions are addressed.

What biological and molecular mechanisms underlie the regenerative, anti inflammatory and pro healing effects of PRP, MSCs and exosomes in musculoskeletal tissues.

How do these therapies compare in clinical effectiveness across different injury types, including tendon, cartilage, muscle and ligament damage.

What are the safety, feasibility and tolerability profiles of PRP, MSCs and exosomes, particularly with regard to preparation methods, dosing protocols and delivery approaches.

How can these biologic therapies be integrated into personalized, mechanism driven treatment strategies in sports medicine, and which evidence gaps should be addressed in future clinical trials.

METHODS

This review was conducted as a narrative, evidence based synthesis of regenerative biologic therapies, including platelet rich plasma, mesenchymal stem cells and exosomes, in the management of sports related musculoskeletal injuries. The analysis relied exclusively on peer reviewed publications identified in major international scientific databases and was complemented by relevant literature obtained through cross referencing.

SEARCH AND STRATEGY

The search strategy was designed as a targeted selection of literature for a narrative review and aimed at identifying experimental and clinical data on the use of PRP, mesenchymal stem cells and exosomes in sports related musculoskeletal injuries.

The search was conducted in the electronic scientific databases PubMed, Scopus and Google Scholar. These databases were selected as primary sources of peer reviewed biomedical and clinical literature in the fields of sports medicine, orthopedics and regenerative medicine. The search period covered publications from January 2000 to May 2024, allowing inclusion of both early foundational studies and recent clinical and translational research.

Search queries were constructed using combinations of key terms reflecting both biologic therapies and their clinical contexts. The following terms were used: platelet rich plasma, PRP, mesenchymal stem cells, MSC, exosomes, extracellular vesicles, sports injuries, musculoskeletal injuries, tendinopathy, cartilage regeneration, osteochondral defects, regenerative medicine and orthobiologics. These terms were combined in different ways to maximize retrieval of relevant publications. No formal language restrictions were applied, although the analysis included studies available in English.

Additional sources were identified through manual review of reference lists from key systematic and narrative reviews, as well as through cross citation of highly relevant publications. This approach enabled inclusion of studies that may not have been captured during the initial database search but were important for understanding mechanisms of action and clinical application of the reviewed therapies.

Study selection was performed manually based on relevance to the topic of the review, with priority given to publications reporting biological mechanisms, regenerative effects, safety considerations and clinical outcomes of PRP, MSC and exosome based therapies in injuries of tendons, cartilage, muscles and ligaments.

SELECTION PROCESS

Publications were selected manually based on their direct relevance to the biological mechanisms, therapeutic applications and reported clinical outcomes of platelet rich plasma, mesenchymal stem cells or exosomes in musculoskeletal injuries, consistent with the methodological approach of narrative reviews. Eligible sources included randomized controlled trials, cohort and observational studies, in vitro and in vivo experimental research, as well as systematic and narrative reviews addressing these biologic therapies. Studies were excluded if they were not peer reviewed, were limited to conference abstracts without full datasets, focused exclusively on pediatric populations, or addressed conditions unrelated to musculoskeletal or sports related injury models. Overall, 73 publications providing mechanistic or therapeutic information on PRP, MSCs or exosomes were included in the analysis.

DATA EXTRACTION AND SYNTHESIS

Data were extracted qualitatively from the included studies with emphasis on cellular and molecular mechanisms of action, tissue specific regenerative effects, safety and tolerability profiles, and clinical outcomes such as pain reduction, structural healing and functional recovery. Given the substantial heterogeneity in study design, biologic preparation protocols and outcome measures, quantitative meta analysis was not performed. The findings were therefore synthesized narratively with focus on translational relevance and clinical applicability.

RESULTS

SCOPE OF EVIDENCE

The included studies encompassed a broad spectrum of regenerative strategies. PRP studies investigated leukocyte-rich and leukocyte-poor formulations, single- versus double-spin preparation techniques and variable platelet concentrations [25,26,29,30]. MSC-based therapies included bone marrow–derived, adipose-derived and synovium-derived cell sources, with both autologous and allogeneic approaches [43–47,50]. Exosome-related evidence focused on MSC-derived extracellular vesicles, engineered vesicles and biomaterial-supported delivery systems [60–65,71–73]. Collectively, the evidence addressed mechanistic foundations, therapeutic efficacy and emerging clinical roles of PRP, MSCs and exosomes in tendon injuries, cartilage degeneration, ligament damage and muscle injuries [9,16,32,46–49,66].

PATHOPHYSIOLOGY OF SPORTS-RELATED INJURIES

Sports musculoskeletal tissue injuries typically have three phases: inflammation, repair, and remodeling [9,10]. Acute inflammatory response is characterized by vasodilation, leukocyte migration, and release of pro-inflammatory cytokines, mainly IL-1β and TNF-α. While inflammation is necessary during healing, excessive levels of these cytokines might be implicated in tissue damage and worsening of the healing process [11]. The existing therapy is NSAIDs and RICE protocol, but the former has the possibility to down regulate important inflammatory processes. New approaches include modulating the inflammatory process, e.g., with the help of growth factors to enhance muscle repair or TGF-β1 antagonists to hinder fibrosis [9]. Early use of IL-1 inhibitors is also in the pipeline as a method of prevention of post-traumatic arthritis [12]. Chronic musculoskeletal diseases, such as tendinopathies and cartilage degeneration, are caused by broken healing mechanisms. They are characterized by prolonged inflammation, pathological angiogenesis, and disruption of extracellular matrix homeostasis [13]. Articular cartilage, for instance, has very weak regenerative capacities in consideration of the fact that it is avascular [14]. Repair difficulties in cartilage involve matrix degradation, differentiation deficiencies, and cell loss [15]. Tendinopathies also have limited capacity for self-healing due to low vascularization and high frequencies of loading [16]. Musculoskeletal sports injuries pose significant challenges, leading to the majority of the chronic conditions due to defective processes in healing [13]. Tissue degeneration is initiated by chronic mechanical overload, cyclical microtrauma, and inefficient recovery [8]. Traditional therapies limit tissue regeneration to optimal function, hence promoting interest in regenerative therapies [17]. New creative approaches are aimed at enhancing tissue repair and regeneration through varied mechanisms like PRP therapy, stem cell therapy, and tissue engineering technologies [18]. An understanding of the biological basis of musculoskeletal trauma is essential to choose right regenerative intervention in specific tissue types and phases of trauma and achieve optimal outcomes.

PLATELET-RICH PLASMA

Platelet-rich plasma is a low volume of plasma with a high concentration of platelets. It is derived from autologous blood [19]. Some of the growth factors in PRP that are involved in the healing of tissues include vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), transforming growth factor beta (TGF-β) and platelet-derived growth factor (PDGF) [20,21]. The healing and regeneration of different tissues depend on these growth factors sequestered from activated platelet alpha granules [22,23]. Methods for preparing PRP on a daily basis entail centrifugation of whole blood to concentrate platelet [24]. The cellular content and the concentration of growth factor of PRP can vary due to the wide range of preparation methods [25,26]. Two of the most common forms are leukocyte-rich PRP (LR-PRP) and leukocyte-poor PRP (LP-PRP), with LR-PRP containing higher levels of some growth factors [27]. PRP can be produced by single or double centrifugation in a manner akin to commercial devices [28]. Whereas LP-PRP might be more suited to cartilage disease, LR-PRP would seem to be more suitable in the treatment of tendinopathies [29]. There is no uniformity in preparation and reporting of PRP and thus comparison among studies is difficult [30]. PRP has also been shown to be beneficial in the treatment of musculoskeletal conditions such as patellar tendinopathy, knee and lateral epicondylitis osteoarthritis [31]. There have also been reports of favorable clinical outcomes in the treatment of tendinopathies with ultrasound-guided intratendinous injection of LR-PRP [32]. PRP is clinically utilized in sports medicine, orthopedics, and periodontal therapy [33]. Platelet-rich plasma therapy is gaining popularity as it has the potential to accelerate healing of tendon and ligament injuries. PRP contains a mixture of growth factors that enhance cell proliferation, angiogenesis, and collagen synthesis [34]. In vitro and in vivo studies showed that PRP is able to cause proliferation, migration, and collagen synthesis of tendons and ligaments [35]. PRP regulates inflammation and creates an environment conducive to tissue regeneration [36]. While basic science justifies the potential of PRP, clinical results are unpredictable [37]. The effectiveness of PRP depends on the patient's injury status, application timing, and preparation [21,38]. In spite of its increasing application, further research needs to be conducted to standardize PRP protocols and determine its effectiveness for the variety of musculoskeletal ailments.

STEM CELLS

The ability to differentiate and their immunomodulatory function make MSCs multipotent stromal cells with significant potential in regenerative medicine [39,40]. MSCs release a variety of bioactive compounds that modulate immune response, stimulate tissue regeneration and preserve homeostasis stability [41,42]. Stem cell therapy has the potential for various diseases, including orthopedic applications and spinal cord injury. All types of tissues can produce MSCs including bone marrow, fat tissue and synovium, while MSCs derived from the latter have the best chondrogenic potential [43,44]. Low immunogenicity of MSCs facilitates allogeneic transplantation without the possibility of rejection [45]. Recent studies have shown that MSC therapy is helpful for a variety of sports-related injuries and ailments. When it comes to knee osteoarthritis, MSCs have shown promise in improving cartilage quality, function and pain in comparison to hyaluronic acid injections or placebos [46,47]. In patellar tendinopathy, bone marrow-derived MSCs performed superiorly in tendon structure compared to platelet-rich plasma [48]. In high tibial osteotomy, MSC treatment enhanced cartilage healing and clinical outcomes [49]. Multiple MSC injections have yielded superior results compared to single injection in the treatment of knee osteoarthritis [50]. Allogeneic MSCs have also been found to be successful in treatment of degenerative disc disease [51]. Even then, there was little efficacy demonstrated in the treatment of spinal cord injury [52]. Overall, these findings suggest that MSC therapy is safe and may be effective for musculoskeletal disorders, but further research is required to optimize treatment protocols.

EXOSOMES

Exosomes are extracellular small vesicles (30-150 nm) secreted by most cell types, including stem cells and play a crucial role in intercellular communication [53,54]. Various substances like proteins, lipids, mRNA and microRNAs found in exosomes are transported between cells and have the ability to affect how recipient cells function [55,56]. Stem cell exosomes were reported to be of potential significance in tissue regeneration and cancer research [57,58]. The miRNA content of mesenchymal stem cell exosomes in particular has been shown to be therapeutically effective in a variety of disease models [59,60]. In sports medicine and orthopedics exosomes are showing promise as a treatment for soft tissue injuries and degenerative diseases [61,62]. They have benefits over conventional stem cell treatments and are involved in tissue repair and cell-to-cell communication [63,64]. Exosomes are useful in osteoarthritis treatment, cartilage regeneration, and they enhance sports performance [65]. To boost their therapeutic potential they can be engineered or mixed with biomaterials as well as purified from a variety of sources such as mesenchymal stem cells [5]. Exosome-based therapies have numerous benefits over stem cell-based therapies, e.g., less chance of tumorigenicity and immune rejection. Exosomes have the potential to revolutionize orthopedic regenerative medicine by enabling cell-free methods of tissue regeneration and repair, provided that further research is conducted [6,64]. Exosomes present less risky and more convenient therapeutic options, albeit more studies are required to effectively exploit and maximize their therapeutic potential [60].

CURRENT EVIDENCE ON EFFECTIVENESS

Research shows that stem cell therapy and platelet-rich plasma are effective treatments for tendinopathies and other musculoskeletal conditions. PRP has demonstrated efficacy in treating chronic tendinopathies specifically patellar tendinopathy and lateral epicondylitis [66,67]. Results however are not reliable due to variation in preparation methods and protocols [68]. Large-scale clinical trials are lacking for stem cell therapy despite its encouraging preclinical data. Although their relative efficacy is unknown stem cells and PRP both seem to have positive clinical effects with few side effects [7]. PRP has the potential to relieve pain in tendinopathies, while stem cells have the potential to regenerate tissue and display anti-inflammatory effects [67]. Despite these promising outcomes, stricter studies are needed to define the optimal preparation, dosing, and delivery of these therapies for specific diseases [69,70]. Mesenchymal stem cell-derived exosomes have tremendous therapeutic potential in healing musculoskeletal injury and osteoarthritis. Several animal models have shown that MSC-derived exosomes improve tendon healing, encourage chondrocyte proliferation and reduce inflammation [71]. Exosomes are more effective compared to cell-based therapies since they have reduced risks of tumorigenesis and immunogenicity [72,73]. More high-quality randomized controlled trials are needed to validate the long-term safety and effectiveness of exosome therapy in sports medicine and regenerative applications, as well as to set standardized treatment parameters.

DISCUSSION

This review provides an integrative overview of the available literature on platelet rich plasma, mesenchymal stem cells and exosome based therapies as regenerative approaches in sports related musculoskeletal injuries [1,2,18]. The analyzed evidence suggests that all three modalities are associated with improvements in tissue repair processes, pain related outcomes and functional measures across tendon, cartilage, ligament and muscle injuries, although the strength, consistency and clinical maturity of evidence differ between approaches [7,66].

Platelet rich plasma remains the most extensively studied and clinically implemented strategy, supported by a relatively larger body of clinical data in conditions such as patellar tendinopathy, knee osteoarthritis and lateral epicondylitis [32,67]. Its effects are largely attributed to the local delivery of autologous growth factors that support extracellular matrix remodeling, angiogenesis and cellular proliferation. In contrast, mesenchymal stem cell based therapies act through broader immunomodulatory and pro regenerative mechanisms and may offer advantages in selected cartilage and tendon related applications, including reports of superior outcomes compared with PRP in specific contexts [46].

Exosome based approaches represent an emerging cell free strategy that aims to preserve key paracrine effects of MSCs while potentially reducing safety and regulatory concerns associated with live cell therapies [53,60]. At present, however, the supporting evidence for exosomes remains predominantly preclinical, and robust clinical data are limited.

From a mechanistic perspective, the reviewed studies indicate partially overlapping but distinct biological pathways underlying the effects of these therapies, including modulation of inflammatory signaling, enhancement of extracellular matrix synthesis, stimulation of resident cell proliferation and support of angiogenic responses [11,35]. These mechanisms reflect the multifactorial nature of musculoskeletal tissue repair and help explain why different biologic strategies may be more appropriate for specific tissues or stages of injury.

Both mesenchymal stem cells and exosomes appear to promote tissue repair predominantly through paracrine signaling mechanisms, whereas platelet rich plasma exerts its effects mainly via the local delivery of platelet derived growth factors. Together, these complementary mechanisms illustrate the multifaceted regenerative potential of biologic therapies and their relevance to the complex pathophysiology of musculoskeletal injuries [10,13].

Despite this encouraging body of evidence, substantial heterogeneity across studies limits the strength of current conclusions. Variability in PRP preparation protocols, differences in MSC sources and administration strategies, and the predominantly preclinical nature of exosome research complicate direct comparison between modalities and hinder identification of optimal treatment protocols [7,30]. In addition, many studies are characterized by small sample sizes, short follow up periods and heterogeneous outcome measures, which restrict assessment of long term efficacy, durability of tissue repair and delayed adverse effects [31,66].

The reviewed literature also highlights a persistent translational gap between experimental promise and routine clinical application. While PRP is currently the most accessible and widely used biologic therapy in sports medicine, MSC based and exosome based approaches remain constrained by regulatory, logistical and economic barriers [18,45]. The absence of standardized guidelines for preparation, dosing and delivery across all three modalities further limits reproducibility and consistent clinical implementation [7,30].

In summary, PRP, MSCs and exosomes each demonstrate regenerative potential in the management of sports related musculoskeletal injuries. However, broader clinical adoption will require well designed, large scale and long term studies to define comparative advantages, establish standardized protocols and clarify their role within personalized, mechanism oriented treatment strategies [7,30].

LIMITATIONS

Several methodological limitations should be considered when interpreting the findings of this review. The available literature on platelet rich plasma, mesenchymal stem cells and exosomes is characterized by substantial heterogeneity in preparation techniques, biologic composition, dosing strategies, delivery methods and duration of follow up, which complicates direct comparison between studies and limits the establishment of standardized therapeutic protocols. In addition, a considerable proportion of the evidence is derived from small scale, single center or preclinical studies, reducing generalizability and the strength of clinical inference.

Long term outcomes, including durability of symptom improvement, structural tissue regeneration and potential delayed adverse effects, are insufficiently reported across studies. Furthermore, outcome measures vary widely, ranging from pain and functional scores to imaging, cellular or histologic endpoints, which hampers unified assessment of treatment effects and comparative evaluation. High quality randomized controlled trials directly comparing PRP, MSCs and exosome based therapies remain scarce, leaving uncertainty regarding their relative effectiveness. Evidence supporting exosome based interventions is predominantly preclinical, and the limited availability of human data currently restricts conclusions regarding their clinical applicability. Finally, publication bias cannot be excluded, as studies reporting positive findings may be overrepresented in the published literature.

CONCLUSIONS

This narrative review compared platelet rich plasma, mesenchymal stem cells and MSC derived exosomes as regenerative therapies for sports related musculoskeletal injuries, focusing on mechanisms, clinical effectiveness, safety and translational potential. All three demonstrate regenerative and anti inflammatory properties, but differ in biological mechanisms, strength of clinical evidence and readiness for routine use.

Platelet rich plasma is the most established modality in clinical practice, with consistent symptomatic improvement in tendinopathies and early degenerative conditions, although outcomes are influenced by variability in preparation and application. Mesenchymal stem cell therapies offer broader immunomodulatory and regenerative potential, particularly for cartilage and tendon repair, yet their implementation is limited by regulatory, financial and methodological heterogeneity. MSC derived exosomes represent a promising cell free approach with favorable safety and strong paracrine effects, but clinical use remains restricted due to limited human trial data.

Direct comparative clinical evidence is scarce, and current conclusions rely mainly on indirect comparisons across heterogeneous studies. None of these therapies can be considered universally superior. Their optimal application depends on tissue type, injury characteristics and stage of pathology.

AUTHORS’ CONTRIBUTIONS

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All authors have read and agreed with the published version of the manuscript.

USE OF AI

Artificial intelligence tools were used solely to assist with vocabulary refinement and language editing. All ideas, analyses, and conclusions are entirely the author’s own.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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