

Risk factors for symptoms of stroke in a community-based observational study in
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Abstract

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Background: Stroke is currently the third leading cause of death and sixth highest cause of premature death in Nepal. While studies have been conducted at tertiary care facilities to describe the epidemiology of hospitalized stroke, there has been limited research using population-level data that can reveal major risk factors for stroke in the Nepalese population. This study describes the prevalence of and risk factors for self-reported symptoms of stroke in participants of the Dhulikhel Heart Study (DHS), Dhulikhel, Nepal.

Methods: We conducted analysis of cross-sectional data collected at baseline from participants enrolled in the Dhulikhel Heart Study, a population-based, longitudinal cohort study focused on investigating risk factors for cardiovascular disease in Dhulikhel, Nepal. The study included 1073 individuals aged 18 or older who were randomly sampled from residents of Dhulikhel at the household level. Participants were surveyed with a battery of instruments that included the Questionnaire for Verifying Stroke-Free Status (QVSFS), a validated questionnaire used to

assess whether individuals exhibit stroke symptoms. Pearson's chi-squared tests and t-tests were used to examine associations between demographic, physical, and behavioral risk factors stratified by sex as well as binary stroke outcome. Multivariate logistic regression models were developed hierarchically for further assessment of risk factors. Fully adjusted models included the following covariates: demographic characteristics (sex, age [categorical], ethnicity, education, annual income, employment status, marriage status), physical risk factors (BMI, hypertension, diabetes, severe chest pain lasting at least half an hour, depression), and behavioral risk factors (fruit/vegetable/fat consumption, smoking, exposure to secondhand smoke, alcohol use, physical activity, stress).

Results: The mean age of study participants was 40.5 (SD=16.4) years and 58.4% were female.

A total of 126 individuals in the study (11.7%) had at least one self-reported stroke symptom assessed from the QVSFS. In the fully adjusted linear regression model, females had a 2.7-fold greater odds of exhibiting stroke symptoms compared to males ($p=0.003$, 95% CI: 1.4, 5.2).

Obesity ($BMI \geq 30$) was found to be protective and associated with an odds of stroke symptoms 0.3 times that of normal weight ($p=0.03$, 95% CI: 0.1, 0.9), as was a high level of physical activity (≥ 5000 MET-min per week) with an odds of stroke symptoms 0.2 times that of the lower recommended level of physical activity ($p=0.001$, 95% CI: 0.1, 0.5). The presence of at least one major life stressor was associated with an odds of stroke symptoms 2.1 times that of individuals with no major stressors ($p=0.003$, 95% CI: 1.3, 3.5).

Discussion: Nepal has a unique stroke symptom profile. The prevalence of individuals who exhibited stroke symptoms in this study was twice as high as in the United States and suggests a potentially high burden of stroke in Nepal. This burden of stroke symptoms was skewed toward younger ages and females compared to the global burden. Significant risk factors for an

increased risk of exhibiting stroke symptoms included sex, age, and having at least one major life stressor. Unemployment was marginally associated with higher odds of stroke symptoms. Significant protective factors included high levels of physical activity and, surprisingly, obesity. Collinearity between variables and the fact that the QVSFS has higher negative predictive value than positive predictive value may explain why traditional behavioral and metabolic risk factors were not found to be significant in this study's fully adjusted logistic regression model. Obesity and access to foods such as fruits and fats may also have been protective due to being an indicator of increased household wealth.

Conclusion: The results of this study confirm the high burden of stroke symptoms and risk factors within Nepal. Prospective longitudinal studies are needed to verify these results and monitor trends in stroke and other chronic disease risk factors to strengthen the country's ability to prevent and respond to the growing burden of non-communicable diseases.

BACKGROUND

The Global Burden of Disease study reported that in 2013 stroke was the second leading cause of death worldwide after ischemic heart disease and the third leading cause of disability after ischemic heart disease.² While stroke mortality and disability-adjusted life years (DALYs)—years of life lost due to a disability—have declined since 1990, the overall burden of the disease, including the number of people who died from stroke, remain disabled, were affected (i.e. incidence of new strokes), or survived has increased significantly.² The overall increased burden is attributed to aging, population growth, improved stroke care reducing mortality but increasing disability, and the increase of modifiable stroke risk factors.² Metabolic risk factors such as obesity and diabetes mellitus, which have increased among youth and adults, are major contributors towards the rise in stroke incidence in individuals younger than 70.² In 2016, the estimated global lifetime risk of stroke from 25 years of age onward was

approximately 25% among both men and women, with 18.3% risk of ischemic stroke and 8.2% risk of hemorrhagic stroke.³ Notably, the shift in burden has been primarily in low and middle-income (LMIC) countries which contribute 75% of stroke deaths and 81% of stroke-related DALYs.⁴

In Nepal, classified as a low-income country by the World Bank,⁵ infectious diseases accounted for 70% of both morbidity and mortality until the beginning of the 21st century.⁶ However, in recent years the country has undergone an epidemiologic shift toward a higher burden of non-communicable diseases (NCDs). Years of life lost (YLLs) to infectious diseases such as lower respiratory infections and diarrheal diseases, which were major causes of premature death, have decreased.¹ Meanwhile, YLLs to NCDs such as ischemic heart disease, chronic obstructive pulmonary disease, and stroke have increased.¹ NCDs now account for more than 44% of deaths and 80% of outpatient contacts in the country, and are projected to cause 66% of all deaths by 2030.⁷ Nearly one-third of the population have hypertension and 15% have diabetes. Both obesity and hypertension—major known risk factors for stroke—have dramatically increased in prevalence, especially in rural areas.⁸ Compared to other South Asian countries, Nepal is second after Pakistan as having the highest prevalence of hypertension in community settings.⁹ Nepal also has the highest percentage of females over 15 who have smoked, and the highest percentage of stroke patients from hospital-based registries who have reported a history of smoking.⁹

As a result, stroke is now the third leading cause of death and sixth highest cause of premature death in Nepal.¹ Stroke is also the sixth highest cause of DALYs due to the high burden of disability associated with the disease.¹ Rates of disability and mortality from stroke are at least 10 times greater in medically underserved regions due to lack of primary care treatment to screen patients for stroke risk and mitigate risk factors.³⁷ While age-standardized prevalence of stroke and mortality due to stroke in Nepal is similar to surrounding countries, between 1990-2013 age-standardized mortality rates due to stroke increased for both ischemic and hemorrhagic stroke.¹⁰ Outside of the Global Burden of Disease study, existing information on the burden of stroke in Nepal is limited primarily to estimates of prevalence, morbidity, and mortality in urban areas using hospital-based studies.^{7,11} Common risk factors seen in hospital-based studies include hypertension, smoking, alcohol use, and diabetes.¹² A high prevalence of hemorrhagic strokes,

which are often associated with severe disability, have also been reported.¹² Due to a lack of healthcare facilities that are equipped to treat stroke, most stroke patients, particularly in rural areas, seek treatment through traditional healers.¹¹

Due to the limitations of hospital-based studies, there is a need for population-level research to gain a better understanding of stroke epidemiology in the general Nepalese population. The Dhulikhel Heart Study (DHS) is a population-based, prospective cohort study on cardiovascular diseases and its modifiable and non-modifiable risk factors in Dhulikhel, a suburban town outside Kathmandu. As a result of this collaborative effort between Dhulikhel Hospital and the University of Washington, researchers have found that hypertension awareness was positively associated with increasing age, and while over three-fourths of those aware of their hypertensive status were on treatment, only 35% had their blood pressure under control.¹³ The prevalence of hypertension was 62.5% among individuals aged 65 and older, but 9% of individuals under age 30 also had hypertension. A reliable and validated food frequency questionnaire (FFQ) designed to measure the dietary practices of adult Nepalese was developed for the DHS and risk factors for depressive symptoms were assessed.^{14,15}

As part of the DHS, the Questionnaire for Verifying Stroke-Free Status (QVSFS), an 8-item questionnaire designed to identify stroke-free individuals, was administered during in-home interviews.¹⁶ This questionnaire has been validated through medical record review in a U.S. cohort with a low prevalence of stroke or transient ischemic attack (TIA), as well as in culturally diverse low-income populations in West Africa.^{16,17} Risk of stroke may increase up to 20% in the first three months after a TIA.³⁸ The DHS utilized a shortened version of the QVSFS—excluding questions on whether the patient had previously been diagnosed with stroke—to gather data on symptoms indicative of potential silent strokes or transient ischemic attacks (TIAs) that were not severe enough to require physician consult. Inclusion of this instrument provides a unique opportunity to investigate self-reported stroke symptoms in Nepal.

Nepal's Multisectoral Action Plan on the Prevention and Control of NCDs 2014-2020 has highlighted the need to take action in health promotion and risk reduction to reduce overall mortality from prevalent NCDs.⁸ Given that much of the population of Nepal does not have access to hospitals or neurologists for diagnosis and treatment, the QVSFS in the DHS provides a cheap, efficient way to identify individuals most at risk for stroke who could be referred to a

primary care provider at Dhulikhel Hospital for risk factor assessment, treatment of major risk factors, counseling, and enrollment in prevention programs. The specific aims of this study are to describe the prevalence of self-reported symptoms of stroke in DHS participants to better characterize stroke epidemiology in the general population, and analyze risk factors for stroke symptoms to provide information for how Nepal can focus resources and research to reduce the impact of stroke on its country's population.

METHODS

Dhulikhel is a municipality in Nepal just over an hour's drive southeast from the capital city of Kathmandu. In 2011, Dhulikhel had a population of around 34,000.¹⁸ This study utilized cross-sectional data from the DHS that surveyed 1,073 adults 18 years of age or older between November 2013 and February 2015. The recruitment team consisted of bachelor-educated graduates from Kathmandu University who were trained to conduct door-to-door surveys and measure variables. All of the 2225 households in the city were enumerated and about a third of the households ($n=735$) were randomly selected and stratified by ward (nine administrative divisions).¹⁴

Inclusion criteria for the DHS was being a permanent resident of Dhulikhel or residing in Dhulikhel for at least six months at time of being surveyed. Exclusion criteria included individuals who were pregnant at time of data collection, temporary residents who lived in hostels or motels, individuals who were unable to provide appropriate responses to survey questions due to health concerns or inability to communicate in Nepali or Newari language, and individuals who did not provide informed consent.¹⁴

Data on demographic variables, physical risk factors, and behavioral risk factors was collected through a standardized personal questionnaire using electronic tablets, physical exams, and laboratory testing. Demographic variables included *age, sex, ethnicity, education, employment status, annual income, and marriage status*. Self-reported age was used except for one outlier where the self-reported age of 15 was younger than the inclusion criteria. The age of that individual was recalculated based on their reported year of birth. Employment status was dichotomized as employed (government employee, non-government employee, or self-

employed), unemployed (non-paid, home-maker, retired, unemployed, others) based on self-reported occupation, or students. Annual income was presented in US dollars (USD) and cut points were set for relatively even distribution of subjects within each income category.

Stroke symptom questionnaire

Five questions related to previous stroke symptoms were asked in the DHS personal questionnaire based on the QVSFS. Participants were asked to answer if he/she had ever had: 1) sudden painless weakness on one side of the body; 2) sudden numbness or a dead feeling on one side of the body; 3) sudden painless loss of vision in one or both eyes; 4) sudden loss of the ability to understand what people are saying; and 5) sudden loss of the ability to express oneself verbally or in writing. Wording of the vision question was a modification of the original QVSFS in order to increase its understandability within the context of the Nepalese language. This was done based on problems encountered in interpretation of these symptoms in a previous study done in Vietnam.¹⁹ Stroke symptoms were summarized as a binary variable (0/1) calculated as response of “yes” to at least one of the questions on the QVSFS, with 1 indicating positive presentation of stroke symptoms and 0 indicating no presentation of stroke symptoms.

Physical risk factors

Height, weight, and waist and hip circumference were measured by the study team using standardized instruments. Using World Health Organization (WHO) expert consultation guidelines for South Asia, *Body Mass Index (BMI)* was categorized as underweight (<18.5 kg/m²), normal (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²), and obese (>30 kg/m²).²⁰ Blood pressure was measured three times with the participant in a sitting posture using a standard digital blood pressure machine on the right arm over loose clothing. The mean of the three measurements was used for analysis and *hypertension* was defined as a systolic blood pressure (SBP) \geq 140 mmHg, diastolic blood pressure (DBP) \geq 90 mmHg, or a participant receiving antihypertensive medications.²¹ History of *diabetes* was ascertained through self-report.

The Rose Angina Questionnaire, developed to detect coronary heart disease, has been validated with cardiologists' diagnoses in Bangladesh.²² History of *severe chest pain lasting over half an hour* was ascertained as part of the questionnaire through self-report.

Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D), a validated 20-item measure that is frequently used in both clinical and research settings to determine depression symptomatology in the general population.^{27,28} The CES-D asks participants to rate how often in the past week they experienced certain symptoms associated with depression such as restless sleep, sadness, poor appetite, and hopelessness. The four response options include rarely (<1 day), some (1-2 days), occasionally (3-4 days), and most (5-7 days). Each item is scored between 0-3 for a total instrument range of 0-60, with higher scores being indicative of greater frequency of depressive symptoms and correlating with an increased risk of clinical depression. Scores <16 were categorized as no depressive symptoms, 16-20 as mild depressive symptoms, and ≥ 21 as severe depressive symptoms.²⁹

Behavioral risk factors

A 115-item semiquantitative food frequency questionnaire (FFQ) was developed for Nepalese foods and validated prior to its use in the DHS.¹⁴ The aspects of diet that will be focused on in this study are intake of *vegetables*, *fruits*, and *fats* summarized as number of portions per week. The WHO recommends at least five servings of fruits and vegetables per day; high-fat diets have been linked with stroke risk.^{23,30} *History of smoking* (former smoker, current smoker, or never smoked), *household exposure to secondhand smoke*, and *alcohol consumption* (number of drinks per week) were all self-reported variables.

The WHO developed the Global Physical Activity Questionnaire (GPAQ) to assess several components of *physical activity* including intensity, duration, and frequency split across the domains of occupational, transport-related, and leisure time physical activity. Combined, activity across the domains should ideally be between 500-1000 MET-minutes of physical activity per week. The variable for physical activity was therefore categorized as <500, 500-999, 1000-4999, and ≥ 5000 MET-minutes of physical activity per week for analysis.^{24,31}

Chronic stress was measured with an 8-item instrument that assessed exposure and extent of psychological stress across multiple life domains including work, relationships, finances, and personal or family health problems.²⁵ Each item is assessed on chronicity (≥ 6 months), and perceived stressfulness (“not very,” “moderately,” “very”). A binary variable was generated to reflect whether there was at least one stressor with a minimum of six months’ duration that was

perceived to be moderately or very stressful.²⁶ Scores have been shown to be associated with chronic stress, depression, and anxiety.²⁶

Statistical Analysis

The data was managed and analyzed with RStudio Version 3.5.3. Descriptive statistics on demographic variables, physical risk factors, and behavioral risk factors were presented by sex and binary stroke outcome using means/standard deviations for continuous variables and counts/percentages for categorical variables. Differences by sex and binary stroke outcome were assessed using t-tests for continuous variables and Pearson's chi-square tests for categorical variables. Sex, employment status, hypertension, diabetes, severe chest pain, exposure to secondhand smoke, and the presence of at least one major stressor were treated as binary variables. Depression; dietary intake of vegetables, fruits, and fats; smoking; and alcohol use were treated as continuous variables. Ethnicity, education, annual income, BMI, and physical activity were treated as categorical variables. Age was presented as both a continuous and categorical variable.

Logistic regression models were developed hierarchically showing unadjusted results, adjustment for demographic variables, and adjustment for physical/behavioral risk factors. Crude (unadjusted) logistic regression was used to quantify the association of self-reported stroke symptoms (binary dependent variable) and individual demographic characteristics (sex, age [categorical], ethnicity, education, annual income, employment status, marriage status) as well as individual physical (BMI, hypertension, diabetes, severe chest pain lasting at least half an hour, depression) and behavioral (fruit/vegetable/fat consumption, smoking, exposure to secondhand smoke, alcohol use, physical activity, stress) risk factors. Multivariate logistic regression was then used to assess the association between self-reported stroke symptoms and individual physical and behavioral risk factors, adjusting for all demographic characteristics (age adjusted as a continuous variable). The full model for association between stroke symptoms and risk factors included all variables and age as a categorical variable, but exposure to secondhand smoke was excluded due to collinearity between variables and inability of models to converge. Results presented include crude and adjusted odds ratios (OR), 95% confidence intervals (CI), and p-values. For our analysis, $p < 0.05$ was considered a statistically significant association, and results of $0.05 \leq p < 0.1$ were considered of marginal significance.

RESULTS

Socio-demographic Characteristics and Risk Factors of Participants by Gender

Among 1,073 study participants, the mean age was 40.5 (SD=16.4) years and 58.4% were female. The ethnicity of 49.1% of participants was Newar, and 27.8% were Brahmin or Chhetri. Table 1 highlights the differences in socio-demographic variables based on sex. While there were no significant differences in age, ethnicity, or marital status, there were sex differences in education level, employment, and annual income. Women were significantly more likely to have less education than men, with 41.9% of women having no formal education compared to 17.3% of men ($p<0.0001$). Men were significantly more likely to be employed than women (33.6% vs 7.3%) ($p<0.0001$). However, women in this study were more likely to be in school, with 49.9% compared to 2.0% of men. Women were also significantly more likely to have lower income than men, with 78.0% of women earning an annual income of less than \$500 USD compared to 47.5% of men ($p<0.0001$).

Table 2 presents the differences in physical risk factors based on sex. In the study population, 56.9% had normal BMI, 6.0% were underweight, 29.4% were overweight, and 7.7% were obese. Only 1.9% of the participants had self-reported diabetes and 2.4% had previously experienced chest pain that lasted for at least half an hour. Women were significantly less likely to have hypertension (23.1%) than men (39.5%) ($p<0.0001$). CES-D scores were significantly different between sexes, with women more likely to have mild and severe depressive symptoms than men ($p=0.03$).

Table 3 highlights the differences in behavioral risk factors based on sex. There were significant differences in smoking status, exposure to secondhand smoke, drinking status, physical activity, and stress. On average, study participants consumed 11.5 portions of vegetables per week (SD=8.6), 12.2 portions of fruits (SD=7.2), and 5.3 portions of fats (SD=5.1). Women were significantly more likely to have never smoked (78.9% vs 51.8%) and men were more likely to be current smokers (35.7% vs 14.2%) ($p<0.0001$). Men were also significantly more likely to have been exposed to secondhand smoke than women (31.6% vs 11.5%) ($p<0.0001$) and be current drinkers, with 29.6% of the men drinking over 3 glasses per week compared to 7.8% of women ($p<0.0001$). Men were more likely to have higher net MET-

min per week than women ($p=0.007$), and women were significantly more likely to have at least one major stressor in their lives ($p=0.03$).

Self-Reported Stroke Symptoms

A total of 126 individuals in the study (11.7%) had at least one self-reported stroke symptom from the QVSFS. Differences in socio-demographic variables based on self-reported stroke symptoms (Table 4) revealed significant differences in sex, age, education, employment, and annual income. Women were significantly more likely to report stroke symptoms ($p<0.0001$). While the average age of individuals with no self-reported stroke symptoms was 39.2 (SD=16.0), the average age of individuals with self-reported stroke symptoms was 50.1 (SD=16.4) ($p<0.0001$). The majority of individuals who did not report any stroke symptoms were under age 40, but among those who reported stroke symptoms, the majority were in the 40-49 (27.8%), 50-64 (25.4%), and 65 and over (23.0%) age categories ($p<0.0001$). Over half of individuals who reported stroke symptoms had no formal education (57.1%) compared to 28.3% of individuals without stroke symptoms ($p<0.0001$), and 8.7% were employed compared to 19.5% among individuals without stroke symptoms ($p<0.0001$). Those who reported having stroke symptoms were also significantly more likely to have a lower annual income ($p=0.02$).

Tables 5 and 6 highlight the differences in physical and behavioral risk factors based on self-reported stroke symptoms. Individuals with stroke symptoms were significantly more likely to have hypertension ($p=0.01$), diabetes ($p=0.002$), and a history of experiencing at least half an hour of chest pain ($p=0.0008$) than individuals without stroke symptoms. Additional significant differences were found in depression, diet, smoking status, exposure to secondhand smoke, physical activity, and stress. Severe depressive symptoms were significantly more common among individuals with stroke symptoms (11.1%) than individuals without stroke symptoms (3.5%) ($p=0.0002$). Weekly portions consumed of vegetables ($p=0.0004$) and fats ($p=0.0002$) were significantly lower among individuals who reported stroke symptoms while fruit consumption was marginally lower ($p=0.08$). A higher portion of individuals had never smoked (69.3%) among those with no stroke symptoms than among those with stroke symptoms (55.6%), and there were significantly more former smokers among those with stroke symptoms (18.3% vs 8.0%) ($p=0.0003$). Individuals with self-reported stroke symptoms were significantly

more likely to be exposed to secondhand smoke ($p=0.004$), have less physical activity per week ($p=0.005$), and have at least one major life stressor ($p<0.0001$).

Major risk factors for stroke symptoms

Table 7 presents the results from unadjusted logistic regression analysis of individual demographic, physical risk factor, and behavioral risk factor variables as predictors of stroke symptoms. In the unadjusted models, the presence of stroke symptoms was significantly associated with demographic variables of sex, age, ethnic group, education, and annual income. It was also marginally associated with unemployment. Notably, odds of stroke symptoms for females was 2.5 times higher than that for men ($p<0.0001$, 95% CI: 1.6, 3.9). The odds of stroke symptoms increased with increasing age categories, with individuals who were 65 or older having an odds 8.6 times that of individuals 18-29 years of age ($p<0.0001$, 95% CI: 4.4, 16.9). Being part of the Brahmin/Chhetri ethnic group was associated with an odds of stroke symptoms 1.6 times that of the Newari ethnic group ($p=0.03$, 95% CI: 1.1, 2.5). Individuals with no education had an odds of stroke symptoms 2.9 times that of those who received less than high school education ($p<0.0001$, 95% CI: 1.9, 4.3). Finally, those who made between \$500-1499 USD had an odds of stroke 0.4 times that of individuals who made less than \$500 USD ($p=0.007$, 95% CI: 0.2, 0.8).

In terms of physical risk factors, stroke symptoms were significantly associated with hypertension, diabetes, chest pain, and CES-D score. Hypertension was associated with a 64% higher odds of having stroke symptoms ($p=0.01$, 95% CI: 1.1, 2.4); diabetes with a 281% higher odds ($p=0.01$, 95% CI: 1.5, 9.8); and experiencing chest pain for at least half an hour with a 321% higher odds ($p=0.001$, 95% CI: 1.8, 9.7). While there was no significant association of mild depression with presentation of stroke symptoms, severe depression was associated with an odds of stroke symptoms 3.2 times that of those with no depressive symptoms ($p=0.0005$, 95% CI: 1.7, 6.3).

Evaluation of behavioral risk factors found that stroke symptoms were significantly associated with diet, smoking status, physical activity, and stress. Consumption of one more portion per week of vegetables was associated with a 3.9% lower odds of stroke symptoms ($p=0.004$, 95% CI: 0.9, 1.0) while consuming one more portion of fats was associated with a 4.7% lower odds ($p=0.04$, 95% CI: 0.9, 1.0). A history of smoking was associated with an odds

of stroke symptoms 2.8 times that of individuals who had never smoked ($p=0.0001$, 95% CI: 1.7, 4.8). High levels of physical activity, with 5000 or greater MET-min per week, was associated with a 69.1% lower odds of stroke symptoms ($p=0.001$, 95% CI: 0.2, 0.6) while the presence of at least one major life stressor was associated with a 195% higher odds ($p<0.0001$, 95% CI: 2.0, 4.4).

Table 8 presents results from multivariate logistic regression models adjusted for all demographic variables. After adjustment, hypertension, consumption of fats, and smoking status were no longer significantly associated with the outcome of stroke symptoms while BMI category and chest pain became marginally associated with the outcome. Self-reported diabetes, consumption of vegetables, and the presence of at least one major stressor remained significantly associated with presence of stroke symptoms in the same direction as the unadjusted models. However, in the partially adjusted model, mild depression became statistically significant with a 46.5% lower odds of stroke symptoms ($p=0.047$, 95% CI: 0.3, 1.0) and netting less than 500 MET-min per week of physical activity became associated with a 50% lower odds of stroke symptoms ($p=0.02$, 95% CI: 0.3, 0.9).

Table 9 presents results from the fully adjusted multivariate logistic regression model. Among demographic variables, sex and age remained statistically significant in the same direction as the unadjusted models, but ethnic group, education, and annual income were no longer significant. Employment as a predictor was only marginally significant. The odds of stroke symptoms among those age 65 or older was 5.9 times the odds among 18-29 year olds ($p=0.001$, 95% CI: 2.0, 17.3) compared to 8.6 in the unadjusted model. Additionally, in the fully adjusted model, the previously significant associations between physical risk factors and stroke symptoms were no longer present. Instead, being obese ($BMI \geq 30$) was associated with an odds of stroke symptoms 0.3 times that of individuals with normal weight ($p=0.03$, 95% CI: 0.1, 0.9). Finally, the behavioral risk factor of smoking status was no longer significant, and dietary consumption was only marginally associated with presence of stroke symptoms. In the full model, only the highest level of physical activity with 5000 or greater MET-min per week was statistically significant and associated with a 75.8% lower odds of stroke symptoms ($p=0.001$, 95% CI: 0.1, 0.5). The presence of at least one major life stressor was associated with 113%

higher odds ($p=0.003$, 95% CI: 1.3, 3.5) of stroke symptoms compared to the 195% higher odds in the unadjusted model.

DISCUSSION

Prevalence of stroke symptoms

This analysis of the DHS dataset of adults aged 18 and older found a prevalence of stroke symptoms of 11.7%. Historically, Nepal has had no population-based studies on prevalence of stroke in the general population.³² According to a 2012 systematic review, in neighboring South Asian countries the prevalence estimates ranged from 0.8% in India to 21.8% in Pakistan, which included TIAs.³² However, studies in the review had various limitations including non-rigorous epidemiologic design, differing case definitions, differing instruments, and differing methods of sampling that may have resulted in inaccurate estimates.³² In the United States (US), the overall prevalence of stroke in 2010 was estimated by the Centers for Disease Control and Prevention (CDC) to be 2.6%; the prevalence of TIA symptoms in adults was approximately 2.3%.^{33,34} Combined, the prevalence of stroke symptoms in the US, which includes TIA symptoms, was approximately 4.9%. The results of this study suggest that Nepal may have a prevalence of stroke and TIA two times that of the US. While LMICs are known to have overall stroke incidence rates exceeding that of incidence rates seen in high-income countries by 20%, this study suggests that Nepal has a higher burden of stroke and TIA in the general population than expected.³⁵

Risk factors for stroke symptoms

The fully adjusted model showed that risk factors significantly associated with stroke symptoms were sex, age, and the presence of at least one major life stressor. Unemployment was also marginally associated with a higher odds of stroke symptoms. Unemployment was an unsurprising risk factor given that experiencing at least one spell of unemployment was associated with higher risks of stroke incidence and mortality in Japan.⁴⁷ Increasing age is also a well-known risk factor for stroke, with incidence doubling each decade after the age of 45 years and over 70% of all strokes occurring above the age of 65.⁴⁶ However, the average age of stroke in the DHS dataset was relatively young at 50 years. Over 20% of individuals exhibiting stroke

symptoms were under age 40, and only 23% were age 65 or older, suggesting that Nepal's burden of stroke is skewed towards younger populations compared to the global burden.

In contrast with the aforementioned known risk factors, the evidence linking chronic stress with stroke has not been fully established despite demonstrated association between stress and cardiovascular disease.⁴⁸ While stressful habits such as high consumption of energy-providing beverages is associated with high risk of stroke, and individuals with high stress intensity have a doubled risk of fatal stroke, one study found no evidence of stress having an impact on nonfatal strokes.^{48,49} However, a case-control study conducted in Spain provided evidence that increased levels of stress in the past year is strongly associated with an almost four-fold odds of stroke.⁴⁸ The hypothesis for the association between stress and stroke is that chronic stress can increase cerebrovascular disease risk by affecting blood pressure reactivity, cerebral endothelium, coagulation, or heart rhythm.⁵⁰ This study provides further evidence that chronic stress may a risk factor for stroke, particularly in LMICs. This association with stress could not be explained by the high prevalence of hypertension in the study population because the presence of at least one major life stressor was not associated with hypertension in the analysis.

Interestingly, the significantly higher odds of stroke symptoms in the DHS associated with being female does not align with global trends. Globally as of 2013, there were no significant differences between sexes in the proportion of stroke burden (in DALYs) although a greater portion of the burden in men could be attributed to behavioral risk factors.³⁶ Worldwide, stroke is more common among men although women have more 1-month case fatalities.³⁹ However, among DHS study participants, 76.2% of individuals with stroke symptoms were female and even after adjustment for all variables in the fully adjusted model, the odds of stroke symptoms for females was 2.7 times that of men. While this data suggests that women in Nepal have a higher burden of stroke symptoms, there have been no other studies conducted that reflect this association. One hospital-based study on stroke at Kathmandu Medical College Teaching Hospital found that 39.5% of patients who presented with stroke were female.¹² Another hospital-based study of 150 CT-confirmed stroke cases found that 30% were female.⁵⁷ While a separate retrospective hospital study reported stroke being more common in females by a factor of 2.6, it may have been biased due to lack of use of CT scanning and exclusion of TIA cases.⁵⁷ Lower rates of education in women may be associated with lower health literacy and difficulty

understanding survey questions, leading to potentially inaccurate estimates of stroke symptoms and other health issues. Symptoms of moderate and severe depression in women was also found to be highly correlated with report of chest pain ($R = 0.27$), suggesting possible somatization of psychological concerns. Other possible explanations for the difference between this study's results and existing literature may be that women in Nepal have lower access to care or conduct less care-seeking behavior. Women in Nepal have long faced social and legal discrimination beginning at birth that place their long-term health at risk.⁵⁸ Beyond issues such as having high maternal mortality rates, women face social restrictions that contribute to lack of perceived autonomy, lack of social support, and increased psychological morbidity, all of which may be risk factors that could not be accounted for in the variables included in the logistic regression models.⁵⁹

The fully adjusted model also showed that a high level of physical activity was a significant protective factor for stroke symptoms. There is substantial evidence that supports moderate and high levels of activity being associated with a 25% lower risk of stroke incidence compared to inactivity.⁵¹ This is due to physical activity favorably modifying stroke risk factors including hypertension, diabetes, and obesity.⁵⁴ The literature suggests that physical activity intensity needs to be moderate to vigorous for men for maximum benefit, compared to women who benefit most from long durations of low to moderate intensity activities.⁵¹ Differences between intensity of exercise was not evaluated in this study, but clarifying which types of physical activity would be most beneficial to reducing stroke risk in the Nepalese population can allow healthcare providers to promote physical activity in primary and secondary prevention of stroke, as well as rehabilitation.⁵³

Obesity was also found to be associated with a reduced risk of stroke symptoms, a finding not consistent with current literature. According to the literature, both overweight and obesity increase risk of stroke with a J-shaped dose-response relation.⁵⁵ There is an obesity paradox in stroke in which mortality and number of recurrent strokes is lower in obese stroke patients compared to normal weight patients, but that would bias results towards obesity being a risk factor rather than a protective factor.⁵⁶ That obesity was a protective factor in this dataset may be explained by the QVSFS having a higher negative predictive value than positive predictive value, therefore being better at identifying stroke-free individuals than individuals

with stroke or TIA.¹⁶ An alternate explanation is that obesity simply reflects more wealth, better access to food, and better socioeconomic status than those that are underweight in this low income country. The study participants categorized as having symptoms of stroke may not be reflective of the actual distribution of stroke in the general Nepalese population.

The same rationale, as well as collinearity between variables, may explain why other traditional behavioral and metabolic risk factors were not significant in this study's fully adjusted logistic regression model. According to the 2013 Global Burden of Disease (GBD) Study, behavioral risk factors such as smoking, poor diet, and low physical activity were the primary cause of stroke burden; metabolic factors such as hypertension and high BMI were the second largest contributors to DALYs.³⁶ In one of Nepal's hospital-based studies, stroke was more likely to occur among individuals who exhibited common risk factors like hypertension, smoking, and diabetes.¹² The estimate of hypertension prevalence in the DHS (29.9%) is aligned with previous study estimates; it is higher than in surrounding South Asian countries and similar to the prevalence in the US.^{61,62} However, none of these metabolic variables proved to be significant risk factors in the fully adjusted model. While being a former smoker was a significant risk factor in the bivariate logistic regression model, it became non-significant after adjusting for demographic variables, likely due to its strong correlation with sex (6.9% of women vs. 12.6% of men). Similarly, many metabolic risk factors like hypertension, diabetes, and chest pain were significant in bivariate logistic regression models but not in the fully adjusted model, likely due to collinearity between metabolic and other variables such as physical exercise.⁴⁴

Finally, South Asian countries are known to have nontraditional risk factors for stroke such as water-pipe use, desi ghee (a type of fat), chewable tobacco, and infectious causes of stroke.¹¹ While this study did not consider all of these nontraditional risk factors, it found that dietary variables—consumption of vegetables, fruits, and fats (which included desi ghee)—were associated with a lower odds of stroke symptoms in the unadjusted model. After adjusting for demographic variables, only higher consumption of vegetables was associated with a lower odds of stroke symptoms. This suggests that greater access to foods such as fruits and fats may be indicative of higher household wealth or socioeconomic standing, which are protective against stroke.⁴⁵ Given that 6% of adults over age 18 in the DHS dataset were underweight, and that malnutrition is considered a silent crisis in parts of Nepal, access to certain foods may be a

privilege for wealthier households.⁵² This also provides an explanation for why obesity was considered a protective factor in this dataset despite the current understanding of obesity as a risk factor for stroke. Ethnicity, which may also be an indicator for household wealth, was not a risk factor in the fully adjusted model. However, in the bivariately adjusted model, Brahmin/Chhetri had a significantly higher odds of stroke compared to Newars, which is interesting because both ethnic groups are considered to be affluent.¹⁵ This association could not be explained by collinearity with other variables and may require further research.

Strengths and Limitations

To our knowledge, this is the first study providing population-level analysis of risk factors of stroke symptoms within the general Nepalese population. The random sampling technique to recruit adults in a community setting, large sample size, and detailed collection of information on demographic and clinical risk factors using standardized and validated study instruments are major strengths of the study. The study was conducted by local Nepalese surveyors who could communicate in Nepalese and translate difficult health concepts to individuals with low health literacy, strengthening the results of the data collection. Given that the majority of Nepalese patients suffering from stroke and other neurological disorders such as epilepsy often ascribe their conditions to the wrath of God and turn to traditional healers, using the QVSFS to ascertain information about stroke symptoms rather than self-reporting stroke status gives strength to the study's estimates.¹⁰

However, the study also has many limitations. Due to using observational, cross-sectional data from the DHS study, conclusions about the major risk factors for stroke in Nepal are limited to drawing inference about correlation and not causation. Exclusion of individuals unable to respond due to inability to communicate in Nepali or Newari language may have biased results by not collecting records on individuals who exhibit aphasia or dysarthria—two language disorders that may result from stroke. Furthermore, due to many variables being self-reported responses, there is a potential for inaccurate reporting (i.e. age) or biased responses due to stigma around a disease, for example depression. Self-reported stroke symptoms may also be an inaccurate indicator of the presence of stroke due to potential inaccuracies in the QVSFS and the lack of neurologist evaluation or neuroimaging, which are far more reliable methods to confirm stroke. Furthermore, while the study participants were randomly selected, the sample may not be

fully representative of the underlying population of Dhulikhel and is certainly not an accurate representation of the larger country of Nepal. Therefore, any inferences drawn from this study may not be generalizable to other regions of Nepal such as rural communities.

Several additional factors could have strengthened this study's conclusions. The 2013 GBD Study highlighted that reducing exposure to air pollution should be one of the priorities to reduce stroke burden, especially in LMICs.³⁶ Given that environmental factors were the third largest contributors to DALYs, analysis of environmental risk factors in the DHS dataset would have been beneficial to better understand risk factors for stroke symptoms. While the DHS collected household-level data on fuel used for cooking—one of the contributors to household air pollution—there was too much missing data to use the variable in the analysis.⁴³ At the country level, Nepal resumed air quality monitoring at multiple sites in Nepal in mid-2016, seven years after previous monitoring stations were closed, and this continuous data on particulate matter and other air pollutants may be used for future analysis of air pollution as a stroke risk factor.^{41,42}

Finally, the study did not distinguish between hemorrhagic stroke, which is caused by bleeding, and ischemic stroke, which is caused by blockage of an artery, but the different categories of stroke have differing etiologies and prevalences.⁴⁰ A retrospective study of stroke patients in a Kathmandu University found that 63% of patients experienced ischemic stroke while 37% experienced hemorrhagic.¹⁰ In a Nepalese hospital-based study, active smokers were found to be more at risk of hemorrhagic stroke and diabetic patients for ischemic stroke.¹² Understanding the different risk factors for each type of stroke could allow the government and healthcare facilities to better direct resources for care and prevention.

Conclusions

Major issues with stroke in South Asia include lack of rigorous studies into stroke risk factors, limited access to tertiary stroke care, low awareness of stroke risk factors and management by the public and caregivers, and the lack of interests in addressing stroke from governments.¹¹ As of 2012, there were approximately 10 registered neurologists in Nepal, and most advanced healthcare facilities were located in Kathmandu, Nepal's capital, causing rural patients needing to travel three or four days to reach the nearest primary healthcare centers.¹⁰ Promisingly, Nepal has made a commitment to tackling NCDs in its Multisectoral Action Plan on the Prevention and Control of NCDs 2014-2020 as well as its prioritization of universal health

coverage in the country's 2018/19 healthcare budget.⁶⁰ The results of this study confirm the high burden of stroke symptoms and risk factors within the country. Further prospective longitudinal studies are needed to verify these results and provide data to monitor trends in stroke and other chronic disease risk factors with the long-term goal of strengthening the country's ability to prevent and respond to the growing burden of non-communicable diseases such as stroke during the country's epidemiological transition.

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APPENDIX

Table 1: Demographic variables by sex

	Female	Male	
	n (%) or Mean (SD)	n (%) or Mean (SD)	p-value
n	627	446	
Reported Age in Years (mean (SD))	40.15 (16.34)	40.87 (16.59)	0.50
Categorical Age in Years (%)			0.88
18-29	208 (33.2)	142 (31.8)	
30-39	111 (17.7)	77 (17.3)	
40-49	141 (22.5)	95 (21.3)	
50-64	108 (17.2)	87 (19.5)	
≥ 65	59 (9.4)	45 (10.1)	
Ethnicity (%)			0.28
Newar	313 (49.9)	214 (48.0)	
Brahmin/Chhetri	163 (26.0)	135 (30.3)	
Other	151 (24.1)	97 (21.7)	
Education (%)			<0.0001
Less than high school	238 (38.0)	240 (53.8)	
No formal education	263 (41.9)	77 (17.3)	
High school or more	126 (20.1)	129 (28.9)	
Unemployed (%)	268 (42.7)	287 (64.3)	<0.0001
Employed	46 (7.3)	150 (33.6)	
In school	313 (49.9)	9 (2.0)	
Annual Income in USD (%)			<0.0001
< 500	489 (78.0)	212 (47.5)	
500-1499	87 (13.9)	100 (22.4)	
1500-1999	19 (3.0)	70 (15.7)	
≥2000	32 (5.1)	64 (14.3)	
Not married (%)	182 (29.0)	107 (24.0)	0.08

Table 2: Physical risk factor variables by sex

	Female	Male	
	n (%)	n (%)	p-value
n	627	446	
BMI (%)			0.09
18.5 – 24.9	346 (55.2)	265 (59.4)	
< 18.5	36 (5.7)	28 (6.3)	
25.0 – 29.9	186 (29.7)	129 (28.9)	
≥ 30	59 (9.4)	24 (5.4)	
Hypertension (%)	145 (23.1)	176 (39.5)	<0.0001
Self-Reported Diabetes (%)	11 (1.8)	9 (2.0)	0.41
Missing data	234 (37.3)	149 (33.4)	
Chest pain for half an hour (%)	19 (3.0)	7 (1.6)	0.18
CES-D Score (%)			0.03
<16: No depressive symptoms	476 (75.9)	369 (82.7)	

16-20: Mild depressive symptoms	119 (19.0)	62 (13.9)	
≥ 21: Severe depressive symptoms	32 (5.1)	15 (3.4)	

Table 3: Behavioral risk factor variables by sex

	Female	Male	
	n (%) or Mean (SD)	n (%) or Mean (SD)	p-value
n	627	446	
Number of weekly portions			
Vegetables (mean (SD))	11.63 (8.84)	11.25 (8.24)	0.50
Fruits (mean (SD))	12.37 (7.56)	12.05 (6.53)	0.50
Fats (mean (SD))	5.40 (5.27)	5.23 (4.79)	0.60
Smoking Status (%)			<0.0001
Never smoked	495 (78.9)	231 (51.8)	
Former smoker	43 (6.9)	56 (12.6)	
Current smoker	89 (14.2)	159 (35.7)	
Exposure to Secondhand Smoke (%)	72 (11.5)	141 (31.6)	<0.0001
Missing data	495 (78.9)	231 (51.8)	
Drinking Status (%)			<0.0001
None	506 (80.7)	229 (51.3)	
< 1 glass per week	52 (8.3)	46 (10.3)	
1-3 glasses per week	20 (3.2)	39 (8.7)	
> 3 glasses per week	49 (7.8)	132 (29.6)	
MET-min per week (%)			0.007
500 – 999	83 (13.2)	37 (8.3)	
< 500	244 (38.9)	152 (34.1)	
1000– 4999	159 (25.4)	136 (30.5)	
≥ 5000	141 (22.5)	121 (27.1)	
Presence of at least 1 major stressor (%)	135 (21.5)	71 (15.9)	0.03

Table 4: Demographic variables by self-reported stroke symptom status

	No stroke symptoms	Positive stroke symptoms	
	n (%) or Mean (SD)	n (%) or Mean (SD)	p-value
n	947	126	
Sex			<0.0001
Female	531 (56.1)	96 (76.2)	
Male	416 (43.9)	30 (23.8)	
Reported Age in Years (mean (SD))	39.16 (16.0)	50.14 (16.4)	<0.0001
Categorical Age in Years (%)			<0.0001
18-29	335 (35.4)	15 (11.9)	
30-39	173 (18.3)	15 (11.9)	
40-49	201 (21.2)	35 (27.8)	
50-64	163 (17.2)	32 (25.4)	
≥ 65	75 (7.9)	29 (23.0)	
Ethnicity (%)			0.08

Newar	476 (50.3)	51 (40.5)	
Brahmin/Chhetri	251 (26.8)	44 (34.9)	
Other	217 (22.9)	31 (24.6)	
Education (%)			<0.0001
Less than high school	437 (46.1)	41 (32.5)	
No formal education			
High school or more			
Unemployed (%)			<0.0001
Employed	268 (28.3)	72 (57.1)	
In school	242 (25.6)	13 (10.3)	
Annual Income in USD (%)	499 (52.7)	56 (44.4)	0.02
< 500	604 (63.8)	97 (77.0)	
500-1499	175 (18.5)	12 (9.5)	
1500-1999	80 (8.4)	9 (7.1)	
≥2000	88 (9.3)	8 (6.3)	
Not married (%)	260 (27.5)	29 (23.0)	0.34

Table 5: Physical risk factor variables by self-reported stroke symptom status

	No stroke symptoms	Positive stroke symptoms	
	n (%)	n (%)	p-value
n	947	126	
BMI (%)			0.43
18.5 – 24.9	532 (56.2)	79 (62.7)	
< 18.5	59 (6.2)	5 (4.0)	
25.0 – 29.9	280 (29.6)	35 (27.8)	
≥ 30	76 (8.0)	7 (5.6)	
Hypertension (%)	271 (28.6)	50 (39.7)	0.01
Self-Reported Diabetes (%)	13 (1.4)	7 (5.6)	0.002
Missing data	347 (36.6)	36 (28.6)	
Chest pain for half an hour (%)	17 (1.8)	9 (7.1)	0.0008
CES-D Score (%)			0.0002
<16: No depressive symptoms	747 (78.9)	98 (77.8)	
16-20: Mild depressive symptoms	167 (17.6)	14 (11.1)	
≥ 21: Severe depressive symptoms	33 (3.5)	14 (11.1)	

Table 6: Behavioral risk factor variables by self-reported stroke symptom status

	No stroke symptoms	Positive stroke symptoms	
	n (%) or Mean (SD)	n (%) or Mean (SD)	p-value
n	947	126	
Number of weekly portions			
Vegetables (mean (SD))	11.76 (8.78)	9.37 (6.66)	0.0004
Fruits (mean (SD))	12.34 (7.39)	11.44 (4.95)	0.08
Fats (mean (SD))	5.44 (5.28)	4.46 (2.99)	0.002
Smoking Status (%)			0.0003

Never smoked	656 (69.3)	70 (55.6)	
Former smoker	76 (8.0)	23 (18.3)	
Current smoker	215 (22.7)	33 (26.2)	
Exposure to Secondhand Smoke (%)	182 (19.2)	31 (24.6)	0.004
Missing data	656 (69.3)	70 (55.6)	
Drinking Status (%)			0.80
None	646 (68.2)	89 (70.6)	
< 1 glass per week	85 (9.0)	13 (10.3)	
1-3 glasses per week	53 (5.6)	6 (4.8)	
> 3 glasses per week	163 (17.2)	18 (14.3)	
MET-min per week (%)			0.005
500 – 999	98 (10.3)	22 (17.5)	
< 500	344 (36.3)	52 (41.3)	
1000 – 4999	260 (27.5)	35 (27.8)	
≥ 5000	245 (25.9)	17 (13.5)	
Presence of at least 1 major stressor (%)	159 (16.8)	47 (37.3)	<0.0001

Table 7: Odds ratios from unadjusted logistic regression models

Variable	Odds Ratio	95% Confidence Interval	p-value
Demographic Variables			
Sex			
Male (reference)	---	---	
Female	2.507	(1.63, 3.85)	<0.0001
Categorical Age in Years			
18-29 (reference)	---	---	
30-39	1.936	(0.93, 4.05)	0.08
40-49	3.889	(2.07, 7.30)	<0.0001
50-64	4.384	(2.31, 8.33)	<0.0001
≥65	8.636	(4.41, 16.90)	<0.0001
Ethnic group			
Newar (reference)	---	---	
Brahmin/Chhetri	1.617	(1.05, 2.49)	0.03
Other	1.333	(0.83, 2.14)	0.24
Education			
Less than high school (reference)	---	---	
No education	2.863	(1.90, 4.33)	<0.0001
High school or more	0.573	(0.30, 1.09)	0.09
Unemployment	1.887	(0.97, 3.68)	0.06
Annual Income in USD			
<500 (reference)	---	---	
500-1499	0.427	(0.23, 0.80)	0.007
1500-1999	0.701	(0.34, 1.44)	0.33
≥2000	0.566	(0.27, 1.20)	0.14
Not married	0.790	(0.51, 1.23)	0.29
Physical risk factors			
BMI Category			

18.5-24.9 (reference)	---	---	
<18.5	0.571	(0.22, 1.47)	0.24
25.0-29.9	0.842	(0.55, 1.29)	0.43
≥30	0.620	(0.28, 1.39)	0.25
Hypertension	1.641	(1.12, 2.41)	0.01
Self-Reported Diabetes	3.808	(1.48, 9.82)	0.01
Chest pain for half an hour	4.208	(1.83, 9.66)	0.001
CES-D Score			
<16: No depressive symptoms (reference)	---	---	
16-20: Mild depressive symptoms	0.639	(0.36, 1.15)	0.13
≥21: Severe depressive symptoms	3.234	(1.67, 6.25)	0.0005
Behavioral risk factors			
Dietary consumption (portion per week)			
Vegetables	0.961	(0.94, 0.99)	0.004
Fruits	0.982	(0.96, 1.01)	0.19
Fats	0.953	(0.91, 0.998)	0.04
Smoking Status			
Never smoked (reference)	---	---	
Former smoker	2.836	(1.67, 4.81)	0.0001
Current smoker	1.438	(0.93, 2.24)	0.11
Exposure to Secondhand Smoke	0.743	(0.42, 1.32)	0.31
Drinking Status			
None (reference)	---	---	
< 1 glass per week	1.110	(0.60, 2.07)	0.74
1-3 glasses per week	0.822	(0.34, 0.66)	0.66
> 3 glasses per week	0.802	(0.47, 0.42)	0.42
MET-min per week			
500 – 999 (reference)	---	---	
< 500	0.673	(0.39, 1.16)	0.16
1000 – 4999	0.600	(0.34, 1.07)	0.09
≥ 5000	0.309	(0.16, 0.61)	0.001
Presence of at least 1 major stressor (%)	2.948	(1.98, 4.40)	<0.0001

Table 8: Odds ratios from multivariate logistic regression models adjusting for all demographic variables—sex, reported age (continuous), ethnic group, education level, unemployment status, annual income in USD (categorical), and marriage status

Variable	Odds Ratio	95% Confidence Interval	p-value
Physical risk factors			
BMI Category			
18.5-24.9 (reference)	---	---	
<18.5	0.379	(0.14, 1.04)	0.06
25.0-29.9	0.787	(0.50, 1.25)	0.31
≥30	0.442	(0.19, 1.05)	0.07
Hypertension	1.426	(0.90, 2.26)	0.13
Self-Reported Diabetes	2.957	(1.02, 8.56)	0.046
Chest pain for half an hour	2.212	(0.91, 5.36)	0.08

CES-D Score			
<16: No depressive symptoms (reference)	---	---	
16-20: Mild depressive symptoms	0.535	(0.29, 0.99)	0.047
≥21: Severe depressive symptoms	2.182	(1.05, 4.54)	0.04
Behavioral risk factors			
Dietary consumption (portion per week)			
Vegetables	0.965	(0.94, 0.99)	0.01
Fruits	1.006	(0.98, 1.04)	0.67
Fats	0.984	(0.94, 1.03)	0.47
Smoking Status			
Never smoked (reference)	---	---	
Former smoker	1.671	(0.87, 3.21)	0.12
Current smoker	1.204	(0.72, 2.03)	0.49
Exposure to Secondhand Smoke	1.050	(0.54, 2.05)	0.89
Drinking Status			
None (reference)	---	---	
< 1 glass per week	1.475	(0.74, 2.96)	0.27
1-3 glasses per week	1.232	(0.48, 3.16)	0.66
> 3 glasses per week	1.095	(0.57, 2.11)	0.79
MET-min per week			
500 – 999 (reference)	---	---	
< 500	0.500	(0.28, 0.91)	0.02
1000 – 4999	0.588	(0.31, 1.10)	0.098
≥ 5000	0.249	(0.12, 0.52)	0.0002
Presence of at least 1 major stressor (%)	1.964	(1.27, 3.05)	0.003

Table 9: Odds ratios from a fully adjusted multivariate logistic regression model

Variable	Odds Ratio	95% Confidence Interval	p-value
Demographic Variables			
Sex			
Male (reference)	---	---	
Female	2.693	(1.40, 5.19)	0.003
Categorical Age in Years			
18-29	---	---	
30-39	2.378	(0.98, 5.75)	0.05
40-49	4.416	(1.84, 10.62)	0.001
50-64	4.043	(1.54, 10.64)	0.005
≥ 65	5.893	(2.01, 17.26)	0.001
Ethnic group			
Newar (reference)	---	---	
Brahmin/Chhetri	1.536	(0.83, 2.85)	0.17
Other	1.303	(0.66, 2.57)	0.45
Education			
Less than high school (reference)	---	---	
No education	1.060	(0.59, 1.92)	0.85
High school or more	1.128	(0.51, 2.52)	0.77

Unemployment	2.093	(0.95, 4.60)	0.07
Annual Income in USD			
<500 (reference)	---	---	
500-1499	0.705	(0.35, 1.42)	0.33
1500-1999	1.587	(0.67, 3.79)	0.30
≥2000	1.293	(0.52, 3.21)	0.58
Not married	0.922	(0.52, 1.65)	0.79
Physical risk factors			
BMI Category			
18.5-24.9 (reference)	---	---	
<18.5	0.389	(0.13, 1.13)	0.08
25.0-29.9	0.641	(0.39, 1.07)	0.09
≥30	0.346	(0.14, 0.89)	0.03
Hypertension	1.372	(0.82, 2.30)	0.23
Self-Reported Diabetes	1.804	(0.56, 5.81)	0.32
Chest pain for half an hour	2.108	(0.81, 5.48)	0.13
CES-D Score			
<16: No depressive symptoms	---	---	
16-20: Mild depressive symptoms	0.556	(0.27, 1.13)	0.10
≥21: Severe depressive symptoms	2.031	(0.91, 4.54)	0.08
Behavioral risk factors			
Dietary consumption (portion per week)			
Vegetables	0.962	(0.92, 1.00)	0.05
Fruits	1.036	(0.99, 1.08)	0.09
Fats	0.998	(0.94, 1.06)	0.95
Smoking Status			
Never smoked (reference)	---	---	
Former smoker	1.458	(0.70, 3.03)	0.31
Current smoker	1.164	(0.64, 2.10)	0.62
Drinking Status			
None	---	---	
< 1 glass per week	1.005	(0.47, 2.17)	0.99
1-3 glasses per week	0.988	(0.35, 2.78)	0.98
> 3 glasses per week	1.139	(0.54, 2.40)	0.73
MET-min per week			
500 – 999 (reference)	---	---	
< 500	0.552	(0.29, 1.04)	0.07
1000 – 4999	0.571	(0.29, 1.11)	0.099
≥ 5000	0.242	(0.11, 0.54)	0.001
Presence of at least 1 major stressor (%)	2.134	(1.30, 3.51)	0.003