



Higher Density of Primary Care Facilities Is Inversely Associated with Ischemic Heart Disease Mortality, but Not with Stroke Mortality: A Japanese Secondary Medical Service Area Level Ecological Count Data

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Poor accessibility to physicians might be linked to the inadequate control of cardiovascular risk factors. The aim of this study was to investigate whether the accessibility of primary care physicians was related to a lower incidence of ischemic heart disease and stroke mortality via ecological data analyses of both primary care facility density and internal physician density. The unit of observation was the Japanese secondary medical service area, the basic unit for healthcare planning and administration. A primary care facility was defined as a clinic or medical institution with less than 200 inpatient beds, whose specialty included internal medicine. The number of primary care facilities per 10,000 population and the number of internal physicians per 10,000 population were used as explanatory variables. Bayesian hierarchical models were used to analyze the relative risks (RR) of primary care facility density and internal physician density using the socioeconomic confounders of designated emergency hospitals, natural log-transformed population density, birth rate, secondary and tertiary industrial workers, and taxable income. In multivariate models for ischemic heart disease mortality, primary care facility density was significantly related to the total population (RR = 0.986, 95% credible interval [CrI]: 0.979-0.993), men (RR = 0.988, 95% CrI: 0.981-0.996), and women (RR = 0.986, 95% CrI: 0.979-0.993). No significant results were obtained for internal physician density. In the multivariate models for stroke mortality, neither primary care facility density nor internal physician density showed any significant effects. Increasing primary care facility density may reduce ischemic heart disease mortality.

Keywords: integrated nested Laplace approximation; internal physician; ischemic heart disease; primary care facility; stroke

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Introduction

As ischemic heart disease and stroke remain the leading causes of premature death in the world (Roth et al. 2015), the control of cardiovascular risk factors (including hypertension, diabetes, dyslipidemia, smoking, and low physical activity) is essential. Primary care physicians/general practitioners play a key role in assessing and managing cardiovascular risk factors to prevent cardiovascular diseases through lifestyle modification and medication (Ju et al. 2018). Furthermore, ecological studies in the U.S. have reported that primary care physician density is negatively

correlated with stroke and cardiovascular disease mortality (Shi et al. 2003b; Basu et al. 2019).

Many countries have primary care-based health systems that require a visit to a general practitioner who acts as a gatekeeper for the continuous care of patients (Velasco Garrido et al. 2011; Sripa et al. 2019). In Japan, all citizens are covered by the national insurance system, and patients in Japan can freely choose between visiting a physician's office or a hospital. This is because the healthcare system has no officially defined general physicians or gatekeepers (Ikegami and Campbell 1999), although the government encourages patients to choose their preferred doctors.

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Furthermore, there are patient disincentives for self-referral, including extra charges for initial consultations at large hospitals with 200 beds or more (Mossialos et al. 2017). Thus, Japanese patients have no officially defined general physicians, but Japanese primary care physicians (general physicians and family doctors) function in almost the same capacities as primary care physicians in clinics and small hospitals in other countries (Maruyama 2013).

Our previous municipality-level ecological study reported that a longer distance (by road) to the nearest primary care facility was significantly related to increased stroke mortality, whereas internal physician density was not. This finding was related to Hokkaido, which is the second largest northern island and the largest prefecture, and has the lowest prefecture population density in Japan (Saijo et al. 2018). However, to the best of our knowledge, in Japan, the relationships between the accessibility of primary care physicians and the prevalence of ischemic heart disease and stroke have not been fully determined.

Because one of the priorities of primary care physicians is to control coronary heart disease and stroke risk factors, poor accessibility to physicians might be linked to the inadequate control of cardiovascular risk factors. The aim of this study was to elucidate whether the accessibility of primary care physicians (evaluated via an ecological data analysis of primary care facility density and internal physician density) is related to lower levels of ischemic heart disease and stroke mortality.

Methods

Study design

This was an ecological study based on statistical data in Japan. The unit of observation was the secondary medical service area, which is comprised of several municipalities, and is regarded as the basic unit for healthcare planning and administration. There were 344 secondary medical service areas during the period from April, 2013 to March, 2018. However, in the present study, the Soso area was excluded because it contained evacuation zones contaminated with radioactive substances from the Fukushima Daiichi Nuclear Power Plant that was crippled by the 2011 Great East Japan Earthquake (Ochi et al. 2016). Thus, 343 secondary medical service areas were analyzed. Since this study used anonymized aggregated data, ethical approval was not required.

Outcomes

The numbers of deaths from ischemic heart disease (I20-I25 of ICD-10) and stroke (I60-I69 of ICD-10) were obtained from the Vital Statistics of Japan website (<http://www.mhlw.go.jp/toukei/list/81-1.html>) and the numbers of five-year deaths (2013-2017) within each secondary medical service area in Japan were used as outcomes. To calculate the expected number of deaths, the whole Japanese population was used as the reference population. Sex and five-year age groups, stratified for each five-year

population (2013-2017), were used based on the 2015 census and population estimates (2013-2017, <http://www.stat.go.jp/data/jinsui/2.htm>). The total and the sex-stratified standard mortality ratios (SMR) of ischemic heart disease and stroke were calculated by dividing the observed numbers by the expected number of deaths.

Accessibility to primary care physicians

A primary care facility was defined as follows: 1) a clinic whose specialty included internal medicine and 2) a medical institution with less than 200 inpatient beds, whose specialty included internal medicine.

The numbers of each secondary medical service area were extracted from the Japanese medical analysis platform constructed in December, 2018 data by the Japan Medical Association (Japan Medical Association 2018). The number of primary care facilities and internal physicians per 10,000 population were used as explanatory variables. The number of internal physicians per population of each secondary medical service area was obtained from the Survey of Physicians, Dentists and Pharmacists in 2014 (Health Statistics Office Japanese Ministry of Health Labour and Welfare 2015).

Confounders

The number of designated emergency hospitals in each secondary medical service area in 2015 was obtained (Health statistics Office Japanese Ministry of Internal Affairs and Communication 2016), and their per 100,000 population values were calculated. Population density (per km²) of each secondary medical service area was calculated by dividing the area (from the 2015 census) by the five-year average population. Since its distribution was skewed, the natural log-transformed population density was introduced into the models. The birth rate per 1,000 population in each secondary medical service area in 2015 was obtained from the Vital Statistics of Japan (<http://www.mhlw.go.jp/toukei/list/81-1.html>). The percentages of secondary and tertiary industry workers were obtained from the 2015 census. Taxable income data were acquired (Japanese Ministry of Internal Affairs and Communications, 2016), and taxable income per population head was used as a variable.

Statistical analysis

First, the crude and multivariate relative risks (RR) of primary care facility density, internal physician density, designated emergency hospitals, population density (km²), birth rate, secondary industry workers (%), tertiary industry workers (%), and taxable income for total and sex-stratified ischemic heart disease and stroke mortalities were analyzed via univariate and multivariate Poisson regression analyses with an offset variable (the expected number of deaths).

Regarding area-based ecological studies, the uneven population distribution in different areas corresponds to differences in the mortality rate. A small change in the number of observed outcomes could cause extreme changes

in RR, which is known as a small number problem (Matthews 1990). To address this issue, smoothing techniques for RR estimation have been developed (Kang et al. 2016). Therefore, in the present study, Bayesian hierarchical models with integrated nested Laplace approximation (INLA) were applied to estimate the smoothed standardized mortality rates for each secondary medical service area (Rue et al. 2009, 2017). Another possible approach was to use Markov Chain Monte Carlo (MCMC) methods using the BUGS (Bayesian inference Using Gibbs Sampling) software, but INLA for spatial models is able to return accurate parameter estimates in a much shorter time than MCMC (Kang et al. 2016), and convergence diagnostics are not necessary (Paul et al. 2010). The priors were set to the default (Gómez-Rubio 2020). For the default settings, the fixed effect parameter estimates were the same for INLA and OpneBUGS (Carroll et al. 2015). These were based on Poisson regression models with random effects allowing for both nonstructural variability (heterogeneity across all areas in the study region) and structural variability (autocorrelation between neighboring areas). The crude and adjusted RR of primary care facility density and internal physician density were analyzed. Secondary medical service areas that shared a border were defined as neighboring areas. If the area comprised an isolated island or several islands, the area that had a regular sea route (or a regular air route if a sea route did not exist) was defined as the neighboring area.

Statistical analyses of regular Poisson regressions were performed using Stata statistical software version 16.0 for Windows (StataCorp, College Station, TX, USA). Statistical analyses of Bayesian hierarchical models were conducted using the R-INLA library (19.09.3) in R-3.6.2 to obtain RRs and their 95% credible intervals. There were no missing values in the dataset. $P < 0.05$ was defined as statistically significant, aside from the Bayesian estimation analyzed by INLA. In the Bayesian estimation, since it was not possible to obtain direct P values, a 95% credible interval that did not include 1 was deemed to be a significant result.

Results

Table 1 presents the characteristics of 343 secondary medical service areas in Japan. The mean number of primary care facilities (per 10,000 population) was 6.9 and ranged from 2.6 to 20.0, while the mean number of internal physicians (per 10,000 population) was 7.4 and ranged from 0.6 to 36.6.

The RRs for ischemic heart disease mortality in crude and adjusted regular Poisson regression models are shown in Table 2. In multivariate models, high primary care facility density (per 1 facility/10,000 population increase) was significantly related to reduced RR in terms of the total population (RR = 0.989, 95% confidence interval (CI): 0.987-0.990), men (RR = 0.989, 95% CI: 0.987-0.991), and women (RR = 0.989, 95% CI: 0.987-0.991). There was a

Table 1. Characteristics of 343 secondary medical service areas in Japan.

	N	Mean	SD	Median	Min	25 Percentiles	75 Percentiles	Max
Primary care facility per 10,000 population	343	6.9	1.7	6.8	2.6	5.6	7.9	20.0
Internal physicians per 10,000 population	343	7.4	3.3	7.0	0.6	5.7	8.2	36.6
Designated emergency hospital per 100,000 population	343	3.9	2.1	3.5	0.8	2.5	4.9	16.8
Population density (km^2)	343	1,233	2,777	249	12	93	722	18,061
Ln population density	343	5.7	1.6	5.5	2.5	4.5	6.6	9.8
Birth rate per 1,000 population	343	7.5	1.4	7.5	4.1	6.6	8.3	12.2
Secondary industry workers (%)	343	23.8	6.6	23.0	10.0	18.8	28.5	43.4
Tertiary industry workers (%)	343	61.5	6.0	61.1	47.8	56.9	65.9	77.3
Taxable income per population (100,000 yen)	343	12.3	3.1	11.9	7.3	10.1	13.6	36.4
SMR of total death (men and women)	343	102.1	6.3	102.1	88.2	97.5	106.1	121.2
SMR of total death (men)	343	102.5	7.3	102.3	85.5	97.7	107.4	125.0
SMR of total death (women)	343	101.8	6.0	101.6	86.5	97.4	105.5	118.5
SMR of malignant neoplasms (men and women)	343	100.1	7.7	99.7	81.7	95.0	104.1	125.9
SMR of malignant neoplasms (men)	343	100.9	8.6	100.5	80.2	95.3	106.2	131.8
SMR of malignant neoplasms (women)	343	99.1	7.6	98.6	78.5	95.1	104.0	125.1
SMR of ischemic heart disease (men and women)	343	103.1	14.4	101.9	63.1	93.9	112.0	153.3
SMR of ischemic heart disease (men)	343	102.8	15.4	102.0	56.8	93.4	112.9	146.3
SMR of ischemic heart disease (women)	343	103.3	14.7	102.6	66.5	93.1	112.0	160.5
SMR of stroke (men and women)	343	105.5	18.0	103.3	70.3	92.1	115.0	163.5
SMR of stroke (men)	343	105.7	18.9	102.9	63.8	92.3	115.9	168.7
SMR of stroke (women)	343	105.4	18.8	102.6	61.5	91.7	115.3	166.8

SMR, standardized mortality rate.

Table 2. Results of regular Poisson regression analyses for relative risk of ischemic heart disease mortality.

	Crude			Multivariate*		
	RR	95% CI	P value	RR	95% CI	P value
Men and women						
Primary care facilities per 10,000 population (per 1 increase)	0.988	0.987 - 0.989	< 0.001	0.989	0.987 - 0.990	< 0.001
Internal physicians per 10,000 population (per 10 increase)	0.974	0.967 - 0.982	< 0.001	1.017	1.007 - 1.027	0.001
Designated emergency hospitals per 100,000 population (per 1 increase)	1.017	1.016 - 1.018	< 0.001	1.014	1.012 - 1.016	< 0.001
Ln population density (per 1 increase)	0.990	0.988 - 0.991	< 0.001	1.033	1.030 - 1.035	< 0.001
Birth rate per 1,000 population (per 1 increase)	0.957	0.956 - 0.959	< 0.001	0.956	0.954 - 0.958	< 0.001
Secondary industry workers (%) (per 10 increase)	1.016	1.013 - 1.020	< 0.001	0.959	0.953 - 0.964	< 0.001
Tertiary industry workers (%) (per 10 increase)	0.952	0.949 - 0.955	< 0.001	0.920	0.914 - 0.926	< 0.001
Taxable income per population (10,000 yen) (per 1 increase)	0.993	0.993 - 0.994	< 0.001	0.998	0.997 - 0.998	< 0.001
Men						
Primary care facilities per 10,000 population (per 1 increase)	0.990	0.988 - 0.991	< 0.001	0.989	0.987 - 0.991	< 0.001
Internal physicians per 10,000 population (per 10 increase)	0.988	0.977 - 0.998	0.025	1.022	1.007 - 1.037	0.005
Designated emergency hospitals per 100,000 population (per 1 increase)	1.018	1.016 - 1.020	< 0.001	1.011	1.009 - 1.014	< 0.001
Ln population density (per 1 increase)	0.990	0.989 - 0.992	< 0.001	1.032	1.029 - 1.036	< 0.001
Birth rate per 1,000 population (per 1 increase)	0.954	0.952 - 0.957	< 0.001	0.952	0.949 - 0.955	< 0.001
Secondary industry workers (%) (per 10 increase)	1.003	0.998 - 1.007	0.229	0.932	0.924 - 0.940	< 0.001
Tertiary industry workers (%) (per 10 increase)	0.959	0.954 - 0.963	< 0.001	0.902	0.894 - 0.911	< 0.001
Taxable income per population (10,000 yen) (per 1 increase)	0.994	0.993 - 0.994	< 0.001	0.998	0.997 - 0.999	0.002
Women						
Primary care facilities per 10,000 population (per 1 increase)	0.986	0.985 - 0.988	< 0.001	0.989	0.987 - 0.991	< 0.001
Internal physicians per 10,000 population (per 10 increase)	0.962	0.953 - 0.972	< 0.001	1.012	0.998 - 1.027	0.087
Designated emergency hospitals per 100,000 population (per 1 increase)	1.017	1.015 - 1.018	< 0.001	1.016	1.014 - 1.019	< 0.001
Ln population density (per 1 increase)	0.989	0.987 - 0.991	< 0.001	1.033	1.030 - 1.036	< 0.001
Birth rate per 1,000 population (per 1 increase)	0.960	0.958 - 0.962	< 0.001	0.960	0.957 - 0.963	< 0.001
Secondary industry workers (%) (per 10 increase)	1.029	1.025 - 1.033	< 0.001	0.982	0.974 - 0.990	< 0.001
Tertiary industry workers (%) (per 10 increase)	0.947	0.943 - 0.951	< 0.001	0.935	0.927 - 0.943	< 0.001
Taxable income per population (10,000 yen) (per 1 increase)	0.993	0.992 - 0.994	< 0.001	0.997	0.996 - 0.998	< 0.001

All regular Poisson regression analyses were performed using Stata statistical software version 16.0 for Windows (StataCorp, College Station, TX, USA).

RR, relative risk; CI, confidence interval.

*All listed variables were included in the models.

significant relation between increasing internal physician density (per 10 physician/10,000 population increase) and higher RR in the total population (RR = 1.017, 95% CI: 1.007-1.027) and men (RR = 1.022, 95% CI: 1.007-1.037), but not women (RR = 1.012, 95% CI: 0.998-1.027).

Table 3 shows the RRs for stroke mortality in crude and adjusted regular Poisson regression models. In the multivariate models, high primary care facility density was significantly related to lower RR among the total population (RR = 0.994, 95% CI: 0.992-0.996), men (RR = 0.995, 95% CI: 0.992-0.998), and women (RR = 0.992, 95% CI: 0.989-0.995), while high internal physician density was significantly related to reduced RR only among women (RR = 0.979, 95% CI: 0.961-0.998).

Table 4 presents the RRs for ischemic heart disease and stroke mortalities in Bayesian hierarchical models with INLA. In the multivariate models for ischemic heart disease mortality, high primary care facility density was

significantly related to reduced RR among the total population (RR = 0.986, 95% credible interval [CrI]: 0.979-0.993), men (RR = 0.988, 95% CrI: 0.981-0.996), and women (RR = 0.986, 95% CrI: 0.979-0.993). No significant results were seen for internal physician density. In the stroke mortality multivariate models, neither primary care facility density nor internal physician density was associated with significant RR.

Discussion

In the Bayesian hierarchical models with INLA, the increased primary care facility density was significantly related to lower RR for ischemic heart disease, but neither primary care facility density for stroke nor the internal physician density for both ischemic heart disease and stroke showed statistically significant results. To the best of our knowledge, this is the first report of a possible protective effect of increasing primary care facility density of Japanese

Table 3. Results of regular Poisson regression analyses for relative risk of stroke mortality.

	Crude			Multivariate*		
	RR	95% CI	P value	RR	95% CI	P value
Men and women						
Primary care facilities per 10,000 population (per 1 increase)	0.971	0.969 - 0.972	<0.001	0.994	0.992 - 0.996	<0.001
Internal physicians per 10,000 population (per 10 increase)	0.923	0.913 - 0.932	<0.001	0.987	0.973 - 1.001	0.067
Designated emergency hospitals per 100,000 population (per 1 increase)	1.020	1.018 - 1.022	<0.001	0.990	0.988 - 0.992	<0.001
Ln population density (per 1 increase)	0.951	0.949 - 0.952	<0.001	0.972	0.969 - 0.975	<0.001
Birth rate per 1,000 population (per 1 increase)	0.945	0.943 - 0.947	<0.001	0.975	0.973 - 0.978	<0.001
Secondary industry workers (%) (per 10 increase)	1.103	1.099 - 1.107	<0.001	0.995	0.988 - 1.003	0.222
Tertiary industry workers (%) (per 10 increase)	0.875	0.872 - 0.879	<0.001	0.922	0.914 - 0.930	<0.001
Taxable income per population (10,000 yen) (per 1 increase)	0.982	0.981 - 0.982	<0.001	1.000	0.999 - 1.001	0.924
Men						
Primary care facilities per 10,000 population (per 1 increase)	0.976	0.974 - 0.978	<0.001	0.995	0.992 - 0.998	0.002
Internal physicians per 10,000 population (per 10 increase)	0.952	0.939 - 0.966	<0.001	0.996	0.976 - 1.016	0.677
Designated emergency hospitals per 100,000 population (per 1 increase)	1.024	1.021 - 1.027	<0.001	0.992	0.989 - 0.996	<0.001
Ln population density (per 1 increase)	0.953	0.951 - 0.956	<0.001	0.979	0.975 - 0.983	<0.001
Birth rate per 1,000 population (per 1 increase)	0.948	0.945 - 0.951	<0.001	0.980	0.976 - 0.984	<0.001
Secondary industry workers (%) (per 10 increase)	1.080	1.074 - 1.086	<0.001	0.970	0.959 - 0.981	<0.001
Tertiary industry workers (%) (per 10 increase)	0.888	0.883 - 0.894	<0.001	0.912	0.901 - 0.923	<0.001
Taxable income per population (10,000 yen) (per 1 increase)	0.981	0.979 - 0.982	<0.001	0.996	0.994 - 0.997	<0.001
Women						
Primary care facilities per 10,000 population (per 1 increase)	0.966	0.964 - 0.968	<0.001	0.992	0.989 - 0.995	<0.001
Internal physicians per 10,000 population (per 10 increase)	0.895	0.883 - 0.908	<0.001	0.979	0.961 - 0.998	0.034
Designated emergency hospitals per 100,000 population (per 1 increase)	1.016	1.014 - 1.019	<0.001	0.988	0.985 - 0.991	<0.001
Ln population density (per 1 increase)	0.948	0.946 - 0.950	<0.001	0.966	0.962 - 0.970	<0.001
Birth rate per 1,000 population (per 1 increase)	0.941	0.938 - 0.944	<0.001	0.971	0.968 - 0.975	<0.001
Secondary industry workers (%) (per 10 increase)	1.125	1.118 - 1.131	<0.001	1.019	1.008 - 1.029	<0.001
Tertiary industry workers (%) (per 10 increase)	0.863	0.858 - 0.869	<0.001	0.932	0.921 - 0.942	<0.001
Taxable income per population (10,000 yen) (per 1 increase)	0.983	0.982 - 0.984	<0.001	1.004	1.002 - 1.006	<0.001

All regular Poisson regression analyses were performed using Stata statistical software version 16.0 for Windows (StataCorp, College Station, TX, USA).

RR, relative risk; CI, confidence interval.

*All listed variables were included in the models.

secondary medical service area level on ischemic heart disease mortality in the whole of Japan.

Although our previous study was a municipal-level analysis in a northern island of Japan, a longer road distance to the nearest primary care facility was significantly related to increased stroke mortality, while internal physician density was not (Saijo et al. 2018). Because no Japanese statistics on the number of absolute primary care physicians were available, we used the number of multispecialty internal physicians working at facilities that included all types of clinics and hospitals for the present study and the previous study (Saijo et al. 2018). The number of physicians therefore may not reflect the absolute primary physician density because they may have other main specialties. Meanwhile, as a general practitioner is not officially defined and there are patient disincentives for self-referral (including extra charges for initial consultations at large hospitals with 200 beds or more), primary care

facilities were defined as clinics and medical institutions with less than 200 inpatient beds, whose specialty included internal medicine. Thus, primary care facility density referred to the number of places where people were able to receive primary care in a secondary medical service area. We considered that this parameter reflected primary care accessibility more accurately than internal physician density. We therefore hypothesized that primary care facility density had more protective effects on ischemic heart disease and stroke mortality compared with internal physician density.

In state-level studies of the USA, increased primary care physician density was significantly related to reduced all-cause and stroke mortality (Shi et al. 2003a, b, 2005). A county-level study in the USA reported that temporary increases in primary care physician density were significantly correlated with reduced cardiovascular mortality (Basu et al. 2019). Thus, though there are wide

Table 4. Results of Bayesian hierarchical modeling with integrated nested Laplace approximation (INLA).

	Crude		Multivariate*	
	RR	95% CrI	RR	95% CrI
Ischemic heart disease				
Men and women				
Primary care facilities per 10,000 population (per 1 increase)	0.989	0.983 - 0.994	0.986	0.979 - 0.993
Internal physicians per 10,000 population (per 10 increase)	0.990	0.955 - 1.026	1.014	0.978 - 1.051
Men				
Primary care facilities per 10,000 population (per 1 increase)	0.991	0.984 - 0.997	0.988	0.981 - 0.996
Internal physicians per 10,000 population (per 10 increase)	1.000	0.962 - 1.039	1.022	0.982 - 1.064
Women				
Primary care facilities per 10,000 population (per 1 increase)	0.988	0.982 - 0.994	0.986	0.979 - 0.993
Internal physicians per 10,000 population (per 10 increase)	0.979	0.945 - 1.015	1.003	0.967 - 1.040
Stroke				
Men and women				
Primary care facilities per 10,000 population (per 1 increase)	0.999	0.993 - 1.005	1.007	1.000 - 1.014
Internal physicians per 10,000 population (per 10 increase)	0.974	0.933 - 1.016	0.984	0.948 - 1.021
Men				
Primary care facilities per 10,000 population (per 1 increase)	0.998	0.990 - 1.006	1.006	0.999 - 1.014
Internal physicians per 10,000 population (per 10 increase)	0.986	0.945 - 1.030	0.992	0.953 - 1.033
Women				
Primary care facilities per 10,000 population (per 1 increase)	0.998	0.992 - 1.004	1.006	0.999 - 1.013
Internal physicians per 10,000 population (per 10 increase)	0.979	0.943 - 1.017	0.979	0.941 - 1.018

All statistical analyses of the Bayesian hierarchical models were conducted using the R-INLA library (19.09.3) in R-3.6.2.

RR, relative risk; CrI, credible interval.

*Two listed variables, designated emergency hospitals, population density, birth rate, secondary and tertiary industrial workers, and taxable income were included in the models

disparities in the accessibility and quality of healthcare in the USA, and patients in Japan are several times more likely to access healthcare (Ruggles et al. 2019), our findings of reduced ischemic heart disease mortality were consistent with those studies. However, we found that primary care facility density had no significant impact on stroke mortality. Reasons for the discrepancy between the benefits associated with ischemic heart disease mortality in the present study and that of stroke mortality in the previous Hokkaido study may be due to both the indicator difference between density and distance, and the area unit difference between Japanese prefecture levels and municipality levels in Hokkaido.

As previously mentioned, one possible mechanism of decreased mortality is that easier access to primary care physicians could correspond to better cardiovascular risk factor control due the important role of physicians in reducing coronary heart disease and stroke risk factors (Ju et al. 2018). A primary care service area study (6,542 areas) in the USA reported that the temporary increase in primary care physician density was significantly related to decreased all-cause mortality and ambulatory-care sensitive-condition hospitalization (Chang et al. 2017). The better primary care access for diabetic patients may be associated with reduced ambulatory-care sensitive-condition hospitalization (Gibson

et al. 2013). Thus, improving primary care accessibility may also decrease ambulatory-care sensitive-condition hospitalizations due to the decline in cardiovascular risk factors.

Several socioeconomic factors that were used as possible confounders and emergency hospital density have also been reported as factors related to cardiovascular mortality (Kada et al. 2016). The present study used the percentages of secondary and tertiary industrial workers but did not include primary industry employees. Because the percentage of primary industry workers was the opposite of the other values, it did not need to be introduced to the model as a confounder (Otsubo et al. 2009).

In contrast to primary percutaneous coronary intervention to treat acute myocardial infarction that occurs even after 12 hours from onset (Nomura et al. 2010), administration of recombinant tissue plasminogen activator (rt-PA) has been restricted to within 4.5 hours from onset to improve the prognosis of cerebral infarction, which is the most prevalent stroke type, and access to the facilities that administer rt-PA have a wide disparity (Imai et al. 2014). Thus, the density of those facilities was not adjusted in our models, which may have affected the stroke results.

Our study has some limitations. First, since there was no individual data available, an adjusted analysis for the

fully confounding factors was not conducted, and since this was an ecological study, ecological fallacy may have occurred. No cause-effect relationships were thus inferred. However, we applied hierarchical models that considered spatial correlation and included several socioeconomic indicators. Second, the RR (0.986) of primary care facilities density meant only a 1.4% reduction in ischemic heart disease mortality. Thus, the effect size was rather small, and 1.4% of the number of ischemic heart disease deaths (Year 2017: N = 69,857) was 978. Third, the primary care facility density data was based on 2019 data because there had been no public data from which to obtain the number of defined primary care facilities between 2013 and 2017. According to the Survey of Medical Institutions, the number of general hospitals (with 20 beds or more, including more than 199-bed hospitals) changed from 7,474 in 2013 to 7,314 in 2018 (-2.1%). The number of clinics (with no beds or less than 20 beds, including other than internal medicine clinics) increased from 100,528 in 2013 to 102,105 in 2018 (+1.6%). We therefore believed that the number of primary medical care facilities in 2019 could be used as a substitute for those between 2013 and 2017. Finally, although in many countries primary care is delivered mainly through general practitioners in clinics, a primary care facility in this present study was defined as a clinic or medical institution with less than 200 inpatient beds, whose specialty included internal medicine, because primary care services are generally available both in outpatient departments of small and medium-sized hospitals with less than 200 beds (Maruyama 2013; Kaneko and Matsushima 2017; Aoki et al. 2020).

In conclusion, higher primary care facility density may be related to reduced ischemic heart disease mortality. The Japanese medical plan for secondary medical service areas should thus consider the issue of accessibility to primary care physicians.

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Conflict of Interest

The authors declare no conflicts of interest.

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