

## RESEARCH COMMUNICATION

## Socioeconomic Status and Lung Cancer Risk in Nepal

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## Abstract

**Background.** Lung cancer is the most common cancer among men and the third most common cancer among women in Nepal. Socioeconomic disparities in lung cancer have not been studied in the Nepalese population. **Methods.** We conducted a lung cancer case-control study, including 209 cases and 313 controls at the main cancer hospital in Nepal, the B.P. Koirala Memorial Cancer Hospital (BPKMCH). **Results.** We observed differences in lung cancer risk by ethnicity; the Rai, Limbu and Magar groups had a higher risk of lung cancer than Brahmin (OR=3.11, 95% CI=1.55-6.23). An inverse association was observed between education and lung cancer risk (p for trend=0.0008). We also observed greater lung cancer risk among unmarried individuals (OR=2.25, 95% CI=1.12-4.53), and lower risk in individuals who lived in the Central region compared to the West (OR=0.47, 95% CI=0.26-0.85). There were greater proportions of late stage cancers among women compared to men, in the Rai/Limbu/Magar ethnic groups, in individuals with lower education and in older age groups. **Conclusions.** Disparities in lung cancer risk were observed by race/ethnicity, education, marital status, and by region of residence. Further research on socioeconomic influence on lung cancer in Nepal is warranted to develop better prevention efforts against the disease.

**Keywords:** Cervical cancer - control measures - screening - risk factors - natural history

*Asian Pacific J Cancer Prev*, 12, 1083-1088

## Introduction

Of the 1.3 million cases of lung cancer estimated to occur each year worldwide, 672,000 cases occur in low and middle income countries (LMCs). Consequently, of the 1.2 million annual deaths attributable to lung cancer, 591,000 deaths (49%) occur in LMCs (Ferlay et al., 2004). Cancer is already a major burden in LMCs and the burden is expected to increase in the next decades due to the growing population, better management of infectious diseases, and adoption of western lifestyles (Sloan and Gelband, 2007). However, very little data is available from LMCs such as Nepal, on the disparities in lung cancer risks as well as on the established risk factors, as the majority of epidemiologic studies on lung cancer have been conducted in North America and Europe.

Nepal is one of the poorest countries in the world, with a gross domestic product per capita of 470 US dollars in 2009 (<http://www.worldbank.org.np>). The estimated total population for 2010 is 28.9 million, consisting of race/ethnic groups Chettri, Brahmin, Tharu, Tamang, Newar and other smaller subgroups (15.5, 12.5, 7.0, 6.6, 5.5, 5.4 and 47%, respectively) (CIA). The labor force is 75% agriculture, 18% service and 7% industry while the unemployment rate is 46%. Approximately 29.3% of men

and 26.2% of women in Nepal smoke tobacco (<http://www.tobaccoatlas.org>). The high smoking prevalence among Nepalese women is in contrast to corresponding figures observed in neighboring countries such as India and China.

At present, the development of a national cancer control program in Nepal is at a very early stage. A national meeting held at the B.P. Koirala Memorial Cancer Hospital (BPKMCH) in Bharaptur with support from the World Health Organization identified the urgent need to formulate a national cancer control program and communicate primary prevention messages on tobacco smoking, tobacco chewing, and other major cancer risk factors. However, such future efforts may have limited scope because currently there is no data available on the most at risk population in Nepal.

Socioeconomic factors have been associated with an increased risk of lung cancer in Central and Eastern Europe (Hrubá et al., 2009), New Zealand (Mao et al., 2001), and Canada (Sidorchuk et al., 2009). There have been fewer studies in Asia and in low income countries investigating socioeconomic factors and lung cancer risk. Understanding the role of socioeconomic factors on lung cancer risk in Nepal will facilitate formulation of a culturally sensitive and effective cancer control program.

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The present case-control study is designed to investigate the lung cancer risk profile in a LMC with special emphasis among never smokers. In this manuscript, we present results on socioeconomic, geographic, ethnic disparities of lung cancer risk in Nepal.

## Materials and Methods

A hospital-based case-control study was conducted at the B. P. Koirala Memorial Cancer Hospital (BPKMCH) in the city of Bharatpur, Chitwan district, between November 2009–November 2010. The BPKMCH hospital is located 150km southwest of Katmandu, the capital of Nepal. Since its establishment in 1999, BPKMCH has undergone significant growth in terms of both resources/infrastructure and the number of patients treated. In 2003, it provided treatment to 3,500 patients compared to just 262 patients in 1999. The hospital now is the premier cancer referral center in Nepal and includes 16 different departments, including surgical oncology, radiation oncology, medical oncology and cancer prevention, control and research branch.

Of the 239 eligible lung cancer cases invited to participate in the study 209 lung cancer patients agreed to take part in the study and were interviewed (participation rate = 87.4%). Of the 446 eligible controls invited to participate in the study, 313 controls agreed to take part in the study for a participation rate of 70.2%. The reasons for nonparticipation among the cases (n=30) were: person deceased (3%), ill health (67%), the study doesn't make sense to the respondent (23%), confidentiality reasons (3%) and other reasons (3%). The reasons for nonparticipation among the controls (n=133) were: person deceased (3.5%), ill health (46%), study doesn't make sense to the respondent (42%), confidentiality reasons (0.8%), and other reasons (7.5%). The distribution of age among the nonparticipating cases and controls were similar to their corresponding participating case and control groups. However, the proportion of women in the nonparticipating control group (63.2%) was higher than that in the participating control group (29.5%). The proportions of men and women in the nonparticipating and participating case groups were very similar.

In this study, we included 209 lung cancer cases (ICD-O2 codes C33 and C34), and 313 controls matched on age ( $\pm 5$  years), sex and geographical area of residency (mountain, hilly and plain region). All eligible cases were recruited as soon as possible after initial diagnosis of lung cancer, with a target interval of one day between initial diagnosis and recruitment, and a maximum interval of 3 months to ensure that very few cases are not recruited because they die before there is an opportunity to interview them. The source of controls were visitors of non-lung cancer patients at the hospital. A standardized questionnaire was administered to all study participants by trained staff members, who collected data on demographic and socioeconomic status, family history of cancer, tobacco and alcohol consumption habits, dietary factors, occupation, residential history and usage of different chewing products available locally. All study subjects gave informed consent. This study has been approved by the

IRB committees at the University of Utah, University of Maryland and the Nepal Health Research Council.

### Statistical analysis

Unconditional logistic regression was used to estimate the odds ratios (OR) and their 95% confidence intervals (95%CI), to evaluate the risk of lung cancer according to various potential disparity factors. We first adjusted for age (in 5 year categories), sex, and residence (plains, hill, mountain), then additionally adjusted for race/ethnicity (categories), education (categories as shown in table 2), and packyears of smoking (categories: 0, 1-9 packyears, 10-19 packyears, 20-29 packyears,  $\geq 30$  packyears).

The rurality variable was calculated based on self reported number of years lived in urban areas. The majority of cases (83.3%) and controls (78.2%) had never lived in urban areas, thus these subjects were categorized as rural. The other subjects who had ever lived in urban areas were categorized as urban. The socioeconomic index variable was created by summing across three variables on whether there was a toilet in the house (1=attached, 2=away from house, 3=no toilet), running water in the house (1=yes, 2=no), and a separate kitchen (1=yes, 2=no). Thus the range of the SES index score was from 3 to 7, with 3 indicating the highest level of SES and 7 indicating the lowest SES. Since very few subjects had a score of 7, we combined these subjects with those who had a score of 6. Chi-square tests were conducted to assess associations between the demographic and socioeconomic factors.

Packyears of tobacco smoking was estimated by combining the cigarettes per day and duration information for cigarettes with filter, cigarettes without filter and bidi cigarettes (packyears = cigarettes per day/20 \* years of smoking). Very few individuals reported smoking other products such as choor/kankat (n=27 cases and 12 controls), hookapipe (n=17 cases and 7 controls) and hashish (n=4 cases and 3 controls). Since cigarette equivalents are difficult to calculate for these tobacco products and the frequency/duration of these habits were fairly low, we categorized these individuals into the 1-9 packyears of tobacco smoking if they had not been categorized into a packyear category due to other tobacco cigarette habits. In other words, if an individual had smoked only hashish, they were categorized into 1-9 packyears. However, if an individual had smoked hashish and smoked 25 packyear equivalents of cigarettes, then they would be categorized into the 20-29 packyear category. Never smokers are thus defined as individuals who did not smoke any tobacco products (cigarettes with filter, cigarettes without filter, bidi, choor/kankat, hookapipe, or hashish).

We also report the tumor characteristics overall for all lung cancer patients, and stratified by gender. Chi-square tests were conducted to determine whether there were associations between these tumor characteristics and gender. We also calculated the proportion of individuals missing T stage, missing N stage, missing M stage, and with late overall stage by potential disparity groups. Chi-square tests were conducted to examine associations between missing stage or late stage data with patient

characteristics. All analyses were conducted on SAS version 9.2.

## Results

The demographic characteristics of the lung cancer cases and controls are shown in Table 1. A higher proportion of cases were in the oldest age group compared to controls. The majority of cases (60.3%) and controls (70.6%) were male. The ethnicity was quite diverse as expected, while the majority of subjects were Hindu in religion. Since the BPKMC hospital is located in the plains, it was expected that the majority of patients and controls are from the plains region.

There were substantially higher proportion of controls who did not smoke in the younger age groups and among women compared to men. The median packyears was higher among controls who were older and was slightly higher for men compared to women. Among people living in the mountain region there appeared to be a lower proportion of never smokers. Increased risks of lung cancer were observed for individuals who were Rai/Limbu/Magar ethnicity compared to the Brahmin ethnicity (adjusted OR=3.11, 95%CI=1.55-6.23; Table 1). The proportion of never smoker controls was not particularly low for this ethnic group and the median packyears was

not necessarily among the highest in comparison to other ethnic groups. The Rai/Limbu/Magar group, however, had the highest proportion of controls in the lowest education category of <3rd standard (data not shown). A decreased risk of lung cancer was observed in individuals who lived in the Central region relative to the Western region (OR=0.47, 95%CI=0.26-0.85).

For socioeconomic characteristics (Table 2), we observed a decreased risk of lung cancer among individuals with higher education and an increased risk of lung cancer among individuals who were not married. No association was observed between lung cancer risk and rurality of residence. The median tobacco packyear was higher among controls with lower education and among controls who were married, but appeared to be fairly similar among controls by rurality. There was an inverse association observed between the low SES index score 6-7 and lung cancer risk, but a trend was not suggested (p=0.2359).

We examined the associations among the demographic and socioeconomic factors among controls with Chi-square tests. Race/ethnicity was associated with religion (p=0.0008), residence (plains, hilly, mountain; p<0.0001), residence (east-west; p<0.0001), education (p=0.0325), rurality (p<0.0001), and SES index (p<0.0001). Education was also associated with marital status (p=0.0446),

**Table 1. Demographic Characteristics of Lung Cancer Cases and Controls in Nepal**

	Cases n=209		Controls n=313		Adjusted 95% CI		Adjusted 95% CI %		Never smokers		Median packyears	
	N	%	N	%	OR <sup>1</sup>		OR <sup>2</sup>		cases	controls	cases	controls
Age												
<40	13	6.2%	22	7.0%					61.5%	63.6%	3.2	1.4
40-49	10	4.8%	91	29.1%					30.0%	64.8%	11.3	4.7
50-59	47	22.5%	112	35.8%					0.0%	31.3%	25.5	8.8
60-69	78	37.3%	77	24.6%					9.0%	26.0%	23.2	26.3
≥70	61	29.2%	11	3.5%					1.6%	27.3%	31.8	18.7
	p-value for chi-square <0.0001											
Gender												
Male	126	60.3%	221	70.6%					7.9%	32.1%	29.5	10.5
Female	83	39.7%	92	29.4%					10.8%	65.2%	17.0	7.5
Residence												
Plains	107	51.9%	208	66.9%					14.0%	42.8%	30.6	14.9
Hill	95	46.1%	97	31.2%					4.2%	40.2%	26.4	11.9
Mountains	4	1.9%	6	1.9%					0.0%	33.3%	24.0	9.5
	p-value for chi-square 0.0025											
Race/Ethnicity												
Brahmin	47	22.5%	78	24.9%	1.00		1.00		6.4%	39.7%	38.0	10.5
Chettri	33	15.8%	51	16.3%	0.97	0.51-1.84	0.88	0.44-1.78	3.0%	37.3%	24.5	11.2
R,L,M	58	27.8%	31	9.9%	3.55	1.89-6.68	3.11	1.55-6.23	6.9%	41.9%	24.9	7.45
T,M	25	12.0%	71	22.7%	1.09	0.56-2.14	1.15	0.55-2.39	20.0%	46.5%	16.5	5.6
Other	46	22.0%	82	26.2%	1.10	0.62-1.95	1.00	0.53-1.87	13.0%	42.7%	25.2	11.6
	p-value for chi-square <0.0001											
Religion												
Hindu	189	90.4%	285	91.4%	1.00		1.00		9.5%	42.5%	28.0	10.0
Other	20	9.6%	27	8.7%	1.01	0.51-1.98	0.97	0.48-1.96	5.0%	33.3%	14.0	8.6
	p-value for chi-square 0.7207											
Residence - east/west												
Far west	8	3.9%	10	3.2%	0.92	0.32-2.65	1.04	0.34-3.20	0.0%	30.0%	12.1	16.8
Mid west	33	16.0%	40	12.9%	1.11	0.60-2.03	0.97	0.51-1.86	3.0%	32.5%	30.0	9.6
West	90	43.7%	100	32.2%	1.00		1.00		6.7%	42.0%	26.7	8.7
Central	33	16.0%	99	31.8%	0.49	0.28-0.86	0.47	0.26-0.85	12.1%	48.5%	26.4	11.4
East	42	20.4%	62	19.9%	1.12	0.64-1.96	1.18	0.65-2.13	19.0%	38.7%	21.6	10.0
	p-value for chi-square 0.0014											

<sup>1</sup>adjusted for age, sex, residence (plain, hill, mountain); <sup>2</sup>adjusted for age, sex, residence (plain, hill, mountain), race/ethnicity, education and packyears of tobacco smoking (categories); RLM, Rai, Limbu, Magar; T,M, Tharu, Madishe

**Table 2. Socioeconomic Characteristics of Lung Cancer Patients and Controls in Nepal**

	Cases n=209		Controls n=313		Adjusted OR <sup>1</sup>	95% CI	Adjusted OR <sup>2</sup>	95% CI	Never smokers		Median packyears	
	N	%	N	%					cases	controls	cases	controls
Age <40	13	6.2%	22	7.0%					61.5%	63.6%	3.2	1.4
Education												
<3rd Std.	170	81.3%	159	50.8%	1.00		1.00		7.6%	34.6%	23.4	11.5
4th-High	33	15.8%	116	37.4%	0.36	0.14-0.91	0.41	0.24-0.68	18.2%	44.4%	34.1	8.5
≥Tertiary	6	2.9%	37	11.8%	0.40	0.24-0.66	0.39	0.14-1.10	0.0%	64.9%	25.5	5.3
p-value for chi-square			<0.0001		p trend		<0.0002		p trend		0.0008	
Marital Status												
Married	165	80.0%	295	94.3%	1.00		1.00		9.7%	42.7%	26.7	9.6
Other	44	21.1%	18	5.8%	2.34	1.21-4.55	2.25	1.12-4.53	6.8%	27.8%	22.5	11.8
p-value for chi-square			<0.0001									
Rurality												
Rural	175	84.1%	240	76.7%	1.00		1.00		9.1%	39.6%	26.7	10.0
Urban	33	15.9%	73	23.3%	0.73	0.44-1.21	0.99	0.54-1.74	9.1%	49.3%	23.0	9.6
p-value for chi-square			0.0384									
SES index												
3 (high SES)	23	11.1%	52	16.7%	0.54	0.29-0.99	0.68	0.35-1.30	8.7%	48.1%	20.0	10.4
4	104	50.0%	111	35.6%	1.00		1.00		8.7%	38.7%	28.5	11.3
5	52	25.0%	85	27.2%	0.75	0.46-1.23	0.77	0.45-1.30	9.6%	40.0%	20.0	9.6
6-7 (low SES)	29	13.9%	64	20.5%	0.68	0.38-1.21	0.52	0.28-0.98	10.3%	43.8%	25.7	9.1
p-value for chi-square			0.0066		p trend		0.9216		p trend		0.2359	

<sup>1</sup>adjusted for age, sex, residence (plain, hill, mountain); <sup>2</sup>adjusted for age, sex, residence (plain, hill, mountain), race/ethnicity, education and packyears of tobacco smoking (categories)

**Table 3. Tumor Characteristics**

	Total		Males		Females	
	N	%	N	%	N	%
ICD						
p-value for chi-square			0.3179			
C34.0 (main bronchus)	9	4.3	3	2.4	6	7.2
C34.1 (upper lobe)	104	49.8	69	54.8	35	42.2
C34.2 (middle lobe)	8	3.8	4	3.2	4	4.8
C34.3 (lower lobe)	28	13.4	17	13.5	11	13.3
C34.8 (overlapping)	10	4.8	7	5.6	3	3.6
C34.9 (lung NOS)	50	23.9	26	20.6	24	28.9
Histology						
p-value for chi-square			0.0980			
Small cell carcinoma	36	17.2	22	17.5	14	16.9
Non-small cell carcinoma	53	25.4	40	31.7	13	15.7
Adenocarcinoma	21	10.0	9	7.1	12	14.5
Squamous cell carcinoma	80	38.3	43	34.1	37	44.6
Others	3	1.4	2	1.6	1	1.2
Missing	16	7.7	10	7.9	6	7.23
Stage T						
p-value for chi-square			0.4304			
T1	1	0.5	0	0.0	1	1.2
T2	8	3.9	4	3.2	4	4.8
T3	45	22.0	28	22.2	18	21.7
T4	66	31.6	37	29.4	29	34.9
missing	88	42.1	57	45.2	31	37.3
Stage N						
p-value for chi-square			0.6547			
N0	20	9.6	13	10.3	7	8.4
Nx	35	16.7	17	13.5	18	21.7
N1	44	21.1	25	19.8	19	22.9
N2	19	9.1	11	8.7	8	9.6
N3	1	0.5	1	0.8	0	0.0
missing	90	43.1	59	46.8	31	37.3
Stage M						
p-value for chi-square			0.2979			
M1	24	11.5	11	8.7	13	15.7
M2	10	4.8	7	5.6	3	3.6
Mx	88	42.1	51	40.5	37	44.6
missing	87	41.6	57	45.2	30	36.1
Combined stage						
p-value for chi-square			0.1180			
1	2	1.0	2	1.6	0	0.0
2	7	3.3	6	4.8	1	1.2
3	78	37.3	43	34.1	35	42.2
4	34	16.3	18	14.3	16	19.3
missing	88	42.1	57	45.2	31	37.3

rurality ( $p<0.0001$ ) and SES index ( $p=0.0006$ ). Since in Table 1 and 2, the adjusted OR2 included adjustment for race/ethnicity, education and residence (plains, hilly, mountain), we accounted for most of these correlations when examining the various demographic or socioeconomic variables as disparity factors. The association which was not accounted for, was between rurality and SES index ( $p<0.0001$ ), and between residence (east-west) and SES index ( $p<0.0001$ ). However, we did not observe any association with lung cancer risk for rurality or any clear dose-response trend between the SES index and the lung cancer risk, thus we did not consider this for further adjustment.

The tumor characteristics of the lung cancer patients are shown overall and by gender in Table 3. Tumors in the upper lobe of the lung were most common, followed by unspecified site. The most common histology was squamous cell carcinoma of the lung, followed by non-small cell carcinoma. Unfortunately, a fairly large proportion of patients were classified as non-small cell carcinoma which includes both squamous cell carcinoma and adenocarcinoma histologies. As expected, a high proportion of patients had late T stage, were node positive and had metastasis. There did not appear to be differences by gender when considering T stage, N stage and M stage separately or combined.

When we examined the proportion of patients with latestage tumors by demographic and SES groupings, we observed a higher proportion of patients with late stage for women (98.1%) compared to men (88.4%;  $p$ -value for chi-square=0.0447). Though the differences were not statistically significant, we observed higher proportions of late stage for the Chettri ethnic group (100%) compared to the Brahmin group (87.1%) and other ethnic groups, in the lowest education group (94.9%) compared to the highest education group (66.7%), in lower SES index groups (96.4% and 95.2%) compared to the high SES

group (83.3%), and in individuals who lived in rural regions (94.3%) compared to urban regions (81.3%). There did not appear to be large differences by age groups or by marital status in the proportion of late stage tumors. Finally, though statistically significant differences were not observed, higher proportions of late stage tumors were observed in patients from the mountains (100%) and hills (96.7%) compared to the plains (87.5%), and in patients from far east (100%) and Midwest (100%) than patients from the central (84.6%) and east (88.5%) regions.

## Discussion

We observed differences in lung cancer risk and the distribution of tumor characteristics by various demographic and socioeconomic factors for the Nepalese population. More specifically, increased lung cancer risks were observed for the Rai/Limbu/Magar ethnicity, and in individuals who live in the Western region relative to the Central region (where the BPKMC hospital is located). These groups did not in particular have higher medians of packyear exposure among controls nor an especially high proportion of ever smokers, thus it does not appear that tobacco smoking would be the major culprit behind these differences in risk. The Central region is known to be more advanced with great number of health facilities available.

We also observed higher risk of lung cancer among individuals who had lower education or were unmarried, but did not observe differences by lung cancer risk by rurality or SES index. It did appear that individuals with lower education had a higher median packyear exposure and a higher proportion of ever smokers. Differences in packyear medians were not great between controls who were married vs. unmarried, however, the proportion of never smokers among the married controls was much greater (42.7%) than among unmarried individuals (27.8%). Thus the higher lung cancer risk observed for individuals with lower education and individuals who were unmarried may be partly due to the cigarette smoking. Though we did adjust for cigarette smoking in packyear categories, residual confounding is still a concern. Interestingly, differences in median packyear exposure were not apparent whether individuals lived in urban areas or rural areas.

Statistically significant differences by gender for the tumor characteristics were not observed. There did appear however to be a higher proportion of women with squamous cell carcinomas and adenocarcinomas compared to men. However, this comparison is difficult due to the large proportion of patients who were classified as 'non-small cell carcinoma' which includes both squamous cell carcinomas and adenocarcinomas. There was difficulty in histological classification of the tumor. Though our research team plans to improve the histological classification of lung cancer patients being recruited in the future, this situation may be part of the difficulties of lung cancer management in a LMC.

Late stage tumors were more prevalent among women, and possibly in individuals who lived in rural regions and had lower education. Though the result for

women is surprising, the late stage diagnosis, though unfortunate, may be expected for the lower education and rural residents because of limited access to healthcare. From our results, we may predict that female lung cancer patients would have lower survival than male lung cancer patients.

There are some limitations in our study, including the self reported measure of demographic variables that were used to calculate the respondent's socioeconomic status. However, we would not expect any inaccuracies in the self report to be different by case or control status, thus we may expect bias toward the null assuming no other sources of bias. Another limitation is that our study is hospital-based in a major cancer hospital, thus it is unlikely that our cases are representative of all lung cancer cases in Nepal. We expect that an unknown but significant proportion of lung cancer cases may not even be diagnosed, thus at present it would be impossible to capture all lung cancer cases in Nepal with a population-based approach. We believe however that it is important to start examining the major risk factors of the lung cancer patients who can be captured.

Our control series is not population-based, thus it is possible that the distribution of the factors of interest do not reflect the distribution in the base population. Hospital-based controls from the surrounding hospitals are difficult to match on geographic region since people from various regions of Nepal come to the cancer hospital for treatment. Additionally, typically used approaches to recruit population-based controls are not possible in Nepal. Random digit dialing is not possible because the majority of Nepalese do not have home phones or cell phones. Population-based records such as census records are not available. Though visitors are not an ideal source because they may share environmental characteristics with the cancer patients, we believe this is the best source of controls that is possible at the moment. Finally, since our case-control study is somewhat limited in sample size at present, some of the associations we observe may be due to chance and we may also not have adequate power to detect moderate risks.

In summary, within the medically underserved population of Nepal, disparities in lung cancer risk were observed by race/ethnicity, education, marital status, and by region of residence. This is the first epidemiologic study of lung cancer in Nepal. Further research on disparities in lung cancer in Nepal is warranted, in order to develop better prevention efforts against lung cancer. More specifically it would be of interest to understand survival differences between women and men, and by other disparity groups.

## Acknowledgments

We would like to thank all of the study participants for taking part in this study. We would also like to thank Dr. Paolo Boffetta and Dr. Peter Boyle for their support of this study. The study was carried out with funds from the International Agency for Research on Cancer (Lyon, France), the Huntsman Cancer Institute (Salt Lake City, Utah) and the University of Maryland (College Park,

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