

Cancer Epidemiology in Populations of the United States—with Emphasis on Hawaii and California—and Japan¹

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Summary

The population of California and the San Francisco Bay Area has a number of ethnic components that differ in the frequency with which certain cancers occur. Mortality rates for California Japanese and incidence data from the cancer reporting system of the Bay Area are analyzed for the cancer sites considered related to nutrition. The American Japanese of California are particularly amenable to epidemiological study because of the cancer data available from Japan for comparison with that of the California Japanese. The cancer rates occurring among the successive generations of the Japanese in California are compared to the rates in Japan and the white rates for the Bay Area. Gastric cancer rates undergo a stepwise reduction from the high rates in Japan to the intermediate rates of immigrant Japanese and the lower rates for the American born. Colon cancer rates are increased about equally in both generations of Japanese and are approaching the white rates. Cancers of the breast, uterine corpus, and ovary in women and the prostate for men are rapidly approaching the rates for the white population. Etiologies are continually being identified or indicated for a number of these cancers by epidemiological studies, and more specific identification of carcinogenic mechanisms should be possible by other disciplines.

The purpose of this conference is to consider the role of nutrition in the causation of cancer. This is a subject of obvious importance. However, to paraphrase Mark Twain's comment concerning the weather, as epidemiologists we like to talk about the relationship between nutrition and cancer but no one does much about it. If we accept the premise that much of cancer can be ascribed to our environment, we have to recognize that we encounter our environment largely through our skin, our respiratory tract, and our alimentary tract. I presume we shun the last-named environmental exposure route because of the complexity it presents. Defining adverse environmental exposures for the skin and respiratory tract presents no great problem, but this is not true for the alimentary tract. The food and water we consume provide vehicles for a wide range of non-nutrient chemicals used in the processing and preserving of nutrients, as a route for the many drugs taken for medicinal and other

reasons, and the inadvertent contaminations that may occur in food production and handling. In addition to the vehicular role of alimentation, there is presumptive evidence that the normal constituents of diet may play a carcinogenic role through metabolites or indirectly through influencing the endocrine milieu. Given the carcinogenic potentialities of both normal and abnormal constituents of nutrition, the difficulty in conversion of food constituents to qualitative and quantitative measurements and the need to have historical information for the time when carcinogenesis is presumed to have been initiated should explain the reluctance of epidemiologists to invade this field of work.

"Natural experiments" have developed in which dietary changes have occurred among populations of people with concomitant changes in cancer occurrence for specific tissue sites. These experiments have served to select between competing genetic and environmental hypotheses as explanations of regional population differences. The United States has been the setting for many of these experiments, and we are all familiar with the leading role of Bill Haenszel of the National Cancer Institute in determining the cancer experience of the many migrant populations as they become fused into the United States culture and way of life.

California provides points of entry for a large portion of the Asiatic migrant populations. It has also attracted sizeable Mexican American and southern black populations seeking improved economic opportunities that are lacking in the areas of their birth.

In Table 1, incidence rates for all sites and for certain sites of cancer for the 5 countries of the San Francisco Bay Area (Table 1, Footnote *b*) are presented. The sites were chosen for their possible relationship to digestion and nutrition. It may come as a surprise to see that black males exceed all population groups for total cancer. Census underenumeration may be responsible for some of the excess of total cancer, but the excesses of specific cancer sites can be shown to be real by examining the site distribution in age-specific groups. The excesses of black males are most pronounced for esophagus, stomach, and pancreas as digestive organs. The excess for prostate is also pronounced and included here as an endocrine-dependent organ. The white population otherwise leads all populations in total cancer occurrence. For the oriental populations, the Chinese exceed the Japanese for total cancer.

For specific cancer sites, the nasopharynx is included to show that it persists as a remarkable excess for Chinese that has so far defied explanation and has been under study by Dr. Brian Henderson of the University of Southern Califor-

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Table 1
Average annual age-adjusted cancer incidence rates^a for selected sites in the San Francisco-Oakland standard metropolitan statistical area^b for the years 1969-1973

Site	White		Black		Chinese		Japanese	
	Male	Female	Male	Female	Male	Female	Male	Female
All cancer	336.1	306.4	390.4	258.4	292.8	231.6	157.5	187.2
Nasopharynx	0.8	0.4	1.2	0.4 ^c	21.8	7.4	1.0 ^c	0.0
Esophagus	4.5	2.2	17.0	4.1	10.8	2.2 ^c	2.8 ^c	2.2 ^c
Stomach	13.6	6.9	25.6	7.7	14.0	12.0	19.8	23.7
Colon	32.7	27.3	28.1	23.8	27.5	15.9	16.0	22.5
Rectum and anus	11.7	10.5	12.4	9.0	22.3	10.8	19.9	8.3
Liver	3.2	1.5	5.0	1.6	23.5	5.5	0.0	1.6 ^c
Pancreas	11.1	7.1	17.5	10.3	10.6	5.9	6.8 ^c	7.1 ^c
Breast	0.8	88.7	1.5	64.5	0.4	49.1	0.0	44.1
Corpus		33.6		15.1		17.9		15.9
Ovary		15.1		10.2		7.3		6.0
Prostate	51.6		89.9		20.5		20.7	

^a Rates/100,000.

^b Counties included: San Francisco, San Mateo, Marin, Alameda, and Contra Costa.

^c Based on 5 cases or less.

nia and the late Phil Buell of our staff. Esophageal cancer is excessive among Chinese males along with black males, as mentioned earlier. Gastric cancer, which leads all other cancer sites among men in Japan and has the usual male:female sex ratio of nearly 2:1 (4), does not differentiate between the sexes in our incidence data. This had previously been found for the American-born Japanese (Nisei) from statewide mortality data, which reflected a reduction in the male rates without a similar change in the female rates (2). The surprising finding is that black males have the highest gastric cancer rate, exceeding the Japanese male rate in the San Francisco Bay Area. This excess seems to be peculiar to the black male, since the rate for black women is about the same as for white women and less than that for either Japanese or Chinese women.

Before considering cancer of the large bowel, attention should be drawn to the large excess of liver cancer among Chinese males. This excess, to a lesser extent, also applies to Chinese women as compared to other women of the Bay Area. These excesses are limited to hepatocellular cancers and do not extend to those of the gallbladder and bile ducts.

Cancer of the pancreas, as pointed out before, is another site for which there is a considerable excess among black males, which seems to be true as well for black women when compared to other women.

One of the cancer sites most responsive to new environmental surroundings experienced by migrant populations is cancer of the colon. In Japan the rate for colon cancer is roughly one-tenth of that for stomach cancer. The San Francisco Bay Area incidence data indicate the rates for these 2 sites among Japanese are nearly the same, and the female colon cancer rate exceeds that for men. This Japanese female excess had been found earlier in California mortality data (5).

In Table 2, incidence rates for colon and colon plus rectum from the Third National Cancer Survey for 1969 are shown for blacks and whites by region of the United States. Both blacks and whites of the south have lower rates than for the other regions. The western cities have attracted large segments of their growing populations from the middle-western and eastern parts of the United States. The colon cancer rates for the white population most closely

Table 2
Age-adjusted incidence rates^a for colon cancer and colon cancer plus rectum from the Third National Cancer Survey^b for the north, south, and west regions by race and sex, 1969

Area ^c	White				Negro			
	Males		Females		Males		Females	
	Colon ^d	Colon and rectum	Colon	Colon and rectum	Colon	Colon and rectum	Colon	Colon and rectum
North	34.5	52.7	30.8	42.4	34.5	53.3	30.5	43.2
South	28.5	41.3	26.0	34.7	23.5	30.8	22.7	30.3
West	37.3	55.4	30.8	42.3	21.2	34.7	20.5	27.8

^a Rates/100,000 and adjusted to 1970 United States population.

^b Preliminary Report, Third National Cancer Survey, 1969 Incidence, Biometry Branch, National Cancer Institute.

^c North, Detroit, Iowa, Minneapolis-St. Paul, Pittsburgh; South, Atlanta, Birmingham, Dallas-Ft. Worth; West, Denver, San Francisco-Oakland.

^d Colon excludes rectosigmoid; rectum includes rectosigmoid.

matches that for northern whites. For the blacks, the colon cancer rates are more comparable to those of the southern blacks. The data for northern blacks are nearly identical to those of northern whites. Since three-fourths of blacks in the San Francisco Bay area were born in the south, it is expected that their colon cancer rates will increase with time to reach the white rates, as has already happened in the northern areas. The Kaiser Foundation Research Institute has a case-control study underway to determine dietary differences between black colon cancer patients and controls in the Bay Area. A collaborative study is being carried on at the same time in Atlanta.

Of the Asiatic populations of California, the 1 that is most amenable to epidemiological study is the Japanese. This is largely because there are reasonably good data for the Japanese in Japan for comparison with the immigrant Japanese American population and their progeny, along with other components of the United States population. The well-known contrasts between the Japanese of Japan and the American white population are: high gastric cancer rates in Japan; low colon cancer rates in Japan; low rates for cancers of the breast, uterine corpus, and ovary among Japanese women; and low prostatic cancer rates among Japanese men. These are the cancer sites most likely to be related directly or indirectly to nutrition.

The gastric cancer rates exceed by far those of any other site for both sexes in Japan. Intuitively, one would feel this must be related to carcinogenic action of something ingested, since the stomach is the organ of initial and prolonged exposure to the environmental components of nutrition. The possibility of achlorhydria as a precursor of cancer was not supported from general population findings among Japanese of California (6). Pernicious anemia as a precursor disease and the higher frequency of blood group A among Japanese and its association with gastric cancer cannot explain more than a small fraction of the high gastric cancer rate among the Japanese of Japan. The recent publication by Haenszel *et al.* (9), based on a dietary study of Japanese in Hawaii and in Japan, quite convincingly incriminates pickled vegetables and dried, salted fish as the important constituents of the traditional Japanese diet related to the occurrence of gastric cancer. This is supported by observations of gastric mucosal damage from pickled vegetables (10).

Colon and gastric cancer incidence rates often have reciprocal relationships in various populations. This is true for the Japanese in Japan, and among American Japanese the reduction in gastric cancer rates is accompanied by a rise in colon cancer rates. Haenszel *et al.* (7) have recently published a companion study to the gastric cancer study indicating that colon cancer in Hawaiian Japanese is related to the consumption of meat and legumes, with beef and string beans being the leading representatives of these food items.

The very low breast cancer rate for Japanese women in Japan has always been of interest as possibly harboring an answer to the question of why this is the most frequent cancer of women in the United States. The work of MacMahon *et al.* (11), demonstrating the differences in the estrogen profiles of Japanese and American women,

particularly in younger women, and the recent report of the shifting of the profile toward that of Caucasian women in Hawaiian Oriental women (3), suggests the possible role of dietary change mediated through hormonal changes.

Prostatic cancer as a clinical disease occurs very infrequently among Japanese men in Japan as compared to men in the United States. However, the finding of latent disease in the histopathological examination of prostatic glands of Japanese men in Japan and men in the United States do not differ markedly. A histopathological study of prostatic glands of Japanese men of Hawaii and Japan found proliferative activity of latent cancers more frequent in Hawaii (1). This is compatible with the increase in mortality from prostatic cancer found in American Japanese as compared to those in Japan (2, 8).

In the light of what has been presented, the cancer experience of California Japanese will now be considered. In Chart 1, the population of Japanese in California at the time of the 1970 census is presented by age, sex, and place of birth. The distribution by place of birth is based on a 1% sample of the population. At this time 77% of the Japanese are American born and 23% are foreign born. The male and female American born are about equal numerically, and all but 3 to 4% are still under age 60. On the other hand, the foreign-born segment (Issei) of the Japanese population is two-thirds female and one-third male. The excess of females is almost completely accounted for by those ranging in age from their 20's to their 50's, with the largest proportion in the 35- to 44-year age bracket. These women are predominantly identified with marriages to American men serving assignments in Japan and elsewhere. In the present context they would be quite different from Issei immigrants of the past as to degree and rate of acculturation.

Aside from the excess of Issei females just discussed, the numbers of Issei males and females are comparable over the younger and older ages. The California Japanese population over age 60 is composed of two-thirds Issei in both sexes.

Mortality Rates

The age-specific gastric cancer mortality rates for California Japanese for the period 1968 through 1972 are shown

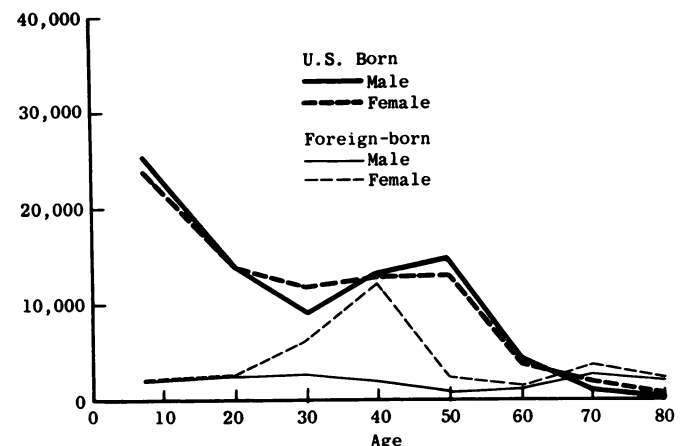


Chart 1. California Japanese by age, sex, and nativity in 1970.

in Chart 2. The rates for Japanese males and females in Okayama Prefecture of Japan for the years 1963 to 1967 are also presented for comparison. It is readily apparent that the gastric cancer mortality rates have undergone a stepwise reduction, 1st in the Issei or immigrant population and a 2nd further reduction in their progeny. The male and female components of the latter have quite comparable rates through age 60. The small proportion of the American-born Japanese population beyond age 60 makes the rates for older ages very unstable. The age-adjusted gastric cancer incidence rates among the San Francisco Bay Area Japanese males and females show no significant differences, indicating that there has been a greater reduction in male rates than in females (Table 1). If this were true, then Chart 2 suggests that this has taken place primarily in the American-born population. This question will be considered further with incidence data.

In Chart 3, the age-specific mortality rates for cancer of the colon by sex and nativity are shown for the California Japanese population. Cancer of this site occurs at a low frequency in Japan. From Chart 3 it is apparent that the stepwise reductions seen for gastric cancer in successive generations are not repeated by stepwise generation increases for colon cancer. In fact, the rates are higher for the immigrant than for the American-born Japanese, although this is more likely attributable to the small numbers, particularly for the Nisei population over age 60. In any case, no conditioning protective effect is evident for the earlier years of life spent in Japan in connection with colon cancer, such as the opposite susceptibility effect that seems to be the case with cancer of the stomach.

Incidence Data

In Table 1, age-adjusted incidence rates were given for the Japanese males and females of the San Francisco Bay Area in comparison with other ethnic groups for cancer sites considered to have some relationship to nutrition in its broadest sense. Unfortunately, the Japan incidence data cannot be examined by nativity because we do not have this information routinely available for cases. However, from the nativity data for the Japanese population of California, we know that the population under age 60 is predominantly American born, whereas over age 60 the Japanese population is two-thirds foreign born. The incidence cases developing during the 5 years from 1969 to 1973 will be examined first in comparison to the expected cases if the Japanese population of the Bay Area were experiencing the age-specific cancer rates of the white population of this area, and also with the rates for the Prefecture of Okayama, Japan.

In Table 3, the observed number of cases of various cancer sites occurring among Japanese males and females of the San Francisco Bay Area are compared to the expected numbers of cases if the rates for the white population of the area and those for Okayama were experienced. Gastric cancer cases for males were only one-fourth as frequent as Okayama rates would predict and only two-thirds greater than would be expected using white rates. Japanese females

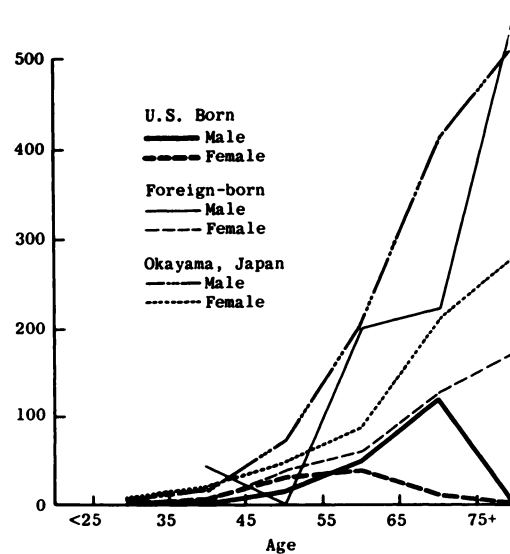


Chart 2. Cancer of the stomach mortality rates/100,000 for California Japanese in 1968 to 1972 and for Okayama, Japan, in 1963 to 1967 by age and sex, and by nativity for California Japanese.

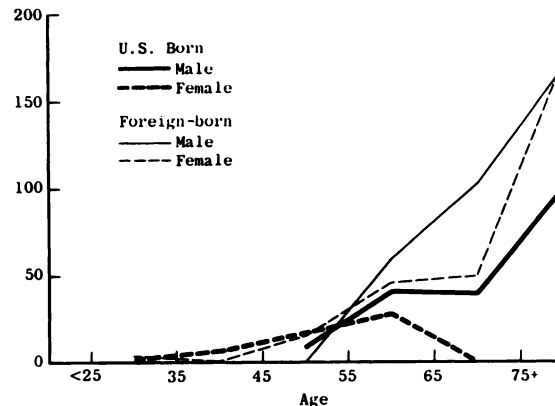


Chart 3. Mortality rates for cancer of the colon per 100,000 for California Japanese by sex and nativity.

had 3 times as many gastric cancers as would be expected with white rates and 40% of the number expected from Okayama rates. These findings are consistent with the previous observation that male Japanese gastric cancer rates are reduced to a greater extent than are the rates for females among American Japanese, when compared to Japanese rates in Japan. In Table 1, it was seen that the usual sex difference in that rate for this site has disappeared in the Bay Area Japanese population.

For colon cancer both males and females have 3 to 4 times the number of cases that Okayama rates would predict. Females have 80% of the number of cases that would make them comparable to white females and Japanese males a little over one-half of that for white males. Cancers of the rectum and anus are about twice the number Okayama rates would provide, and there appears to be no deficiency as compared to whites.

Among women, more than 3 times the number of cancers of the breast occurred than would have been expected with Okayama rates and 57% of the cases that would have

resulted from rates for white women. Similarly, for cancers of the ovary and uterine corpus there are about one-half of the cases that would result from rates for white women, and 6 times the number of ovarian cancers and 3.5 times the number of uterine corpus cancers predicted from Okayama rates. Similarly, for prostatic cancer in males there are one-half of the cases that would be expected from white rates but over 5 times the cases that Okayama rates predict.

In Table 4, the observed cases of the various cancer sites in Table 3 are divided between those occurring among Japanese men and women of the Bay Area before age 60 and for those that age and older. The expected cases using rates for the white population of the area are presented for comparison. Again, it should be pointed out that the

Japanese younger than 60 years are predominantly American born, while those 60 and older are largely Issei.

For males under age 60, the gastric cancers observed are one-third more than expected, while older males had almost twice the number expected from white rates. Females under age 60 had twice as many gastric cancers as rates for white women would predict and over 3 times the number among those 60 years and older. Again, Japanese male rates are proportionately nearer to white male rates than Japanese women are to the rates for white women.

The observed cases of colon cancer for Japanese under age 60 are very close to the expected number from white rates for both men and women. For those 60 years and older, this is close to being true for females, but males have

Table 3
Observed cancer cases of indicated sites among Japanese of the San Francisco-Oakland SMSA,^a 1969-1973, compared to expected cases using age-specific rates of Okayama, Japan and white population of the San Francisco-Oakland SMSA

Cancer site	Japanese observed cases	Expected cases; Okayama ^b age-specific rates	Expected cases; San Francisco-Oakland SMSA white age-specific rates ^c
<i>Males</i>			
Stomach	15	63.3	9.0
Colon	11	3.2	20.3
Rectum and anus	13	5.3	10.8
Prostate	16	3.0	33.1
<i>Females</i>			
Stomach	18	45.0	6.2
Colon	19	4.6	23.4
Rectum and anus	7	4.8	9.7
Breast	47	13.5	82.1
Uterine corpus	13	2.2	26.1
Ovary	6	1.8	13.2

^a SMSA, standard metropolitan statistical area.

^b Ref. 4, pp. 208, 209.

^c San Francisco Bay Area Resource for Cancer Epidemiology.

Table 4
Observed and expected cancers of certain sites among Japanese of the San Francisco-Oakland SMSA,^a 1969-1973

Cancer site	Ages < 60		Ages 60+	
	Observed	Expected ^b	Observed	Expected ^b
<i>Males</i>				
Stomach	3	2.3	12	6.7
Colon	4	5.2	7	15.1
Rectum and anus	4	3.2	9	7.6
Prostate	2	2.7	14	30.4
<i>Females</i>				
Stomach	4	1.8	14	4.4
Colon	6	6.8	13	16.5
Rectum and anus	3	3.3	4	9.7
Breast	41	55.7	6	26.4
Corpus uteri	11	15.6	2	10.4
Ovary	5	9.4	1	3.8

^a SMSA, standard metropolitan statistical area.

^b Expected number computed using age-specific white rates for San Francisco-Oakland SMSA 1969-73.

one-half of the expected number. Cancers of the rectum and anus are not deficient for Japanese people compared to white, with the possible exception of older women.

Women under age 60 had three-fourths of the expected number of breast cancers that white rates would predict, 71% of the cancers of the uterine corpus, and a little over one-half of the ovarian cancers. For those 60 years and older, these proportions are 23, 19, and 26%, respectively. This indicates that the American-born Japanese are approaching the white population in the frequency of occurrence of cancer in these sex organs. Similarly, for prostatic cancer among men, Japanese men under age 60 have nearly three-fourths of the expected cases from white rates and almost one-half of the number expected for men 60 years and older.

Conclusions

The Japanese are a particularly interesting population to study for cancer occurrence because of the strikingly different diet in Japan as compared to the United States. The comparability of the available data in Japan with those in the United States and the opportunity this provides for comparing the Japanese in their homeland with those migrants who have adopted the United States as their new homeland show some remarkable results. The shifting of emphasis of gastrointestinal cancer from stomach to colon and the remarkable increases in breast, uterine corpus, and ovarian cancer in women and prostatic cancer in men from the low rates in Japan toward those indigenous in the United States has to have explanations waiting for elucidation. Progress has been made in the epidemiological studies referred to, and now it should be possible to identify more specifically the chemical, biological, and endocrinological

mechanisms that may be involved in the carcinogenic process.

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