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A Systematic Survey of Breast Cancer Incidence in the Département of Rhône, France

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A systematic survey of all centres of diagnosis and care of breast cancer patients in the Rhône "département" of France was carried out to evaluate, for the year 1985, the incidence rate of breast cancer in an urban, industrialised part of France not covered by a cancer registry. Two hundred and fifty seven institutions or individuals were involved, covering the public and private sectors in the Rhône département, but also in neighbouring cities and elsewhere in France, which also enabled a search to be carried out for cases diagnosed or treated outside the département. Altogether, over this 1-year period, 801 new cases were identified (791 women and 10 men). This study demonstrated a high incidence of female breast cancer (80.5 new cases per 100 000 woman-years, standardised to the world population) which was particularly marked among women aged 40–60. This incidence is higher than that described by the cancer registry of the neighbouring département of Isère, but is close to the incidence found in Geneva. Results also concur with the relatively high mortality rate from breast cancer observed in the Rhône département.
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INTRODUCTION

DESCRIPTIVE EPIDEMIOLOGY, the aim of which is to describe the occurrence of diseases in populations and subgroups, often provides the first clues which lead to aetiological research. In Europe, France is divided from an administrative and geopolitical point of view into "départements".

The Rhône département, mostly urban and highly industrialised, is situated in the northern part of the south-east region, close to the Swiss border, and is centered around Lyon. Statistics and maps of cancer mortality in France, published regularly by the INSERM [1–3] indicate only limited variations of rates among départements with higher rates in the most urbanised parts of France, particularly around Paris and Lyon [2]. In contrast, we have only sparse information on cancer incidence. Population-based cancer registries are recent and only exist in a limited number of départements, therefore not providing national coverage.

As breast cancer is the leading cancer site in women [4, 5] in most European countries and shows some tendency to increase over time [3], it was decided to collect information on breast cancer occurrence in the Rhône, in order to quantify it and obtain a good picture of the disease. This study was also considered necessary for the assessment of the feasibility of setting up a site-specific or all sites cancer registry in this part of France. An additional motivation was to obtain a baseline measure of disease incidence and stage distribution which could be used in the future, along with continuous monitoring of changes in breast cancer mortality rates as well as in the stage-specific incidence rates, for evaluating the impact of a cancer screening programme which was due to be launched in 1987.

PATIENTS AND METHODS

The goal of the study was to identify and collect standardised information on all incident cases of breast cancer diagnosed between 1 January 1985 and 31 December 1985 among the resident population of the Rhône département. In the absence of a cancer registry, this was done by surveying all providers of medical care who may encounter breast cancer cases for diagnosis, treatment or other reasons, such as administrative or insurance purposes. After consultation with key individuals, groups of specialists prepared lists of surgeons, clinicians, pathologists, radiotherapists and chemotherapists and Social Security doctors who were connected in any way with breast cancer. These lists were later checked and compared with those of appropriate medical and scientific societies in order to avoid any omissions. In addition, all diagnostic and treatment institutions were approached. Altogether 257 providers of care were contacted: those in the public and private sectors of health care, specialised cancer institutions or general hospitals, from the small rural hospitals to the largest university hospital in Lyon. This survey also included the institutions and clinicians of the neighbouring cities of the adjacent départements. Finally, information could be made available on subjects, residing in the Rhône but treated in other parts of France via the French Social Security system.

Data collection

After the necessary authorisations had been granted, data collection began in September 1986 and ended in March 1988. Letters were sent to the heads of hospitals and health institutions

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and then to all individual doctors accompanied by a brief document describing the methods to be used for the conduct of the study, including a sample record form and listing the scientists involved. Permission was sought from the doctors for access to patients' records. In those cases where no reply was received, a second letter was sent after a 4-month delay, followed 2 months later by a telephone contact.

Record form

The record form comprised three parts: the first aimed at identifying the patient with cancer, and included social security number, which in France contains information on sex, year, month and place of birth as well as a unique identifier; the second described the subject (record number, sex, date and place of birth, address) and contained some information for characterisation of the data source (date and place of diagnosis, place(s) of treatment and health insurance) and finally the third described the tumour itself (diagnosis, laterality, site, histocytology, stage, size, nodes). In compliance with the rather stringent French confidentiality regulations, data of a nominal nature or which could be linked to an individual were not entered on the computer and were only temporarily manipulated by two of us (A.J.S. and M.O. C.-L.) under strict control.

Data abstraction and codification

The data were abstracted from the original clinical, radiological, pathological and administrative records, and transcribed on a standardised form. This work was always carried out by a doctor, in the vast majority of cases by one of us (M.O.C.-L.). In less than 5% of the cases, the data forms were filled in by the doctors who had been treating the patients. For some variables, the information was recorded as originally presented. The description by the individual pathologists was later recoded for all the cases according to the WHO classification, under the supervision of a certified pathologist, the Head of Pathology at the Regional Cancer Institute (B.F.). A similar procedure was applied for the staging of tumours.

Data preparation and analysis

The first step was to eliminate multiple entries for a given patient. For most subjects in the data base, two to three sources had been used, the most frequent being clinical and pathological records, in addition to information of an administrative nature. The elimination of multiple entries per individual was mainly done by hand, using the identification data. Later on, control by computer runs on the data entered, such as date and place of birth, was also carried out.

Statistical analyses were performed using Minitab [6] and SPSS [7]. Descriptive statistics included computation of mean, median and percentiles. Standardisation was done by the direct method. Analysis of variance and Mann–Whitney test were used.

RESULTS

Number of breast cancer cases

The total number of incident cases of breast cancer occurring in the resident population of the Rhône département between 1 January 1985 and 31 December 1985 was 801. This number did not include prevalent or recurrent cases, nor cases diagnosed in the Rhône but occurring in persons who are not resident in the département, yet it included cases in women living in the Rhône, but diagnosed outside.

Table 1. Female breast cancer cases and incidence rates by age-group in the Rhône in 1985

Age-group (years)	Number of incident cases	Incidence rate (per 100 000 woman-years)
20–24	3	4.8
25–29	5	8.5
30–34	10	18.0
35–39	41	73.3
40–44	79	186.7
45–49	84	208.8
50–54	101	236.2
55–59	101	244.4
60–64	92	253.9
65–69	47	245.5
70–74	87	304.7
75+	141	252.2
Total	791	105.9

Age and sex distribution

The 801 cases comprised 791 women and 10 men. The age structure is given in Table 1. For women, the youngest case was 22 years old, the oldest 95; the median age at diagnosis was 58.0 and the mean 59.2. For men, the youngest case was 53 years old, the oldest 82, the median age was 67.0 and the mean 67.8. Among women, the largest proportion of the total number of cases (25.4%) came from the 50 to 59 year age-group. Over half of the cases were diagnosed before the age of 60.

The results discussed below only refer to women.

Breast cancer incidence

The incidence rate of breast cancer was computed using the total number of incident cases diagnosed in 1985 in the resident population of the Rhône. The population at risk was taken as the total resident population of the Rhône for 1985. The size of the population was 1444702 in the census conducted by the National Institute of Statistics and Economic Studies [8] in 1982. The estimation of the figures for the year 1985 took into account the national changes in the population (births and deaths) as well as immigration and emigration, using the Prudent model [9]. For women, we had 791 cases diagnosed among 746870 women, for a crude incidence rate of 105.9 cases per 100000 woman-years. The age-specific incidence rates are shown in Fig. 1 and Table 1. Rates were higher in Lyon (128.6 cases per 100000 woman-years) than in the rural part of the Rhône (84.5 cases per 100000).

Age-standardised rates were computed by the direct method [10]; for women, they are 108.0 cases per 100000 woman-years (European standard) and 80.5 per 100000 (World standard). Computation of age-adjusted rates was also done separately for left and right breasts for women with unilateral tumours. The rate is higher for left (78.6 per 100000 left breasts) than for right breast (73.7 per 100000 right breasts).

Place of origin

The country of birth was known for 624 women (78.9%). The vast majority (88%) were born in France. Other countries of birth with more than 1% of cases were Algeria (3.7%), Italy (1.9%), Spain (1.8%) and Tunisia (1.4%). Among the 549 women born in France, half (50.6%) were born in the Rhône

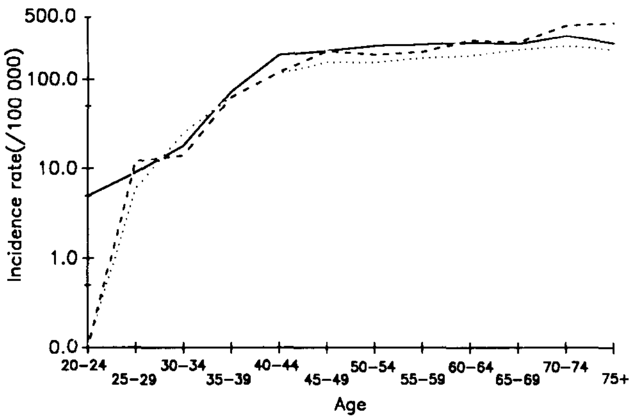

Fig. 1. Age-specific incidence rate of female breast cancer in the Rhône and two neighbouring cancer registries. —— Rhône, ···· Isère, --- Geneva.

département and an additional 23.8% were born in the neighbouring départements.

Treatment institutions

The place of treatment was known for all patients and totalled 50 institutions (39 private clinics, 10 public hospitals and one regional cancer institute) in the Rhône (out of a total of 57 treatment institutions surveyed). In the majority of cases (436 cases or 55.1%) treatment took place in a private institution. The regional specialised cancer centre treated 103 incident cases (13.0%), and the public hospitals 235 (29.7%), the vast majority of these being cared for in large university hospitals situated in Lyon (203 cases or 25.7%) and only a limited number in rural or small urban hospitals located in other cities of the Rhône. Finally, 17 cases (2.1%) were treated in other parts of France. The number of new cases seen by a given institution varied from a minimum of 1 to a maximum of 126. Patients' characteristics were examined according to place of treatment. The only significant difference concerned age, with the youngest patients being treated more frequently in the specialised cancer institute (mean age: 54.9 years).

Order of cancer

For 29 cases (3.7%), cancer represented a second occurrence of breast cancer. For 27 cases, the year of first diagnosis of breast cancer was known and varied from 1942 to 1984. For 29.6% of cases, it was 1980 or later.

Circumstances of diagnosis

Whereas a mammography had been performed on 654 women (82.7%), the reason for carrying out this examination was labelled as screening (carried out in the absence of any suspicious clinical symptom) in only 3.2% of all breast cancer cases. The delay between mammography and final diagnosis was known for 569 women and for 82.1% was less than 2 months. The longest period was 18 months, the shortest was less than a week and the median interval was 1 month.

Tumours discovered by screening mammography were compared to cases having had a diagnostic mammography. Comparisons of medians were carried out using the Mann-Whitney test and were found significant at the 0.05 level for age (55-years-old for screening vs. 57 for diagnostic mammography) and for the largest diameter of the tumour, either for radiological size (12.5 mm vs. 22) or for macroscopical size of the tumour on surgical piece (15 mm vs. 20 mm). Therefore, tumours are found by screening mammography at an earlier age and tend to be smaller.

Description of the tumour

Laterality of the tumour was known for 789 women (99.7%). There was no strong preponderance of either left (48.9%) or right (49.8%) breast. Bilateral cases represented 1.3% of cases. The precise localisation within the breast was known for 761 cases (96.2%) and results are presented in Fig. 2.

Staging of the tumour

Staging according to the TNM classification [11] was available for 690 women (87.2%). For the vast majority, 497 women (72.0%), clinical staging had been carried out and was reported prior to any intervention. For 153 cases (22.2%), only surgical TNM was given and in 40 cases, although a TNM was reported, its mode of determination was unknown. Both clinical and surgical TNM were given for 7.7% of the cases. Complete TNM were only available for 404 women (51.1%). Values of tumour (T) were given for 690 (87.2%), nodes (N) for 652 (82.4%) and metastases (M) for only 420 (53.1%). Results are presented in Table 2.

Histocytology

The histological types of breast cancer are presented in Table 3. Carcinomas were largely predominant (97.6%) and non-epithelial tumours were rare (0.8%). Carcinomas were classified according to the major component of the tumour and combined forms were seldom notified (14 cases). Infiltrating duct carcinoma was the most frequent invasive mammary cancer (79.0%) in women and the only type of male breast cancer, whereas lobular carcinoma represented only 6.4% of women's tumours. Tumours found at histology as being non-infiltrating carcinomas were included in this survey (4.3%). They were represented by 31 *in situ* carcinomas and 3 cases of Paget's disease of the nipple without any underlying breast tumour. Metastatic tumours in the breast were excluded from this survey. For 13 patients (1.6%), the histology was unknown. Table 4 gives the status of node distribution.

DISCUSSION

Even in the absence of a formal cancer registry, evaluation of the incidence of a disease at a population level can be made. The major determinant of the success of this work was the active participation of all clinicians and medical personnel involved. For the first time it provides direct evidence of a high incidence of breast cancer in a French urban population. Table 5 gives

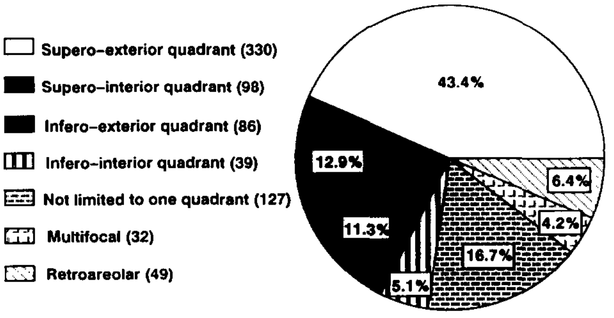

Fig. 2. Tumour localisation within the breast. No. of cases is given in parentheses.

Table 2. Distribution of stage at diagnosis of female breast cancer cases

Stage	Brief description	No.	%
T	extension of tumour	(available for 690 women)	(87.2%)
is *in situ*		14	2.0
0	no palpable breast tumour	9	1.3
1	< 2 cm	204	29.6
2	> 2 cm < 5 cm	312	45.2
3	> 5 cm	66	9.6
4	extension to skin or costal ribs	65	9.4
x	cannot be appreciated	20	2.9
N	regional node involvement	(available for 652 women)	(82.4%)
0	no node involvement	403	61.8
1	mobile homolateral axillary nodes	206	31.6
2	fixed homolateral axillary nodes	27	4.1
3	other nodes involved	9	1.4
x	cannot be appreciated	7	1.1
M	metastasis	(available for 420 women)	(53.1%)
0	no metastasis	386	91.9
1	metastasis	28	6.7
x	cannot be appreciated	6	1.4

crude and age-standardised incidence rates for the Rhône and two neighbouring registries, the Isère in France [12] and Geneva in Switzerland [13]. The age-standardised incidence in the Rhône is much higher than in Isère, but only slightly higher than in Geneva. On a world scale, higher rates are only found in a limited number of registries in the USA, Hawaïi and New Zealand. Our rates are similar to most US rates for white women [5] (Table 6). Age-specific incidence rates for the Rhône, Isère and Geneva are given in Fig. 1. The high rates are especially to be noted among young women. The rates for the 40–59 age-group are among the highest observed in the world, whereas among older women our rates tend to decline, in contrast to some registries such as Geneva or most US registers where they continue to increase [5]. Apparently, this figure cannot be explained by bias or error in the design or conduct of the survey and has been confirmed by other sources. Several potential sources of error were considered. The denominator of the incidence rate provided by the census office is reliable. We explored several sources of error in the numerator. Inclusion of prevalent cases could lead to an increase in the number of reported cases. The month and year of diagnosis (based on date of surgery or date of biopsy for a small minority of cases) were available for all subjects and the exact day was known for 97%. These dates were confronted with dates of mammography and found to be consistent. Unusual dates or delay between mammography and diagnosis were checked from the original records. Variation in the number of cases diagnosed by month was examined to rule out, for example, overdiagnosis in January, which could give an indication of inclusion of cases of the preceding year. The months with the highest number of cases (June: 89, July: 88 and October: 82) may reflect an increased awareness by women of their breasts just before or after the summer period. The lowest number, 38, was for August, and most probably results from the reduced availability of surgeons

Table 3. Histology of female breast cancer

Histological type	No.	%
Carcinoma	772	97.6
Invasive	738	93.3
Ductal carcinoma:	625	79.0
Common type	553	69.9
Comedocarcinoma	20	2.5
Colloïd carcinoma	12	1.5
Medullary carcinoma	12	1.5
Cribriform carcinoma	5	0.6
Papillary carcinoma	2	0.3
Tubular carcinoma	12	1.5
Apocrine carcinoma	4	0.5
Metaplastic carcinoma	5	0.6
Lobular carcinoma	51	6.4
Combined forms	14	1.7
Invasive carcinomas NOS*	48	6.1
In situ carcinoma	34	4.3
Intraductal carcinoma:	25	3.2
Solid carcinoma	18	2.3
Comedocarcinoma	1	0.1
Cribriform carcinoma	5	0.6
Papillary carcinoma	1	0.1
Lobular *in situ* carcinoma	6	0.8
Paget's disease without tumour	3	0.4
Non-epithelial cancer	6	0.8
Sarcoma	3	0.4
Non-Hodgkin lymphoma	3	0.4
Histology unknown	13	1.6
Total	791	

*NOS = Not otherwise specified.

Table 4. Lymph node status of female breast cancer cases

Node status	No.	%
Negative	398	58.4
1–3 Positive	144	21.1
4–9 Positive	96	14.1
>10 Positive	44	6.4
Total	682	100.0

Table 5. Incidence rate of female breast cancer in the Rhône and in neighbouring registries

	Rhône (1985)	Isère (1979–1984) [12]	Geneva (1983–1986) [13]
Incidence rate (per 100 000 woman-years)			
Crude	105.9	77.9	125.6
World standardised	80.5	59.5	77.4
Europe standardised	108.0	80.1	106.8

Table 6. World standardised incidence rate of female breast cancer in selected cancer registries [5]

Registry	Incidence rate (per 100 000 woman-years)
China, Tianjin	18.2
Brazil, Recife	48.2
France, Martinique	31.1
France, Bas-Rhin	62.4
France, Calvados	55.1
France, Doubs	52.9
France, Isère	57.7
USA, Alemada, White	78.4
USA, Bay Area, White	87.0
USA, Los Angeles, White	77.3
USA, Connecticut, White	77.8
USA, Atlanta, White	75.4
USA, New Orleans, White	67.8
USA, Detroit, White	74.9
USA, Hawaii, White	84.4

and other health professionals during the holidays. A recent confirmation of our figures came from unpublished data for 1988 with a similar number of incident cases (A. Bremond, Hôpital E-Herriot). In the regional anticancer centre, 628 cases of breast cancer were seen in 1985 among the Rhône resident population, but we only counted 103 cases as incident. They represent 13.0% of all Rhône cases and correspond almost exactly to the 12.5% figure given by Lagarde for the proportion of new cancer patients diagnosed in a cancer hospital as opposed to other institutions [14]. We therefore feel confident that no substantial number of prevalent cases was included.

Inclusion of cases of women who were treated in the Rhône but were not usually resident in the département could also have occurred. Women's residence was defined as their usual address and was checked against administrative records used for reimbursement of medical expenses. The addresses can therefore be considered as accurate and up-to-date. A number of checks on the identity of subjects and by computer were made. We do not believe multiple counting did occur to any significant extent.

We also compared our estimate with an unpublished document prepared by a Social Security doctor for 1985 [15] and covering about 85% of the Rhône population. 665 new cases were discovered in a population of 642 300 women, corresponding to a crude incidence rate of 104.5 per 100 000 woman-years which was almost identical to our figures.

The high incidence of breast cancer in the Rhône is reflected in mortality rates (standardised mortality rate of 34 per 100 000 as compared to an overall rate of 29 for France) with a mortality/incidence ratio of 35% which is similar to Isère (37%) [12].

The origin of the cases reflects the composition of the population in the Rhône. For the total Rhône population and according to the INSEE, 84.3% of residents were born in France, 5.3% in Algeria, 1.9% in Italy, 1.3% in Spain and 1.3% in Tunisia [8]. The only country of birth showing a slight deficit of cases is Algeria.

If we were to later evaluate stage shift as a result of screening, and with the added proviso that this reflects lead-time as well as the potential effectiveness of screening, the low proportion of known TNM in the past would be a problem. It is particularly regrettable for the M not to be coded. In most cases, this may represent a lack of complete ascertainment of occult metastasis which is not done systematically, particularly for small primary tumours. A further difficulty may arise from slight modification in TNM criteria over time [11, 16]. Also of relevance is the description of *in situ* tumours. According to clinical staging (Table 2), only 14 cases were *in situ* (2.0%). This can be contrasted with 4.3% (Table 3) according to histology. Part of this difference may be explained by a much higher proportion of missing values for TNM classification (15.3%) than for histology (1.6%). Excluding *in situ* cases from the computation of the incidence rate leads to a crude rate of 101.3 cases per 100 000 woman-years instead of 106.9.

This study indicates that, for one French urban population at least, the rates are as high as among white American women, which is in contradiction with data from existing French cancer registries. This clearly illustrates the fact that extrapolation from a limited number of registries to a whole national population may be a hazardous exercise. On the other hand, a thorough one-site, in-depth survey like the one presented here may yield more cases that routine cancer registration where under-registration may be more likely to occur. One study conducted in the UK found an under-registration of 8% for breast cancer [17].

A specific *ad hoc* survey like the one reported here can also provide a complete description of a population-based series of breast cancer, therefore eliminating potential biases present in hospital-based case series. Further investigations are needed to explain this high incidence of breast cancer, in particular among women of 40 to 60 years of age. As clearly stressed by Muir *et al.* [18] and Doll [19], monitoring of cancer incidence among young age-groups is the most informative way of identifying new risks. Potential fields to examine include diet, alcohol and reproductive life. In particular, use of oral contraceptives mainly at a young age or before first full-term pregnancy should be explored as a factor.

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Feature Articles

Cancer Registration and Incidence in Hawaii

Marc T. Goodman and Grant N. Stemmermann

INTRODUCTION

THE HAWAII Tumor Registry was established in 1960 by the Hawaii Medical Association, and developed as a collaborative effort between the Hawaii Medical Association, the Hawaii Department of Health and the local chapter of the American Cancer Society. In 1973, this registry provided the basis for a Hawaii component to the newly established Surveillance, Epidemiology, and End Results programme of the United States' National Cancer Institute [1].

The Hawaii Tumor Registry comprises a system of individual hospital tumour registries and a statewide central registry which participate in a programme to study cancer incidence and survival from neoplastic disease. Information concerning diagnostic procedures and findings, treatment, histology and staging is gathered to provide data on which to monitor trends and base patient management. Follow-up information is obtained annually. The registry uses a computer-linkage program adapted to the linguistic characteristics of the Asian and Polynesian groups that comprise the state's population. This facilitates checking for duplicate entries in the files.

Nearly all cancer epidemiology research and cancer control activities in Hawaii depend in a significant way on the database provided by the Hawaii Tumor Registry. The registry has several special features. It covers populations dispersed over a wide geographic area, encompassing several different islands in the Pacific Ocean. Yet, 75% of the cancer cases are registered by hospitals within a 3-mile radius of the central registry, leading to a close interaction of hospitals and central registry. Furthermore, because of the state's insular nature, the population is very much contained and outmigration rates are low, allowing for more efficient and complete follow-up.

The ethnic diversity of the population of approximately 1.1 million inhabitants covered by the registry creates a distinctive scientific resource. Only 24% of the population is white. Japanese comprise 23%, providing the largest concentration of Japanese in the Surveillance, Epidemiology, and End Results programme. Substantial numbers of Filipinos (11%) and Chinese (5%) are represented; growing numbers of Koreans (1%) and Samoans (1%) are present in the population; and the registry produces the only incidence and survival rates for Hawaiians (part-Hawaiians) (20%), a native American population. The mixed race group amounts to about 11% of the registry population. This ethnic diversity makes possible a variety of comparisons on incidence and survival that can contribute to the general understanding of cancer aetiology and responses to therapy.

With some exceptions, cancer rates in Hawaii are lower than rates for the mainland of the USA (Fig. 1), although the patterns of cancer incidence are similar. Lung cancer is the most common cancer among men, followed by cancers of the prostate and colon. Among women, cancers of the breast, colon and lung are the three most common sites.

Most descriptive and analytic epidemiology conducted in Hawaii has shown wide variation in the incidence and mortality for cancer and other diseases by ethnic group [2]. These data have been useful in generating hypotheses regarding cancer aetiology. In general, Asian-Americans experience lower rates than do whites and Hawaiians for many of the more common malignancies (Table 1). Dramatic shifts in the cancer rates among migrants in the parent country compared with those in the host country have shown that environmental factors, versus

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