

# Prevention Program for People Living with Stroke in Low and Middle-Income Country: A Systematic Review

Aisyah Lahdji<sup>1</sup>, Dwi Pudjonarko<sup>2</sup>, Zahroh Shaluhiah<sup>3</sup>

<sup>1</sup>Doctoral Study Program of Medical and Health Science, Faculty of Medicine, Universitas Diponegoro

<sup>2</sup>Department of Neurology, Faculty of Medicine, Universitas Diponegoro

<sup>3</sup>Department of Health Promotion, Faculty of Public Health, Universitas Diponegoro

## ABSTRACT

**Background:** Non-communicable diseases (NCDs) are the primary factors responsible for mortality and impairment on a global scale. By 2030, it is estimated that non-communicable diseases will comprise 80% of the global population. According to the World Health Organization (WHO), the risk of stroke will grow by 50% for the entire global population by 2022. Currently, it is projected that 1 in 4 individuals will suffer from a stroke

**Method:** This review was reported using the "Preferred Reporting Items for Systematic Reviews and Meta-Analysis" guideline and written using the "Synthesis without Meta-Analysis" method. The included studies for this review followed several criteria, including randomized controlled trials (RCT), English and Bahasa articles, using population was people living with stroke, intervention was any prevention and disability limitation, and outcomes were prevention measurements (primary, secondary, and tertiary prevention).

**Results:** The study yielded multiple efficacious and streamlined preventive interventions implemented for stroke patients. Emphasizing risk factors as the main strategy for preventing health issues, using pharmacological treatments such as polypill, aspirin, and vitamins as a supplementary measure under the guidance of medical physicians and cardiologists. In addition, tertiary preventive initiatives encompass more than just administering drug treatment; they also require adherence to pharmaceutical protocols.

## Correspondence

lahdjiaa@unimus.ac.id

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## INTRODUCTION

Non-communicable diseases (NCDs) are the primary factors responsible for mortality and impairment on a global scale. By 2030, it is estimated that non-communicable diseases will comprise 80% of the global population.<sup>1</sup> There is a direct correlation between the incidence of non-communicable diseases and the number of individuals affected by strokes. According to the World Health Organization (WHO), the risk of stroke will grow by 50% for the entire global population by 2022. Currently, it is projected that 1 in 4 individuals will suffer from a stroke.<sup>2</sup>

In 2018, the incidence rate of stroke in Indonesia was 10.9 cases per 1000 individuals. East Kalimantan Province had the highest prevalence rate of 14.7 per 1000 population, while Papua Province had the lowest rate of 4.1 per 1000 population. The frequency in Central Java Province was 11.8 per 1000 population, indicating a relatively high rate.<sup>3</sup> Individuals of all age groups are susceptible to stroke. The occurrence of stroke among

individuals aged 20-24 years was 2.4 per 100,000 individuals, but among those aged 45-49 years, it was 32.9 per 100,000 individuals. Additionally, a separate study reported that among a total of 77 samples, 13.2% fell between the age range of 21-45 years (7-9 individuals), with 88% experiencing non-hemorrhagic stroke and 12% experiencing hemorrhagic stroke.<sup>4</sup>

Recurrent stroke is a common consequence of stroke. A study conducted in Sweden indicates that between 23% and 30% of those who have had a stroke will suffer from a subsequent stroke.<sup>5</sup> In 2019, a study conducted in China revealed that the occurrence rate of recurrent stroke was 12%. The proportion of recurrent stroke episodes in the first three years showed an increase of 11.51%, 16.76%, and 20.07% respectively.<sup>6</sup> The rate of recurring stroke ranged from 1.15% to 15% within the first month, 7% to 20.6% within the first year, 16.2% to 35.3% within 5 years, and 14% to 50% within 10 years.<sup>7</sup> In 8 Asian countries, the occurrence of repeated stroke was 25%, while in Norway it ranged from 5.4% to

11.3%. The proportion of repeated strokes that were non-hemorrhagic was 90%.<sup>8</sup> A study conducted in Korea likewise demonstrated a recurrence incidence of 64% for non-hemorrhagic strokes.<sup>9</sup> In Indonesia, the occurrence rate of repeated stroke is 62%, with 46.8% of these cases being recurrent non-hemorrhagic strokes. According to multiple studies, the occurrence of recurring stroke is significantly elevated, with rates ranging from 25% to 60%.<sup>11</sup>

The elevated prevalence of stroke necessitates a focus on optimizing preventive measures. Adopting preventative measures such as lifestyle modifications might effectively reduce the occurrence of stroke cases.<sup>11</sup> Engaging in physical exercise, maintaining a regulated diet, refraining from smoking, and abstaining from alcohol consumption are proactive measures that can be optimized for prevention.

Prevention approaches implemented in low and middle-income countries are not yet at their peak effectiveness. The fluctuation is evident in the annual number of instances. The purpose of this study was to assess the optimization, efficacy, and efficiency of stroke prevention interventions in people living with stroke and in low and middle-income countries.

## **METHOD**

### **Study Design**

A systematic review was conducted of randomized controlled trials (RCTs) comparing prevention program implementation with usual care interventions. This systematic review was reported by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis).

A comprehensive search was conducted to find relevant English and Bahasa articles from electronic databases published between 2013 to 2023. Electronic databases including PubMed, Emerald, Scopus, and ScienceDirect. Literature searches were carried out to identify studies investigating the effect of prevention programs in low and middle-income countries that focused on decreasing the number of people living with stroke. An initial search was performed based on the PICO (participants, comparison, intervention, and outcomes) framework and key terms. The following key terms were used "Prevention", "Stroke", and "Low and Middle Country".

For inclusion and exclusion criteria in this study, the inclusion criteria were RCTs including prevention programs for people living with stroke. Studies were

included if they were non-RCTs, and did not have intervention, or prevention programs for people living with stroke in low and middle countries.

The authors independently conducted a screening process for study selection. In the first stage, reviewers independently extracted information from potentially relevant titles and abstracts. The screened studies were then included in the second stage for a full-text review. Again, independently, the authors read and evaluated the full-text articles based on predefined exclusion and inclusion criteria. Finally, the authors compared the results, and any differences were resolved by reaching a consensus.

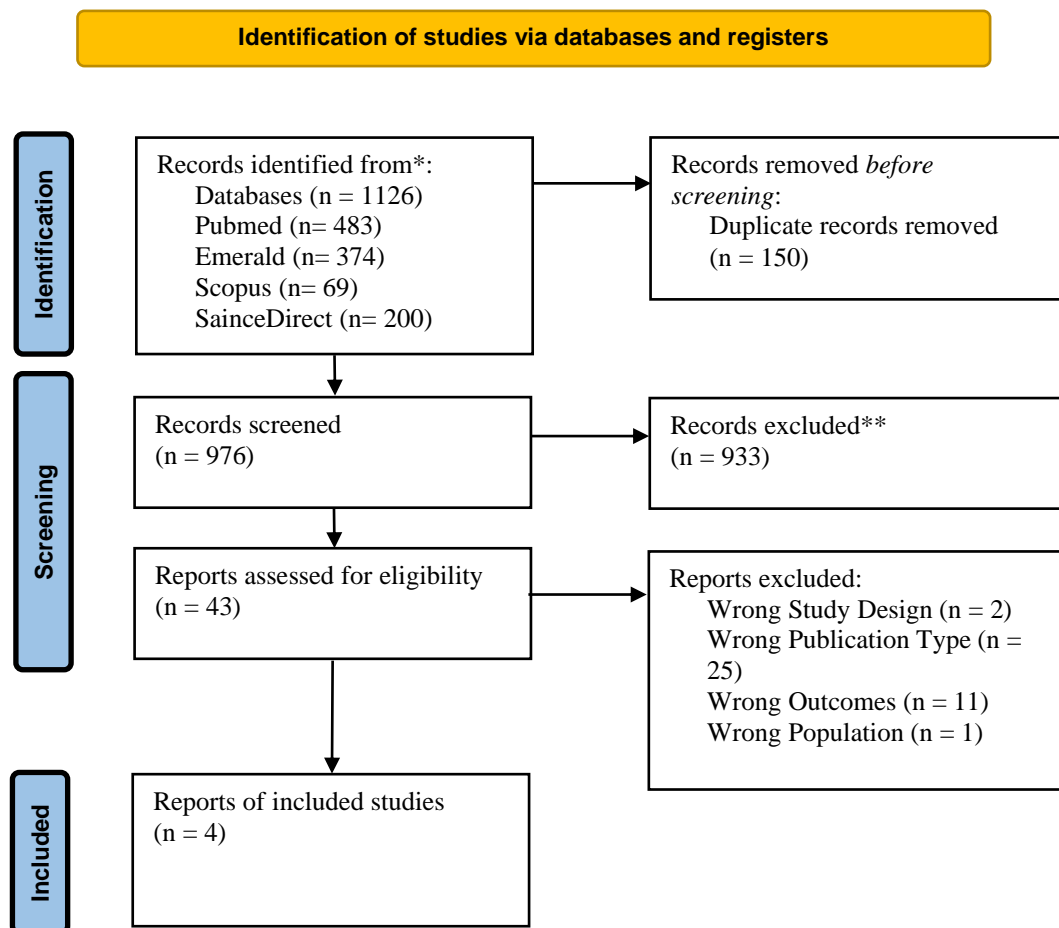
For extraction data, the authors independently extracted data from the included articles into a structured table. The extracted data consisted of the first author, year of publication, study design, population, intervention, primary outcomes, and secondary outcomes. Additionally, information was recorded on the intervention characteristics, including the type of prevention program for people living with stroke, and the duration of the program.

Because of random sequence generation, all studies had a low risk of selection bias. In this review, assessing the risk of bias using CASP (Critical Appraisal Skills Programme) Randomized Controlled Trial Tools. The total of questions is eleven with the detail i.e. "Q1) Did the study address a focused research question? Q2) Was the assignment of participants to the intervention randomized?, Q3) Were all participants who entered the study accounted for at its conclusion?, Q4) Were the participants "blind" to the intervention they were given? Were the investigators "blind" to the intervention they were given to participants? Were the people assessing/analyzing outcomes "blinded"?, Q5) Were the study groups similar at the start of the randomized controlled trial? Q6) Apart from the experimental intervention, did each study group receive the same level of care (that is, were they treated equally)?, Q7) Were the effects of intervention reported comprehensively?, Q8) Was the precision of the estimate of the intervention or treatment effect reported?, Q9) Do the benefits of the experimental intervention outweigh the harms and costs?, Q10) Can the results be applied to your local population/ In your context?, Q11) Would the experimental intervention provide greater value to the people in your care than any of the existing interventions?" (see Table 1).

**Table 1.** CASP tools for assessing the risk of bias for randomized controlled trial

Authors	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Roshandel <i>et al.</i> ,	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Shi <i>at al.</i> ,	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Pagidipati <i>et al.</i> ,	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Bosch <i>et al.</i> ,	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Y= Yes, N= No, and C= Can't tell



**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analysis Flowchart

**RESULTS AND DISCUSSION**

In total 1,126 published articles were collected from online databases, including PubMed, ScienceDirect, Emerald, and Scopus. All articles were published between 2013 to 2023. After deleting duplicates, 976 articles are obtained. After reviewing the abstract, 933 were excluded because of irrelevant studies. 43 articles are reported assessed for eligibility, 2 articles inappropriate study

design, 25 articles inappropriate publication type, 11 articles inappropriate outcome, and 1 article inappropriate population. The final articles in this study were four articles. Table 2 summarizes each article included in a systematic assessment of preventative programs for people living with stroke in low and middle-income countries.

**Table 2.** Summary of included studies

Author(s)	Year	Study design	Population	Intervention	Primary outcome	Secondary outcome
Roshandel <i>et al.</i> ,	2019	Randomize Controlled Trial	A total of 50.045 participants aged 40 – 75 years old were diagnosed with stroke during pregnancy and not during pregnancy	<ul style="list-style-type: none"> <li>•All participants in both study groups received minimal care, a package of non-pharmacological interventions that included educational training about healthy lifestyle—eg, a healthy diet with low salt, sugar, and fat content, exercise, weight control, and abstinence from smoking and opium (a common habit in this population). The interventions were delivered at follow-up visits by the Poly Iran field follow-up team;</li> <li>•Face-to-face training session (3 – 6 months);</li> <li>•Minimal care was supplemented by a short text message twice per month;</li> <li>•Participant who has hypertension needs a healthcare network for hypertension control</li> </ul>	According to the study on the use of polypill medicine for preventing stroke recurrence, it was found that 80.5% of the individuals who received the treatment were considered to be adherent in taking their prescriptions. The efficacy of tertiary prevention measures, aimed at preventing the worsening of stroke, is demonstrated by a reduction in the severity incidence of 5 to 9% among participants who consistently adhere to medication.	Both groups' training sessions (education) yielded no meaningful results. Nevertheless, adhering to a certain lifestyle can mitigate the severity of a stroke.
Shi <i>at al.</i> ,	2021	Randomize Controlled Trial	A total of 38 Community Health Centers (19 with Clinical Decision Support System (CDSS) and 19 Non-CDSS)	<ul style="list-style-type: none"> <li>•Diabetes Complication Control in Community Clinics (D4C) ;</li> <li>•Phase I : 18 month</li> <li>•Phase II : 36 month</li> </ul>	The prevalence of smoking among diabetes patients with stroke was 20.8%. The utilization of a community-based approach as a preventive measure for stroke cases in individuals with diabetes as a comorbid condition has demonstrated significant efficacy, leading to a notable 60.3% decrease in the likelihood of disease severity.	-
Pagidipati <i>et al.</i> ,	2017	Randomize Controlled Trial	A total of 13.616 participants from 38 countries aged more than 50 with diabetes mellitus and	<ul style="list-style-type: none"> <li>•Open-label use of antihyperglycemic therapy;</li> <li>•Total follow-up 3 years</li> </ul>	Overall, 29.9% of patients with diabetes mellitus and cardiovascular disease (stroke) achieved all 5 secondary	-

			known cardiovascular disease at entry into TECOS (Trial Evaluating Cardiovascular Outcomes With Sitagliptin).		prevention parameters at baseline, although 71.8% achieved at least 4 parameters.
Bosch <i>et al.</i> ,	2023	Randomize Controlled Trial	A total of 12.705 participants from 21 countries aged 55 to 65 years old with vascular risk factors but without overt cardiovascular	<ul style="list-style-type: none"> <li>• a fixed-dose combination of candesartan 16 mg and hydrochlorothiazide 12.5 mg daily or placebo and rosuvastatin 10 mg daily or placebo as tertiary prevention;</li> <li>• Follow-up clinic visits were at 6 weeks and 6 months after randomization and every 6 months thereafter.</li> </ul>	Administering medicine as a tertiary preventive measure in the intervention group resulted in a reduction in blood pressure. Nevertheless, the decrease in blood pressure did not lead to a decrease in the intensity of any form of stroke.

In this systematic review, the variation in stroke prevention incurred by each article is due to the type of prevention and period. The majority of the experiments were done on a group and individual scale. Primary stroke prevention involves the management of persons who have not previously experienced a stroke. Secondary stroke prevention pertains to the management of persons who have previously experienced a stroke or transient ischemic attack.<sup>12</sup>

The study that conducted in Iran with a total participant of 50.045 aged 40 to 70 years old with regular stroke and stroke while pregnant. The study findings indicate that those who regularly consume a certain medication experience a decline in their health condition, specifically among those living with stroke. The reduction in health conditions was observed to range from 5% to 9%. The study demonstrates that the preventative strategy consists of three distinct steps. During the initial phase, individuals who had experienced a stroke participated in an in-person training session that lasted for a period of 3 to 6 months. The second stage received minimal care. During this session, the intervention participants were presented with the option of using the polypill medicine. In the final session, all participants, particularly those in the intervention group with more severe conditions, required a healthcare network to manage their illness.<sup>13</sup> The endeavors undertaken are akin to a study completed throughout 9 nations, which showed the efficacy of employing a composite medication regimen (polypill, aspirin, and vitamins) as a main preventive measure in

individuals afflicted with stroke.<sup>14</sup> Combining primary, secondary, and tertiary prevention programs maximizes the effectiveness of prevention efforts. A comprehensive study was conducted to integrate primary, secondary, and tertiary prevention strategies, focusing on engaging in regular physical activity and monitoring dietary consumption. Subsequently, the administration of polypill and aspirin, the management of risk factors post-hospitalization, and the utilization of antiplatelet medications were implemented to prevent stroke. The combination decreased the patient's annual chance of experiencing a more severe stroke by a factor of 1.39.<sup>15</sup>

It is vital to combine preventive measures to prevent stroke patients from worsening. Research conducted in Europe demonstrates that integrating preventive measures with adopting healthy behaviors, such as abstaining from smoking, limiting alcohol consumption, and engaging in regular physical activity, can effectively mitigate the risk factors associated with obesity. Moreover, it is imperative to enhance self-awareness to manage health conditions as a primary preventive measure, particularly in cases where there is a familial predisposition to stroke. Implementing primary prevention measures is considerably more challenging in comparison to secondary and tertiary prevention. The secondary preventive efforts aim to integrate the services offered by internal medicine physicians and cardiologists. Moreover, tertiary interventions aim to offer preventive measures to ensure that stroke survivors do not have worsening symptoms.<sup>16</sup>

The results of the study that conducted in Iran are in direct opposition to the findings of the study conducted in Indonesia. The use of drugs as a tertiary prevention strategy effectively manages blood pressure, but does not serve as a preventive measure against further deterioration in stroke patients. A study conducted in Indonesia demonstrated that medication treatment was administered to 53 stroke patients. Remarkably, 84.9% of the patients experienced a reduction in high blood pressure, while 15.09% exhibited an increase in blood pressure.<sup>17</sup> The utilization of medication as a means of secondary and tertiary prevention does not always prove successful in preventing stroke patients from deteriorating. A study conducted in Europe revealed that the use of medication as a preventive measure for stroke patients is ineffective to a significant extent, with a rate of 32.28%.<sup>18</sup> The primary concern in tertiary prevention for stroke patients extends beyond the efficacy of medications, encompassing the issue of patient adherence to medication, which hinders the attainment of ideal tertiary preventive outcomes. A multi-center study conducted in a hospital revealed that 70% of the patients who received pharmacological treatment exhibited an increase in severity following drug therapy. In addition, a significant proportion of patients (27.9%) who suffered severity had extremely low drug adherence.<sup>19</sup>

According to an about the therapy of stroke necessitates the involvement of multiple disciplines.<sup>20</sup> Therefore, the utilization of medication treatment as a tertiary preventive measure is unsuitable if the objective is to mitigate the severity of the disease. According to another study, the effectiveness of pharmacological treatment as a tertiary preventive measure is reduced due to the need to consider risk factors and other disorders to optimize its application.<sup>4</sup> Multi-disciplinary engagement entails the implementation of all levels of stroke prevention measures to patients, ensuring that preventative activities are executed at their highest level of efficiency.<sup>20,21</sup>

The study conducted in 38 countries has a diverse viewpoint on the prevention of strokes. The stroke patient who adheres to the prescribed treatment has become a standard in this preventive endeavor. The results show that only 29,9% of stroke patients received 5 parameters of prevention while the others received 4 parameters of prevention. The efficacy of secondary prevention is shown in the program's ability to effectively manage blood pressure and smoking behaviors. Patients who meet all five characteristics get a decrease in blood pressure of over 50%, while for smoking habits, the reduction is over 80%.<sup>22</sup> The other study used community approaches as secondary prevention for reducing worse conditions.<sup>23</sup> The findings indicated that 60.3% of stroke patients who received community-based interventions exhibited a

reduction in the severity of their condition. The efficacy ascribed to the emphasis on secondary prevention was evidenced by a study done in Surakarta. Administering antiplatelet therapy and optimizing stroke patients' adherence to medication has been shown to decrease the occurrence of recurrent stroke in patients. The efficacy of antiplatelet therapy and patient compliance in reducing recurrent stroke events was demonstrated in a cohort of 82 patients. Initially, 69% of patients experienced recurrent stroke episodes. However, after implementing antiplatelet therapy and optimizing patient compliance, the incidence of recurrent stroke was reduced to 23%.<sup>24</sup>

Previous studies have shown inadequate execution of primary, secondary, and tertiary preventative measures individually. Therefore, it is necessary to integrate all prevention efforts into a comprehensive stroke prevention strategy. A comprehensive prevention approach was implemented in India, Iran, Mozambique, Nigeria, and the Russian Federation, including basic to tertiary levels. At the primary level, health promotion is optimized by focusing on risk factors. In primary preventive endeavors, alongside optimizing health promotion, policies are employed to mitigate risk factors, such as levying higher charges on cigarette manufacturers and establishing smoke-free zones. Moreover, in the management of hypertension, the approach involves implementing dietary regulation by closely monitoring the quantity and quality of food consumed. Additionally, secondary prevention involves optimizing treatment for individuals who have experienced a stroke. Drug therapy, including optimizing the administration of antiplatelet medications, managing blood pressure, and considering surgical intervention if necessary, is employed as part of the treatment regimen for stroke patients with severe symptoms. The final step in the tertiary treatment process involves optimizing pharmacological therapy, ensuring compliance with medication, and receiving support from the community to aid in rehabilitation.<sup>25</sup>

The same strategy is also employed in wealthy nations like the United States. The initial approach to addressing the issue of stroke is concentrating on those with elevated risk factors. Activities such as screening are conducted to identify individuals with prehypertension and dysglycemia to determine the number of people at risk of developing hypertension and diabetes mellitus. Hypertension and diabetes mellitus are recognized as risk factors for stroke. The second approach involves modifying lifestyle habits such as reducing cigarette and alcohol intake, managing salt consumption, boosting fruit and vegetable consumption, maintaining a healthy body weight, and engaging in physical activity. The third strategy is to optimize pharmacological intervention. To optimize pharmaceutical usage to uphold blood pressure

and lower blood lipid levels. Optimizing medicine usage has been shown to effectively control blood pressure and blood lipids in several countries like Argentina, China, and India. In the previous policy, the United States targeted the populace. The population method involves planning, monitoring, and assessing efforts, with each strategy being characterized by this approach. This technique involves implementing policy and legislative changes.<sup>26</sup>

India's Ministry of Health and Family Welfare implemented a strategy under a stroke prevention guideline. India's policy is to target the people by implementing preventive programs for strokes that emphasize high-risk tactics. The initial action in the preventative program is screening individuals between the ages of 10 and 20 years. Screening is conducted to identify and exclude individuals with hypertension and diabetes mellitus. The second action is reducing cigarette usage by offering counseling and therapy to prevent high-risk stroke patients from smoking. The next step to decrease cigarette usage involves implementing a smoke-free area policy. The upcoming task involves administering medical therapy to people with arrhythmia. The treatment provided is anticoagulant therapy. The upcoming task involves decreasing alcohol intake by offering counselling to patients exhibiting unhealthy alcohol use habits. The upcoming task is to optimize the utilization of medications like aspirin for their antiplatelet properties. The final task is lifestyle management through monitoring food consumption, engaging in physical activity, and managing body weight.<sup>27</sup>

Additional stroke preventive efforts in Illinois include aspirin therapy, blood pressure regulation, cholesterol control, and reducing cigarette smoking. Implementing multiple activities simultaneously in the stroke prevention program in Illinois has been demonstrated beneficial based on the annual patient statistics.<sup>28</sup> Malaysia offers a preventative program for stroke that targets lifestyle risk factors like cigarette usage, alcohol intake, physical activity, and consumption of an unhealthy diet. Another focus is also applied to activities centered on the danger associated with body metabolism. This activity targets stroke patients with elevated systolic blood pressure, high blood cholesterol levels, high BMI, and high fasting sugar levels. In addition, the government prioritizes environmental concerns such as air pollution and environmental instability, which impact the occurrence of stroke.<sup>29</sup> Observing the successful execution of preventive programs by different countries to manage and decrease stroke occurrences highlights the significance of enhancing primary prevention, secondary prevention, and tertiary prevention initiatives. Moreover, enhancing the involvement of the community and caregivers might optimize the effectiveness of these prevention measures.

## CONCLUSION

Preventive programs in low-to-middle countries are typically categorized into primary, secondary, and tertiary prevention. The most ideal, effective, and efficient approach to prevention is to integrate all prevention initiatives. Prevention entails addressing risk factors such as smoking, alcohol intake, and insufficient physical activity. In addition, regular health check-ups are beneficial as a preventive measure. In addition, pharmacological therapy can be employed for secondary and tertiary prevention.

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