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# Attributable causes of cancer in Japan in 2005—systematic assessment to estimate current burden of cancer attributable to known preventable risk factors in Japan

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**Background:** To contribute to evidence-based policy decision making for national cancer control, we conducted a systematic assessment to estimate the current burden of cancer attributable to known preventable risk factors in Japan in 2005.

**Methods:** We first estimated the population attributable fractions (PAFs) of each cancer attributable to known risk factors from relative risks derived primarily from Japanese pooled analyses and large-scale cohort studies and the prevalence of exposure in the period around 1990. Using nationwide vital statistics records and incidence estimates, we then estimated the attributable cancer incidence and mortality in 2005.

**Results:** In 2005, ~55% of cancer among men was attributable to preventable risk factors in Japan. The corresponding figure was lower among women, but preventable risk factors still accounted for nearly 30% of cancer. In men, tobacco smoking had the highest PAF (30% for incidence and 35% for mortality, respectively) followed by infectious agents (23% and 23%). In women, in contrast, infectious agents had the highest PAF (18% and 19% for incidence and mortality, respectively) followed by tobacco smoking (6% and 8%).

**Conclusions:** In Japan, tobacco smoking and infections are major causes of cancer. Further control of these factors will contribute to substantial reductions in cancer incidence and mortality in Japan.

**Key words:** cancer, Japan, population attributable fraction, risk factor

## introduction

Japan has experienced a drastic change in disease structure and pattern over the past five decades [1, 2], due to economic, demographic, and lifestyle changes experienced after World War II. Together with rapid aging, the transition in patterns of disease from communicable diseases such as tuberculosis and pneumonia to noncommunicable diseases, including cancer [1, 2], poses challenges to health systems and to public health in Japan. Cancer has been the leading cause of death in Japan since 1981, accounting for ~30% of all deaths in recent years. Cancer registry data in 2005 suggest that 54% of Japanese men and 41% of Japanese women will be diagnosed with cancer during their lifetime [3].

It is well known that cancers are largely caused as a result of lifestyle and environmental factors that are potentially preventable. On the other hand, substantial differences in the pattern of cancer by geographical region and socioeconomic level may be identified [4]. Cancer control policies in any country must therefore be tailored to reflect the local burden of cancer and characteristics of the health system.

The first national systematic quantitative assessment of multiple cancers was reported in the United States in 1981 [5] and was followed by updated estimates for the United States [6, 7], estimates for European countries including the Nordic countries [8, 9], and France [10, 11] and global estimates [12]. Although the cancer burden attributable to sectioned individual risk factors has been reported for East Asian countries [13–16], no single study has provided a reliable estimation of attributable fraction for known risk factors on multiple cancer risks in Japan.

In the present study, we conducted a systematic assessment to estimate the current burden of cancer attributable to known preventable risk factors in Japan in 2005.

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## methods

We estimated the population attributable fraction (PAF) of site-specific cancers occurring in Japan in 2005. PAF in the present study is the fraction of total cancer incidences or mortality that is attributable to a particular exposure and that could be avoided if that exposure were eliminated or reduced to an alternative scenario that would result in the lowest risk, or in other words, the theoretical minimum risk exposure distribution [17].

### data sources

Estimation of PAF of known causes of cancer in Japanese requires the availability of cancer incidence and mortality data in Japan, data on the prevalence of exposure to each risk factor and relative risk (RR) for each causally related cancer.

*selection of risk factors for cancer in Japan.* Risk factors included in this study were those for which there is evidence for a causal association with cancer (Table 1). These factors were selected based on the agents classified by the International Agency for Research on Cancer (IARC) [18] as Group 1 carcinogens in humans; risk and protective factors that were judged as 'convincing', with the exception of 'convincing' or 'probable' for vegetable, fruit, and salt intake by the second 'Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective' report, produced by the World Cancer Research Fund and American Institute for Cancer Research in 2007 [19]; and the conditions evaluated by the IARC Cancer Prevention Handbook Series [20] as causally associated with a reduced risk. Some established carcinogens, such as infection with *Schistosoma haematobium* (blood fluke), *Opisthorchis viverrini* (liver fluke), human immunodeficiency virus, and intake of aflatoxin, were not included in this study due to their very rare or very low prevalence in Japan. Further, due to the lack of reliable prevalence data in Japan, we did not include risk factors such as occupational exposure, air pollution, and ultraviolet and radiation exposure.

*cancer incidence and mortality in Japan in 2005.* Cancer incidence data in 2005 were obtained from the annual estimate by the Japan Cancer Surveillance Research Group as part of the Monitoring of Cancer Incidence in Japan project [3] on the basis of data collected from population-based cancer registries in Japan. We obtained sex- and age-specific incidence data for target cancers using code of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10), with morphology code of the International Classification of Disease for Oncology, 3rd Edition (ICD-O-3).

Data on cancer mortality statistics in 2005 were obtained from the vital statistics of Japan. We extracted sex-, age-, and cause-specific mortality from an electronic database obtained from the Japanese Ministry of Health, Labour and Welfare, with permission. Cause of death was classified using the ICD-10.

Table 2 summarizes cancer incidence and mortality in Japan in 2005.

*prevalence of exposures to each risk factor.* The current burden of cancer reflects the cumulative effect of past exposures. For most cancers and risk factors, average latency between first exposure and diagnosis is ~15 years [11]. We therefore assumed a latency time of ~15 years and considered exposures around 1990. We collected prevalence data of exposures to each risk factor from different sources, giving priority to representative Japanese surveys. No latency time was considered and current prevalence was applied for exogenous hormone use (hormone replacement therapy and oral contraceptive use) in women given the assumption that cancer risk decreases rapidly after the cessation of use of exogenous hormones [21]. Occupational exposures such as asbestos, etc. were not included in this analysis due to a lack of reliable prevalence data in Japan.

*selection of RR for each causally related cancer.* Data on RR included in this study were obtained from epidemiologic studies identified from different sources, including PubMed, *Ichushi*, and websites, in either English or Japanese. We employed priority ranking for the inclusion and selection of RRs as follows: for selection, a study should include RR and corresponding 95% confidence intervals (CIs). Among these studies, highest priority was given to meta-analyses that included pooled analyses of Japanese populations. When meta-analyses were not available, we selected the most

**Table 1.** Risk factors and cancers included in the present analysis

| Risk factor | Definition of theoretical minimum risk exposure distribution | Target cancers associated with risk factor |
|---|---|---|
| Tobacco smoking (active) | Never smoking | Oral and pharynx, esophagus, stomach, colorectum, liver, pancreas, larynx, lung, cervix uteri, ovary, bladder, kidney, myeloid leukemia |
| Passive smoking | No exposure | Lung (nonsmokers) |
| Alcohol drinking | No alcohol intake | Oral and pharynx, esophagus, colorectum, liver, female breast |
| Overweight and obesity | Body mass index <25 | Colon, pancreas, postmenopausal breast, endometrial, kidney |
| Physical inactivity | Average daily total physical activity level + three METs/day | Colon, breast, endometrial |
| Vegetable intake | Higher than the lowest intake group | Esophagus, stomach |
| Fruit intake | Higher than the lowest intake group | Esophagus, stomach, lung |
| Salt intake | Intake of ≤6 g/day | Stomach |
| Infection | No infection | |
| *Helicobacter pylori* | | Noncardia stomach, gastric MALT lymphoma |
| Hepatitis C virus | | Liver |
| Hepatitis B virus | | Liver |
| Human papillomavirus | | Oral cavity, oropharynx, anus, penis, vulva, vagina, cervix uteri |
| Human T-cell leukemia type I | | Adult T-cell lymphoma/leukemia |
| Epstein–Barr virus | | Nasopharynx, Burkitt lymphoma, Hodgkin lymphoma |
| Exogenous hormone use | No use | Female breast |
| Hormone replacement therapy | | |
| Oral contraceptives | | |

MALT, mucosa-associated lymphoid tissue; MET, metabolic equivalents.

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**Table 2.** Incidence[a] and mortality[b] of cancer in Japan in 2005

| Site | ICD-10 | Men | | Women | | Both sexes | |
|---|---|---|---|---|---|---|---|
| | | Incidence | Mortality | Incidence | Mortality | Incidence | Mortality |
| Oral and pharynx | C00–C14 | 7417 | 4151 | 3498 | 1528 | 10 915 | 5679 |
| Esophagus | C15 | 14 818 | 9465 | 2678 | 1717 | 17 496 | 11 182 |
| Stomach | C16 | 80 102 | 32 643 | 37 035 | 17 668 | 117 137 | 50 311 |
| Colon | C18 | 37 126 | 13 436 | 31 069 | 13 685 | 68 195 | 27 121 |
| Rectum | C19–C20 | 22 344 | 8710 | 13 517 | 4999 | 35 861 | 13 709 |
| Anus | C21 | 430 | 137 | 248 | 130 | 678 | 267 |
| Liver | C22 | 28 729 | 23 203 | 13 465 | 11 065 | 42 194 | 34 268 |
| Gall-bladder, etc. | C23–C24 | 9237 | 7845 | 9399 | 8741 | 18 636 | 16 586 |
| Pancreas | C25 | 13 108 | 12 284 | 11 691 | 10 643 | 24 799 | 22 927 |
| Sinonasal | C30–C31 | 826 | 261 | 673 | 174 | 1499 | 435 |
| Larynx | C32 | 3903 | 1006 | 214 | 84 | 4117 | 1090 |
| Lung | C33–C34 | 58 264 | 45 189 | 25 617 | 16 874 | 83 881 | 62 063 |
| Skin | C44 | 4405 | 347 | 3702 | 321 | 8107 | 668 |
| Breast | C50 | 312 | 87 | 47 582 | 10 721 | 47 894 | 10 808 |
| Vulva | C51 | | | 704 | 226 | 704 | 226 |
| Vagina | C52 | | | 221 | 102 | 221 | 102 |
| Cervix uteri | C53 | | | 8474 | 2465 | 8474 | 2465 |
| Corpus uteri | C54 | | | 8189 | 1459 | 8189 | 1459 |
| Ovary | C56 | | | 8304 | 4467 | 8304 | 4467 |
| Penis | C60 | 308 | 128 | | | 308 | 128 |
| Prostate | C61 | 42 997 | 9265 | | | 42 997 | 9265 |
| Kidney | C64 | 6871 | 2600 | 3153 | 1233 | 10 024 | 3833 |
| Renal pelvis | C65–C66, C68 | 2887 | 1419 | 1731 | 880 | 4618 | 2299 |
| Bladder | C67 | 12 619 | 4141 | 3858 | 1888 | 16 477 | 6029 |
| Thyroid | C73 | 2126 | 446 | 7093 | 1024 | 9219 | 1470 |
| Hodgkin disease | C81 | 422 | 89 | 501 | 43 | 923 | 132 |
| Non-Hodgkin lymphoma | C82–C85, C96 | 8571 | 4772 | 7386 | 3676 | 15 957 | 8448 |
| Multiple myeloma | C88–C90 | 2242 | 1972 | 2171 | 1917 | 4413 | 3889 |
| Leukemia | C91–C95 | 5200 | 4311 | 3832 | 2972 | 9032 | 7283 |
| All sites | C00–C97 | 379 436 | 196 603 | 267 366 | 129 338 | 646 802 | 325 941 |

[a]Japan Cancer Surveillance Research Group as part of the Monitoring of Cancer Incidence in Japan project [3].
[b]Vital statistics of Japan [1].
ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision.

comprehensive studies of Japanese available. Results from cohort studies had priority over case–control studies. When RRs for Japanese populations were not available, we then substituted the data with those for other Asian populations and finally with non-Asian values from the literature.

### analysis

PAF was calculated based on the RR of cancer associated with exposure to the risk factor and the prevalence of exposure to the risk factor in the total population ($P$) [22] using the following formula:

$$\mathrm{PAF} = \frac{P\times(\mathrm{RR}-1)}{P\times(\mathrm{RR}-1)+1}.$$

When RR or exposure data were reported in multiple exposure categories, they were combined in a dichotomous variable [10, 23].

Different methods were used for estimations related to infection. To estimate major infectious causes of cancer in Japanese such as *Helicobacter pylori*, hepatitis B virus and hepatitis C virus (HCV), we used an alternative formula [23, 24] based on the distribution of exposure in cases (Pc) since the prevalence of each infection among cases was more stable than that among control or reported populations in the literature:

$$\mathrm{PAF} = Pc\times\frac{\mathrm{RR}-1}{\mathrm{RR}}.$$

For other infectious agents, we applied the PAF values from a previous estimation [25] due to a lack of prevalence or RR data for Japanese.

For physical inactivity and salt intake, we derived the risk of cancer per unit increase in exposure and average RR for the whole population based on the average level of exposure, assuming a log-linear relationship between exposure and risk, by means of the following formula [10]:

$$\mathrm{Risk} = [\ln(\text{risk per unit})\times\text{average exposure level}];$$

$$\mathrm{PAF} = \frac{\mathrm{Risk}-1}{\mathrm{Risk}}.$$

To account for interactions among multiple risk factors, such as tobacco smoking and alcohol drinking, we used the following formula under the assumption of independent exposures and effect [26]:

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$$PAF = 1 - \prod_{i=1}^{n} (1 - PAF_i),$$

where $i$ refers to $i$th risk factor.

To account for uncertainty in the estimation of PAFs arising from RRs and the exposure prevalence of risk factors, the 95% CI of PAF was calculated using the variance of PAF based on a delta method, where $P$ was the prevalence of exposure and $\beta$ was defined as ln (RR):

$$\mathrm{Var(PAF)} = \frac{[Exp(\beta)-1]^2 \cdot Var(P) + [P.Exp(\beta)]^2 \cdot Var(\beta)}{\{P[Exp(\beta)-1]+1\}^4}$$

The variance of prevalence was considered null when the prevalence data were based on the whole population. When PAF was derived directly from the literature, as with some infectious agents, estimation of 95% CI was carried out under the assumption of no variability for the PAF.

## results

Overall, ~55% of cancer (53% for incidence and 57% for mortality, respectively) among men was attributable to preventable risk factors in Japan. The corresponding figure was lower among women, but preventable factors still accounted for nearly 30% of cancer (28% and 30%; Table 3; detailed results of cancer burden by risk factor are shown in supplemental Appendix Tables A1–A8, available at *Annals of Oncology* online).

The estimated PAFs for each risk factor are summarized in Table 3. Tobacco smoking and infectious agents are the major risk factors for cancer in Japan, followed by alcohol drinking. Other risk factors such as salt intake, excess body mass index (BMI), vegetable intake and fruit intake, physical inactivity, and female exogenous hormone use accounted for a small share (<2%) of both cancer incidence and mortality. A substantial difference is seen in the pattern of cancer attributable to preventable risk factors by sex, primarily due to differences in the past cumulative exposure to tobacco smoking. In men, tobacco smoking, including both active and passive smoking, had the highest PAF (30% and 35% for incidence and mortality, respectively), followed by infectious agents (23% and 23%). Among women, in contrast, infectious agents had the highest PAF (18% and 19% for incidence and mortality, respectively), followed by tobacco smoking, including active and passive (6% and 8%).

Summary results for individual cancers are shown in Table 4. In both sexes, infections and tobacco smoking remained the major causes of site-specific cancer, i.e. oral cavity and pharynx, stomach, and liver in men and nasopharynx, liver, and cervix uteri in women due to both tobacco smoking and infection; esophagus, larynx, and urinary tract in men due to tobacco smoking; and anus in men and women due to infection. For other cancers, on the other hand, such as pancreas and leukemia; male prostate; and female colorectum, breast, corpus uteri, ovary, and urinary tract, no strong associations with the currently known preventable risk factors were seen.

## discussion

This is the first study in Japan to systematically analyze the current burden of cancer attributable to multiple known preventable risk factors. Our study suggests that ~45% of cancer incidence and mortality in Japan in 2005 was potentially preventable.

The major advantage of the present study was the use of best available evidence from the Japanese population, particularly given that exposure–disease relationships can vary substantially between populations even after adjustment for potential confounders. A well-known example of this is the difference in tobacco smoking and BMI between Western and Asian populations [27, 28]. RRs of cancer incidence and mortality used in the present study were derived primarily from pooled analyses or large-scale cohort studies of Japanese, which enabled a more appropriate and realistic estimation than studies that extrapolate RRs from other populations.

Our results confirmed that tobacco smoking and infectious agents are currently the major causes of cancer in Japan.

The prevalence of current smokers among Japanese men has constantly decreased, from 53% in 1990 to 39% in 2005. The higher prevalence of ever smokers in 1990 (73%) than recently led to the large attribution of tobacco smoking in Japanese men. In women, in contrast, the prevalence of current smoking has been stable since 1990 (10%–11%) despite an increasing trend in younger age groups (aged 20–40 years: 11% in 1990 and 18% in 2005) [2]. We anticipate that the burden of cancer attributable to tobacco smoking will decrease in men but not in women in the next few decades due to the 20- to 30-year time lag between tobacco exposure and diagnosis.

Previous studies have consistently shown that the RR of tobacco smoking on cancer is lower in the Japanese as well as other East Asian populations than in Western populations [29]. There are several potential reasons for this. First, the uptake of smoking began later in the Japanese than in Western populations and the shortage of cigarettes during and shortly after World War II meant that consumption in this period at least was lower [27]. Secondly, Japanese nonsmokers have a higher incidence of cancers due to environmental tobacco smoke [30] and other indoor air pollutants [31]. Thirdly, susceptibility to tobacco smoke appears to have a genetic component; and finally, other lifestyle or environmental factors commonly found in the Japanese population appear to have a protective effect [27].

Another important finding from our study is its confirmation of the notion that infectious agents are a major cause of cancer in the East Asian region [16]. Its advanced socioeconomic status and high degree of hygiene and sanitation notwithstanding, Japan is not an exception: *H. pylori* and HCV are major infectious causes that account for a relatively large share of preventable cancers. In contrast, the contribution of infectious agents has recently been reported as <5% in Western populations [6, 9, 10]. The prevalence of these infectious agents shows a strong cohort effect, namely a huge variation by birth cohort, and has been declining rapidly among younger birth cohorts.

The majority of gastric cancer in Japan is derived from the noncardia stomach (91% in men and 94% in women in 2000) [32], and the prevalence of *H. pylori* is >80% in the birth cohort born before 1950 and 40%–50% in those born after 1950 [33, 34]. Because of this cohort effect, gastric cancer is expected to decline rapidly in a next few decades after the reduction of *H. pylori* infection in Japan. Hepatocellular carcinoma, which accounts for 90% of all liver cancer cases, is primarily caused by

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**Table 3.** Number and PAF (%) of cancer incidence and mortality attributable to selected risk factors in Japan in 2005

| Risk factor | Definition of exposure category | Incidence | | Mortality | |
|---|---|---|---|---|---|
| | | PAF (%) (95% CI) | Number | PAF (%) (95% CI) | Number |
| Men | | | | | |
| Total number | | | 379 436 | | 196 603 |
| Tobacco smoking | Ever smoking | 29.7 (29.6–29.8) | 112 622 | 34.4 (34.3–34.5) | 67 697 |
| Passive smoking | Passive smoking | 0.2 (0.2–0.2) | 913 | 0.4 (0.4–0.4) | 708 |
| Infection | Positive (*Helicobacter pylori*, HCV, HBV, HPV, EBV, HTLV-I) | 22.8 (22.8–22.8) | 86 529 | 23.2 (23.2–23.2) | 45 619 |
| Alcohol drinking | Alcohol intake | 9.0 (9.0–9.0) | 34 151 | 8.6 (8.6–8.6) | 16 905 |
| Salt intake | >6 g/day | 1.9 (1.8–1.9) | 7137 | 1.5 (1.4–1.5) | 2908 |
| Body mass index | ≥25 (overweight and obesity) | 0.8 (0.7–0.8) | 2848 | 0.5 (0.5–0.5) | 1046 |
| Fruit intake | Lowest intake group | 0.7 (0.7–0.7) | 2621 | 0.7 (0.7–0.8) | 1441 |
| Vegetable intake | Lowest intake group | 0.7 (0.7–0.7) | 2549 | 0.7 (0.7–0.7) | 1395 |
| Physical inactivity | Without three METs/day exercise | 0.3 (0.3–0.3) | 1169 | 0.2 (0.2–0.2) | 423 |
| All above risk factors (adjusted for overlaps) | | 53.3 (53.2–53.4) | 202 257 | 56.9 (56.8–57.0) | 111 901 |
| Women | | | | | |
| Total number | | | 267 366 | | 129 338 |
| Tobacco smoking | Ever smoking | 5.0 (4.9–5.0) | 13 276 | 6.2 (6.1–6.2) | 8002 |
| Passive smoking | Passive smoking | 1.2 (1.2–1.2) | 3238 | 1.6 (1.6–1.7) | 2133 |
| Infection | Positive (*H. pylori*, HCV, HBV, HPV, EBV, HTLV-I) | 17.5 (17.5–17.6) | 46 869 | 19.4 (19.3–19.4) | 25 040 |
| Alcohol drinking | Alcohol intake | 2.5 (2.5–2.6) | 6769 | 2.5 (2.4–2.5) | 3176 |
| Salt intake | >6 g/day | 1.2 (1.2–1.3) | 3300 | 1.2 (1.2–1.2) | 1574 |
| Body mass index | ≥25 (overweight and obesity) | 1.6 (1.5–1.6) | 4167 | 1.1 (1.1–1.1) | 1431 |
| Fruit intake | Lowest intake group | 0.8 (0.8–0.8) | 2162 | 0.8 (0.8–0.9) | 1079 |
| Vegetable intake | Lowest intake group | 0.4 (0.4–0.4) | 1082 | 0.4 (0.4–0.5) | 562 |
| Physical inactivity | Without three METs/day exercise | 0.6 (0.5–0.6) | 1462 | 0.4 (0.4–0.4) | 521 |
| Exogenous hormone use | Current use | 0.4 (0.4–0.4) | 999 | 0.2 (0.2–0.2) | 241 |
| All above risk factors (adjusted for overlaps) | | 27.8 (27.6–27.9) | 74 234 | 29.9 (29.8–30.1) | 38 736 |
| Both sexes | | | | | |
| Total number | | | 646 802 | | 325 941 |
| Tobacco smoking | Ever smoking | 19.5 (19.4–19.5) | 125 898 | 23.2 (23.2–23.3) | 75 699 |
| Passive smoking | Passive smoking | 0.6 (0.6–0.7) | 4152 | 0.9 (0.9–0.9) | 2842 |
| Infection | Positive (*H. pylori*, HCV, HBV, HPV, EBV, HTLV-I) | 20.6 (19.7–21.5) | 133 398 | 21.7 (20.4–22.9) | 70 660 |
| Alcohol drinking | Alcohol intake | 6.3 (6.3–6.4) | 40 920 | 6.2 (6.1–6.2) | 20 081 |
| Salt intake | >6 g/day | 1.6 (1.6–1.6) | 10 437 | 1.4 (1.3–1.4) | 4483 |
| Body mass index | ≥25 (overweight and obesity) | 1.1 (1.1–1.1) | 7014 | 0.8 (0.7–0.8) | 2476 |
| Fruit intake | Lowest intake group | 0.7 (0.7–0.8) | 4783 | 0.8 (0.8–0.8) | 2520 |
| Vegetable intake | Lowest intake group | 0.6 (0.5–0.6) | 3631 | 0.6 (0.6–0.6) | 1957 |
| Physical inactivity | Without three METs/day exercise | 0.4 (0.4–0.4) | 2631 | 0.3 (0.3–0.3) | 945 |
| Exogenous hormone use | Current use | 0.2 (0.2–0.2) | 999 | 0.1 (0.1–0.1) | 241 |
| All above risk factors (adjusted for overlaps) | | 42.7 (42.6–42.9) | 276 491 | 46.2 (46.1–46.3) | 150 637 |

PAF, population attributable fraction; CI, confidence interval; HCV, hepatitis C virus; HBV, hepatitis B virus; EBV, Epstein–Barr virus; HPV, human papillomavirus; HTLV-I, human T-cell leukemia type I; MET, metabolic equivalents.

chronic HCV infection in Japan. The peak incidence between the 1970s and the 1990s in Japanese men was affected by the birth cohort effect among those born during 1931–1935, which was attributed to HCV outbreaks in Japan [35]. This spread was ended by the early 1990s by the control of parenteral HCV transmission and interferon therapy for patients with chronic HCV infection, followed by a community-based anti-HCV screening system started in 2002. Japanese liver cancer incidence is therefore likely to decline further in the next decade [35].

Other important infections in Japan include human T-cell leukemia type I (HTLV-I), which is the main cause of adult T-cell leukemia (ATL). However, the attribution of this agent to total cancer burden is small due to the low prevalence of HTLV-I and small proportion of carriers (6% and 2% among men and women, respectively) who develop ATL [36].

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**Table 4.** PAF (%) of incidence and mortality attributable to known risk factors by site of cancer in Japan in 2005

| Site | ICD-10 | Men | Women | Both sexes | |
|---|---|---|---|---|---|
| | | Incidence/mortality, PAF (%) (95% CI) | Incidence/mortality, PAF (%) (95% CI) | Incidence, PAF (%) (95% CI) | Mortality, PAF (%) (95% CI) |
| Oral cavity | C00–C09 | 72.8 (72.5–73.1) | 30.3 (30.0–30.7) | 54.9 (54.6–55.3) | 56.1 (55.8–56.4) |
| Oropharynx | C10 | 75.3 (75.0–75.6) | 36.8 (36.5–37.1) | 71.2 (70.9–71.5) | 70.5 (70.2–70.9) |
| Nasopharynx | C11 | 97.2 (97.2–97.2) | 92.8 (92.8–92.9) | 95.9 (95.7–95.9) | 96.3 (96.3–96.3) |
| Hypopharynx, etc. | C12–C14 | 71.9 (71.6–72.3) | 28.2 (27.8–28.5) | 64.9 (64.5–65.2) | 66.9 (66.5–67.2) |
| Esophagus | C15 | 84.8 (84.7–85.0) | 51.6 (51.2–52.0) | 79.7 (79.5–80.0) | 79.7 (79.5–79.9) |
| Stomach | C16 | 82.5 (82.3–82.6) | 72.0 (71.7–72.2) | 79.1 (79.0–79.3) | 78.8 (78.6–79.0) |
| Colon | C18 | 51.0 (50.8–51.1) | 12.8 (12.6–13.0) | 33.6 (33.4–33.8) | 31.7 (31.5–31.9) |
| Rectum | C19–C20 | 46.6 (46.5–46.7) | 6.5 (6.4–6.6) | 31.5 (31.3–31.6) | 31.9 (31.8–32.1) |
| Anus | C21 | 90.0 (90.0–90.0) | 90.0 (90.0–90.0) | 90.0 (90.0–90.0) | 89.9 (89.9–89.9) |
| Liver | C22 | 92.2 (92.1–92.3) | 91.8 (91.6–92.0) | 92.1 (91.9–92.2) | 92.1 (91.9–92.2) |
| Pancreas | C25 | 23.9 (23.7–24.1) | 11.6 (11.5–11.8) | 18.1 (18.0–18.3) | 18.2 (18.0–18.4) |
| Larynx | C32 | 71.9 (71.5–72.2) | 30.1 (29.7–30.5) | 69.7 (69.3–70.1) | 68.6 (68.3–69.1) |
| Lung | C33–C34 | 69.1 (69.0–69.2) | 36.5 (36.3–36.8) | 59.2 (59.0–59.3) | 60.2 (60.1–60.4) |
| Breast | C50 | | 10.5 (10.4–10.7)/11.0 (10.8–11.1) | 10.5 (10.4–10.7) | 11.0 (10.8–11.1) |
| Vulva | C51 | | 40.0 (40.0–40.0) | 40.1 (40.1–40.1) | 39.8 (39.8–39.8) |
| Vagina | C52 | | 40.0 (40.0–40.0) | 39.8 (39.8–39.8) | 40.2 (40.2–40.2) |
| Cervix uteri | C53 | | 100 (100.0–100.0) | 100 (100.0–100.0) | 100 (100.0–100.0) |
| Corpus uteri | C54 | | 15.5 (15.2–15.8) | 15.5 (15.2–15.8) | 15.5 (15.2–15.8) |
| Ovary | C56 | | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) |
| Penis | C60 | 40.0 (40.0–40.0) | | 39.9 (39.9–39.9) | 39.8 (39.8–39.8) |
| Prostate | C61 | 0.0 (0.0–0.0) | | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) |
| Kidney | C64 | 37.4 (37.0–37.8) | 12.0 (11.7–12.2) | 29.4 (29.0–29.7) | 29.2 (28.9–29.6) |
| Renal pelvis | C65–C66, C68 | 70.7 (70.5–70.9) | 3.6 (3.4–3.7) | 45.5 (45.3–45.7) | 45.0 (44.8–45.2) |
| Bladder | C67 | 70.7 (70.5–70.9) | 3.6 (3.4–3.7) | 54.9 (54.8–55.1) | 49.6 (49.5–49.8) |
| Hodgkin disease | C81 | 48.0 (48.0–48.0) | 48.0 (48.0–48.0) | 48.0 (48.0–48.0) | 48.5 (48.5–48.5) |
| NHL | C82–C85, C96 | 4.0 (4.0–4.0) | 3.8 (3.9–3.9) | 3.9 (3.9–4.0) | 3.8 (3.8–3.8) |
| Leukemia | C91–C95 | 29.2 (29.0–29.4)/32.0 (31.8–32.2) | 14.7 (14.7–14.7) | 23.0 (22.9–23.1) | 25.0 (20.8–25.1) |

PAF, population attributable fraction; CI, confidence interval; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision; NHL, non-Hodgkin lymphoma.

Alcohol consumption in Japan and the proportion of heavy drinkers increased for decades until 1990 and have now peaked [2]. Our estimates of the PAF of alcohol drinking should be interpreted with caution because Japanese have a high prevalence of an aldehyde dehydrogenase 2-deficient phenotype, a deficiency that results in greater exposure to acetaldehyde, which is a known carcinogen in alcohol. This genetic difference may be one reason for the stronger RR in Japanese than Western populations [37]. In addition, the nonexposure referent group in many Japanese studies includes lifetime abstainers who are genetically unable to metabolize acetaldehyde, as well as past drinkers who quit drinking due to symptoms caused by alcohol drinking, which may have resulted in the underestimation of RR.

Other risk factors tended to contribute only a relatively small portion of the overall burden. For example, the prevalence of overweight and obesity (BMI ≥25) in Japan has gradually increased in men (22% in 1990 and 29% in 2005) but has been stable in women at ~21%–22% for decades according to the National Nutrition Survey [38]. In addition, the prevalence of obesity (BMI ≥30) has been ~3% in both sexes. As long as the Japanese maintain current BMI levels, the overall cancer burden derived from excess BMI may be small. Rather, the prevalence of underweight (BMI <18.5) in Japan has been greater (5% in men and 10% in women) than that of obesity. Given that many previous studies in Japanese and Asian populations have associated low BMI with an increased risk of cancer [28, 39], PAF for low BMI may warrant further investigation.

Physical inactivity, high salt intake, low vegetable and fruit intake, and female exogenous hormone use are associated with an increased risk of some cancers, but the contribution from these exposures based on our definition of exposed category was modest, due to the low prevalence of exposed category and/or an insufficient or inadequate definition of exposure level. It is notable that the intake of highly salt-concentrated preserved foods rather than salt intake as a whole salt equivalent is suggested to increase the risk of cancer [40], and estimation by the latter instead of the former may underestimate the real PAF. In addition, the prevalence of exogenous hormone use in Japan was and remains significantly low compared with Western populations, which may have led to its small contribution. More accurate estimates of the impact of these factors in Japanese will require a better scientific understanding of the association and more reliable data for Japanese.

Several limitations of these estimates warrant mention. Due to a lack of reliable prevalence data in Japan, we did not include

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risk factors such as occupational, air pollution, or ultraviolet or radiation exposures. From previous estimates from Western populations [41], the PAF of occupational exposure may be expected to be ~5% in men, which is not negligible, while the PAF of other factors may not be substantial. Regarding infectious agents, we substituted our estimates with the PAF obtained in a previous estimate [25] due to a lack of prevalence and RR data in Japan, such as for human papillomavirus and Epstein–Barr virus, or excluded them from the present estimate due to the very small number of cases in this population. In addition, the RR estimates and prevalence data were extracted independently. Combining biases by using data from multiple sources would increase the bias of PAF estimation. More generally, most cancers have a multifactorial etiology, and a logically multivariate approach is more realistic. Due to an absence of information on most interactions and the joint prevalence of multiple exposures, we took account of the overlap of risk factors. Nevertheless, the results should be interpreted with caution due to uncertainties over the interactions among risk factors of cancer [8, 11, 42]. Since we used the best estimate of RR and prevalence currently available for Japanese, measured with the most suitable methodology, we believe that our estimates of PAFs are the best that can be currently calculated for Japanese. Nevertheless, many PAFs in the present analysis were based on RRs derived from a single study, not from pooled or meta-analyses, and estimates based on them will require updating when more appropriate evidence become available. At the same time, the cause of more than half of Japanese cancers remains unexplained. Solving this issue will require more research targeted at cancer etiology.

Allowing for these methodological issues, this first comprehensive assessment of cancer burden attributable to multiple risk factors in Japan showed that ~55% of cancer in men, 30% of cancer in women, and 45% of cancer in both sexes was attributable to known risk factors. Our estimate also confirmed that tobacco smoking and infectious agents are currently the main causes of cancer in Japan. These estimates have major implications for national health policy for cancer prevention and control strategies in Japan, namely that public health targeting aimed at substantial reductions in current Japanese cancer incidence and mortality should more strongly focus on the control of tobacco smoking and reduction of chronic infections such as *H. pylori* and HCV.

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Contributors—MIn and ST developed the study concept. MIn, NS, MIw, SS, and TS undertook reviews of published studies. TM and KS prepared statistical data for analysis. MIn and NS analyzed the data and prepared the results. MIn wrote the draft of the report. NS, TM, MIw, SS, TS, KS, and ST critically revised the manuscript. All authors have seen and approved the final version.

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## disclosure

The authors declare no conflicts of interest.

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RESEARCH

# Trends in cause specific mortality across occupations in Japanese men of working age during period of economic stagnation, 1980-2005: retrospective cohort study

OPEN ACCESS

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## Abstract

**Objective** To assess the temporal trends in occupation specific all causes and cause specific mortality in Japan between 1980 and 2005.

**Design** Longitudinal analysis of individual death certificates by last occupation before death. Data on population by age and occupation were derived from the population census.

**Setting** Government records, Japan.

**Participants** Men aged 30-59.

**Main outcome measures** Age standardised mortality rate for all causes, all cancers, cerebrovascular disease, ischaemic heart disease, unintentional injuries, and suicide.

**Results** Age standardised mortality rates for all causes and for the four leading causes of death (cancers, ischaemic heart disease, cerebrovascular disease, and unintentional injuries) steadily decreased from 1980 to 2005 among all occupations except for management and professional workers, for whom rates began to rise in the late 1990s ($P<0.001$). During the study period, the mortality rate was lowest in other occupations such as production/labour, clerical, and sales workers, although overall variability of the age standardised mortality rate across occupations widened. The rate for suicide rapidly increased since the late 1990s, with the greatest increase being among management and professional workers.

**Conclusions** Occupational patterns in cause specific mortality changed dramatically in Japan during the period of its economic stagnation and resulted in the reversal of occupational patterns in mortality that have been well established in western countries. A significant negative effect on the health of management and professional workers rather than clerks and blue collar workers could be because of increased job demands and more stressful work environments and could have eliminated or even reversed the health inequality across occupations that had existed previously.

## Introduction

During the past half century Japan has achieved considerable success in population health.[1] Since 1986, the country has ranked first internationally in female life expectancy at birth.[2] A primary driver of this prolonged life expectancy could be strong socioeconomic development, the achievement of universal healthcare coverage, improved diet, and changes in health behaviour.[1 3] Japan's strong economic growth, however, stopped in the 1990s after its "bubble economy" collapsed, and in 1998, triggered by the Asian financial crisis and a series of bankruptcies among big finance firms, Japan experienced the first negative economic growth in its postwar history.[4] Over the past two decades, the Japanese economy has been basically stagnant. The unemployment rate, still lower than that in other

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Appendix 1: Occupational classification and specific occupations from Japanese vital statistics
Appendix 2: Supplementary tables (A-C)



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developed countries, rose from 2.0% in 1991 to 5.5% in 2003.[5] The easing in employment contract regulations in the late 1990s increased the proportion of non-regular workers among male employees from 9% in 1991 to about 19% in the late 2000s.[5]

There is an ongoing debate about Japan's unstable labour market, including concerns about increased unemployment, job insecurity, and widening social disparities and income inequality.[6] The relatively poorer performance of life expectancy in Japanese men in recent years, compared with women, could be attributable to these rapid changes in the labour market, most remarkably symbolised by the record high male suicide rate since 1998.[7 8] We analysed the temporal trends in occupation specific, all cause, and cause specific mortality among Japanese men aged 30-59 in the three decades from 1980 to 2005, when Japan experienced an economic expansion followed by its most serious postwar economic crisis.

## Methods

### Data sources

We obtained individual death certificates from the occupation specific vital statistics recorded by the Ministry of Health, Labour, and Welfare, Japan from 1980 to 2005.[9] Every five years, in the same year as the national population census, the government collects information on occupation as well as cause of death from death certificates submitted to the local government by the family of a person who had died.[10] To calculate occupation specific death rates, we also obtained information on occupation specific populations from the national population census, which is implemented at five year intervals on 1 October.[11] Following relevant studies,[12 13] we used data only on men because of the poor reliability of the information on occupations for women. In Japan, women are more likely to work on a part time or a non-regular basis (range 44-53% of total workers in 2007), and 27% of married women were full time homemakers in 2000.[11]

### Measurements

Data on the death certificate include the underlying cause of death, filled out by physicians and based on the sequence of morbid events leading to death and coded according to ICD-9 (international classification of diseases, ninth revision, 1980-90) and ICD-10 (10th revision, 1995-2005).[14 15] Some codes were inappropriate for analysis of cause of death or were ill defined (such as heart failure) and were redistributed to be comparable and consistent across data by using an algorithm developed by Naghavi and colleagues.[16] Occupations were classified into 10 categories: professional and engineering (hereinafter professional); management; clerical; sales; services; security services (security); agriculture, forestry, and fisheries (agriculture); transportation and communication (transportation); production and labour work (production/labour); and unemployed. We used the International Standard Classification of Occupations to create these categories.[17 18] In the years when occupation specific vital statistics were undertaken, the family members of dead people were required to select one occupational category from the list of 10 occupations. The list was provided to the family with detailed descriptions and definitions of those categories, as well as job examples for each category (see appendix 1 on mbj.com) and jobs that were not included in the category.

### Statistical analysis

We used data for people aged 30-59. We excluded those aged 20-29, including students in universities and other higher education institutions. We also excluded the population aged 60 and over, which was the typical retirement age in Japan during the study period. With data based on a five year age interval, we computed the age standardised mortality rate, directly adjusted to the 1985 Japan standard population[19] with the same occupational categorisation as the national census (denominator) and the number of deaths (numerator) for all causes and the five leading causes of death: cancers, ischaemic heart disease, cerebrovascular disease, unintentional injuries, and suicide. We then computed the age standardised mortality rate for the four leading cancers (stomach cancer; larynx, trachea, bronchus, and lung cancer; colorectal cancer; and liver cancer) and categorised occupations into management, professional, the unemployed, and "others" including clerical, sales, services, security, agriculture, transportation, and production/labour on the basis of our analysis of the trend of the age standardised mortality rates.

Data were analysed with a generalised estimating equation model, with an assumed Poisson distribution for the outcome and an exchangeable correlation structure. To model the possible change in mortality in the two specific occupational groups in 2000, we included a term in all models for management and professional workers. A simple step term was included to reflect the potential change in 2000 across all occupational categories, and an interaction of the step term with management and professional workers was used to identify any additional changes in mortality in these two specific occupations. Time and an interaction between time and management and professional workers were also included in the model, to allow for the possibility of differential changes in death rates over time in these occupational categories. Models were built with backwards stepwise model building.

To evaluate if the variability of age standardised mortality rates across occupations has increased over time, we computed the coefficient of variation of rates. The coefficient of variation is a commonly used normalised measure of variability, defined as the ratio of the standard deviation to the mean. It is suitable for evaluating temporal changes in variability and deals with the possible incomparability of the original standard deviation when its average changes over time.

We analysed the data using Stata version 11 (StataCorp, College Station, TX).

## Results

In the study period, a third of the total male working population were employed in production/labour. The population share of each occupation was mostly stable, although the proportion of professionals increased from 7.4% to 12.6%. The proportion of management workers decreased from 8.2% to 3.2% (table 1⇓, and see table A in appendix 2 on bmj.com for details).

Age standardised mortality rates from all causes and from major conditions declined from 1980 to 2005, whereas the decline in mortality from cardiovascular diseases stabilised after 1995 (table 2⇓). The exception was suicide, for which the age standardised mortality rates in 2005 increased by 21.2 per 100 000 compared with 1990. Cancer, the leading cause of death among working age men, showed the largest reduction (−42%) followed by mortality from cerebrovascular disease (−33%).

Age standardised mortality rates for all causes substantially declined for all occupations and for unemployed people, except



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for management and professional workers. Rates for management and professional workers began to increase in the late 1990s: from 152 in 1995 to 245 in 2000 for management and from 192 in 1995 to 272 in 2000 for professionals (fig 1⇓, and see table B in appendix on bmj.com for complete data).

From 1980 to 1995, the all causes age standardised mortality rate largely decreased among sales (−71%), clerical (−66%), and production/labour workers (−64%), while the reductions among other occupations were relatively small (−26% to −40%). The age standardised mortality rates for all cancers, ischaemic heart disease, cerebrovascular disease, and unintentional injuries showed mostly similar occupation specific trends to the all causes rate. The rate for suicide, however, did not show a declining trend. In particular, management workers showed the highest increase in the rate for suicide from 1980 to 2005 (271%), followed by security (138%) and services (95%) workers, whereas the rate for suicide among sales, clerical, and production/labour workers did not rise even in the most recent period (after 1995) (see table B in appendix 2 on bmj.com).Table 3 shows the results of the generalised estimating equation model⇓. All professions showed a long term downward trend in mortality across the study, though management and professional workers had lower risk of death in the period before 2000. There was, however, evidence of a large change in risk in 2000, with management and professional workers having increased risk of some categories of death (and in all cause mortality) relative to other professions. There was an increase in suicide mortality in 2000 across all occupations but a larger increase among management and professional workers. All workers saw an increase in suicide mortality in 2000, but this increase was greater among management and professional workers. Increases in the suicide mortality rate among the management and professional workers were similar to those for other illnesses, representing about a 70% increase in deaths after 2000. Before 2000, however, the management and professional workers experienced significantly lower mortality rates across all six causes of death, with rate ratios of 0.61 to 0.82 (table 4⇓), all of which were significant. After 2000 this situation was reversed for all cause and all cancer mortality, and the mortality rate for suicide and cerebrovascular disease equalised to those of the non-management and professional workers.

The coefficient of variations of the age standardised mortality rate across occupations, excluding unemployed people, showed an increased trend for all causes and the five leading causes of death (table 5⇓). The coefficient of variation for the all causes rate across occupations increased from 0.29 in 1980 to 0.46 in 2005. The temporal trend of the coefficient of variation for the suicide rate increased from 0.33 in 1980 to 0.58 in 2005, while the coefficient of variation for the suicide rate including unemployed people became smaller (table 5[5]).

Figure 2⇓ (and table C in the appendix on bmj.com) shows the trends in age standardised mortality rates by the four leading sites of cancer. Mortality from stomach cancer showed the largest reduction in this period, whereas rates for lung cancer and colorectal cancer seem to have plateaued. The occupational patterns described for all cancer mortality also seem to be reflected in these cancer specific data series, suggesting that the reversal in declining cancer mortality among management and professional workers occurred across a broad range of cancer sites.

## Discussion

In Japan, trends in mortality varied substantially across occupations and the variability widened from 1980 to 2005, but socioeconomic disparities between occupational groups reduced because of rising mortality among management and professional workers. Many studies in other countries have reported growing health inequality across social classes in from 1980 to 2000.[13 20-23] For example, Mackenbach and colleagues reported widening disparities in health between manual and non-manual workers in five European countries between 1981-5 and 1991-5.[24] The overall mortality in management and professional workers in Japan, in particular among management, has increased since 2000, whereas that in other workers has showed a steady decline. It should also be noted that, unlike the other four leading causes of death, mortality from suicide showed an upward trend regardless of occupation, along with stagnation in the declining trend in mortality from ischaemic heart disease. As with other causes, management workers showed the poorest performance, with the largest increase in mortality from suicide in later years.

Economists have argued that lingering economic stagnation has been responsible for changes in work environments and employment systems, making the lives of working age people erratic and stressful.[6] Together with the introduction of ICD-10, this might be one of the potential factors to account for the trend in cardiovascular mortality ceasing to fall after 1995. This could also explain Japan's counterintuitive trends in occupation specific age standardised mortality rates in recent years. Companies downsized their organisations after the economic recession in the 1990s and consequently the share of managers in the labour market decreased from 6.7% in 1995 to 3.2% in 2005.These changes in work environment could increase responsibilities and job demands of managers compared with manufacturing and clerical workers. Yearly working hours for clerical, sales, and production/labour workers decreased from 2162 hours in 1980 to 1970 hours in 2000.[25] Growing evidence suggests a strong link between job stress and various health outcomes, including metabolic risk factors, mental disorders, and mortality.[26]

Our results are consistent with those from some recent studies that reported that risk factors for cancers and cardiovascular disease—such as being overweight, high alcohol consumption, lower concentrations of high density lipoprotein cholesterol, and physical inactivity—are more prevalent in higher grades of occupations such as professional and management workers in recent years in Japan, potentially because of high job demands among those workers.[27-29] The authors of these studies have suggested the existence of unique patterns in occupational health gradients in Japan, which could be in part because of strong pressures on high grade workers in Japan, stemming from Japan's particular work culture.[3 30] On the other hand, the observed increased gradients in age standardised mortality rates of professionals and managements from 1995 to 2000 might be attributable to the radical changes in socioeconomic conditions of the 1990s rather than to inherent characteristics of Japan's work environment. This observation is, however, contrary to the reduced mortality rates from unintentional injuries and some other causes after the economic crisis.[31]

A possible explanation for the observed increasing trend in mortality for lung cancer and colorectal cancer could be in part because of differences in access to preventive services across occupations. In Japan, under the Industrial Safety and Health Law employers must pay for annual health screening for all employees. In 2004, 73% of men aged 45-54 had an annual health examination.[32] Given the increased pressures on management and professional workers, however, their tight daily schedules might prevent them from using the opportunity of health examination and subsequent healthcare benefits, as well as necessary medical care, despite universal health



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coverage.[1] According to the official cancer registry statistics, the incidence rates of the four cancers analysed here have been stable or declining since 1990.[33] Therefore, it is unlikely that the observed reversal in trends in mortality from cancer among management and professional workers is because of increased incidence.

Interestingly, we found that variability in suicide rate decreased among all men of working age. When we excluded unemployed men from our analysis, however, the rate increased (table 5⇓). At the same time, the age standardised mortality rate from suicide increased among workers and not among unemployed people (see table B in appendix on bmj.com). These data support claims that the changing work environment could be primarily responsible for increasing suicide rates in recent years. In a prospective cohort study in Japan, Fujino and colleagues showed that unemployment was not associated with the risk of suicide,[34] while Granados suggested countercyclical trends of suicide mortality related to Japan's economic fluctuations.[35] Kondo et al also reported that the percentage of reported poor health among unemployed people was 16.5% before the economic crisis in 1998 and 12.6% afterwards.[7] Because of potential misclassification in this category, these findings require further studies with better data, but the evidence from available studies suggests that unemployment per se is not the driving force behind the changes in mortality patterns observed in this study. An alternative explanation could be that during the study period the unemployment rate doubled, with a relatively higher increase among younger people, and the characteristics of unemployed people could have changed over time, becoming closer to that of general workers in terms of their health risks.[36]

## Limitations

Our study has substantial advantages because of the complete enumeration data used and the application of multiple approaches to standardise the variability in age composition and definitions of cause of death across years. Some caution is nevertheless needed when interpreting our findings, primarily because of potential information bias or misclassifications in occupational categories. Lack of further information, such as employment conditions and company size, prevented us from examining the detailed mechanisms underlying our findings. In addition, numerator-denominator bias attributable to the use of different sources to gather information on the number of deaths and occupations, which can occur if the distribution of populations across occupations are different between the two data sources,[37] must be considered. For example, the family of a dead person choose his or her last occupation from 10 occupational categories that included unemployment, opening the risk of misclassification bias, especially when, for example, unemployment occurred only shortly before death. To deal with this potential problem, we excluded unemployed people from our primary analysis because misclassification is most likely in this category.[12] Furthermore, family members might be less likely to report that the person who had died was unemployed if he or she had had a prestigious job before death, potentially resulting in overestimation of mortality rates among such groups. We conducted a sensitivity analysis under the assumption that the entire reduction of professional and management workers of working age represented a shift of these employees into the "other" category, but that dead people continued to be recorded as "professional and management" on death certificates. If we adjust for this effect, the relative risk of death among professional and management workers in 2005 remained higher than it was before 1995 (0.99, 95% confidence interval 0.87 to 1.13). Our results, though not as strong, remain unchanged under even the most unrealistic assumptions about the strength of this numerator-denominator bias. Another possible limitation of our research is the model selection method. Our statistical analysis modelled the effect of the recession with a step term estimated from a combination of published work on the point at which increased mortality was observed and empirical observation of the trends in the data. Because of the small number of data points available, we could not test a wider range of model choices without a high risk of spurious statistical results. There were also only six time points, so the findings might be sensitive to boundary effects in the model. A more robust analysis of a wider range of time points might enable a more sensitive comparison of mortality between occupational categories. More time will need to pass before a longer series can be analysed and definitive judgments made about the apparent changes in mortality rates presented here.

## Conclusion

This study has implications for the health effects of the spread of globalisation over the past two decades, which has made global and domestic economies more and more volatile and unstable. In the case of Japan, a major economic collapse in the 1990s, followed by years of economic stagnation and changes in working environment, could have been a factor associated with radical changes in patterns of mortality that had been established since 1980. In addition, certain trends in key causes of mortality were reversed or arrested, and there was a rapid increase in the suicide rate. This emphasises the priority that needs to be placed on suicide prevention among working age men and the importance of reacting quickly to the health consequences of economic collapse. Economic crises might not simply constitute a threat to health equality but can have a complex impact on various subpopulations regardless of their socioeconomic status.

The lessons of Japan's reversal of health outcomes in the 1990s would be particularly relevant given that many similar economies might be beginning to experience the same phenomenon since the 2008 global financial crisis. Policymakers and health professionals should be aware of the pace and magnitude of the impact on population health from a major economic event. The changes experienced in Japan also serve as a reminder that the health gains in modern societies might not necessarily be guaranteed and could be vulnerable to sudden socioeconomic changes.

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**What is already known on this topic**

Japanese health is now under threat, especially among men of working age, because of the lingering economic stagnation since the 1990s, which is characterised by the record high rate of suicide among men

Trends in occupational variations in the mortality rate during the period of Japan's recent economic stagnation are largely unknown

**What this study adds**

Risk of mortality in management workers in Japan, which was previously the lowest, largely increased after 1995, whereas in other non-professional workers mortality steadily decreased between 1980 and 2005

During this time mortality from suicide increased in all occupations, with the largest increase among management and professional workers

Economic crises might not simply negatively affect health equality but can have a complex impact on various subpopulations regardless of their socioeconomic status

the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Not required

Data sharing: No additional data available.

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# Tables

Table 1| **Proportion of population by occupation among Japanese men aged 30-59 according to national population census, 1980-2005 (%)**

| Occupation | 1980 (n=24 250 948) | 1985 (n=25 896 538) | 1990 (n=25 961 345) | 1995 (n=26 059 598) | 2000 (n=25 935 755) | 2005 (n=25 621 203) |
|---|---|---|---|---|---|---|
| Professional | 7.4 | 9.5 | 10.6 | 12.1 | 13.2 | 12.6 |
| Management | 8.2 | 6.3 | 6.6 | 6.7 | 4.1 | 3.2 |
| Others* | 80.3 | 78.9 | 78.4 | 76.0 | 75.7 | 75.9 |
| Unemployed | 4.1 | 5.3 | 4.4 | 5.2 | 7.0 | 8.3 |

*Clerical, sales, services, security, agriculture, transportation, and production/labour.



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Table 2| **Number of deaths and age standardised mortality rates per 100 000 (95% confidence intervals) from all causes and five leading causes of death among men aged 30-59 in Japan, 1980-2005**

| Cause of death | 1980 (n=87 629) | 1985 (n=94 214) | 1990 (n=87 915) | 1995 (n=83 634) | 2000 (n=85 545) | 2005 (80 702) | *% change | †Absolute difference |
|---|---|---|---|---|---|---|---|---|
| All causes | 388.5 (385.9 to 391.1) | 365.7 (363.4 to 368.0) | 306.6 (304.5 to 308.8) | 295.7 (293.7 to 297.7) | 293.6 (291.6 to 295.6) | 279.2 (277.2 to 281.1) | −28 | −109 |
| All cancers | 144.5 (142.9 to 146.1) | 121.4 (120.1 to 122.8) | 116.1 (114.9 to 117.4) | 106.9 (105.7 to 108.1) | 100.3 (99.1 to 101.4) | 102.4 (101.3 to 103.5) | −29 | −42 |
| Ischaemic heart disease | 43.9 (43.0 to 44.8) | 40.4 (39.6 to 41.2) | 38.4 (37.7 to 39.2) | 30.8 (30.2 to 31.5) | 30.5 (29.9 to 31.2) | 32.3 (31.6 to 32.9) | −26 | −12 |
| Cerebrovascular disease | 57.9 (56.9 to 58.9) | 41.9 (41.1 to 42.7) | 33.8 (33.1 to 34.5) | 30.5 (29.8 to 31.1) | 26.8 (26.2 to 27.4) | 25.4 (24.8 to 26.0) | −56 | −33 |
| Unintentional injuries | 37.3 (36.5 to 38.1) | 34.6 (33.8 to 35.3) | 32.2 (31.5 to 32.9) | 31.7 (31.1 to 32.4) | 28.3 (27.6 to 28.9) | 25.7 (25.1 to 26.3) | −31 | −12 |
| Suicide | 33.7 (33.0 to 34.5) | 43.2 (42.4 to 44.0) | 30.9 (30.2 to 31.6) | 31.9 (31.1 to 32.5) | 50.3 (49.4 to 51.1) | 53.1 (52.2 to 54.0) | 57 | 19 |

*Difference between 1980 and 2005 rates expressed as percentage of 1980 rate.

†Absolute difference in age standardised mortality rate per 100 00 between 1980 and 2005.



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Table 3| **Ratios of age standardised mortality rates for all causes, all cancers, ischaemic heart disease, cerebrovascular disease, unintentional injuries, and suicide mortality: results of generalised estimating equation models for trend analysis**

| Cause of death/variable | Rate ratio | z statistic | P value |
|---|---|---|---|
| **All causes** | | | |
| Intercept | 342.85 | 291.73 | <0.001 |
| Time | 0.9 | −34.75 | <0.001 |
| Occupation: | | | |
| Non-management/professional* *v* management/professional | 0.7 | −7.38 | <0.001 |
| Step function: | | | |
| 1980-95* *v* 2000-5 | 0.96 | −3.94 | <0.001 |
| Occupation and step: | | | |
| Non-management/professional after 2000* *v* management/professional after 2000 | 1.69 | 32.71 | <0.001 |
| **All cancers** | | | |
| Intercept | 113.42 | 138.58 | <0.001 |
| Time | 0.94 | −9.3 | <0.001 |
| Occupation: | | | |
| Non-management/professional *v* management/professional | 0.82 | −2.6 | 0.009 |
| Step function: | | | |
| 1980-95 *v* 2000-5 | 0.76 | −9.67 | <0.001 |
| Occupation and step: | | | |
| Non-management/professional after 2000* *v* management/professional after 2000 | 1.86 | 17.38 | <0.001 |
| **Ischaemic heart disease** | | | |
| Intercept | 39.75 | 62.9 | <0.001 |
| Time | 0.88 | −12.61 | <0.001 |
| Occupation: | | | |
| Non-management/professional* *v* management/professional | 0.77 | −1.91 | 0.06 |
| Step function: | | | |
| 1980-95* *v* 2000-5 | 0.99 | −0.2 | 0.8 |
| Occupation and step: | | | |
| Non-management/professional after 2000* *v* management/professional after 2000 | 1.55 | 8.56 | <0.001 |
| **Cerebrovascular disease** | | | |
| Intercept | 49.87 | 75.88 | <0.001 |
| Time | 0.8 | −22.13 | <0.001 |
| Occupation: | | | |
| Non-management/professional* *v* management/professional | 0.63 | −3.83 | <0.001 |
| Step function: | | | |
| 1980-95* *v* 2000-5 | 1.03 | 0.91 | 0.4 |
| Occupation and step: | | | |
| Non-management/professional after* 2000 *v* management/professional after 2000 | 1.72 | 10.54 | <0.001 |
| **Unintentional injury** | | | |
| Intercept | 38.42 | 60.68 | <0.001 |
| Time | 0.94 | −8.45 | <0.001 |
| Occupation: | | | |
| Non-management/professional* *v* management/professional | 0.54 | −3.71 | <0.001 |
| Step function: | | | |
| 1980-95* *v* 2000-5 | 0.9 | −3.71 | <0.001 |
| Occupation and step: | | | |
| Non-management/professional after 2000* *v* nmanagement/professional after 2000 | 1.55 | 9.88 | <0.001 |
| **Suicide** | | | |
| Intercept | 32.61 | 55.1 | <0.001 |
| Time | 0.97 | −2.32 | 0.02 |



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**Table 3 (continued)**

| Cause of death/variable | Rate ratio | z statistic | P value |
|---|---|---|---|
| Occupation: | | | |
| Non-management/professional* *v* management/professional | 0.61 | −3.07 | 0.002 |
| Step function: | | | |
| 1980-95* *v* 2000-5 | 1.49 | 8.53 | <0.001 |
| Occupation and step: | | | |
| Non-management/professional after 2000* *v* management/professional after 2000 | 1.68 | 6.79 | <0.001 |

*Reference category.



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Table 4| **Ratios of age standardised mortality rates by cause of death, before 1995 and after 2000, for management/professional versus non-management/professional**

| Causes of death | Before 1995 | After 2000 |
|---|---|---|
| All causes | 0.70 (0.63 to 0.76)* | 1.18 (1.07 to 1.31)* |
| All cancers | 0.82 (0.78 to 0.95)* | 1.52 (1.29 to 1.80)* |
| Ischaemic heart disease | 0.77 (0.59 to 1.01) | 1.19 (0.89 to 1.59) |
| Cerebrovascular disease | 0.63 (0.50 to 0.80)* | 1.08 (0.84 to 1.40) |
| Unintentional injury | 0.54 (0.40 to 0.75)* | 0.84 (0.61 to 1.18) |
| Suicide | 0.61 (0.45 to 0.84)* | 1.03 (0.73 to 1.45) |

*P<0.05.



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Table 5| **Trend in variability of mortality rates across occupations. Figures are coefficient of variation (95% confidence interval) of age standardised mortality rate from all causes and five leading causes of death among working men aged 30-59 in Japan, 1980-2005**

| | 1980 | 1985 | 1990 | 1995 | 2000 | 2005 |
|---|---|---|---|---|---|---|
| **Excluding unemployed men** | | | | | | |
| All causes | 0.29 (0.14 to 0.44) | 0.27 (0.13 to 0.42) | 0.34 (0.16 to 0.53) | 0.40 (0.18 to 0.63) | 0.43 (0.18 to 0.67) | 0.46 (0.19 to 0.73) |
| All cancers | 0.21 (0.10 to 0.32) | 0.20 (0.10 to 0.30) | 0.27 (0.13 to 0.40) | 0.35 (0.16 to 0.53) | 0.40 (0.17 to 0.62) | 0.44 (0.19 to 0.69) |
| Ischaemic heart disease | 0.28 (0.13 to 0.42) | 0.29 (0.14 to 0.45) | 0.35 (0.16 to 0.53) | 0.37 (0.17 to 0.58) | 0.40 (0.17 to 0.62) | 0.46 (0.19 to 0.73) |
| Cerebrovascular diseases | 0.35 (0.16 to 0.54) | 0.32 (0.15 to 0.49) | 0.39 (0.17 to 0.61) | 0.44 (0.19 to 0.69) | 0.47 (0.19 to 0.75) | 0.48 (0.20 to 0.77) |
| Unintentional injuries | 0.49 (0.20 to 0.78) | 0.44 (0.19 to 0.70) | 0.48 (0.20 to 0.77) | 0.53 (0.21 to 0.85) | 0.56 (0.21 to 0.92) | 0.55 (0.21 to 0.90) |
| Suicide | 0.33 (0.15 to 0.51) | 0.36 (0.16 to 0.57) | 0.46 (0.19 to 0.75) | 0.50 (0.20 to 0.81) | 0.56 (0.21 to 0.87) | 0.58 (0.21 to 0.92) |
| **Including unemployed men** | | | | | | |
| All causes | 1.10 (0.16 to 2.03) | 1.05 (0.18 to 1.92) | 1.20 (0.11 to 2.30) | 1.18 (0.12 to 2.25) | 1.07 (0.17 to 1.97) | 1.08 (0.17 to 2.00) |
| All cancers | 0.81 (0.24 to 1.38) | 0.82 (0.24 to 1.39) | 0.96 (0.21 to 1.72) | 0.89 (0.23 to 1.56) | 0.85 (0.24 to 1.47) | 0.94 (0.22 to 1.67) |
| Ischaemic heart disease | 0.99 (0.20 to 1.77) | 1.03 (0.19 to 1.86) | 1.25 (0.08 to 2.43) | 1.16 (0.13 to 2.19) | 1.06 (0.18 to 1.93) | 1.09 (0.16 to 2.02) |
| Cerebrovascular diseases | 0.92 (0.22 to 1.61) | 0.89 (0.23 to 1.55) | 0.99 (0.20 to 1.78) | 1.05 (0.18 to 1.93) | 0.95 (0.22 to 1.68) | 1.00 (0.20 to 1.81) |
| Unintentional injuries | 0.65 (0.24 to 1.06) | 0.59 (0.24 to 0.95) | 0.75 (0.24 to 1.26) | 0.90 (0.23 to 1.58) | 0.79 (0.24 to 1.34) | 0.81 (0.24 to 1.37) |
| Suicide | 1.20 (0.10 to 2.33) | 1.05 (0.18 to 1.94) | 1.22 (0.10 to 2.34) | 1.13 (0.13 to 2.17) | 1.03 (0.18 to 1.94) | 0.93 (0.21 to 1.69) |



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# Figures

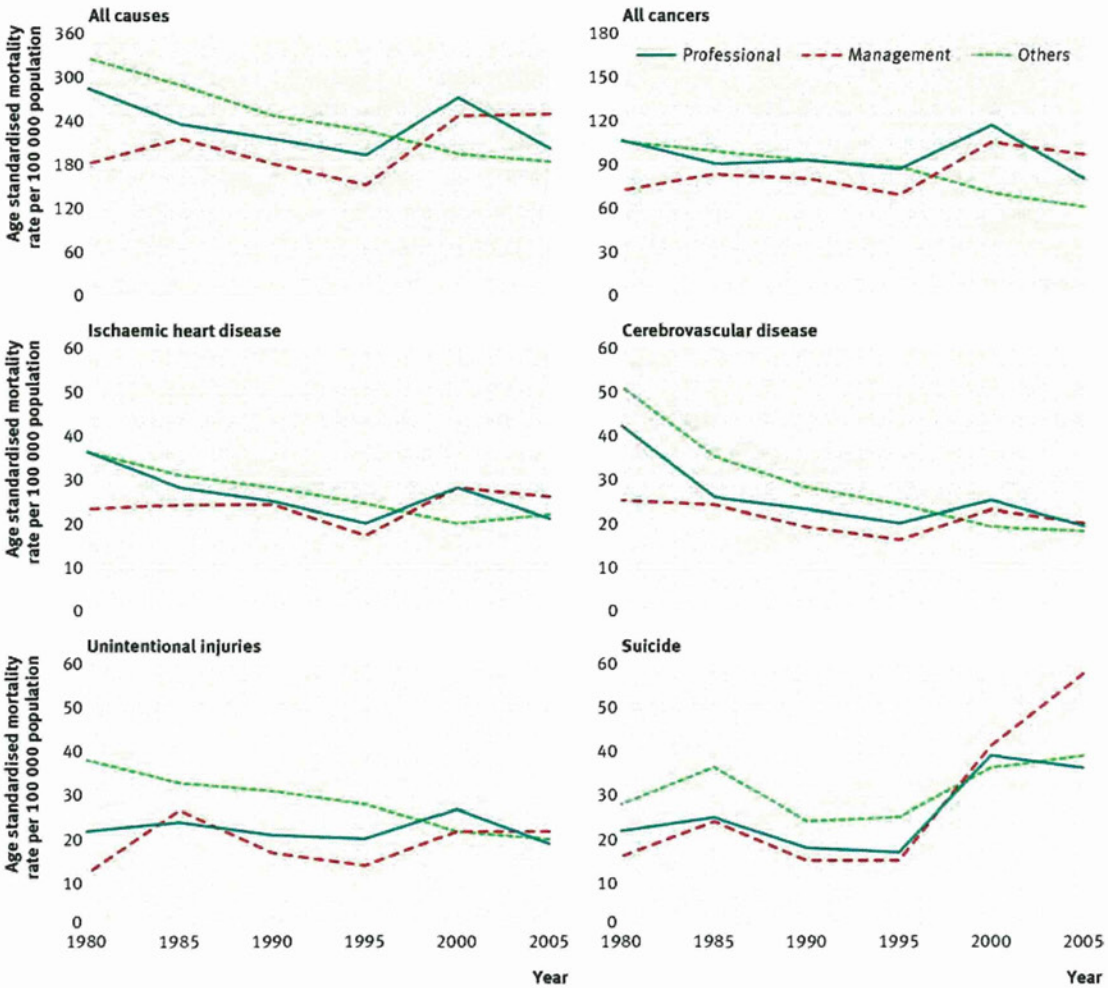


**Fig 1** Temporal trends and comparisons of age standardised mortality rates (per 100 000) from all causes and five leading causes of death, 1980-2005, among men aged 30-59 in Japan



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