PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Lifestyle Approaches to Hypertension for Prevention of Stroke and Vascular Cognitive Impairment: A Realist Review Protocol
AUTHORS	Ibrahim, Sarah; Bielecki, Joanna; Kocabas, Emine; Singh, Sanjula; Senff, Jasper; Casaubon, Leanne; Rosand, Jonathan; Rac, Valeria E.; Pikula, Aleksandra

VERSION 1 - REVIEW

REVIEWER NAME	Chen, Qihui
REVIEWER AFFILIATION	China Agricultural University, College of Economics and Management
REVIEWER CONFLICT OF INTEREST	There are no competing interests.
DATE REVIEW RETURNED	27-May-2024

| GENERAL COMMENTS | I think the review protocol is well-motivated and well-written. I have only a few minor suggestions for improving the paper.

1) The authors mentioned that a Realistic review is theory-driven. Thus, including a discussion on the potential theories to use as the framework/basis in the paper would be nice.

2) Why only search for studies from 2000 onward?

3) Would it be possible to combine your review with some meta-analysis to really pin down the effectiveness of LSM interventions?

4) What are some potential risks for your review? This should be part of your Discussion section.

5) When do you expect the review to be completed? |
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REVIEWER NAME	Zhang, Xiaofei
REVIEWER AFFILIATION	Beijing Tsinghua Changgung Hospital, Department of Clinical Epidemicology and Biostatistics
REVIEWER CONFLICT OF INTEREST	I have no competing interests.
DATE REVIEW RETURNED	03-Jul-2024

GENERAL COMMENTS	This realist review protocol is a novel one that works beyond the traditional evaluative review approaches and conducts a black box evaluation of LSM interventions in terms of understanding how and why they work, under what circumstances, and for whom to reduce the risk of stroke and VCI.

	I have no more comments about this good protocol except one below:
	Figure 1, modifiable Risk Factors (28): "Behavioural MRFs accounting for ~50% of stroke burden. Metabolic MRFs accounting for 70% of stroke burden". The literature citation in Figure 1 is not completely matched with that expressed in the risk factor paragraph on page 4. In addition, Figure 1 requires further explanation as to why the Behavioural MRFs + Metabolic MRFs are greater than 100%.

REVIEWER NAME	Tu, Hung-Pin
REVIEWER AFFILIATION	Kaohsiung Medical University
REVIEWER CONFLICT OF INTEREST	None
DATE REVIEW RETURNED	11-Jul-2024

GENERAL COMMENTS	The authors present a study protocol for a realist review, comprising four stages: 1) clarifying the scope; 2) searching for evidence; 3) critically appraising primary studies and extracting data focusing on the Context-Mechanism-Outcome (CMO) configuration; and 4) synthesizing evidence and drawing conclusions.

I would like to raise the following concerns.
1.
Page 4, lines 38-41: Specifically, non-modifiable risk factors (e.g., age, genetics, sex) and modifiable risk factors (MRFs) have been linked to stroke, with 10 MRFs (Fig. 1). However, Fig. 1 appears to show only 9 MRFs: behavioral MRFs (smoking, alcohol use, substance use, poor diet, low physical activity) and metabolic MRFs (high BMI, fasting glucose, total cholesterol, low GFR).
Low 'phisical' activity and total 'cholestoral' appear to be typographical errors.
2.
Page 5, lines 22-23: Lifestyle Medicine (LSM) focuses on 6 pillars: Nutrition, Physical activity, Sleep health, Stress reduction, Social Connections, and Substance use (Fig. 2).
To ensure that the role of Lifestyle Medicine is not overlooked in the comprehensive management of patients with hypertension (HTN), a schematic presentation of the factors contributing to the impact of uncertainty on stroke and vascular cognitive impairment (VCI) is proposed. |

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Dr. Qihui Chen's Comments	
The authors mentioned that a Realistic review is theory-driven. Thus, including a discussion on the potential theories to use as the framework/basis in the paper would be nice.	A list of potential theories that will be used has been presented on pg 7.
2) Why only search for studies from 2000 onward?	Studies from 2000 onwards will be searched because Lifestyle Medicine was founded as a new medical speciality in 2004.
3) Would it be possible to combine your review with some meta-analysis to really pin down the effectiveness of LSM interventions?	Appreciating the overall intent/aim of the realist review, which is to unpack how and why LSM interventions may or may not work, how they work for different populations, and the mechanisms and contextual influences (interactions) that may reduce the risk of stroke and cognitive decline such as VCI, a meta-analysis is not appropriate. Further, there have been published systematic review and meta-analysis on the effectiveness of LSM interventions for various chronic diseases.
4) What are some potential risks for your review? This should be part of your Discussion section.	Mention of limitations has been included on pg 9.
5) When do you expect the review to be completed?	Completion date has been included on pg 6.
Reviewer 2: Dr. Xiaofei Zhang's Comments	
Figure 1, modifiable Risk Factors (28): "Behavioural MRFs accounting for -50% of stroke burden. Metabolic MRFs accounting for 70% of stroke burden". The literature citation in Figure 1 is not completely matched with that expressed in the risk factor paragraph on page 4. In addition, Figure 1 requires further explanation as to why the Behavioural MRFs + Metabolic MRFs are greater than 100%.	The figure has been revised.
Reviewer 3: Prof. Hung-Pin Tu's Comments	
Page 4, lines 38-41: Specifically, non-modifiable risk factors (e.g., age, genetics, sex) and modifiable risk factors (MRFs) have been linked to stroke, with 10 MRFs (Fig. 1). However, Fig. 1 appears to show only 9 MRFs: behavioral MRFs (smoking, alcohol use, substance use, poor diet, low physical activity) and metabolic MRFs (high BMI, fasting glucose, total cholesterol, low GFR). Low 'phisical' activity and total 'cholestoral' appear to be	The figure has been revised.

typographical errors.	
Page 5, lines 22-23: Lifestyle Medicine (LSM) focuses on 6 pillars: Nutrition, Physical activity, Sleep health, Stress reduction, Social Connections, and Substance use (Fig. 2). To ensure that the role of Lifestyle Medicine is not overlooked in the comprehensive management of patients with hypertension (HTN), a schematic presentation of the factors contributing to the impact of uncertainty on stroke and vascular cognitive impairment (VCI) is proposed.	Appreciating that the focus is on LSM interventions and exploring how, why, for whom, and under what circumstances such interventions may/or may not work rather than LSM as a discipline/medical speciality, the proposed schematic presentation of factors contributing to the impact of the uncertainty on stroke and VCI may not be appropriate in illustrating the comprehensive management of HTN for patients through LSM. A schematic presentation of the generated theory and findings will be provided following completion of the data analysis (final publication and KT plans).