A COHORT STUDY ON THE PRIMARY PREVENTION OF STROKE INCIDENCE IN ADULT POPULATION IN BOGOR, WEST JAVA

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ABSTRACT

Background: Incidence of stroke showed an increasing trend in Indonesia, 12 new cases per 1,000 in 2013, and 19 new cases per 1,000 in 2018 despite the stroke control programs from the government. This study aimed to estimate Cumulative Incidence, Incidence Rate, and Population Attributable Fraction (PAF). This study also estimated the effect of blood pressure, physical activity, blood sugar levels, and smoking habits on the risk of stroke in adults.
Subjects and Method: This was a cohort study conducted for 6 years in 5 Districts, Bogor City, West Java. An adult population of 5,189 subjects with aged ≥25 years was selected. The dependent variable was stroke. The independent variables included blood pressure, physical activity, blood sugar level, and smoking habits. Data for independent variables (except blood sugar level) were collected by using questioners. Data were analyzed by Cox Proportional Hazard Model.
Results: The Cumulative Incidence was 2.09% and Incidence Rate was 480 new stroke cases per 100,000 person-year (CI 95%= 130 to 670) over 6 years. Predictors of stroke incidence were hypertension (HR= 2.50; CI 95%= 1.50 to 4.10; p= 0.001), low physical activity (HR= 2.40; CI 95%= 1.50 to 3.90; p< 0.001), high blood sugar level (HR= 3; CI 95%= 1.70 to 5.50; p= 0.001), and heavy smoking (HR= 3.90; CI 95%= 1.40 to 11.10; p= 0.007). PAF of blood sugar level and physical activity was 67.75%, and able to reduce stroke incidence by 1,990 from 2,937.
Conclusion: Hypertension, low physical activity, high blood sugar level, and heavy smoking are predictors of stroke in adult. Primary prevention by increasing physical activity and decreasing blood sugar level can reduce incidence of stroke.

Keywords: stroke, Cumulative Incidence, Incidence Rate, PAF, primary prevention

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BACKGROUND

WHO estimated that in 2020 non communicable diseases (NCD) will cause 73% of deaths and 60% of all morbidity in the world (WHO, 2017). In Indonesia, stroke ranks first as the leading cause of death and neurological disability (Kim and Johnson, 2011). National stroke prevalence is still sta-ble at 120 per 100,000 person-years in 2013 (Balitbangkes, 2014), increasing to 190 cases per 100,000 person-years and in Bogor city at 110 per 100,000 per-son--years (Balitbangkes, 2014). However, various efforts to prevent and control stro-ke have been carried out. The NCD risk factor cohort study results in the city of Bogor during 4 years of monitoring showed that the rate of emergence of new cases (incidence) of stroke was 5 new cases every 1,000 person-years or 500 per 100,000 person-years (Pradono et al., 2017).

Risk factors for stroke include modifiable risk factors and non-modifiable risk factors. The main determinants of stroke

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in-cluded hypertension (OR= 4.20; 95% CI = 2.20 to 8.03; p <0.001), coronary heart disease (OR= 2.74; 95% CI= 1.51 to 4.99; p = 0.001), diabetes mellitus (OR= 2.89; 95% CI= 1.47 to 5.64; p= 0.002), and poor economic status (OR= 1.83; 95% CI= 1.03 to 3.33; p= 0.038) (Riyadina and Rahajeng, 2013). Interventions can be carried out on modifiable risk factors that can be changed or modified in community groups, especially groups that are more at risk. The government has launched NCD prevention pro-gram through the periodic health check pro-gram, get rid of cigarette smoke, be diligent in physical activity, a healthy diet with balanced calories, adequate rest and ma-nage stress (Ministry of Health, 2015). The implementation of programs related to risk factor intervention in the community movement consists of 6 main activities, including (1) Increasing physical activity; (2) Increasing hygiene and healthy living behavior; (3) Provision of healthy food and accelerating improvement of nutrition; (4) Increasing disease prevention and early detection; (5) Environmental quality improvement; and (6) Increasing education on healthy living. The main focus is carried out in physical activity, con-sump-tion of vegetables and fruit, and re-gular health checks (Ministry of Health, 2017).

The risk of stroke can be prevented, among others, by controlling one or more stroke risk factors according to the ability and capacity of the at-risk group. The stroke cohort data of the research "Cohort Study of Non-Communicable Disease Risk Factors" in Bogor City has been run-n-ing for 6 years of monitoring, from 2011/-2012 to 2017/2018. Selection of appro-priate and effective forms of intervention in risk groups requires information on the value of Population Attributable Risk (PAF) to determine the factors to be selected for intervention so that the incidence of stroke can be reduced. PAF is an impact measure that calculates the population that can be pre-vented against a health disorder if there is an intervention on the causative factor. PAF is the proportionate reduction in population disease or death that would occur if exposure to risk factors was reduced un-der conditions ideal.

Many diseases are caused by multi-ple risk factors, and individual risk factors can interact in their impact on overall dis-ease risk. As a result, PAF for individual risk factors often overlaps and increases by more than 100 percent (WHO, 2005). This study aims to calculate the PAF number to determine the steps for selecting the right intervention and preventive measures in general.

SUBJECTS AND METHODS

1. Study Design

This was a follow-up analysis design of prospective cohort stroke data for 6 years of follow-up (2011/2012 to 2017/2018). The secondary data source was a subset of research data "Cohort Study of Non-Communicable Disease Risk Factors (FRNCD)" in 5 sub-districts (Kebon Kalapa, Babakan Pasar, Babakan, Ciwaringin, Panaragan) in Central Bogor sub-district, Bogor City.

2. Population and Sample

The population is the permanent residents of Bogor city aged 25 years and over. The target population is permanent residents over 25 years of age and domiciled in 5 sub-districts (Kebon Kalapa, Babakan Pasar, Babakan, Ciwaringin, Panaragan), Bogor Tengah sub-district, Bogor City. The stroke cohort sample was adult respondents aged 25 years and over who did not have a stroke (initial screening results). The sampling technique in the NCD risk factor cohort study used total sampling with the criteria of permanent residents aged 25 years and over and willing to be routinely checked 3 times per year and

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every 2 years. The inclusion criteria for the analyzed stroke cohort data were complete stroke incidence data at examination years 2, 4, and 6, stroke-free sample at baseline, and periodic check-up data for at least 1 examination during the 6-year follow-up.

Secondary data for a complete cohort sample and analyzed were 5,198 stroke-free subjects at the start of the study. The total cumulative incidence of stroke during 6 years of follow-up was 109 cases (2.08%). The stroke incidence rate as an event status (hazard) was the first diagnosed stroke. It was calculated taking into account the sample's presence at the time of examination at 2 years, 4 years, and 6 years of follow-up at 480 cases per 100,000 person-years.

3. Study Variables

The dependent variable was PAF as a measure of impact. Independent variables include status characteristics (age, sex, education, and marital status), health status (obesity, hypertension, lipid profile, blood sugar levels), and risky behaviours such as smoking, physical activity, intake of nutrients (carbohydrates, sodium, and fat).

4. Operational Definition of Variables

PAF can be defined as the proportion of new cases that can be prevented if risk factors are removed. The incidence of stroke is the result of a neurological examination by a neurologist through anamnesis and sequelae.

Age was categorized into 3 groups: age <35 years, 35-44 years, and 45 years and over.

Gender was categorized into male and female.

Education was categorized into lower education (no school and primary school), moderate education (graduated junior high and high school), and higher education (graduated D3 and Graduate).

Marital status was categorized as not married, married, and divorce (divorce life and die).

The health status of study subjects included hypertension, obesity, lipid profile, blood sugar, and mental health (stress).

Hypertension was classified according to JNC 2003 if the systolic blood pressure is ≥ 140 mmHg or diastolic ≥ 90 mmHg.

Obesity (overweight) was categorized according to the classification of Body Mass Index (BMI) for the Asian population, including underweight (BMI <18.5), normal (18.5 to 22.9), overweight (23 to 24.9), and obesity (≥25).

Lipid profile consists of levels of LDL, HDL, and triglycerides in the blood. The lipid profile was abnormal if the LDL cholesterol level was ≥100 mg/ dL, HDL ≥ 40 for men and ≥50 for women, and triglycerides ≥150 mg/ dL.

Blood sugar level fasting was abnormal (diabetes mellitus) if the level was ≥126 mg/ dL.

Mental health was measured through emotional disturbance symptoms (stress) using the instrument Self Reporting Questionnaire (SRQ). Stress criteria determined if the answer at least 6 of 20 symptoms. According to the WHO Steps 2004 classification, physical activity was calculated, including the amount of daily physical activity during work, travel, and leisure in units Metabolic Equivalent Turnover (MET). Lack of physical activity= <600 MET and sufficient= ≥600 MET.

Smoking habit was calculated using the Brinkman Index (the number of cigarettes times the length of time smoked during the lifetime). It was categorized into heavy smokers (> 600 cigarettes/ year), moderate smokers (<20-599 cigarettes/ year), light smokers (0-199 cigarettes/ year), and non-smokers.

Nutrients associated with stroke include intake of carbohydrates, fat, and sodium. The collection of data on nutrient intake was done using the 24-hour recall method, and the

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percentage of nutrient intake was categorized according to the 2013 PUGS criteria. Excess intake of carbohydrates was ≥60 percent, fat ≥2 percent, and sodium ≥2000 grams.

5. Study Instruments

Secondary data collected using the WHO STEPS method includes interviews, physical measurements, and laboratory examinations with regular measurement intervals every 4 months and every 2 years.

6. Data analysis

Cox regression method was used to determine the hazard ratio for stroke incidence by controlling for other covariates. PAF was calculated using the Stata program from the available fit models due to multivariate logistic regression analysis. The fit model obtained was carried out by statistical tests with multiple logistic regression. PAF value calculation was performed for each risk factor and the combination of risk factors. The determination of the selection of risk factors that will be intervened is based on the PAF percentage.

7. Research Ethics

The data source was a subset of cohort study research data that focuses on monitoring for a period of 6 years and had received ethical permission from the Ethics Commission of the Indonesian Ministry of Health Research and Development Agency in 2018 with letter number LB 02.01 / 2 / - KE.076 / 2018 dated on March 1, 2018.

RESULTS

Characteristics of the sample included gender, age, education level, and marital status. The description of the stroke cohort sample distribution according to the characteristics, was presented in Table 1. The majority of the sample were women, aged 45 years and over, had moderate education (graduated from high school) and were married. The number of data as a cohort sample (free outcome at the beginning of the study) was 5,198, and it was found that the cumulative incidence of stroke during the 6-year period was 109 cases (2.09%). The incidence of stroke (incidence rate) calculated as a hazard rate of stroke in 6 years was 480 person-years per 100,000 inhabitants with a 95% confidence interval (CI) 130 up to 670 per 100,000 person-years. The rate of occurrence of new stroke cases was 480 per 100,000 person-years inhabitants for 6 years of observation.

Risk factors affecting the stroke at the beginning and when monitoring 6 years included sample characteristics (age and marital status), health status (BMI, lipid profile, hypertension, and stress), and behaviors (smoking, physical activity, and nutrient intake) was shown in Table 2. Risk factors experiencing positive changes (smaller proportion at 6 years of baseline monitoring) included stress risk factors, physical activity, and fat and sodium (salt). Risk factors experiencing negative changes for stroke (greater proportion at 6 years of monitoring) included hypertension, lipid profiles, blood sugar profiles, carbohydrate intake, and obesity.

The Cox proportional-hazards model results showed in Table 3 that the factors included as predictors in the stroke incidence model included hypertension, inadequate physical activity, abnormal fasting blood sugar levels, and abnormal triglyceride levels after considering age.

Table 4 showed the results of the calculation of the PAF value the best choice of intervention with one risk factor was eliminating the abnormal fasting blood sugar level of 47.79 percentage, eliminating two risk factors (abnormal fasting blood sugar level and physical inactivity) of 67.75 percentage, eliminating three risk factors (lack of physical activity, hypertension, and abnormal fasting blood sugar levels) was 77.11 percentage while eliminating four risk factors (lack of physical

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activity, hypertension, abnormal fasting blood sugar levels, and heavy smoking) was 80.9 percentage.

Table 1. Characteristics of the cohort samples stroke

Variable	Categories	Total sample (n= 5,198)	Percentage (%)
Gender	Male	1,497	28.8
	Female	3,701	71.2
Age (years)	<35	1,086	20.9
	35-44	1,658	31.9
	≥45	2,453	47.2
Education	Low	1,835	35.3
	Medium	3,056	58.8
	High	307	5.9
Marriage	Unmarried	182	3.5
	Married	4,200	80.8
	Divorced	816	15.7

Table 2. Changes in risk factors for stroke incidence at baseline and monitoring 6 years of study cohort NCD risk factor 2018

Risk factors	Categories	Initial (%)	Monitoring 6-year (%)
Age (Years)	<35	22.6	20.9
	35-44	30.4	31.9
	≥45	46.9	47.2
Marital status	Not married	6.5	3.5
	Married	85.0	80.8
	Divorced	2.3	3.1
	Widowed	6.2	12.5
Hypertension	No	70.0	61.7
	Yes	30.0	38.3
BMI	Underweight	6.6	4.7
	Normal	29.8	23.1
	Excess	16.6	16.5
	Obese	45.8	54.9
Stress	No	73.1	93.3
	Yes	26.9	6.7
Physical activity	Enough	50.2	67.7
	Less	49.8	32.2
Smoking	Non-smoker	58.6	53.4
	Light smokers	19.7	16.2
	Medium smokers	10.6	12.7
	Heavy smoker	2.0	3.6
HDL	Normal	59.5	56.4
	Risk	39.2	42.8
LDL	Normal	18.1	15.7
	risk	81.9	84.3
Triglycerides	Normal	81.9	73.0
	Risk	18.1	27.0
Sugar intake/ KH	<60%	47.3	22.6
	≥60%	52.7	77.4
Fat	<25%	31.3	56.4
	≥25%	68.7	42.8
Sodium	<2000 mg	51.9	59.8
	≥2000 mg	44.1	40.2

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Table 3. Predictors of stroke incidence at 6-years of monitoring

Predictor	Hazard Ratio (HR)	95% CI		p
		Lower Limit	Upper Limit	
Hypertension (systolic ≥140 mmHg/ diastolic ≥90 mmHg)	2.49	1.50	4.12	0.001
Physical activity <600 MET	2.45	1.50	3.99	0.001
Fasting glucose level ≥126 mg/ dl	3.01	1.65	5.47	0.001
Status smoking				
Not smoking	1	-	-	0.007
Light smoking	1.40	0.73	2.77	
Moderate smoking	1.75	0.94	3.26	
Heavy smoking	3.89	1.36	11.09	

Table 4. Value of population attributable fraction (PAF) risk factors for stroke at 6-years of follow-up. (NCD risk factor cohort study 2018)

Physical activity	Hypertension	Fasting blood sugar levels	Heavy smokers	PAR	PAF	Number of stroke cases in Bogor City (HR 0.48%)	Number of stroke cases can be reduced
√				0.86	38.52	2,937	1,131
	√			0.64	28.81	2,937	846
		√		1.07	47.79	2,937	1,404
			√	12.37	16:38	2,937	481
√	√			1.26	56.35	2,937	1,655
√		√		1.51	67.75	2,937	1,990
√			√	1.10	49.35	2,937	1,449
	√	√		1.41	63.05	2,937	1,852
	√		√	0.89	39.70	2.937	1.166
		√	√	1.27	56.82	2,937	1,669
√	√	√		1.72	77.11	2,937	2,265
√	√		√	1.42	63.43	2,937	1,863
√		√	√	1.65	73.63	2,937	2,163
	√	√	√	1.54	68.88	2,937	2,023
√	√	√	√	1.81	80.90	2,937	2,376

DISCUSSION

The results of further analysis of the stroke cohort data aged 25 years and over in Bogor City during 6 years of monitoring, the cumulative incidence of stroke was 2.09 percentage, and speed of emerging new cases (hazard rate) of strokes of 480 per 100,000 person-years. The incidence of stroke was higher than in some countries in China= 120,42 per 100,000 person-years (95% CI= 26.17 to 214.67) (Wu et al., 2013) and 200 per 100,000 person-years in Australia (Clissold et al., 2017). The incidence rate showed an increase in line with the respondents' increasing age (Honjo et al., 2008). The study results in the older age group (50 years and over) showed a greater incidence rate. In the Netherlands in 2008, the incidence rate of stroke in the population aged 55-94 years was 627 per 100,000 person-years, and in Spain, in 2011 it was found to be 453 per 100,000 person-years, at age 60 years and over and 1,006 per 100,000 person-years at

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the age of 80 years and over. After adjusting for age, the incidence of stroke in East Asian countries was around 24,753-34,778 per 100,000 person-years, which was higher than in the United States of 22,066 per 100,000 person-years, and in the United Kingdom was 14,197 per 100,000 person-years (Kim et al., 2016).

The majority of stroke had over 45 years old, married, low education, and do not work. The findings of stroke patient age were equal to the previous epidemiological studies in Indonesia, which showed a mean age of 58 stroke patients, 8 years with a prevalence of 1.2%. The risk of recurrent stroke occurrence and stroke patients' death was associated with increasing age (Sun et al., 2013). Stroke disease was more experienced by vulnerable people, including people with low education levels and who did not work ($p < 0.050$). The relationship between education level and stroke incidence was still controversial. Research in America and Europe had a relationship between education level and stroke incidence, while studies in Japan did not show this relationship (Abboud et al., 2012; Christiansen et al. 2016; Honjo et al., 2008). Status did not work a higher risk of having a stroke according to research in France, where people who did not have a job are more likely to have a stroke than employees (Grimaud et al., 2011). In Bangladesh, the largest proportion of stroke patients are unemployed (21%) (Hossain et al., 2011).

Several risk factors that experienced negative changes include hypertension, obesity, lipid profile, and fasting blood sugar. Hypertension was the main determinant of stroke (Riyadina and Rahajeng, 2013). Hypertension patients who did not seek treatment were three times the risk of having a stroke than seeking treatment (OR= 3; 95% CI= 1.18 to 7.62) (Riyadina and Kristanti, 2016). Research in Bangladesh showed the same results, hypertension as a major risk factor for stroke (63%) and the majority of stroke patients (42.85%) did not seek treatment or treatment is irregular (Hossain et al., 2011). The results of the analysis reported obesity was associated with the incidence of stroke. Obesity is an independent risk factor for stroke, and increased BMI is associated with the cause of death in the general population (Whitlock et al., 2009). An increase in body weight change by 2.7 percentage over a long period (since age 25 years) is associated with an increased risk of stroke (Stevens et al., 2013). The relationship between BMI and ischemic stroke risk was linear and comparable between sexes and between races (Bazzano et al., 2010). Based on the results of lipid profile examination, respondents with LDL levels (>100 mg/ dL) and triglycerides (> 150 mg/ dL) were significantly ($p < 0.050$) associated with the incidence of stroke at the age of 25 years and over.

The multivariate Cox regression analysis results showed that stroke incidence predictors were fasting blood sugar levels, hypertension, physical activity, and heavy smoking, after controlling for age factors. Several Western and Asian countries, especially in China, Japan, and the Republic of Korea, showed that the risk of stroke was associated with a higher increase in blood pressure among Asian populations than Western countries. The fact showed that systolic blood pressure ≥140 mmHg indicates 6.22 times higher risk of hypertensive conditions which was 2.84 times in the Asian population than Western countries with HR 2.39 and HR 1.79, respectively (Chen et al., 2014).

Hypertension as a predictor for atherosclerosis carotid has been widely proven, and inflammation is an important mechanism (Li and Chen, 2005). Hypertension via vasoactive peptides accelerates the atherosclerotic process. However, the relationship between hyper homocysteine and atherosclerotic carotid disease is still controversial. Some studies suggested a potential mechanism. Hyper homocysteine contributes to atherosclerosis development, such as increased oxidative stress, impaired endothelial function, and lipid changes. It has metabolism to promote the formation of atherosclerotic plaques and improve the adhesion of plate-

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lets, and induction of thrombosis (Steven et al., 2013).

The synergistic effect of hypertension and hyper homocysteine can be explained that hyper homocysteine activates angiotensin-converting enzymes by inhibiting endogenous hydrogen sulphide production, which worsens hypertension (Antoniades, 2009). When hypertension and hyper homocysteine are combined, the effect on atherosclerosis can be increased. Biological mechanisms can explain the relationship of cholesterol to the incidence of stroke. Serum cholesterol and non-cholesterol HDL is a predictor of stroke. Recent research results showed that low non-HDL cholesterol is the best predictor of stroke (Tanabe et al., 2010). Several studies had reported that subjects with low blood cholesterol are more prone to experience intracerebral hemorrhage (intracerebral haemorrhage).

This can be explained because low cholesterol induces angioneurosis feature, allows combination with hypertension, and low cholesterol can also be a result of poor nutritional status (Olsen et al., 2007). Cohort studies in Asian and Asia Pacific countries showed a weak positive association between total cholesterol and death and cerebral infarction (Pan et al., 2010). Serum cholesterol was inversely related to stroke severity. The survival analysis showed the same results, every 1 mmol/ L increase in cholesterol showed HR= 0.89 (95% CI= 0.82 to 0.97; p <0.001). These results supported the hypothesis that high cholesterol levels are associated with the development of minor strokes. Serum total cholesterol level in acute phase non-cardioembolic ischemic stroke is a predictor of functional outcome-independent over the long term.

Total cholesterol is associated with the risk of major strokes such as strokes haemorrhagic or embolic, while high levels of total cholesterol are associated with minor ischemic strokes. Cholesterol can exhibit neuroprotective effects due to its antioxidant properties. High cholesterol increases the adaptation of cardiac myocytes to ischemia and slows down oxidative stress to brain tissue in vitro. When brain tissue is ischemic injury, nerve cells can produce free radicals, which then attack the cell membrane. Cholesterol can protect brain tissue from ischemic injury and limit the level of lesions by neutralizing free radicals (Pan et al., 2010).

Research on the magnitude of the disease problem globally indicated that high systolic blood pressure has an effect on stroke problems in East Asian countries. The results showed that an attributable risk fraction is around 52-73 per cent of strokes associated with DALYs (Hossain et al., 2011). The results of the multivariate model, a minimum diastolic blood pressure of 90 mmHg (HR= 2.45; 95% CI= 1.47 to 4.08; p= 0.001) and a systolic blood pressure of at least 160 mmHg vs <140mmHg (HR= 2.80; 95% CI= 1.53 to 5.14; p= 0.001) was associated with the incidence of stroke. Systolic blood pressure (≥160 mmHg) and diastolic blood pressure (≥90 mmHg), and atrial fibrillation (TIA) are risk factors for the incidence of stroke among the elderly population (Hornsten et al., 2016).

Globally 90.5 % (CI 95%= 88.5 to 92.2) the burden of stroke (DALYs) was due to risk factors that can be modified by 74.2 percentage (95% CI= 70.7 to 76.7) in these are caused by behavioural risk factors (smoking, poor eating habits, and lack of physical activity). Risk factors associated with the metabolic (high systolic blood pressure, high BMI, high fasting plasma glucose, high total cholesterol, low glomerular filtration rate caused DALYs by 72.4 percentage (95% CI= 70.2 to 73.5) and environmental risk factors (pollution air and lead exposure) amounting to 33.4 percentage (95% CI= 32.4 to 34.3) respectively, the second and third largest contributor to DALYs (Feigin et al., 2013). Although the ten most important risk factor is the systolic blood pressure high, low fruit diet, high BMI, high sodium intake, smoking, low vegetable diet, PM environmental pollution, household air pollution due to use of solid fuels, low-grain diet, and high fasting glucose, there is the heterogeneity of PAF risk factors from DALYs associated with stroke between different countries. The hetero-

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geneity is consistent with previous studies on risk factors for cardiovascular disease (Joseph et al., 2014).

This study showed that the contribution of different risk factors to stroke burden varies with time of day and between countries and continents. Therefore, regular monitoring of PAF and implementation of country-specific strategies as appropriate is necessary for stroke prevention. Considering that various risk factors contribute to the burden of stroke, government policies for stroke prevention strategies covering health services, non-governmental organizations, communities, and individuals were very important. Although the government has the authority and responsibility to control environmental, social, medical factors and lifestyle through tax laws and policies (e.g. taxes on tobacco, alcohol, salt sugar, or saturated fat), health services also have a responsibility to identify these factors. Risks that require detection and medical attention (such as high blood pressure, atrial fibrillation, dyslipidaemia, or symptomatic carotid artery stenosis) to reduce risk factors in the population (Feigin et al., 2016).

This study's limitation was that it uses secondary data so that there were some information biases that the researcher may not be able to control directly even though it was used structured instruments and trained interviewers and examiners. The population represented 5 sub-districts from 11 sub-districts in Central Bogor District, so generalization was limited to populations with the same characteristics. The best choice of intervention that the community can do independently in controlling fasting blood sugar levels through routine checks at Community Health Centre and limiting carbohydrate intake and doing physical activity routinely.

CONTRIBUTORS

Woro Riyadina was the main contributor in writing this article, while the member contributors were Yuda Turana, Dewi Kristanti, Julianty Pradono, and Ekowati Rahajeng.

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CONFLICT OF INTEREST

There is no conflict of interest at the writing of this article.

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