Determining rural risk for aneurysmal subarachnoid hemorrhages: A structural equation modeling approach

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ABSTRACT

An aneurysmal subarachnoid hemorrhage (aSAH) carries a high disability burden. The true impact of rurality as a predictor of outcome severity is unknown. Our aim is to clarify the relationship between the proposed explanations of regional and rural health disparities linked to severity of outcome following an aSAH. An initial literature search identified limited data directly linking geographical location, rurality, rural vulnerability, and aSAH. A further search noting parallels with ischemic stroke and acute myocardial infarct literature presented a number of diverse and interrelated predictors. This *a priori* knowledge informed the development of a conceptual framework that proposes the relationship between rurality and severity of outcome following an aSAH utilizing structural equation modeling. The presented conceptual framework explores a number of system, environmental, and modifiable risk factors. Socioeconomic characteristics, modifiable risk factors, and timely treatment that were identified as predictors of severity of outcome following an aSAH and within each of these defined predictors a number of contributing specific individual predictors are proposed. There are considerable gaps in the current knowledge pertaining to the impact of rurality on the severity of outcome following an aSAH. Absent from the literature is any investigation of the cumulative impact and multiplicity of risk factors associated with rurality. The proposed conceptual framework hypothesizes a number of relationships between both individual level and system level predictors, acknowledging that intervening predictors may mediate the effect of one variable on another.

Key words: Aneurysmal subarachnoid hemorrhage, rural vulnerability, structural equation modeling

Introduction

With a predicted 40% of case fatality aneurysmal subarachnoid hemorrhage (aSAH) is the most feared stroke event among clinicians. Affecting younger adults and individuals in their prime, the individual disability burden and consequential social impact is devastating. The severity of outcome, herein referred to as outcome, includes both functional and cognitive losses resulting in a loss of productive years for individuals

that were previously healthy and active.^[1,2] Classified as a hemorrhagic stroke and defined as extravasation of blood into the subarachnoid space following the rupture of a cerebral aneurysm, aSAH account for 5–10% of strokes.^[3] Despite shared risk with ischemic events aSAH are disengaged from general stroke epidemiological and clinics studies.^[4] This disengagement has resulted in less knowledge about predictors of incidence and outcome of aSAH, particularly in terms of rurality and any associated social determinants of health.

Low socioeconomic rural cohorts have a consistent pattern of both a higher incidence and increased

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mortality following vascular and cerebrovascular events.^[5,6] Differential health outcomes and increased mortality rates are suggested to be associated with a range of influences including lower socioeconomic status, impaired access to care, and poorer rural risk factor profiles.^[7] As a cerebrovascular event aSAH has been extensively linked to a number of modifiable risk factors including smoking and excessive alcohol consumption^[8,9] as well as increased risk-taking and the higher prevalence of modifiable risk factors.^[10,11] There has been a limited analysis of the complex phenomenon that is the cumulative impact and multiplicity of risk factors associated with rurality and outcome following an aSAH.

Current recommendations propose that ruptured aneurysms are secured as early as feasible to reduce the risk of secondary complications and increased mortality.^[12] At a system level, timely treatment is likely to be difficult to achieve for individuals residing in rural areas who through factors of distance alone are likely to face a number of delays. The impact of remoteness is more than the linear distance to services.^[13,14] While topography and transportation are important considerations, the cumulative impact of timely presentation, diagnosis, treatment, and inter-hospital transfers must be assessed. The proposed conceptual framework encapsulates how rurality exacerbates regional disparities associated with geographical location and access to health care.

Linking rurality, with a wider range of health status measures including individual risk factors, is vital to understanding the true impact of rurality on health outcomes.^[14] The previous research relating to aSAH has focused on the analysis of clinical variables, limiting our understanding of the potential social determinants of this disease. This review challenges this concept by proposing structural equation modeling (SEM) as a methodology to identify the direct and indirect hypothesized relationships while acknowledging mediating effects.

As a statistical method, SEM adopts a hypothesis testing approach enabling the multivariate analysis of identified covariates,^[15] and the proposed predictors of outcome including socioeconomic characteristics, modifiable risk factors, and timely treatment. Given, the complexity of rurality and the impact on health outcomes, SEM is proposed as a methodology for the multivariate analysis of proposed relationships and interrelationships of predictors and covariates set within a structural theory that is both rationalized and based on previous empirical findings.^[16,17] This knowledge is then transferred to a conceptual framework that is presented pictorially identifying proposed relationships and

interrelationships among proposed predictors.^[18] This review develops and presents a conceptual framework of rural vulnerability, based on the substantial theory this framework will form the empirical basis of the SEM.

Methods

This literature review has been undertaken as part of a large retrospective study explores the interplay of predictors influencing outcome following an aSAH for individuals residing outside metropolitan areas. While a number of definitions in the literature reflect rurality, this study acknowledges geographical classification in terms of environmental parameters and remoteness from population centers as reflecting rurality.

An initial search was conducted utilizing MEDLINE, PubMed, Proquest, and CINAHL electronic databases. The databases were searched utilizing a number and combination of terms including “subarachnoid hemorrhage, rurality, urban, rural, time to treatment, outcomes, risk factors, socioeconomic, and inter-hospital transfer.” Boolean operators were included to encompass a number of possible combinations of the search terms. Titles and abstracts were initially screened with 504 articles initially identified. Full-text copies of 242 articles were further reviewed with 72 articles that included subarachnoid hemorrhage and one or more of the search terms included in the final selection. Of the 72 articles, 15 were linked to individual and modifiable risk factors, 12 to system-level factors, 8 articles to socioeconomic factors, and only 3 articles specifically looked at aSAH and rural/urban considerations.

Articles were then individually assessed in terms of relevance on the basis of the title, keywords, and abstract. To ensure saturation, the reference lists were also searched to identify the additional publications. Earlier seminal works (pre 2000) were reviewed and included as required, and all articles were evaluated according to the following criteria:

- The article was in English, with a full text available and was either peer reviewed or published as reputable gray literature
- The article included some reference to health outcomes associated with rurality and/or factors associated with rurality that has been identified as potentially influencing outcome following an aSAH.

Analysis

From an initial broad search, a number of individual factors were identified within each of the proposed

predictors. The identified individual factors have all been reviewed in varying combinations within the literature in relation to the prevalence of vascular and cerebrovascular events. What is absent from the literature is how these individual factors impact on outcome following an event. That is, are there common or distinct factors that influence both prevalence and outcome? Due to the dearth of literature pertaining to the influence of rurality on outcome following an aSAH, relevant representative evidenced-based literature was reviewed noting parallels with ischemic stroke and acute myocardial infarction in terms of the impact of rurality on health outcomes. A conceptual framework including identified individual factors of outcome is shown in Figure 1. The framework is presented as a path diagram to enable a clearer conceptualization of the underlying theory that rurality does impact on outcome.

Ethics approval

The Tasmanian Health and Medical Human Research Ethics Committee approved this study in December 2014 (H0014563).

Results

Socioeconomic status

Poor prognosis and increased mortality rates following aSAH are associated with low socioeconomic status.^[19,20] Socioeconomic factors have been consistently identified as predictors of both the prevalence and outcome of cerebrovascular events.^[6,21] Socioeconomic variations are associated with shifting demographics, aging populations, and an increased prevalence of vascular risk factors,^[22] with Heeley *et al.*^[23] reporting an increased

risk ratio of 1.70 within low socioeconomic areas. Despite considerable geographical and social diversity within rural areas, aggregate level socioeconomic disproportions have been well-described with rural populations predominantly characterized by a low socioeconomic status.^[24-27] The presented model identifies socioeconomic status as potentially increasing the probability of a poor outcome following an aSAH.

Proposed explanations for health outcome differences associated with socioeconomic status include both health literacy and financial security.^[10,26] Within rural and regional settings, health literacy is proposed as a significant barrier to symptom recognition and early presentation to emergency care.^[28] Individuals fail to seek medical attention following a stroke due to both a lack of awareness of symptoms and failure to understand the significance of symptoms.^[29] While higher income and socioeconomic status is correlated with improved stroke knowledge, prehospital delays following an aSAH have not been studied in detail.^[30]

Income and employment have been associated with outcome in a number of stroke studies with both unemployment and low income identified as predictors of mortality.^[21,31] When specifically looking at aSAH, Jaja *et al.*^[32] further identified a significant inpatient mortality risk following an aSAH for those with low compared to higher socioeconomic status. However, this study, like many others, utilized median income at a postcode level as indicative of socioeconomic status. Despite evidence supporting the correlation of socioeconomic status and outcome, the factors mediating or interrelating with this effect to a large extent are unknown^[33] because

Figure 1: Conceptual framework

broad population-based registries may not adequately represent individual socioeconomic status. This warrants the analysis of socioeconomic status by identifying the individual factors of health literacy measures (such as presentation time and symptom awareness) as well as financial security (mainly reported health insurance status as well as the indicators of health literacy and financial security utilizing the socioeconomic indexes for areas).

Modifiable health risk factors

Modifiable risk factors and an underlying risk-taking culture are associated with a number of negative health outcomes.^[26,34] Smoking and hypertension are two of the leading causes of diseases burden in Australia.^[7] Consideration of both risk factors and risk-taking is imperative when considering rural disparities in health outcomes.^[10,11] A higher prevalence of modifiable risk factors in rural areas may in part explain the poor health outcomes following vascular and cerebrovascular events, including aSAH.^[23,26,35] This contributes to what Thorogood *et al.*^[36] described as an epidemic of vascular disease in rural areas. The proposed explanations of aSAH outcome related to modifiable risk factors include smoking status, hypertension, and patterns of alcohol consumption.^[37-40]

Hypertension is identified as the most important and common modifiable factor associated with cerebrovascular events including aSAH.^[7,29,41] Hypertension is an independent risk factor for both the severity of the initial hemorrhage and post aSAH complications.^[42-44] Hypertension is purported as being more common in rural areas with an estimated one-third of individuals residing in rural areas hypertensive. McLaughlin *et al.*^[45] identify that among women, there is a higher morbidity related to hypertension for women residing in outer and inner regional areas mainly due to modifiable risk factors. Janus *et al.*^[46] further note that suboptimal detection and treatment of hypertension within rural areas are of particular concern given the increased rates of cerebrovascular disease in rural areas.

Current smoking status is identified as the most significant risk factor for a fatal aSAH.^[41] Within rural and regional areas smoking has been linked to a number of poor health outcomes with Eberhardt and Pamuk^[26] predicting that future health disparities will be portended by a higher prevalence of smoking within rural areas. Smoking is a risk factor for both aneurysm formation and severity of outcome,^[47,48] with smoking linked to increased complications including vasospasm, delayed cerebral infarction as well as increased mortality.^[49,50]

Alcohol is identified to have a distinct dose relationship with aSAH secondary to transient peaks in systolic blood pressure.^[51,52] Excessive alcohol consumption is identified as a significant problem linked to rural health outcome.^[23,53] Alcohol is difficult to associate with aSAH given differing definitions, the questionable reliability of self-reporting as well as the transient effects of alcohol in terms of short- and long-term harm. Despite this, excessive alcohol consumption and/or daily intake of alcohol is associated with post aSAH complications, including an increased risk of mortality.^[41,49]

Timely treatment

Delayed and/or misdiagnosis, prolonged transfer times and inter-hospital transfers are key predictors of outcome following an aSAH.^[54-60] However, little is known relating the impact of rurality and health access as a direct determinant of outcome post aSAH.^[61] Regional disparities have been linked to distance from emergency services with Murata and Matsuda^[62] claiming that increased distance to hospital is associated with a significant risk of mortality following an aSAH. A broader view of explanations for health outcome differences associated with timely treatment includes access to neurosurgical expertise, presenting symptom recognition and triage, delayed/missed diagnosis, and inter-hospital transfers.

Rural emergency departments lack the experience and resources required to manage an aSAH.^[63,64] Access to neurosurgical services is linked with improved outcomes following an aSAH,^[55,56] but in small rural hospital initial evaluation and a critical period of stabilization will likely occur in the emergency department without this expertise. An increased availability of diagnostic imaging is also suggested to have a positive impact on the diagnosis of aSAH.^[65,66] However, within rural and regional hospitals, this availability does not always include appropriate radiologist services with experience in interpreting cerebral imaging.^[67] Physician led, rather than radiologist led, interpretation of imaging has previously been identified as a leading cause of diagnostic errors in emergency settings.^[68]

An estimated 12–50% of aSAH are misdiagnosed.^[57-59] Failure to recognize and appropriately triage, the classical headache presentation of an aSAH is associated with poor outcomes and increased mortality.^[69,70] Diagnosing aSAH is a clinical challenge, given its rarity the odds of misdiagnosis significantly increase in smaller centers where medical staff may not have ever encountered an aSAH.^[30,61] Individuals who present with mild symptoms are the most likely to be misdiagnosed;^[71] yet sadly these are the individuals most likely to benefit from timely treatment.^[69]

Inter-hospital transfers are also associated with increased complications with adverse events occurring in up to one-third of inter-hospital transfers.^[55,56,60] Despite this inter-hospital transfers are vital to access neurosurgical services that are not offered in smaller and rural hospitals.^[54] The majority of inter-hospital transfers occur during a time of medical instability. Despite an estimate of 2% risk of death during transfers,^[72] consideration of the imminent need for neurosurgical interventions and the potential for improved outcomes make transfers likely from rural and regional areas.

Covariates

Independently identified predictors of outcome following an aSAH must also be included as part of the model. These covariates are consistent across geographical locations and are fundamental to the severity of outcome following an aSAH. Older age, male sex, aneurysm size, and the severity of the initial bleed have been previously identified as predictors of outcome following an aSAH.^[55,73] These identified demographic and clinical covariates will be simultaneously considered when fitting the data and analyzing the final model. Females face an increased risk of aSAH, yet the prevalence of modifiable risk factors and poor outcomes is higher in men.^[74] Older age is identified as a predictor of poor outcome, perhaps reflecting the resilience of younger individuals and a superior ability for recovery posttraumatic events.^[44,75] Larger aneurysms, particularly those >10 mm, are associated with poor outcomes;^[76,77] however, the epidemiology of aneurysm size is relatively unknown. A clinical presentation including the presenting level of consciousness and the severity of initial symptoms is identified as the most important predictor of outcome following an aSAH.^[76-78] The inclusion of these identified covariates is fundamental for controlling bias and reducing the residual variance when analyzing the data.^[79]

Discussion

From this review, a conceptual framework of rural vulnerability has been developed, including the predictors of socioeconomic characteristics, modifiable risk factors, and timely treatment as well as identified covariates [Figure 1]. From these three predictors, a number of individual factors are identified as influencing the outcome. Socioeconomic factors include health insurance status, health literacy (particularly symptom recognition) as well as indicators of financial security utilizing health insurance status and the socioeconomic indexes for areas. Identified modifiable risk factors include hypertension, smoking, and alcohol intake. System level predictors associated with timely treatment

include access to neurosurgical expertise, missed/delayed diagnosis, the recognition, and triage of individuals and inter-hospital transfers. The proposed conceptual framework also contains a number of paths that illustrate the proposed interrelationships between the predictors.

Following an aSAH, the period of time before the securement of an aneurysm is a modifiable period where decisions and interventions can significantly impact outcome.^[80] There is a significant amount of literature pertaining to outcome post-aSAH, however, there is limited literature linking rurality to outcome. In linking predictors to a conceptual framework of rural vulnerability, explanations of poor outcomes post-aSAH within rural populations can be established. The proposed conceptual framework does not aim to distinguish or differentiate between the causes of delayed/missed diagnosis and treatment. Rather it focuses on the diagnostic process from a regionalized perspective, identifying initial admission location, triage score, and diagnosis process as proposed predictors of outcome following an aSAH.

The proposed predictors linked to outcome reflect a complex web of individual and system differences. This review provides the supporting basis for the proposed hypothesis that outcome following an aSAH is associated with rurality. The identification of the model is crucial to determine whether the model can be feasibly evaluated fundamental to this is the specification of the model. The presented conceptual framework guides the specification of the proposed relationships among the proposed predictors that will guide future analysis of the model.^[17,18] Importantly, SEM does not involve a data-driven analysis rather it is the analysis of a carefully defined conceptual framework that presents hypothesized relationships between the predictors.^[81] This review does not aim to address decision-making related to individual cases; rather it attempts to identify the predictors of outcome linked to rurality, informing the conceptual framework that will underpin SEM impact of the situation, decisions, and interventions to be measured at an aggregate level.

Limitations

From a public health perspective defining the risks for aSAH is important. However, with a relatively low incidence and limited prospective studies, identifying the risk factors is difficult. The majority of studies have been retrospective with clear inclusion and exclusion criteria, with some studies focusing on very selected groups for example, excluding those who died before their hospital admission or shortly after. The second

limitation is that the majority of studies has been small and has only included a small number of risk factors, often looking at limited age groups.

Conclusion

The complexity of the impact of rurality on outcome following an aSAH can only begin to be understood though a theory testing approach to the study of the predictors associated with outcome following an aSAH. This review highlights the paucity of epidemiological evidence exploring the impact of rurality on outcome following an aSAH. Socioeconomic characteristics, modifiable risk factors, and timely treatment are identified as predictors of outcome following an aSAH, however, the relationship between predictors is complex with intervening predictors potentially mediating the effect of one variable on another. A sound theoretical foundation of the proposed predictors and the hypothesized relationships is fundamental for the future data analysis. To best of our knowledge, this is the first study that will examine the individual factors associated with rurality and the concept of rural vulnerability on time to treatment and severity of outcome following an aSAH.

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Conflicts of interest

There are no conflicts of interest.

References

- Al-Khindi T, Macdonald RL, Schweizer TA. Cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. *Stroke* 2010;41:e519-36.
- Khan M, Ahmed B, Ahmed M, Najeeb M, Raza E, Khan F, *et al.* Functional, cognitive and psychological outcomes, and recurrent vascular events in Pakistani stroke survivors: A cross sectional study. *BMC Res Notes* 2012;5:89.
- Togha M, Sahraian MA, Khorram M, Khashayar P. Warning signs and symptoms of subarachnoid hemorrhage. *South Med J* 2009;102:21-4.
- Nichols LJ, Smith L, Allen PL. Pathways to enhancing the quality of stroke care through national data monitoring systems for hospitals. *Med J Aust* 2014;200:392-3.
- Godley J, McLaren L. Socioeconomic status and body mass index in Canada: Exploring measures and mechanisms. *Can Rev Sociol* 2010;47:381-403.
- Kim AS, Johnston SC. Global variation in the relative burden of stroke and ischemic heart disease. *Circulation* 2011;124:314-23.
- Stevenson CE, Mannan H, Peeters A, Walls H, Magliano DJ, Shaw JE, *et al.* The effect of modifiable risk factors on geographic mortality differentials: A modelling study. *BMC Public Health* 2012;12:79.
- Beseoglu K, Holtkamp K, Steiger HJ, Hänggi D. Fatal aneurysmal subarachnoid haemorrhage: Causes of 30-day in-hospital case fatalities in a large single-centre historical patient cohort. *Clin Neurol Neurosurg* 2013;115:77-81.
- Zhang J, Liu G, Arima H, Li Y, Cheng G, Shiue I, *et al.* Incidence and risks of subarachnoid hemorrhage in China. *Stroke* 2013;44:2891-3.
- Davis S, Bartlett H. Healthy ageing in rural Australia: Issues and challenges. *Australas J Ageing* 2008;27:56-60.
- Jackson JE, Doescher MP, Jerant AF, Hart LG. A national study of obesity prevalence and trends by type of rural county. *J Rural Health* 2005;21:140-8.
- Connolly ES Jr, Rabinstein AA, Carhuapoma JR, Derdeyn CP, Dion J, Higashida RT, *et al.* Guidelines for the management of aneurysmal subarachnoid hemorrhage: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2012;43:1711-37.
- Boscoe FP, Henry KA, Zdeb MS. A nationwide comparison of driving distance versus straight-line distance to hospitals. *Prof Geogr* 2012;64:1-12.
- Jordan H, Roderick P, Martin D, Barnett S. Distance, rurality and the need for care: Access to health services in South West England. *Int J Health Geogr* 2004;3:21.
- Kupek E. Beyond logistic regression: Structural equations modelling for binary variables and its application to investigating unobserved confounders. *BMC Med Res Methodol* 2006;6:13.
- Wu JR, Moser DK, Riegel B, McKinley S, Doering LV. Impact of prehospital delay in treatment seeking on in-hospital complications after acute myocardial infarction. *J Cardiovasc Nurs* 2011;26:184-93.
- Beran TN, Violato C. Structural equation modeling in medical research: A primer. *BMC Res Notes* 2010;3:267.
- Fox-Wasylyshyn SM, El-Masri M, Artinian NT. Testing a model of delayed care-seeking for acute myocardial infarction. *Clin Nurs Res* 2010;19:38-54.
- Jakovljevic D, Sivenius J, Sarti C, Torppa J, Mähönen M, Immonen-Räihä P, *et al.* Socioeconomic inequalities in the incidence, mortality and prognosis of subarachnoid hemorrhage: The FINMONICA stroke register. *Cerebrovasc Dis* 2001;12:7-13.
- Schievink WI, Riedinger M, Jhutti TK, Simon P. Racial disparities in subarachnoid hemorrhage mortality: Los Angeles County, California, 1985-1998. *Neuroepidemiology* 2004;23:299-305.
- Kapral MK, Wang H, Mamdani M, Tu JV. Effect of socioeconomic status on treatment and mortality after stroke. *Stroke* 2002;33:268-73.
- Strong K, Mathers C, Bonita R. Preventing stroke: Saving lives around the world. *Lancet Neurol* 2007;6:182-7.
- Heeley EL, Wei JW, Carter K, Islam MS, Thrift AG, Hankey GJ, *et al.* Socioeconomic disparities in stroke rates and outcome: Pooled analysis of stroke incidence studies in Australia and New Zealand. *Med J Aust* 2011;195:10-4.
- Humphreys JS. Delimiting 'rural': Implications of an agreed 'rurality' index for healthcare planning and resource allocation. *Aust J Rural Health* 1998;6:212-6.
- James R. Participation disadvantage in Australian higher education: An analysis of some effects of geographical location and socioeconomic status. *High Educ* 2001;42:455-72.
- Eberhardt MS, Pamuk ER. The importance of place of residence: Examining health in rural and nonrural areas. *Am J Public Health* 2004;94:1682-6.
- Australian Institute of Health and Welfare. Rural, Regional and Remote Health: Indicators of Health System Performance. Canberra: Australian Institute of Health and Welfare; 2008.
- Zahnd WE, Scaife SL, Francis ML. Health literacy skills in rural and urban populations. *Am J Health Behav* 2009;33:550-7.
- Alkadry MG, Wilson C, Nicholson D. Stroke awareness among rural residents: The case of West Virginia. *Soc Work Health Care* 2005;42:73-92.
- Larsen CC, Eskesen V, Hauerberg J, Olesen C, Romner B, Astrup J. Considerable delay in diagnosis and acute management of subarachnoid haemorrhage. *Dan Med Bull* 2010;57:A4139.
- Langagergaard V, Palnum KH, Mehnert F, Ingeman A, Krogh BR, Bartels P, *et al.* Socioeconomic differences in quality of care and clinical outcome after stroke: A nationwide population-based study. *Stroke* 2011;42:2896-902.
- Jaja BN, Saposnik G, Nisenbaum R, Schweizer TA, Reddy D, Thorpe KE, *et al.* Effect of socioeconomic status on inpatient mortality and use of postacute care after subarachnoid hemorrhage. *Stroke* 2013;44:2842-7.
- Addo J, Ayerbe L, Mohan KM, Crichton S, Sheldenkar A, Chen R, *et al.* Socioeconomic status and stroke: An updated review. *Stroke* 2012;43:1186-91.
- Hartley D. Rural health disparities, population health, and rural culture. *Am J Public Health* 2004;94:1675-8.

35. Kerr GD, Slavin H, Clark D, Coupar F, Langhorne P, Stott DJ. Do vascular risk factors explain the association between socioeconomic status and stroke incidence: A meta-analysis. *Cerebrovasc Dis* 2011;31:57-63.
36. Thorogood M, Connor M, Tollman S, Lewando Hundt G, Fowkes G, Marsh J. A cross-sectional study of vascular risk factors in a rural South African population: Data from the Southern African stroke prevention initiative (SASPI). *BMC Public Health* 2007;7:326.
37. Korja M, Silventoinen K, Laatikainen T, Jousilahti P, Salomaa V, Hernesniemi J, et al. Risk factors and their combined effects on the incidence rate of subarachnoid hemorrhage – a population-based cohort study. *PLoS One* 2013;8:e73760.
38. Larrew T, Pryor W 3rd, Weinberg J, Webb S, Battenhouse H, Turk AS, et al. Aneurysmal subarachnoid hemorrhage: A statewide assessment of outcome based on risk factors, aneurysm characteristics, and geo-demography. *J Neurointerv Surg* 2015;7:855-60.
39. Murthy SB, Moradiya Y, Shah S, Naval NS. In-hospital outcomes of aneurysmal subarachnoid hemorrhage associated with cocaine use in the USA. *J Clin Neurosci* 2014;21:2088-91.
40. Ruigrok YM, Buskens E, Rinkel GJ. Attributable risk of common and rare determinants of subarachnoid hemorrhage. *Stroke* 2001;32:1173-5.
41. Yamada S, Koizumi A, Iso H, Wada Y, Watanabe Y, Date C, et al. Risk factors for fatal subarachnoid hemorrhage: The Japan collaborative cohort study. *Stroke* 2003;34:2781-7.
42. De Marchis GM, Lantigua H, Schmidt JM, Lord AS, Velander AJ, Fernandez A, et al. Impact of premorbid hypertension on haemorrhage severity and aneurysm rebleeding risk after subarachnoid haemorrhage. *J Neurol Neurosurg Psychiatry* 2014;85:56-9.
43. Tang C, Zhang TS, Zhou LF. Risk factors for rebleeding of aneurysmal subarachnoid hemorrhage: A meta-analysis. *PLoS One* 2014;9:e99536.
44. Chotai S, Ahn SY, Moon HJ, Kim JH, Chung HS, Chung YG, et al. Prediction of outcomes in young adults with aneurysmal subarachnoid hemorrhage. *Neurol Med Chir (Tokyo)* 2013;53:157-62.
45. McLaughlin D, Hockey R, Mishra G. Heart disease in women in remote Australia: Urban-rural differences after adjusting for lifestyle behaviours and socio-demographic factors. *Aust N Z J Public Health* 2013;37:90.
46. Janus ED, Bunker SJ, Kilkkinen A, McNamara K, Philpot B, Tideman P, et al. Prevalence, detection and drug treatment of hypertension in a rural Australian population: The greater green triangle risk factor study 2004-2006. *Intern Med J* 2008;38:879-86.
47. de Rooij NK, Rinkel GJ, Dankbaar JW, Frijns CJ. Delayed cerebral ischemia after subarachnoid hemorrhage: A systematic review of clinical, laboratory, and radiological predictors. *Stroke* 2013;44:43-54.
48. Isaksen J, Egge A, Waterloo K, Romner B, Ingebrigtsen T. Risk factors for aneurysmal subarachnoid haemorrhage: The Tromsø study. *J Neurol Neurosurg Psychiatry* 2002;73:185-7.
49. Dalbjerg SM, Larsen CC, Romner B. Risk factors and short-term outcome in patients with angiographically negative subarachnoid hemorrhage. *Clin Neurol Neurosurg* 2013;115:1304-7.
50. Inagawa T, Yahara K, Ohbayashi N. Risk factors associated with cerebral vasospasm following aneurysmal subarachnoid hemorrhage. *Neurol Med Chir (Tokyo)* 2014;54:465-73.
51. Hillbom M, Saloheimo P, Juvela S. Alcohol consumption, blood pressure, and the risk of stroke. *Curr Hypertens Rep* 2011;13:208-13.
52. Leppälä JM, Paunio M, Virtamo J, Fogelholm R, Albanes D, Taylor PR, et al. Alcohol consumption and stroke incidence in male smokers. *Circulation* 1999;100:1209-14.
53. Inder KJ, Handley TE, Fitzgerald M, Lewin TJ, Coleman C, Perkins D, et al. Individual and district-level predictors of alcohol use: Cross sectional findings from a rural mental health survey in Australia. *BMC Public Health* 2012;12:586.
54. Catalano AR, Winn HR, Gordon E, Frontera JA. Impact of interhospital transfer on complications and outcome after intracranial hemorrhage. *Neurocrit Care* 2012;17:324-33.
55. Nuño M, Patil CG, Lyden P, Drazin D. The effect of transfer and hospital volume in subarachnoid hemorrhage patients. *Neurocrit Care* 2012;17:312-23.
56. Drazin D, Rosner J, Nuño M, Alexander MJ, Schievink WI, Palestrant D, et al. Type of admission is associated with outcome of spontaneous subarachnoid hemorrhage. *Int J Stroke* 2015;10:529-33.
57. Edlow JA, Malek AM, Ogilvy CS. Aneurysmal subarachnoid hemorrhage: Update for emergency physicians. *J Emerg Med* 2008;34:237-51.
58. Lorenzi L, Kerr ME, Yonas H, Alexander S, Crago E. Influence of delaying treatment after symptoms develop from subarachnoid hemorrhage: A preliminary analysis. *J Neurosci Nurs* 2003;35:210-4.
59. Singh A, Soares WE. Management strategies for acute headache in the emergency department. *Emerg Med Pract* 2012;14:1-23.
60. Miyazaki T, Ohta F, Moritake K, Nagase A, Kagawa T. The key to improving prognosis for aneurysmal subarachnoid hemorrhage remains in the pre-hospitalization period. *Surg Neurol* 2006;65:360-5.
61. Newman-Toker DE, Moy E, Valente E, Coffey R, Hines AL. Missed diagnosis of stroke in the emergency department: A cross-sectional analysis of a large population-based sample. *Diagnosis* 2014;1:155-66.
62. Murata A, Matsuda S. Association between ambulance distance to hospitals and mortality from acute diseases in Japan: National database analysis. *J Public Health Manag Pract* 2013;19:E23-8.
63. Sharma S, Gomez D, de Mestral C, Hsiao M, Rutka J, Nathens AB. Emergency access to neurosurgical care for patients with traumatic brain injury. *J Am Coll Surg* 2014;218:51-7.
64. Leira EC, Hess DC, Torner JC, Adams HP Jr. Rural-urban differences in acute stroke management practices: A modifiable disparity. *Arch Neurol* 2008;65:887-91.
65. Lovelock CE, Rinkel GJ, Rothwell PM. Time trends in outcome of subarachnoid hemorrhage: Population-based study and systematic review. *Neurology* 2010;74:1494-501.
66. Sarmiento JM, Mukherjee D, Nosova K, Schievink WI, Alexander MJ, Patil CG, et al. Predictors of treatment delay in aneurysmal subarachnoid hemorrhage patients. *J Neurol Surg A Cent Eur Neurosurg* 2015;76:46-55.
67. Smith KB, Humphreys JS, Wilson MG. Addressing the health disadvantage of rural populations: How does epidemiological evidence inform rural health policies and research? *Aust J Rural Health* 2008;16:56-66.
68. Guly HR. Diagnostic errors in an accident and emergency department. *Emerg Med J* 2001;18:263-9.
69. Kowalski RG, Claassen J, Kreiter KT, Bates JE, Ostapovich ND, Connolly ES, et al. Initial misdiagnosis and outcome after subarachnoid hemorrhage. *JAMA* 2004;291:866-9.
70. Vermeulen MJ, Schull MJ. Missed diagnosis of subarachnoid hemorrhage in the emergency department. *Stroke* 2007;38:1216-21.
71. Bo SH, Davidsen EM, Gulbrandsen P, Dietrichs E. Acute headache: A prospective diagnostic work-up of patients admitted to a general hospital. *Eur J Neurol* 2008;15:1293-9.
72. Bardach NS, Olson SJ, Elkins JS, Smith WS, Lawton MT, Johnston SC. Regionalization of treatment for subarachnoid hemorrhage: A cost-utility analysis. *Circulation* 2004;109:2207-12.
73. Cong W, Zhongxin Z, Tiangui L, Zhang Y, Min H, Chao Y. Risk factors for rebleeding of aneurysmal subarachnoid hemorrhage based on the analysis of on-admission information. *Turk Neurosurg* 2012;22:675-81.
74. Algra AM, Klijn CJ, Helmerhorst FM, Algra A, Rinkel GJ. Female risk factors for subarachnoid hemorrhage: A systematic review. *Neurology* 2012;79:1230-6.
75. Schöller K, Massmann M, Markl G, Kunz M, Fesl G, Brückmann H, et al. Aneurysmal subarachnoid hemorrhage in elderly patients: Long-term outcome and prognostic factors in an interdisciplinary treatment approach. *J Neurol* 2013;260:1052-60.
76. Claassen J, Carhuapoma JR, Kreiter KT, Du EY, Connolly ES, Mayer SA. Global cerebral edema after subarachnoid hemorrhage: Frequency, predictors, and impact on outcome. *Stroke* 2002;33:1225-32.
77. Naidech AM, Janjua N, Kreiter KT, Ostapovich ND, Fitzsimmons BF, Parra A, et al. Predictors and impact of aneurysm rebleeding after subarachnoid hemorrhage. *Arch Neurol* 2005;62:410-6.
78. Wostrack M, Sandow N, Vajkoczy P, Schatlo B, Bijlenga P, Schaller K, et al. Subarachnoid haemorrhage WFNS grade V: Is maximal treatment worthwhile? *Acta Neurochir (Wien)* 2013;155:579-86.
79. Bollen KA, Bauldry S. Three Cs in measurement models: Causal indicators, composite indicators, and covariates. *Psychol Methods* 2011;16:265-84.
80. Sharma B, Satija V, Dubey P, Panagariya A. Subarachnoid hemorrhage with transient ischemic attack: Another masquerader in cerebral venous thrombosis. *Indian J Med Sci* 2010;64:85-9.
81. Hays RD, Revicki D, Coyne KS. Application of structural equation modeling to health outcomes research. *Eval Health Prof* 2005;28:295-309.