Potential crowdedness of mechanical thrombectomy and cerebral infarction mortality in Japan: Application of inverted two-step floating catchment area method

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Abstract

Objectives: This study aimed to evaluate a stroke medical delivery system based on population coverage and the potential crowdedness index (PCI) of mechanical thrombectomy and investigate the relationship between PCI and cerebral infarction mortality in Japan.

Materials and Methods: This cross-sectional study defined 662 facilities and 1605 neurointerventionalists as supply, population aged 55 years or older as demand, and set the reachable area for demand as 120 min in driving time. Multiple regression analysis adjusted for spatial autocorrelation was used to examine the relationship between PCI and cerebral infarction mortality.

Results: In the 2020 data, 99% of the population aged 55 years or older had access to mechanical thrombectomy (≤ 120 min), and the PCI ranged from 5876 to 129838, with a median of 30426. From 2020 to 2035, the PCI is estimated to increase (30426 to 32510), decreasing after 2035 (32510 to 29469). The PCI distribution exhibited geographical heterogeneity. High PCI values emerged in eastern Japan. According to regression analysis, the increase in PCI by 1% led to an increase of 0.13% in standardized mortality ratio of cerebral infarction in men. However, PCI did not significantly correlate with cerebral infarction mortality in women.

Conclusions: PCI for hospitals based on supply and demand was geographically heterogeneous in Japan. Optimization of PCI contributes equalization of mechanical thrombectomy provision system and may improve cerebral infarction mortality.

Introduction

Cerebrovascular diseases lead to the death of approximately 100,000 people every year in Japan (1), being the fourth most common cause of death among all causes in 2020 (1). Although most of the deaths were distributed in the age group of 65 years and above, it accounts for 5% to 10% of the cause of death in the group from 20 to 65 years old and is also a threat to the younger generation (1). Cerebrovascular diseases are classified into ischemic stroke, cerebral hemorrhage, and subarachnoid hemorrhage. Advances in treatment and medical technology have improved the outcome of patients with acute ischemic stroke (AIS). Nevertheless, AIS accounts for more than half of deaths caused by cerebrovascular diseases (1). Recently, two main treatments for AIS have become commonly available in Japan (2). The first is thrombolysis by recombinant tissue plasminogen activator (rt-PA), and the other is mechanical thrombectomy (MT) using MT devices (2,3). Unfortunately, both treatments have a time limit: within 4.5 h for rt-PA and within 6–24 h for MT to obtain a clinical effect (4–7). Moreover, early initiation of treatment can lead to a good prognosis in patients (4,6,8). In short, a shortened "onset to reperfusion time" along with a system that can provide early and effective treatment whenever and wherever possible will reduce the number of deaths and patients with severe sequelae from AIS.

A variety of studies have indicated options to shorten the time from stroke onset to reperfusion, such as cooperative method (9), workflows in hospitals (10,11), rapid diagnoses (12), and public awareness campaigns (13). However, infrastructure and human resources such as spatial accessibility (14–16), facilities (i.e., the number of beds, equipment), and human resources (17) are critical. Optimization of supply against demand is a crucial issue because the allocation of facilities and human resources affects the onset-to-reperfusion time in stroke.

In Japan, the geographical distribution of physicians between urban and rural areas is significantly different

(18,19). Although the disparity has narrowed due to the declining population in rural areas, equalization has not been reached. Additionally, in Japan, overtime regulations for physicians will be enforced from April 2024 (20). Thus, more physician resources are needed to provide stroke treatment 24 h/7 days.

Primary stroke centers (PSCs) were certified to equalize stroke treatment by the Japan Stroke Society. In 2021, over 900 PSCs provided rt-PA treatment for 24 h/7 days (21). However, the feasibility of MT differs from hospital to hospital. Takagi et al. reported that only 6.06 per 100,000 person-years were given MT in Japan (22). The first-ever ischemic stroke incidence rate was 106.6 per 100,000 person-years (23), and the implementation rate of MT was estimated to be only 5%. Moreover, Maeda et al. clarified that the density of high-level stroke hospitals and neuroendovascular specialists was positively associated with the use of MT (24). This means that accessibility to MT exhibits a disparity depending on the place. Spatial accessibility has been commonly evaluated worldwide in equalizing medical resources (16,25). Recently, two-step floating catchment area methods (2SFCA) have been applied to assess the spatial accessibility of medical resources (26) from the perspective of supply (i.e., the number of physicians or hospital beds), demand (i.e., population), and travel cost (i.e., distance or time) (26). Japan has faced a serious decline in birthrate and the working-age population is estimated to reduce in the future (27). The shortage of workers impacts the burden on medical professionals and the effect of overcrowding in hospitals. Crowding in emergency departments is associated with delays in starting treatment and discharge before treatment is completed and deteriorates the quality of medical care (28). In other words, in a society with a reducing working-age population, adequate placement of human resources will result in medical equalization and enable to reach sustainable development goals. Wang focused on the supply of medical resources to develop a potential crowdedness index (PCI) of facilities by altering the 2SFCA to inverted 2SFCA (I2SFCA) (29). A positive correlation between PCI and the actual number of patients discharged from facilities has been previously demonstrated (30). Although the I2SFCA can be used to focus on the supply of medical resources, no research on stroke treatment has been conducted, to the best of our knowledge. Therefore, the purposes of this study were 1) to examine and visualize simple population coverage for MT, 2) to evaluate the PCI per neurointerventionalist at facilities providing MT, and 3) to determine whether PCI is related to cerebral infarction mortality in the region. This study can contribute to the equalization and sustainability of the medical care provider system.

Methods and Materials

Study Design

This is a cross-sectional study. First, the simple population coverage rate for MT was evaluated by categorizing ≤ 30 min, ≤ 60 min, ≤ 90 min, and ≤ 120 min based on driving time. Next, PCI per neurointerventionalist at facilities that can provide MT for AIS in Japan was calculated using I2SFCA. Finally, the relationship between PCI and cerebral infarction mortality in the prefecture unit was analyzed using the ordinary least squares (OLS), spatial error (SEM), and spatial lag models (SLM).

Facilities and Human Resources

This study targeted 969 facilities, including PSCs and training center hospitals for MT, and 1745 neurointerventionalists (as of September 2021). From the 969 facilities, 307 facilities without neurointerventionalists were excluded, resulting in 662 facilities and 1605 neurointerventionalists. Facilities with neurointerventionalists can provide MT (31). Data on PSC, hospitals of training centers for MT, and the number of neurointerventionalists at each facility were presented to the public by the Japan Stroke Society (32) and JSNET (33).

Population and Grid Data

The study population included individuals aged 55 years with an increased incidence of AIS (23). The study used 500-m square grid data with an estimated population based on the 2015 census ranging from 2020 to 2050 by the Ministry of Land, Infrastructure, and Transport (MLIT) (34). Shapefiles of Japan on the prefecture-level and grid data are available from MILT (35).

Catchment area Size and Distance Decay Function

The driving time between the location and facility (< 120 min) by car was adopted as the catchment area size in this study. The catchment area size was set for the driving time (< 60 min) in another study (14,36). However, the average transportation time by ambulance was approximately 40 min, and 99% of the transport was completed within 120 min (37). Next, by implementing the distance decay function, the study was designed to select a hospital closer to the demand location for treatment. In 2SFCA, various distance decay functions have been introduced depending on the medical field (26). The widely used Gaussian distance decay function was used in this study (38,39) (Equation (A) and Figure 1).

$$f(d_{ij}) = \begin{cases} \frac{e^{-\frac{1}{2}*(\frac{d_{ij}}{d_0})^2} - e^{-\frac{1}{2}}}{1-e^{-\frac{1}{2}}}, & d_{ij} < d_0 \\ 0, & d_{ij} \geq d_0 \end{cases} \quad \text{(A)}$$

where i, j mean grid i and facility j, d_0 is 120 min, $d_{ij}$is the driving time (min) from grid i to facility j. Thus, a population of the grid I with a driving time of >120 min has no chance of receiving MT at facility j.

I2SFCA Method

The I2SFCA consists of three main factors: supply, demand, and the distance decay function (29). The I2SFCA process consists of two steps, as shown in equations (B) and (C).

For the first step, the demand to supply ratio was calculated for each grid *i*.

$$r_i = \frac{D_i}{\sum_{l \in \{d_{il} < d_0\}} \sum_{l=1}^{n} (S_l f(d_{il}))} \quad \text{(B)}$$

where r_i is the demand to supply ratio at grid *i*, D_i is the population aged 55 years and older at grid *i*, S_l is the number of neurointerventionalists at facility *l*, $f(d_{il})$ is the distance decay function based on the driving time between i and l.

In the second step, C_j was calculated for each facility j.

$$C_j = \sum_{i \in \{d_{ij} < d_0\}} (r_i f(d_{ij})) \quad \text{(C)}$$

where C_j is the PCI per neurointerventionalist at facility j and $f(d_{ij})$ is the distance decay function based on the driving time between i and j.

Finally, according to Jenks natural breaks classification, the PCI was classified into 4 groups, and 662 facilities were plotted on the map. Jenks' natural classification is a statistical classification method that minimizes differences within groups and maximizes differences between groups (40).

Cerebral Infarction Mortality Risk

This study used the standardized mortality ratio (SMR) of cerebral infarction mortality for 47 prefectures as the cerebral infarction (ICD-10 code I63) mortality risk. SMR was calculated by an indirect method using the population stratified by sex and age groups into 18 groups every 5 years old, from 0–4 years old to 85 years and older, and the number of deaths due to cerebral infarction in sex and age groups. The population and number of deaths were obtained from Vital Statistics 2020 (41).

Covariate Variables

Covariate variables identified as risk factors for cerebral infarction were adopted in the regression analysis, which were: socioeconomic status (unit, year), which is ratio of people that completed college and university studies (%, 2010), income of the taxpayers (Japanese yen, 2019) (42), lifestyle factors, salt intake (g/day, 2016) (43), proportion of smokers (%, 2019) (44), and participation rate in general health examinations (%, 2015) (45,46)(46). The proportion of smokers was obtained from the Cancer Registry and Statistics (47). Other data were obtained from the Statistical Observations of Prefectures (48).

Ordinary Least Square and Spatial Regression Models

The relationship between PCI and cerebral infarction SMR was analyzed using the following three models: non-spatial OLS as in Equation (D), SEM as in Equation (E), and SLM as in Equation (F). The error term in OLS follows normality and identical independent distribution (i.i.d). However, when managing spatial data, i.i.d. may not be satisfied because of the error term with spatial autocorrelation. This is a result from Tobler's first law of geography, which states that geographically close data have similar properties (49). SEM can adjust the error term and consider an unmeasurable variable with spatial autocorrelation. In contrast, the SLM considers the response variable with spatial autocorrelation. Thus, we considered the positive and negative spatial autocorrelations of the cerebral infarction mortality risk between neighboring prefectures.

$$y = a + X\beta + \varepsilon \quad \text{(D)}$$

$$y = a + X\beta + \mu$$

$$\mu = \lambda W \mu + \varepsilon \quad \text{(E)}$$

$$y = a + \rho W y + X\beta + \varepsilon \quad \text{(F)}$$

where y is the cerebral infarction SMR in the prefecture, a is a constant, X is a variable, β is a parameter of X, μ, ε are error terms, λ, ρ are spatial parameters, and W is the spatial weight matrix.

Spatial Weight Matrix

The spatial weight matrix was defined based on Queen's contiguity method; it was set to 1 if the prefectures shared either a common vertex or edge or were connected by bridges or tunnels, and 0 otherwise. Additionally, Okinawa Prefecture was defined as connecting to Kagoshima Prefecture, which was the nearest, because Okinawa Prefecture still had no neighbor even after the above definition. Regardless of the number of neighbors, a spatial weight matrix was used for row standardization, where the sum of rows was 1.

Analysis

First, the population coverage rate was examined and visualized for MT in four categories: ≤30 min, ≤60 min, ≤90 min, and ≤120 min. This means that the population can reach facilities, regardless of the supply. Next, the PCI of each facility was evaluated by the I2SFCA and expressed by the Jenks' natural breaks classification. Finally, the relationship between PCI and cerebral infarction SMR was analyzed using Pearson correlation and OLS, SEM, and SLM. Normality and uniform dispersion of the error term were verified using the Jarque–Bera and Breusch–Pagan tests after OLS regression. The Moran's I was calculated to evaluate the spatial autocorrelation of the error term. Multicollinearity between variables was evaluated using the variance inflation factor (VIF). When VIF > 5, one variable with a slight correlation to the response variable was excluded. Model fitness was verified using Akaike's information criterion. In addition, the PCI, cerebral infarction SMR, and income per taxpayer were used after the logarithmic phase.

The degrees of latitude and longitude of the facilities were obtained using the "CSV address matching service" provided by the Center for Spatial Information Science at the University of Tokyo (50). The driving time was calculated from the centroids of the 2015 census grid to the facility. The visualization of results was performed using ArcGIS pro-2.8 (ESRI Inc., Redlands, USA) and ArcGIS Geo Suite Network Road 2021 Japan version (Esri Japan, Sumitomo Denko, Japan). Other analyses were performed using R (version 4.1.1) (51).

Ethics statement

This study used only public data available for secondary use. Thus, this study did not require approval from the ethics committee. We followed the data source rules before using the data and publishing it.

Results

Population coverage rate

In 2020, the population coverages in the four categories analyzed (≤30 min, ≤60 min, ≤90 min, and ≤120 min) were 86.0%, 96.1%, 98.3%, and 98.8%, respectively. This indicated that 85% more over of population aged 55 years and older could access MT within 30 min, and approximately 99% of the population had access to MT within 120 min (Figure 2).

Potential crowdedness index

The PCI per neurointerventionalist at facilities was 30426 (median) in 2020 and increased to 32374 in 2035 (Table 1). However, the PCI decreased from 2040 to 2050. This tendency was due to a decreasing population, as the number of facilities and neurointerventionalists was fixed. However, the PCI values in 2020 and 2045 were at the same level. This means that MT accessibility does not improve congestion without increasing the number of neuro-interventionalists. The gap between the minimum and maximum values in 2020 was 5876–129838. Subsequently, the gap gradually narrowed; in 2050, it was 5888–94692. In addition to increasing the number of neurointerventionalists, overall optimization can be achieved by moving neurointerventionalists from facilities with low PCI to those with high PCI.

Figure 3 shows the PCI in 2020 at each facility in four categories using the Jenks' natural break classification. High PCI value facilities were concentrated in eastern Japan, in contrast to low PCI facilities located in urban areas on the Pacific side of southern Japan.

Relationship between PCI and Cerebral Infarction SMR

The analysis of the relationship between PCI and Cerebral Infarction SMR in each prefecture indicated a positive correlation coefficient (men: r=0.51 [95% confidence interval (CI): 0.19–0.70]) and (women r=0.45, [95% CI: 0.19–0.65]) (Figure 4). In short, prefectures with high PCI values had a higher risk of *Cerebral Infarction* mortality than prefectures with low PCI values.

The results for the three models are listed in Table 2. The income per taxpayer was excluded from the models after checking the VIF. Consequently, five variables are included in the model. The analysis results for men and the OLS model were accepted based on the Akaike's Information criteria (AIC). The normality and uniform dispersion of the error term were not rejected in the error term. In addition, no spatial autocorrelation was observed (Moran's I = 0.13, p=0.08). The PCI (B=0.13, [95% CI, 0.01–0.25]) and ratio of people that completed up to colleges and universities (B=-2.35, [95% CI, -3.39 to -1.32]) were significant variables. In other words, a high PCI was related to a high *cerebral infarction* mortality risk after adjustments for other factors. In the analysis of women, the SEM model was accepted based on AIC. Spatial parameter λ (B=0.42, [95% CI, 0.12–0.72) indicated spatial autocorrelation in the unmeasurable variable. PCI was not significant in all models, and the ratio of people that completed up to colleges and universities (B=-3.06, [95% CI, -3.75 to -2.37]), salt intake (B=14.78, [95% CI, 9.29–20.27]), participation rate in general health examinations (B=0.63, [95% CI, 0.06–1.20]), and proportion of smoking (B=-2.00, [95% CI, -3.61

to -0.39]) were significant variables. Therefore, socioeconomic status and lifestyle are more important than PCI in women.

Discussion

Population Coverage Rate and PCI

This study showed that the percentage of the population aged 55 years or older who could access MT within 120 min was approximately 99%. Hospitals with high PCI values were concentrated in the eastern area of Japan. To avoid overestimating the demand, we focused only on the population aged 55 years or older, which has a high risk of cerebral infarction (23). In other words, the population needing MT was almost entirely covered by the present hospital locations. However, considering the amount of supply, the PCI value ranged from 5876 to 129,838, and the distribution of human resources for MT did not meet requirements. Therefore, the present study implies the need to optimize the allocation of neurointerventionalists.

This study evaluated the PCI per neurointerventionalist at the hospitals using I2SFCA. PCI was approximately 30,000 (interquartile range: 25,799 to 37,194) in 2020. This indicates that one neurointerventionalist covered 30,000 people aged 55 years or older. Wang demonstrated that the actual number of discharged patients was higher in hospitals with higher PCI rates using the I2SFCA (30). Accordingly, when the PCI is high, the supply is insufficient, and physicians are required to diagnose or treat many patients. Hence, the hospital becomes crowded. Hospital crowding causes serious problems, such as patients being transferred with incomplete treatment, delayed diagnosis, examination, and treatment, and ambulances being diverted (28). Hospitals with high PCI values were located in eastern Japan, whereas those with low PCI values were concentrated in urban areas such as Tokyo and Osaka. This result was consistent with a previous report on physician distribution (18). PCI was linked to physician distribution because it was calculated based on the number of neurointerventionalists. This index can be used as an indicator of physician allocation, considering the demand. However, when the PCI was low, the amount of supply was adequate or excessive. Thus, this hospital can increase the provision of treatment or dispatch physicians to other hospitals with a high PCI.

Allocating physicians from low to high PCI hospitals is expected to improve accessibility to MT, reduce overwork of physicians, and adapt overtime regulations for physicians from April 2024 (20).

Relationship between PCI and Cerebral infarction mortality

Our findings indicated that PCI and cerebral infarction SMR were positively correlated by prefecture. To the best of our knowledge, this study is the first to report PCI-related health outcomes in this region. cerebral infarction SMR in men was higher in prefectures with high PCI; in contrast, the SMR in women was not significantly related to PCI after adjusting for socioeconomic status. Regression analysis showed that a 1% increase in PCI led to a 0.13% increase in SMR in men. This result supported the hypothesis that a high PCI is associated with high mortality risk. In addition, regional health outcomes with higher geographical accessibility to primary care using 2SFCA, which is the prototype of I2FCA, have a lower heart disease mortality (52) and a lower hospitalization rate for the elderly (53). This finding is consistent with our results. In particular, this study emphasized that accessibility to and crowdedness of hospitals are related to mortality in the emergency department. For women, the SEM had the lowest AIC, and the spatial parameter λ was significant, indicating that the unmeasurable variable had a positive spatial autocorrelation. Factors with similar characteristics between prefectures were associated with SMR and require further research.

Finally, we compared the results of previous studies on gender differences. In Japan, women develop AIS at an older age than men (54). Therefore, the effect of age increases the risk of death regardless of the availability of treatment. Salt intake, participation rate in general health examinations, and smoking rate were significant factors in women's results. Salt intake is undoubtedly a risk factor for stroke in Japan (55). Although general health examinations aim to identify the risk factors for hypertension or metabolic syndrome, their effect is unclear and has been controversial in previous studies (45,56). As this study only used data from 2015, longitudinal data must be analyzed. This study indicates that a high smoking rate is associated with low mortality in women. Past studies indicated that smoking increases the risk of developing AIS (44). Furthermore, smoking patients were 10 years younger than non-smokers at the first onset of stroke (57). This implies that developing AIS at a younger age reduces mortality at the regional level. A future analysis requires setting the AIS incidence rate as a regional health outcome.

Limitations and Perspectives

This study has several limitations. First, this study defined the demands as a population over 55 years old and did not manage the actual demands. In addition, the catchment area and distance decay functions were based on assumptions. Thus, the PCI was not the same as the crowdedness per physician or hospital. The population was set as actual reference data (23); however, the Gaussian distance decay function may underestimate demands in areas far from hospitals. The value of 120 min varied from resident to resident. Residents value the first option even if a hospital is 120 min away. Second, this study did not include cerebrovascular treatment practitioners. The JSNET certified them in September 2020 (58), and they can provide MT to patients. Thus, they will contribute to decreasing PCI in the future. Third, this analysis has a modifiable areal unit problem; in other words, if we aggregate data from different regions, different results can be obtained. However, it is reasonable to analyze the results at the prefectural level because prefectures have formulated medical plans for emergency medical care. This study did not consider demand on remote islands. Therefore, a neurointerventionalist at the hospital that accepts an air ambulance has a higher PCI than others. Finally, this study only mentioned the correlations by conducting a cross-sectional study. Further research using panel data is needed to clarify the causal relationship between PCI and mortality risk.

Conclusions

MT covered approximately 99% of the population aged 55 years or older within 120 min. However, PCI based on supply and demand is geographically heterogeneous. Hospitals with high PCI were concentrated in eastern Japan. Furthermore, a high PCI was correlated with high cerebral infarction mortality in men. Therefore, optimizing PCI by allocating or educating neurointerventionalists is a crucial challenge in the stroke medical system.

Author Contributions

Kazuki Ohashi designed the study, collected the data, carried out the analysis and drafted the manuscript.

Kensuke Fujiwara designed the study and provided the critical revision of the manuscript.

Toshiya Osanai provided the critical revision of the manuscript.

Takumi Tanikawa provided the critical revision of the manuscript.
Kyohei Bando collected the data and carried out the analysis.
Shojiro Yamazaki provided the critical revision of the manuscript.
Tomohiro Aoki provided the critical revision of the manuscript.
Songzi Gu: designed the study and collected the data.
Katsuhiko Ogasawara: designed the study and managed the overall project.
All of author approved the final version of manuscript to be published.

Conflicts of interest

The authors of this manuscript declare no competing interests in association with this study.

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Figure Legends:

Fig 1. The vertical axis means the weight obtained by converting the driving time into the range from 0 to 1. The horizontal axis means the driving time from 0 to 120 min.

Fig 2. Fig 2 shows the areas where a resident can reach a facility that can provide MT in driving times divided into 4 stages.

Fig 3. Fig 3 expresses the location of facilities. The PCI increases from white to dark red.

Fig 4. Fig4 shows the correlation (A: men, B: women) between log PCI and log SMR.

Table 1 Potential crowdedness index from 2020 to 2050.

year	Median	1st Qu	3rd Qu	Min – Max
2020	30426	25799	37194	5876–129838
2025	31275	26466	38497	6078–126682
2030	32374	27376	40407	6324–124588
2035	32510	27219	40837	6351–120021
2040	31891	26616	40137	6260–112707
2045	30709	25694	38670	6077–103620
2050	29469	24637	37416	5888–94692

Table 2　Relationship between PCI and SMR for men in 2020

	OLS		SEM	SLM
	Unadjusted B (95% CI)	Adjusted B (95% CI)	Adjusted B (95% CI)	Adjusted B (95% CI)
PCI	0.25 (0.06)***	0.13 (0.01–0.26) **	0.11 (0.01–0.22) **	0.11 (-0.00–0.23) *
Ratio of people that completed up to colleges and universities (%)		-2.35 (-3.39– -1.32) ***	-2.38 (-3.34– -1.41) ***	-2.26 (-3.22– -1.31) ***
Salt intake (g/day)		2.41 (-3.50– -8.33)	1.14 (-3.90–6.17)	1.68 (-3.69–7.06)
Participation rate in general health examinations (%)		0.42 (-0.30–1.13)	0.40 (-0.24–1.04)	0.44 (-0.20–1.07)
Smoking rate (%)		-0.27 (-1.91–1.37)	-0.01 (-1.54–1.52)	-0.33 (-1.82–1.16)
Intercept	-2.57 (0.65) ***	-1.37（-2.60– -0.14）**	-1.11 (-2.27–0.05)	-1.08 (-2.28–0.12) *
ρ				0.14 (-0.16–0.43)
λ			0.27 (-0.07–0.60)	
Wald Test			2.43	0.81
LR Test			1.67	0.86
Moran's I		0.13*	-0.00	0.04
Adjusted R^2	0.25	0.54		
AIC		-77.41	-77.09	-76.27

*** p<0.01, ** p<0.05, *p<0.1

OLS, ordinary least squares; CI, confidence interval; SEM, spatial error model; SLM, spatial lag model; PCI, potential crowdedness index

AIC, Akaike's Information Criteria.

OLS model: Jarque–Bera test = 0.74, p=0.69, Breush–Pagan test = 3.47, p=0.63

Table 3 Relationship between PCI and SMR for women in 2020

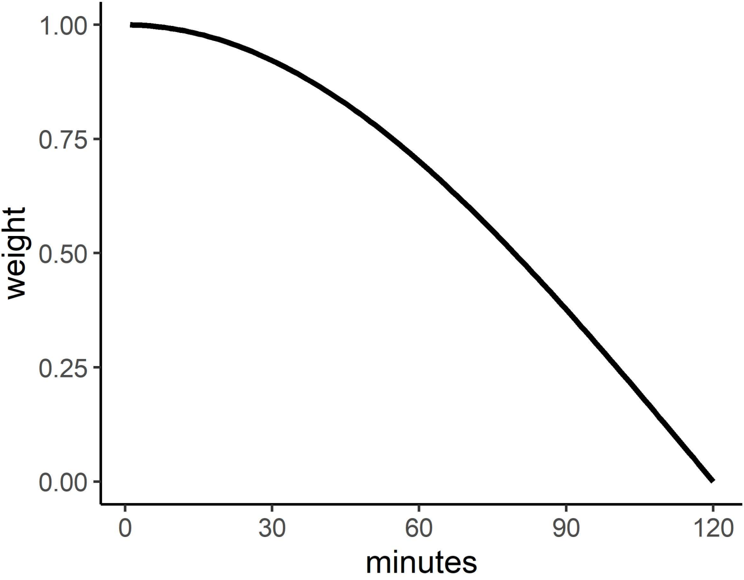
	OLS		SEM	SLM
	Unadjusted B (SE)	Adjusted B（95% CI）	Adjusted B（95% CI）	Adjusted B（95% CI）
PCI	0.27 (0.08) ***	0.06 (-0.04–0.17)	0.05 (-0.04– -0.14)	0.03 (-0.06–0.14)
Ratio of people that completed up to colleges and universities (%)		-2.94 (-3.67– -2.22) ***	-3.06 (-3.75– -2.37) ***	-2.70 (-2.70– -1.96) ***
Salt intake (g/day)		17.72 (11.07–24.38) ***	14.78 (9.29–20.27) ***	16.41 (10.47– -22.35) ***
Participation rate in general health examinations (%)		0.78 (0.13–1.43) **	0.63 (0.06–1.20) **	0.68 (0.09–1.26) **
Smoking rate (%)		-1.45 (-3.08–0.19) *	-2.00 (-3.61– -0.39) **	-1.84 (-3.35– -0.33) **
Intercept	-2.79 (0.83) ***	-2.04 (-3.15– -0.93) ***	-1.54 (-2.55– -0.53) ***	-1.60 (-2.70– -0.51) ***
ρ				0.19 (-0.06–0.43)
λ			0.42 (0.12–0.72)*	
Wald Test			7.65 ***	2.24
LR Test			3.18 *	1.83
Moran's I		0.16*	-0.02	0.08
Adjusted R^2	0.19	0.77		
AIC		-91.17	-92.35	-91.00

*** p<0.01, ** p<0.05, *p<0.1

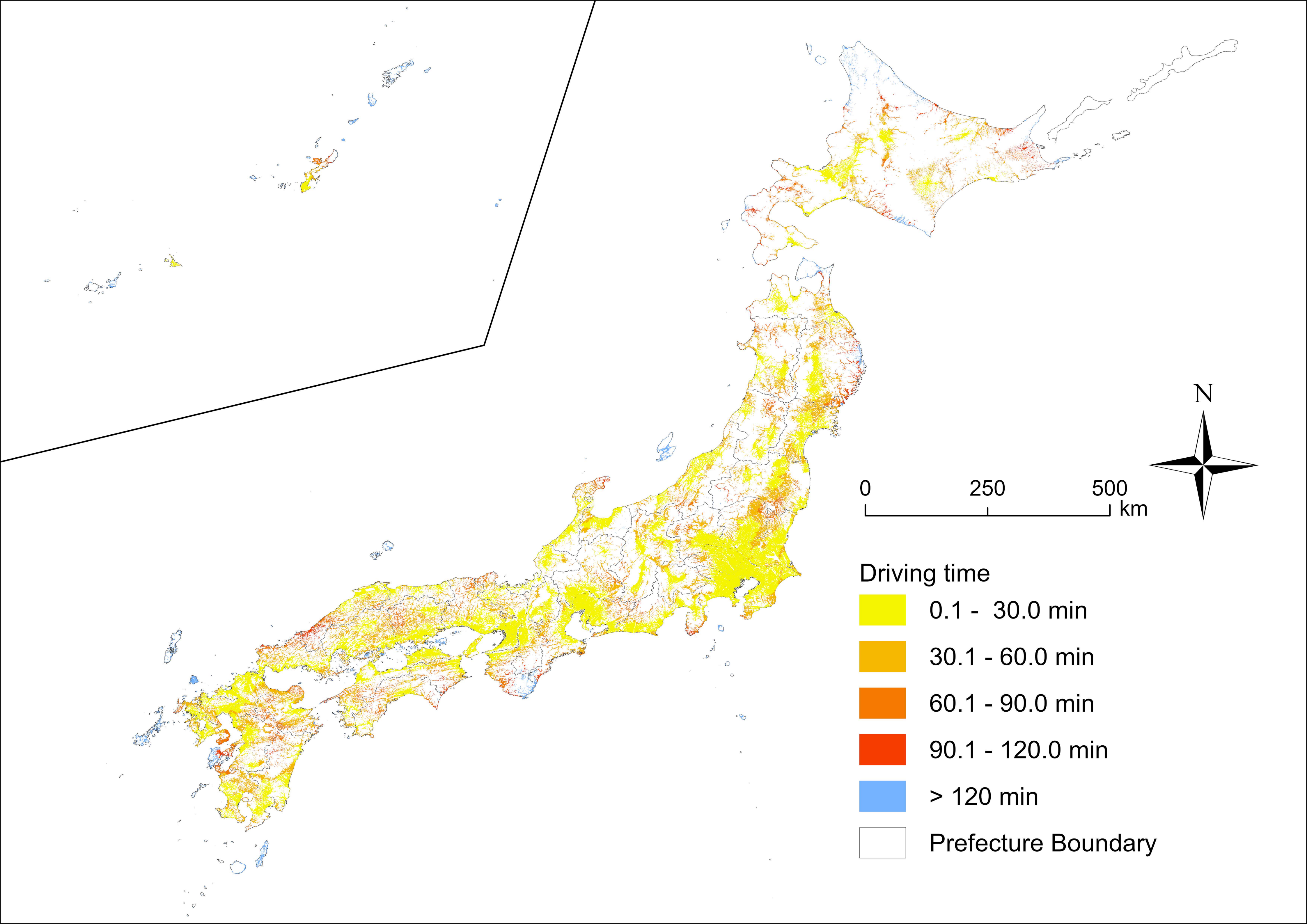
OLS, ordinary least squares; CI, confidence interval; SEM, spatial error model; SLM, spatial lag model; PCI, potential crowdedness index

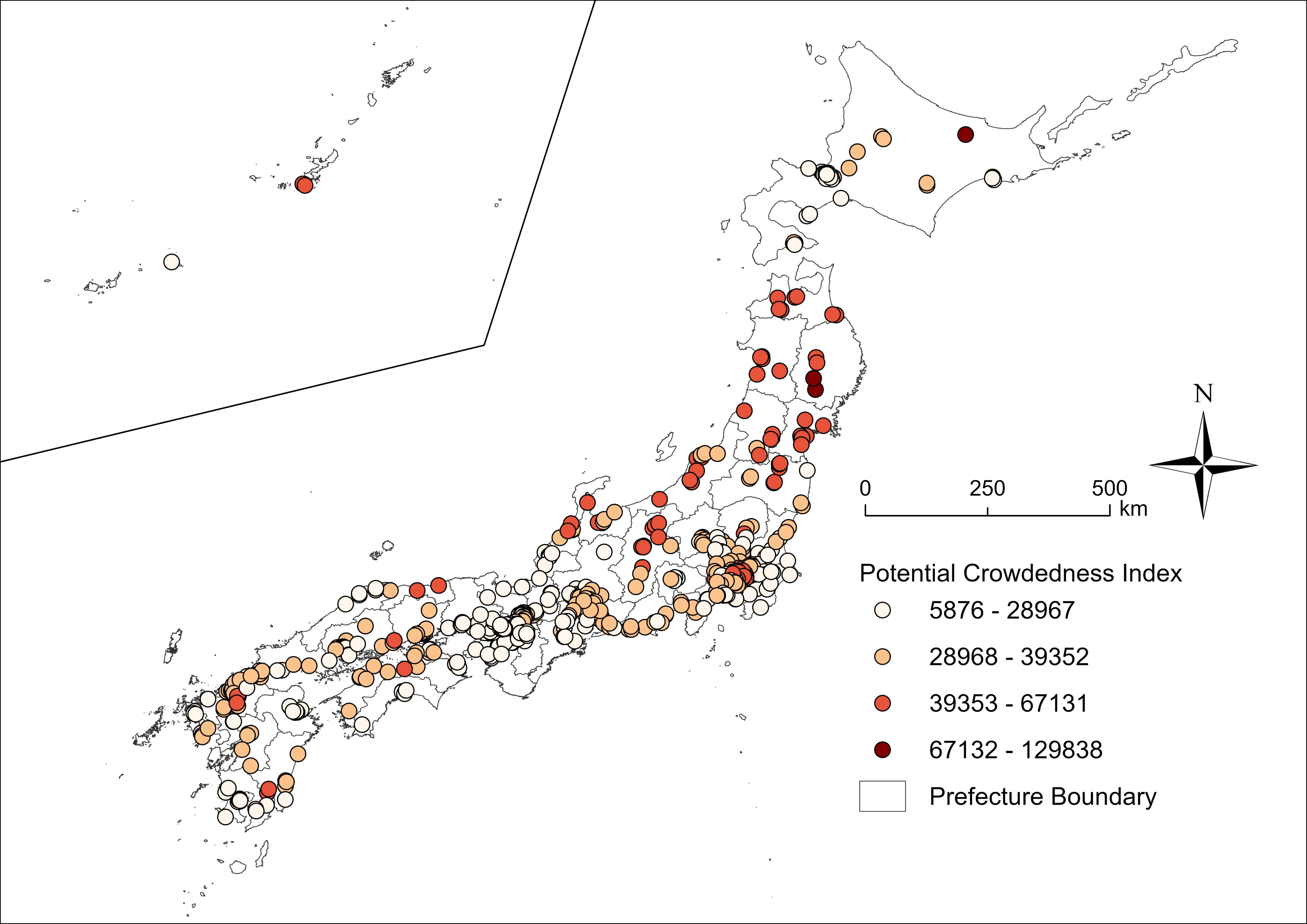
AIC, Akaike's Information criteria.

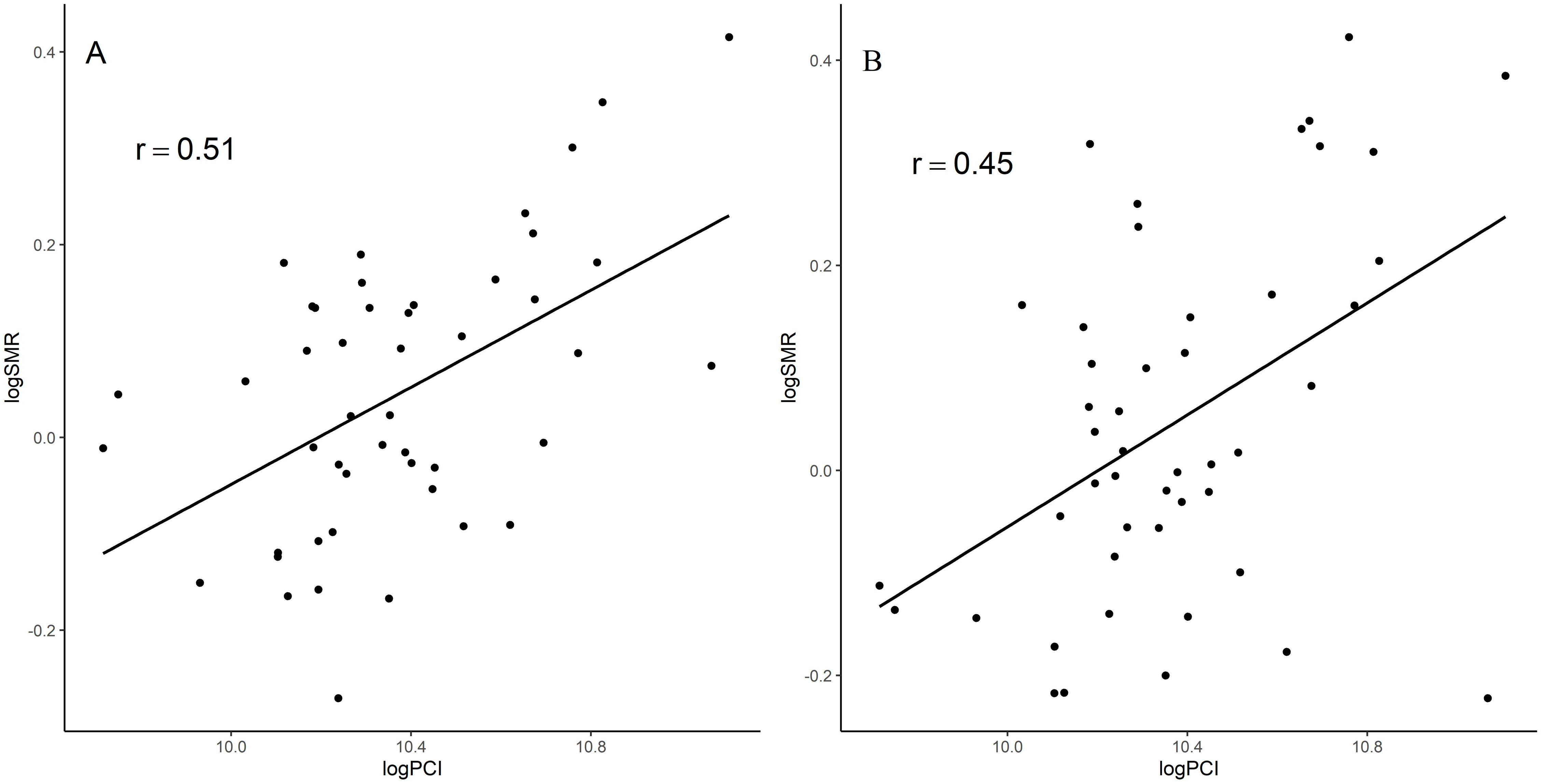
OLS model: Jarque–Bera test = 3.47, p=0.33, Breush–Pagan test = 2.07, p=0.84



1.00
0.75
0.50
0.25
0.00
weight
0
30
60
90
120
minutes


N
0
250
500
km
Driving time
0.1 - 30.0 min
30.1 - 60.0 min
60.1 - 90.0 min
90.1 - 120.0 min
> 120 min
Prefecture Boundary


N
0
250
500
km
Potential Crowdedness Index
5876 - 28967
28968 - 39352
39353 - 67131
67132 - 129838
Prefecture Boundary


A
r = 0.51
0.4
0.2
0.0
-0.2
logSMR
10.0
10.4
10.8
logPCI
B
r = 0.45
0.4
0.2
0.0
-0.2
logSMR
10.0
10.4
10.8
logPCI