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Comprehensive strategies for stroke prevention: A narrative review of population-level risk factor mitigation

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Abstract:

Stroke remains a leading cause of global mortality and is projected to become the second-largest contributor to the global disease burden by the year 2050. Despite advancements in medical technology, a definitive cure for stroke is still unavailable, and effective management heavily depends on timely intervention after its occurrence. In recent decades, stroke incidence has declined in developed nations due to improved preventive measures while it has surged in developing regions, particularly among younger populations. This highlights the urgent need for comprehensive prevention strategies to address modifiable factors and reduce long-term disabilities. This review categorizes modifiable stroke risk factors into three key domains: metabolic, behavioral, and environmental. It synthesizes current knowledge and evaluates intervention strategies targeting hypertension, diabetes, smoking, dietary habits, and air pollution, among others. The review also examines emerging evidence on the benefits and limitations of these interventions, providing critical insights into their effectiveness. Notably, the discussion also encompasses the interplay and combined impacts of these risk factors, offering a thorough insight into etiology and emphasizing the importance of adopting a comprehensive strategy for risk management. By providing a general view of stroke prevention efforts, the paper aims to guide future research and support the development of evidence-based, population-level strategies to mitigate stroke risk globally.

Keywords:

Population intervention, prevention, risk factors, stroke

Introduction

Stroke is defined as a sudden neurological malfunction caused by either blockage or rupture of blood vessels supplying the central nervous system. Stroke is considered a common consequence of vascular aging, but can also occur at any age, with increased cases in young adults.[1] According to the latest reports from the Global Burden of Disease Study (GBD), stroke is the third leading cause of global deaths and the fourth cause of disability-adjusted life years (DALYs) in 2021.[2,3] As one of the major noncommunicable diseases, stroke is among the top two causes of global disease burden projected for 2050, indicating a persistent disease burden in the future.[4] The incidence, mortality, and DALY rates of stroke are negatively correlated with the sociodemographic index, and although stroke incidence has significantly decreased in the high-income regions due to the health education and surveillance, it continues to increase in developing regions due to evolving living habits and aging trend.[5] Therefore, interventions against stroke play a vital role in the sustainable reduction of global mortality, especially in improving the health of people in the low-income regions.

Significant advancements have been made in the treatment of the acute onset of stroke in the past decades, and strategies such as endovascular therapy and thrombolytics

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have been proven to effectively reduce mortality and disabilities caused by acute stroke.[6,7] However, these measures are accessible for a brief period right after the symptoms appear, and only a fraction of patients with a sudden stroke can promptly get therapy. Furthermore, patients who survive an initial stroke are still subject to stroke recurrence. Although the 5-year-recurrence rates decline in developed countries, they remain at over 10% and have barely changed over the last two decades.[8] Therefore, primary and secondary prevention remains essential in mitigating the constant threats of stroke, especially in reducing stroke-related mortality in the population with primary cardiometabolic disease.

According to the American Heart Association's (AHA) most recent guideline (2024) for stroke prevention strategies, rational modification of stroke-associated cardiometabolic, behavioral, and dietary risk factors can effectively reduce the incidence and burden from stroke.[9] The GBD study estimates that approximately 87% DALYs of stroke could be attributed to 19 major risk factors, such as high blood pressure (BP), hypercholesterolemia, diabetes, overweight, tobacco use, alcohol intake, and air pollution.[10] In accordance with the classification of stroke-related risk factors in the GBD study, this review summarizes the current knowledge of metabolic, behavioral, and environmental risk factors associated with stroke incidence or mortality [Figure 1]. By adding mechanistic insights and updated evidence on intervention strategies for these risk factors, we believe this review can be a theoretical guide for future actions and investigations in stroke prevention. In addition, we discuss the interplay of these risk factors, promoting the understanding of their relative significance and leading to the development of more comprehensive prevention strategies.

Metabolic Risk Factors

Blood pressure

High BP (hypertension) is regarded as the leading contributor to stroke,[11] and patients with systolic BP (SBP) ≥ 130 mmHg or diastolic BP (DBP) ≥ 80 mmHg are recommended to take antihypertensive medications and lifestyle modifications to reduce stroke risk [Figure 2].[9] Over 30% of adults worldwide are predicted to have hypertension,[12] and high BP is linked to approximately 56.8% of the burden of stroke.[13] Hypertension has a profound effect on the circulatory system, and there is a delay between the elevated BP and subsequent complications. It can impair both the structure and function of the cerebral vasculature by imposing oxidative stress, inflammation, and baroreflex dysfunction.[14] It also reduces the cerebral blood flow (CBF) by disturbing endothelium-dependent vascular relaxation, which may trigger cerebral ischemia and white matter injuries. Meanwhile, hypertension-mediated endothelial dysfunction can lead to the overproduction of nitric oxide (NO) and increase vascular permeability, resulting in brain edema and hemorrhagic stroke. Although the brain has an

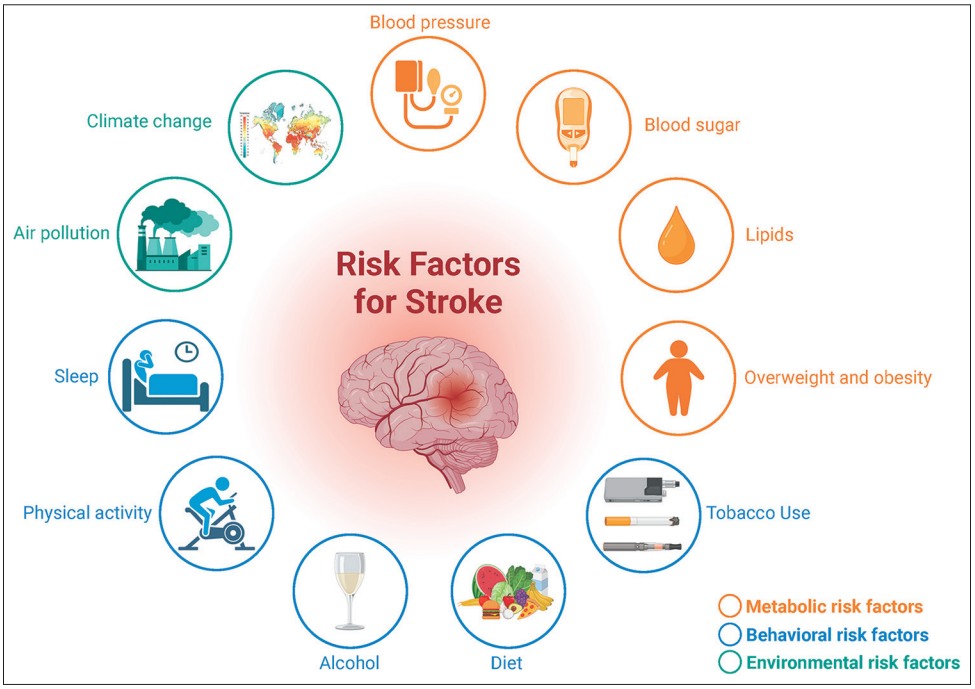

Figure 1: Central illustration of stroke-related metabolic, behavioral, and environmental risk factors. The diagram utilizes orange circles to denote metabolic risk factors, blue circles to represent behavioral risk factors, and green circles to indicate environmental risk factors. This figure was created in BioRender. Ding, R. (2025) https://BioRender.com/a44l738

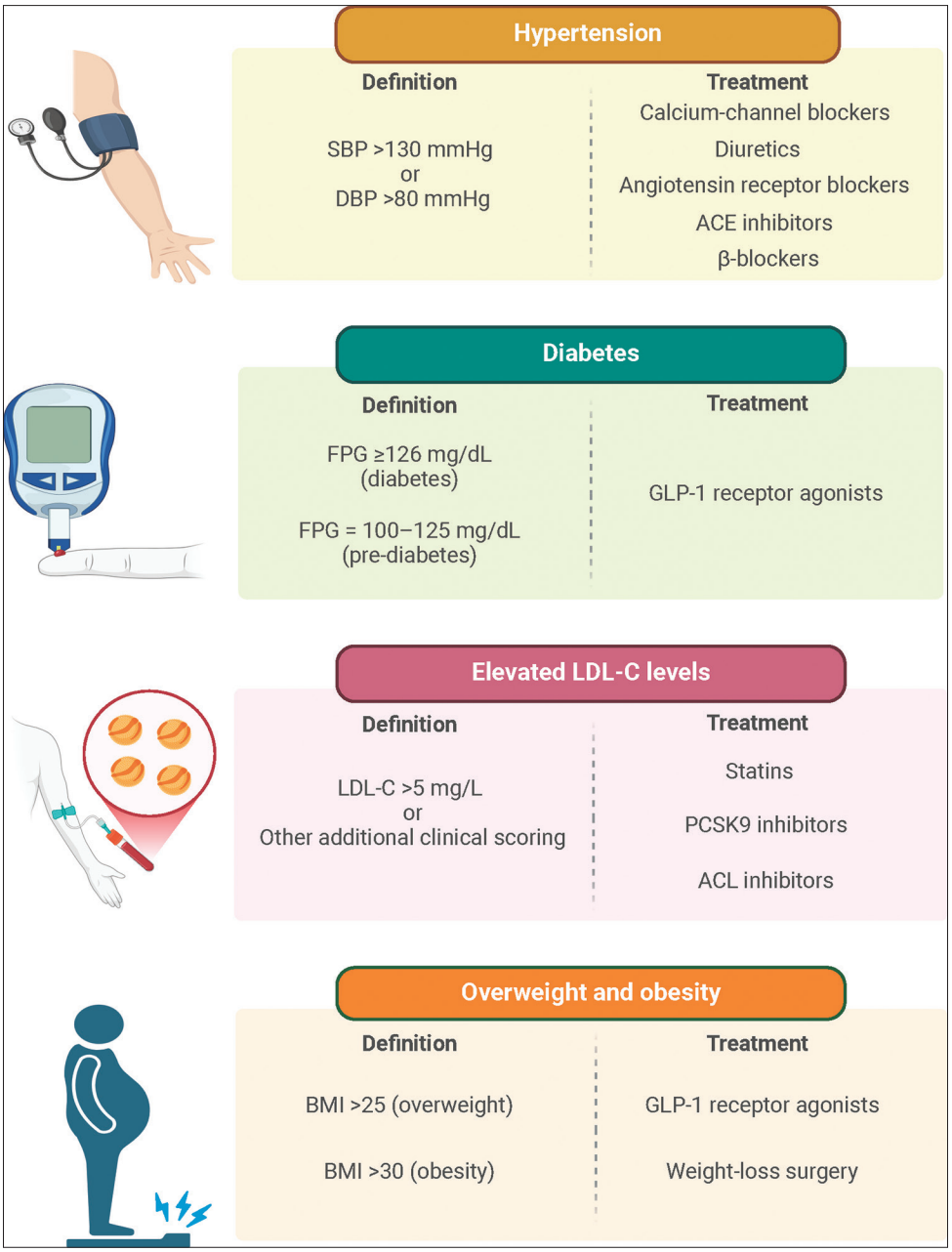

Figure 2: Definition and correlated treatment of stroke-related metabolic risk factors. The figure presents four major modifiable risk factors – hypertension, diabetes, elevated low-density lipoprotein cholesterol (LDL-C) levels, and overweight/obesity – organized into distinct color-coded sections. Each section provides (1) diagnostic criteria (left) and (2) evidence-based treatment options (right), including pharmacological interventions and procedural therapies. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, ACE inhibitors: Angiotensin-converting enzyme inhibitors, β-blockers: β-adrenergic receptor blockers, FPG: fasting plasma glucose, GLP-1 receptor: glucagon-like peptide 1 receptor, LDL-C: Low-density lipoprotein cholesterol, PCSK9 inhibitors: Proprotein convertase subtilisin/kexin type 9 inhibitors, ACL inhibitors: ATP citrate lyase inhibitors, BMI: Body mass index. This figure was created in BioRender. Ding, R. (2025) https://BioRender.com/j73z719

autoregulation system to maintain a constant CBF when the arterial pressure ranges from 60 to 150 mmHg,[15] patients with hypertension still require additional medication to maintain adequate cerebral perfusion.[14] In addition, SBP/DBP levels exceeding 115/75 mmHg, which are not typically classified as hypertensive, may still increase stroke risk compared to ideal BP levels.[16,17] Among modifiable risk factors, hypertension is identified as the most significant contributor to stroke risk.

Pharmacological management of BP through antihypertensive therapy is well-documented to prevent stroke, regardless of age, gender, or race. A large meta-analysis included 48 large randomized-controlled trials (RCTs) examining BP-lowering medications estimated that a 5 mmHg reduction in SBP could decrease the risk of major cardiovascular events, including both fatal and nonfatal stroke, by about 10%.[18] A recent RCT from China reported that reducing SBP/DBP by 23.1/9.9 mmHg could lower stroke risk

by 34%.[19] Pharmacological interventions including diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, β-adrenergic receptor blockers (β-blockers), and calcium-channel blockers (CCBs) were all proven to mitigate stroke incidence among patients with hypertension. CCBs are consistently the most effective in mitigating stroke risk, while β-blockers are comparatively less effective.[9] Combining multiple antihypertensive medications is generally more effective, and national surveys indicate that about 60% adults in the United States use two or more medications to control BP.[20]

Furthermore, longer duration of hypertension independently correlates with higher antihypertensive medication use, elevated SBP, and increased stroke risk, indicating that delaying hypertension onset could reduce stroke burden.[21] Patient-driven antihypertensive management and routine hypertension screening in the general population are the crucial preventive measures. A recent RCT also demonstrated that intensive BP management (targeting < 120 mmHg) significantly reduced stroke incidence compared to standard targets (< 140 mmHg) in patients with type 2 diabetes.[22] These findings strongly support the recommendation for intensive BP control among high-risk populations.

Blood sugar

Diabetes (fasting plasma glucose [FPG] ≥ 126 mg/dL) and prediabetes (FPG 100–125 mg/dL) are both associated with stroke incidence and mortality.[23,24] The GBD study estimated that approximately 529 million people were living with diabetes in 2021 (an age-standardized prevalence of 6.1%), and this number is projected to surge to 1.31 billion by the year 2050.[25] Type 2 diabetes (T2D) accounts for over 95% of diabetes cases, which is a progressive condition characterized by inadequate insulin secretion from pancreatic β-cells, often in the context of insulin resistance and metabolic syndrome.[23] Individuals with diabetes can develop stroke at a relatively younger age and may suffer from more serious comorbidities.[26] Diabetes primarily exacerbates atherosclerosis in large arteries to induce ischemic stroke, while triggers cerebral small vessel disease and arterial stiffness to cause hemorrhagic risk. Moreover, it increases the risk of atrial fibrillation (AF), a major cause of cardioembolic stroke,[27] likely through atrial remodeling triggered by reactive oxygen species and advanced glycation end products.[28] Thus, high blood sugar not only increases the incidence of stroke but also influences the severity and recovery outcomes of acute ischemic stroke, highlighting the critical importance of glucose control in stroke prevention and management.

Although diabetes is an established risk factor for cerebrovascular events, there is currently no direct evidence that screening asymptomatic adults or those with unrecognized diabetes symptoms reduces stroke risk.[29] However, RCTs reported that treatment with GLP-1 receptor agonists (GLP-1RAs), such as dulaglutide and semaglutide, can significantly lower the risk of ischemic stroke in T2D patients.[30-32] Nevertheless, intensive glycemic control (HbA1c ≤ 6.5%) in type 1 or 2 diabetes has not demonstrated a reduction in stroke risk more than standard control (HbA1c 7%–8%) and may increase the risk of hypoglycemia and treatment burden.[9] Balancing the prevention of cerebrovascular complications with the potential drawbacks of intensive glucose management is therefore essential.

Lipids

Elevated serum lipid levels are regarded as an indirect and complex risk factor for stroke, while elevated levels of low-density lipoprotein cholesterol (LDL-C) are a definite risk factor for cardiovascular diseases. LDL-C is closely connected with the development of atherosclerosis, a key pathological basis for the occurrence of stroke. Cumulative exposure to LDL-C results in chronic inflammatory state and endothelial damage, while the internalization of LCL-C into vascular smooth muscle cells and macrophages leads to the development of foam cells, which then contributes to the atherosclerotic plaques.[33] Moreover, triglyceride-rich lipoproteins are commonly identified as an indicator for the risk of atherosclerosis-related disease.[34] Although high-density lipoprotein cholesterol (HDL-C) has generally been considered a beneficial factor in the vascular environment, evidence from genetic analyses has not consistently demonstrated HDL-C's beneficial role in preventing atherosclerosis and therapies targeting to improve HDL-C levels have not significantly altered cardiovascular events.[33]

Despite the inconsistency and ambiguity regarding the association between plasma cholesterol levels and stroke risk, LDL-C > 190 mg/dL (4.9 mmol/L) has been associated with long-term cardiovascular risks, and it is recommended to define LDL-C > 5 mg/dL as hypercholesterolemia.[35] Statins are the most well-known medications used to diminish cholesterol production in the liver via the inhibition of HMG-CoA reductase, which are considered the greatest advances in preventing stroke since the advent of aspirin and antihypertensive therapy.[36] Stain treatment is consistently associated with declined stroke risk.[37,38] An RCT enrolled patients with vascular risk factors but no prior cardiovascular diseases indicated that statin treatment reduced stroke risk by 30%.[39]

For patients with elevated cardiovascular risk who cannot tolerate statin treatment, bempedoic acid may provide a potential benefit in improving cardiovascular outcomes,[40] although its effect on preventing first

strokes was not statistically significant in a large RCT involving over 4,000 participants.[41] A meta-analysis reported that cholesterol-lowering treatment with PCSK9 inhibitors, including alirocumab and evolocumab, may help prevent stroke. However, there was insufficient data to conclude their protective effects against the first occurrence of stroke, and no significant difference was observed when comparing their effects with other active treatments in reducing LDL-C.[42]

Overweight and obesity

According to the latest report from the WHO in 2023, about 38% of the world's population is currently overweight, generally characterized by a body mass index (BMI) > 25 kg/m^2.[43] In addition to BMI, other metrics for overweight, such as waist circumference, waist-to-hip ratio, waist-to-height ratio, and weight-adjusted waist index are also positively associated with stroke incidence.[9] Obesity, defined as a BMI > 30 kg/m^2, is closely linked to other metabolic disorders including hypercholesterolemia, diabetes, and hypertension. Obesity fosters a chronic, low-grade inflammatory state that promotes cardiovascular complications, as demonstrated by the correlation between elevated inflammatory markers and stroke incidence.[44]

Interestingly, although obese patients are at increased risk for stroke, individuals with overweight or obesity may have lower mortality and recurrence risks following a stroke, a phenomenon termed the obesity paradox. These potential protective effects against stroke mortality and functional outcome may stem from the protective role of adipose tissue, such as secreting tumor necrosis factor-α receptors that neutralize inflammation. However, the roles of other mechanisms such as adiponectin and leptin resistance remain uncertain and require further investigation.[45]

A meta-analysis of 7 RCTs demonstrated that treatment with GLP-1RAs could reduce both body mass and blood sugar in patients with diabetes, which was further associated with a 16% reduction in stroke risk.[46] A recent RCT enrolled participants averaging a BMI of 33.34 kg/m^2 found that treatment with semaglutide could lower stroke risk by 23.3%.[47] In addition, bariatric surgery, aimed at achieving significant weight loss in patients with severe obesity (class II: BMI = 35–39.9 kg/m^2 and class III: BMI ≥ 40 kg/m^2), has shown to reduce stroke risk. A study tracking over 200,000 diabetic patients found that those who underwent bariatric surgery had a 33% lower risk of cerebrovascular disease compared to their nonsurgery counterparts.[48] A retrospective cohort of obese patients (class II with comorbidities or class III) also reported that those who underwent weight loss surgery had a much lower risk of cerebrovascular events compared to the matched nontreated group.[49]

Furthermore, a recent meta-analysis comprising 39 studies indicated that bariatric surgery was associated with a 36% reduction in stroke incidence.[50] However, additional RCTs are needed to confirm the benefits of weight-loss surgery in stroke prevention.

Lifestyle Factors Influencing Stroke Risk

Tobacco use

In 2020, it was estimated that approximately 32.6% of the global adult males and 6.5% of females were the regular tobacco users.[51] Smoking impairs vasodilation primarily by reducing nitric oxide bioavailability, and exacerbates inflammation, increasing leukocyte recruitment and adhesion to the vessel wall. Furthermore, the use of tobacco promotes atherosclerosis by altering lipid profiles, particularly facilitating foam cell formation through the oxidation of LDL. These processes, along with effects on platelet function and coagulation factors, significantly increase the risk of thrombotic events. The GBD study revealed that tobacco smoking accounted for 13.8% of stroke DALYs in 2021, ranked first among all behavioral risk factors.[13]

Substantial epidemiological evidence indicates that traditional cigarettes, waterpipe smoking, smoke-less tobacco, and environmental tobacco smoke are consistently linked to stroke incidence [Figure 3].[9,52] Notably, as a novel tobacco product, electronic cigarettes (e-cigs) are becoming increasingly popular worldwide, especially among younger users, and may potentially substitute combustible cigarettes in future.[53] The cardiopulmonary effects of e-cigs remains controversial, and current evidence does not indicate any statistical correlations between e-cig use and cardiovascular risk.[54] Another national survey-based study also declared that compared to the current users of combustible cigarettes, the current e-cig users may have a relatively lower stroke risk.[55] Therefore, additional studies are warranted to determine whether switching from cigarettes to e-cigs could reduce stroke risk.

This significant body of evidence supports the benefit in preventing smoking initiation among nonsmokers to reduce the risk of stroke. A higher likelihood of initiating traditional cigarette smoking has been observed among users of novel tobacco products, particularly those who first used e-cigarettes.[56] Therefore, using any substitute for cigarettes should be discouraged among nonsmokers to avoid subsequent smoking tendencies. Meanwhile, smoking cessation in former smokers can significantly reduce the incidence of stroke.[57] A longitudinal study demonstrated a reduction in stroke risk within 5 years of smoking cessation compared to continued smoking; however, a persistently elevated risk relative to never-smokers was observed for 1,015 years postcessation.[58] Moreover, it was also concluded that

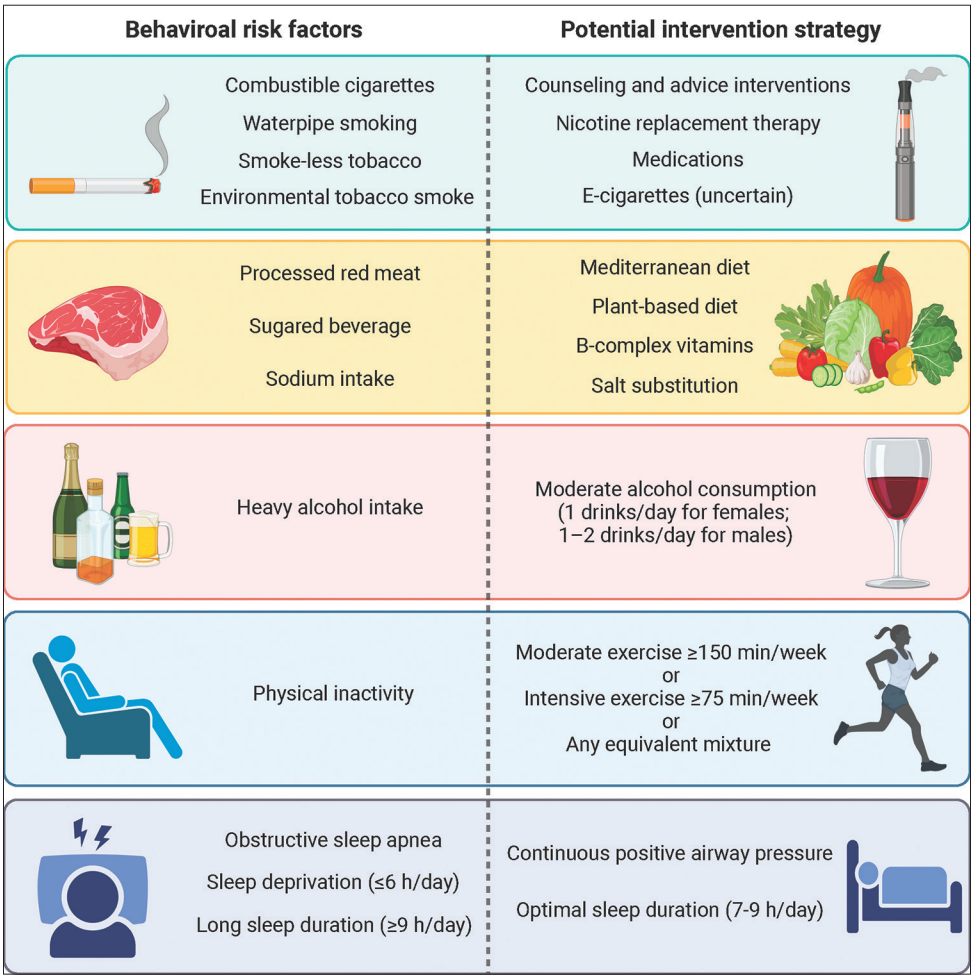

Figure 3: Behavioral risk factors of stroke and potential intervention strategies. The figure categorizes five key behavioral domains (tobacco use, dietary patterns, alcohol consumption, physical activity, and sleep health) with evidence-based prevention approaches. Color-coding distinguishes between: (1) tobacco-related risks (combustible products, smokeless tobacco, and secondhand smoke) and cessation strategies; (2) dietary modifications (Mediterranean/plant-based diets, salt substitution); (3) alcohol intake; (4) recommended exercise thresholds; and (5) sleep optimization interventions. All recommendations align with current stroke prevention guidelines.[9] This figure was created in BioRender. Ding, R. (2025) https://BioRender.com/4j3iga2

smoking cessation before the age of 65 years resulted in an 18% reduction in stroke risk.[59]

While no randomized trials directly examined how different cessation methods impact stroke risk specifically, RCTs show that various counseling intervention measures, from brief physician interactions to more extensive telephone or in-person support, are effective in helping people quit smoking.[60] The efficacy of smoking cessation interventions is enhanced when medication is used in conjunction with counseling. Substantial evidence indicated that medications including varenicline, bupropion, and nicotine replacement therapy (NRT) significantly improved smoking quit rates.[61,62] Varenicline appears to be the most effective single medication, outperforming bupropion and single-form NRT. However, combining different types of NRT may be more effective than using just one, and this combination therapy is comparable in effectiveness to varenicline.[63]

Recent research suggested that "opt-out" smoking cessation interventions, where all patients are automatically enrolled unless they decline, may be more effective than traditional "opt-in" approaches. An RCT found that the opt-out approach led to higher quit rates at 1 month, although this difference disappeared by 6 months. Nonetheless, engagement with cessation resources (medication and counseling) was significantly higher in the opt-out group.[64] These findings support guidelines recommending proactive intervention, such as offering varenicline, even for smokers not yet ready to quit.[65]

In addition, updated meta-analysis included 78 studies reported that nicotine-contained e-cigs demonstrated superior efficacy in smoking cessation compared to either nicotine-free e-cigs or NRT.[66] Moreover, another comprehensive RCT recruited 886 participants also demonstrated that the 1-year cessation rate (18%) in the e-cig use group was almost doubled versus the group

that received NRT (9.9%).[67] While e-cigs appear to help more people quit smoking for a year compared to nicotine replacement, most of those who quit smoking with e-cigs may convert to continued e-cig users. Since there is still a lack of long-term data on the health effects of e-cigs are limited, it remains unknown whether switching to e-cigs could alleviate stroke risk and prevent relapses to smoking or combined use over time.

Diet

Dietary patterns are closely linked to nutritional status and cardiovascular homeostasis. Since the diet directly affects the intake of nutrients including carbohydrates, salts, total fat, and cholesterol, it can modify metabolic risk factors such as diabetes, hypertension, hyperlipidemia, and obesity, which are associated with increased stroke risk as discussed above. Recent studies suggest that diet may have a substantial impact on stroke prevention.[68] In developed countries like the US, it was estimated that only 0.1% of the population adheres to a healthy diet. This trend was also observed in developing countries. For example, in China, there was a significant increase in the western dietary pattern, with a marked increase in meat consumption and a decline in the intake of fruits and vegetables.[69] The latest report from the GBD study also recorded that dietary risk factors, including elevated sodium intake and reduced consumption of fruits and vegetables, accounted for more than 15% of stroke mortality.[13] Furthermore, it was reported that the attributable burden from increased sugared beverage intake has risen by 23.4% in the past two decades.

A comprehensive meta-analysis including 16 epidemiological studies with over 160 million participants reported that the intake of processed red meat was strongly associated with stroke incidence.[70] Another meta-analysis included 123 reports also suggested that the consumption of vegetables, fruits, and fish was associated with a reduced stroke risk, whereas the intake of sugared beverage intake might increase stroke risk.[71]

The Mediterranean diet is an effective approach to reducing stroke risk. It generally includes whole grains, nuts, fresh fruits, and vegetables, with an emphasis on olive oil and a relatively restricted intake of animal products.[68] The Mediterranean diet, known for its cardiovascular health benefits, is part in Life's Essential 8 Advisory from the AHA.[72] A meta-analysis of 40 RCTs suggested that for participants at a high-risk of cardiovascular disease, a Mediterranean diet was significantly associated with a reduced incidence of stroke compared to minimal interventions (regular diet or minimal healthy diet advice).[73] Furthermore, a large RCT from Spain also indicated that a Mediterranean diet had a more pronounced protective effect against major cardiovascular events (including ischemic stroke) in patients with recorded coronary heart disease than a low-fat diet in a 7-year follow-up.[74]

Higher adherence to a plant-based diet was recently reported to reduce the incidence of stroke.[75,76] Two prospective cohorts in Taiwan found that a vegetarian diet could decrease stroke risk, and vitamin B_{12} intake may modify the association between plant-based diet and decreased stroke risk.[77] Conversely, another cohort study showed that plant-based diet index was not statistically associated with stroke risk.[78] Despite inconsistencies across studies focusing on vegetarian diet, a meta-analysis reported that supplementation with B-complex vitamins (a combination of dual-or more use of B_6, B_{10}, and B_{12}) could reduce stroke risk.[79]

The Dietary Approaches to Stop Hypertension (DASH) emphasizes fruits, vegetables, whole grains, and lean proteins, with low levels of sodium, saturated fat, and sugars to promote cardiovascular health.[80] Increased adherence to the DASH diet has been reported to reduce stroke risk, particularly in the prevention of ischemic stroke.[81,82]

Salt intake is another well-established risk factor for stroke incidence. Historically, humans consumed < 1 g of salt per day for millions of years, but this intake increased to > 10 g/day approximately 5,000–10,000 years ago, suggesting that the human body may not be evolutionarily adapt to high salt consumption. Increased salt intake is strongly associated with elevated BP due to impaired renal excretion, and it also increases arterial stiffness and left ventricular (LV) mass, independently of BP.[83]

In a large RCT involving participants over 60 years of age with hypertension or stroke history, using a salt substitute containing 25% NaCl and 75% KCl was associated with a reduced incidence of stroke compared to regular salt intake.[84] Similarly, another large RCT that included more than 20,000 participants with a mean follow-up of 4.7 years also suggested that salt substitution with reduced NaCl and excessive KCl resulted in a 14% reduction of stroke riskand also lowered healthcare costs compared to the nonintervention group.[85] No current evidence indicates that salt substitution can induce any severe cardiovascular events.[9] However, this strategy may not be suitable for countries added sodium in food processing, and potassium intake may increase the burden in patients with pre-existing renal disease.

Alcohol

High intake of alcohol is a traditional risk factor for stroke, accounting for 5.2% of the global stroke burden in 2021.[13] Alcohol consumption has a complex relationship with cardiovascular disease, and the effect of alcohol

on cardiovascular health varies with population characteristics. Light to moderate consumption of alcohol (1 drinks per day for females and 1–2 drinks per day for males) may have a cardioprotective effect, indicating a J-or U-shape associations between alcohol use and cardiovascular diseases.[86] Epidemiological evidence also suggests that light to moderate drinking may be associated with a reduced incidence of ischemic stroke.[87] However, recent findings indicate that the benefits from light to moderate drinking may be confounded by concurrent healthy lifestyle behaviors, as adjusting for these factors significantly weakens the association between moderate alcohol intake and cardiovascular protection.[88]

In contrast, habitual and heavy alcohol intake is consistently associated with an increased risk of stroke, even in populations aged < 50 years.[88-90] Recent studies also emphasize that heavy alcohol intake contributes significantly to hemorrhagic stroke incidents among young adults.[91,92] Methodological variability in defining heavy and moderate alcohol consumption across studies limits the comparability of their conclusions, highlighting the need for standardized alcohol intake thresholds linked to stroke risk.

A prospective study reported that reducing alcohol intake among heavy drinkers (3 drinks per day for females and 4 drinks per day for males) could significantly reduce major cardiovascular events, especially beneficial in preventing ischemic stroke.[93] These findings indicate that while the potential benefit of light alcohol consumption on stroke risk remains uncertain, population-wide reduction in alcohol intake should be prioritized as a primary stroke prevention strategy.

Physical activity

Exercise improves cardiovascular health through shear stress, which stimulates endothelial cells to release molecules promoting vasodilation and nitric oxide production. In addition, exercise mobilizes endothelial progenitor cells, contributing to the repair of damaged vessel linings and promoting blood vessel growth.[94] The intensity of physical activity can be expressed in metabolic equivalent of task (MET) units.[95] Moderate-intensity activities have MET values ranging from 3 to 5.9, while vigorous-intensity exercises have MET values of 6 or higher. Long-term vigorous activities for 150–300 min per week and moderate exercises for 300–600 min per week are consistently associated with reduced mortality.[96]

Increased physical activity consistently contributes to stroke prevention and is not impacted by hypertension.[97] A comprehensive meta-analysis suggested that even exercise for 1–150 min per week in leisure time can significantly lower the risk of stroke. Interestingly, a more pronounced effect was observed for physical activity < 150 min per week compared to higher levels of exercise.[98] This evidence suggests that even relatively low-strength exercise is better than none.

According to the latest scientific guidelines for stroke prevention, adults are encouraged to engage in at least 150 min of moderate-intensity exercise, 75 min of vigorous-intensity exercise, or any equivalent combination of both modalities per week.[9] Moreover, exercise patterns and sexual differences may affect the role of physical activity in stroke prevention. For instance, recent evidence suggests that morning physical activity is associated with a lower stroke incidence, regardless of total activity levels.[99] Additionally, intermittent vigorous exercise may exhibit a more substantial effect against stroke among females than in males.[100]

In contrast, low physical activity is a well-established risk factor for stroke related mortality and DALYs, accounting for 2.1% of the total stroke burden in 2021.[13] Emerging evidence suggests that sedentary behavior may represent a growing risk factor for stroke, particularly among young adults.[101-103] Future studies should further validate whether physical activity can counteract the impact of sedentary behavior on stroke risk, either through independent effect or interactive relationships. Developing public health and clinical intervention strategies to simultaneously reduce sedentary time and increase physical activity time remains essential.

Sleep

Sleep is a central physiological process that maintains cardiovascular homeostasis. Disruptions to the sleep cycle or sleep curtailment from any cause, including obstructive sleep apnea (OSA), insomnia, and hypersomnia, may compromise cardiovascular recovery and health.[104] A large prospective cohort study revealed that unhealthy sleep patterns are associated with increased incidence of stroke.[105] OSA, which is characterized by recurrent breathing pauses or shallow breaths during sleep due to upper airway obstruction, has been widely linked to an increased risk of stroke.[106]

A comprehensive meta-analysis indicated that both sleep deprivation (≤ 6 h/day) and prolonged sleep duration (≥ 9 h/day) were associated with an increased risk of stroke and cardiometabolic diseases. Both observational and Mendelian randomization studies suggested a link between insomnia and stroke.[107] This evidence supports the notion that nonapnea sleep disorders might increase stroke risk by disturbing circadian rhythm and could also impair the neuroplasticity during stroke recovery.[108]

Continuous positive airway pressure (CPAP) therapy has been observed in observational studies to reduce stroke risk among OSA patients. A meta-analysis of 13 studies (9 RCTs, 4 cohort studies) showed CPAP therapy might reduce stroke risk in patients with OSA, particularly those with good adherence and moderate-to-severe OSA.[109] However, this benefit was not consistently demonstrated across all RCTs. However, not all RCTs have consistently demonstrated this benefit. Therefore, more RCTs are needed to clarify the role of CPAP in stroke prevention. The AHA recommends 7–9 h of sleep per day as beneficial for cardiovascular health,[9] although no RCTs have specifically evaluated the effects of sleep duration on stroke incidence or mortality.

Environmental Risk Factors

Air pollution

Air pollution has been widely regarded as a persistent risk factor that increases the incidence and mortality of cardiovascular disease. Air pollutants are the mixtures of particulate matter, gaseous pollutants (SO_2, CO, NO_X, O_3, etc.), organic compounds (polycyclic aromatic hydrocarbons, persistent organic pollutants), and metals. These can originate from both artificial and natural sources.[110] Among them, particulate matter with aerodynamic diameters < 2.5 μm ($PM_{2.5}$) is the most well-known contributor to cardiorespiratory diseases. These can deposit in the pulmonary alveoli and may even penetrate the air-blood barrier to enter the circulation.[111]

Recent studies have reported the presence of airborne magnetic particles in human brain samples and cerebrospinal fluid, suggesting that these nanoparticles with particle sizes smaller than 200 nm might directly enter the brain through the olfactory bulb or be translocated through the lung to the brain.[112,113] $PM_{2.5}$ may contribute to cerebrovascular disease by increasing permeability of the blood-brain barrier, triggering systemic inflammation, imposing thrombosis and atherosclerosis in the cardiovascular system, and elevating BP by disturbing the autonomic nervous system [Figure 4].[114]

Substantial evidence confirms the association between air pollution and stroke, especially highlighting the casual relationship between $PM_{2.5}$ exposure and stroke incidence.[114] In a meta-analysis that included 94 articles with over 6.2 million events, it was reported that short-term exposure to multiple air pollutants,

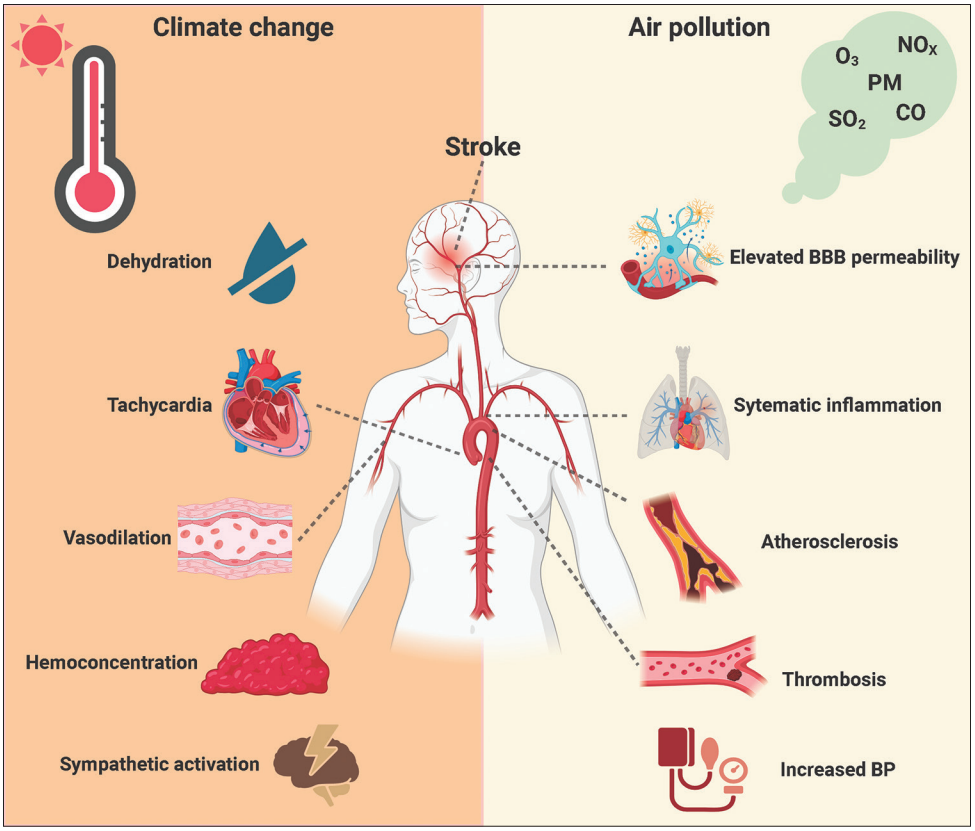

Figure 4: Potential mechanisms for air pollution and climate change-induced stroke. Left: Climate change effects (dehydration, tachycardia, and hemoconcentration) may contribute to stroke incidence through sympathetic activation and hemodynamic changes. Right: Air pollution components (PM, NO_x, O_3, SO_2, CO, etc.) may trigger stroke onset by inducing blood-brain barrier disruption, systemic inflammation, and atherosclerosis. BBB: Blood-brain barrier, BP: Blood pressure. This figure was created in BioRender. Ding, R. (2025) https://BioRender.com/r0t838o

including $PM_{2.5}$, PM_{10}, CO, NO_2, and SO_2 had a weak but statistically significant association with stroke hospital admissions and mortality.[115] Another meta-analysis suggested long-term exposure to $PM_{2.5}$ and PM_{10} was consistently associated with increased stroke incidence and mortality.[116]

More importantly, pooled-analysis from the ELAPSE study, which included over 32,000 participants from developed countries in Europe also suggested that even relatively lower exposure to $PM_{2.5}$ (< 25 μg/m^3) was linked to increased stroke mortality.[117] An additional analysis of the same project showed that $PM_{2.5}$ (< 25 μg/m^3) was also associated with increased stroke incidence. Interestingly, the study found that a more restricted exposure load (< 15 μg/m^3, lower than the WHO Air Quality Guideline [AQG] level 3 interim limit),[118] showed an even stronger association.[119]

The exposure-response curve of particulate matter and stroke mortality does not show a clear threshold, and the curve appears steeper at lower concentrations of $PM_{2.5}$.[120] This finding underscores the importance of continuous efforts to reduced air pollution, even in regions where air quality has improved over recent decades.

The GBD study demonstrated that both ambient $PM_{2.5}$ and indoor $PM_{2.5}$ pollution are the established risk factors for stroke, accounting for 16.6% and 11.2% of the total burden, respectively.[13] Ambient $PM_{2.5}$ pollution ranked first among all environmental risk factors. However, no RCTs have directly assessed the effects of reducing air pollution on stroke risk. The WHO AQG guideline has tightened the annual limit for $PM_{2.5}$ from 15 μg/m^3 to 5 μg/m^3, indicating an ambitious orientation to constantly improve the global air quality in future. Nevertheless, such a goal requires more stringent energy conservation and emission reduction policies as well as global energy structure transformation, which cannot be accomplished immediately.

Currently, it is estimated that more than 94% of the world's population still lives in areas with $PM_{2.5}$ concentrations exceeding the WHO annual limitation, and more than 80% of those people live in countries with low- and middle-income status.[121] Therefore, for older adults or those with preexisting complications that are more susceptible to the incidence of stroke, the most practical approach may involve reducing outdoor activities in polluted weather.

Notably, pioneering RCTs conducted by Kan *et al*. reported that the application of high-efficacy air purifiers significantly reduced BP, circulating inflammatory and thrombotic biomarkers, and stress hormones in healthy young adults, implicating potential benefits in reducing indoor air pollution to prevent cardiovascular disease.[122,123] In addition, in cases where outdoor activities are necessary, N95 and N99 masks have demonstrated protective effects against air pollution, while their potential cardiovascular benefits require further confirmation.[114] For patients with chronic respiratory or cardiovascular conditions, prolonged mask use or wearing a mask in high temperature environments may exacerbate existing symptoms, so caution is advised.[114,124]

Climate change and extreme weather events

Global climate change is primarily driven by increasing atmospheric concentrations of greenhouse gases (GHGs), largely due to anthropogenic activities such as fossil fuel combustion, deforestation, and industrial processes. This enhanced GHG effect traps more outgoing longwave radiation, leading to a warming planet and cascading consequences including rising sea levels, more frequent and intense extreme weather events, altered precipitation patterns, and disruptions to ecosystems and biodiversity.[125] The most direct and detrimental effects of climate change are increased ambient temperature and the occurrence of heat waves. The *Lancet Countdown* declared that record-breaking global temperatures were witnessed in 2023, exceeding those of the past 100,000 years. This extreme heat significantly increased the number of heatwave days impacting vulnerable populations (e.g., the elderly and infants). Climate change attribution studies have shown that human activity has more than doubled the likelihood of these dangerous heat events, leading to a substantial rise in heat-related deaths among the elderly.[126]

Modeling studies have indicated the long-term impacts of air pollution on cardiovascular and stroke mortality. Modeling conducted by Mazidi *et al*. has suggested that increased ambient temperature is associated with substantial increases in cardiovascular deaths by 2099, ranging from 8,844 to 25,486 annually, and stroke deaths increasing by 2,063 to 13,039 annually in the U.S., exceeding increases expected from population growth alone.[127] Another modeling study estimated that although temperature-related years of life lost for stroke may decrease from 0.85% to 1.02% in 2050–2070, heat-related deaths were projected to increase dramatically in summer months, exceeding 157% by the 2050s and 296% by the 2070s.[128] Compared to the 1980s, Li *et al*. projected a 100% increase in heat-related stroke mortality in the 2080s in Beijing, China, while no significant changes were observed for mortality from temperature-related hemorrhagic stroke.[129] Moreover, Zhou *et al*. predicted that without mitigation efforts, heat-related stroke mortality would increase by 9.2% in 22 Asian cities by the 2090s, while effective air pollution control could limit this increase to 2.4%.[130]

Two comprehensive reviews suggested a nonlinear association between ambient temperature and stroke risk, with increased risk at both extremes of heat and cold. A 1°C increase in temperature was associated with a 1%–2% increase in ischemic stroke risk.[131] Hot temperatures had a more immediate effect on ischemic stroke, while cold temperatures were associated with a longer lag effect and higher intracerebral hemorrhage risk.[131,132] High temperatures may increase stroke risk through dehydration, electrolyte imbalances, vasodilation, hemoconcentration, and potentially increased cardiac arrhythmias.[133] Cold temperatures may increase risk via vasoconstriction, blood flow disturbance, sympathetic activation, and hemoconcentration.[131] However, the exact mechanisms of temperature-related stroke remain ambiguous. Prevention strategies for extreme temperature-related stroke are crucial for the elderly population and residents in extreme weather prone areas (tropical areas and cold regions).[134] Older adults are particularly susceptible to temperature extremes due to impaired thermoregulation and insufficient awareness of heat stroke symptoms.[135]

Wildfires and severe weather can further exacerbate their risks by disrupting healthcare access and limiting their ability to escape dangerous situations. For heatwaves, early warning systems, increased access to air conditioning and cooling centers, and urban planning modifications (e.g., increased reflectivity and tree canopy) are crucial to reducing correlated cardiovascular risk. Strategies against cold weather include individual actions (e.g., exercise and appropriate clothing), home modifications (e.g., weatherization and heating), and community initiatives (e.g., warming centers).[131] However, there is a lack of well-designed RCTs to assess the actual impact of these preventive measures on stroke risk.

Secondary Prevention

Secondary prevention focuses on reducing the recurrence of acute stroke events in patients with previous cerebrovascular conditions or other high-risk cardiovascular multimorbidity. Although most patients survive the first occurrence of stroke or TIA, they are at a higher risk of experiencing a secondary stroke.[136] Understanding the etiology and existing vascular risk factors in this high-risk population can provide targeted and effective strategies to lower stroke recurrence rates and improve quality of life.[137] Globally, ischemic stroke accounts for 65% of the total stroke incidence, while hemorrhagic stroke accounts for 29% as of 2021.[13] As it constitutes most cases, most established secondary prevention measures focus on ischemic stroke.

Over the last six decades, the recurrence rate of ischemic stroke has declined steadily due to anticoagulant, antiplatelet, and antihypertensive treatment.[138] These strategies are thoroughly discussed in several comprehensive reviews, and as we mentioned in previous sections, effective control of canonical risk factors such as blood pressure, hyperlipidemia, diabetes, and smoking has also been critical for long-term secondary prevention.[139-141] Therefore, we briefly summarize the essential progress about anti-thrombotic treatment in this section.

Anticoagulant therapy

According to the TOAST classification, cardioembolic events caused by AF, myocardial infarction (MI), LV thrombus, and other cardiomyopathy account for the majority (27%) of ischemic stroke incidence, followed by atherosclerosis in large arteries (13%).[139] Among them, AF accounts for 10%–12% of total ischemic strokes.[142] As the most well-documented condition to cause stroke, monotherapy with aspirin is not effective for preventing stroke in AF patients, and dual-antiplatelet treatment with aspirin and clopidogrel has shown limited efficacy.[139]

Oral anticoagulation (OAC) treatment represents a milestone in preventing stroke among patients with AF, significantly reducing the thromboembolic stroke incidence and all-cause mortality.[143] Treatment options mainly include vitamin K antagonists (VKAs) such as warfarin and non-VKA OACs (NOACs, or direct OACs) including dabigatran, rivaroxaban, and apixaban. Maintaining therapeutic anticoagulation levels (time in therapeutic range [TTR] > 70% for VKAs and label-adherent dosing [LAD] for NOACs) and managing bleeding risk factors are essential for successful embolism-related stroke prevention. As for VKAs, TTR is negatively correlated with the occurrence of bleeding and thromboembolic events.[144] For NOACs, LAD has been associated with better outcomes in OAC treatment, while off-dosage use is linked to a higher risk of ischemic stroke but not hemorrhage.[145,146]

Prospective studies have shown that compared to VKAs, NOACs offer superior effects in reducing the risk of ischemic stroke and systemic embolism, with a lower risk of major bleeding or other adverse effects.[147-149] For older patients with AF who are especially susceptible to stroke, a meta-analysis suggested that compared to VKAs, NOACs demonstrated greater efficacy in reducing stroke and embolic events, without increasing the risk of major bleeding.[150]

Current guidelines recommend initiating anticoagulation within 14 days poststroke in AF patients, yet the optimal timing for balancing embolic recurrence and hemorrhage risks remains uncertain.[151] The START RCT primarily indicated that starting

direct OAC therapy earlier within the first 2 weeks poststroke resulted in better outcomes than delaying initiation. While this study did not identify a definitive optimal day for OAC initiation, it provides valuable guidance for clinical decision-making regarding OAC therapies.[152] Despite advancements in NOACs, optimal stroke prevention strategies for high-risk AF patients remain in the area of ongoing research, particularly regarding individualized treatment choices and managing the balance between stroke and bleeding risks in patients with multiple comorbidities such as extreme age, kidney failure, a history of brain bleeds, and recent gastrointestinal bleeding.[153] Further research, especially RCTs, is needed to guide decision-making in these complex cases.

Antiplatelet therapy

As we mentioned above, atherosclerosis in large arteries is a significant cause of ischemic stroke, posing a high risk of stroke recurrence, similar to carotid artery disease.[154] Secondary prevention strategies for patients with atherosclerosis mainly include stabilizing plaques and restoring blood flow.[137] Both surgical intervention and medications are effective in this process. Studies have shown that carotid endarterectomy (CEA) plus medical therapy is more effective than medical therapy alone for preventing recurrent stroke in patients with severe carotid stenosis, especially when performed within 2 weeks of a recent stroke.[155,156]

While CEA remains the preferred method for older patients with favorable anatomy, carotid artery stenting (CAS) is a less invasive alternative with comparable outcomes and stroke risk for younger patients with moderate carotid stenosis and low perioperative risk.[137,157] For strokes caused by large artery occlusion or small vessel disease, antiplatelet drugs (either single or dual therapy) are usually the preferred treatment. However, anticoagulants are recommended if the stroke is due to low blood flow or a tendency for blood clots.[139]

Antiplatelet medications, on average, reduce the yearly risk of vascular events by 2%, but this benefit is accompanied by a slightly increased risk of serious bleeding outside the skull (0.1% to 0.3%).[158,159] The use of antiplatelet medications like aspirin has not been well-established for primary stroke prevention. For patients with diabetes and other common vascular risk factors, aspirin treatment has not been associated with a reduced stroke risk.[160,161] Similarly, aspirin is ineffective at preventing a first stroke in aging populations (≥ 70 years old) or patients with chronic kidney disease.[162,163] Although most RCTs report limited overall benefits of aspirin for primary prevention, future studies are still required to explore its potential in high-risk subgroups (e.g., those with subclinical vascular abnormalities or high lipoprotein (a) levels) and evaluate differential effects across racial/ethnic populations with elevated cardiovascular risks.[9]

Although posterior circulation-related stroke has generally been considered to carry a lower risk of recurrence than anterior circulation, recent studies suggest that it may also present a high-risk of recurrence in the first few weeks.[154,164] There is no significant difference in secondary prevention strategies of anterior and posterior circulation disease stroke.[165] For noncardioembolic patients with high stroke risk, mono-antiplatelet therapy with either aspirin or clopidogrel is commonly used for long-term secondary prevention.

Aspirin remains the most affordable and widely used medication for preventing a second stroke, and the FDA recommends daily doses ranging from 50 to 325 mg for this purpose.[156] While clopidogrel has not demonstrated superiority over aspirin alone for preventing strokes, it appears more effective in preventing serious circulatory problems overall.[166]

Recent pooled analyses of RCTs indicated that compared to single-use aspirin, dual therapy with aspirin and clopidogrel immediately after a noncardioembolic stroke was more effective in reducing the recurrence rate.[167] A recent multi-center RCT conducted in 222 hospitals in China included patients with moderate stroke or TIA attributed to atherosclerotic diseases. The results showed that, compared to aspirin monotherapy, dual treatment with aspirin and clopidogrel within 72 h after a minor stroke or TIA significantly reduced the risk of recurrence within 90 days.[168] Therefore, for patients with a minor stroke or TIA that carries a high risk of recurrence, guidelines recommend using two antiplatelet drugs (aspirin plus either clopidogrel or ticagrelor) in the first 3 weeks and then switch to clopidogrel alone.[167,169]

However, for stroke from small-vessel disease, which is more often associated with microbleeds, secondary prevention with dual antiplatelet therapy may not reduce the recurrence rate and could increase mortality risk.[170] In these cases, anticoagulant strategy is also discouraged due to elevated bleeding risks, while cilostazol has emerged as a promising alternative.[171,172] Cilostazol is particularly suitable for small-vessel disease as it not only acts as an antiplatelet agent but also improves endothelial function.[173] Studies have demonstrated that cilostazol offers comparable efficacy to aspirin in preventing stroke in patients with high bleeding risk, providing enhanced long-term benefits and superior performance, especially in small-vessel disease.[174-176]

Interactions of Risk Factors

We have discussed the most established risk factors in the three main areas, while the occurrence of stroke may result from complex interplays between multiple adverse conditions. Metabolic risk factors such as high BP, blood sugar, and blood lipids have a more direct effect on stroke etiology, while behavioral and environmental factors may enhance stroke risk by modifying metabolic conditions. High BP is considered the most essential player in stroke etiology and can exacerbate the adverse effects of other metabolic disorders. Hypertension itself may have a much stronger impact on cardiovascular health than other coexisting conditions, as a critical RCT reported that reducing SBP to < 120 mmHg significantly reduced stroke risk compared to a target of 140 mmHg, and such effects were not influenced by diabetes status or stroke history.[177]

Hypertension is generally considered to drive the association between prediabetes and cardiovascular events.[178,179] However, a recent prospective study found that prediabetes was associated with ischemic stroke in participants without hypertension but not in hypertensive patients, suggesting that although other metabolic conditions contribute to stroke risk in nonhypertensive populations, such effects may not be significant among those with hypertension.[180] In addition, hyperlipidemia and hyperuricemia have both been reported to have synergetic effects with hypertension on the risk of ischemic stroke, which may be attributed to similar mechanisms they share in promoting atherosclerosis.[181,182]

Diabetes and obesity frequently coexist, while their separate contributions remain a topic of debate. Although overweight or obesity has been associated with increased carotid intima-media thickness and arterial stiffness in nondiabetes populations, this association is diminished in patients with diabetes.[183] A large multi-center RCT reported that intensive modification of lifestyle in patients with diabetes resulted in moderate weight loss and a significant decline in glycated hemoglobin, but no specific benefits were recorded for the improvement of cardiovascular outcomes.[184]

Although the interactions remain controversial, as we mentioned above, treatment with GLP-1RAs has been shown to reduce stroke risk in patients with either diabetes or obesity. Elevated plasma triglyceride and glucose levels are both causally linked to cardiovascular events,[185] and cumulative evidence suggests that the triglyceride-glucose (TyG) index may be an emerging predictor of stroke risk and prognosis.[186] The TyG index provides a readily available and easily calculated estimate of insulin resistance, combining both fasting triglycerides and glucose levels.

Comprehensive meta-analyses have concluded that the TyG index is positively correlated with the incidence and recurrence of ischemic stroke.[186,187] However, the clinical utility of the TyG index for predicting insulin resistance remains debated, with concerns regarding its sensitivity to hyperglycemia and hyperlipidemia, limited longitudinal data, and uncertain predictive value in younger populations.[188] Interestingly, as insulin resistance is prevalent in populations with overweight or obesity, it was recently reported that TyG mediated more than 50% of BMI-associated stroke risk in a middle-aged and elderly population in China.[189]

Behavioral risk factors may contribute to stroke risk by modifying metabolic disorders. Smoking has demonstrated a combined effect with hypertension, exceeding their individual effects on stroke risk, with the joint effects being more profound among women with ischemic stroke.[190] Although hypertension contributes more to stroke risk than other risk factors, lifestyle modifications (including BMI, smoking, diet patterns, and physical activity) can significantly reduce stroke risk in patients with hypertension.[191]

Smoking and diabetes may synergistically induce systemic oxidative stress, chronic inflammation, and reduced cerebral blood flow, cooperatively contributing to stroke development. A large cross-sectional study in China reported that smoking could exacerbate stroke risk in patients with diabetes, indicating the importance of smoking cessation to prevent stroke in those high-risk patients.[192] Additionally, smoking can negate the protective effects of a healthy diet on stroke risk and worsen the impact of low socioeconomic status.[190,193]

Environmental risk factors also contribute to stroke incidence and mortality by inducing metabolic dysfunction. Patients with existing metabolic conditions or cardiovascular complications may be particularly vulnerable to cardiometabolic effects from environmental exposure. Air pollution is consistently associated with elevated BP, arterial stiffness, and increased hypertension hospitalizations.[194-196] Although a recent study suggested that NO_2 exposure led to an elevated re-admission rate of heart failure in patients with hypertension,[197] the interactions between air pollution and major risk factors of stroke remain unclear. Furthermore, air pollution has also been linked to the development of dysfunction, including insulin resistance, type 2 diabetes, and obesity.[198-200] Moreover, increasing evidence also suggests that extreme weather conditions are associated with diabetes and other metabolic disorders, while patients with diabetes may be particularly vulnerable to

adverse effects arising from climate change.[201] However, there is still limited evidence elucidating the joint effects between environmental threats and other risk factors.

Future studies are needed to examine whether environmental exposure can increase stroke risk in patients with existing metabolic disorders. In summary, as reported by the GBD study, metabolic conditions account for the majority of stroke burdens and thus should be targeted with the highest priority in stroke prevention.[13] The impact of environmental factors on individuals is long-lasting and often difficult to control through short-term, individual-level interventions. However, for individuals already experiencing major metabolic risk factors, targeted reduction in exposure to adverse environmental risk factors remains important in preventing acute stroke onset.

Prospective and Perspectives

Considerable strides have been made in preventing stroke over recent decades, particularly in the management of metabolic risk factors. Robust evidence from RCTs has shown that effective control of conditions such as hypertension and diabetes can significantly reduce stroke incidence and mortality. These advancements underscore the importance of evidence-based strategies for primary and secondary stroke prevention.

However, addressing behavioral and environmental risk factors remains challenging. Many of the intervention strategies targeting these areas lack validation through comprehensive RCTs, leaving uncertainties about their precise roles in stroke prevention. Furthermore, the implementation and efficacy of these strategies are often shaped by geographical, cultural, and economic factors, complicating their adoption and scalability in diverse populations. In addition, the complex interplay of certain risk factors, such as alcohol consumption, lipid profiles, and the increasing use of novel tobacco products, has not been fully understood. Environmental risks, including air pollution and climate change, also require further investigation to establish effective protective approaches.

Taken together, future research should prioritize comprehensive prospective studies and large-scale RCTs to evaluate the effectiveness of interventions targeting behavioral and environmental factors. Efforts should also aim to modify strategies to address socio-economic and cultural variations, ensuring equitable and effective implementation. More importantly, future studies should clarify the relative importance and interactions of various risk factors to inform the development of targeted and comprehensive preventive strategies for populations with differing metabolic profiles.

Addressing these gaps will support the development of stronger population-level interventions and advance global efforts to reduce the burden of stroke.

Author contributions

Ruiyang Ding: Formal analysis, investigation, visualization, writing-original draft. Omar Elmadhoun: Writing-review and editing. Rui Chen: Writing-review and editing. Xunming Ji: Conceptualization, project administration, supervision, resources, writing-review and editing.

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Not applicable.

Data availability statement

Data sharing is not applicable to this article as no datasets were generated and/or analyzed during the current study.

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Conflicts of interest

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