

REVIEWER'S REPORT

Manuscript No.: IJAR-56750

Title: The Exercise Pillar of Lifestyle Medicine: Emerging Evidence, Novel Modalities, Molecular Mechanisms, and Pharmacological Synergies A Narrative Review

Recommendation:

Accept

Rating	Excel.	Good	Fair	Poor
Originality	Yes			
Techn. Quality		Yes		
Clarity	Yes			
Significance		Yes		

Reviewer Name: Dr. Ashish Yadav

Detailed Reviewer's Report

Reviewer's Comment for Publication.

Acceptance comments are mentioned below suitable for the paper titled "The Exercise Pillar of Lifestyle Medicine: Emerging Evidence, Novel Modalities, Molecular Mechanisms, and Pharmacological Synergies A Narrative Review"

Reviewer Comments: Accept

Reviewer Comments –

Introduction:

The introduction compellingly positions physical activity as the most potent non-pharmacological intervention within lifestyle medicine, highlighting transformative recent evidence that redefines exercise prescription. The authors effectively establish the context of paradigm-shifting discoveries, from landmark cancer trials to novel ultra-short activity paradigms and exercise-derived molecular mediators. Four interconnected frontiers are clearly outlined, providing a coherent roadmap for the narrative review. The introduction successfully engages readers across disciplines and sets the stage for the synthesis that follows.

Literature Review:

The literature review is methodically organized around the four stated frontiers, drawing from a well-designed search of PubMed, Scopus, and Google Scholar with relevant keywords spanning exercise prescription, VILPA, exerkinetics, and GLP-1 exercise interactions. The emphasis on publications from 2022 through March 2026 ensures currency and captures the most transformative recent evidence. The synthesis effectively bridges classical exercise physiology with cutting-edge molecular discoveries,

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including the emerging role of Lac-Phe as an exercise-responsive metabolite. A more critical appraisal of methodological limitations across the cited studies would further strengthen this section.

Solution Approach:

The authors appropriately employ a narrative review methodology, which is well-suited for synthesizing diverse and rapidly evolving evidence across multiple interconnected domains. The structured literature search strategy is clearly described, encompassing three major databases with well-defined keywords and a focused timeframe that ensures relevance. The organization around four distinct yet interconnected frontiers provides a coherent framework that balances breadth across emerging modalities with depth in selected areas such as exercise oncology and GLP-1 synergies. This approach effectively supports the objective of identifying opportunities for translation into clinical practice.

Results and Discussion:

The results present transformative evidence, including the CHALLENGE trial showing that structured exercise after colon cancer chemotherapy reduces recurrence by 28% and mortality by 37%, outcomes rivaling many approved drugs. VILPA research from the UK Biobank reveals that just 1.2–3.4 minutes of vigorous incidental activity daily reduces major cardiovascular events by 30–45% in non-exercising women, fundamentally challenging traditional exercise paradigms. The discussion of exer kines, particularly Lac-Phe, and the synergy between exercise and GLP-1 receptor agonists addresses critical clinical challenges such as lean mass preservation during pharmacological weight loss. The integration of these diverse findings is skillfully executed, though a more explicit discussion of implementation barriers in clinical practice would enhance translational relevance.

Conclusion:

The conclusion succinctly captures the central thesis that the exercise pillar of lifestyle medicine is undergoing a scientific renaissance driven by transformative evidence across clinical outcomes, novel modalities, molecular mechanisms, and pharmacological synergies. The authors effectively articulate the potential for integrating traditional exercise prescription with emerging frontiers to enable personalized physical activity interventions across the spectrum of chronic disease. The conclusion appropriately offers a forward-looking perspective while acknowledging the need for continued research.