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NSC93-2745-B-039-001-URD

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Abstract

The objective of this study was to investigate the roles of spatio-temporal factors in the incidence and mortality of breast cancer among Taiwanese women from 1979 to 1998. Breast cancer incidence and mortality data were provided by Taiwan's Department of Health (DOH). The spatial factors included urbanization, residential areas, population density and allocation of medical resources. The rate of increase of breast cancer incidence over the 20-year period was much higher than that of breast cancer mortality. Overall, the peak of breast cancer incidence was in the age range of 45 to 49 years. Breast cancer incidence in the 336 regions varied considerably and correlated strongly with mortality (r=0.37). Breast cancer incidence and mortality were strongly correlated with each of the four spatial factors. In conclusion, the significant differences in breast cancer incidence and mortality based on spatio-temporal factors indicate that environmental factors play an important role in the etiology of this disease. The results of this study may be used as a reference in strategies aimed at preventing breast cancer.

Keywords: Spatio-temporal factors, breast cancer incidence, mortality

1979   1998

20

45   50

336

(r=0. 37)

Introduction

Breast cancer is a major cause of death among Taiwanese women. In 2000, breast cancer mortality rate among women was 10.61 per 100,000. There has been a steady rise in breast cancer incidence over the last twenty years which may reflect, in part, changes in lifestyle, such as diet. In 1990, Taiwan's DOH implemented a nationwide breast cancer screening program in the community. Between 1999 and 2001, one million women aged over 35 years were given breast palpitation. The screening program included education about self-examining and the importance of early detection. Suspected positive cases were referred to local hospitals for diagnosis and treatment. Tabar (2003) investigated mortality in breast cancer patients and found that mammography service screening substantially reduced mortality rates. In Taiwan, such screening programs have not been comprehensively evaluated. Recent reports in Taiwan indicate that the age of onset of malignant breast cancer has become lower over the past few decades. Family history of breast cancer is a well-known risk factor in early onset of this disease. Claus (1990) conducted a population-based case-control study. A total of 4730 breast cancer patients were age- and residence-matched with 4688 controls. Family history of breast cancer, especially in a first-degree relative, was found to be a significant factor, after adjustment for confounders. Sattin (1985) found that risk of developing breast cancer was 2.3 times higher in patients with a

family history of breast cancer compared to those without family history of the disease. The Collaborative Group on Hormonal Factors in Breast Cancer (2001) concluded that the lifetime excess incidence of breast cancer is 5.5% with one affected first-degree relative and 13.3% for women with two. Although family history most likely affects incidence of breast cancer through genetic predisposition, various environmental factors may also play important roles. Currently, there are no available data in Taiwan on relationships between the incidence and mortality of breast cancer. Moreover, there are no data on the spatio-temporal factors that may affect incidence and mortality of this disease in Taiwan. The findings of this study will be used to establish baseline data on breast cancer incidence and mortality in order to develop nationwide breast cancer prevention programs.

Materials and Methods

Data on the general population from 1979 to 1998 in Taiwan were provided by the Ministry of the Interior, while data on breast cancer cases and breast cancer death cases were provided by the Department of Health. Data from 1996 were used as the standard population to calculate the standardized incidence and mortality of breast cancer in each year. Standardized incidence and mortality in each district from 1992 to 1996 were categorized into five levels (>80%, 60-80%, 40-60%, 20-40%, <20%),

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labeled as high risk, moderate high risk, moderate, moderate low risk and low risk.

Urbanization data, residential areas, population density and medical resources (no. of medical staff) and population density were provided by the government office of statistics (Executive Yuan). The urbanization level was classified into seven categories according to population density, social index, and economic status. In the current study three main categories of urbanization were used: metropolitan (high), suburban (moderate) and rural areas (low). Residential areas were classified into three categories: plains, mountains and outlying islands. The proportions of the population and medical staff were calculated by dividing numbers in each district by numbers in the total population. These proportions were classified into high (over 33.3%), low (under 66.6%) and medium (between 33.3% and 66.6%). Population density in each district was calculated in the same way. Age-adjusted incidence and mortality were graded into five levels. Breast cancer incidence was graded from 0-11.95, 11.95-15.95, 15.95-20.75, 20.75-27.24, 27.24-67.46 per 100,000 population. Breast cancer mortality was graded from 0-3.93, 3.93-6.61, 6.61-8.41, 8.41-10.45, 10.45-26.25 per 100,000 population.

The statistical model used was proportional odds model

$$\log(ODD_{j(x)}) = \alpha_j + \beta_1 x_1 + \beta_2 x_2 + \Lambda + \beta_k x_k,$$

where x meant spatial factors, j represented the mortality or incidence level

, $j = 5,4,3,2$. Since the assumption of proportional odds hold (which was shown by the goodness-of-fit test for model fit), for any fixed j, the estimated odds that a spatial situation (denoted by A) is in the high risk direction rather than the low risk direction equal exp(β) times the estimated odds for the other spatial situation (denoted by B).

For example, for urbanization, let x=A meant in the moderate urbanization area, x=B meant in the low urbanization area, the odds ratio (OR) was calculated from these results as follows:

$$Odds\ Ratio = \frac{p_{5(x=A)}/1-p_{5(x=A)})}{p_{5(x=B)}/1-p_{5(x=B)}} = \frac{p_{4(x=A)}/1-p_{4(x=A)})}{p_{4(x=B)}/1-p_{4(x=B)}} = \frac{p_{3(x=A)}/1-p_{3(x=A)})}{p_{3(x=B)}/1-p_{3(x=B)}} = \frac{p_{2(x=A)}/1-p_{2(x=A)})}{p_{2(x=B)}/1-p_{2(x=B)}}.$$

When OR was over 1, this meant that the population in the moderate urbanization area had a higher risk of developing breast cancer than the population in areas with low level urbanization. The same calculation method was used for the other spatial factors. Age standardized incidence and mortality were plotted for each year (1979 to 1998), for each age group, and for each birth cohort. Age standardized incidence and mortality of breast cancer in the 336 districts were calculated and classified into five categories and plotted on the map of Taiwan. The Pearson's correlation coefficient between incidence and mortality was calculated.

Results

Age standardized incidence and mortality of breast cancer in the 336 districts in Taiwan are shown in Figure 1. Breast cancer incidence and mortality were graded into five levels with the darkest areas indicating highest incidence and mortality. The darkest areas tend to coincide with the metropolitan areas, such as in the north. Pearson's correlation coefficient between incidence and mortality of breast cancer was 0.37. Incidence was lowest in the east of Taiwan, although some areas with low breast cancer incidence had high mortality.

Figure 2 shows the trends in age-specific breast cancer incidence and mortality rates from 1979 to 1998. Incidence of breast cancer increases with time, with a sharp increase at 1990. However, the mortality rate increases only slightly (range from 5/100,000 population to 10/100,000 population). The peak in mortality rate occurred in 1997 and decreased gradually afterwards.

Figure 3 shows the trends in age-specific incidence and mortality rates of breast cancer by birth cohort (1902-1911, 1907-1916, …, 1942-1951). Incidence of breast cancer occurred at an earlier age in the younger generations. Also, the rate of increase in incidence of breast cancer was higher in the younger generations.

The trends in age-specific incidence and mortality rates of breast cancer in three five-year time periods (1982-1986, 1987-1991, 1992-1996) can be seen in Figure 4.

There was a similar trend to that in Fig.3 with an increase of breast cancer mortality with age. The increase in incidence was highest in the most recent five-year time period (1992-1996), with a peak at 45-49 years for each five-year age interval. In principle, mortality rates increased in each of the three five-year time periods. Mortality rate was highest at ages over 80 years. Except for ages over 80 years, the mortality in the most recent five-year time period was consistently higher than in the other time periods. For all ages below 65, incidence of breast cancer was higher than breast cancer mortality.

Table 1 shows the correlations of the five levels of breast cancer incidence and mortality with the spatial factors. Overall, there were significant associations of both incidence and mortality of breast cancer with each of the spatial factors. There was a significant positive correlation of high urbanization with breast cancer incidence and mortality. There was an even spread of levels of breast cancer incidence and mortality in the plain areas, but for the mountainous areas and outlying islands, there were negative correlations with breast cancer incidence and mortality. Population density correlated negatively with breast cancer incidence and mortality. Low population density correlated significantly with high incidence of breast cancer, but breast cancer mortality was similar in each level of mortality at low population density. There was a positive correlation of medical resources with breast cancer incidence and mortality.

The odds ratios of breast cancer incidence and mortality within levels of each spatial factor can be seen in Table 2. There were dose-dependently significant correlations of urbanization with breast cancer incidence and mortality. There was a significant difference between plains and mountains in breast cancer incidence and mortality, but there were no significant associations among other topographical areas. Significant negative correlations between each of the levels of population density were found in breast cancer incidence, but for breast cancer mortality only high and low population density correlated significantly. High level of medical resources was higher than medium and low levels of medical resources in both breast cancer incidence and mortality. Incidence and mortality of breast cancer were similar between medium and low level of medical resources.

Discussion

Previous studies of breast cancer in Taiwan have shown that breast cancer mortality is highest in urban areas, while it is highly variable around the island as a whole, which may be due to the small number of breast cancer cases. Long-term monitoring of breast cancer mortality is required to identify trends in different parts of the country. In addition, cancer mapping, such as the "Geographic Information System" (GIS) can provide a dynamic exhibition of patterns and trends which yields information about the clustering and diffusion process in breast cancer mortality and incidence, as well

their intercorrelations. The current study found that breast cancer mortality and incidence were highly correlated and has increased gradually over the past twenty years. This may be attributed to the introduction of the national cancer screening program in 1995 in Taiwan. Furthermore, dietary and lifestyle changes may have contributed to the increase in breast cancer mortality and incidence. Another important trend is the considerably earlier onset of breast cancer incidence over the past twenty years. As such, the Department of Health may lower the age of breast cancer screening. Ongoing health awareness programs have also helped to catch breast cancer in many women in Taiwan. Levi (1994) reported that overall incidence of various cancers increased from 10% to 30% but the cancer mortality remained approximately the same. This may be due to improved diagnosis and therapeutic advancements. Menegoz (1997) investigated the cancer incidence and mortality in France in 1975-95 and found that mortality remained relatively even while incidence increased.

Cancer mapping studies have shown that the south-west of Taiwan has a clustering effect for certain cancers, such as cancer of the bladder, skin, liver and lung which have been attributed to arsenic in the groundwater. However, breast cancer incidence in this part of the country was not significantly from that in other areas. Factors other than lifestyle and diet that affect breast cancer incidence include

pesticides, such as DDT which was used 50 years ago to eradicate malaria in Taiwan, and air pollutants from incinerators, such as dioxin. The Taiwan EPA has recently reduced the maximum permissible limit for dioxin. Breast cancer incidence is generally much higher in highly urbanized areas. This finding is consistent with those of many other studies in other countries, such as Japan and Spain. Previous studies have identified other factors associated with increased incidence of breast cancer, such as decreasing age of menarche, increasing age at first marriage, age at first birth, decreasing fertility rate and increasing adult height. Minami (1996) reported significant period effects on breast cancer incidence, although the cohort effect was marginal. The relative risks by birth cohort suggested a declining trend in younger birth cohorts. Mackillop (2000) evaluated associations between community incomes and cancer incidence in North America and found that breast cancer incidence was highest among highest socioeconomic status, although the underlying mechanisms remain unclear. Over the years the cancer registry has developed comprehensive data on breast cancer. In addition, breast cancer diagnostic techniques have improved considerably, as proven by follow-up biopsy in 80% of diagnoses. This database can be used to correlate with environmental and ecological factors as well as personal risk factors, such as predisposition, alcohol consumption and smoking habit. Analyses of the significant associations are vital in the development of national cancer prevention

programs. The database can also be used to evaluate the effectiveness of such

programs.

ACKNOWLEDGEMENTS

REFERENCES

1. Tabar L ,Yen MF ,Vitak B ,Tony Chen HH. Mammography service screening and mortality in breast cancer patients: 20-year follow-up before and after introduction of screening. The Lancet 2003; 361:9367.

2. Claus EB ,Risch NJ ,Thompson WD. Using age of onset to distinguish between subforms of breast cancer. Ann Hum Genet 1990, 54(2):169-77.

3. Claus EB ,Stowe M ,Carter D ,Holford T. The risk of a contralateral breast cancer among women diagnosed with ductal and lobular breast carcinoma in situ: data from the Connecticut Tumor Registry. The Breast 2003;12: 451-56.

4. Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. Lancet. 2001;358(9291):1389-99.

5. Sattin RW ,Rubin GL ,Webster LA ,Huezo CM ,Wingo PA ,Ory HW ,Layde PM. Family history and the risk of breast cancer. JAMA 1985;253(13):1908-13.

6. Levi F ,Lucchini F ,La Vecchia C. Worldwide patterns of cancer mortality, 1985-89. Eur J Cancer Prev 1994;3(2):109-43.

7. Hannoun-Levi J M, Courdi A, Marsiglia H , Namer H, Gerard J P. Breast cancer in elderly women: is partial breast irradiation a good alternative? Breast Cancer Research and Treatment 2003;81(3): 243.

8. Menegoz F ,Black RJ ,Arveux P ,Magne V ,Ferlay J ,Buemi A ,Carli PM ,Chapelain G ,Faivre J ,Gignoux M ,Grosclaude P ,Mace-Lesec'h J ,Raverdy N ,Schaffer P.

Cancer incidence and mortality in France in 1975-95. Eur J Cancer Prev 1997 ;6(5):442-66.

9. Minami Y ,Takano A ,Okuno Y ,Fukao A ,Kurihara M ,Hisamichi S. Trends in the incidence of female breast and cervical cancers in Miyagi Prefecture, Japan, 1959-1987. Jpn J Cancer Res 1996;87(1):10-7.

10. Colonna M ,Grosclaude P ,Faivre J ,Revzani A. Cancer registry data based estimation of regional cancer incidence. Journal of Epidemiology and Community Health 1999, 53(9):558

11. Minami Y ,Ohuchi N ,Fukao A ,Hisamichi S ,Determinants of Infant Feeding Method in Relation to Risk Factors for Breast Cancer. Preventive Medicine 2000,30.363-370).

12. Mackillop WJ ,Zhang-Salomons J ,Boyd CJ ,Groome PA. Associations between community income and cancer incidence in Canada and the United StatesCancer 2000,89(4): 901-912.

13. Chen CJ, You SL, Pwu RF, Wang LY, Lin YP, Hsi GC, Hsi MS, Ho HC, Lee CT, Lin CG, et al. Community-based cervical cancer screening in seven townships in Taiwan. J Formos Med Assoc. 1995;94(2):103-11.

Table1.Correlations of the five levels of breast cancer incidence and mortality with the

spatial factors(1992 to 1996)

Spatial factors	N	Rate of Incidence rate					#P	Rate of Mortality					#P
		Low	Mod Low	Mod	Mod high	High	r*	Low	Mod Low	Mod	Mod high	High	r*
Urbanization							<. 0001						<. 0001
Low	168	35.7	24.4	19.0	14.9	6.0	0. 476	32.7	21.4	17.3	12.5	16.1	0. 327
Moderate	143	7.7	20.3	23.8	27.3	21.0		10.5	23.1	24.5	25.9	16.1	
High	48	4.2	12.5	16.7	66.7	0.0		2.1	6.3	16.7	29.2	45.8	
Region							<. 0001						<. 0001
Outlying islands	9	22.2	44.4	11.1	11.1	11.1	0. 273	44.4	11.1	22.2	0.0	22.2	0. 204
Mountainous areas	29	65.5	13.8	10.3	6.9	3.4		58.6	10.3	10.3	6.9	13.8	
Plain areas	321	15.6	19.9	21.2	21.5	21.8		15.6	21.2	20.9	21.8	20.6	
Pop. Density													
Low	119	13.4	10.9	16.8	23.5	35.3	<. 0001	12.6	18.5	21.0	21.8	26.1	<. 0001
Moderate	120	14.2	23.3	23.3	22.5	16.7	- 0. 298	16.7	20.8	19.2	25.8	17.5	- 0. 194
High	120	31.7	25.8	20.0	14.2	8.3		30.0	20.8	20.0	12.5	16.7	
Dist. of Medical Resources													
Low	119	23.5	26.9	22.7	19.3	7.6	<. 0001	23.5	31.9	18.5	9.2	16.8	<. 0001
Moderate	120	25.8	20.8	18.3	17.5	17.5	0. 271	21.7	19.2	19.2	22.5	17.5	0. 218
High	120	10.0	12.5	19.2	23.3	35.0		14.2	9.2	22.5	28.3	25.8	

#P   P value is according to chi-square tendency test

r*   r denotes Pearson's correlation coefficient

Table2. Odds ratios of breast cancer incidence and mortality within levels of each spatial

Factor (1992 to 1996)

Spatial factor	Incidence rate		Mortality rate	
	Odds ratios (95%CI)	P	Odds ratios (95%CI)	P
Urbanization				
Low	1	-	1	-
Moderate	2. 9(1. 9-4. 5)	<. 0001	2. 0(1. 3-3. 0)	<. 0001
High	22. 4(11. 2-45. 0)	<. 0001	6. 1(3. 4-11. 2)	<. 0001
Region				
Outlying islands	1	-		-
Mountainous areas	1. 3(0. 3-5. 1)	0. 002	0. 4(0. 1-1. 9)	<. 0001
Plain areas	3. 4(1. 0-11. 8)	0. 054	2. 0(0. 5-7. 9)	0. 318
Pop. Density				
Low	1	-	1	-
Moderate	0. 4(0. 3-0. 7)	0. 010	0. 7(0. 4-1. 1)	0. 105
High	0. 2(0. 1-0. 4)	<. 0001	0. 5(0. 3-0. 8)	0. 002
Distribution of Medical Resources				
Low	1	-	1	-
Moderate	1. 4(0. 9-2. 2)	<. 0001	1. 3(0. 8-2. 0)	0. 014
High	3. 8(2. 4-6. 0)	<. 0001	2. 3(1. 4-3. 6)	0. 001

P   P value is according to chi-square test
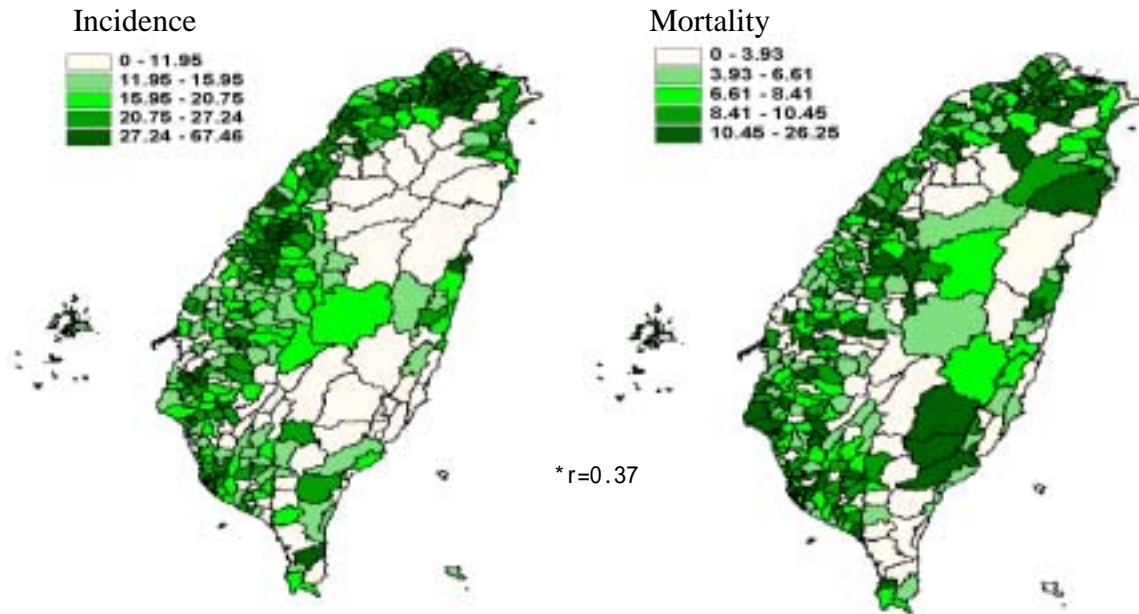
Figure 1. Age standardized incidence and mortality of breast cancer in the 336 districts in Taiwan.

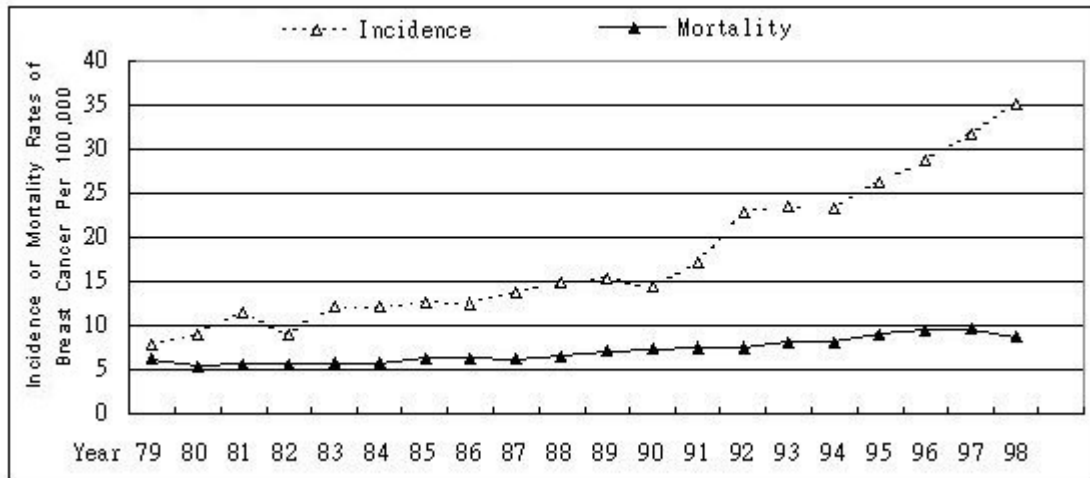*r   Pearson's correlation coefficient between incidence and mortality

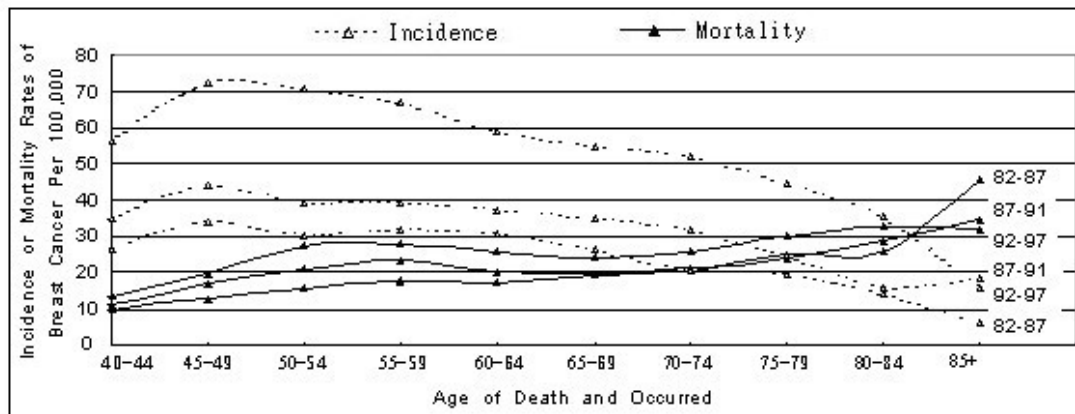**Figure 2. Trends in age-specific breast cancer incidence and mortality rates from 1980 to 1998.**

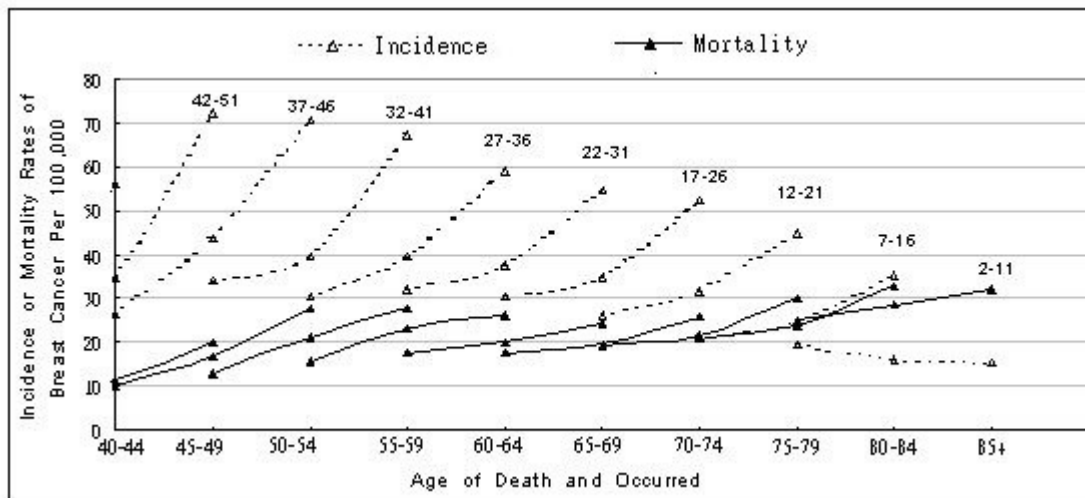**Figure 3. Trends in age-specific incidence and mortality rates of breast cancer by year of birth**

Figure 4. Trends in age-specific incidence and mortality rates of breast cancer in three five-year time periods.