

Ethnicity and Health Care in Cervical Cancer Survival: Comparisons between a Filipino Resident Population, Filipino-Americans, and Caucasians

Maria Theresa Redaniel,¹ Adriano Laudico,^{2,3,5} Maria Rica Mirasol-Lumague,⁵ Adam Gondos,¹ Gemma Leonora Uy,³ Jean Ann Toral,⁴ Doris Benavides,⁴ and Hermann Brenner¹

¹Division of Clinical Epidemiology and Aging Research, German Cancer Research Center, Bergheimer Str 20, Heidelberg, Germany; ²Manila Cancer Registry, Philippine Cancer Society; Departments of ³Surgery and ⁴Obstetrics and Gynecology, Philippine General Hospital, University of the Philippines-Manila, Manila, Philippines; and ⁵Department of Health-Rizal Cancer Registry, Rizal Medical Center, Pasig City, Philippines

Abstract

Few studies have assessed and compared cervical cancer survival between developed and developing countries, or between ethnic groups within a country. Fewer still have addressed how much of the international or inter-racial survival differences can be attributed to ethnicity or health care. To determine the role of ethnicity and health care, 5-year survival of patients with cervical cancer was compared between patients in the Philippines and Filipino-Americans, who have the same ethnicity, and between Filipino-Americans and Caucasians, who have the same health care system. Cervical cancer databases from the Manila and Rizal Cancer Registries and Surveillance, Epidemiology, and End Results 13 were used. Age-adjusted 5-year survival estimates were computed and compared between the three patient groups. Using Cox proportional hazards modeling, potential determinants of survival differences were examined. Overall 5-year relative survival was similar in Filipino-

Americans (68.8%) and Caucasians (66.6%), but was lower for Philippine residents (42.9%). Although late stage at diagnosis explained a large proportion of the survival differences between Philippine residents and Filipino-Americans, excess mortality prevailed after adjustment for stage, age, and morphology in multivariate analysis [relative risk (RR), 2.07; 95% confidence interval (CI), 1.68-2.55]. Excess mortality decreased, but persisted, when treatments were included in the multivariate models (RR, 1.78; 95% CI, 1.41-2.23). A moderate, marginally significant excess mortality was found among Caucasians compared with Filipino-Americans (adjusted RR, 1.22; 95% CI, 1.01-1.47). The differences in cervical cancer survival between patients in the Philippines and in the United States highlight the importance of enhanced health care and access to diagnostic and treatment facilities in the Philippines. (Cancer Epidemiol Biomarkers Prev 2009;18(8):2228-34)

Introduction

Cancer of the uterine cervix is the most common gynaecological malignancy worldwide, with an increased burden of disease in developing countries, where 83% of the cases occur (1, 2). For developing countries, average incidence was estimated to be 19.1 per 100,000 women-years, almost twice the estimated incidence of 10.3 per 100,000 women-years in developed countries (3). Larger differences in cervical cancer mortality, with estimates of 11.2 and 4 deaths per 100,000 women-years in less developed and more developed countries, respectively, point to persisting major survival differences (1). Human papillomavirus (HPV) prevalence rates among women with normal cytology in developing and developed countries were estimated at 15.5% and 10%, respectively (4). Human papillomavirus types 62 and 84 (both 3.3%) and 53 (2.3%) were the most common in the United States (5),

whereas types 18 (1.6%), 16 (1.3%), 31, 45, and 52 (all 0.5%) were the most common in the Philippines (6).

Between ethnicities within countries, the epidemiology of cervical cancer has also been reported to differ. In the United States, incidence ranges from 4.9 per 100,000 among American Indians/Alaska Natives, to 7.3 per 100,000 among African Americans.⁶ Mortality likewise varies, from 1.5 to 3.5 per 100,000 between Asian or Pacific Islanders and African Americans, respectively.⁶ Five-year survival was reported to be higher among Americans of Korean or South-Asian descent (85.7% and 85.8%) compared with non-Hispanic White women (77.5%; ref. 7). Filipino-Americans were found to have similar survival rates with those of non-Hispanic White women (7, 8).

Few studies have assessed and compared cervical cancer survival in developed and developing countries, as well as between population groups of different ethnic origin within the same country (2, 7-10). Between developed and developing nations, survival differences from

Received 4/6/09; revised 5/20/09; accepted 5/29/09; published online 8/6/09.

Grant support: Maria Theresa Redaniel was supported by a scholarship from the German Academic Exchange Service.

Requests for reprints: Hermann Brenner, Division of Clinical Epidemiology and Aging Research, German Cancer Research Center, Bergheimer Str. 20, D-69115 Heidelberg, Germany. Phone: 49-6221-548140; Fax: 49-6221-548142. E-mail: h.brenner@dkfz-heidelberg.de

Copyright © 2009 American Association for Cancer Research.

doi:10.1158/1055-9965.EPI-09-0317

⁶ Surveillance Epidemiology and End Results (SEER) Program (<http://www.seer.cancer.gov>). Limited-Use Data (1973-2005) National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2008, based on the November 2007 submission.

gynaecological cancers were mainly attributed to advanced stage at diagnosis and deficiencies in treatment availability, accessibility, and affordability (11). However, the distribution of tumor histology, which has been found to be related to cervical cancer survival (12-14), also varies between ethnic groups (12). Few studies have addressed how much of the international cervical cancer survival differences are explained by ethnicity or by exposure to health care conditions.

To examine the role of health care and ethnicity on cervical cancer survival, up-to-date estimates of 5-year relative survival of Filipino-Americans with cervical cancer registered in the United States Surveillance, Epidemiology, and End Results (SEER) database were compared with survival of cancer patients in the Philippines from the National Capital Region (NCR), who have the same ethnicity, and to Caucasians in SEER, who are exposed to the same health care system.

Materials and Methods

Databases

SEER 13. Filipino-American and Caucasian ethnic populations from the United States were included in the study. Filipino-Americans are the second largest Asian group in the United States and among the most acculturated, with majority being either native born (32%) or naturalized citizens (42%; ref. 15). They are among the groups with the highest levels of income, education, and health insurance (15). Although cultural similarities with Philippine residents tend to diminish with longer stay in the United States and younger age at migration, majority of Filipino-Americans still observe Philippine customs.

From the SEER 13 database,⁶ patients identified to be of Filipino or Caucasian ethnicity were selected. Those ages 15 y and older, diagnosed from January 1, 1993 to December 31, 2002, and were followed with respect to vital status until December 31, 2002 were included in the study. After exclusion of 24,262 *in situ* cases (63.3%) and 73 cases who were identified by death certificates and autopsy only (<1%), a total of 485 Filipino-American and 13,576 Caucasian cancer patients were used in the analysis.

Manila and Rizal Cancer Registries. The Philippine population is represented by residents of the NCR, more commonly known as Metro Manila, which covers ~13% of the Philippine population (16). It is the largest urban metropolis, and the political, social, educational, and economic center. With a gross regional domestic product amounting to a third of the national total gross domestic product, its population is wealthier and has better access to health care and cancer diagnostic and treatment facilities than the rest of the country (16).

Information on cervical cancer cases was abstracted from the databases of the Philippine Cancer Society-Manila Cancer Registry and the Department of Health-Rizal Cancer Registry. The Philippine registries are regarded as among the high-quality cancer registries from developing countries and have been regularly included in Cancer Incidence in Five Continents (17-23). Furthermore, they follow the cancer registration definitions and data collection guidelines set by the International Agency for

Research on Cancer and the International Association of Cancer Registries.

Subsamples of 200 cases diagnosed in each calendar year from 1993 to 2002 and followed with respect to vital status until December 31, 2002 were randomly selected, using the same inclusion and exclusion criteria as for the SEER databases. From Local Civil Registry Offices, death certificate notifications mentioning cancer as the cause of death were collected to determine survival status. For those not identified as dead, active follow-up by personal visits to the patients or their families in the last known place of residence was used to confirm vital status. From the original sample of 2,000 patients, 155 patients (7.8%) were excluded due to invalid data and 265 patients (13.2%) were excluded due to absence of any follow-up information. A total of 1,580 cervical cancer patients (79%) were included in the analysis, for whom anonymized data sets were prepared and used.

The project proposal was approved by the Ethics Review Board of the NIH of the University of the Philippines Manila. The information obtained strictly conformed to the code of conduct stipulated by the Guidelines on Confidentiality for Population-based Cancer Registries (24).

Data Analysis

Estimation of Survival using Period Analysis. In the past, cohort-based analyses such as the conventional life-table (actuarial) method or the Kaplan-Meier method (25, 26) have typically been used to derive survival estimates. In this study, however, we used period analysis, introduced by Brenner and Gefeller (27) in 1996, to derive more up-to-date survival estimates. With this approach, only the survival experience of patients within some recent time period is considered. Here, only the survival experience of patients for the 1998 to 2002 period was included. It has been shown by extensive empirical evaluation that period analysis provides more up-to-date estimates of survival for patients diagnosed in the respective period (28-32).

Estimation of Relative Survival. According to common practice in population-based cancer survival analysis, relative survival was calculated in addition to absolute survival. Relative survival reflects the survival experience of cancer patients in the absence of competing causes of death, and is estimated as the ratio of the observed survival of cancer patients and the expected survival of a group of people with the same age and sex distribution from the general population (33, 34). For all groups, expected survival was derived from life tables for the year 2000 using the so-called Ederer II method (35). Due to the absence of life tables for other races, the life table for Whites from the U.S. National Center for Health Statistics (36) was used for both SEER populations. The life table for the Philippine resident population was derived from the projected population estimate and the actual mortality data for the NCR, which were obtained from the Philippine National Statistics Office.

Age Adjustment. To compare overall cancer survival estimates between the different cancer populations, age adjustment was done. Using age groups 15 to 39 y, 40 to 49 y, 50 to 59 y, and 60 y and above, age-specific period survival estimates were first obtained for the Philippine resident, the Filipino-American, and the Caucasian

populations. For each of the cancer populations, the age-specific estimates were then weighted, using weights from the World Standard Cancer Patient Population (37), and summed.

Tests for Survival Differences between Cancer Populations. To test for differences in absolute and relative survival estimates between the three populations, a novel modeling approach for period analysis (38) was used. For that purpose, age-specific numbers of patients at risk and of deaths by year of follow-up were first calculated for each population group. Poisson regression models were then fitted, wherein the numbers of deaths were modeled as a function of the population group (Philippine residents or Filipino-Americans or Caucasians), year of follow-up (1, 2, 3, 4, 5—entered as a categorical variable), and age-group (as described above—entered as a categorical variable), using the logarithm of the persons at risk as offset, and accounting for late entries and withdrawals as half persons, as described in detail elsewhere (38). Based on *P* values for the population parameter estimate, this allowed for testing of significance of survival differences after adjustment for age. A significance level of $\alpha = 0.05$ (two-sided testing) was used.

Multivariate Analysis. To assess the factors affecting survival for each population group and potentially explain survival differences, the Cox Proportional Hazards model was used (39). Individual Cox models by population group were used to determine bivariate associations of age, stage, histology, surgery, and radiotherapy with survival within each population. Age at diagnosis was categorized into the same groupings used in age adjustment. Stage was categorized according to the Federation of Gynecology and Obstetrics (FIGO) stage I, II III, and IV (40).

Histology was classified based on the WHO Classification of Tumors (41) as follows: squamous cell carcinoma (SCC), adenocarcinoma, and other types. Binary variables were used for receipt of surgical treatment and of radiotherapy. However, chemotherapy and hormone therapy were not included in the SEER public use database and were not covered in the analysis.

To compare survival probabilities between populations, a multivariate model was then built jointly for all three population groups. Using Filipino-Americans as the reference group, relative hazards were calculated for the Philippine resident population and for Caucasians, while controlling for the effects of age, stage, histology, surgery, and radiotherapy, first individually and then simultaneously. Two multivariate models were estimated: the first only included age, stage, and histology, whereas the second included the three aforementioned factors and treatment (surgery and radiotherapy).

For each variable included in the Cox models, the assumption of proportional hazards was checked by using log (–log) graphs. No violations of the assumptions were found as the plotted lines were roughly parallel over time. All analyses were done with the SAS Statistical Analysis Software. Special macros were used for standard and modeled period survival analysis as previously described (38, 42).

Results

Table 1 shows the distribution of cases for each population group by age groups, FIGO stage, histology, surgery, and radiotherapy. Filipino-American cervical cancer patients were on average older than the other groups, with

Table 1. Tumor characteristics of cervical cancer patients in the NCR, Philippines, and Filipino-Americans and Caucasians from U.S. SEER, 1993 to 2002

Variable	NCR (n = 1,580)		Filipino-Americans (n = 485)		Caucasians (n = 13,505)		P*
	Freq	%	Freq	%	Freq	%	
Age group							
<40	332	21.0	80	16.5	4,255	31.5	<0.0001
40-49	511	32.3	137	28.3	3,537	26.2	
50-59	404	25.6	116	23.9	2,241	16.6	
60+	333	21.1	152	31.3	3,472	25.7	
FIGO							
I	300	23.9	265	57.1	8,119	63.9	<0.0001
II	415	33.1	112	24.1	2,304	18.1	
III	440	35.1	58	12.5	1,282	10.1	
IV	100	8.0	29	6.3	995	7.8	
Unknown	325		21		805		
Morphology							
SCC	979	76.0	289	60.7	7,972	61.8	<0.0001
Adenocarcinoma	221	17.2	100	21.0	2,305	17.9	
Others	89	6.9	87	18.3	2,630	20.4	
NOS [†]	291		9		598		
Surgery							
Without surgery	757	71.5	172	35.5	4,333	32.2	<0.0001
With surgery	302	28.5	313	64.5	9,144	67.9	
Unknown	521		0		28		
Radiotherapy							
Without radiotherapy	335	25.1	215	45.0	7,185	54.0	<0.0001
With radiotherapy	1,000	74.9	263	55.0	6,121	46.0	
Unknown	245		7		199		

Abbreviations: Freq, frequency; NOS, not otherwise specified.

*Comparing the distributions of the variables in the three population groups.

[†]Includes: Neoplasms; Carcinoma, NOS; Carcinoma, Undifferentiated, NOS.

Table 2. Five-year absolute and relative survival (in %) of cervical cancer patients adjusted to the World Standard Cancer Patient Population, Philippine resident population, and Filipino-Americans and Whites from U.S. SEER, 1998 to 2002

Variable	(1) Philippine resident patients		Between (1) and (2)		(2) Filipino-Americans		Between (2) and (3)		(3) Caucasians	
	%	SE	Diff	P	%	SE	Diff	P	%	SE
Absolute survival										
Over all survival	39.8	2.4	25.2	<0.001	65.1	3.1	-2.0	0.44	63.0	0.6
Age group										
<40	48.6	5.3	25.4	0.01	74.0	7.2	10.0	0.05	84.1	0.8
40-49	39.9	4.3	30.3	<0.001	70.2	5.3	7.5	0.12	77.7	1.0
50-59	49.1	4.8	20.6	0.01	69.7	6.1	-6.4	0.34	63.3	1.5
60+	30.0	4.5	24.9	<0.001	54.8	5.9	-11.0	0.05	43.8	1.2
Relative survival										
Over all survival	42.9	2.7	26.0	<0.001	68.8	3.4	-2.2	0.53	66.6	0.7
Age group										
<40	49.1	5.4	25.3	0.01	74.4	7.2	10.0	0.05	84.5	0.8
40-49	40.7	4.4	30.3	<0.001	71.0	5.4	7.6	0.12	78.6	1.0
50-59	51.3	5.0	20.3	0.02	71.6	6.3	-6.5	0.32	65.1	1.5
60+	36.1	5.4	27.2	<0.002	63.3	6.8	-11.5	0.05	51.8	1.4

Abbreviation: Diff, difference.

>30% ages 60 years or above. Caucasians were youngest with >30% below age 40 years. Both SEER patient groups were diagnosed more often at earlier stages than Filipinos in the Philippines, with more than half of patients being diagnosed at stage I. The distribution of histologic profiles also varied between populations, with 76% of Filipinos in the Philippines having SCC, compared with around 60% in the SEER populations. Only a minority of patients residing in the Philippines (28.5%) underwent surgery, compared with 64.5% and 67.9% of Filipino-Americans and Caucasians, respectively, but almost 75% of the Philippine resident patients received radiotherapy.

Age adjusted and age-specific estimates of 5-year absolute and relative survival are shown in Table 2. With few exceptions, survival estimates decrease with increasing

age. Much lower survival was seen in Filipinos living in the Philippines than in the U.S. cancer populations in all age groups, with differences from survival in Filipino-Americans ranging from 20 to 30 percentage units. Five-year overall absolute and relative survival estimates were similar among Filipino-Americans and Caucasians. However, survival differences were significant among the youngest and the oldest age groups, with Caucasians having higher survival in the former and Filipino-Americans in the latter.

As shown in Table 3, late stage at diagnosis and not receiving surgery all strongly increased the risk of death in each of the three populations. For Caucasians, increasing age and being diagnosed with SCC also increased the risk of death. Having received radiotherapy was related to a

Table 3. RR of death according to various prognostic factors among cervical cancer patients, Philippine resident population and from Filipino-Americans and Caucasians from U.S. SEER, 1993 to 2002, Bivariate analysis

Variable	Philippine resident patients		Filipino-Americans		Caucasians	
	RR	95% CI	RR	95% CI	RR	95% CI
Age group						
<40	1.00		1.00		1.00	
40-49	1.07	0.84-1.36	0.89	0.49-1.62	1.55	1.39-1.72
50-59	0.88	0.69-1.13	0.98	0.54-1.81	2.63	2.36-2.93
60+	1.28	1.00-1.64	1.91	1.11-3.29	4.89	4.46-5.36
FIGO stage						
I	1.00		1.00		1.00	
II	2.34	1.66-3.29	4.87	3.04-7.79	3.95	3.60-4.32
III	5.22	3.75-7.26	6.00	3.50-10.28	8.93	8.12-9.83
IV	15.04	10.17-22.23	21.61	12.12-38.51	20.39	18.51-22.47
Morphology						
SCC	1.00		1.00		1.00	
Adenocarcinoma	0.90	0.71-1.16	0.79	0.51-1.23	0.72	0.66-0.79
Others	0.85	0.59-1.22	0.55	0.32-0.94	0.56	0.51-0.61
Surgery						
With surgery	1.00		1.00		1.00	
Without surgery	2.91	2.18-3.89	3.82	2.69-5.43	5.53	5.18-5.91
Radiotherapy						
With radiotherapy	1.00		1.00		1.00	
Without radiotherapy	1.85	1.52-2.24	0.36	0.24-0.53	0.30	0.28-0.32

Table 4. RR of death for cervical cancer patients from the Philippine resident population and for Caucasian patients compared with Filipino-American patients from U.S. SEER, 1993 to 2002

Variable	Philippine resident patients		Filipino-Americans (reference group)		Caucasians	
	RR	95% CI	RR	95% CI	RR	95% CI
Bivariate analysis	2.79	2.31-3.38	1.00	—	1.04	0.87-1.24
After controlling for other variables						
Age	3.10	2.56-3.75	1.00	—	1.23	1.03-1.46
FIGO stage	1.83	1.49-2.24	1.00	—	1.15	0.96-1.38
Morphology	2.58	2.12-3.14	1.00	—	1.03	0.87-1.23
Surgery	1.54	1.26-1.89	1.00	—	1.16	0.97-1.38
Radiotherapy	2.27	1.87-2.76	1.00	—	1.17	0.98-1.39
Multivariate analysis						
Controlling for age, FIGO stage and morphology	2.07	1.68-2.55	1.00	—	1.23	1.02-1.47
Controlling for age, FIGO stage, morphology, surgery and radiotherapy	1.78	1.41-2.23	1.00	—	1.22	1.01-1.47

higher risk of dying for the Filipinos in the Philippines, but showed an inverse association for the SEER populations.

In bivariate analysis, the risk of death was almost thrice higher among cervical cancer patients from the Philippines than among Filipino-American cervical cancer patients (Table 4). This strong excess mortality was substantially reduced when stage at diagnosis and receipt of surgery were controlled for. Nevertheless, excess mortality prevailed even after age, stage, and histology were controlled simultaneously in multivariate analysis [relative risk (RR), 2.07; 95% confidence interval (CI), 1.68-2.55]. Excess mortality further decreased, but still persisted, when treatments were included in the multivariate models (RR, 1.78; 95% CI, 1.41-2.23). Comparing Filipino-American and Caucasian patients, no difference in mortality was observed in the bivariate analysis. However, a moderate marginally statistically significant excess mortality for Caucasian patients emerged after controlling for age and other covariates in multivariate analysis (RR, 1.22; 95% CI, 1.01-1.47).

Discussion

This comparative analysis disclosed very large survival deficits of Philippine resident patients with cervical cancer compared with Filipino-American patients, whereas the latter even had slightly more favorable survival expectations than Caucasian patients in the United States. These very clear cut patterns underline the overwhelming role of health care related factors in international cancer survival differences.

Due to availability of effective early detection measures, a comprehensive evaluation of progress against cervical cancer also has to consider trends in incidence and mortality. In the United States, between 1973 and 2005, incidence and mortality from cervical cancer have both been reduced by 60%,⁶ and most of this reduction has been attributed to widespread dissemination of cancer screening (43). Along with increased access to screening is the shift toward earlier detection, which is apparent in the differences in the stage distributions between the Philippine residents, and the Filipino-Americans and Caucasians.

The reduction in cervical cancer burden through screening is likewise possible in developing countries, as

illustrated by a large community-based intervention trial in India (44). Using visual inspection with 4% acetic acid (VIA), as much as 25% decrease in incidence and 35% decrease in mortality is achievable within 7 years, provided that good training of health personnel, sustained quality assurance, and monitoring are also in place (44). Other methods such as visual inspection after application of Lugol's iodine or with magnifying device (VIAM; ref. 45), as well as loop electrosurgical procedure (46), were likewise shown to be feasible and effective screening methods.

In the Philippines, however, cancer screening is not coordinated or appropriately targeted and there has been no sustained public health campaign to promote its benefits (47). Consequently, cervical cancer incidence has only decreased by 7.3% between 1980 and 2002 (23, 48). Whereas VIA and VIAM were shown to be effective and acceptable screening methods in the country (49), their implementation and use are yet to be assessed. Pap smears are available through family planning clinics and relevant societies, but the screening coverage for Filipino women is low, with only 12% of the population being screened (47).

In addition, the proportion of Philippine patients not receiving surgery and those receiving radiotherapy differ considerably from the U.S. SEER populations. It was estimated that only 50% to 60% of cervical cancer patients in the Philippines had received some form of treatment (50). Treatment access and affordability likely pose barriers to a considerable number of patients. Cancer care services, including treatment facilities, are mainly provided by private institutions, with government hospitals and clinics accounting for only a fraction of the total number of hospitals in the NCR (16). Although public institutions offer subsidized services, diagnostic procedures and treatment regimens are still costly for the average Filipino. With NCR residents receiving an average annual income of US\$6,211 (16), surgery costs of US\$1,676 to 3,434, radiotherapy costs of US\$952 to 1,014, and chemotherapy costs of US\$621 to 1,241 (51) in government hospitals are deemed too high.

In recent years, efforts to increase cervical cancer screening awareness and use, as well as access to treatment, have been done by various sectors in the Philippines. These include the establishment of the Cervical Cancer Screening Program in 2005 and the Cervical Cancer Prevention Network Program in 2006 (6, 52). Both aim

to increase education and awareness about cervical cancer in Filipino women and provide access and information to screening and effective treatments (6). However, the cervical cancer screening program is not yet fully implemented, whereas Cervical Cancer Prevention Network Program is still currently limited to several pilot sites all over the country. Their impacts in decreasing cancer mortality are still to be seen.

Between Filipino-Americans and Caucasians, there is not much difference in the overall relative survival rates for cervical cancer. The differences between the youngest and oldest age groups can be explained by the stage distributions between populations. For patients younger than 40 years, the proportion of those with stage IV disease among Filipino-Americans is twice that of Caucasians (5.19% versus 2.39%). In contrast, more Caucasians in the 60 years and above age group were diagnosed with stage IV disease, compared with Filipino-Americans (14.94% versus 7.64%). With the exception of age, the distribution of the variables studied was the same for both populations. After adjustment for age in the Cox model, Caucasians even showed a modest, marginally increased risk of death compared with Filipino-American cervical cancer patients. The reasons for this possible difference are unclear and warrant further investigation.

Our analyses, however, have limitations. Despite maximum possible efforts of follow-up, including personal visits to the homes of patients who could not otherwise be traced, survival information was still not complete for all patients in the Philippines. Of those who could not be matched to death certificates, 38.8% had complete 5-year survival, whereas some survival information was available for an additional 42.9%. The active migration and high mobility of most of the residents of the NCR and incomplete addresses in the medical records are the main reasons for losses to follow-up. Nevertheless, measures to locate the patients and to gather survival information were exhausted, and were believed to have kept losses at the possible minimum.

Although various prognostic factors have been included in the analysis, not all have been taken into consideration. Information on life-style or other individual factors such as screening access and use, socioeconomic status, comorbidities, and immigration history was not available. Likewise, data were also lacking for organization, training and skills of health care professionals, application of patient care guidelines, and diagnostic and treatment facilities.

Despite these limitations, the differences in cervical cancer survival clearly highlight the importance of access to and use of diagnostic and treatment facilities for international differences in cervical cancer survival, and making adequate facilities affordable should be given priority. Emphasis should also be given to promoting early diagnosis through screening programs in the Philippines and other low and middle income countries.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

We thank the staff of the Manila and Rizal Cancer Registries (Siony Alcos, Zoila Bautista, Lydia Navarro, Ellen Santos, Antonette Tad-y, Minda Turano, Melinda Visoria, Wilma Grafilo, Tess Medes, Herly Sy-Menco, Elena Marquez, Josephine Isla, Portia de Guzman, and Arlene Sasot) who facilitated data abstraction and patient follow-up, Vincent Olaiwar of the National Statistics Office for his help in obtaining population information, and Editha Dumo of the National Economic and Development Authority for her assistance in obtaining mortality data and report on the NCR profile. Special mention also goes to the Philippine Cancer Society and the Rizal Medical Center.

References

- Parkin D, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005;55:74-108.
- Sankaranarayanan R, Ferlay J. Worldwide burden of gynaecological cancer: the size of the problem. *Best Pract Res Clin Obstet Gynaecol* 2006;20:207-25.
- GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide. IARC CancerBase No. 5. version 2.0. Lyon: IARC Press.
- de Sanjose S, Diaz M, Castellsague X, et al. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. *Lancet Infect Dis* 2007;7:453-9.
- Dunne EF, Unger ER, Sternberg M, et al. Prevalence of HPV infection among females in the United States. *JAMA* 2007;297:813-9.
- Domingo EJ, Noviani R, Noor MR, et al. Epidemiology and prevention of cervical cancer in Indonesia, Malaysia, the Philippines, Thailand and Vietnam. *Vaccine* 2008;26 Suppl 12:M71-9.
- Bates JH, Hofer BM, Parikh-Patel A. Cervical cancer incidence, mortality, and survival among Asian subgroups in California, 1990-2004. *Cancer* 2008;113:2955-63.
- Lin SS, Clarke CA, Prehn AW, Glaser SL, West DW, O'Malley CD. Survival differences among Asian subpopulations in the United States after prostate, colorectal, breast, and cervical carcinomas. *Cancer* 2002; 94:1175-82.
- Gondos A, Brenner H, Wabinga H, Parkin D. Cancer survival in Kampala, Uganda. *Br J Cancer* 2005;92:1808-12.
- McGuire V, Jessor CA, Whittemore AS. Survival among U.S. women with invasive epithelial ovarian cancer. *Gynecol Oncol* 2002;84:399-403.
- Sankaranarayanan R. Overview of cervical cancer in the developing world. FIGO 6th Annual Report on the Results of Treatment in Gynecological Cancer. *Int J Gynaecol Obstet* 2006;95 Suppl 1:S205-10.
- Vinh-Hung V, Bourgain C, Vlastos G, et al. Prognostic value of histopathology and trends in cervical cancer: a SEER population study. *BMC Cancer* 2007;7:164.
- Grisaru D, Covens A, Chapman B, et al. Does histology influence prognosis in patients with early-stage cervical carcinoma? *Cancer* 2001;92:2999-3004.
- Alfsen GC, Kristensen GB, Skovlund E, Pettersen EO, Abeler VM. Histologic subtype has minor importance for overall survival in patients with adenocarcinoma of the uterine cervix: a population-based study of prognostic factors in 505 patients with nonsquamous cell carcinomas of the cervix. *Cancer* 2001;92:2471-83.
- Reeves T, Bennett C. *We the People: Asians in the United States*. Census 2000 Special Reports, CENSR-17. Washington (DC): US Census Bureau; 2004.
- NSCB. *Metro Manila — a Gateway to the Philippines*, 2005 Edition. Makati: National Statistical Coordinating Board, 2006.
- Laudico A, Esteban D, Bustamante G, Farre C, Maramba T, Baltazar J, Rizal Province. In: Muir C, Waterhouse J, Powell J, Mack T, Whelan S, editors. *Cancer Incidence in Five Continents Vol. V*. Lyon: International Agency for Research on Cancer; 1987. p. 474-7.
- Laudico A, Esteban D, Bustamante G. Philippines, Rizal Province. In: Parkin D, Muir C, Whelan S, Gao Y, Ferlay J, Powell J, editors. *Cancer Incidence in Five Continents Vol. VI*. Lyon: International Agency for Research on Cancer; 1992. p. 526-9.
- Laudico A, Esteban D, Ngelangel C, Eufemio G, Maramba T. Philippines, Manila. In: Parkin D, Muir C, Whelan S, Gao Y, Ferlay J, Powell J, editors. *Cancer Incidence in Five Continents Vol. VI*. Lyon: International Agency for Research on Cancer; 1992. p. 522-5.
- Laudico A, Esteban D, Ngelangel C, Eufemio G, Guzman C. Manila, Philippines. In: Parkin D, Whelan S, Ferlay J, Raymond L, Young J, editors. *Cancer Incidence in Five Continents Vol. VII*. Lyon: International Agency for Research on Cancer; 1997. p. 418-21.
- Esteban D, Laudico A, Cruz R. Philippines, Rizal. In: Parkin D, Whelan S, Ferlay J, Teppo L, Thomas D, editors. *Cancer Incidence in*

- Five Continents Vol. VII. Lyon: International Agency for Research on Cancer; 2002. p. 418–9.
22. Laudico A, Esteban D, Reyes L. Philippines, Rizal. In: Parkin D, Whelan S, Ferlay J, Teppo L, Thomas D, editors. *Cancer Incidence in Five Continents Vol. VIII*. Lyon: International Agency for Research on Cancer; 2002. p. 286–7.
 23. Laudico A, Lumague M, Esteban D, Reyes L, Mapua C, Redaniel M. *Cancer Incidence in Manila, Philippines (1998-2002)*. In: Curado M, Edwards B, Shin H, Storm H, Ferlay J, Heanue M, Boyle P, editors. *Cancer Incidence in Five Continents Vol. VIII*. Lyon: International Agency for Research on Cancer; 2007.
 24. International Association of Cancer Registries, and International Agency for Research on Cancer. *Guidelines On Confidentiality For Population-based Cancer Registries, Internal Report No. 2004/03*. Lyon: IARC; 2004.
 25. Cutler S, Ederer F. Maximum utilization of the life table method in analyzing survival. *J Chron Dis* 1958;8:699–712.
 26. Kaplan E, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457–81.
 27. Brenner H, Gefeller O. An alternative approach to monitoring cancer survival. *Cancer* 1996;78:2004–10.
 28. Brenner H, Hakulinen T. Up-to-date long-term survival curves of patients with cancer by period analysis. *J Clin Oncol* 2002;20:826–32.
 29. Brenner H, Hakulinen T. Advanced detection of time trends in long-term cancer patient survival: experience from 50 years of cancer registration in Finland. *Am J Epidemiol* 2002;156:566–77.
 30. Brenner H, Soderman B, Hakulinen T. Use of period analysis for providing more up-to-date estimates of long-term survival rates: empirical evaluation among 370,000 cancer patients in Finland. *Int J Epidemiol* 2002;31:456–62.
 31. Tälback M, Stenbeck M, Rosen M. Up-to-date long-term survival of cancer patients: an evaluation of period analysis on Swedish Cancer Registry data. *Eur J Cancer* 2004;40:1361–72.
 32. Ellison L. An empirical evaluation of period survival analysis using data from the Canadian Cancer Registry. *Ann Epidemiol* 2006;16:191–6.
 33. Ederer F, Axtell LM, Cutler SJ. The relative survival rate: a statistical methodology. *Natl Cancer Inst Monogr* 1961;6:101–21.
 34. Henson DE, Ries LA. The relative survival rate. *Cancer* 1995;76:1687–8.
 35. Ederer F, Heise H. *Instructions to IBM 650 programmers in processing survival computations*. Bethesda (MD): National Cancer Institute; 1959.
 36. Arias E. *United States abridged life tables, 2000*. National vital statistics reports; vol 51 no 3. Hyattsville (MD): National Center for Health Statistics; 2002.
 37. Sankaranarayanan R, Black R, Parkin D. *Cancer Survival in Developing Countries*. Lyon: International Agency for Research on Cancer; 1998.
 38. Brenner H, Hakulinen T. Up-to-date and precise estimates of cancer patient survival: model-based period analysis. *Am J Epidemiol* 2006;164:689–96.
 39. Cox D. Regression models and life tables (with discussion). *J Royal Stat Soc Series B* 1972;34:187–220.
 40. Quinn MA, Benedet JL, Odicino F, et al. Carcinoma of the cervix uteri. FIGO 6th Annual Report on the Results of Treatment in Gynecological Cancer. *Int J Gynaecol Obstet* 2006;95 Suppl 1:S43–103.
 41. Tavassoli FA, Deveilee P. *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Breast and Female Genital Organs*. Lyon: IARC Press; 2003.
 42. Brenner H, Gefeller O, Hakulinen T. Period analysis for 'up-to-date' cancer survival data: theory, empirical evaluation, computational realisation and applications. *Eur J Cancer* 2004;40:326–35.
 43. Jemal A, Thun MJ, Ries LA, et al. Annual report to the nation on the status of cancer, 1975–2005, featuring trends in lung cancer, tobacco use, and tobacco control. *J Natl Cancer Inst* 2008;100:1672–94.
 44. Sankaranarayanan R, Esmey PO, Rajkumar R, et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. *Lancet* 2007;370:398–406.
 45. Arbyn M, Sankaranarayanan R, Muwonge R, et al. Pooled analysis of the accuracy of five cervical cancer screening tests assessed in eleven studies in Africa and India. *Int J Cancer* 2008;123:153–60.
 46. Rema P, Suchetha S, Thara S, Fayette JM, Wesley R, Sankaranarayanan R. Effectiveness and safety of loop electrosurgical excision procedure in a low-resource setting. *Int J Gynaecol Obstet* 2008;103:105–10.
 47. Faro S. Proceedings from the first Asia-Oceania Research Organisation on Genital Infections and Neoplasia (AOGIN) Meeting. *Infect Dis Obstet Gynecol* 2006;14:1–38.
 48. Laudico A, Redaniel T, Esteban D, Reyes L. Cancer incidence (1993–1997) and incidence trends (1980–1997) in Metro Manila and Rizal Province. *Philipp J Surg Spec* 2005;60:10–5.
 49. Ngelangel C, Limson G, Cordero C, et al. Acetic-acid guided visual inspection vs. cytology-based screening for cervical cancer in the Philippines. *Int J Gynecol Obstet* 2003;83:141–50.
 50. Ganzon E, Luna J. Recurrent and persistent cervical cancer cases in a tertiary hospital: a 21 year experience. *Philipp J Oncol* 2006;7:28–43.
 51. Sotto L. Cancer of the cervix: the Philippine experience; has anything changed? *Philipp J Gyn Oncol* 2004;1:1–5.
 52. Administrative order 2005-0006. *The establishment of a cervical cancer screening program*. Manila: Department of Health Philippines; 2005.