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REGULAR ARTICLE

Changes in pancreatic cancer mortality, period patterns, and birth cohort patterns in Japan: analysis of mortality data in the period 1968–2002

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Abstract
Objectives The 5-year survival rate for pancreatic cancer is known to be lower than that for cancer at any other site in the body, and the proportion of pancreatic cancer deaths among all cancer deaths has been increasing in Japan. The aim of this study was to investigate pancreatic cancer mortality in the light of temporal and geographical trends in the 47 prefectures of the country between 1968 and 2002.
Methods To survey the geographical aspects of pancreatic cancer mortality, we mapped the direct age-adjusted mortality rates of persons aged 40 years and older by sex in seven 5-year periods (1968–1972 to 1998–2002). We also evaluated the changes in period and birth cohort trends using estimable functions based on the age–period–cohort models in each prefecture.
Results During the observation period the Hokkaido and Tohoku regions had high mortality rates for both sexes. No significant increase in period trends was observed from 1973 to 2002, but significant increases in cohort trends were observed from 1913 to 1962—in two prefectures, for males, and in four prefectures, for females.
Conclusions The results of this study reveal a combination of time trends in pancreatic cancer mortality and changes in period or birth cohort trends. The changes in cohort trends in each prefecture were more variable than the period trends. This finding probably indicates the need for further investigation of the cohort-related factors involved in the prevalence of pancreatic cancer. Further research on mortality in the 47 prefectures needs to be conducted while taking the two time effects into account.

Keywords Age–period–cohort model · Cohort effect · Estimable functions · Pancreatic cancer · Period effect

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Introduction

Pancreatic cancer is generally characterized as being difficult to diagnose and having a poor prognosis. The 5-year survival rate for pancreatic cancer is known to be the lowest of all cancers [1], and in recent years the proportion of deaths from pancreatic cancer has been increasing. In 1993, 8139 male patients died from pancreatic cancer, accounting for 5.7% of all cancer deaths among males; among females with pancreatic cancer, 6574 patients died, accounting for 7.0% of all cancer deaths among females [2]. In 2003, however, the corresponding figures were 11,280 (6.0%) for males and 9868 (8.0%) for females [3].

In a previous study [4], we provided a map of the standardized mortality ratio (SMR) for pancreatic cancer in the 47 prefectures of Japan. This SMR map was based on census data and vital statistics from 1998 to 2002, and it showed high death rates for both sexes in the Hokkaido and the Tohoku region. The SMRs for pancreatic cancer in

Japan in 2000 had the same characteristics [5]. In the study reported here, we extended the observation period and attempted to identify regional and temporal trends in pancreatic cancer death rates in Japan. We also investigated curvatures from period trends in different eras as well as birth cohort trends, using age–period–cohort models for the 47 prefectures of Japan. By means of these analyses, we attempted to clarify one of the aspects of pancreatic cancer and contribute to further research.

Materials and methods

Mortality data

The mortality data for pancreatic cancer (ICD-8: 157, ICD-9: 157, ICD-10: C25) in all 47 Japanese prefectures were obtained from CD-ROMs of the National Vital Statistics, Statistics and Information Department of the Minister's Secretariat of the Ministry of Health, Labor and Welfare, which granted us the permission to use the data. Deaths at 40 years of age and over stratified by sex and 5-year age groups for the period 1968–2002 were abstracted in our study, with the exception of Okinawa, where the data are only for the period 1973–2002 because of insufficient data.

Before beginning the statistical analysis, we categorized the mortality data into seven periods—1968–1972, 1973–1977, 1978–1982, 1983–1987, 1988–1992, 1993–1997, and 1998–2002—and averaged them by 5 years in each period. These averages were used to calculate the age-specific death rates for ten 5-year age groups (40–44 to 85+ years) by period. The population in the census year that fell in the middle of each period (1970, 1975, 1980, 1985, 1990, and 2000) was used as the denominator. The age-specific death rates in Okinawa in the period 1968–1972 were not calculated for the reason stated above.

Statistical methods

To construct the disease maps, we calculated the direct age-adjusted mortality rates for persons aged 40 years and older using the Japanese 1985 model population as the standard. We graded the mortality rates into the five levels provided on the web page of the Ministry of Health, Labour and Welfare [6] and calculated these levels as follows. First, the average and the standard deviation of the mortality rate in each period were calculated. Second, level 1 and level 5 were defined as the rates below the average beyond the standard deviation and the rates above the average beyond the standard deviation, respectively. Finally, dividing the rest of the range, including the average, into tertiles, levels 2, 3, and 4 were defined as intertertile range, in order of size.

In terms of the estimates of parameters from the age–period–cohort models, it is known that these cannot be uniquely estimated because of the exact linear dependency among the three factors [7]. Many solutions to this dependency have been proposed [8, 9]. Here, we used the estimable functions for age–period–cohort analyses provided by Tarone and Chu [10] to investigate the curvatures from the period and cohort trends for analyzing the direction and magnitude of two time trends. The age–period–cohort model used in our study is

$$E_{ijk} = \alpha_i + \pi_j + \gamma_k,$$

where E_{ijk} is the logarithm of the mortality rate $R_{ij} = \frac{d_{ij}}{N_{ij}}$ (d_{ij}: number of cancer deaths, N_{ij}: number of persons at risk), and α_i is the effect of age group i; π_j is the effect of time period j; and γ_k is the effect of birth cohort k. A unique set of parameter estimates for the model was obtained by setting constraints on the parameters by the maximum likelihood method, and regression programs that make use of a particular model sometimes select these constraints arbitrarily. With respect to the arbitrariness, Clayton and Shifflers [11] showed that changes of parameters were uniquely estimated regardless of any constraints. Tarone and Chu [10] extended the estimable function of Clayton and Shifflers and developed a methodology for testing curvatures from trend between two successive groups of cohorts. The Tarone and Chu approach is named a contrast and is also applicable to trends in period [8].

In this study the populations were divided into ten 5-year age groups (40–44 to 85+ years), and time was divided into seven 5-year periods (1968–1972 to 1998–2002). As a result, we obtained 16 overlapping birth cohorts of 10 years each (1878–1887 to 1953–1962). Since there is the relationship among three indices: $k = j - i + 10$.

We used the following estimable function [8, 10] to investigate curvatures from the period trend.

$$C_1 = \pi_7 - \pi_5 - (\pi_4 - \pi_2),$$

where C_1 is the contrast for comparing the period trend in 1988–2002 with the period trend in 1973–1987. This function was designed to enable an approximate comparison between the group from 1990 onward and the group before 1990. To investigate curvatures from the cohort trend, we grouped the birth cohorts into an early cohort (1888–1897 to 1903–1912), a middle cohort (1913–1922 to 1928–1937), and a recent cohort (1938–1947 to 1953–1962).

The contrast [8, 10] between the middle cohort and early cohort can be estimated by

$$C_2 = 3\gamma_{11} + \gamma_{10} - \gamma_9 - 3\gamma_8 - (3\gamma_6 + \gamma_5 - \gamma_4 - 3\gamma_3).$$

Similarly, the contrast between the recent cohort and middle cohort can be estimated by

$$C_3 = 3\gamma_{16} + \gamma_{15} - \gamma_{14} - 3\gamma_{13} - (3\gamma_{11} + \gamma_{10} - \gamma_9 - 3\gamma_8).$$

The particular parameter estimates were maximum likelihood estimates and obtained by using the generalized linear model for univariate analyses and SPSS ver. 12.0J software for Windows (SPSS, Chicago, IL). The parameter constraint was default (the last period effect and the last two cohort effects are zero). Contrast coefficient matrices defined by the SPSS software package were customized according to the hypotheses $C_1 = 0$, $C_2 = 0$, and $C_3 = 0$ and were analyzed by the F test [12, 13]. Two-sided P values less than 0.05 were considered to be statistically significant.

Results

Mortality map

According to the direct age-adjusted mortality rates for pancreatic cancer, all prefectures showed increasing trends in both sexes during the observation period (these rates are not shown). The overall age-adjusted mortality rates for pancreatic cancer for the first period (1968–1972) to the seventh period (1998–2002) increased by 70.3% among males and by 68.3% among females. Figure 1 shows the mortality map based on the levels described in the Materials and methods. This map illustrates the following findings: (1) Iwate, even in the Tohoku region, tended to have the average national mortality rates, (2) in the west of Japan, in Tottori, a relatively high number of males had level 5, and (3) level 5 occurred in the northern Kyushu area several times between the second period, 1973–1977, and the fifth period, 1988–1992, but did not occur in the sixth period, 1993–1997, or the seventh period, 1998–2002.

In the light of level 1 and level 5, Yamaguchi and Okinawa, for males, and Yamaguchi, Kagoshima, and Okinawa, for females, had level 1 for five or more

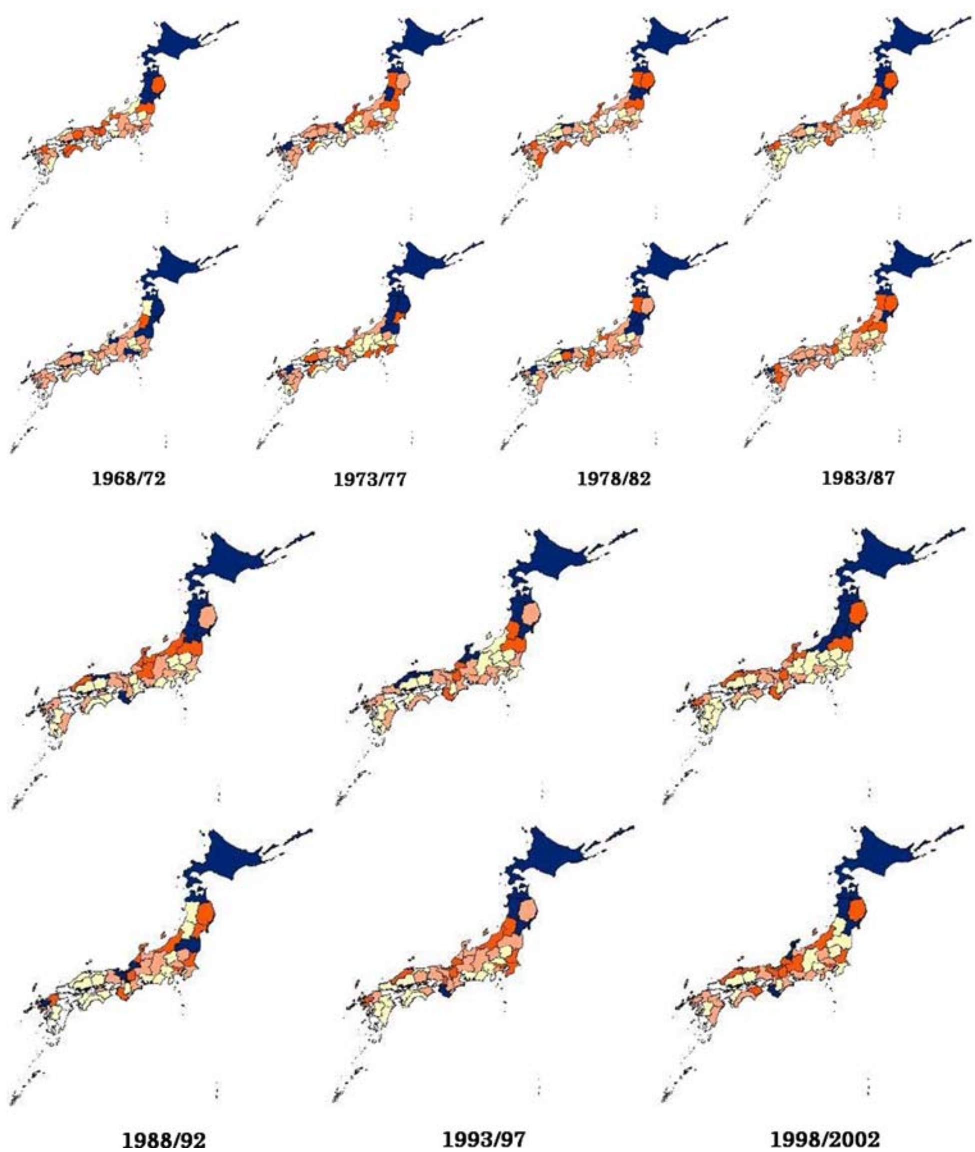

Fig. 1 Direct age-adjusted mortality rates for pancreatic cancer in the 47 prefectures during the period 1968–2002. *White* level 1, *yellow* level 2, *orange* level 3, *red* level 4, *black* level 5 (see online version for color coding). Level 1 and level 5 were defined as the rates below the average beyond the standard deviation and the rates above the average beyond the standard deviation, respectively. Levels 2, 3, and 4 were defined as the rate of intertertile range within the standard deviation, in order of size. The maps at the *top* are for males, and the maps at the *bottom* are for females

successive times. Hokkaido, Aomori, Miyagi, Akita, and Yamagata, for males, and Hokkaido, Aomori, and Miyagi, for females, had level 5 for five or more successive times. Many level 5 regions were observed in Hokkaido and most of the Tohoku region during the observation period. Level 5 was identified in Hokkaido and Aomori in every period.

Age–period–cohort models

The model evaluation in each prefecture is shown in Table 1. Because we used the generalized linear model in this study, based on the assumption that the logarithm of the mortality rate is a linear function of regressor valuables, the goodness-of-fit of the age–period–cohort models was evaluated by residual sum of squares [13]. There were 40 *df*, except in Okinawa, where there were only 32 *df* because of the lack of mortality data for the first period, 1968–1972. The effect of period and cohort factors was evaluated by the *F* test. The period effect was statistically significant for males in Miyagi, Akita, Gumma, Saitama, Chiba, Toyama, Shiga, Osaka, and Wakayama, and for females in Hokkaido, Miyagi, Saitama, Fukui, and Yamanashi. The cohort effect was statistically significant for both sexes in all prefectures, with the exception in Shimane for males. Table 2 shows the results of the *F* test for the estimable function C_1. Among the prefectures with bias toward level 1 or level 5, the estimated curvatures from the period trend C_1 decreased significantly in Miyagi and Kagoshima, for males, and in Hokkaido, for females. Hokkaido had the largest decrease in females: $C_1 = -0.264$ ($P = 0.001$). Among the prefectures with no bias toward level 1 and level 5, Iwate, Saitama, Chiba, Osaka, Nara, and Wakayama showed a significant decrease in C_1 for males. Wakayama had the largest decrease in males: $C_1 = -0.590$ ($P = 0.003$). The C_1 values showed that curvatures from the period trends between 1988–2002 and 1973–1987 were small in every prefecture. Table 3 shows the results of the *F* test for the estimable function C_2. Every prefecture that had a level 1 or level 5 five or more times in succession had a significant decrease in C_2. Aomori had the largest decrease, $C_2 = -2.779$ ($P < 0.001$) for males, and Okinawa had the largest decrease, $C_2 = -5.275$ ($P < 0.001$) for females. All of the prefectures with no bias toward level 1 and level 5, with the exception of Tottori, for males, and Gifu, Tottori, and Miyazaki, for females, showed a significant decrease in C_2. Toyama had the largest decrease in males, $C_2 = -4.078$ ($P < 0.001$), and Akita had the largest decrease in females, $C_2 = -4.560$ ($P < 0.001$). The C_2 values showed a decrease in cohort trends between 1913–1937 and 1888–1912 in most of the 47 prefectures. Table 4 shows the results of the *F* test for the estimable function C_3. Among those prefectures with a bias toward level 1 and level 5, the C_3 values showed a significant increase between 1938–1962 and 1913–1937 in Okinawa for both sexes, and a significant decrease in Hokkaido for both sexes. Yamaguchi had the largest decrease for males, $C_3 = -2.826$ ($P = 0.002$), and Hokkaido had the largest decrease for females, $C_3 = -1.057$ ($P < 0.032$). Hokkaido and Okinawa showed a clear contrast between the age-adjusted mortality rate and the estimated curvatures from the cohort trends C_3. Among the prefectures with no bias toward level 1 or level 5, Kochi had the largest increase for males, $C_3 = 2.835$ ($P = 0.002$), and Shiga had the largest increase for females, $C_3 = 4.054$ ($P < 0.006$). Tochigi had the largest decrease for males, $C_3 = -4.342$ ($P < 0.001$), and Ehime had the largest decrease for females, $C_3 = -4.485$ ($P < 0.001$). Based on the C_3 values between 1938–1962 and 1913–1937, curvatures from the cohort trends appeared to be different overall.

Discussion

The geographical trend in pancreatic cancer mortality in Japan that we detected in our study is consistent with that reported by Kato et al. [14]. Our previous SMR analysis of the 1998–2002 data showed the same geographical trend. The study reported here also showed the time trend of the mortality described in the Results.

Using an age–period–cohort analysis, we investigated the curvatures from the period and cohort trends for analyzing the direction and magnitude of two time trends in accordance with to Tarone and Chu's suggested use of estimable functions C_1, C_2 , and C_3 These functions include information on whether the trends are concave upward or downward [12]. C_1 was used to investigate the curvatures from the period trends in the 1990s onwards. C_2 was used to investigate curvatures from the cohort trends between the early cohort (1888–1897 to 1903–1912) and the middle cohort (1913–1922 to 1928–1937), while C_3 was used to investigate curvatures from the cohort trends between the middle cohort and the recent cohort (1938–1947 to 1953–1962). These functions are the comparisons of period-based or cohort-based trends in different eras, but it is clear that they do not show direct associations with increases or decreases in pancreatic cancer mortality rates [8]. Furthermore, Tarone and Chu's approach was based on prior hypotheses which determined the groups of cohorts in female breast cancer mortality rates to be investigated [10, 15]. In our study we did not conduct a survey of the grouping of periods and cohorts in each prefecture and, consequently, the validity of the grouping is a limitation of this study.

We did not observe any statistically significant changes in period trend between two groups in most of the prefectures. The classification code was changed three times during the observation periods, but there were no major changes in the classification of causes of pancreatic cancer

Table 1 Residual sum of squares for age–period–cohort models and *P* values (based on the *F* test) for the significance of period effects and cohort effects during 1968–2002

Prefecture	Male			Female			Prefecture	Male			Female		
	Residual[a]	*P* value for period[b]	*P* value for cohort[c]	Residual	*P* value for period	*P* value for cohort		Residual	*P* value for period	*P* value for cohort	Residual	*P* value for period	*P* value for cohort
Hokkaido	0.536	0.402	<0.001	0.519	0.008	<0.001	Shiga	2.197	0.011	<0.001	4.528	0.732	<0.001
Aomori	1.985	0.930	<0.001	1.511	0.405	<0.001	Kyoto	1.250	0.320	<0.001	2.058	0.151	<0.001
Iwate	2.052	0.137	0.007	2.987	0.454	0.004	Osaka	0.444	0.024	<0.001	0.758	0.446	<0.001
Miyagi	0.610	<0.001	<0.001	2.178	0.002	<0.001	Hyogo	0.713	0.733	<0.001	0.641	0.650	<0.001
Akita	2.675	0.049	<0.001	3.022	0.133	<0.001	Nara	3.151	0.114	0.006	3.471	0.428	<0.001
Yamagata	2.148	0.496	<0.001	2.282	0.520	<0.001	Wakayama	3.153	0.005	<0.001	5.046	0.794	0.011
Fukushima	1.334	0.854	<0.001	1.579	0.564	<0.001	Tottori	5.253	0.903	0.016	5.011	0.096	<0.001
Ibaraki	2.532	0.361	<0.001	1.058	0.379	<0.001	Shimane	3.419	0.523	0.079	3.299	0.098	<0.001
Tochigi	1.759	0.266	<0.001	1.560	0.148	<0.001	Okayama	3.023	0.403	<0.001	2.290	0.646	<0.001
Gumma	0.637	0.022	<0.001	2.908	0.781	<0.001	Hiroshima	0.739	0.451	<0.001	1.710	0.963	<0.001
Saitama	0.843	0.014	<0.001	1.825	0.021	<0.001	Yamaguchi	1.611	0.255	<0.001	3.663	0.781	<0.001
Chiba	0.803	0.013	<0.001	1.806	0.285	<0.001	Tokushima	4.440	0.140	0.039	8.568	0.961	0.001
Tokyo	0.425	0.929	<0.001	0.585	0.384	<0.001	Kagawa	6.566	0.127	0.012	4.967	0.312	<0.001
Kanagawa	0.456	0.732	<0.001	1.551	0.164	<0.001	Ehime	2.415	0.941	<0.001	2.030	0.636	<0.001
Niigata	1.523	0.352	<0.001	1.261	0.943	<0.001	Kochi	1.744	0.110	<0.001	4.515	0.538	0.013
Toyama	1.425	0.020	<0.001	2.859	0.279	<0.001	Fukuoka	0.471	0.460	<0.001	1.752	0.761	<0.001
Ishikawa	6.575	0.741	0.030	2.619	0.112	<0.001	Saga	4.306	0.488	0.007	5.040	0.429	<0.001
Fukui	2.551	0.773	<0.001	3.613	0.019	<0.001	Nagasaki	2.602	0.439	<0.001	2.456	0.270	<0.001
Yamanashi	6.597	0.305	0.025	2.636	0.046	<0.001	Kumamoto	1.508	0.984	<0.001	2.190	0.078	<0.001
Nagano	5.135	0.262	0.011	1.964	0.318	<0.001	Oita	1.920	0.851	<0.001	2.317	0.497	<0.001
Gifu	2.539	0.492	<0.001	4.876	0.942	<0.001	Miyazaki	3.998	0.493	<0.001	4.916	0.575	0.004
Shizuoka	0.905	0.545	<0.001	1.206	0.949	<0.001	Kagoshima	1.335	0.294	<0.001	2.801	0.790	<0.001
Aichi	0.898	0.396	<0.001	1.101	0.886	<0.001	Okinawa[d]	2.998	0.268	0.039	4.176	0.430	0.008
Mie	1.623	0.377	<0.001	2.549	0.700	<0.001	Total	0.081	0.006	<0.001	0.149	0.103	<0.001

There were 40 *df*, except in Okinawa, where there were 32 *df*. The *F* test was used

[a] Residual sum of squares

[b] *P* value for the significance of period effects

[c] *P* value for the significance of cohort effects

[d] Except for the period 1968–1972

Table 2 Contrasts for comparing period trends in 1988–2002 with those in 1973–1987 for pancreatic cancer in the 47 prefectures of Japan, and the totals

Prefecture	Male		Female		Prefecture	Male		Female	
	Contrast (95% CI)	P[a]	Contrast (95% CI)	P[a]		Contrast (95% CI)	P[a]	Contrast (95% CI)	P[a]
Hokkaido	−0.115(−0.271 to 0.040)	0.141	−0.264(−0.417 to −0.111)	0.001	Shiga	−0.172(−0.486 to 0.143)	0.277	−0.132(−0.583 to 0.320)	0.559
Aomori	0.086(−0.213 to 0.385)	0.564	0.196(−0.065 to 0.457)	0.136	Kyoto	−0.046(−0.283 to 0.191)	0.697	0.039 (−0.265 to 0.344)	0.795
Iwate	−0.319(−0.623 to −0.015)	0.040	−0.040(−0.407 to 0.326)	0.826	Osaka	−0.240(−0.382 to −0.099)	0.001	−0.169(−0.354 to 0.016)	0.072
Miyagi	−0.391(−0.557 to −0.225)	<0.001	−0.033(−0.346 to 0.280)	0.831	Hyogo	−0.135(−0.315 to 0.044)	0.134	−0.099(−0.269 to 0.071)	0.245
Akita	−0.226(−0.573 to 0.121)	0.195	0.276(−0.093 to 0.645)	0.138	Nara	−0.468(−0.844 to −0.091)	0.016	−0.054(−0.449 to 0.341)	0.783
Yamagata	−0.045(−0.356 to 0.266)	0.770	0.224(−0.096 to 0.545)	0.165	Wakayama	−0.590(−0.966 to −0.213)	0.003	−0.003(−0.479 to 0.474)	0.991
Fukushima	−0.132(−0.377 to 0.113)	0.283	−0.090(−0.356 to 0.177)	0.501	Tottori	−0.173(−0.659 to 0.314)	0.477	−0.053(−0.528 to 0.422)	0.823
Ibaraki	−0.183(−0.520 to 0.155)	0.281	−0.135(−0.353 to 0.084)	0.220	Shimane	−0.359(−0.751 to 0.033)	0.072	0.058(−0.327 to 0.444)	0.761
Tochigi	−0.018(−0.300 to 0.263)	0.895	0.043(−0.222 to 0.308)	0.745	Okayama	−0.254(−0.555 to 0.047)	0.096	−0.196(−0.517 to 0.125)	0.225
Gumma	−0.046(−0.215 to 0.124)	0.590	0.186(−0.176 to 0.547)	0.306	Hiroshima	−0.004(−0.186 to 0.179)	0.967	0.031(−0.247 to 0.308)	0.824
Saitama	−0.244(−0.439 to −0.049)	0.015	−0.139(−0.426 to 0.148)	0.333	Yamaguchi	−0.197(−0.466 to 0.072)	0.147	−0.038(−0.444 to 0.368)	0.852
Chiba	−0.278(−0.468 to −0.088)	0.005	0.198(−0.087 to 0.483)	0.168	Tokushima	−0.189(−0.636 to 0.258)	0.397	0.049(−0.572 to 0.670)	0.875
Tokyo	−0.040(−0.178 to 0.098)	0.564	0.028(−0.135 to 0.190)	0.732	Kagawa	−0.519(−1.063 to 0.024)	0.061	−0.219(−0.692 to 0.254)	0.355
Kanagawa	−0.100(−0.244 to 0.043)	0.165	0.018(−0.246 to 0.282)	0.891	Ehime	−0.041(−0.371 to 0.288)	0.801	0.227(−0.075 to 0.529)	0.137
Niigata	−0.091(−0.353 to 0.171)	0.487	−0.064(−0.302 to 0.174)	0.591	Kochi	0.169(−0.111 to 0.449)	0.230	−0.112(−0.562 to 0.339)	0.620
Toyama	−0.033(−0.286 to 0.220)	0.793	0.205(−0.154 to 0.564)	0.255	Fukuoka	−0.071(−0.217 to 0.074)	0.329	0.114(−0.166 to 0.395)	0.416
Ishikawa	0.085(−0.459 to 0.629)	0.753	0.120(−0.223 to 0.463)	0.483	Saga	0.113(−0.327 to 0.553)	0.608	−0.196(−0.672 to 0.280)	0.410
Fukui	−0.056(−0.395 to 0.283)	0.740	0.089(−0.314 to 0.493)	0.656	Nagasaki	0.069(−0.274 to 0.411)	0.687	0.239(−0.094 to 0.571)	0.154
Yamanashi	−0.439(−0.984 to 0.106)	0.111	0.048(−0.296 to 0.393)	0.778	Kumamoto	0.040(−0.220 to 0.301)	0.757	−0.044(−0.358 to 0.270)	0.780
Nagano	−0.027(−0.507 to 0.454)	0.912	0.014(−0.283 to 0.311)	0.925	Oita	0.137(−0.156 to 0.431)	0.350	0.094(−0.229 to 0.417)	0.560
Gifu	−0.176(−0.514 to 0.162)	0.299	0.148(−0.320 to 0.617)	0.526	Miyazaki	0.155(−0.269 to 0.579)	0.465	0.088(−0.382 to 0.559)	0.706
Shizuoka	−0.104(−0.305 to 0.098)	0.305	0.102(−0.131 to 0.335)	0.381	Kagoshima	−0.251(−0.497 to −0.006)	0.045	−0.015(−0.370 to 0.340)	0.932
Aichi	0.003(−0.198 to 0.204)	0.976	0.009(−0.213 to 0.232)	0.934	Okinawa	0.076(−0.343 to 0.496)	0.713	0.030(−0.465 to 0.525)	0.903
Mie	−0.182(−0.452 to 0.088)	0.181	0.054(−0.284 to 0.393)	0.747	Total	−0.118(−0.178 to −0.058)	<0.001	0.003(−0.079 to 0.085)	0.942

CI, Confidence interval

[a] The F test was used

Table 3 Contrasts for comparing cohort trends in 1913–1937 with those in 1888–1912 for pancreatic cancer in the 47 prefectures of Japan, and the totals

Prefecture	Males		Females		Prefecture	Males		Females	
	Contrast (95% CI)	P[a]	Contrast (95% CI)	P[a]		Contrast (95% CI)	P[a]	Contrast (95% CI)	P[a]
Hokkaido	−1.983(−2.670 to −1.296)	<0.001	−2.351(−3.027 to −1.675)	<0.001	Shiga	−3.444(−4.836 to −2.053)	<0.001	−4.546(−6.544 to −2.548)	<0.001
Aomori	−2.779(−4.102 to −1.456)	<0.001	−2.521(−3.676 to −1.367)	<0.001	Kyoto	−1.937(−2.987 to −0.887)	0.001	−3.780(−5.127 to −2.432)	<0.001
Iwate	−1.944(−3.289 to −0.598)	0.006	−3.134(−4.756 to −1.511)	<0.001	Osaka	−2.557(−3.183 to −1.932)	<0.001	−3.936(−4.753 to −3.118)	<0.001
Miyagi	−2.065(−2.798 to −1.332)	<0.001	−2.832(−4.217 to −1.446)	<0.001	Hyogo	−2.426(−3.219 to −1.633)	<0.001	−4.007(−4.758 to −3.255)	<0.001
Akita	−2.663(−4.199 to −1.128)	0.001	−4.560(−6.192 to −2.928)	<0.001	Nara	−3.318(−4.985 to −1.651)	<0.001	−3.580(−5.329 to −1.830)	<0.001
Yamagata	−2.925(−4.301 to −1.548)	<0.001	−4.208(−5.627 to −2.789)	<0.001	Wakayama	−3.205(−4.872 to −1.537)	<0.001	−3.073(−5.183 to −0.964)	0.005
Fukushima	−1.734(−2.819 to −0.649)	0.002	−3.152(−4.333 to −1.972)	<0.001	Tottori	−1.589(−3.741 to 0.563)	0.144	−2.084(−4.186 to 0.018)	0.052
Ibaraki	−1.748(−3.243 to −0.254)	0.023	−3.965(−4.931 to −2.999)	<0.001	Shimane	−2.939(−4.676 to −1.203)	0.001	−3.465(−5.170 to −1.759)	<0.001
Tochigi	−2.737(−3.982 to −1.491)	<0.001	−3.827(−5.000 to −2.654)	<0.001	Okayama	−1.776(−3.107 to −0.444)	0.010	−3.909(−5.330 to −2.488)	<0.001
Gumma	−2.180(−2.930 to −1.431)	<0.001	−3.691(−5.293 to −2.090)	<0.001	Hiroshima	−3.156(−3.963 to 2.349)	<0.001	−2.552(−3.780 to −1.324)	<0.001
Saitama	−2.523(−3.385 to −1.660)	<0.001	−3.571(−4.840 to −2.303)	<0.001	Yamaguchi	−1.800(−2.992 to −0.608)	0.004	−3.508(−5.305 to −1.711)	<0.001
Chiba	−2.492(−3.334 to −1.651)	<0.001	−4.054(−5.316 to −2.792)	<0.001	Tokushima	−2.664(−4.643 to −0.686)	0.010	−4.135(−6.884 to −1.387)	0.004
Tokyo	−1.811(−2.423 to −1.199)	<0.001	−2.992(−3.710 to −2.274)	<0.001	Kagawa	−2.868(−5.274 to −0.461)	0.021	−4.542(−6.635 to −2.449)	<0.001
Kanagawa	−1.921(−2.555 to −1.286)	<0.001	−1.823(−2.993 to −0.654)	0.003	Ehime	−3.136(−4.595 to −1.676)	<0.001	−3.237(−4.574 to −1.899)	<0.001
Niigata	−2.441(−3.600 to −1.282)	<0.001	−3.502(−4.556 to −2.447)	<0.001	Kochi	−3.009(−4.249 to −1.769)	<0.001	−2.801(−4.797 to −0.806)	0.007
Toyama	−4.078(−5.199 to −2.957)	<0.001	−4.169(−5.757 to −2.581)	<0.001	Fukuoka	−2.476(−3.121 to −1.832)	<0.001	−2.755(−3.998 to −1.512)	<0.001
Ishikawa	−3.958(−6.367 to −1.550)	0.002	−3.395(−4.915 to −1.875)	<0.001	Saga	−2.618(−4.567 to −0.670)	0.010	−4.279(−6.387 to −2.170)	<0.001
Fukui	−2.724(−4.223 to −1.224)	0.001	−3.356(−5.141 to −1.571)	<0.001	Nagasaki	−2.944(−4.459 to −1.429)	<0.001	−3.376(−4.848 to −1.905)	<0.001
Yamanashi	−2.436(−4.848 to −0.024)	0.048	−3.107(−4.632 to −1.583)	<0.001	Kumamoto	−2.962(−4.115 to −1.809)	<0.001	−4.127(−5.517 to −2.738)	<0.001
Nagano	−3.577(−5.705 to −1.449)	0.002	−2.261(−3.577 to −0.944)	0.001	Oita	−3.154(−4.455 to −1.853)	<0.001	−2.310(−3.739 to −0.880)	0.002
Gifu	−2.977(−4.473 to −1.480)	<0.001	−1.980(−4.054 to 0.094)	0.061	Miyazaki	−3.376(−5.254 to −1.498)	0.001	−1.579(−3.661 to 0.503)	0.133
Shizuoka	−2.968(−3.861 to −2.074)	<0.001	−3.038(−4.069 to −2.006)	<0.001	Kagoshima	−2.732(−3.817 to −1.647)	<0.001	−2.688(−4.260 to −1.117)	0.001
Aichi	−2.961(−3.851 to −2.071)	<0.001	−3.400(−4.386 to −2.415)	<0.001	Okinawa	−2.686(−4.843 to −0.529)	0.016	−5.275(−7.820 to −2.729)	<0.001
Mie	−2.895(−4.091 to −1.699)	<0.001	−4.536(−6.035 to −3.036)	<0.001	Total	−2.483(−2.749 to −2.216)	<0.001	−3.168(−3.530 to −2.806)	<0.001

CI, Confidence interval

[a] The F test was used

Table 4 Contrasts for comparing cohort trends in 1938–1962 with those in 1913–1937 for pancreatic cancer in the 47 prefectures of Japan, and the totals

Prefecture	Males		Females		Prefecture	Males		Females	
	Contrast (95% CI)	P^a	Contrast (95% CI)	P^a		Contrast (95% CI)	P^a	Contrast (95% CI)	P^a
Hokkaido	−1.580(−2.557 to −0.603)	0.002	−1.057(−2.018 to −0.096)	0.032	Shiga	−0.818(−2.796 to 1.160)	0.408	4.054(1.214 to 6.894)	0.006
Aomori	0.062(−1.818 to 1.943)	0.947	−0.194(−1.835 to 1.446)	0.812	Kyoto	−0.388(−1.880 to 1.105)	0.603	−0.047(−1.961 to 1.868)	0.961
Iwate	1.407(−0.505 to 3.319)	0.145	−0.755(−3.062 to 1.551)	0.512	Osaka	−0.808(−1.697 to 0.081)	0.074	0.036 (−1.126 to 1.198)	0.950
Miyagi	0.030(−1.012 to 1.072)	0.954	−0.147(−2.117 to 1.823)	0.881	Hyogo	−0.196(−1.323 to 0.931)	0.727	0.789(−0.279 to 1.858)	0.143
Akita	−1.817(−4.000 to 0.366)	0.100	−1.244(−3.563 to 1.076)	0.285	Nara	0.995(−1.373 to 3.364)	0.401	−0.033(−2.519 to 2.454)	0.979
Yamagata	−0.575(−2.530 to 1.381)	0.556	2.418(0.402 to 4.434)	0.020	Wakayama	−1.001(−3.371 to 1.368)	0.398	1.682(−1.316 to 4.680)	0.264
Fukushima	0.866(−0.676 to 2.408)	0.263	−1.160(−2.837 to 0.517)	0.170	Tottori	−0.467(−3.525 to 2.592)	0.759	−0.017(−3.004 to 2.971)	0.991
Ibaraki	−0.291(−2.415 to 1.832)	0.783	0.734(−0.639 to 2.107)	0.287	Shimane	2.074(−0.394 to 4.541)	0.097	−0.528(−2.952 to 1.896)	0.662
Tochigi	−4.342(−6.112 to −2.572)	<0.001	−1.068(−2.735 to 0.599)	0.203	Okayama	−0.312(−2.204 to 1.581)	0.741	1.367(−0.652 to 3.387)	0.179
Gumma	−0.437(−1.502 to 0.629)	0.412	−0.543(−2.819 to 1.733)	0.632	Hiroshima	0.684(−0.464 to 1.831)	0.236	0.182(−1.563 to 1.927)	0.834
Saitama	0.245(−0.981 to 1.471)	0.688	−2.180(−3.983 to −0.378)	0.019	Yamaguchi	−2.826(−4.520 to −1.132)	0.002	−2.348(−4.903 to 0.206)	0.071
Chiba	0.705(−0.491 to 1.901)	0.241	0.603(−1.190 to 2.396)	0.501	Tokushima	0.602(−2.210 to 3.414)	0.668	3.474(−0.432 to 7.381)	0.080
Tokyo	−1.329(−2.199 to −0.460)	0.004	−0.608(−1.628 to 0.413)	0.236	Kagawa	0.255(−3.165 to 3.675)	0.881	−2.493(−5.468 to 0.481)	0.098
Kanagawa	−0.694(−1.595 to 0.208)	0.128	0.979(−0.683 to 2.641)	0.241	Ehime	−1.683(−3.757 to 0.391)	0.109	−4.485(−6.386 to −2.584)	<0.001
Niigata	1.350(−0.297 to 2.997)	0.105	1.901(0.402 to 3.400)	0.014	Kochi	2.835(1.072 to 4.597)	0.002	2.091(−0.745 to 4.927)	0.144
Toyama	−1.128(−2.721 to 0.465)	0.160	2.030(−0.226 to 4.287)	0.077	Fukuoka	−0.393(−1.309 to 0.523)	0.391	−0.085(−1.852 to 1.681)	0.923
Ishikawa	−0.085(−3.507 to 3.337)	0.960	−1.662(−3.822 to 0.498)	0.128	Saga	−1.555(−4.325 to 1.214)	0.263	1.768(−1.229 to 4.764)	0.240
Fukui	−1.240(−3.371 to 0.892)	0.247	−2.886(−5.423 to −0.349)	0.027	Nagasaki	0.918(−1.235 to 3.071)	0.394	−2.359(−4.450 to −0.267)	0.028
Yamanashi	−0.329(−3.756 to 3.099)	0.847	−1.023(−3.190 to 1.144)	0.346	Kumamoto	0.612(−1.027 to 2.251)	0.455	1.111(−0.864 to 3.086)	0.262
Nagano	0.613(−2.411 to 3.637)	0.684	−3.496(−5.367 to −1.626)	0.001	Oita	1.772(−0.077 to 3.622)	0.060	−2.655(−4.686 to −0.623)	0.012
Gifu	−2.300 (−4.427 to −0.174)	0.035	−0.688(−3.635 to 2.260)	0.640	Miyazaki	1.676(−0.993 to 4.344)	0.212	1.201(−1.758 to 4.160)	0.417
Shizuoka	0.213(−1.057 to 1.482)	0.737	−0.745(−2.211 to 0.721)	0.310	Kagoshima	−0.547(−2.089 to 0.994)	0.477	0.119(−2.114 to 2.353)	0.915
Aichi	−1.252(−2.517 to 0.013)	0.052	0.440(−0.961 to 1.841)	0.529	Okinawa	3.805(1.130 to 6.480)	0.007	3.429(0.272 to 6.586)	0.034
Mie	−2.893(−4.593 to −1.193)	0.001	2.118(−0.013 to 4.249)	0.051	Total	−0.450(−0.829 to −0.071)	0.021	−0.185(−0.700 to 0.330)	0.471

CI Confidence interval

[a] The F test was used

death. Changes in diagnostic and detection techniques or treatment are period factors that would affect all ages simultaneously [16]. These factors, however, were considered to have a minimal influence on the number of deaths in our analysis. On the other hand, almost all prefectures showed a statistically significant decline in cohort trend between the middle cohort and the early cohort, which would be more of an age effect than a cohort effect, partly because nearly 80% of the patients with pancreatic cancer were between 60 and 80 years of age [17]. In contrast, each prefecture showed a different change in cohort trend between the recent cohort and the middle cohort. There was a statistically significant increase in Okinawa and Kochi, for males, and in Yamagata, Niigata, Shiga, and Okinawa, for females. Okinawa had level 1 six successive times, and so this finding may mean that the generation gap in terms of mortality is becoming smaller between Okinawa and the other prefectures in recent years. However, it is not yet certain what sorts of cohort-related factor are involved. Long-term habits and long-term exposures are associated with cohort effects that result in different generations being exposed to different risks [9]. Several environmental factors affecting cohort effects have been presented [16], and one of the suspected risks among different generations is dietary habit. High cholesterol intake has been indicated as being related to the increment of pancreatic cancer risk according to population-based case-control study in Japan [18]. The westernization of the Japanese diet in the younger generations may partly account for the increase in pancreatic cancer over the past decades [19].

Tango et al. [20] considered the possibility of an age-period and an age-cohort interaction in age–period–cohort models and advocated period or cohort effects being constant within certain age groups. They adopted the conventional grouping: young age (20–34 years), middle age (35–54 years), and advanced age (55–79 years). In their study, the parameters of the models were estimated close between the middle age and the advanced age [20]; our present study incorporated the middle age into the advanced age. However the influence of an age interaction on period or cohort trends was not as clear as the two situation of the age groups.

In conclusion, this study carried out a combination of time trend analyses in mortality rates and the evaluation of changes in period or cohort trend based on estimable functions. The results reveal variations in mortality from pancreatic cancer from a different perspective in each prefecture. Further study is required to improve our statistical methods, and we need to continue to analyze pancreatic cancer mortality based on time effects.

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