Introduction

Hypertension is a major risk factor for cardiovascular disease mortality, and accumulated evidence has demonstrated the effectiveness of reducing dietary salt intake for controlling hypertension and cardiovascular disease incidence at the individual level. At the ecological level, a lower level of average salt intake is shown to be related to lower mortality and a lower prevalence of hypertension-related diseases. A recent population-based intervention in the UK successfully reduced population-level salt intake through food standards regulation and a public campaign on the salt content of processed foods, although the impact on population health remains to be seen.

Japan has experienced a drastic decrease in cardiovascular mortality, although this varies across regions. This regional variation does not necessarily match the local patterns of reported average salt intake. In this study, we examined population-level risk factors for hypertension-related disease mortality, focusing on the average household dietary consumption of salt intake sources. Methods: We prepared an ecological panel dataset, with prefecture as the unit of analysis, by referring to public statistics and market research data from 2012 to 2015. We collected prefectural averages of household dietary consumption related to salt intake and other nutrients that may affect hypertension control. We used demographic characteristics, medical care availability and local economy indices as covariates. Panel data analysis with fixed-effects modelling was performed, regressing prefectural-level mortality from ischaemic heart diseases, subarachnoid and intracerebral haemorrhage and cerebral infarction on dietary consumption and the selected covariates. Results: We confirmed the average household consumption of salt equivalents of discretionary salt intake sources to be positively but only weakly associated with mortality from ischaemic heart diseases and cerebral infarction. Household expenditure on processed foods was positively associated with ischaemic heart disease mortality. Conclusions: These findings may suggest that the reduction of salt in processed foods, in addition to individual behavioural change, could be useful for decreasing mortality from ischaemic heart diseases in the Japanese population. Ecological factors related to decreasing cerebrovascular disease mortality in the context of the ageing Japanese population require further investigation.

Household dietary salt consumption and mortality from cardiovascular diseases: an ecological panel analysis in Japan

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Background: Epidemiological evidence has shown that lower salt intake reduces hypertension-related disease mortality. Japan has experienced a drastic decrease in cardiovascular mortality, although this varies across regions. This regional variation does not necessarily match the local patterns of reported average salt intake. In this study, we examined population-level risk factors for hypertension-related disease mortality, focusing on the average household dietary consumption of salt intake sources. Methods: We prepared an ecological panel dataset, with prefecture as the unit of analysis, by referring to public statistics and market research data from 2012 to 2015. We collected prefectural averages of household dietary consumption related to salt intake and other nutrients that may affect hypertension control. We used demographic characteristics, medical care availability and local economy indices as covariates. Panel data analysis with fixed-effects modelling was performed, regressing prefectural-level mortality from ischaemic heart diseases, subarachnoid and intracerebral haemorrhage and cerebral infarction on dietary consumption and the selected covariates. Results: We confirmed the average household consumption of salt equivalents of discretionary salt intake sources to be positively but only weakly associated with mortality from ischaemic heart diseases and cerebral infarction. Household expenditure on processed foods was positively associated with ischaemic heart disease mortality. Conclusions: These findings may suggest that the reduction of salt in processed foods, in addition to individual behavioural change, could be useful for decreasing mortality from ischaemic heart diseases in the Japanese population. Ecological factors related to decreasing cerebrovascular disease mortality in the context of the ageing Japanese population require further investigation.
potential confounders. We selected the following causes of death (with International Statistical Classification of Diseases and Related Health Problems, Tenth Revision codes): ischaemic heart diseases (I20–I25), subarachnoid haemorrhage (I60, I69.0), intracerebral haemorrhage (I61, I69.1) and cerebral infarction (I63, I69.3).

Average household consumption of dietary salt and related food items
A previous study in Japan identified the average share of discretionary sodium intake from self-cooking as 54.7% of the total dietary sodium intake, with processed foods consumed at home and dining out accounting for the rest.16 The largest food group in terms of dietary sodium intake was seasoning with seasoning salt, soy sauce and miso paste, contributing more than 60% of the total sodium intake.

We estimated the average household consumption of salt equivalents from soy sauce, seasoning salt and miso paste as a surrogate marker of discretionary dietary salt consumption in the household. More specifically, we referred to publicly available data derived from the governmental Family Income and Expenditure Survey (FIES) to obtain the prefecture-specific average household consumption of these food items each year from 2012 to 2015.17 The FIES randomly sampled households with two or more persons in the prefectural capital cities to collect consumption records for 6 consecutive months, refreshing half of the sample every 3 months. The sample size was around 5500 households each year. Due to the above sampling frame, one-person households and households in rural areas may not be adequately reflected in our dataset.

For this study, we assembled data on the yearly household consumption of soy sauce (l/year), salt (kg/year) and miso paste (kg/year) in each prefecture. Furthermore, we calculated salt equivalents (kg/year) from the data on the consumption of these three seasonings by referring to the mean salt equivalents of each seasoning, published in the Standard Tables of Food Composition in Japan, 2010.18 More specifically, the salt equivalent of soy sauce is 15.0 g/84.7 ml, that of seasoning salt is 99.1 g/100 g and that of miso paste is 12.0 g/100 g.

Because processed foods consumed at home and dining out are also significant sources of salt intake,16 we assembled data on the yearly amount of household expenditure (in tens of thousands of Japanese yen, or 90 US dollars) on processed food and eating out from the FIES. In the FIES, processed foods included lunch boxes, sandwiches, fried and grilled foods (e.g. fried/grilled chicken or fish) and other ready-to-eat foods (e.g. stewed/flavoured/seasoned/simmered fish, beans or vegetables). To make comparisons across prefectures and years, we calibrated the expenditure values using the consumer price index of prefectural differences and the over-year calibrator, with the indices of 2015 as a reference.19

Other household dietary consumption
We added salted and dried fish as a minor source of salt consumption.18 We also adopted five other food items from the FIES: fresh vegetables, fresh fruits, raw fish/shellfish, seaweed and bean curd. These food items are rich in potassium, calcium, omega-3 fatty acids, dietary fibre and vegetable protein, all of which can affect hypertension control.20

Demographic characteristics, economic factors and medical care at the prefecture level
We considered demographic characteristics, economic factors and medical care accessibility to be potential confounders. The percentage of the prefectural population aged ≥65 years and the sex ratio (men per 100 women) for each prefecture were obtained from estimates issued by the National Institute of Population and Social Security Research.21

We also included the crude prevalence of metabolic syndrome and candidate obese conditions for those aged 40–74 years as a conventional cardiovascular risk factor, available at https://www.mhlw.go.jp/bunya/shakaihoshio/iryouuseido01/info02a-2.html. The National Health Checkup Programme was newly introduced by the Ministry of Health, Labour and Welfare for all persons aged 40–74 years in the nation to specifically screen for metabolic syndrome conditions (waist circumference of >85 cm for males and >90 cm for females, plus more than two of the following conditions: dyslipidaemia, hypertension or high blood sugar).22

To account for the influence of household size, we obtained the average size of households with two or more persons for each prefecture from the FIES. We included the prefectural average taxable income by referring to the number of taxpayers and total amount of taxable income issued by the National Tax Agency of Japan.23 We also included population density per inhabitable area, drawn from the System of Social and Demographic Statistics of Japan.24

Finally, as a surrogate marker of medical care accessibility, we used the number of medical care institutions per 100,000 population for each prefecture and year.24 We also referred to JRSR–CI for Academia, a commercial data source provided by IMS Japan, Inc. that included the entire monthly market sales of antihypertensive drugs in Japan from June 2012 to December 2015. We limited these data to orally administered drugs mainly used in the outpatient treatment of hypertension. We estimated annual sales in 2012 by doubling the data from July to December 2012. We counted the number of tablets per person per year. We did not use the defined daily dose as a standardized measurement unit because this information was not available for some of the newer drugs. We expected little variance in healthcare availability under the universal public health coverage in Japan.

Statistical analysis
We conducted a panel data analysis, taking the prefectural mortality as a target variable, regressed on household dietary consumption and other covariates. Panel data analysis is useful to counteract misspecification by unobserved and time-invariant confounders.25 We expected that prefectural characteristics that were not likely to change over the study period (e.g. medical technology, performance of the local health care system, dietary habits and culture and welfare policy) should be adequately controlled in the fixed-effects model. We estimated a fixed-effects model and a random-effects model, and we then used the Hausman–Wu test. We also added an ad hoc analysis stratified by average yearly salt-equivalent consumption at the median of 3.54 kg/year/household.

For the data processing and statistical analysis, we used Stata version 12.1 (StataCorp., College Station, TX, USA). No internal review board approval was needed for this study because the data were obtained from databases that were open to the public or anonymously constructed for commercial use.

Results
Table 1 shows the descriptive statistics on the panel data from 2012 to 2015.

We confirmed that the mortality from hypertension-related diseases and the household consumption of soy sauce, seasoning salt and miso paste and the consumption of salt equivalents from seasonings varied widely across the prefectures. There was a decreasing trend in mortality from hypertension-related diseases over the study period.

Table 2 shows the results of the panel data regression analysis. The Hausman–Wu test suggested that for mortality from ischaemic heart diseases (P = 0.735), the results of the random-
The test results for subarachnoid and intracerebral haemorrhage ($P = 0.020$) and for cerebral infarction ($P = 0.000$) suggested that the fixed-effects model produced less biased estimates and should be adopted. Because the differences in coefficient estimation were observed for the covariates and not for salt-related consumption, the tables present the results of the fixed-effects models. The results of the Hausman–Wu test were similar for the salt-equivalent variable.

As the left column of table 2 shows, the average household expenditure on processed foods was positively associated with mortality from ischaemic heart diseases (coefficient = 1.288, $P = 0.013$ with each seasoning variable), suggesting that each increase by 10 000 Japanese yen (90 US dollars) in the average annual household expenditure on processed foods was associated with an increase in disease-related mortality of about 1.2 deaths per 100 000 population. When we categorized the expenditure by tertiles, we confirmed a dose-response increasing trend with the mortality (data not shown). We did not find consistent results for the consumption of soy sauce or seasoning salt or for the salt equivalents of discretionary salt sources. Contrary to our expectations, the consumption of miso paste showed a negative association with mortality from ischaemic heart diseases (coefficient = $-0.950$, $P = 0.013$).

As for mortality from subarachnoid and intracerebral haemorrhage, seasoning salt showed the largest positive coefficient (coefficient = 0.382, $P = 0.238$), and expenditure on processed food also showed a relatively large positive effect (coefficient = 0.309, $P = 0.397$), while the consumption of soy sauce (coefficient = $-0.396$, $P = 0.057$) and miso paste (coefficient = $-0.442$, $P = 0.085$) unexpectedly showed negative associations. Finally, seasoning salt

Table 1 Descriptive statistics on hypertension-related disease mortality, household dietary consumption, demographic characteristics and economic factors for 47 prefectures, 2012–15, Japan (N = 188)

|                          | Mean  | SD    | Min   | Max   | Mean by year |
|--------------------------|-------|-------|-------|-------|--------------|
|                          | 2012  | 2013  | 2014  | 2015  |
| Hypertension-related disease mortality (per 100 000 population) Ischemic heart diseases (I20–I25) | 60.2  | 15.48 | 33.3  | 105.3 | 62.8  | 60.7  | 59.9  | 57.3  |
| Subarachnoid (I60, I69.0) and intracerebral (I61, I69.1) haemorrhage Cerebral infarction (I63, I69.3) | 40.0  | 8.15  | 25.4  | 65.6  | 40.9  | 39.8  | 39.8  | 39.5  |
| Subarachnoid (I60, I69.0) | 64.1  | 17.18 | 27.9  | 105.3 | 67.2  | 65.8  | 62.4  | 60.8  |
| Intracerebral (I61, I69.1) haemorrhage | | | | |
| Cerebral infarction (I63, I69.3) | | | | |
| Household dietary salt consumption per household per year Soy sauce (l) | 5.9   | 1.23  | 3.5   | 11.2  | 6.3   | 6.1   | 5.7   | 5.7   |
| Seasoning salt (kg) | 2.0   | 0.81  | 0.7   | 5.9   | 2.0   | 2.2   | 2.0   | 1.9   |
| Miso paste (kg) | 5.7   | 1.42  | 3.1   | 9.5   | 5.9   | 5.8   | 5.6   | 5.4   |
| Salt equivalents of the above seasonings (kg)* | 3.7   | 1.01  | 2.1   | 8.1   | 3.8   | 3.9   | 3.7   | 3.6   |
| Expenditure on processed foods (10 000 JPY)b | 11.3  | 1.15  | 8.6   | 13.9  | 11.2  | 11.3  | 11.2  | 11.4  |
| Expenditure on eating out (10 000 JPY)b | 15.3  | 2.66  | 8.1   | 23.9  | 15.2  | 15.4  | 15.4  | 15.3  |
| Other household dietary consumption per household per year Fresh vegetables (kg) | 173.7 | 17.67 | 137.1 | 222.6 | 174.8  | 175.0  | 174.1  | 170.9  |
| Fresh fruit (kg) | 82.4  | 11.32 | 54.4  | 112.5 | 86.4  | 83.5  | 82.0  | 77.7  |
| Raw fish and shellfish (kg) | 29.9  | 5.33  | 17.8  | 49.5  | 31.2  | 30.6  | 29.1  | 28.9  |
| Salted and dried fish (kg) | 8.4   | 2.40  | 1.9   | 15.7  | 8.6   | 8.7   | 8.1   | 8.2   |
| Seaweed (kg) | 1.2   | 0.43  | 0.5   | 3.6   | 1.2   | 1.2   | 1.2   | 1.2   |
| Bean curd (cake portion) | 79    | 9.27  | 54    | 119   | 77    | 79    | 79    | 80    |
| Demographic characteristics, economic factors and medical care availability in the prefecture Percentage of the population aged ≥65 years (%) | 27.0  | 2.85  | 17.7  | 33.9  | 25.6  | 26.6  | 27.5  | 28.3  |
| Sex ratioc | 93.1  | 3.70  | 87.7  | 100.4 | 93.1  | 93.1  | 93.1  | 93.2  |
| Average size of households comprising two or more people | 3.0   | 0.13  | 2.8   | 3.5   | 3.0   | 3.1   | 3.0   | 3.0   |
| Average income of taxpayers (1000 JPY) | 5152  | 912.36 | 3966  | 9732  | 4917  | 5227  | 5191  | 5274  |
| Population density of inhabitable areas (per inhabitable km²) | 1365.2 | 1735.95 | 240.6 | 9609.4 | 1369.3 | 1367.9 | 1365.4 | 1358.1 |
| Crude prevalence of metabolic syndrome and candidate conditions (age 40–74) in the National Health Checkup Program (%) | 26.5  | 0.02  | 23.3  | 33.0  | 26.6  | 26.4  | 26.5  | 26.6  |
| Medical care institutions per 100 000 population | 88.2  | 13.28 | 61.8  | 119.4 | 87.7  | 88.2  | 88.3  | 88.8  |
| Sales of antihypertensive drugs (per prefectural population) | 105   | 13.87 | 71    | 159   | 110   | 106   | 103   | 101   |

a: Salt equivalent of soy source = 15.0 g/84.7 ml, salt equivalent of seasoning salt = 99.1 g/100 g and salt equivalent of miso paste = 12.0 g/100 g.
b: Adjusted for the consumer price index as of 2015.
c: Number of men per 100 women in each prefecture.
Table 2: Results of an ecological panel data analysis with fixed-effects estimation for hypertension-related mortality by prefecture, 2012–15, Japan

| Causes of mortality | Coeff. 95% CI | Coeff. 95% CI | Coef. 95% CI | Coef. 95% CI | Coef. 95% CI |
|---------------------|--------------|--------------|--------------|--------------|--------------|
| Soy sauce (l)       | 0.231 - 0.371 | 0.383 - 0.515 | 0.396 - 0.804 | 0.104 - 0.423 | 0.417 - 0.731 |
| Seasoning salt (kg) | 0.396 - 0.804 | 0.256 - 1.019 | 0.113 - 0.746 | 0.113 - 0.746 | 0.113 - 0.746 |
| Miso paste (kg)     | 0.950 - 1.550 | 0.206 - 0.743 | 0.143 - 0.383 | 0.143 - 0.383 | 0.143 - 0.383 |
| Expenditure on processed foods (10,000 JPY) | 1.288 - 2.277 | 1.128 - 2.389 | 1.027 - 1.207 | 1.027 - 1.207 | 1.027 - 1.207 |
| Expenditure on eating out (10,000 JPY) | 0.066 - 0.430 | 0.041 - 0.262 | 0.041 - 0.262 | 0.041 - 0.262 | 0.041 - 0.262 |

Discussion

Our ecological panel data analysis confirmed that the salt-equivalent consumption of major discretionary salt sources was positively associated with increased mortality from ischaemic heart diseases and cerebral infarction; a 1-kg increase in the salt-equivalent consumption per household per year corresponded to ~0.40 more deaths per 100,000 population. Likewise, an increase in household seasoning salt consumption of 1 kg per year was related to higher mortality from all three of the examined conditions, corresponding to about 0.40 more deaths per 100,000 population. However, the association between seasoning salt consumption and mortality differed between prefectures with high and low salt consumption. We further found that each increase by 10,000 Japanese yen in expenditure on processed foods was related to nearly 1.28 additional deaths caused by ischaemic heart diseases per 100,000 population, especially in prefectures with higher salt consumption. These findings are in line with previous epidemiological findings showing that reducing salt intake resulted in lower blood pressure and reduced cardiovascular disease mortality at the individual level. 1,6 This study results are also in accordance with recent nutrition surveys in Japan, which showed that the source of salt intake has extended from discretionary intake using seasonings to less discretionary intake through processed foods. 16

This study may add to the existing literature showing that at the ecological level, the influence of non-discretionary salt consumption on ischaemic heart disease mortality may be larger than that of discretionary salt consumption. Salt intake among Japanese people remained higher than that recommended for the effective prevention of cardiovascular diseases 1,12 and adherence to salt reduction in dietary habits is very low. 27 Our findings suggest that public policy seeking to regulate the salt content of processed foods, in addition to individual behavioural modification to reduce discretionary salt use, may effectively achieve population-level reductions in ischaemic heart disease and related mortality in Japan, as has been seen in other countries such as the UK. 10

Our models did not show consistent associations between salt intake sources and stroke mortality, which requires some discussion. An epidemiological evaluation in a Japanese community setting confirmed the attribution of hypertension to the incidence and mortality of cerebral infarction and subarachnoid haemorrhage in the 1970s and 1980s. 28 However, the most recent results from a large registry of stroke patients indicated that the type of cerebral infarction changes from atherosclerosis-based infarction to cardiogenic thrombotic infarction with atrial fibrillation, which may not be attributable to hypertension. 29 This registry also indicated that the prevalent use of anti-thrombotic medication in older patients may be an emerging risk factor for intracerebral haemorrhage. 30 These observations may indicate that the attribution of stroke incidence to hypertension and salt intake is attenuated in the context of Japan’s ageing population, and further epidemiological evaluation is required. Our models did not show a consistent association of the local availability of health care institutions, antihypertensive medication use, demographics and average income with hypertension-related...
Table 3  Results of an ecological panel data analysis with fixed-effects estimation for hypertension-related mortality by prefecture, 2012–15, Japan  Stratiﬁed by total salt-equivalent consumption

| Causes of mortality | Cerebral infarction | Subarachnoid and intracerebral haemorrhage | Ischaemic heart diseases |
|---------------------|---------------------|------------------------------------------|-------------------------|
| Soy sauce (l)       | Coef. 95% CI        | Coef. 95% CI                             | Coef. 95% CI            |
| 0.525               | 0.514 – 1.565       | 0.260 – 0.569                            | 0.090 – 0.405           |
| Miso paste (kg)     | Coef. 95% CI        | Coef. 95% CI                             | Coef. 95% CI            |
| 2.279               | 1.530 – 3.053       | 1.034 – 2.479                            | 1.053 – 1.053           |
| Expenditure (JPY/y) | Coef. 95% CI        | Coef. 95% CI                             | Coef. 95% CI            |
| 0.751               | 0.743 – 0.751       | 0.031 – 0.041                            | 0.031 – 0.041           |

- Higher salt consumption
- Lower salt consumption

\[ a: \text{Salt equivalent of soy source = 15.0 g/84.7 ml, salt equivalent of seasoning salt = 99.1 g/100 g and salt equivalent of miso paste = 12.0 g/100 g.} \]
\[ b: \text{Adjusted for the consumer price index as of 2015.} \]
\[ c: \text{Adjusted for other food groups, as well as demographic characteristics, economic factors and medical care availability in the prefecture (variables described in table 1).} \]

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Conflicts of interest: None declared.

Key points
- A recent decrease trend in cardiovascular mortality in Japan was accompanied by remaining high salt intake and regional disparity in this mortality.
- An ecological panel data analysis was conducted to identify prefectural-level determinants of cardiovascular mortality.
- Mortality from ischaemic heart diseases was related to household expenditure on non-discretionary salt intake sources, rather than that on discretionary intake sources.
- Results indicated that regulation on the salt content of processed food may reduce cardiovascular mortality in Japan.
- Ecological factors related to stroke mortality need further investigation in the context of population ageing in Japan.

References
1. Fujiyoshi A, Ohkubo T, Miura K, et al. Blood pressure categories and long-term risk of cardiovascular disease according to age group in Japanese men and women. Hypertens Res 2012;35:947–53.
2. Takashima N, Ohkubo T, Miura K, et al. Long-term risk of BP values above normal for cardiovascular mortality: a 24-year observation of Japanese aged 30 to 92 years. J Hypertens 2012;30:2299–306.
3. Intersalt Cooperative Research Group. INTERSALT: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. BMJ 1988;297:319–28.
4. He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ 2013;346:f3132.
5. Aburto NJ, Ziolkowska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. BMJ 2013;346:f3126.
6. He F, Brinserd H, MacGregor G. Salt reduction in the United Kingdom: a successful experiment in public health. J Hum Hypertens 2014;28:345–52.
7. Ikeda N, Saito E, Kondo N, et al. What has made the population of Japan healthy? J Cardiovasc Prev Prev Treat 2011;18:109–15.
8. Ueshima H. Explanation for the Japanese paradox: prevention of increase in coronary heart disease and death in stroke. J Atheroscler Thromb 2007;14:278–86.
9. Miura K. Epidemiology and prevention of hypertension in Japanese: how could Japan get longevity? EPMA J 2011;2:59–64.
10. He FJ, MacGregor GA. A comprehensive review on salt and health and current experience of worldwide salt reduction programmes. J Hum Hypertens 2009;23:363–84.
11. Anderson CA, Appel LJ, Okuda N, et al. Dietary sources of sodium in China, Japan, the United Kingdom, and the United States, women and men aged 40 to 59 years: the INTERMAP study. J Am Diet Assoc 2010;110:736–45.
12. Asakura K, Uechi K, Sasaki Y, et al. Estimation of sodium and potassium intakes assessed by two 24 h urine collections in healthy Japanese adults: a nationwide study. Br J Nutr 2014;112:1195–205.
13. Ministry of Health, Labour and Welfare. Vital Statistics 2012–2015. 2017.
14. Rose G. Sick individuals and sick populations. Int J Epidemiol 2001;30:427–32.
15. Uechi K, Asakura K, Masayasu S, Sasaki S. Within-country variation of salt intake assessed via urinary excretion in Japan: a multilevel analysis in all 47 prefectures. Hypertens Res 2017;40:598–605.
16. Asakura K, Uechi K, Masayasu S, Sasaki S. Sodium sources in the Japanese diet: difference between generations and sexes. Public Health Nutr 2016;19:2011–23.
17. Statistics Bureau at Ministry of Internal Affairs and Communication, Statistics Japan. Family Income and Expenditure. Available at: http://www.stat.go.jp/english/data/sav/index.html (5 May 2018, date last accessed).
18. Ministry of Education, Culture, Sports, Science and Technology. Standard Tables of Food Composition in Japan 2010. 2010.
19. Statistics Bureau at Ministry of Internal Affairs and Communication, Statistics Japan. Consumer Price Index 2012–2015. 2017.
20. Stamler J, Chan Q, Daviglus ML, et al. Relation of dietary sodium (salt) to blood pressure and its possible modulation by other dietary factors: the INTERMAP study. Hypertens 2018;71:631–7.
21. The National Institute of Population and Social Security Research. Population Estimates 2012–2015. 2017.
22. Sakamoto H, Rahman M, Nomura S, et al. Japan Health System Review, Vol. 8. New Delhi: World Health Organization, Regional Office for South-East Asia, 2018.
23. National Tax Agency JAPAN. Income Tax Return 2012–2015. 2017.
24. Statistics Bureau at Ministry of Internal Affairs and Communication, Statistics Japan. Social Indicators by Prefecture 2012–2015. 2017. Available at: http://www.stat.go.jp/english/data/shihyou/index.html (5 May 2018, date last accessed).
25. Jeffrey WM. Ecometric Analysis of Cross Section and Panel Data. Cambridge, MA: The MIT Press, 2002.
26. Tsunemileto J, Jouslabhi P, Rastenyte D, et al. Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study. Lancet 2001;357:848–51.
27. Okuda N, Stamler J, Brown JJ, et al. Individual efforts to reduce salt intake in China, Japan, UK, USA: what did people achieve? The INTERMAP Population Study. J Hypertens 2014;32:2385–92.
28. Kubo M, Kiyohara Y, Kato I, et al. Trends in the incidence, mortality, and survival rate of cardiovascular disease in a Japanese community: the Hisayama study. Stroke 2003;34:2349–54.
29. Kato Y, Hayashi T, Tanahashi N, et al. Cardioembolic stroke is the most serious problem in the aging society: Japan standard stroke registry study. J Stroke Cerebrovasc Dis 2015;24:811.
30. Kato Y, Hayashi T, Nagamine Y, et al. Antithrombotic drugs play a significant role in intracerebral hemorrhage in the elderly patients. J Stroke Cerebrovasc Dis 2015;24:1986–90.
31. Beaglehole R, Bonita R, Horton R, et al. Priority actions for the non-communicable disease crisis. Lancet 2011;377:1438–47.
32. Okechukwu C, Gottlieb L. The social determinants of health: it’s time to consider the causes of the causes. Public Health Rep 2014:129:19–31.
33. Hyseni L, Elliot-Green A, Lloyd-Williams F, et al. Systematic review of dietary salt reduction policies: evidence for an effective hierarchy? PLoS One 2017;12:e0177535. Available at: https://doi.org/10.1371/journal.pone.0177535.
34. Yang Q, Liu T, Kuklina EV, et al. Sodium and potassium intake and mortality among US adults: prospective data from the Third National Health and Nutrition Examination Survey. Arch Intern Med 2011;171:1183–91.
35. van Mierlo LA, Arends LR, Struppel MT, et al. Blood pressure response to calcium supplementation: a meta-analysis of randomized controlled trials. J Hum Hypertens 2006;20:571–80.
36. Iso H, Kobayashi M, Ishihara J, et al. Intake of fish and n3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based (IPCHC) Study Cohort 1. Circulation 2006;113:195–202.
37. Yang H, Chen J, Chang L. Effects of soy protein hydrolysate on blood pressure and angiotensin-converting enzyme activity in rats with chronic renal failure. Hypertens Res 2008;31:957–63.
Framingham score and work-related variables for predicting cardiovascular disease in the working population

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Background: The Framingham score is commonly used to estimate the risk of cardiovascular disease (CVD). This study investigated whether work-related variables improve Framingham score predictions of sickness absence due to CVD. Methods: Eleven occupational health survey variables (descent, marital status, education, work type, work pace, cognitive demands, supervisor support, co-worker support, commitment to work, intrinsic work motivation and distress) and the Framingham Point Score (FPS) were combined into a multi-variable logistic regression model for CVD sickness absence during 1-year follow-up of 19 707 survey participants. The Net Reclassification Index (NRI) was used to investigate the added value of work-related variables to the FPS risk classification. Discrimination between participants with and without CVD sickness absence during follow-up was investigated by the area under the receiver operating characteristic curve (AUC). Results: A total of 129 (0.7%) occupational health survey participants had CVD sickness absence during 1-year follow-up. Manual work and high cognitive demands, but not the other work-related variables contributed to the FPS predictions of CVD sickness absence. However, work type and cognitive demands did not improve the FPS classification for risk of CVD sickness absence [NRI = 2.3%; 95% confidence interval (CI) = 2.7 to 9.5%; P = 0.629]. The FPS discriminated well between participants with and without CVD sickness absence (AUC = 0.759; 95% CI 0.724–0.794). Conclusions: Work-related variables did not improve predictions of CVD sickness absence by the FPS. The non-laboratory Framingham score can be used to identify health survey participants at risk of CVD sickness absence.

Introduction

The World Health Organization estimates that 17.7 million people worldwide died from cardiovascular disease (CVD) in 2015, representing 31% of all global deaths.¹ Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke. In Europe, CVD caused 3.9 million deaths, which accounts for 45% of all deaths in 2015.² Moreover, CVDs are responsible for the loss of more than 64 million disability-adjusted life years, which is about a quarter of all disability-adjusted life years lost due to disease in Europe.³ Most CVDs can be prevented by addressing lifestyle risks such as tobacco use, unhealthy diet, overweight and physical inactivity. People who are at high CVD risk need early detection and management by counseling and medicines.⁴

In the past seven decades, the Framingham heart study has identified age, sex, high blood pressure, smoking, dyslipidemia and diabetes as the major risk factors for developing CVD.⁵ The point scores on these risk factors were combined into a Framingham score which is predictive of the 10-year CVD risk.⁶,⁷ Framingham scores are widely used in primary health care to early detect people at risk of CVD when they consult their general practitioner (GP). The use of Framingham scores in public and occupational health care is restricted, because the scores rely on blood pressure measurements and blood cholesterol levels. D’Agostino et al.⁴ developed a non-laboratory version of the Framingham score, in which blood pressure measurement is replaced by patient-reported systolic blood pressure and blood cholesterol measurements are replaced by the body mass index calculated from patient-reported length and weight. The non-laboratory Framingham score predicts CVD as accurately as the original, and therefore it was concluded that the non-laboratory Framingham score can be used for CVD risk assessments in situations where laboratory testing is inconvenient or unavailable.⁸⁻¹⁰ Potentially large numbers of individuals at risk of CVD could be detected if the non-laboratory Framingham score were implemented in occupational health surveys.

Occupational health surveys focus on health risks and work stress. In a recent overview of systematic reviews, Fishta and Backe⁹ found that work stress was significantly associated with an increased CVD risk. In a review of 27 cohort studies in Europe, the USA and Japan, Kivimäki and Kawachi¹⁰ found evidence that job strain and long working hours were associated with work stress and elevated risk of both coronary heart disease and stroke. The excess risk for