


BMJ Open Lifestyle approaches to hypertension for prevention of stroke and vascular cognitive impairment: a realist review protocol

Sarah Ibrahim ^{1,2,3,4} Joanna Bielecki,⁵ Emine Kocabas,³ Sanjula Singh,^{6,7,8,9} Jasper R Senff,^{6,7,8,9} Leanne K Casaubon,^{10,11} Jonathan Rosand,^{6,7,8,9} Valeria E Rac,^{1,2} Aleksandra Pikula^{3,10,11,12}

To cite: Ibrahim S, Bielecki J, Kocabas E, *et al.* Lifestyle approaches to hypertension for prevention of stroke and vascular cognitive impairment: a realist review protocol. *BMJ Open* 2024;**14**:e088631. doi:10.1136/bmjopen-2024-088631

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<https://doi.org/10.1136/bmjopen-2024-088631>).

Received 10 May 2024
Accepted 05 September 2024



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For numbered affiliations see end of article.

Correspondence to

Dr Aleksandra Pikula;
aleksandra.pikula@uhn.ca

ABSTRACT

Introduction Stroke and vascular cognitive impairment (VCI) are major global public health pandemics. The increased incidence of stroke and VCI is in part due to modifiable risk factors (MRFs), with hypertension (HTN) being the strongest single MRF. Even though the underlying causes of HTN are multifactorial, lifestyle choices (eg, poor diet, physical inactivity, alcohol consumption) are chief contributors. Lifestyle medicine (LSM) is a medical and evidence-based discipline that is a promising approach for preventing stroke and cognitive impairment, including VCI. The empirical evidence from systematic reviews, meta-analyses and large population-based studies has reported on the effectiveness of LSM interventions. However, the evaluation of such complex, social and behavioural interventions warrants more information to allow its successful implementation into innovative clinical care models. More importantly, we need to understand how such interventions work, who it works for and under what circumstances to successfully manage HTN and other MRFs (eg, hyperlipidaemia, smoking, alcohol use and diet). **Methods and analysis** This realist review will follow the Realist and Meta-narrative Evidence Synthesis: Evolving Standards. The review will comprise four stages: (1) clarify the scope, (2) search for the evidence, (3) critically appraise primary studies and extract data focusing on the context, mechanism and outcome configuration and (4) synthesise evidence and draw conclusions.

Ethics and dissemination Research ethics board approval is not required for this review. The primary output of this review will be an evidence-based programme theory for LSM interventions for the management of HTN and other MRFs to reduce the risk of stroke and VCI. Findings from this review will be disseminated at three levels: micro (eg, patients, caregivers, clinicians, non-research partners), meso (eg, public, national not-for-profit organisations, professional associations and centres) and macro (eg, policymakers and government partners). **PROSPERO registration number** CRD42024511566.

INTRODUCTION

Neurological disorders affect 43.1% (3.4 billion) of the global population,¹ making it a global pandemic and profound public health

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The review will facilitate an understanding of the CMO configuration; context mechanisms and outcomes of lifestyle medicine (LSM) interventions that account for specific contexts and populations and work towards reducing health disparities and the burden of stroke, vascular cognitive impairment and neurodegenerative disease.
- ⇒ A multidisciplinary team with methodological, epidemiological, neurological, LSM and implementation science-related experience and patient partners will be involved in the development, refinement and finalisation of the programme theory.
- ⇒ The development of the CMOs will be limited based on the inclusion criteria of this review and potentially oversimplify the CMO configuration for LSM interventions.

concern. Among the neurological disorders, stroke is the greatest global contributor of nervous system disability-adjusted life years.¹ Further, over the past 30 years, stroke prevalence has increased by 86.1%¹ with 12.2 million new stroke cases annually.²⁻³ Stroke (ischaemic or haemorrhagic)⁴ contributes to the radiographic and clinical definition of vascular cognitive impairment (VCI).⁵⁻⁶ Globally, an estimated 40% of strokes have been occurring among the working population (<65 years of age) over the past decade.⁷⁻⁹ Such occurrence may have substantial implications on persons' cognition (eg, deficit in processing speed, attention, executive function, memory)¹⁰⁻¹¹ and mental health (eg, depression,¹²⁻¹⁴ anxiety¹⁵). It may also impact quality of life due to changes in role, self-identity, relationship(s), as well as physical, psychological and social functioning.^{9,16}

Stroke also has negative economic implications resulting from premature departure

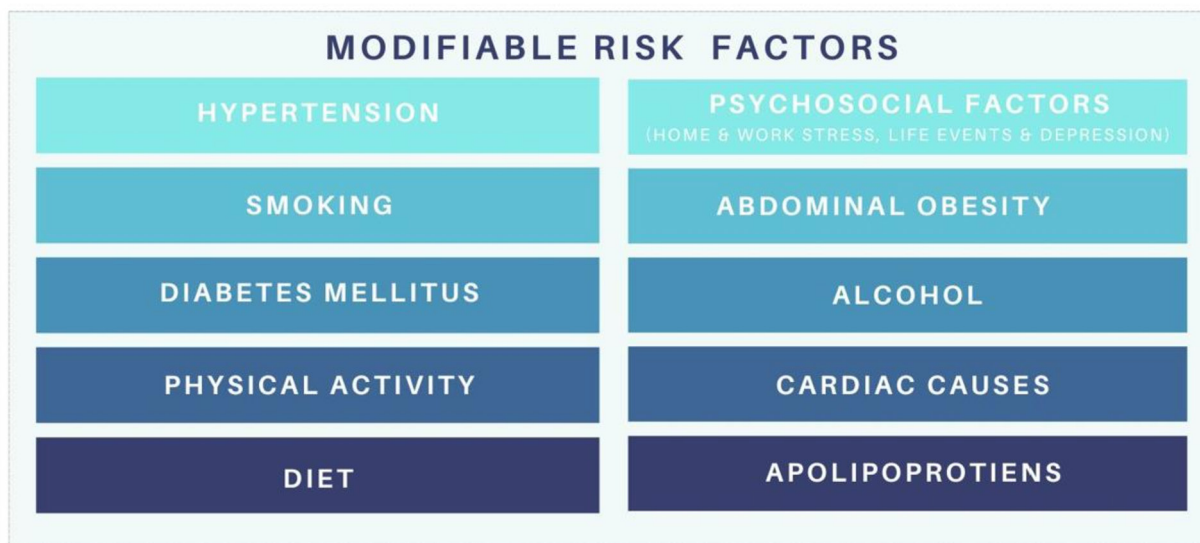


Figure 1 Modifiable risk factors.

from the workforce, reduced productivity, increase in work absenteeism, reliance on government subsidy coupled with the associated healthcare costs.^{17 18} Globally, in 2017, the economic burden of stroke was US\$451 billion.¹⁹ Of note, the average cost of a hospital stay for young adult patients who had a stroke (age range 18–44 years) spans from US\$34 886 for ischaemic stroke to US\$146 307 for subarachnoid haemorrhage in the USA.²⁰ Similarly in Australia, the economic implication of young adult patients who had a stroke was approximately \$A2.0 billion over 5 years, equivalent to \$A149 180 per patient.²¹ Comparably, VCI, which encompasses an entire spectrum of vascular brain pathologies contributing to cognitive deficit—from mild cognitive impairment to vascular dementia²²—is the second most common cause of dementia after Alzheimer’s disease (AD).^{23–25} With both direct and indirect expenses, dementia is among the most expensive medical conditions—costing more than cancer and heart disease.²⁶ Worldwide, the prevalence of overall dementia is forecasted to triple (estimated 152 million persons) by 2050²⁷ with dementia-associated costs also projected to soar to US\$2 trillion by 2030.²⁷

Risk factors

Stroke and VCI incidence have been attributed in most part to shared risk factors. Specifically, non-modifiable (eg, age, genetics, sex) and modifiable risk factors (MRFs) have been linked to stroke, with 10 MRFs (figure 1) collectively associated with up to 90% of attributable stroke risk.^{28 29} Similarly, VCI is predominantly explained by the effect of MRFs²² with the most prevalent vascular MRFs being hypertension (HTN), hyperglycaemia, hyperlipidaemia, limited physical activity (PA) and smoking.³⁰ Of note, HTN is globally the single strongest and the most contributing MRF for both stroke and VCI, making it a harbinger of two major brain diseases.³¹ Worldwide, HTN affects one in three middle-aged adults (40–59 years of age) and an estimated 7% of young adults (18–39 years of

age).^{32 33} HTN is defined as a systolic blood pressure (BP) of ≥ 130 –139 mm Hg or diastolic BP of ≥ 80 –89 mm Hg.³⁴ The prevalence and deleterious effects of HTN highlight the integral importance of BP management and control, and it being a matter of heart and brain health.^{35 36}

This was illustrated in the Honolulu-Asia Aging Study,³⁷ where an association between *midlife* untreated HTN and increased risk of VCI and AD development in older age was found.³⁷ Similarly, in the Coronary Artery Risk Development in Young Adults study, BP variability among young adults (18–30 years old, followed for 25 years) was associated with psychomotor and memory-related impairment in midlife.³⁸ This association with HTN and VCI was confirmed in a prospective study, with midlife HTN resulting in cognitive function decline, brain atrophy and increasing white matter hyperintensity later in life.³⁹ The causes of HTN are multifactorial and complex; however, there is clear evidence that poor lifestyle choices such as unbalanced dietary habits, physical inactivity, smoking and excess alcohol consumption are major contributors.⁴⁰ Current HTN-related national and international guidelines emphasise the importance of lifestyle modifications⁴⁰ as fundamental initial steps to minimise the negative effect on the brain, particularly in relation to stroke and VCI.

Lifestyle medicine (LSM)

LSM is a medical specialty and evidence-based discipline that applies behavioural, motivational, environmental and medical principles to address the complexity of chronic disease(s)^{41 42} through its primary, secondary and tertiary preventative approach. LSM focuses on six pillars: nutrition, PA, sleep health, stress reduction, social connections and substance use⁴³ (figure 2).

LSM was first associated with health outcomes, specifically heart disease at the Nathan Pritikin Longevity Center in the 1970s. The discipline gained further momentum with the Lifestyle Heart Trial led by Ornish⁴⁴

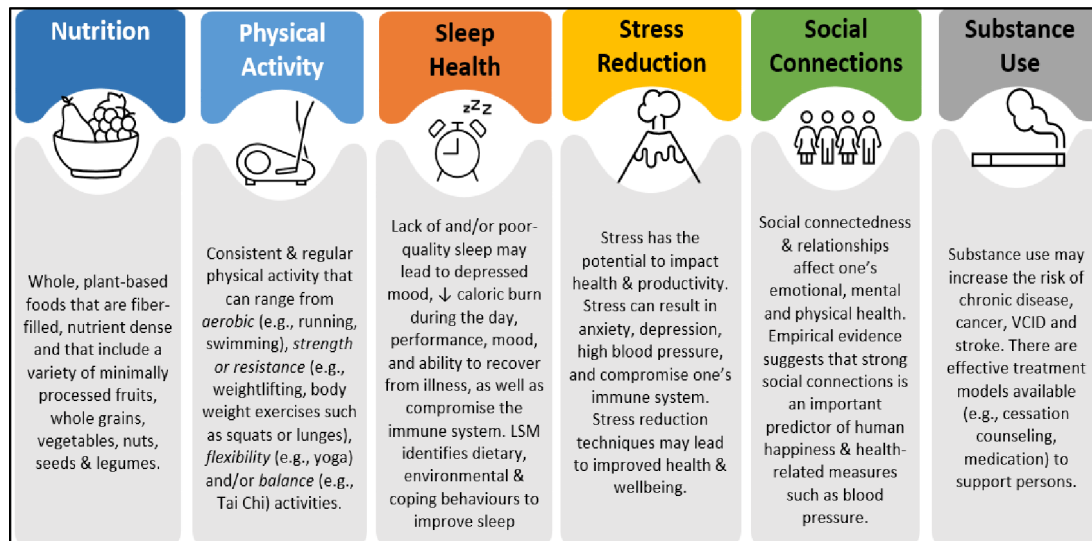


Figure 2 Lifestyle medicine (LSM) pillars. VCI, Vascular Cognitive Impairment and Dementia.

in the 1980s where adherence to a non-pharmacological and intensive lifestyle modification intervention reversed patients' coronary artery disease at 1-year and 5-year follow-up. Over time, with the evolution of this trial and associated research, cardiac patients in the USA now have access to the Ornish intensive cardiac rehabilitation programme through Medicare. Similarly, the Complete Health Improvement Program led by Dr Hans Diehl was established as an outpatient intensive lifestyle change programme in the 1990s for the prevention, treatment and reversal of lifestyle-related chronic conditions.⁴⁵

Healthy lifestyle habits and LSM interventions have also been associated with stroke risk and its recurrence.^{46–49} This was illustrated in a prospective population-based cohort study, the UK Biobank Study, where 306 473 adults who had a healthy lifestyle (eg, non-smoking, healthy diet, regular PA) and followed for a median of 7.1 years reduced their stroke risk by approximately two-thirds.⁵⁰ Similarly, in the Prevención con Dieta Mediterránea trial, which comprised of the Mediterranean diet and supplemented with extra virgin olive oil and nuts, found a 30% relative risk reduction in composite clinical endpoints of cardiovascular death, stroke and myocardial infarction.⁵¹ Such findings are consistent with a meta-analysis of 18 cohort and 5 case-control studies, where moderate-to-high levels of PA lowered stroke incidence and mortality by an estimated 30%,⁵² with high levels of occupational PA associated with a 43% stroke risk reduction.⁵³ Furthermore, in a systematic review on PA and VCI, the overall effect was statistically significant (HR 0.68, 95% CI 0.54 to 0.86, I^2 6.8%), with higher PA levels associated with smaller VCI risk overtime.⁵⁴ Over the past decade, the impetus for LSM integration in the current model of care has accelerated, culminating with the American Board of Lifestyle Medicine landmark article in *JAMA* 2010 on physician competencies for prescribing LSM,⁴³ and recent (2016) implementation of the formal board certification across the globe through the Accredited International, American and European LSM Boards. LSM addresses

principles that are the cornerstone for brain health, and the effectiveness of such interventions has been well documented and in some cases, is the first line of treatment to meaningfully reduce the burden of cerebrovascular and neurodegenerative disorders.⁴⁰

Knowledge gap

Complex interventions, such as LSM, introduce knowledge, information, resources and modifications to behaviour and lifestyle while depending on human reasoning and reaction among diverse groups of populations and in various settings and contexts.⁵⁵ Complex interventions are traditionally evaluated through one or more outcomes, which are often determined a priori.^{56 57} Appreciating that such complex interventions are implemented in the real-world, in different settings, contexts and among diverse groups of populations with differing backgrounds, experiences and social determinants of health (SDOH), the traditional evaluative approach oversimplifies the intervention, participants and context.^{55 58} Additionally, the traditional evaluative approach provides little information about *how*, *why* and *for whom* such complex LSM interventions may or may not work, under what circumstances and for what groups of populations. Such gaps highlight the need for a theory-driven approach for the evaluation of LSM interventions as it provides a '*black box evaluation*' to generate insight on the outcomes, underlying causal mechanism of actions and contextual factors (and the interaction between them).⁵⁶ However, such an evaluation on LSM interventions for the management of HTN and other MRFs (eg, hyperlipidaemia, smoking, alcohol use, diet) to reduce stroke and cognitive decline such as VCI does not currently exist and has implications on the implementation, scale-up and sustainability of these interventions.⁵⁶

Review aims and research questions

This realist review aims to: (1) unpack the evidence gaps on how and why LSM interventions (through the

different pillars) focused on HTN and other MRFs (eg, hyperlipidaemia, smoking, alcohol use, diet) 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 and (2) build evidence-based knowledge and recommendations on LSM interventions that focus on HTN (other MRFs) and the design of such interventions to support brain health (reduce stroke and VCI). The research questions of this review are:

1. What are *the mechanisms of actions* of LSM interventions focused on HTN and other MRFs that would reduce the risk of stroke and VCI?
2. What are *the key contextual factors that determine or influence the mechanisms* of LSM interventions focused on HTN and other MRFs that would reduce the risk of stroke and VCI?
3. What are *the strengths or weaknesses of existing LSM interventions* focused on HTN and other MRFs for reducing the risk of stroke and VCI?

METHODS AND ANALYSIS

Design

A realist review is a theory-driven methodological approach to understand the heterogeneous evidence of complex interventions, such as LSM, that are applied in different contexts and with diverse groups of populations to generate causal explanations that answer the following questions: ‘*What works, for whom, in what circumstances and why?*’.⁵⁹ Extending beyond traditional approaches (eg, systematic reviews and meta-analysis), a realist review is a logic of inquiry that explores inputs and outputs of interventions with consideration to the environment, context, culture, SDOH and human behaviour; all of which are described as the intervention ‘*black box*’.^{60 61}

The hallmark of a realist review methodology is the distinctive exploration and understanding of the generative model of causality—with identification of a complex intervention under specific contextual factors (C) that trigger a particular mechanism (M) and the combination of this, generates a specific outcome (O) which is referred to as the CMO configuration.⁶²

Context

The ‘backdrop’ environmental conditions and background of the intervention that may trigger or modify a mechanism and potentially impact the outcomes.^{59 63}

Examples of context include social (eg, SDOH, cultural and ethnic background) and economic (eg, poverty, income and employment) conditions (figure 3).

Mechanism

The causal force triggered or modified by the context and that leads to the outcome.^{59 64} Mechanism consists of intervention resources (eg, information on sodium intake for HTN management) and a persons’ cognitive, emotional and/or behavioural response (the reasoning).⁶⁴ Examples of mechanism include the participants’ self-efficacy and readiness as well as the interventionists’ competence and confidence (figure 3).

Outcome

The patterns of intended and/or unintended consequences based on the context–mechanism interaction that occurs at different levels: *micro*, *meso* and/or *macro*.⁶³ Examples of outcome for this review include HTN, stroke occurrence, VCI with or without dementia (figure 3).

The realist review approach also acknowledges the complexities of healthcare systems in conjunction with the persons who interact and navigate within the *micro*, *meso* and ecosystems. As such, this understanding has

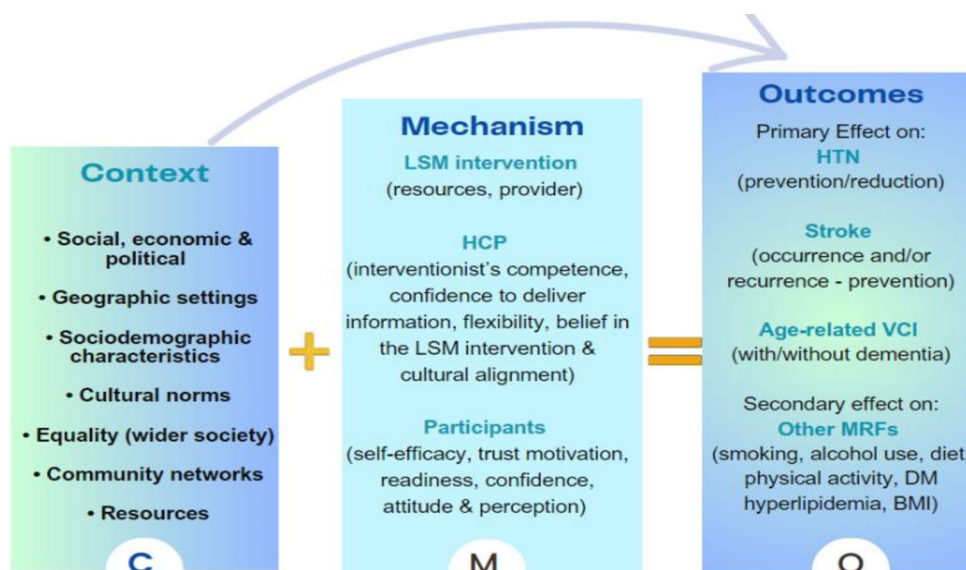


Figure 3 Context, mechanism and outcome configuration. BMI, body mass index; HTN, hypertension; LSM, lifestyle medicine; MRFs, modifiable risk factors; VCI, vascular cognitive impairment; HCP, Health care providers; DM, Diabetes mellitus.

the potential to: (1) yield a more comprehensive understanding about the feasibility of such complex LSM interventions in the real world based on different variables, diverse groups of populations, SDOH and in different contexts and settings—supporting the shift from one-size-fits-all to more personalised/precision brain care; (2) inform meaningful adaptations and scale up of complex LSM interventions; and (3) address inequities in health and other outcomes.⁶⁵ The review commenced in November 2023. The Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols checklist for this protocol is presented in online supplemental appendix 1.

Stages of our realist review

This review will follow the process grounded in the realist approach defined by Pawson *et al*⁶² and adapted by Rycroft-Malone *et al*.⁶⁶ The stages of the review will be iterative and include the following: (1) clarify the scope, (2) search for the evidence, (3) critically appraise primary studies and extract data focusing on the CMO configuration and (4) synthesise evidence and draw conclusions. This protocol was registered with PROSPERO (CRD42024511566).

Stage 1: clarify the scope

An early exploratory search of the literature will be conducted in this stage to investigate the theoretical underpinnings of existing LSM interventions as well as map out the conceptual and theoretical landscape of LSM interventions for the management of HTN and other MRFs to reduce the risk of stroke and VCI.⁶⁷ Theoretical underpinnings of existing LSM interventions may include: Theory of Reasoned Action,⁶⁸ Theory of Planned Behaviour,⁷⁰ Rogers Diffusion of Innovation Theory,⁷¹ Self-Determination Theory,⁷² Social Cognitive Theory⁷³ and Health Behaviour Change Theory.⁷⁴ The exploratory search will also be used to inform and guide discussions with the project team⁶⁷ as we work through the development of an initial programme theory. Additionally, frequent meetings will be held with the multidisciplinary project team that have expertise in mixed methods, realist review methodology, epidemiology, neurodegenerative disease, neurological health, ageing, dementia, stroke/VCI, neuroimaging, quality improvement, economic analysis, complex interventions and family medicine. Furthermore, patient partners will also be engaged to attain an understanding of their perspective on existing theories, how and why LSM interventions work, to what extent, for whom and in what contexts. A final version of the search strategy using the OVID is presented in online supplemental appendix 2.

Stage 2: search for the evidence

The literature search strategy and syntax will be codeveloped by the project team and medical information specialist (JB). The search was from 2000 onwards, which aligns with the time of the landmark textbook publication on LSM.⁷⁵ The following databases will be searched:

Ovid MEDLINE(R) ALL, Ovid Embase, Ovid Healthstar, EBSCO CINAHL and Elsevier Scopus. The medical information specialist will design and tailor the search syntax for each database. An example of the search strategy for OVID is presented in online supplemental appendix 2. The search will be inclusive of study design (eg, non-empirical, quantitative, qualitative and mixed methods), country, setting (eg, primary care, community), year of publication and target population (eg, young adults, older adults, men, women). The search will centre on the following areas: (1) LSM interventions (on any of the six pillars) that are focused on HTN as the primary MRF for the prevention of stroke and/or VCI; (2) LSM interventions focused on other MRFs to reduce the risk of stroke and/or VCI; (3) LSM interventions focused on HTN and other MRFs for diverse groups of populations (eg, women, men, immigrants); and (4) articles that provide evidence on facilitators and barriers on the implementation and uptake of LSM interventions to reduce the risk of stroke and/or VCI.

Two reviewers will screen the titles and abstracts of the selected articles using the Covidence software⁷⁶ and categorise them as ‘include’, ‘exclude’ or ‘maybe’ based on the selection criteria (table 1). Reviewers will discuss and resolve any disagreements by consensus to ensure interrater reliability. Appreciating the iterative nature of this review, in collaboration with the medical information specialist, the project team may revise the search strategy based on the initial screening results. Selected articles, for the full-text review, will be reviewed by two reviewers and any disagreements will be resolved by a third reviewer and consensus.

The selected articles will be reviewed for relevance and rigour.⁷⁷ The Mixed Methods Appraisal Tool V.2018 will be used to critically appraise studies that use quantitative, qualitative and mixed methods research designs.⁷⁸ The following describes the information that will be extracted:

Quantitative data: (1) general article information—author’s last name(s), publication date, study setting, country and continent of publication as well as funding agency; (2) study purpose, research design and target population (where available: age, sex, gender, ethnicity, race, socioeconomic and sample size); (3) LSM pillar—for example, nutrition, smoking, PA; (4) LSM intervention’s key ingredients/elements (eg, theoretical underpinning, dose, mode of delivery); (5) description of the context and/or mechanisms; and (6) outcome data.

Qualitative data: (1) adopted or developed theories, frameworks, or models; (2) description and explanation of the contextual factors that determined or influenced the mechanisms of the LSM intervention; and (3) description of facilitators and/or barriers for implementation of the LSM intervention.

The included literature will be described using descriptive statistics. The principles of realist enquiry articulated by Rycroft-Malone *et al* and Pawson^{66 67 77} will be used for the main analysis of this review, which

**Table 1** Realist review selection criteria

Study characteristics	Inclusion criteria
Language	English
Status	Published peer reviewed
Dates	1980 onwards
Design	All types of RCTs, all quasiexperimental and observational designs, all types of mixed methods, qualitative studies and non-empirical
Population	Persons 18 years of age and older
Settings	No restrictions
Intervention	LSM interventions on any of the six pillars for HTN management and other MRFs for the prevention of stroke and/or age-related VCI Description of key ingredients/ characteristics Description of aspects pertaining to context and/or mechanism
Measures	Both quantitative and qualitative measures.
Outcomes	Clinical: HTN, other MRFs when mentioned (eg, hyperlipidaemia, smoking, alcohol use, diet), all types of strokes (eg, ischaemic, haemorrhagic) occurrence and/or recurrence, and age-related VCI, VCI with no dementia and VCI with dementia Behavioural: self-efficacy, motivation, adherence, barriers

HTN, hypertension; LSM, lifestyle medicine; MRFs, modifiable risk factors; RCTs, randomised controlled trials; VCI, vascular cognitive impairment.

includes: (1) arranging the extracted information into evidence tables representing different bodies of literature; (2) conducting a thematic analysis and organising the information into patterns of CMOs; and (3) linking patterns to define the initial programme theory, accordingly. An intersectionality framework will be used to synthesise the evidence to increase the understanding of ways in which current inequities exist with LSM interventions as race, sex, gender identity, sexual orientation and/or SDOH provide context and found to influence life choices and ability to effect health-related changes.^{79 80} The data will be presented in accordance with the Realist and Meta-narrative Evidence Synthesis: Evolving Standards guidelines.⁸¹

Patient and public involvement

Patients (eg, persons with lived/living experience) and/or the public are involved in the design, conduct and dissemination plans of this work.

ETHICS AND DISSEMINATION

Research ethics board approval is not required for this review. The primary output of this realist review is an evidence-based programme theory for LSM interventions for the management of HTN and other MRFs to reduce the risk of stroke and VCI. Additional outputs include: (1) the development of actionable recommendations to promote brain health and lifestyle approaches that extend beyond a one-size-fits-all approach and towards personalised/precision brain care to reduce health disparities and burden of stroke and VCI; and (2) guidance on modifications to LSM interventions based on the CMO configuration for different settings and diverse groups of populations.

Findings from this review will be disseminated at three levels to promote brain health and risk reduction of stroke and VCI through the prevention, management and treatment of HTN and other MRFs via LSM approaches: (1) *micro*—patients/persons with lived experience (PWLE), caregivers, primary care providers, non-research partners and scientists; (2) *meso*—public, national not-for-profit organisations (eg, Heart and Stroke Foundation) professional associations and organisations (eg, American Heart Association, American Academy of Neurology, World Stroke Organization, American College of Lifestyle Medicine); and (3) *macro*—policymakers and government partners.

Within these three levels, findings will be disseminated through: (1) research and executive summaries/reports; (2) policy briefs; (3) publications and conferences; (4) multimedia channels to reach a diverse audience; (5) digital storytelling for health; (6) research and non-research events; (7) co-led (research and non-academic partners), multidisciplinary educational outreach initiatives via videoconferences, webinars and symposiums/workshops; (8) culturally tailored messaging and products (eg, educational/informational material and fact sheets) by enlisting PWLE, established hospital-based patient engagement structures and members that conduct research with structurally marginalised populations; and (9) codevelopment of Knowledge Mobilization tools.

DISCUSSION

LSM has been embraced as an ‘*epitome of personalised medicine*’⁸² and falls under the prevention pillar of the neurological quadrangle, which aims to strengthen health policies, systems and services, optimise health resources for brain health to achieve the WHO Intersectoral Global Action Plan on Neurological Disorders 2022–2031.⁸³ This realist review is the first, to our knowledge, to collectively work beyond the traditional evaluative review approaches and conduct a *black box evaluation* of LSM interventions to understand *how and why* they work, under what circumstances and *for whom* to reduce the risk of stroke and VCI. However, there are several noteworthy limitations of a realist review: (1) it is time intensive and demanding from the reviewers and research team⁶⁶; and (2) there

may be little description of the intervention with clear reporting of the context, mechanisms and outcomes in the included studies, which may affect the CMO configuration in this review. Although there are potential limitations much like with any methodology, this review has the potential to (1) mobilise knowledge on the current scientific state of LSM interventions in primary care to promote brain health; (2) fill gaps that are left by systematic reviews and meta-analyses in this area; (3) provide a theoretical framework and guide on how to develop and/or modify LSM interventions for different contexts and groups of populations based on the CMO configuration; and (4) promote brain health and brain care through the development and implementation of LSM interventions, based on the CMO configuration, in a synergistic, sustainable and holistic way for diverse groups of populations while accounting for sociocultural, economic and contextual factors.

Author affiliations

¹Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada

²Program for Health System and Technology Evaluation, Toronto General Research Institute, Toronto, Ontario, Canada

³Jay and Sari Sonshine Centre for Stroke Prevention & Cerebrovascular Brain Health, University Health Network, Toronto, Ontario, Canada

⁴Centre for Advancing Collaborative Healthcare & Education (CACHE), University of Toronto, Toronto, Ontario, Canada

⁵Toronto Health Economics and Health Technology Assessment (THETA) Collaborative, University of Toronto, Toronto, Ontario, Canada

⁶Henry and Allison McCance Center for Brain Health, Massachusetts General Hospital, Boston, Massachusetts, USA

⁷Department of Neurology, Massachusetts General Hospital, Boston, Massachusetts, USA

⁸Broad Institute of MIT and Harvard, Cambridge, MA, Massachusetts, USA

⁹Center for Genomic Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA

¹⁰Department of Neurology, Toronto Western Hospital, Toronto, Ontario, Canada

¹¹Department of Medicine, Division of Neurology, University of Toronto Faculty of Medicine, Toronto, Ontario, Canada

¹²Krembil Brain Institute, University Health Network, Toronto, Ontario, Canada

X Aleksandra Pikula @WomensBrain_MD

Contributors SI, AP and VER conceived and designed the project. VER serves as the methodologist and scientific advisor. JB is an experienced information specialist who is conducting the literature search and contributed to the manuscript review and approval. SI wrote the initial manuscript draft. EK is responsible for the data screening and collection as well as manuscript review and approval. JRS, SS, JR and LC all reviewed and approved the manuscript. The guarantor of the study is AP, who accepts full responsibility for the finished work and/or the conduct of the study, had access to the data and controlled the decision to publish.

Funding This work was supported by the Canadian Institutes of Health Research (Grant # 503560).

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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ORCID iD

Sarah Ibrahim <http://orcid.org/0000-0002-3750-2384>

REFERENCES

- Steinmetz JD, Seeher KM, Schiess N, *et al*. Global, regional, and national burden of disorders affecting the nervous system, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet Neurol* 2024;23:344–81.
- Johnson CO, Nguyen M, Roth GA, *et al*. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019;18:439–58.
- Feigin VL, Brainin M, Norrving B, *et al*. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. *Int J Stroke* 2022;17:18–29.
- Bamford J, Sandercock P, Dennis M, *et al*. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *The Lancet* 1991;337:1521–6.
- Feigin VL, Stark BA, Johnson CO, *et al*. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol* 2021;20:795–820.
- Feigin VL, Nichols E, Alam T, *et al*. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019;18:459–80.
- Boot E, Ekker MS, Putaala J, *et al*. Ischaemic stroke in young adults: a global perspective. *J Neurol Neurosurg Psychiatry* 2020;91:411–7.
- Heart and Stroke Foundation. Stroke month 2022 key messages and backgrounds for media. 2022. Available: <https://www.heartandstroke.ca/-/media/pdf-files/what-we-do/news/stroke-month-2022-background-for-media.pdf?rev=a88365a3f5a94dae9ebc8e8f4d0fc310#:~:text=More%20than%2089%2C000%20strokes%20occur,third%20leading%20cause%20of%20death.&text=dramatically%20over%20the%20past%20several%20decades%20and%20stroke%20continues%20to%20rise.&text=research%20breakthroughs%2C%20better%20awareness%20of, and%20enhanced%20access%20to%20care>
- Singhal AB, Biller J, Elkind MS, *et al*. Recognition and management of stroke in young adults and adolescents. *Neurology (ECRicon)* 2013;81:1089–97.
- Maaijwee NAMM, Rutten-Jacobs LCA, Schaapsmeeders P, *et al*. Ischaemic stroke in young adults: risk factors and long-term consequences. *Nat Rev Neurol* 2014;10:315–25.
- Sasikumar S, Pikula A. Psychosocial Needs and Occupational Functioning of Younger Adults after Stroke. *EC Neurology* 2018;10:34–47.
- Ekker MS, Boot EM, Singhal AB, *et al*. Epidemiology, aetiology, and management of ischaemic stroke in young adults. *Lancet Neurol* 2018;17:790–801.
- Amaricai E, Poenaru DV. The post-stroke depression and its impact on functioning in young and adult stroke patients of a rehabilitation unit. *J Ment Health* 2016;25:137–41.
- Ignacio KHD, Diestro JDB, Medrano JMM, *et al*. Depression and Anxiety after Stroke in Young Adult Filipinos. *J Stroke Cerebrovasc Dis* 2022;31:106232.
- Waje-Andreassen U, Thomassen L, Jusufovic M, *et al*. Ischaemic stroke at a young age is a serious event—final results of a population-based long-term follow-up in Western Norway. *Eur J Neurol* 2013;20:818–23.
- Gurková E, Štůrková L, Mandysová P, *et al*. Factors affecting the quality of life after ischemic stroke in young adults: a scoping review. *Health Qual Life Outcomes* 2023;21:4.
- Walters R, Collier JM, Braighi Carvalho L, *et al*. Exploring post acute rehabilitation service use and outcomes for working age stroke

- survivors (≤ 65 years) in Australia, UK and South East Asia: data from the international AVERT trial. *BMJ Open* 2020;10:e035850.
- 18 Pan X, Wang Z, Yao L, *et al.* The reasons for not returning to work and health-related quality of life among young and middle-aged patients with stroke: A cross-sectional study. *Front Neurol* 2023;14:1078251.
 - 19 World stroke organization (WSO). Global stroke fact sheet. 2022. Available: https://www.world-stroke.org/assets/downloads/WSO_Global_Stroke_Fact_Sheet.pdf
 - 20 Ellis C. Stroke in young adults. *Disabil Health J* 2010;3:222–4.
 - 21 Tan E, Gao L, Collier JM, *et al.* The economic and health burden of stroke among younger adults in Australia from a societal perspective. *BMC Public Health* 2022;22:218.
 - 22 Rundek T, Tolea M, Ariko T, *et al.* Vascular Cognitive Impairment (VCI). *Neurotherapeutics* 2022;19:68–88.
 - 23 Gorelick PB, Scuteri A, Black SE, *et al.* Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American heart association/American stroke association. *Stroke* 2011;42:2672–713.
 - 24 Marengoni A, Winblad B, Karp A, *et al.* Prevalence of chronic diseases and multimorbidity among the elderly population in Sweden. *Am J Public Health* 2008;98:1198–200.
 - 25 Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimer's disease prevalence. *Lancet Neurol* 2011;10:819–28.
 - 26 Monetary Costs of Dementia in the United States. *N Engl J Med* 2013;369:489–90.
 - 27 International A, Patterson C. World alzheimer report 2018: the state of the art of dementia research: new frontiers. 2018. Available: <https://www.alzint.org/resource/world-alzheimer-report-2018/>
 - 28 O'Donnell MJ, Chin SL, Rangarajan S, *et al.* Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *The Lancet* 2016;388:761–75.
 - 29 Feigin VL, Roth GA, Naghavi M, *et al.* Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol* 2016;15:913–24.
 - 30 Zlokovic BV, Gottesman RF, Bernstein KE, *et al.* Vascular contributions to cognitive impairment and dementia (VCI): A report from the 2018 National Heart, Lung, and Blood Institute and National Institute of Neurological Disorders and Stroke Workshop. *Alzheimers Dement* 2020;16:1714–33.
 - 31 Livingston G, Huntley J, Sommerlad A, *et al.* Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet* 2020;396:413–46.
 - 32 Centers for Medicare & Medicaid Services (US). Chronic conditions among medicare beneficiaries—chartbook. 2012. Available: <http://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/chronic-conditions/2012chartbook.html>
 - 33 World Health Organization. First who report details devastating impact of hypertension and ways to stop it. 2023. Available: <https://www.who.int/news/item/19-09-2023-first-who-report-details-devastating-impact-of-hypertension-and-ways-to-stop-it#:~:text=Hypertension%20affects%201%20in%203,and%20many%20other%20health%20problems>
 - 34 Whelton PK, Carey RM, Aronow WS, *et al.* ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines, 2017. Available: <https://www.ahajournals.org/doi/10.1161/HYP.0000000000000065>
 - 35 Iadecola C, Gottesman RF. Neurovascular and Cognitive Dysfunction in Hypertension: Epidemiology, Pathobiology, and Treatment. *Circ Res* 2019;124:1025–44.
 - 36 Singh SD, Senff JR, Van Duijn CM, *et al.* Treating Hypertension: Important for Heart Health. *Fund for Brain Health Stroke* 2024;55:1464–6.
 - 37 Launer LJ, Ross GW, Petrovitch H, *et al.* Midlife blood pressure and dementia: the Honolulu-Asia aging study. *Neurobiol Aging* 2000;21:49–55.
 - 38 Yano Y, Ning H, Allen N, *et al.* Long-term blood pressure variability throughout young adulthood and cognitive function in midlife: the Coronary Artery Risk Development in Young Adults (CARDIA) study. *Hypertension* 2014;64:983–8.
 - 39 Swan GE, DeCarli C, Miller BL, *et al.* Association of midlife blood pressure to late-life cognitive decline and brain morphology. *Neurology (Ecricon)* 1998;51:986–93.
 - 40 Valenzuela PL, Carrera-Bastos P, Gálvez BG, *et al.* Lifestyle interventions for the prevention and treatment of hypertension. *Nat Rev Cardiol* 2021;18:251–75.
 - 41 Rippe JM. Lifestyle Medicine: The Health Promoting Power of Daily Habits and Practices. *Am J Lifestyle Med* 2018;12:499–512.
 - 42 Adsul P, Perez LG, Oh A, *et al.* Implementation science across lifestyle medicine interventions. In: Mechanick JI, Kushner RF, eds. *Creating a Lifestyle Medicine Center*. Cham: Springer International Publishing, 2020: 29–36. Available: http://link.springer.com/10.1007/978-3-030-48088-2_4
 - 43 Lianov L, Johnson M. Physician competencies for prescribing lifestyle medicine. *JAMA* 2010;304:202–3.
 - 44 Ornish D. Intensive Lifestyle Changes for Reversal of Coronary Heart Disease. *JAMA* 1998;280:2001.
 - 45 Morton D, Rankin P, Kent L, *et al.* The Complete Health Improvement Program (CHIP): History, Evaluation, and Outcomes. *Am J Lifestyle Med* 2016;10:64–73.
 - 46 Pikula A, Gulati M, Bonnet JP, *et al.* Promise of Lifestyle Medicine for Heart Disease, Diabetes Mellitus, and Cerebrovascular Diseases. *Mayo Clinic Proceedings: Innovations, Quality & Outcomes* 2024;8:151–65.
 - 47 Eguchi E, Iso H, Tanabe N, *et al.* Healthy lifestyle behaviours and cardiovascular mortality among Japanese men and women: the Japan collaborative cohort study. *Eur Heart J* 2012;33:467–77.
 - 48 Larsson SC, Akesson A, Wolk A. Healthy diet and lifestyle and risk of stroke in a prospective cohort of women. *Neurology (Ecricon)* 2014;83:1699–704.
 - 49 Zhang Y, Tuomilehto J, Jousilahti P, *et al.* Lifestyle factors on the risks of ischemic and hemorrhagic stroke. *Arch Intern Med* 2011;171:1811–8.
 - 50 Rutten-Jacobs LC, Larsson SC, Malik R, *et al.* Genetic risk, incident stroke, and the benefits of adhering to a healthy lifestyle: cohort study of 306 473 UK Biobank participants. *BMJ* 2018;363.
 - 51 Rees K, Takeda A, Martin N, *et al.* Mediterranean-style diet for the primary and secondary prevention of cardiovascular disease. *Cochrane Database Syst Rev* 2019;3.
 - 52 Lee CD, Folsom AR, Blair SN. Physical activity and stroke risk: a meta-analysis. *Stroke* 2003;34:2475–81.
 - 53 Wendel-Vos GCW, Schuit AJ, Feskens EJM, *et al.* Physical activity and stroke. A meta-analysis of observational data. *Int J Epidemiol* 2004;33:787–98.
 - 54 Vitor J, Melita C, Rodrigues M, *et al.* Physical activity in vascular cognitive impairment: Systematic review with meta-analysis. *J Stroke Cerebrovasc Dis* 2023;32:107133.
 - 55 Salter KL, Kothari A. Using realist evaluation to open the black box of knowledge translation: a state-of-the-art review. *Implementation Sci* 2014;9:115.
 - 56 Hewitt G, Sims S, Harris R. The realist approach to evaluation research: an introduction. *Int J Ther Rehabil* 2012;19:250–9.
 - 57 Julnes G, Mark MM. Evaluation as sensemaking: Knowledge construction in a realist world. *New Dirctns Evaluation* 1998;1998:33–52.
 - 58 Kernick D. Wanted--new methodologies for health service research. Is complexity theory the answer? *Fam Pract* 2006;23:385–90.
 - 59 Pawson R, Tilley N. Realistic evaluation. Sage; 1997. Available: https://cnxus.org/wp-content/uploads/2022/04/RE_chapter.pdf
 - 60 De Brún A, McAuliffe E. Identifying the context, mechanisms and outcomes underlying collective leadership in teams: building a realist programme theory. *BMC Health Serv Res* 2020;20:261.
 - 61 Jack K. What is realist evaluation? *Evid Based Nurs* 2022;25:111–3.
 - 62 Pawson R, Greenhalgh T, Harvey G, *et al.* Realist review--a new method of systematic review designed for complex policy interventions. *J Health Serv Res Policy* 2005;10 Suppl 1:21–34.
 - 63 Jagosh J. Realist Synthesis for Public Health: Building an Ontologically Deep Understanding of How Programs Work, For Whom, and In Which Contexts. *Annu Rev Public Health* 2019;40:361–72.
 - 64 Dalkin SM, Greenhalgh J, Jones D, *et al.* What's in a mechanism? Development of a key concept in realist evaluation. *Implementation Sci* 2015;10:49.
 - 65 Fletcher A, Jamal F, Moore G, *et al.* Realist complex intervention science: Applying realist principles across all phases of the Medical Research Council framework for developing and evaluating complex interventions. *Evaluation (Lond)* 2016;22:286–303.
 - 66 Rycroft-Malone J, McCormack B, Hutchinson AM, *et al.* Realist synthesis: illustrating the method for implementation research. *Implement Sci* 2012;7:33.
 - 67 Pawson R, Greenhalgh T, Harvey G, *et al.* Realist synthesis: an introduction. research methods an esrc research programme working paper series. 2004. Available: <https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=435146e6617491ff1c4b32b76e0a534c86d6c7>

- 68 Fishbein MA, A theory of reasoned action: some applications and implications. *Nebraska symposium on motivation*. . University of Nebraska Press, 1980:27. 65–116.
- 69 Ajzen I, Fishbein M. *Understanding Attitudes and Predicting Social Behavior*. Englewood Cliffs (NJ): Prentice Hall, 1980.
- 70 Ajzen I. The theory of planned behavior. *Org Behav Hum Decis Process* 1991;50:179–211.
- 71 Rogers EM. *Diffusion of Innovations*. New York City, NY: Free Press, 1962.
- 72 Deci EL, Ryan RM. Self-determination theory: A macrotheory of human motivation, development, and health. *Can Psychol / Psychol can* 2008;49:182–5.
- 73 Bandura A, National Inst of Mental Health. *Social Foundations of Thought and Action: A Social Cognitive Theory*. Prentice-Hall, Inc, 1986.
- 74 Glanz K, Rimer BK, Viswanath KV. *Health Behavior: Theory, Research, and Practice*. Jossey-Bass/Wiley, 2015.
- 75 Rippe J. *Lifestyle Medicine*. NewYork: Blackwell, 1999.
- 76 Veritas health innovation. *Covidence Systematic Review Software*. Melbourne, Australia, Available: www.covidence.org
- 77 Pawson R. Evidence-based policy: a realist perspective. 2006. Available: <http://ndl.ethernet.edu.et/bitstream/123456789/4276/1/8.pdf.pdf#page=40>
- 78 Hong QN, Fàbregues S, Bartlett G, et al. The Mixed Methods Appraisal Tool (MMAT) version 2018 for information professionals and researchers. *EFI* 2018;34:285–91.
- 79 Shurney D, Webb D. Optimizing Health and Well-Being: The Interplay Between Lifestyle Medicine and Social Determinants of Health. *J Fam Pract* 2022;71:eS78–82.
- 80 Cassoobhoy A, Sardana JJ, Benigas S, et al. Building Health Equity: Action Steps From the American College of Lifestyle Medicine's Health Disparities Solutions Summit (HDSS) 2020. *Am J Lifestyle Med* 2022;16:61–75.
- 81 Wong G, Greenhalgh T, Westhorp G, et al. RAMESES publication standards: realist syntheses. *BMC Med* 2013;11:21.
- 82 Abe M, Abe H. Lifestyle medicine – An evidence based approach to nutrition, sleep, physical activity, and stress management on health and chronic illness. *Pers Med Univ* 2019;8:3–9.
- 83 Owolabi MO, Leonardi M, Bassetti C, et al. Global synergistic actions to improve brain health for human development. *Nat Rev Neurol* 2023;19:371–83.