EC NEUROLOGY
Research Article

Selection of Regional Factors Related to Cerebral Function after Out-of-Hospital Cardiac Arrest in Japan

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Received: December 15, 2018; **Published:** April 01, 2019

Abstract

The rate of good cerebral function after out-of-hospital cardiac arrest (OHCA) remains poor and the difference in the rate exists in the regional level in Japan. Large-scale administrative data are available for research of social and demographic variables (SDV). The purpose of the present study was to find SDVs associated with cerebral function after OHCA using the Utstein database of Japan using correlation coefficient (CC) and coefficient of determination (R^2). The rates of good cerebral function after OHCA at 1 month and SDVs from administrative data were surveyed in each prefecture. Five variables were found using CC and R^2 by multiple regression. We concluded that the combination of CC and R2 would contribute to the selection of regional factors from the many variables in the large-scale database.

Keywords: *Cerebral Function; Out-of-Hospital Cardiac Arrest; Utstein Database; Regional Factors; Social and Demographic Variable; Correlation Coefficient; Adjusted R2*

Abbreviations

OHCA: Out-of-Hospital Cardiac Arrest; EMS: Emergency Medical Services; GCFR: Rate of Good Cerebral Function; SDV: Social and Demographic Variables

Introduction

Emergency cases of out-of-hospital cardiac arrest (OHCA) from all over the world are recorded in the Utstein database [1-3]. Each year, 120,000 people suffer from OHCA, which are all recorded by nationwide emergency medical services (EMS), and 7% of all deaths occur in Japan [4-8]. The Utstein database showed that the rate of good cerebral function (GCFR) after OHCA in Japan is still poor and that the difference in the rate exists in the prefectural level [9]. However, it was difficult to explain the regional differences [10]. The extent of regional variation in OHCA outcomes suggests underlying differences in rural and urban features, characteristics of patients, and patient care. Explanatory variables are classified into individual and environmental (neighborhood) levels in case of multivariate analysis. Evidence from other disciplines suggests that neighborhood-level factors influence health outcomes [11-14]. Numerous studies have evaluated socioeconomic status and race/ethnicity and their association with OHCA survival, but the results have been inconsistent [15-18] and none has considered these regional factors to account for survival and cerebral function in addition to the Utstein database variables.

Large-scale administrative data are available for research of social and demographic variables (SDV) in Japan [19]. A great number of these variables are available to use; however, the number of regions is rather small. Therefore, we need efficiently select the potentially related variables from the SDV provided. We tried to elucidate SDV related to the regional factors in the good cerebral function of patients after OHCA.

Purpose of the Study

The purpose of this study was to find SDV related to cerebral function after OHCA using the Utstein database of Japan using a combination of correlation coefficient (CC) and coefficient of determination (R^2).

Materials and Methods

Study setting

The 2014 Utstein database of Japan was analyzed in this study. EMS were managed by 1703 fire stations and 120,766 staff in 2014. EMS comprised basic life support ambulances staffed with paramedics. Ambulances were dispatched from municipal fire defense stations. Request calls for an ambulance (phone: 119) were received by a telephone operator or a dispatcher. EMS is financed by taxes, and completely free access to EMS is guaranteed. The data of patients with OHCA were electronically recorded in the Utstein database at each fire station and the prognosis of OHCA cases was surveyed in 1 month and sent to the Fire Defense and Disaster Agency. All patients with OHCA were gathered and recorded nationwide in the Utstein database, which has been run in all fire stations since 2008 in Japan. The annual reported number of the Utstein database of Japan is the greatest in the world.

Japan consists of 47 prefectures. The median population of each prefecture is 1,668,000, with a minimum of 574,000 and a maximum of 13,390,000. The median area of each prefecture is 4819 km^2, with a minimum of 574 km^2 and a maximum of 78,420 km^2. Japan is covered by a universal public health insurance system for Japanese people and foreigners are entitled to register. The health insurance system is mainly managed by the Health Insurance, the National Healthcare Insurance and the Long Life Medical Care System that have high-cost medical care expense system.

The Japanese Government provides administrative statistical data of Japan at the portal site e-Stat, where SDV are provided by the Japanese Government Statistics [19]. The SDV have 13 statistical tables (Table 1). These data are summarized by prefectures and fiscal years. A fiscal year means the interval from April of the current year to March of the following year.

Study design

Outcome

Among 125,951 patients with OHCA in the 2014 Utstein database, our outcome was good cerebral function, which was defined as category 1 or 2 in the cerebral performance categories at 1 month after OHCA. The GCFR was calculated in each prefecture (Figure 1).

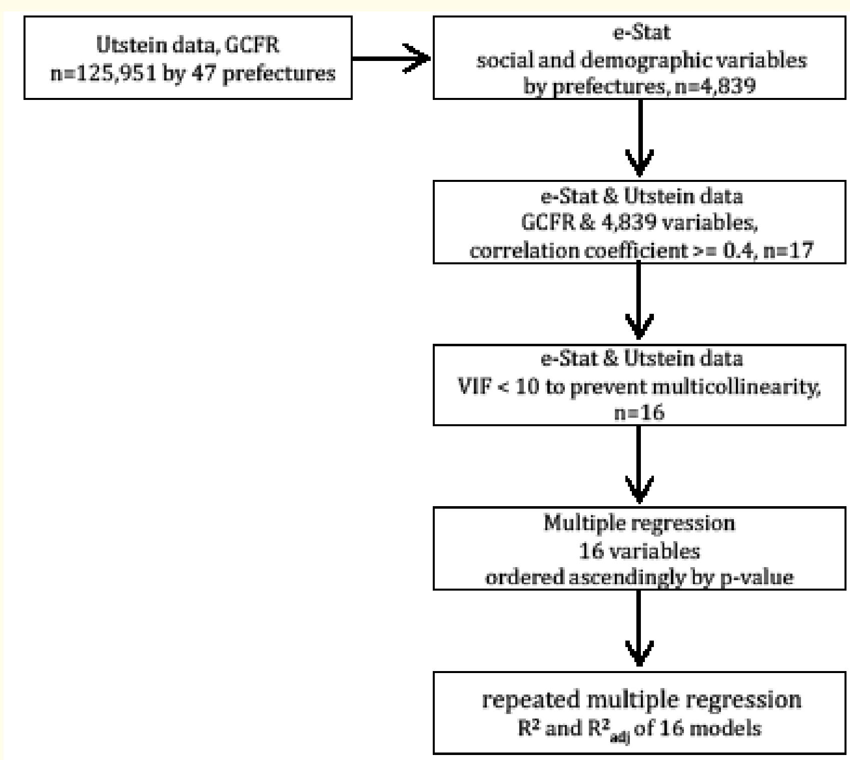

Figure 1: *Flowchart of the study.*

Combination of correlation coefficient and R^2

Correlation coefficient

We downloaded 2800 variables from 13 statistical tables from the SDV in the e-Stat. The original variables were divided by population or area. We obtained a total of 4839 variables for explanatory variables (Table 1). We calculated CC between GCFR and 4839 variables in each prefecture. We chose 17 variables with CC that were ≥ 0.4. We performed multiple regression between GCFR and 17 variables. and calculated variance inflation factors (VIF) in each variable to prevent multicollinearity. When the VIFs were over 10, we deleted the variable of the smaller CC.

Statistical table	Example variables	Number of original variables	Number of modified variables	Number of total variables	Number of variables chosen by correlation coefficients	Number of variables to prevent multicolinearity
Population and households	Population, death, marriage, divorce	136	124	260	1	1
Natural environment	Area, habitable area, temperature, rain	23	16	39	1	1
Economic base	Income, product, shipment, deposit	307	268	575	1	1
Administrative base	Finance, expenditure of health/welfare/education	180	179	359	1	1
Education	School, college and university, teacher, student, graduation	203	117	320	1	0
Labor	Labor force, unemployment rate, part-time work	202	265	467	0	0
Culture and sports	Library, sports facility, swimming pool, travel	90	67	157	0	0
Dwelling	Owned/rented house, floor area, flush toilet, rate of recycling	268	268	536	2	2
Health and medical care	Life expectancy, cause of death, hospital/clinic, medical expense	236	144	380	4	4
Welfare and social security	Livelihood protection, welfare center, visiting care giver, rehabilitation	180	152	332	1	1
Safety	Fire, traffic accident, criminal offence, insurance	154	439	593	2	2
Family budget	Income, wage, expenditure, consumer price index	607	0	607	0	0
Daily time	Type of activity, hobby, TV/radio/newspaper/magazine	214	0	214	3	3
Total	—	2800	2039	4839	17	16

Table 1: *System of social and demographic statistics and selected variables.*

R^2 and R^2_{adj}

R^2 was defined as $1\text{-}SS_{res}/SS_{tot}$, and R^2_{adj} was defined as $1\text{-}(SS_{res}/df_e)/(SS_{tot}/df_t)$, where SS_{tot} was the total sum of squares, SS_{res} was the residual sum of squares, df_t is n-1, df_e is n-p-1, p was the total number of explanatory variables, and n was the sample size.

GCFR was a response variable, and we adopted the top variables from the list (Table 2) as explanatory variables in each model. We repeated the regression analysis 16 times from 1 to 16 explanatory variables of table 2 and gained R^2 and R^2_{adj} in each model. We plotted R^2 and R^2_{adj} and the number of explanatory variables (Figure 2). We also performed stepwise regression with backward elimination to search predictable variables by Akaike information criterion (AIC).

No	Variable (unit)	Statistical table	Estimate	Standard error	t value	Pr(>|t|)
1	Rate of arrests to recognitions of criminal offenses (/100,000)	Safety	0.006	0.002	2.784	0.009
2	Average time of primary activities among 25- to 34-year-old females (minutes)	Daily time	-0.015	0.011	-1.352	0.187
3	Rate of 0- to 14-year-old children (%)	Population and households	0.362	0.304	1.191	0.243
4	Rate of owned houses renovated to be earthquake resistant (%)	Dwelling	0.002	0.002	1.092	0.283
5	Rate of reports of pregnancy (/100,000)	Health and medical care	-0.002	0.002	-1.02	0.316
6	Rate of outpatient rehabilitation stations (/100,000)	Health and medical care	0.004	0.004	0.951	0.349
7	Average time of schoolwork among males (hours)	Education	-0.033	0.036	-0.922	0.364
8	Rate of users of visiting bathing and nursing care (/100,000)	Welfare and social security	-0.007	0.009	-0.78	0.442
9	Lowest temperature among monthly averages of daily lowest (°C)	Natural environment	-0.035	0.057	-0.616	0.543
10	Rate of persons killed by fires (/100,000)	Safety	-0.171	0.300	-0.572	0.572
11	Changes of consumer price index (%)	Family budget	-0.239	0.483	-0.493	0.625
12	Average time of tertiary activities (leisure) among males ages 75 years and older (minutes)	Daily time	0.003	0.007	0.366	0.717
13	Rate of electral roll subscribers (%)	Administrative base	3.766	12.444	0.303	0.764
14	Height among males of the fifth grade at elementary school (cm)	Health and medical care	0.069	0.265	0.26	0.797
15	Rate of Births weighing under 2,500g (/100,000)	Health and medical care	0.005	0.027	0.196	0.846
16	Rate of construction-started residential buildings (/100,000)	Dwelling	0.001	0.005	0.137	0.892

Table 2: *Result of multiple regression of 16 selected variables in ascending order by p-value.*

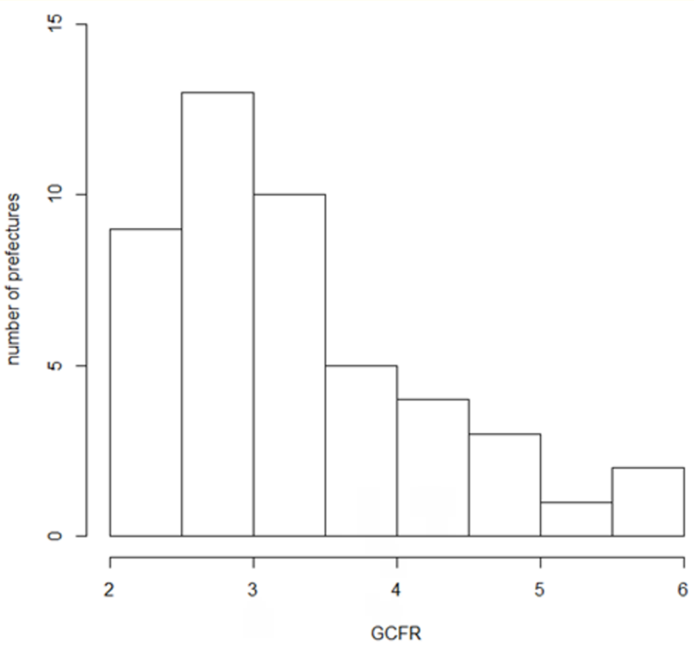

Figure 2: *Distribution of GCFR at 1 month after OHCA by prefecture.*

We used the open statistical software R (version 3.4.2; The R Foundation, Austria) for analysis.

Ethics

The Utstein database was used with permission from the Fire and Disaster Management Agency of the Ministry of Internal Affairs and Communications. This study was approved by the Ethical Committee of Kokushikan University (No. 27-010).

Results

GCFR in each prefecture

The median was 3.1%, the maximum was 5.9%, the minimum was 2.1%, and the mean was 3.1% among 47 prefectures. The distribution of GCFR shown at the prefectural levels was left-sided monophasic and right-tailed (Figure 2).

Selected variables from the e-Stat

Of the original and modified 4839 variables, 17 variables were selected as the correlation coefficients of GCFR and the variables were ≥ 0.4 (variables chosen by correlation coefficients in table 1). Consequently, 16 variables were selected to prevent multicollinearity (variables to prevent multicollinearity in table 1). Then, we obtained the list of 16 variables in ascending order by p-value (Table 2).

R^2 and R^2_{adj} of multiple regression

R^2 showed a plateau as the number of explanatory variables increased. R^2adj also showed plateau-shaped and gradually decreased when the number increased (Figure 3). The maximum R^2 was 0.627 in 16 variables, however the maximum R^2_{adj} was 0.522 in four variables (Figure 3). Only the first variable of "Rate of arrests to recognitions of criminal offenses" (safety) had statistical significance (p = 0.0092) in table 2 and its R^2 and R^2_{adj} were 0.220 and 0.202 (Figure 3). The second variable was "Average time of primary activities among 25- to 34-year-old females (daily time)", the third was "Rate of 0 to-14-year-old children (population and households)", the fourth was "Rate of owned houses renovated to be earthquake resistant (dwelling)", and the fifth was "Rate of reports of pregnancy (health and medical care) " (Table 2).

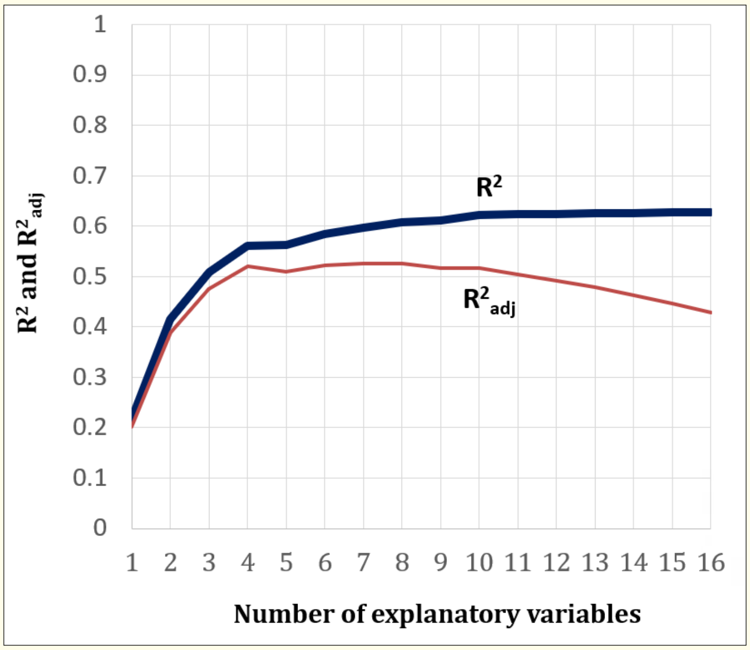

Figure 3: *R^2 and R^2_{adj} and the number of explanatory variables.*
The number of explanatory variables was that of the top variables in ascending order in Table 2.
The upper bold line is R^2 and the lower fine line is R^2adj.

Stepwise regression showed four predictive variables that were the same as the four top variables in table 2.

Discussion

R^2 increased and reached the plateau, however, R^2_{adj} did not increase at four variables afterward (Figure 3) when the number of explanatory variables increased. R^2 was 0.0.561 (89.5% of the maximum) and the R^2_{adj} was 0.520 and the maximum in four explanatory variables (Figure 3), which were quite similar to that of the five or six ones. Stepwise regression with backward elimination showed that four explanatory variables were selected and were the same variables of the four top ones in table 2. Only "Rate of arrests to recognitions of criminal offenses" was statistically significant among 16 social and demographic variables; however, it showed an R^2_{adj} of 0.2025. As the R^2 and the R^2_{adj} mean the descriptive power of the regression model that includes a diverse number of explanatory variables, the four top variables in table 2 seem to demonstrate well regional property in this study.

Correlation coefficient is a measure of association that indicates the degree to which two variables have a linear relationship. The number of regions is limited as there are only 47 prefectures in Japan. Recently, we can use many social and demographic variables that are provided in large-scale databases. However, we have to choose even the smaller number of social and demographic variables, although multilevel analysis is applied to demonstrate regional property. We showed the method of selecting the suitable variables from many ones with a combination of simple correlation and R^2_{adj} by multiple regression analysis in this study.

Health outcomes were reported to be influenced by socioeconomic inequities such as health-care access, quality of health care [20], education [21], health services [22], number of practitioners/hospital beds [23] and workforce [24]. Of the 4839 SDV, we could find no relationship between GCFR and socioeconomic variables of the prefectural income per person, the rate of people having completed colleges and universities, and the rate of hospitals and clinic per population and habitual prefectural area.

We have great concern as to which factor influences the regional differences of good cerebral function after OHCA. The most significant factor was "Rate of arrests to recognitions of criminal offenses" (safety), which means security in the communities and also seems to imply good communication in the communities to keep the community safe. Okubo., *et al.* demonstrated regional variation in favorable outcomes after OHCA using the hierarchical model; however, the suitable variables were still not demonstrated among cases with OHCA [10]. Buick., *et al.* studied the measures of poverty, ethnicity, instability, crime rate, and the density of family physicians as neighborhood variables using hierarchical logistic regression analysis, and only census tracts with a moderate ethnic concentration had an increased likelihood of survival-to-hospital charge [25]. we could select several variables that have correlation with GCFR itself.

The four top variables belonged to diverse fields that were safety, daily time, population and households and dwelling (Table 2). The second variable, "Average time of primary activities among 25- to 34-year-old females" is supposed to be related to allowance and richness. In fact, the four explanatory variables are interesting but much complicated, therefore, further studies would require medical and sociological analyses.

We often postulate the relationship between explanatory variables and outcome variables as a linear model when we use multiple logistic regression or multilevel analysis. We used the multiple regression analysis to demonstrate the relationship between GCFR and finally selected 16 social and demographic variables in this study. However, as the relationship would not always be linear, we need to clarify the nonlinear relationship between exposures and outcomes using methods of machine learning or deep learning.

Limitations of the Study

This method explored the significant factors from many social and demographic variables; however, it did not imply the causality of OHCA and the factors in this study. After meaningful and proper variables were chosen from among the social and demographic variables, multivariate analysis such as multilevel analysis would be required to prove regional property.

Principal component analysis is often used for multiple variables in sociology and psychology, and the statistical method helps the reduction of variables. We used a combined conventional method of correlation coefficient and R^2 to exclude many variables in this study. However, as far as we have surveyed, we could find no reports that described the selection of regional factors from many social and demographic variables among patients with OHCA.

Conclusion

We selected five social and demographic variables related to good cerebral function after OHCA from the Utstein database. The selected variables were the ate of arrests to recognitions of criminal offenses, the average time of primary activities among 25- to 34-year-old females, the rate of 0- to 14-year-old children, the rate of owned houses renovated to be earthquake resistant and the rate of reports of pregnancy.

The combination of correlation coefficient and R^2_{adj} would contribute to the selection of regional factors from the many variables in the large-scale database.

Conflicts of Interest

There were no conflicts of interest through the development of this study.

Authors' Contributions

Kuboyama helped in the study concept, drafting of the manuscript, and design. R. Sagisaka helped in the acquisition of data. S. Ito helped in the statistical analysis. E. Saito helped in the interpretation of data. S. Toyokawa helped in correcting the manuscript. All authors read and approved the final manuscript.

Funding

This study was partially funded by the Institute of Health, Physical Education and Sport Science, Kokushikan University.

Bibliography

1. Lombardi G., *et al*. "Outcome of out-of-hospital cardiac arrest in New York City. The Pre-Hospital Arrest Survival Evaluation (PHASE) Study". *Journal of the American Medical Association* 271.9 (1994): 678-683.
2. Martens P., *et al*. "Utstein style cardiopulmonary-cerebral resuscitation registry for out-of-hospital cardiac arrests between 1991 and 1993. The Belgian CPCR Study Group". *European Journal of Emergency Medicine* 1.3 (1994): 115-119.
3. Kuisma M., *et al*. "Out-of-hospital cardiac arrests in Helsinki: Utstein style reporting". *Heart* 76.1 (1996): 18-23.
4. Hayakawa M., *et al*. "Shortening of cardiopulmonary resuscitation time before the defibrillation worsens the outcome in out-of-hospital VF patients". *American Journal of Emergency Medicine* 27.4 (2009): 470-474.
5. Kitamura T., *et al*. "Nationwide public-access defibrillation in Japan. Implementation Working Group for the All-Japan Utstein Registry of the Fire and Disaster Management Agency". *New England Journal of Medicine* 362.11 (2010): 994-1004.
6. Mitani Y., *et al*. "Public access Defibrillation Improved the Outcome after Out-Of-Hospital Cardiac Arrest in School-Age Children: a Nationwide, Population-Based, Utstein Registry Study in Japan". *Europace* 15.9 (2013): 1259-1266.
7. Sato Y., *et al*. "Timing of Out-of-Hospital Cardiac Arrest and Social Rehabilitation Rate". *International Journal of Therapy and Rehabilitation* 2 (2017): 132-135.
8. Kuboyama I., *et al*. "Prognosis of cerebral function of cerebrovascular disease patients who caused out-of-hospital cardiac arrest in Japan". *EC Neurology* 10.7 (2018): 605-612.
9. Kuboyama I., *et al*. "Regional comparison of survival rate of patients with out-of-hospital cardiopulmonary arrest brought by emergency medical services in Japan". *Kokushi Soc Spor Sci* 11 (2011): 85-93.
10. Okubo M., *et al*. "Regional variation in functional outcome after out-of-hospital cardiac arrest across 47 prefectures in Japan". *Resuscitation* 124 (2018): 21-28.
11. Clarke SO., *et al*. "Socioeconomic status and survival from out-of-hospital cardiac arrest". *Academic Emergency Medicine* 12.10 (2005): 941-947.
12. Sayegh AJ., *et al*. "Does race or socioeconomic status predict adverse outcome after out of hospital cardiac arrest: a multi-center study". *Resuscitation* 40.3 (1999): 141-146.
13. Vaillancourt C., *et al*. "Socioeconomic status influences bystander CPR and survival rates for out-of-hospital cardiac arrest victims". *Resuscitation* 79.3 (2008): 417-423.
14. Ahn KO., *et al*. "Association between deprivation status at community level and outcomes from out-of-hospital cardiac arrest: a nationwide observational study". *Resuscitation* 82.3 (2011): 270-276.
15. Cowie MR., *et al*. "Out-of-hospital cardiac arrest: racial differences in outcome in Seattle". *American Journal of Public Health* 83.7 (1993): 955-959.
16. Becker LB., *et al*. "Racial differences in the incidence of cardiac arrest and subsequent survival. The CPR Chicago Project". *New England Journal of Medicine* 329.9 (1993): 600-606.
17. Chu K., *et al*. "Race and survival after out-of-hospital cardiac arrest in a suburban community". *Annals of Emergency Medicine* 31.4 (1998): 478-482.
18. Galea S., *et al*. "Explaining racial disparities in incidence of and survival from out-of-hospital cardiac arrest". *American Journal of Epidemiology* 166.5 (2007): 534-543.
19. Portal site of Japanese Government (e-Stat).

20. Plug I., *et al*. "Socioeconomic inequalities in mortality from conditions amenable to medical interventions: do they reflect inequalities in access or quality of health care?" *BMC Public Health* 12.1 (2012) 346.

21. Stirbu I., *et al*. "Educational inequalities in avoidable mortality in Europe". *Journal of Epidemiology and Community Health* 64.10 (2010): 913-920.

22. Poikolainen K., *et al*. "The effect of health services on mortality: decline in death rates from amenable and non-amenable causes in Finland, 1969-1981". *Lancet* 327. 8474 (1986): 199-202.

23. Mackenbach JP., *et al*. "Regional differences in decline of mortality from selected conditions: The Netherlands, 1969-1984". *International Journal of Epidemiology* 17.4 (1988): 821-829.

24. Westerling R., *et al*. "Socioeconomic differences in 'avoidable' mortality in Sweden, 1986-1990". *International Journal of Epidemiology* 25.3 (1996): 560-567.

25. Buick JE., *et al*. "The association between neighborhood effects and out-of-hospital cardiac arrest outcomes". *Resuscitation* 103.6 (2016): 14-19.

Volume 11 Issue 4 April 2019