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Heterogeneous trends of premature mortalities in Japan: joinpoint regression analysis of years of life lost from 2011 to 2019

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ABSTRACT

Purpose: To assess long-term premature mortalities in Japan for providing evidence of strategies for sustainable development in population health.
Methods: Descriptive study for observing the trends of premature mortalities due to 10 major causes and all-cause in Japan was conducted using governmental statistics taken between 2011 and 2019. Years of life lost (YLL) was calculated for each cause, and the trends of these were examined by joinpoint regression analysis.
Results: The means of YLL for all-cause through 2011 to 2019 were 8,121,565.1 in males and 6,743,198.4 in females. For each cause, the trends of age-standardized YLL were downward except for malignant neoplasm of pancreas and heart failure in males, and malignant neoplasm of pancreas, malignant neoplasm of breast, and age-related physical debility in females. One significant joinpoint for heart failure was found in males, and one significant joinpoint for each of malignant neoplasm of pancreas and age-related physical debility were found in females.
Conclusions: Premature mortalities due to malignant neoplasm of pancreas in both sexes, heart failure in males and malignant neoplasm of breast in females were issues to be prioritized for promoting population health in Japan.

1. Introduction

Japan is internationally known as a country that managed to improve population health to a surprising level from the mid-1960s [1]. The Global Burden of Disease Study described Japan as having been successful overall in reducing mortality and disability from most major diseases [2]. The Japanese life expectancy for men is 81.64 years (the second longest in the world), and life expectancy for women is 87.74 years (the longest in the world) in 2020 [3]. Life expectancy in Japan have consistently improved for both sexes [4], and the gender gap in Japanese life expectancy has recently declined [5]. The forecast for 2040 is that life expectancy in Japanese will exceed 85 years in both sexes [6]. Considering the implementation of primary and secondary preventive community public health measures and the universal insurance scheme together [7], population health in Japan seems to be in smooth sailing.

In addition to traditional epidemiologic indices such as life expectancy, premature mortality has increasingly been a focus in public health priorities [8,9]. As the Sustainable Development Goal for Health, the United Nations adopted target 3.4: to reduce premature mortality from non-communicable diseases by one-third by 2030, through prevention and treatment and promote mental health and well-being [10]. To monitor premature mortality due to non-communicable diseases (NCDs), years of life lost (YLL) was developed as a comprehensive measure [11]. Differences have been suggested to exist across countries in the risk of dying from different NCDs, so guiding long-term investments and policy implementation strategies aimed at decreasing YLL are thought to depend on the situation in each country as understood by long-term monitoring of potential trajectories in health [6]. On the other hand, in Japan, long-term monitoring systems for population health are in need of improvement [12], and studies of Japanese health status assessing YLL in the public health area are currently insufficient.

From the perspective of premature mortality, forecasting population health in Japan's future is an uncertain prospect. Crude YLLs (per 100,000 population) of atherosclerotic cardiovascular disease (which includes myocardial infarction, ischemic stroke, and peripheral artery disease) and all cancer are increasing from 2017 to 2021 [13], while YLLs for malignancies of the kidney, bladder, and stomach have been decreasing over the last 30 years [14,15]. Although such previous findings help in understanding part of Japan's present situation surrounding premature

Abbreviations: YLL, years of life lost; NCDs, non-communicable diseases; ICD-10, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision; APC, annual percent change.

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mortality, comprehensive epidemiologic studies of YLLs are needed to develop effective public health strategies for controlling premature mortality.

In this study, we aimed to assess the present situation for premature mortality in Japan, as an international leader of population health with the longest life expectancy in the world. Specific issues that would be clarified through the insights in this study would shed light on the direction of strategies for global sustainable development in population health.

2. Materials & methods

2.1. Study design

This descriptive study observed trends in premature mortality due to 10 major causes in Japan, and was conducted using governmental statistics taken between 2011 and 2019. Further details are included in the following subsections.

2.2. Data sources

Vital statistics were used for referring to the number of deaths in Japan from 2011 to 2019. These statistics contain information on death, which is certificated mostly by physicians and subsequently reported to local governments. Causes of death are coded using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10). The number of deaths for each cause is reported by sex and age.

We obtained the population for 2015 from the census that is conducted every five years, including 2015. For each remaining year, population was estimated using census data and demographic variables, including births and deaths in Japan.

Japanese life tables were referred to for obtaining life expectancy in Japan from 2011 to 2019. Each life table is calculated with two different mixes of governmental statistics: one is reported annually and calculated by vital statistics and the size of the population from the Basic Resident Registration Network System; and the other is reported every five years with vital statistics and the population size from censuses in Japan. For the year in which a census is conducted, the life table calculated from census data is recommended to be used instead of the other type of life table. Therefore, in this study, the life table for 2015 that was determined from census data was used in addition to the life tables for other years that were calculated using populations from the Basic Resident Registration Network System.

All these governmental statistics above are reported on a governmental digital platform [16].

2.3. Analysis

YLL were calculated for monitoring premature mortality from 2011 to 2019 in Japan. The concept of YLL is well described by Martinze et al., and its essential parts are: there are various epidemiologic measures to report premature mortality, with measures other than YLL including: i) the proportion of premature deaths under a selected age threshold; ii) age-standardized death rates under a defined age range; iii) years of potential life lost between age at death and a selected age cut-off; iv) probability of survival at a specified age; and v) probability of dying between an exact age range [11]. Although these measures are useful in cases where study goals fit those measures, arbitrarily selecting age-range is considered an important limitation that fails in capturing premature deaths at ages outside the selected age-range [11]. YLL overcomes this issue by calculating time lost based on the potential lifespan of an individual at each age. At the population level, the number of YLL is calculated as the number of deaths due to a cause at a certain age, sex, and time, multiplied by the life expectancy at age of death. The most important advantage of YLL is the avoidance of arbitrary judgments about age cut-offs, which are never methodologically justifiable, and exclusions of older population groups [11]. Therefore, in this study, premature mortality is defined as death before life expectancy, reflecting the concept of YLL which is mentioned above. To calculate YLL, the numbers of deaths between 2011 and 2019 were obtained from the vital statistics according to sex and age (grouped by five-year age strata of 0–4, 5–9, 10–14, 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, and 85 and over). Because life expectancy is reported annually to the public by sex and age (not age-group), we calculated simple averages of life expectancy for each age category of vital statistics, and multiplied the calculated averages of life expectancy with the number of deaths in the same age categories. Finally, the number of YLL was calculated by summing up the YLL of each age-group. To balance the granularity of diseases in ICD-10, three-digit codes (i.e., one letter of the alphabet and a two-digit number) were used to compare each disease. Disease-groups that mix several three-digit ICD-10 codes were beyond the scope of this study. Finally, YLL for diseases that were categorized by three-digit ICD-10 codes were analyzed by sex.

2.4. Statistical analysis

Trends in proportion of YLL (per 1,000 people) and age-standardized YLL were analyzed statistically. Age-standardized YLL were calculated by the direct method with population derived from the 2015 census as a reference. Joinpoint regression analysis was conducted to examine trends by sex. Software for conducting joinpoint regression analysis was downloaded from a website of the US National Cancer Institute [17]. This method detects changes in trends by connecting several different line segments at joinpoints [17]. The maximum number of joinpoints for statistical testing was two in this study because of the limited number of observed points, and analysis started with a straight line (i.e., zero joinpoints) for a model fit asymptotically to two joinpoints. Annual percent changes (APCs) for each line segment were also estimated. The significance of changes in trends and their APCs were therefore reported in the final model [17].

Statistical analyses were conducted using Joinpoint trend analysis software (desktop version 4.9.0.0; National Cancer Institute, Bethesda, Maryland, USA) and STATA (version 13.1 for Mac; Stata Corp, College Station, Texas, USA). All values of $p < 0.05$ were considered statistically significant.

3. Results

Table 1 shows YLL due to all causes, rate of YLL per 1,000 population, and age-standardized rate of YLL (per 1,000 population) from 2011 to 2019 by sex. Mean YLL from 2011 through 2019 were 8,121,565.1 years in males and 6,743,198.4 years in females. Differences between males and females were 1,378,366.7 years for mean YLL, 28.4 for rate of YLL, and 28.2 years for age-standardized YLL. Age-standardized YLL continuously decreased from 2011 to 2019 in both sexes, with the extents of the decreases being 17.3 (2.2 per year) in males and 14.0 (1.8 per years) in females from 2011 to 2019.

All-cause and top-10 YLLs for causes in 2019 are shown in Table 2. Diseases seen only in males were asphyxiation (T71), hanging, strangulation or

Table 1
Years of life lost due to all causes in Japan from 2011 to 2019.

	YLL in males			YLL in females		
	Crude	Rate[i]	Age-standardized rate[ii]	Crude	Rate[i]	Age- standardized rate[ii]
2011	8,327,125	135.5	143.3	6,897,985	106.6	113.3
2012	8,119,043	132.4	137.6	6,650,624	102.9	107.6
2013	8,116,762	132.7	135.7	6,681,045	103.6	106.3
2014	8,124,234	133.1	134.0	6,739,408	104.7	105.5
2015	8,056,099	133.2	133.2	6,664,204	104.5	104.5
2016	8,050,561	132.3	129.3	6,712,288	104.6	102.1
2017	8,057,355	132.8	127.6	6,712,216	104.9	100.4
2018	8,095,264	133.9	126.7	6,798,989	106.6	100.1
2019	8,147,643	135.3	126.0	6,832,027	107.6	99.3

YLL, years of life lost.
i: YLL per 1,000 population
ii: YLL standardized by 1,000 population in 2015

Table 2
Years of life lost due to all causes, top 10 causes, and proportion of each cause, in Japan, 2019.

YLL in males					YLL in females				
ICD10	Crude	Rate[i]	Age-standardized rate[ii]	Proportion of age-standardized rate	ICD10	Crude	Rate[i]	Age-standardized rate[ii]	Proportion of age-standardized rate
All-cause	8,147,643	135.3	126.0	1	All-cause	6,832,027	107.6	99.3	1
C34	635,931	10.6	9.9	0.078	R54	449,561	7.1	5.9	0.060
J18	388,747	6.5	5.7	0.045	I50	359,536	5.7	5.0	0.050
C16	336,160	5.6	5.2	0.041	C50	313,770	4.9	4.8	0.049
T71	304,543	5.1	5.1	0.040	C34	290,936	4.6	4.3	0.043
(X70)	291,127	4.8	4.8	0.038	J18	289,954	4.6	4.0	0.040
I50	287,553	4.8	4.3	0.034	C25	252,800	4.0	3.8	0.038
C25	244,725	4.1	3.8	0.031	C18	232,277	3.7	3.5	0.035
I21	234,234	3.9	3.7	0.029	C16	195,396	3.1	2.9	0.029
C18	218,364	3.6	3.4	0.027	I69	146,372	2.3	2.0	0.020
C22	205,600	3.4	3.2	0.026	I21	134,523	2.1	1.9	0.020

YLL, years of life lost.
i: YLL per 1,000 population
ii: YLL standardized by 1,000 population in 2015
ICD10 codes: C34 = malignant neoplasm of bronchus and lung; J18 = pneumonia, unspecified organism; C16 = malignant neoplasm of stomach; T71 = asphyxiation; X70 = hanging, strangulation or suffocation (which is included in T71); I50 = heart failure; C25 = malignant neoplasm of pancreas; I21 = acute myocardial infarction; C18 = malignant neoplasm of colon; C22 = malignant neoplasm of liver and intrahepatic bile ducts; R54 = age-related physical debility; C50 = malignant neoplasm of breast; and I69 = sequelae of cerebrovascular disease.

suffocation (X70, which is part of T71), and malignant neoplasm of the liver and intrahepatic bile ducts (C22). Conversely, diseases limited to females were age-related physical debility (R54), malignant neoplasm of the breast (C50), and sequelae of cerebrovascular disease (I69). In males, the proportion of age-standardized rates for the top 10 causes ranged from 2.6% to 7.8%, accounting for 38.9% of all-cause YLL. In females, the proportion of age-standardized rates for the top 10 causes ranged from 2.0% to 6.0%, occupying 38.4% of all-cause YLL.

Because of the overlap between asphyxiation (T71) and hanging, strangulation or suffocation (X70), we eliminated hanging, strangulation or suffocation (X70) from subsequent analyses.

Table 3 shows yearly rates of age-standardized YLL (per 1,000 population) for the causes listed in Table 2, from 2011 to 2019 by sex. For each cause in males, rates of age-standardized YLL in 2019 subtracted from rates of age-standardized YLL in 2011 were zero or negative except for malignant neoplasm of the pancreas (C25; 3.6 in 2011 and 3.8 in 2019). Limited to the most recent three years, the rate of age-standardized YLL for heart failure (I50) increased from 4.1 in 2017 to 4.3 in 2019. For each cause in females, rates of age-standardized YLL in 2019 subtracted from rates of age-standardized YLL in 2011 were zero or negative except for malignant neoplasm of the pancreas (C25; 3.3 in 2011 to 3.8 in 2019), malignant neoplasm of the breast (C50; 4.6 in 2011 and 4.8 in 2019), and age-related physical debility (R54; 3.4 in 2011 and 5.9 in 2019). Limited to the most recent three years, rates of age-standardized YLL for malignant neoplasm of the pancreas (C25) increased from 3.6 in 2017 to 3.8 in 2019, and age-related physical debility (R54) from 5.3 in 2017 to 5.9 in 2019. We therefore selected malignant neoplasm of the pancreas and heart failure for males, and malignant neoplasm of the breast, malignant neoplasm of the pancreas, and age-related physical debility for females to conduct further joinpoint regression analysis.

Table 3
Age-standardized years of life lost due to top 10 causes per 1,000 population in Japan, from 2011 to 2019, by sex.

Male		2011	2012	2013	2014	2015	2016	2017	2018	2019
	C34	11.0	10.9	10.9	10.8	10.9	10.4	10.1	9.8	9.9
	J18	9.4	9.0	8.8	8.4	8.3	7.9	5.9	5.7	5.7
	C16	7.3	7.0	6.8	6.6	6.4	6.0	5.8	5.5	5.2
	T71	7.0	6.4	6.5	6.1	5.9	5.3	5.4	5.2	5.1
	I50	4.3	4.3	4.2	4.1	3.9	3.9	4.1	4.1	4.3
	C25	3.6	3.7	3.7	3.8	3.7	3.8	3.8	3.9	3.8
	I21	5.3	5.1	4.8	4.7	4.5	4.3	4.1	3.9	3.7
	C18	3.4	3.5	3.5	3.5	3.6	3.5	3.5	3.5	3.4
	C22	4.8	4.6	4.4	4.2	4.1	3.8	3.6	3.3	3.2
Female										
	R54	3.4	3.8	4.3	4.6	5.0	5.1	5.3	5.5	5.9
	I50	5.5	5.5	5.4	5.2	5.0	4.8	5.0	5.0	5.0
	C50	4.6	4.4	4.6	4.6	4.7	4.8	4.8	4.8	4.8
	C34	4.5	4.6	4.6	4.6	4.6	4.5	4.3	4.4	4.3
	J18	7.3	6.9	6.7	6.4	6.2	5.8	4.3	4.0	4.0
	C25	3.3	3.4	3.4	3.4	3.5	3.5	3.6	3.7	3.8
	C18	3.4	3.5	3.5	3.6	3.6	3.5	3.5	3.5	3.5
	C16	3.9	3.8	3.7	3.6	3.4	3.3	3.1	3.0	2.9
	I69	3.0	2.9	2.8	2.6	2.5	2.3	2.3	2.1	2.0
	I21	3.3	3.1	2.9	2.8	2.6	2.4	2.2	2.1	1.9

ICD10 codes: C34 = malignant neoplasm of bronchus and lung; J18 = pneumonia, unspecified organism; C16 = malignant neoplasm of stomach; T71 = asphyxiation; I50 = heart failure; C25 = malignant neoplasm of pancreas; I21 = acute myocardial infarction; C18 = malignant neoplasm of colon; C22 = malignant neoplasm of liver and intrahepatic bile ducts; R54 = age-related physical debility; C50 = malignant neoplasm of breast; and I69 = sequelae of cerebrovascular disease.

Fig. 1 shows trends for rates of age-standardized YLL for malignant neoplasm of the pancreas, heart failure, and all-cause, which is a reference in males. The final selected model for malignant neoplasm of the pancreas was 0 joinpoints, and APC from 2011 to 2019 was 0.80, which was significant. The final model for heart failure was 1 joinpoint, and APC from 2011 to 2016 was -2.06 and APC from 2016 to 2019 was 2.97; both values were significant. Conversely, the final model for all causes was 0 joinpoints and APC from 2011 to 2019 was significant, at −1.52.

Fig. 2 shows trends in rates of age-standardized YLL for malignant neoplasm of the breast, malignant neoplasm of the pancreas, age-related physical debility, and all causes, which is a reference in females. The final selected model for malignant neoplasm of the breast was 0 joinpoints and APC from 2011 to 2019 was 1.04, which was significant. The final model for malignant neoplasm of the pancreas was 1 joinpoint and APC was 1.27 from 2011 to 2017, and 2.66 from 2017 to 2019; both values were significant. The final model for age-related physical debility was 1 joinpoint, APC from 2011 to 2013 was 13.08, and APC from 2013 to 2019 was 5.01; both values were significant. Conversely, the final model for all causes was 0 joinpoints, and APC from 2011 to 2019 was -1.48, which was significant.

4. Discussion

We found that Japan, which has the longest life expectancy in the world, has points that should be a matter of focus for improving population

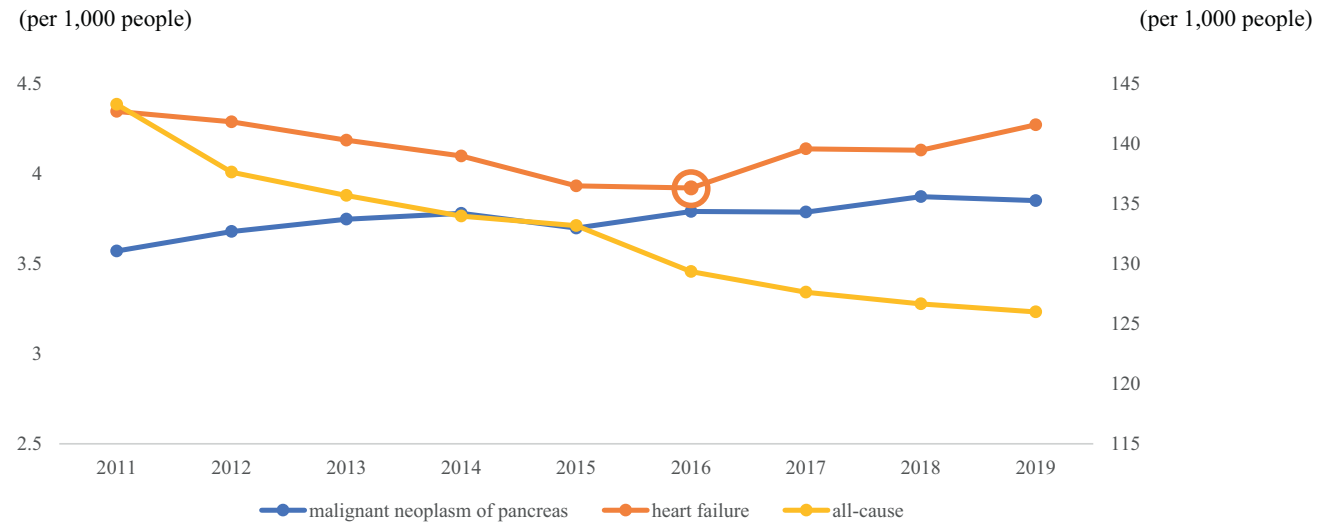

Fig. 1. Trends and joinpoints of year of life lost due to heart failure, malignant neoplasm of pancreas, and all-cause in male from 2011 to 2019. The numbers of left side are for rates of age-standardized YLL for malignant neoplasm of pancreas (C25) and heart failure (I50). The number of right side are for the rate of age-standardized YLL for all-cause. A circled dot means joinpoint which is a changing point for trends. The trend of YLL for all-cause did not have a joinpoint and continuously downward. The trend of malignant neoplasm of pancreas also did not have a joinpoint but continuously upward. The trend of heart failure, on the other hand, had one joinpoint in 2016, and the trend changed from downward to upward at that point.

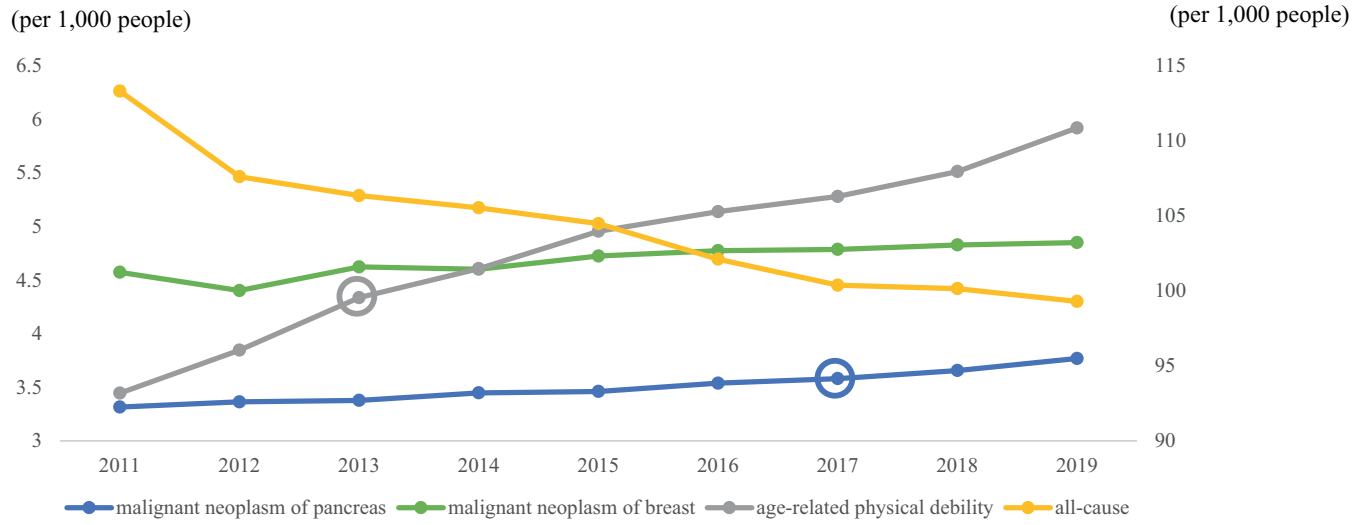

Fig. 2. Trends and joinpoints of year of life lost due to malignant neoplasm of pancreas, malignant neoplasm of breast, age-related physical debility, and all cause in female from 2011 to 2019. The numbers of left side are for rates of age-standardized YLL for malignant neoplasm of pancreas (C25), malignant neoplasm of breast (C50), and age-related physical debility (R54). The numbers of right side are for the rate of age-standardized YLL for all-cause. Circled dots mean joinpoints which are changing points for trends. The trend of YLL for all-cause did not have a joinpoint and continuously downward. The trend of malignant neoplasm of breast also did not have a joinpoint but the trend was upward. The trend of malignant neoplasm of pancreas and age-related physical debility had one joinpoint for each, and the trends before and after the joinpoints were both upward.

health in terms of premature mortality. Due to premature mortality from all causes, more than 8.1 million years (133.5 years per 1,000 population) in males and 6.7 million years (105.1 years per 1,000 population) in females were lost on average from 2011 to 2019. Although trends in the rate of YLL from all causes were linearly downward in both sexes (APC: −1.52 in males; −1.48 in females), malignant neoplasm of the pancreas in both sexes, heart failure in males, and malignant neoplasm of the breast and age-related physical debility in females have been upward heterogeneously. Understandably, YLL for age-related physical debility has increased with life expectancy, but the other diseases mentioned above are needed to be prioritized to improve population health in Japan. The following is the specific discussion including the possible reasons why these heterogeneous trends have been observed.

Malignant neoplasm of the pancreas has been identified as a public health concern not only in Asian countries, but also in Western countries. A recent study by Wang et al. revealed that analysis of YLLs showed that the malignant neoplasm of the pancreas was the most severe cancer in Taiwan [18], and Carrato et al. stated that this cancer represented a substantial burden in Europe, with nearly a million aggregate life-years lost annually and almost complete loss of healthy life in affected individuals

through the poor prognosis and short survival [19]. Social costs, particularly the loss of national productivity due to premature mortality adds to the burden of malignant neoplasm of the pancreas [20], and its substantial increase in burden might continue over the next three decades [21]. Despite these facts, unfortunately, discrepancies between allocation of cancer research funding and societal burdens has been reported [22]. To increase awareness for under-supported but common and highly lethal cancers [22], statistics on YLL should be reported with routine annual reports of governmental statistics alongside the usual incidence and mortality rates and associated age-standardized counterparts [18]. In addition, assessing gaps between burden of diseases, including pancreas cancer, and research funding in Japan would represent a promising research theme for the future.

The burden of heart failure has been growing internationally [23,24], particularly in developed countries such as Japan. Aging is one of the major factors related to premature mortality for heart failure [24]. In addition, comorbidities of heart failure are known to affect its mortality, especially in males [25]. Similar V-shaped changes in trends for the premature mortality of heart failure, as observed in this study, have already been reported, and mortality due to heart failure will likely result in continued increases if current worsening trends in poor-quality diet, physical inactivity, obesity and diabetes continue without intervention [23]. The projected significant increase in heart failure burden highlights the need to set heart failure as a priority for the healthcare system [26] in Japan as well. Developing a system for long-term monitoring of premature mortality due to heart failure would be warranted for considering investments of national resources to develop and allocate effective interventions aimed at controlling heart failure.

Development of interventions to control malignant neoplasm of the breast are urgently required. For women, breast cancer was the most common cancer and the leading cause of cancer deaths in most countries around the world [27]. Unfortunately, large disparities in the burden of breast cancer exist between countries and within countries in terms of ethnicity, deprivation, educational level, and urbanization [28–31]. The economic consequences for society are also considerable [32] through losses in female labor productivity and high work absenteeism costs due to breast cancer [33,34]. In Japan, Saito et al. reported that women with breast cancer experience various job-related problems, including income losses and job losses [35]. Increases in the incidence of breast cancer are to some extent accounted for by a change in the population age structure [27], and rapid changes in age structure and lifestyle during the last decade are expected to strongly increase the burden of breast cancer, particularly in Asian countries [36]. Prevention of premature death due to breast cancer through broad implementation of primary prevention and early detection and treatment are urgently required [37]. YLL is thought to be a useful tool to gauge the effectiveness of the health system with respect to primary prevention, early detection and treatment [9,38]. Although the existence of a relationship between early diagnosis and screening tests and a decrease in breast cancer-related mortality is still disputed [39], measuring the effectiveness of interventions with YLL would find new effective ways of controlling breast cancer. More studies are needed.

Some limitations must be kept in mind when interpreting this study. First, the study used a descriptive study to observe trends for YLL in Japan. Causal relationships for factors associated with a change in trends for YLL could not be examined. Exploring the factors that would affect the trend for male heart failure in Japan, for example, is another topic for future studies. Second, various viewpoints would weight diseases differently for making effective health policy. Therefore, the feasibility of actual preventive methods (practical solutions, organizational capabilities, clear plans, etc.), harmony with existing policies, and realistic budgets should be concerned. Lastly, we used only data until 2019 considering that the trends in YLL we showed here would have changed after 2020 due to COVID-19 and related behavioral changes in patients. Although the effects from COVID-19 are beyond the scope of this study, continuous monitoring for YLL would be needed.

5. Conclusions

In a society where longevity has been expanding to the highest level in the world, the present study revealed that premature mortality due to malignant neoplasm of the pancreas in both sexes, heart failure in males, and malignant neoplasm of the breast in females should be prioritized for promoting population health in Japan. The Japanese situation of research funds in these diseases, monitoring systems with YLL, and the effectiveness of early diagnosis and screening tests as measured by YLL need to be determined in the next step.

Ethics

Ethics approval was not needed for this study.

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CRediT authorship contribution statement

Satoshi Tsuboi: Conceptualization, Project administration, Validation, Writing – original draft. **Tomosa Mine:** Data curation, Formal analysis, Methodology, Software. **Tetsuhito Fukushima:** Resources, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Satoshi Tsuboi is an employee of Nippon Boehringer Ingelheim, which is a pharmaceutical company in Japan.

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