The Effect of Migration on Cancer Incidence Among Japanese in Hawaii

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Objectives: This analysis compared cancer incidence trends among Japanese in Japan, and Japanese and Caucasians in Hawaii, between 1960 and 1997, and estimated the impact of migration on the incidence of different cancers.

Methods: Incidence information was obtained from 8 volumes of Cancer Incidence in Five Continents. The migration effect was estimated from the areas under the incidence curves as the ratio of the geographic and the ethnic difference in cumulative cancer incidence.

Results: Among the 5 more common cancers, the migrant effect was strongest for colon and stomach cancers, prostate and breast cancers were affected to a lesser degree, and lung cancer risk differed little between Japanese in Japan and Hawaii. Migration led to lower risk of stomach, esophageal, pancreatic, liver, and cervical cancers, but to higher rates for all other cancers. The large variation in time for migrants to adopt the host population's cancer risk suggests that risk factors have organ-specific effects, or operate at different times in life. Although the available incidence rates are limited by under-reporting and early detection efforts, mortality rates confirm the significant differences in cancer risk.

Conclusions: The persistent difference in cancer incidence several generations after migration supports the idea that living in the host country is not, alone, sufficient to modify cancer risk for all cancer sites to the level of the host population. Although the migration effect can be partially explained by known etiologic factors, a large proportion of the changing risk remains unexplained. (*Ethn Dis*. 2004;14:431–439.)

Key Words: Cancer, Migration, Risk Factors, Ecologic Studies, Ethnic Groups

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Introduction

The risk for developing cancer varies considerably around the world.[1] Whereas breast and prostate cancer incidence rates are higher in Western countries than in Asia, stomach cancer risk shows the opposite pattern. Depending on the cancer site, migrants have adopted the cancer risk of the host population at different rates,[2] a fact that argues against an exclusive genetic determination of risk, and suggests a variety of etiologic factors. Migrants to the United States from Asia, especially those from Japan, have long been recognized as an informative population to study for the purpose of identifying possible environmental factors that may be responsible for these variations in incidence rates.[3] Immigration from Japan to Hawaii occurred primarily during 1868–1924, when more than 200,000 Japanese came to Hawaii.[4] The population has remained relatively stable, with little in- or out-migration occurring over the years. To this day, the majority of the Japanese population in the US reports only Japanese ethnicity. According to the US Census 2000,[5] there were 796,700 persons with only Japanese ethnicity, whereas 352,232 individuals reported Japanese ethnicity in combination with other backgrounds. Of these two groups, 201,764 and 94,910, respectively, resided in Hawaii.[6]

The large Japanese population in Hawaii provides a good opportunity to study the changes in cancer risk among migrants. The objectives of this paper are to compare cancer incidence trends since 1960 among Japanese in Japan, and Japanese and Caucasians in Hawaii, for the 5 most common cancer sites (stomach, colon, lung, breast, and prostate); to estimate the impact of migration on incidence rates; and to discuss possible risk factors for these developments. In addition, we added an update of incidence rates presented in an earlier report[7] for esophageal, pancreatic, hepatic, cervical, endometrial, and ovarian cancers, as well as for Hodgkin's disease and non-Hodgkin's lymphoma.

Methods

We obtained cancer incidence rates for our populations of interest from the 8 volumes of Cancer Incidence in Five Continents,[8–15] which have been published by the International Agency for Research on Cancer, and cover the time period of 1960 to 1997 (Table 1). This set provides the best comprehensive source for cancer incidence around the world and allows valid comparisons to be drawn between countries, because the rates are age-standardized to the world population. Reports include cancer incidence rates for different ethnic groups within a country. For Japan, we chose the information from the Miyagi registry because it was included in all 8 volumes. This population is not representative of Japanese migrants to Hawaii because the majority came from prefectures (Chugoku, Kyushu, and Okinawa) other than Miyagi in the Tohoku district.[4] However, the great majority of the cancer diagnoses in these registries are tissue confirmed, and the comparison of the Miyagi rates with those in the Hiroshima and Fukuoka registries showed no major discordance.[16]

In Hawaii, cancer incidence data have been collected since 1960, when the statewide Hawaii Tumor Registry was established. Information from Hawaii appeared more suitable for our purposes because of the large number of first generation migrants in Hawaii, and the statewide registry coverage. In addition, the inclusion of Caucasians and Japanese in Hawaii controls for poten-

Table 1. Time periods covered in *Cancer Incidence in Five Continents*

Region	Vol 1 (ICD* 7)	Vol 2 (ICD 7)	Vol 3 (ICD 8)	Vol 4 (ICD 8)	Vol 5 (ICD 9)	Vol 6 (ICD 9)	Vol 7 (ICD 9)	Vol 8 (ICD 10)
Miyagi	1959–60	1962–64	1968–71	1973–77	1978–81	1983–87	1988–92	1993–97
Hawaii	1960–63	1960–64	1968–72	1973–77	1978–82	1983–87	1988–92	1993–97
Site				ICD Code				
Stomach	151	151	151	151	151	151	151	C16
Colon	153	153	153	153	153	153	153	C18
Lung	162, 163	162, 163	162, 163	162	162	162	162	C34
Prostate	177	177	177	185	185	185	185	C61
Breast	170	170	170	174	174	174	174	C50

* ICD (International Classification of Disease).[17]

Table 2. Trends in cancer incidence for less common cancers

Cancer Site	Sex	Population*	1959–63	1960–64	1968–72	1973–77	1978–82	1983–87	1988–92	1993–97
Hodgkin's disease	Men	JJ	0.9	0.4	0.8	0.5	0.5	0.4	0.5	0.5
		JH	1.9	3.2	1.5	1.3	0.9	0.4	0.8	0.5
		CH	3.9	1.9	3.7	2.8	2.4	2.7	2.7	2.7
	Women	JJ	0.1	0.3	0.4	0.2	0.3	0.2	0.2	0.2
		JH	0.8	1.4	1.1	0.4	0.2	0.8	1.3	0.5
		CH	1.2	1.9	2.2	1.7	2.5	2.7	2.9	1.8
Non-Hodgkin's lymphoma	Men	JJ	0.1	0.1	0.4	1.3	3.1	4.3	6.5	6.3
		JH	1.7	1.5	0.5	0.6	1.7	7.8	8.5	9.7
		CH	0	0.4	0.3	2.7	4.0	11.3	15.1	17.2
	Women	JJ	0.2	0.1	0.2	0.9	1.7	2.5	4.2	3.7
		JH	0.7	0.6	0.4	1.6	1.1	5.2	6.3	8.0
		CH	0	0.4	0	0.8	1.7	8.1	6.9	9.0
Esophagus	Men	JJ	13.4	14.5	12.9	13.8	13.3	14.1	14.0	14.4
		JH	6.4	6.8	3.1	4.5	3.7	3.9	3.73	5.4
		CH	5.7	5.7	4.7	2.4	3.5	4.1	4.44	4.1
	Women	JJ	6.3	4.9	4.1	3.2	3.1	2.4	2.21	2.2
		JH	0.7	0.6	0.3	0.6	0.4	0.4	0.6	0.4
		CH	0.3	1.3	1.9	1.9	1.5	0.9	2.02	1.4
Pancreas	Men	JJ	6.1	6.7	7.3	7.4	9.0	10.5	10.9	10.2
		JH	6.7	8.0	7.0	8.6	7.3	8.5	5.8	8.6
		CH	7.5	7.1	9.5	8.6	8.5	9.2	8.5	7.5
	Women	JJ	3.2	3.8	4.5	4.2	5.1	6.1	5.5	5.5
		JH	3.8	4.9	4.7	4.5	5.1	4.5	5.9	5.6
		CH	4.0	5.0	7.4	6.5	8.0	6.1	5.7	6.5
Liver	Men	JJ	N/A	1.3	1.8	2.5	11.2	13.6	15.4	17.1
		JH	7.5	6.7	4.5	5.7	6.2	6.4	5.0	6.2
		CH	4.5	4.3	3.8	2.7	4.2	2.5	4.5	5.0
	Women	JJ	N/A	0.8	0.6	0.9	4.0	4.4	5.43	5.4
		JH	0.6	1.1	1.9	2.2	1.5	2.5	1.9	3.4
		CH	1.9	1.9	1.8	1.4	1.3	1.2	1.5	1.5
Uterine cervix	Women	JJ	22.1	20.6	13.8	12.1	10	6.2	6.4	5.8
		JH	28.2	14.6	7.6	6.4	6.4	3.6	6.4	4.5
		CH	37.6	15.4	13.1	9.3	8.1	7.3	10.5	7.0
Uterine corpus	Women	JJ	2.0	1.3	1.3	2.0	2.8	3.2	4.1	4.2
		JH	9.8	10.8	15.6	19.4	15.5	15.1	14.2	17.3
		CH	15.6	17.5	28.8	34.8	23.4	18.9	15.7	15.5
Ovary	Women	JJ	2.2	1.9	2.8	3.4	4.2	5.1	6.13	7.1
		JH	7.5	9.4	6.9	7	8.0	7.1	8.1	9.8
		CH	11.4	14.8	13.7	9.4	11.0	12.5	14.2	14.4

* JJ=Japanese in Japan; JH=Japanese in Hawaii; CH=Caucasians in Hawaii.

Migrants to the United States from Asia, especially those from Japan, have long been recognized as an informative population to study for the purpose of identifying possible environmental factors that may be responsible for these variations in incidence rates.[3]

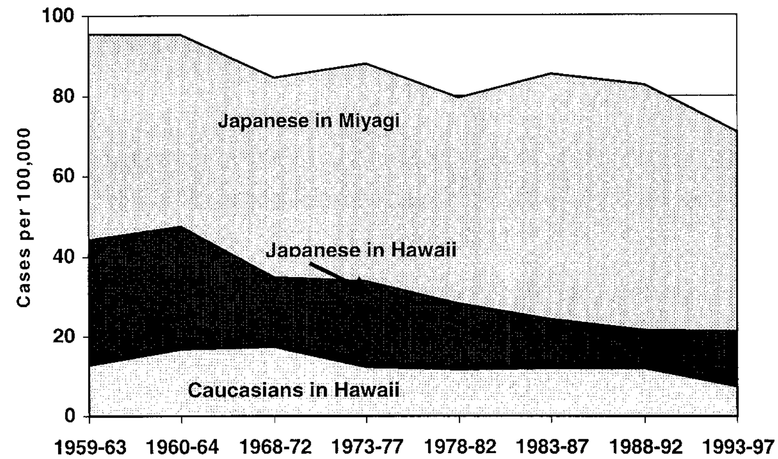

Fig 1. Migration effect by ratio of geographic difference and ethnic difference. Geographic difference = Japanese in Hawaii—Japanese in Japan. Ethnic difference = Caucasians in Hawaii—Japanese in Hawaii

tial environmental confounding factors. Incidence rates covered slightly different time periods (Table 1) in Miyagi and in Hawaii in the first volumes, but later they coincided exactly. Although the codes from the International Classification of Diseases changed from the 7th to the 10th version,[17] the categories included the same cancers over time.

We graphed cancer incidence rates for the most common cancers: lung, colon, stomach, breast and prostate (Figures 2–5). The incidence data for the less common sites of Hodgkin's disease, non-Hodgkin's lymphoma, and cancers of the esophagus, pancreas, liver, uterine cervix, uterine corpus, and ovary, are presented in Table 2. To obtain a crude assessment of the extent to which mi-

Table 3. Estimated migration effect for different cancers

Cancer Site	Geographic Difference (Hawaii Japanese– Japan Japanese)	Ethnic Difference (Hawaii Caucasians– Hawaii Japanese)	Migration Effect Geographic Difference/ Ethnic Difference
Men			
Stomach	−1876	−677	2.77
Colon	567	−85	∞
Lung	182	827	0.22
Prostate	1010	1002	1.01
Esophagus	−327	−7	45.7
Hodgkin's disease	28	51	0.54
Non-Hodgkin's lymphoma	36	82	0.44
Pancreas	−36	32	∞
Liver	−70	−71	0.99
Women			
Stomach	−768	−373	2.06
Colon	378	46	8.28
Lung	43	537	0.08
Breast	1063	1125	0.94
Ovary	134	170	0.79
Uterine cervix	−120	120	∞
Uterine corpus	439	260	1.69
Esophagus	−102	37	∞
Hodgkin's disease	21	48	0.42
Non-Hodgkin's lymphoma	40	15	2.73
Pancreas	3	51	0.06
Liver	−28	−13	2.21

∞ Indicates that the migration effect was so large that the risk in Hawaii Japanese exceeded the Caucasian risk (arithmetically it became negative).

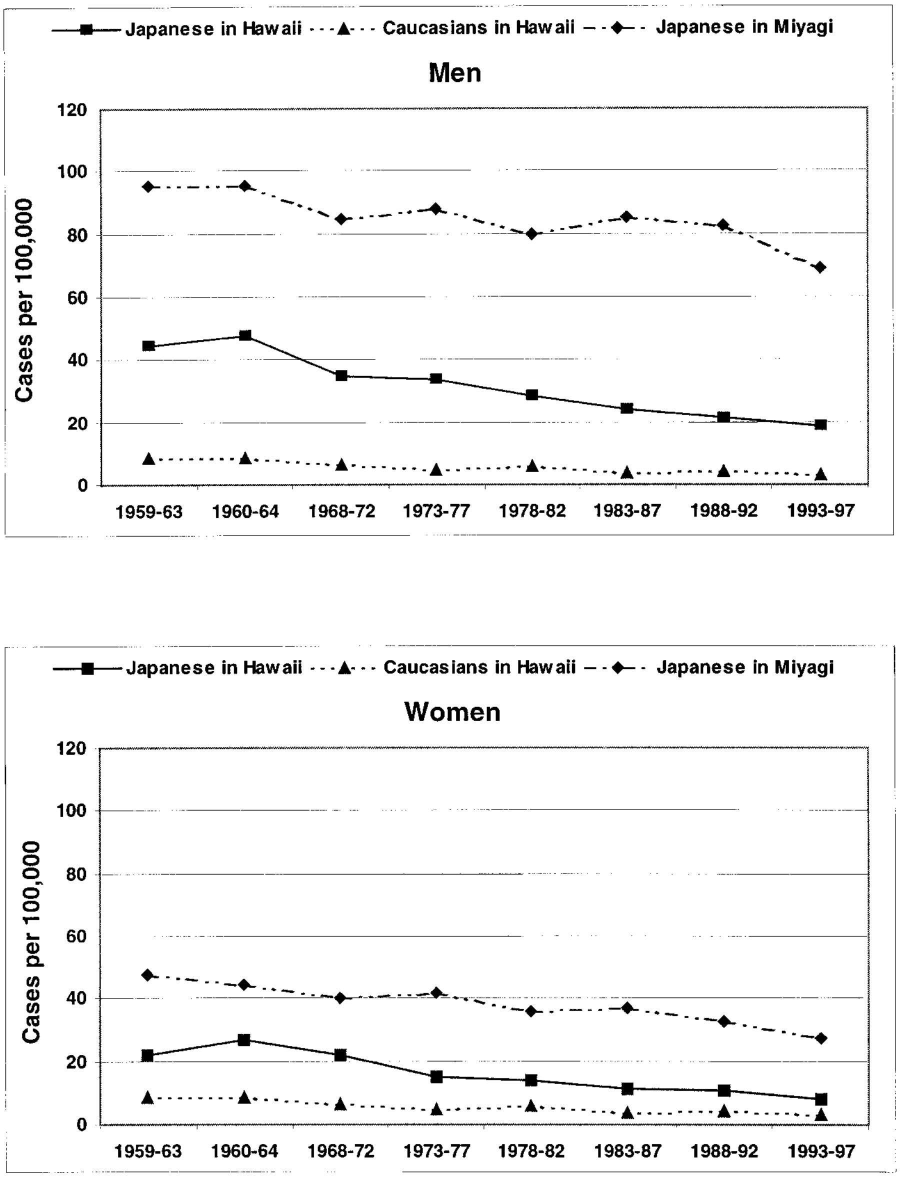

Fig 2. Stomach cancer incidence in three populations[8–15]

gration affects the incidence of specific cancers over time, we estimated the area under the 3 curves as a measure of cumulative cancer incidence during the study period (Figure 1), using the integration method in Mathematica 4.2 (Wolfram Inc., 2003). Then we calculated the difference between the areas for Japanese in Japan and in Hawaii as the geographic difference. Next, we computed the difference between the areas under the curves for Caucasians and Japanese in Hawaii as the ethnic difference. The ratio of geographic to ethnic difference provides a crude assessment of changes in cancer incidence among migrants during 38 years. For example (Figure 1), stomach cancer incidence rates in Japan have been much higher than among Japanese in Hawaii, but there was also a difference between the 2 ethnic populations in Hawaii. The ratio of 2.8 (Table 3) suggests that geographic location was more important in determining cancer risk than ethnicity. We replaced negative ratios with a sign to indicate that the migration effect was so large that the risk in Hawaii for Japanese exceeded that for Caucasians.

RESULTS

Stomach cancer incidence (Figure 2) decreased gradually in all 3 groups, but at different levels. The risk among Japanese men was more than twice as high as that for Japanese in Hawaii, whereas the rates in Caucasians were very small in both sexes. Japanese women experienced approximately half the risk of Japanese men. In a distinctly different pattern, colon cancer incidence (Figure 3) increased among all groups. During the latest time period, the colon cancer rates of Japanese in Hawaii had exceeded the rates of Caucasians. In Miyagi, the very low incidence in the 1960s had started approaching the rates in Hawaii during the late 1980s. Lung cancer incidence trends (Figure 4) showed that men in Hawaii had developed the disease at increasing rates up until 1980, when they started a slow decline, which also occurred in Japanese men, but to a lesser degree. Caucasian women started with very low rates, which rose steadily, but have not reached the male rates. For men and women, lung cancer incidence was similar in Japanese in both locations, but was considerably lower for women for men.

Caucasians in Hawaii had the highest risk of prostate cancer at all times (Figure 5). However, the trend for Japanese in Hawaii followed a similar pattern, at approximately half the risk. Japanese in Miyagi maintained very low prostate cancer incidence rates throughout the study period. Caucasians developed more breast cancer than Japanese in either location until the 1990s, when the incidence among Japanese in Hawaii nearly reached the Caucasian rate (Figure 5). Breast cancer incidence rates for both Caucasian and Japanese women in Hawaii rose most dramatically in the late 1980s, when mammography screen-

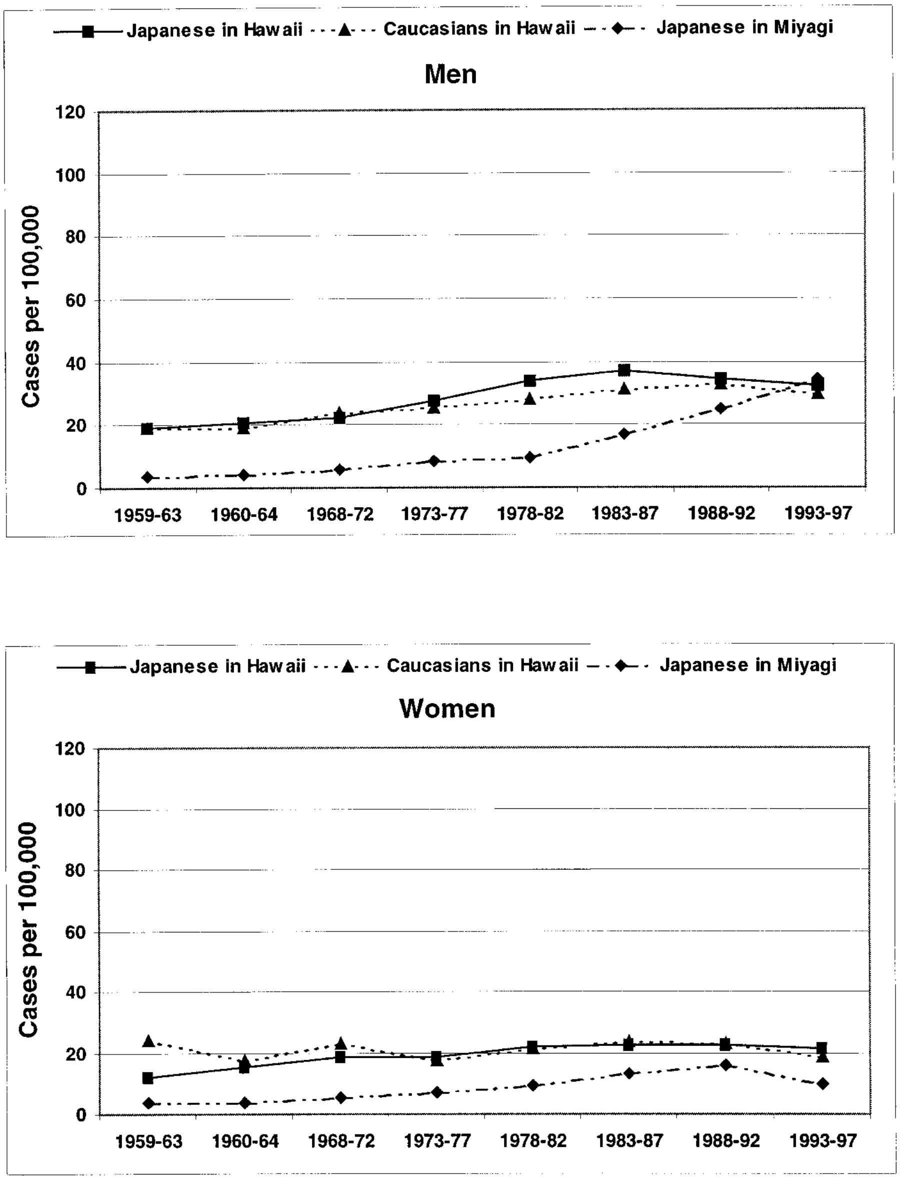

Fig 3. Colon cancer incidence in three populations[8–15]

ing was introduced.[18] Although Japanese women in Miyagi had lower rates than did women in Hawaii, their rates have also been increasing considerably.

The incidence of Hodgkin's disease (Table 2) remained highest in Caucasians, but has been relatively stable over time, whereas the non-Hodgkin lymphoma rates started rising in all populations during the 1980s. This increase was greater among men than among women; Caucasians had the highest rates and migrants had intermediate rates. Throughout the study period, the incidence of esophageal cancer remained considerably higher among men in Japan, compared to men in Hawaii and women of all groups. We observed few differences and little change for the incidence rates of pancreatic cancer. Japanese and Caucasians in Hawaii developed liver cancer at very similar rates over time, while the incidence among men in Japan, and, to a lesser degree, among women in Japan, increased considerably since the late 1970s. Women in all 3 populations experienced a 3- to 4-fold decline in the risk for cervical cancer; Japanese in Hawaii had the lowest incidence. Caucasians and Japanese in Hawaii developed cancer of the uterine corpus at much higher rates than did women in Japan, particularly during the 1970s. The incidence rates for ovarian cancer climbed slightly in both locations, but women in Japan maintained the lowest risk and Japanese migrants preserved their intermediate status.

For stomach and esophageal cancer, disease risk substantially decreased as a result of migration. While the estimated geographical difference in stomach cancer was more than twice as high as the ethnic difference (Table 2), the impact was even greater for esophageal cancer. The migration effect on the development of colon cancer in Japanese migrants was very high, as indicated by the small ethnic difference, but in the opposite direction from the effect on stomach cancer. In fact, the risk in Japanese men has exceeded the risk of Caucasians. On the other hand, the migration effect on the development of lung and pancreatic cancers, as well as Hodgkin's disease, and Non-Hodgkin's lymphoma (except for women), appeared to be minimal. This means that ethnicity, or a behavior among the Japanese, affected risk more than geographic location. In the case of lung cancer, the high smoking rates among Japanese men, and the low smoking rates among Japanese women in either location, contributed to the observed patterns for lung cancer.[19,20] Although the ratios indicated a migration effect for liver cancer, the incidence rates (Table 2) show that the risk was similar in the first 3 time periods, before incidence started to increase among the population in Japan during the 1970s. The migration effect on the development of prostate and breast cancers was estimated to be approximately one, which means that over the study period, geographical and ethnic differences were more or less equal,

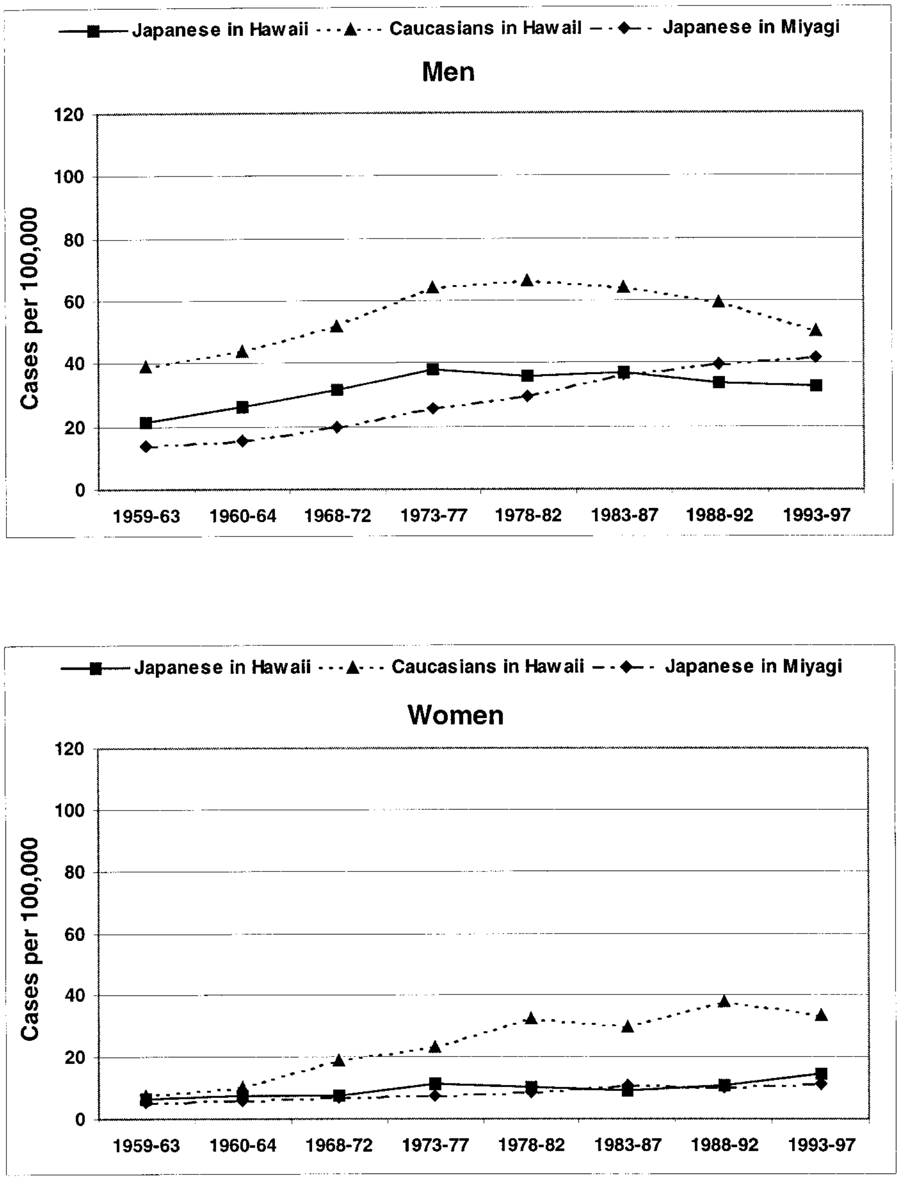

Fig 4. Lung cancer incidence in three populations[8–15]

ie, prostate and breast cancer incidence rates among Japanese in Hawaii were approximately intermediate between those of the other 2 populations. For the three female reproductive sites, ovarian cancer was affected by migration to the same degree as breast cancer, whereas the geographic differences were larger than the ethnic differences for cervical and endometrial cancers, with migration decreasing risk for cervical cancer, and increasing risk for endometrial cancer.

Discussion

Based on cancer incidence data in Hawaii and Japan for nearly 40 years, the effect of migration was by far the strongest for esophageal, stomach, and colon cancers. Women also experienced a considerable migration effect for endometrial cancer and non-Hodgkin's lymphoma. Although risks for prostate and breast cancers were not as strongly affected by migration, these cancers added the greatest number of additional cancer cases in Japanese migrants. Lung cancer risk in migrants remained very close to the incidence in Miyagi. Overall, the migration effect appeared greater in men than in women (Table 3), but the rapid increases in breast cancer incidence from 1978–1982 have reduced that difference.

Numerous lifestyle and biological factors have been investigated to understand these rapid changes in cancer risk. Nutritional factors, such as lower intake of salted and other preserved foods and higher intake of fruits and vegetables in combination with refrigeration[21,22] and H. pylori infection,[23,24] are considered to be the major explanations for the stomach cancer trends. Reductions in stomach cancer incidence are expected when the generation exposed to harsh living conditions that favor H. pylori infection is replaced by people with lower infection rates.[24,25] An additional factor that merits further evaluation is identifying the variable that protects women and Okinawan men in Japan, and Okinawan migrants in Hawaii, from the disease.[26]

First generation Japanese migrants to Hawaii already adopted a colon cancer risk similar to that for Caucasians.[27] Although screening efforts for colon cancer have probably contributed to a faster increase in incidence in the United States[28] than in Japan, a positive energy balance as a result of increased caloric intake and reduced physical activity levels,[21,29,30] high meat consumption,[31] and, especially, exposure to pyrolysis products through consumption of well-done meat,[32] have been associated with the disease. The declining cereal consumption in Japan[33] has also been considered as a possible cause. Therefore, the rising colon cancer incidence among Japanese in both locations is probably a consequence of common lifestyle changes.

Despite heavy smoking among Japanese men in Hawaii and in Japan[19,20] lung cancer incidence for Japanese smokers was significantly lower than in

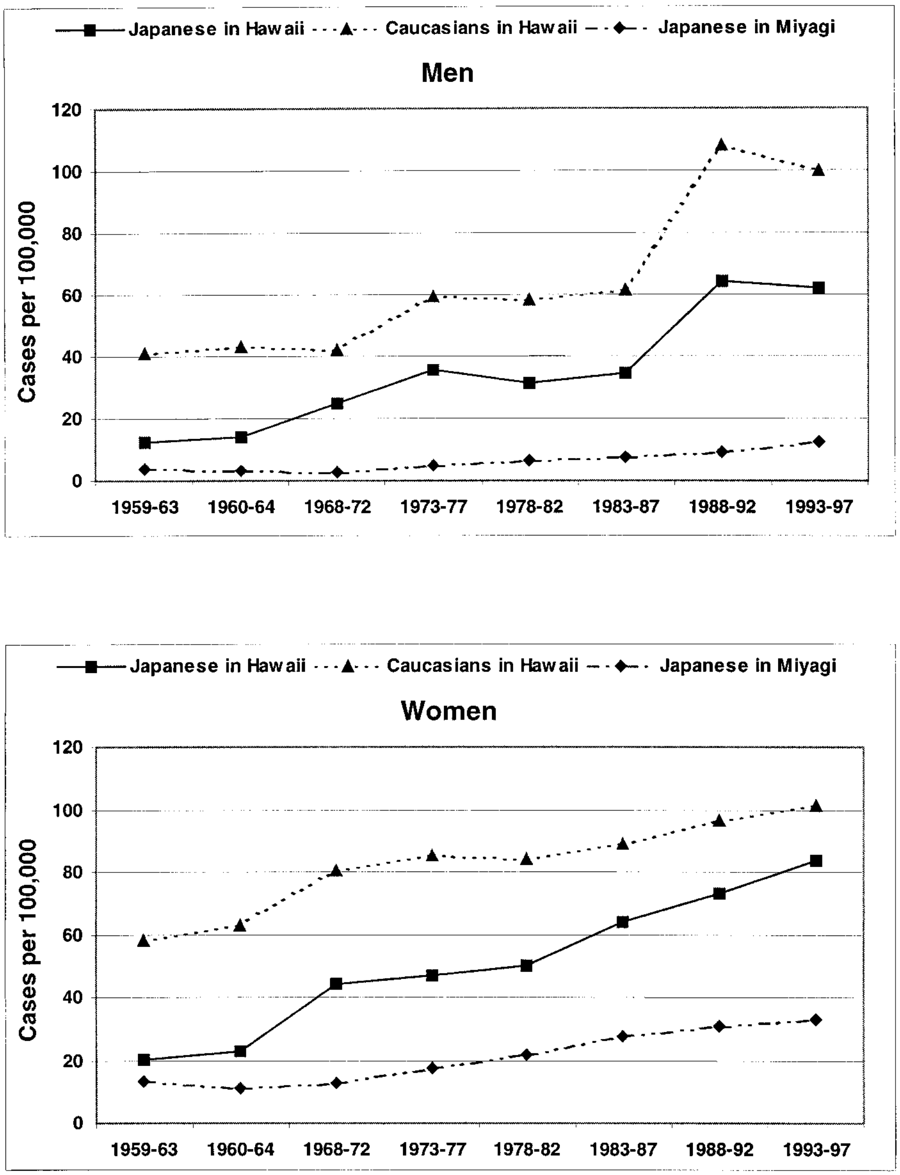

Fig 5. Prostate/breast cancer incidence in three populations[8–15]

Overall, the migration effect appeared greater in men than in women, but the rapid increases in breast cancer incidence from 1978–1982 have reduced that difference.

Caucasians, a phenomenon that has been observed repeatedly. In Hawaii, Caucasian male smokers were at 46% greater risk for lung cancer than Japanese, after adjusting for pack-years of smoking, occupation, education, and age.[34] In a Japanese case-control study,[35] the magnitude of relative risks was substantially lower than in the US or European countries. Genetic polymorphisms in detoxifying enzymes are being investigated as a possible explanation of some of these ethnic difference.[36]

For hormonally related cancers, the dramatic increase during the 1980s is related to increased early detection efforts in Hawaii: testing for Prostate Specific Antigen,[37] and mammography screening.[18] Based on an ecological hypothesis, the trends of prostate and breast cancer have been examined in relation to soy consumption,[38] but the attributable risk is probably small. In contrast to colon cancer, for which risk reaches or exceeds the Caucasian risk in the first generation,[3] the rise in incidence for hormonally related cancers was very gradual and took several generations to manifest. Breast cancer rates doubled among first generation migrants in comparison to Japan, and rates tripled during the second generation.[27] As shown in a multi-ethnic cohort, breast cancer incidence among Japanese American women now equals the risk of Caucasian women.[39] These observations, combined with the increasing breast cancer trends in Japan,[40] suggest that it takes 2 or 3 generations for migrants to adopt the risk of the host country, and that some protective etiologic factors may act during childhood or adolescence. Compared to breast cancer, the incidence of prostate cancer has increased very little in Japan. Although early detection bias due to the PSA screening efforts is likely to account for a large proportion of the additional cases,[37] a comparison of prostate mortality rates between Japan and the United States in 1996 still demonstrated a 3-fold difference.[1] The huge difference in esophageal cancer rates between the 2 locations may be a result of high alcohol consumption among men in Japan.[19,21] The higher risk for endometrial cancer in Hawaii is likely related to higher body weight and dietary factors,[41] whereas the significant elevations during the 1970s have been attributed to the unopposed estrogen use for menopausal symptoms.[42]

This analysis has some limitations related to the comparability of the data.

Under-reporting of cases is a serious concern for disease registries. Whereas the case ascertainment in Hawaii has been virtually complete,[43] a substantial number of cancers in Miyagi were identified by death certificate, alone, during the early periods.[8] Another limitation has to do with modifications in coding,[17] which changed over time for some cancers (Table 1). However, only the revised definition of lung cancer in Volume IV, when the small number of pleural cancers were separated, would have affected the incidence rates. Nevertheless, we are convinced that the incidence trends reflect true differences in disease risk between the 3 populations, although the magnitude of the differences may not be quite accurate, due to differences in reporting and screening. Mortality data, which are less likely to be biased by early detection, support the varying incidence rates.[1] In 1996, stomach cancer mortality was approximately 6-fold greater in Japan than in the United States (31.2 vs 4.5 for men, respectively, and 13.8 vs 2.3 for women, respectively); whereas, mortality from colon cancer differed little by country (17.6 vs 15.9 for men, respectively, and 11.0 vs 12.0 for women, respectively). In agreement with the incidence rates, lung cancer mortality among men was half as high in Japan as in the United States (33.1 vs 53.2, respectively), and one third as high in women (9.6 vs 27.2, respectively). For prostate and breast cancers, the 2 cancers most affected by screening, the difference in incidence was considerably greater than the difference in mortality, but the death rates still showed a 3-fold difference for US vs. Japan (5.5 vs 17.9, respectively, for prostate cancer, and 7.7 vs 21.2, respectively, for breast cancer).

The ecological observations of this analysis provide insight into cancer incidence among migrants, and suggest future directions for research. Despite much progress in etiologic cancer research, a large proportion of risk remains unexplained.[44,45] In the not so distant future, we will not be able to observe much difference in risk between Japanese migrants and the Caucasian population in the United States. Adoption of a Western lifestyle has made a great impact on cancer incidence among migrants, and even in Japan, itself, where cancer incidence rates are approaching those of the United States, as the country has become increasingly Westernized. Colon cancer incidence provides the strongest example of this trend. The interesting research questions in migrants need to be investigated before these unique opportunities disappear. Studies that can include generational analysis will be especially important, as they may be able to generate new hypotheses and determine which aspects of traditional life may have protected Japanese from colon, prostate, and breast cancers. The ultimate goal would be to translate these new ideas into future prevention strategies that could benefit high-risk populations.

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AUTHOR CONTRIBUTION

Design and concept of study: Maskarinec
Acquisition of data: Maskarinec, Noh
Data analysis and interpretation: Maskarinec, Noh
Manuscript draft: Maskarinec, Noh
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