Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Birth-cohort effects and the limits of ecological evaluation of mammography screening: an age-period-cohort analysis of breast cancer mortality in Japan, 1958–2024

Masaaki Kawai

m.kawai.ju@juntendo.ac.jp

Juntendo University School of Medicine Graduate School of Medicine: Juntendo Daigaku Igakubu Daigakuin Igaku Kenkyuka https://orcid.org/0000-0003-1383-0487

Ryoko Semba

Juntendo University School of Medicine Graduate School of Medicine: Juntendo Daigaku Igakubu Daigakuin Igaku Kenkyuka

Misato Okazaki

Juntendo University School of Medicine Graduate School of Medicine: Juntendo Daigaku Igakubu Daigakuin Igaku Kenkyuka

Kotaro Iijima

Juntendo University School of Medicine Graduate School of Medicine: Juntendo Daigaku Igakubu Daigakuin Igaku Kenkyuka

Junichiro Watanabe

Juntendo University School of Medicine Graduate School of Medicine: Juntendo Daigaku Igakubu Daigakuin Igaku Kenkyuka

Goro Kutomi

Juntendo University School of Medicine Graduate School of Medicine: Juntendo Daigaku Igakubu Daigakuin Igaku Kenkyuka

Research Article

Keywords: breast cancer, mammography screening, age-period-cohort analysis, birth cohort, mortality

Posted Date: November 2nd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11368637/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Abstract

Background

Ecological evaluations of mammography screening are confounded by birth-cohort effects and concurrent advances in treatment. We examined the age-period-cohort (APC) structure of breast cancer mortality in Japan and quantified how much screening exposure varies independently of that structure.

Methods

Deaths among Japanese women aged 30–84 years in 1960–2024 were tabulated by 5-year age group and period and analysed with Holford's identifiable APC model and quasi-Poisson errors. Screening eligibility (≥ 50 years from 2000; ≥40 years from 2004) was added as an age × period interaction, as binary or cumulative eligibility with lags of 0, 5 and 10 years. Separability was quantified as the R^2 of exposure on the APC terms. Incidence for 1976–2020 was analysed on the same grid.

Results

Among 437,134 deaths, the age-cohort model fitted far better than the age-period model (deviance 389.2 vs 9,041.8). The cohort deviation from the log-linear trend peaked in women born around 1950 (rate ratio [RR] 1.51; 95% CI, 1.47–1.54). Incidence, including three high-quality regional registries, shared this peak less markedly than mortality (RR 1.22 vs 1.43, 1976–2020). APC terms explained 91% to > 99% of the variation in screening exposure. With a 10-year lag, eligibility was not associated with mortality (RR 1.005; 0.971–1.040); across definitions, RRs ranged from 0.955 to 1.196.

Conclusions

Non-linear changes in breast cancer mortality in Japan were aligned mainly with birth cohort. Less than 10% of the variation in screening exposure was independent of the APC structure, so its effect cannot be reliably estimated from national statistics; individual-level linked data are needed.

Introduction

Breast cancer is the most frequently diagnosed cancer among Japanese women, and annual deaths increased from about 1,700 in 1958 to about 15,900 in 2024 [1]. Age-standardised mortality rose throughout 1963–2006 [2], and by 2008 a downturn was seen only in women younger than 50 years [3]. Mortality has fallen steadily in Western countries since around 1990, whereas in Japan it has declined only slowly or continued to rise [4].

Japan's population-based screening programme developed in stages. Clinical breast examination for women aged 30 years or older was introduced in April 1987 [5, 6]. Biennial mammography was added for women aged 50 years or older in April 2000 [7], and in April 2004 the lower age limit was raised to 40 years and mammography became the standard test [8]. Participation in the municipal programme has remained low, and much screening takes place in workplace or opportunistic settings.

Randomised trials show that invitation to mammography screening reduces breast cancer mortality [9, 10], and large reductions were reported after organised screening in Sweden [11]. Such trials will not be repeated in Japan, so evaluation must rely on observational data, often ecological analyses of mortality trends [12, 13]. Their interpretation is difficult because screening was introduced at the same time as major advances in systemic therapy, and because breast cancer risk differs strongly between birth cohorts [14].

Age-period-cohort (APC) models are the standard tool for separating these influences [15–17], but because cohort equals period minus age, only non-linear components are identifiable. A previous APC analysis of Japanese breast cancer mortality used the intrinsic estimator, whose constraint determines how a linear trend is divided between period and cohort, and attributed the trend mainly to period effects [18]. Incidence has continued to rise in successive cohorts born after 1950 [19]. Because screening eligibility in Japan was defined entirely by age and calendar year, an APC model leaves little independent variation from which a screening effect could be estimated, yet previous ecological evaluations have rarely measured how much remains.

This study had two aims: to describe the APC structure of breast cancer mortality in Japan with an identifiable parameterisation, and to quantify how much of the variation in mammography screening exposure remains independent of that structure, and hence whether a screening effect can be estimated from national statistics.

Materials and Methods

Data and Lexis table

Annual deaths with breast cancer as the underlying cause among Japanese women, by 5-year age group, and mid-year populations were obtained from the national dataset compiled by the National Cancer Center Japan from the Vital Statistics of Japan (1958–2024) [1]. Breast cancer was coded as ICD-7 170, ICD-8 174, ICD-9 174–175 (code 175, male breast, contributes no deaths among women) and ICD-10 C50. Deaths and person-years were tabulated in 11 five-year age groups (30–34 to 80–84 years) by 13 five-year periods (1960–1964 to 2020–2024), defining 23 overlapping 10-year synthetic birth cohorts (1880–1990). Women aged 85 years or older were excluded because the open-ended interval cannot be assigned to a cohort. The study used publicly available aggregate data and did not require ethics review.

Age-period-cohort model

Deaths were modelled with log-linear Poisson regression with log person-years as offset, using Holford's parameterisation [15]: $\log \mu(a,p) = \log N(a,p) + \alpha(a) + \delta \cdot p + \tilde{\pi}(p) + \tilde{\gamma}(c)$, where α is the age effect, δ the net drift, and $\tilde{\pi}$ and $\tilde{\gamma}$ are period and cohort deviations from linearity, constrained to sum to zero and to be orthogonal to a linear trend. Deviations are reported as rate ratios (RRs) relative to the log-linear trend with 95% confidence intervals (CIs), and net drift as an annual percentage change. Age, age-drift, age-period, age-cohort and full APC models were compared by analysis of deviance [20, 21] with F tests using the dispersion of the full APC model. Standard errors were scaled by the Pearson dispersion (quasi-Poisson). Implementation checks are described in Supplementary Methods.

Screening exposure

Mammography eligibility for a woman of single-year age a in year t was $m(a, t) = 1$ if $t \geq 2000$ and $a \geq 50$, or $t \geq 2004$ and $a \geq 40$ [5–8]. With a lag of L years, binary exposure was $m(a - L, t - L)$, and cumulative exposure was the number of years she had been eligible from 1987 to $t - L$, per 10 years. Lags of 0, 5 and 10 years were examined. Cell exposure was the mean over the 25 single-year sub-cells of each Lexis cell (worked examples in **Supplementary Table S2A**), and each exposure was added to the APC model as a single covariate; because it varies with age and period jointly, it is not a linear combination of the APC terms. Eligibility rather than attendance was modelled because attendance data were not available. In a sensitivity analysis, exposure also counted clinical breast examination (1987–2003, ≥ 30 years). All definitions are reported; presenting the 10-year lag first was decided after the initial analyses and is not a prespecified primary analysis.

Separability of screening from the APC structure

The variance of the screening coefficient is $\varphi / \Sigma w_i r_i^2$, where w_i is the fitted number of deaths in cell i, φ the dispersion and r_i the residual from the w_i-weighted regression of exposure on the APC design. We report the weighted R^2 of that regression, the variance inflation factor ($VIF = 1/(1 - R^2)$), the smallest RR detectable with 80% power, and the share of the information $\Sigma w_i r_i^2$ contributed by each cell. An R^2 below 1 means that the coefficient is formally identified; a value close to 1 means that it rests on a small residual part of the exposure variation and is sensitive to misspecification of the APC terms.

Sensitivity analyses

All analyses were repeated for 1975–2024, because Okinawa entered national vital statistics in 1973, and with negative binomial models. Exposure was also defined at annual resolution, with one observation per age group and calendar year (n = 715) and the APC terms of the corresponding cell. A conventional Poisson policy model with grouped ages, a linear trend and binned cohorts was fitted for comparison (Supplementary Methods).

Incidence and comparison with mortality

Breast cancer incidence at ages 30–84 years, including in situ cancer, was obtained from the same source [1]: regional registry estimates for 1975–2015 and the National Cancer Registry from 2016. Incidence and mortality were tabulated on the same grid of nine periods (1976–1980 to 2016–2020), so that the registry change fell on a period boundary, and the same APC model was fitted to each. Because each model's linear trend is fixed by its own constraint, we compared cohort deviations; their ratio, the relative cohort curvature, indicates whether the cohort pattern is more pronounced in mortality than in incidence and is not a measure of survival. Its CIs assume independence of the two models; as a check, a single APC model of deaths with log incident cases as offset estimated it directly. We also calculated local drifts and the mortality-to-incidence ratio by age and period. Robustness of the incidence pattern was examined under five alternative specifications (Supplementary Methods). Because the national series before 2016 consists of estimates, the incidence analysis was repeated with measured data from Yamagata, Fukui and Nagasaki, three prefectures with long-standing high-quality registries [1], for all cases, invasive cancer only and the period before the registry change. Analyses used Python 3 with statsmodels; the code is provided as Supplementary Material.

Results

Mortality trends and APC analysis

There were 437,134 breast cancer deaths at ages 30–84 years in 1960–2024. Age-specific mortality rose in every age group until the 1990s, after which the year of peak mortality advanced with age, from 1997 at 40–44 years to 2015 at 60–64 years; at 70 years or older mortality was still rising in 2024 (Fig. 1; **Supplementary Figure S1**). Each peak corresponds to women born around 1950–1955.

The age-cohort model fitted far better than the age-period model (deviance 389.2 vs 9,041.8; **Table 1**). Adding cohort curvature to the age-period model reduced the deviance by 8,787.6 on 21 df ($F = 163.0$, $P < 0.001$), whereas adding period curvature to the age-cohort model reduced it by 135.0 on 11 df ($F = 4.8$, $P < 0.001$). The dispersion of the full model was 2.57. Net drift was 1.06% per year (95% CI, 0.99–1.14). The cohort deviation rose from 0.79 (0.75–0.83) for women born around 1900 to 1.51 (1.47–1.54) for those born around 1950, then fell to 1.01 (0.98–1.05) for the 1970 cohort and 0.60 (0.50–0.70) for the 1990 cohort (Fig. 2). Period deviations were within ± 5% of the linear trend ($F = 4.8$, $P < 0.001$).

Screening exposure

With a 10-year lag, eligibility was not associated with mortality (RR 1.005; 95% CI, 0.971–1.040), and with a 5-year lag the estimate was similar (0.990; 0.956–1.026) (**Table 2;** Fig. 3). Unlagged eligibility was associated with a 4.5% lower rate (0.955; 0.918–0.994), although an immediate effect is implausible, and cumulative eligibility with higher mortality at every lag (RR per 10 eligible years, 1.10–1.20).

APC terms explained 91–94% of the variation in binary eligibility and 95% to more than 99% in cumulative eligibility. For binary eligibility the VIF was 11–18, so standard errors were 3.3–4.2 times larger than for an uncorrelated exposure (**Supplementary Table S1**). Under the specified model, nominal precision was sufficient to detect a reduction of about 5% (smallest detectable RR, 0.94–0.95), but this does not account for misspecification or alternative exposure definitions. The residual variation was concentrated in a few cells: for the 10-year lag, 2010–2014 contributed 55% of the information, ages 45–59 years 63%, and women born around 1955–1970 66% (**Supplementary Table S2B**), the cohorts in which the cohort deviation fell most steeply (1.44 to 1.01).

Counting clinical breast examination did not resolve the inconsistency: binary programme eligibility with a 10-year lag was associated with lower mortality (RR 0.935; 0.888–0.985), whereas cumulative programme eligibility was associated with higher mortality (1.06–1.11). With annual observations, the mammography estimates were similar (10-year lag, 0.996; 0.970–1.022), but the programme estimate reversed (1.029; 1.005–1.053), so the only nominally protective estimate at a plausible lag was not robust to temporal resolution (**Supplementary Table S1**). Results for 1975–2024, negative binomial models and the conventional policy model (IRR 1.024; 1.003–1.047) are given in Supplementary Results.

Incidence and comparison with mortality

Between 1976 and 2020 there were 2,000,260 new cases (including in situ) and 353,208 deaths. Net drift was 3.96% per year for incidence (95% CI, 3.81–4.11) and 1.17% for mortality. Incidence rose in every age group (2.5–5.1% per year), whereas mortality fell at 30–34 years (− 0.8% per year; −1.2 to − 0.4) and rose by 1.3–2.5% per year from 50 years upward. The incidence model was markedly overdispersed (dispersion 32.6), although 92% of cells had relative residuals within ± 7% (**Supplementary Figure S2**).

Incidence and mortality shared the same cohort pattern, peaking around the 1951 cohort (Fig. 4), but the peak was higher for mortality (RR 1.43 [1.39–1.46] vs 1.22 [1.18–1.26]) and the later decline steeper. The relative cohort curvature was 1.17 (1.13–1.22) for the 1951 cohort and 0.88 (0.82–0.96) for the 1976 cohort; the direct model gave almost identical estimates (1.17 [1.12–1.23] and 0.88 [0.79–0.99]), although for the 1981 cohort its interval included 1 (**Supplementary Table S3**). The direction of the comparison was unchanged under a negative binomial model, before the registry change, after excluding screening ages and after excluding poorly fitting cells (1951 cohort, 1.10–1.20; 1976 cohort, 0.82–0.89; **Supplementary Table S4**), although residual misfit remained. In measured data from the three prefectures, the cohort deviation of incidence also peaked in the 1951 cohort (RR 1.22; 1.17–1.27; invasive cancer only, 1.24; before the registry change, 1.21) and was 0.91 for the 1976 cohort, with little overdispersion (1.3–1.7) (Supplementary Table S5; Supplementary Figure S3). Incidence period deviations showed no apparent upward step at the 2016 registry change (second difference, RR 0.93; 0.89–0.97).

The mortality-to-incidence ratio fell in every age group from around 2000 (Fig. 5), for example from 0.27 to 0.10 at 50–54 years between 1996–2000 and 2016–2020; with invasive cancer alone it fell by about

30% between 2006–2010 and 2016–2020. The share of in situ cancer at 40–49 years rose from 5.9% in 2003 to 16.3% in 2023.

Discussion

Over 65 years, non-linear changes in breast cancer mortality among Japanese women were aligned mainly with birth cohort, peaking in women born around 1950, and period effects beyond the overall drift were small. Screening exposure was almost collinear with the APC structure, and its estimated association with mortality changed size and direction with the exposure definition.

These results should not be read as evidence that mammography screening is ineffective. They show that national mortality statistics cannot reliably separate a screening effect from cohort and period effects. Because eligibility in Japan was defined by age and calendar year and introduced in two steps four years apart, any model that adjusts for age, period and cohort leaves very little exposure variation. The coefficient remains formally identified, and under the specified model its nominal precision is adequate; the difficulty is robustness. The estimate rests on the 6–9% of exposure variation that the APC terms do not explain, which came mostly from women born around 1955–1970 at ages 45–59 years in 2010–2019, where the cohort curve is steepest. Any misspecification there, such as treatment effects that differ by age and period, passes directly into the screening estimate. Equally precise estimates pointed in opposite directions, and the one nominally protective estimate was not robust to temporal resolution. This instability reflects both exposure measurement (eligibility rather than attendance, the assumed timing of any effect and the earlier examination programme) and dependence on the APC model. The positive coefficient of the conventional policy model is better explained by residual confounding along these axes than by harm from screening.

This is consistent with the wider literature. Trials support a mortality reduction with invitation to screening [9, 10], whereas population-level analyses have struggled to attribute mortality trends to screening rather than treatment [14]. Modelling studies combining incidence, stage and survival data have apportioned the US mortality decline between screening and therapy [22, 23]; the most recent attributed 25% of the 58% reduction between 1975 and 2019 to screening and the remainder to treatment of early-stage and metastatic disease, with the share attributable to screening falling as systemic therapy improves [23]. Mortality data alone cannot make this division.

The better fit of the age-cohort model shows that the non-linear changes line up with birth cohort, but does not by itself show that factors acting on cohorts caused them, and the linear component cannot be assigned to period or cohort. Within these limits, the peak in women born around 1950 matches the timing of peak mortality by age. These women grew up during post-war changes in reproductive behaviour, diet and body size, which are recognised determinants of breast cancer risk in Japan [24]; an APC analysis of the Miyagi registry had already detected a rising cohort effect in incidence, attributed to lower parity and less breastfeeding [25]. Incidence shared the cohort peak, so part of the mortality pattern mirrors generational differences in risk; because incidence has risen by about 4% per year,

consistent with registry-based estimates [19], later cohorts still have higher absolute incidence, and the incidence curvature reflects a slowing of that rise.

The mortality peak was, however, more pronounced than the incidence peak and its decline steeper, and the mortality-to-incidence ratio halved in every age group. These findings are compatible with improved survival from earlier diagnosis and systemic therapy [26, 27] but are not direct evidence of it. Deaths in a period arise largely from cases diagnosed earlier, and the ratio is lowered by anything that raises recorded incidence without changing deaths, including lead time, overdiagnosis, the growing share of in situ disease and the registry change. Because a linear change cannot be divided between period and cohort, part of any survival improvement may also appear as cohort decline; the same constraint explains why the intrinsic estimator attributed the Japanese trend mainly to period effects [18]. The continuing rise in mortality at 70 years or older is consistent with the high-risk cohorts entering these ages and is relevant to planning services for older women.

This study used complete national data for 65 years and quantified directly how far screening could be distinguished from age, period and cohort; to our knowledge, no previous ecological evaluation of screening has reported this quantity. Its limitations include the ecological design, without individual screening, stage or treatment data; the use of eligibility rather than attendance, with workplace and opportunistic screening outside the programme; the identifiability constraint and overlapping synthetic cohorts; the exclusion of women aged 85 years or older; possible coding discontinuities; and, for incidence, registry estimates before 2016, inclusion of in situ cancer and marked overdispersion in the national series, although measured data from three high-quality registries reproduced the cohort pattern with little overdispersion.

Comparisons between areas with different screening participation would not resolve the problem: municipal records capture only part of all screening, workplace and opportunistic screening is not recorded by area, and areas with higher participation may also differ in cohort risk and access to treatment. Evaluating screening in Japan will therefore require linkage of screening attendance, cancer registration and death at the individual level. The National Cancer Registry already links incident cases with death certificates, but screening records remain fragmented across municipalities and workplaces, and linkage has so far been limited to regional quality-assurance studies. Even with linked data, self-selection would require designs such as case-control studies with long follow-up. Such data would also allow the stronger screening and treatment strategies called for in Japan [4] to be evaluated directly.

Conclusions

Non-linear changes in breast cancer mortality among Japanese women were aligned mainly with birth cohort, peaking in women born around 1950. Part of this pattern is shared with incidence; the larger cohort decline in mortality is compatible with, but not direct evidence of, improved survival. Screening exposure was almost collinear with the APC structure, so its effect cannot be reliably estimated from national statistics, and individual-level linked data are needed.

Declarations

Ethics approval:

This study used publicly available, anonymised aggregate statistics and did not require ethical review.

Conflicts of interest:

None declared.

Funding:

This study received no specific funding.

Author contributions:

MK conceived and designed the study, analysed the data, developed the software and drafted the manuscript. RS, MO, KI, JW and GK critically revised the manuscript. All authors approved the final version and agree to be accountable for all aspects of the work.

Data availability:

The mortality and population data are publicly available from the National Cancer Center Japan [1].

Code availability:

The analysis code is provided as Supplementary Material.

References

1. National Cancer Center Japan, Cancer Information Service. Cancer statistics in Japan: mortality, 1958–2024 (Vital Statistics of Japan); incidence, 1975–2015 (Monitoring of Cancer Incidence in Japan estimates) and 2016–2023 (National Cancer Registry); incidence in Yamagata, Fukui and Nagasaki, 1985–2023 [datasets]. Available from ganjoho.jp.
2. Shin HR, Boniol M, Joubert C, et al. Secular trends in breast cancer mortality in five East Asian populations: Hong Kong, Japan, Korea, Singapore and Taiwan. Cancer Sci. 2010;101:1241–6.
3. Yako-Suketomo H, Katanoda K. Time trends in breast cancer mortality between 1950 and 2008 in Japan, USA and Europe based on the WHO mortality database. Jpn J Clin Oncol. 2011;41:1240. 10.1093/jjco/hyr143.

4. Katanoda K, Tanaka H, Ito Y. International trends in cancer mortality revisited: Japan's site-specific progress and remaining challenges until 2024. Jpn J Clin Oncol. 2026;56:787–92. 10.1093/jjco/hyag029.
5. Horino T. [The Health and Medical Service Act for the Elderly and mass screening for breast cancer]. Gan Hito. 1988;15:26–8. (In Japanese.).
6. Shibata A, Takahashi T, Ohuchi N, Fukao A. [Evaluation of breast cancer screening by physical examination using population-based cancer registry data]. Nihon Koshu Eisei Zasshi. 2005;52:128–36. (In Japanese.).
7. Ministry of Health. Labour and Welfare. [History of cancer screening in Japan.] Available from mhlw.go.jp. (In Japanese.).
8. Ministry of Health. Labour and Welfare. [Partial revision of the Guidelines for Priority Health Education on Cancer Prevention and Cancer Screening.] Notice No. 0427001, 27 April 2004. Available from mhlw.go.jp. (In Japanese.).
9. Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. Lancet. 2012;380:1778–86.
10. Marmot MG, Altman DG, Cameron DA, et al. The benefits and harms of breast cancer screening: an independent review. Br J Cancer. 2013;108:2205–40.
11. Tabár L, Vitak B, Chen HH, et al. Beyond randomized controlled trials: organized mammographic screening substantially reduces breast carcinoma mortality. Cancer. 2001;91:1724–31.
12. Broeders M, Moss S, Nyström L, et al. The impact of mammographic screening on breast cancer mortality in Europe: a review of observational studies. J Med Screen. 2012;19(Suppl 1):14–25.
13. Autier P, Boniol M, Gavin A, Vatten LJ. Breast cancer mortality in neighbouring European countries with different levels of screening but similar access to treatment: trend analysis of WHO mortality database. BMJ. 2011;343:d4411.
14. Autier P, Boniol M. Mammography screening: a major issue in medicine. Eur J Cancer. 2018;90:34–62.
15. Holford TR. Understanding the effects of age, period, and cohort on incidence and mortality rates. Annu Rev Public Health. 1991;12:425–57.
16. Carstensen B. Age-period-cohort models for the Lexis diagram. Stat Med. 2007;26:3018–45.
17. Rosenberg PS, Check DP, Anderson WF. A web tool for age-period-cohort analysis of cancer incidence and mortality rates. Cancer Epidemiol Biomarkers Prev. 2014;23:2296–302.
18. Wang Z, Bao J, Yu C, Wang J, Li C. Secular trends of breast cancer in China, South Korea, Japan and the United States: application of the age-period-cohort analysis. Int J Environ Res Public Health. 2015;12. 10.3390/ijerph121214993.
19. Abubakar AK, Jamil H, Tanaka H, Katanoda K. Trends in female breast cancer incidence among Japanese, Korean, and US populations: an age–period–cohort analysis. Cancer Epidemiol Biomarkers Prev. 2026;35:1120–8. 10.1158/1055-9965.EPI-26-0101.

20. Clayton D, Schifflers E. Models for temporal variation in cancer rates. I: Age-period and age-cohort models. Stat Med. 1987;6:449–67.
21. Clayton D, Schifflers E. Models for temporal variation in cancer rates. II: Age-period-cohort models. Stat Med. 1987;6:469–81.
22. Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. N Engl J Med. 2005;353:1784–92.
23. Caswell-Jin JL, Sun LP, Munoz D, et al. Analysis of breast cancer mortality in the US—1975 to 2019. JAMA. 2024;331:233–41. 10.1001/jama.2023.25881.
24. Wakai K, Suzuki S, Ohno Y, Kawamura T, Tamakoshi A, Aoki R. Epidemiology of breast cancer in Japan. Int J Epidemiol. 1995;24:285–91.
25. Minami Y, Tsubono Y, Nishino Y, Ohuchi N, Shibuya D, Hisamichi S. The increase of female breast cancer incidence in Japan: emergence of birth cohort effect. Int J Cancer. 2004;108:901–6. 10.1002/ijc.11661.
26. Early Breast Cancer Trialists' Collaborative Group. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet. 2005;365:1687–717.
27. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. N Engl J Med. 2001;344:783–92.

Tables

Tables 1 and 2 are available in the Supplementary Files section.

Figures

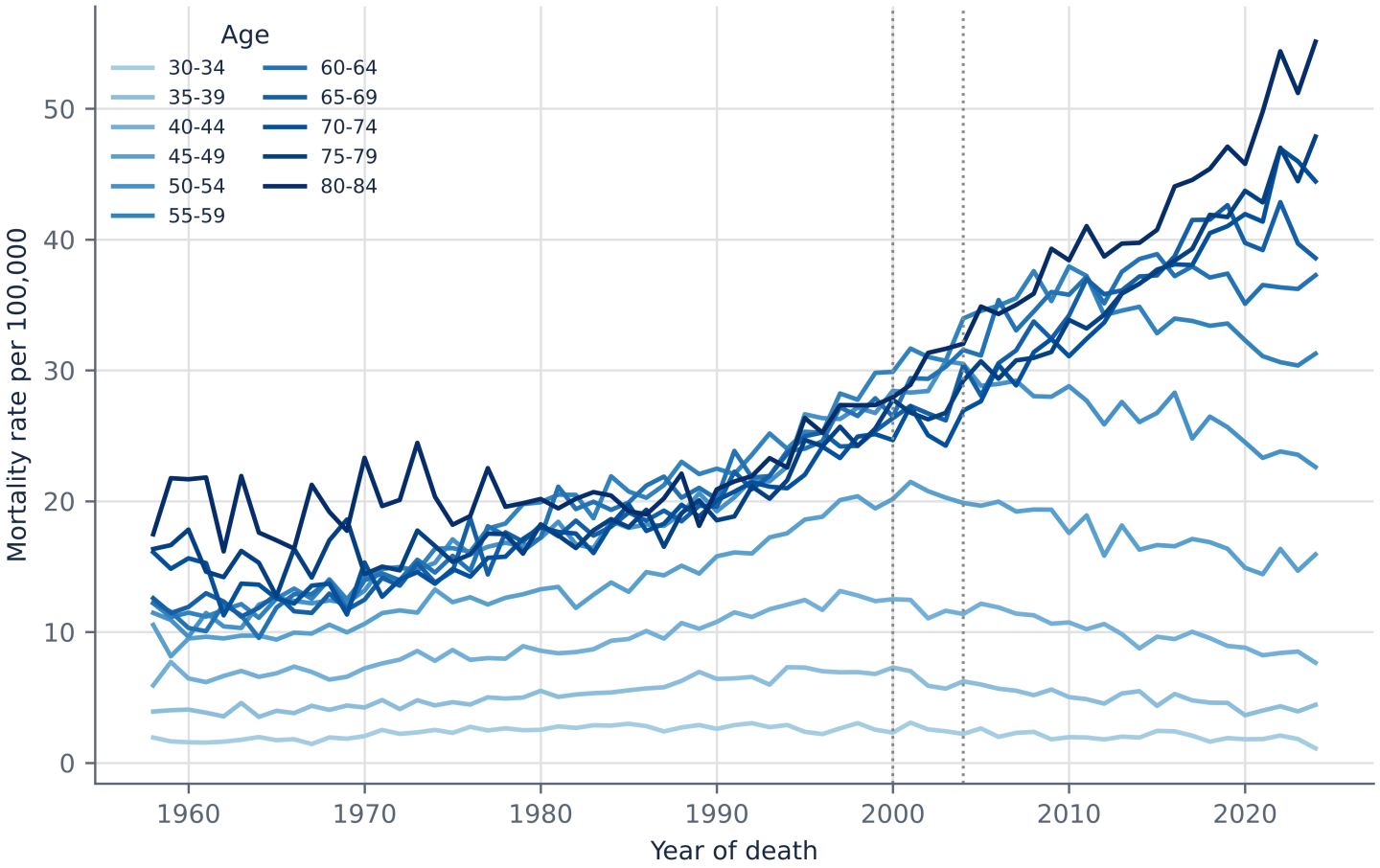


Figure 1

Age-specific breast cancer mortality among Japanese women aged 30–84 years, 1958–2024, by 5-year age group. Dotted vertical lines mark the introduction of mammography screening for women aged ≥50 years (2000) and ≥40 years (2004). Data for 1958–1959 are shown for completeness but were not included in the APC models, which cover 1960–2024.

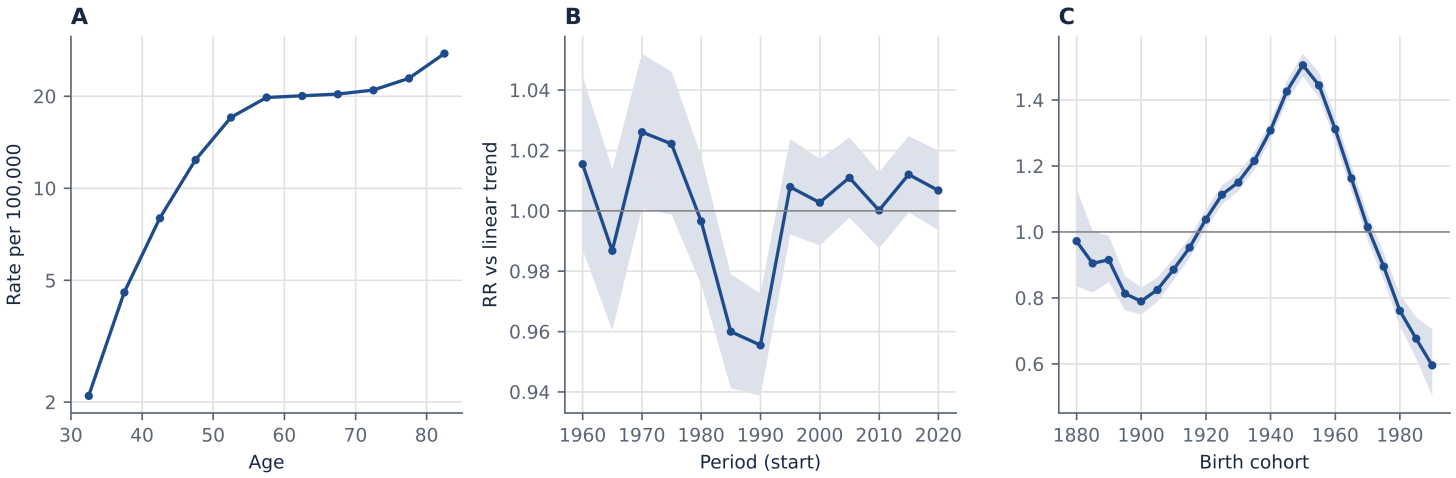


Figure 2

Age-period-cohort model of breast cancer mortality, 1960–2024. (A) Age-specific rates per 100,000 at the reference period, including the net drift. (B) Period deviations and (C) cohort deviations from the log-linear trend, expressed as rate ratios; shaded bands are quasi-Poisson 95% CIs.

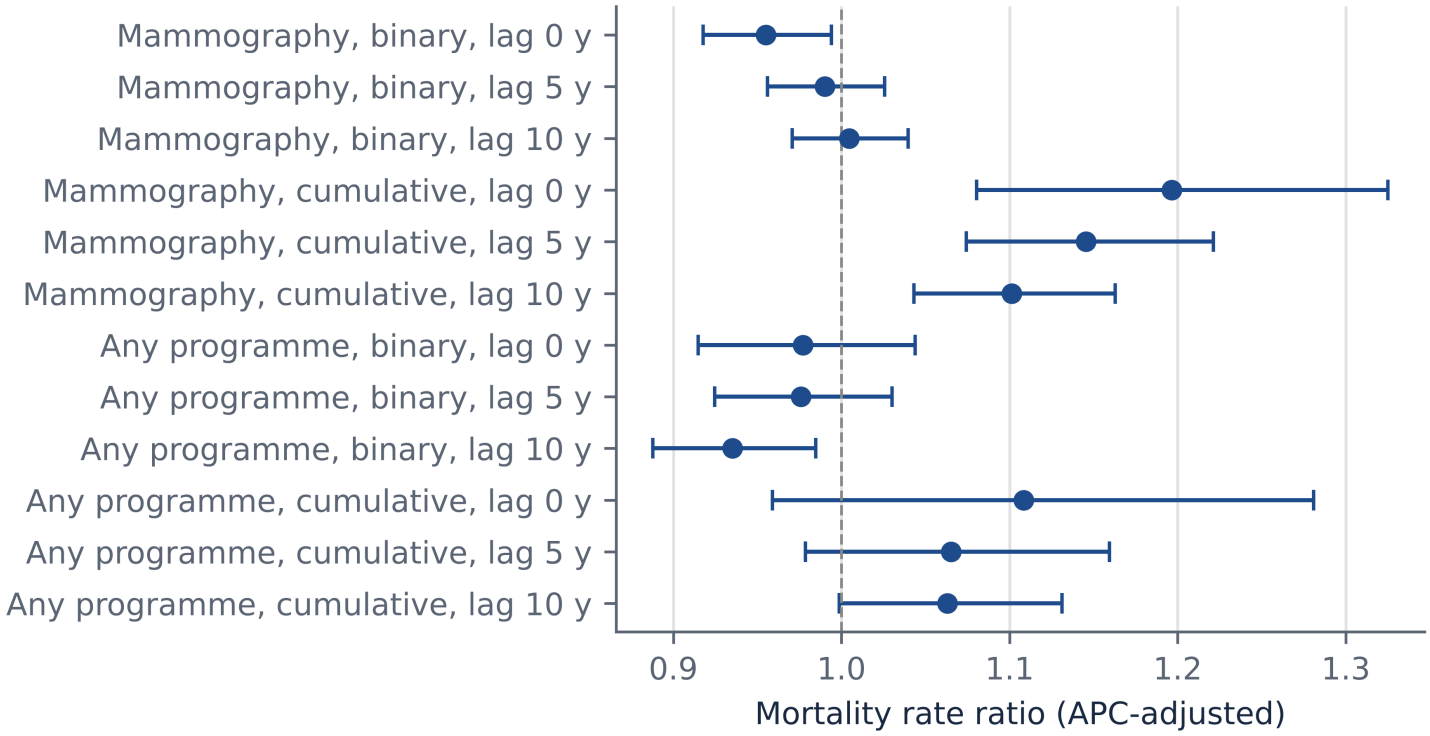


Figure 3

Mortality rate ratios for screening exposure in the APC model, 1960–2024, by exposure definition and lag. Points are rate ratios and bars quasi-Poisson 95% CIs; the dashed line marks a rate ratio of 1. Mammography: eligibility from 2000 at ≥50 years and from 2004 at ≥40 years. Any programme: clinical breast examination (1987–2003, ≥30 years) or mammography eligibility. Cumulative exposure is expressed per 10 years of eligibility.

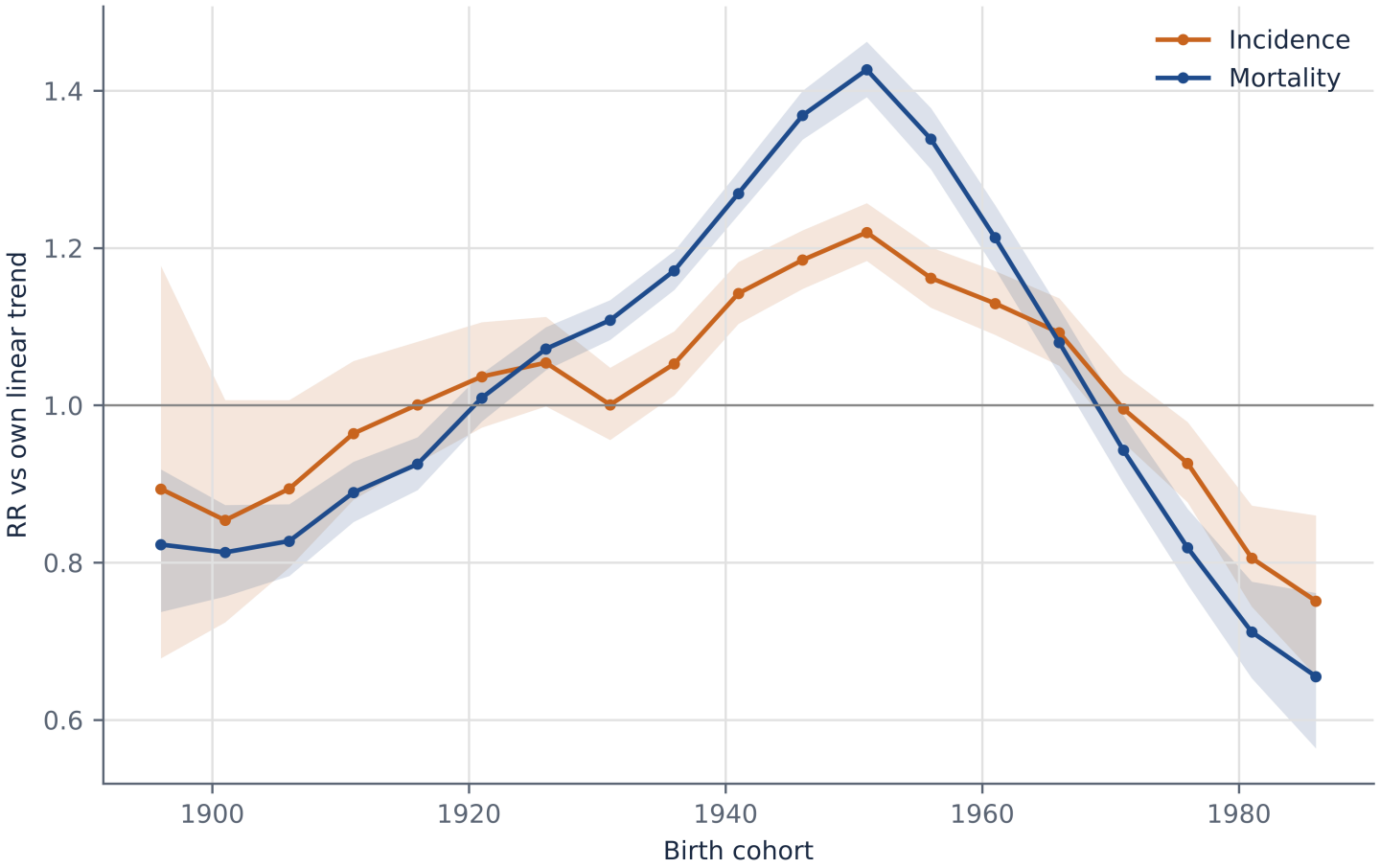


Figure 4

Cohort deviations from linearity for breast cancer incidence (orange) and mortality (blue), 1976–2020. Each curve is relative to its own log-linear trend; shaded bands are quasi-Poisson 95% CIs. Incidence includes in situ cancer.

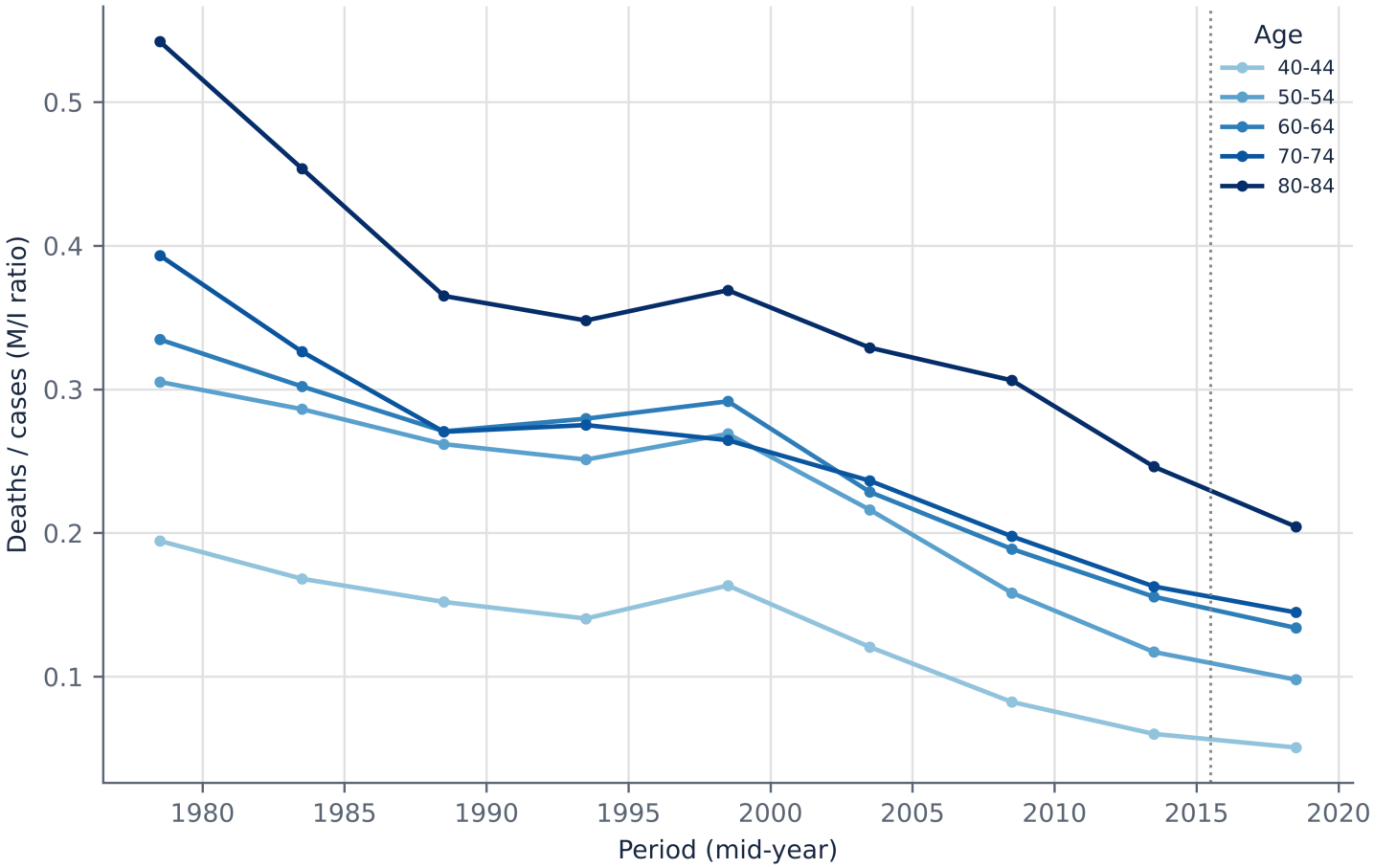


Figure 5

Ratio of breast cancer deaths to new cases (including in situ) by age group and 5-year period, 1976–2020, plotted at period mid-years. The dotted line marks the change from regional registry estimates to the National Cancer Registry in 2016.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Tables.xlsx
- FigureS1.png
- FigureS2.png
- FigureS3.png
- KawaiBreastCancerSupplementaryMaterial.docx