Low Cancer Risk of South Asians: A Brief Report

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ABSTRACT

Context: South Asians (ancestry in India, Pakistan, Bangladesh, or Sri Lanka) may have lower cancer risk than other racial-ethnic groups.

Objective: To supplement published cohort data suggesting low cancer risk in South Asians.

Design: Logistic regression models with 7 covariates to study cancer mortality through 2012 in 273,843 persons (1117 South Asians) with baseline examination data from 1964 to 1985.

Main Outcome Measure: Cancer mortality.

Results: Through 2012, death was attributed to cancer in 28,031 persons, of which 1555 were Asians, including 32 South Asians. The all-Asian vs white adjusted odds ratio was 1.0, and the South Asian vs white odds ratio was 0.5 ($p < 0.001$). In separate regressions, South Asians were at lower risk than blacks, Chinese, Filipinos, Japanese, or other Asians. The South Asian-white disparity was concentrated in men but was generally similar when strata of smoking, body mass index, baseline age, and date of death were compared.

Conclusion: These data support the observation that compared with whites and other Asian groups, South Asians, especially men, have a lower risk of cancer.

INTRODUCTION

Studies of racial-ethnic disparities in cancer risk lead to greater understanding of etiology and point out needs for targeted screening and education. Several reports suggest that South Asians, defined as persons with ancestry in India, Pakistan, Bangladesh, or Sri Lanka, may have lower cancer risk than other racial-ethnic groups.[1-6] Our recent incidence study in 124,193 persons confirmed this and suggested that South Asians may have lower cancer risk than any other US racial-ethnic group.[7] Hoping to cast more light on this, we expanded our study cohort to 273,843 persons and report here an analysis of 28,913 deaths attributed to cancer.

METHODS

Subjects and Data

The institutional review board of Kaiser Permanente approved the study protocols. Subjects were 273,843 persons with available detailed racial classification who underwent health examinations offered by a comprehensive Northern California Health Plan. Taken as a voluntary health appraisal, the examination included health measurements and queries about sociodemographic status, habits, and medical history.[8] As previously described,[9] detailed racial classification was available for 2 time intervals: 1964 to 1973 and 1978 to 1985. For persons with multiple examinations, baseline data from the first examination were used.

Mortality Ascertainment

We followed subjects through December 2012 using an automated matching system[10] that ascertained deaths in California. Presumption of complete follow-up yielded a calculated 8,215,000 person-years of follow-up, but estimates[11] suggest a sensitivity of 89% for the method used. The match found 28,913 deaths attributed to cancer. We accepted primary International Classification of Diseases, Ninth Revision death certificate codes, converting from Eighth Revision codes when necessary. Tables 1 a and b present race-ethnicity distributions.

We used logistic regression with 8 covariates, including sex, race, education, marital status, smoking, alcohol habit, and body mass index (BMI). Race-ethnicity was studied primarily with whites as the referent in 2 sets of models: 1) blacks, all Asians, and others (not white, black, or Asian) and 2) blacks, Chinese, Japanese, Filipinos, South Asians, other Asians, and others. Interethnic Asian comparisons were studied by models using Chinese, Filipinos, Japanese, or other Asians as referents.

We studied total cancer and specific cancer types in all persons, year-of-death endpoints, and stratified by sex, race-ethnicity, BMI, and smoking. We present odds ratios (ORs), 95% confidence intervals (CIs), and associated p values.

RESULTS

Tables 1 a and b show that deaths resulting from cancer made up approximately 25% of all deaths and occurred at a slightly younger age than the average age for all deaths. Ethnic differences in mean age of any death and cancer death seemed to parallel the differences in mean baseline age, with South Asians the youngest (32.2 years at baseline) and whites the oldest (38.2 years at baseline). The unadjusted differences in cancer deaths per 1000 subjects, from 29.1 in South Asians to 107.6 in whites, are noteworthy.

In adjusted models, compared with whites, Asians as a composite had similar cancer mortality risk (Table 2). In models including both sexes with whites as the referent, Chinese had slightly higher risk, Japanese and other Asians had similar risk, Filipinos had slightly lower risk, and South Asians had substantially lower risk (OR = 0.5, CI = 0.3-0.7, $p < 0.001$). For the South Asians vs whites comparison, the OR in men was 0.4 (CI = 0.2-0.6, $p < 0.001$) and in women was 0.8 (CI = 0.5-1.3, $p = 0.4$). Disparities in risk were also present

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Table 1a. Racial-ethnic distribution of study population and cancer deaths[a]

Group	Total in cohort (column %)	Mean base age, years	Cancer deaths (column %)	Cancer deaths per 1000	Cancer deaths as percentage of total deaths	Mean age at any death, years	Mean age at cancer death, years
Total	273,843 (100)	38.2	28,013 (100.0)	102.3	27.1	74.4	71.0
Men	123,361 (45.1)	39.1	14,360 (51.3)	116.4	26.8	76.4	70.7
Women	150,482 (54.9)	37.4	13,653 (48.7)	88.8	27.4	72.6	71.4
White	188,929 (69.0)	39.5	20,328 (72.6)	107.6	26.5	75.8	72.0
Men	87,378 (31.9)	40.1	10,357 (37.0)	119.0	26.2	78.0	71.9
Women	101,551 (37.0)	39.0	9971 (35.6)	97.8	26.85	73.7	72.0
Black	50,573 (18.5)	35.1	5169 (18.5)	102.7	28.9	69.6	68.1
Men	20,462 (7.5)	36.9	2665 (9.5)	130.3	29.3	70.9	66.9
Women	30,111 (11.0)	33.8	2504 (8.9)	83.2	28.5	68.3	69.3
Asians	20,685 (7.6)	35.7	1555 (5.6)	75.1	31.1	73.2	69.5
Men	9462 (3.5)	37.2	838 (3.0)	88.6	30.6	73.2	68.5
Women	11,223 (4.1)	34.4	737 (2.6)	85.7	34.8	73.1	70.3
Other/miscellaneous[b]	13,656 (5.0)	37.2	961 (3.4)	70.4	27.3	70.9	69.3
Men	6059 (2.2)	36.7	500 (1.8)	83.2	25.6	73.8	68.6
Women	7597 (2.8)	37.8	461 (1.6)	60.7	29.4	68.6	70.0

[a] Some column percentages do not total to 100 because of rounding.
[b] Not white, black, or Asian.

Table 1b. Asian subgroup distribution of study population and cancer deaths[a]

Subgroup	Total in cohort (column %)	Mean base age, years	Cancer deaths (column %)	Cancer deaths per 1000	Cancer deaths as percentage of total deaths	Mean age at any death, years	Mean age at cancer death, years
Chinese	9519 (3.5)	35.7	810 (2.9)	85.1	32.7	73.6	69.7
Men	4553 (1.7)	37.1	458 (1.6)	100.7	31.3	74.2	69.1
Women	4966 (1.8)	34.4	352 (1.3)	70.8	34.85	73.2	70.1
Filipino	5898 (2.1)	36.7	369 (1.3)	62.5	27.2	73.1	69.3
Men	2469 (0.9)	39.1	191(0.7)	77.3	24.5	71.4	66.6
Women	3339 (1.2)	35.0	178 (0.6)	53.3	30.9	74.4	71.7
Japanese	2999 (1.1)	36.0	280 (1.0)	93.6	34.3	75.1	71.5
Men	1214 (0.4)	37.2	133 (0.5)	104.0	32.2	75.4	71.0
Women	1785(0.7)	35.2	147 (0.5)	82.1	36.5	74.9	72.1
South Asian	1117 (0.4)	32.2	32 (0.1)	29.1	25.4	66.0	63.5
Men	668 (0.2)	33.6	18 (0.1)	26.9	19.8	67.0	62.8
Women	449 (0.2)	30.2	14 (0.1)	32.1	40.0	65.7	64.0
Other Asian[b]	1242 (0.5)	33.4	64 (0.2)	51.6	28.8	66.1	61.8
Men	558 (0.2)	34.3	38 (0.1)	67.9	28.8	67.4	60.7
Women	684 (0.3)	32.7	26 (0.19)	38.2	28.9	65.1	62.5

[a] Some column percentages do not total to 100 because of rounding.
[b] Largely Korean or Vietnamese.

between Asian ethnic groups (Table 2). Compared with Chinese, Japanese subjects had similar risk, whereas Filipinos, South Asians, and other Asians had lower risk. Compared with Filipinos, Japanese subjects had higher risk and South Asians had lower risk. Compared with Japanese subjects, Filipinos and South Asians had lower risk. Compared with other Asians, only South Asians had lower risk.

The lower risk of South Asians was generally consistent in models stratified by smoking, baseline age, and BMI, and in year-of-death endpoints (Table 3). A model that omitted the 378 deaths attributed to skin cancer showed a similar low risk for South Asians (Table 3).

Table 4 presents ORs of South Asians to whites and to Chinese (the largest Asian group) for risk of death attributed to the 10 most common cancer types in the analysis. These types constituted 77.7% of all cancer deaths (81.3% among South Asians). With small numbers of South Asian cases and wide CIs, few ORs showed p values less than 0.05, but

Table 2. Adjusted odds ratios of death caused by any cancer, odds ratio (95% confidence interval)[a]

Ethnicity	All	Men	Women
Among entire study population vs white as referent			
Asian	1.0 (1.0-1.1) [p = 0.5]	1.0 (0.9-1.1) [p = 0.9]	1.0 (0.9-1.1) [p = 0.5]
Chinese	1.1 (1.1-1.2) [p = 0.002]	1.2 (1.0-1.3) [p = 0.02]	1.1 (1.0-1.3) [p = 0.06]
Japanese	1.1 (1.0-1.3) [p = 0.2]	1.1 (0.9-1.4) [p = 0.2]	1.1 (0.9-1.3) [p = 0.4]
Filipino	0.9 (0.8-1.0) [p = 0.02]	0.8 (0.6-0.9) [p = 0.004]	0.9 (0.8-1.1) [p = 0.4]
South Asian	0.5 (0.3-0.7) [p < 0.001]	0.4 (0.2-0.6) [p < 0.001]	0.8 (0.5-1.3) [p = 0.4]
Other Asian	0.8 (0.6-1.1) [p = 0.2]	0.9 (0.6-1.3) [p = 0.5]	0.8 (0.5-1.1) [p = 0.2]
Among entire study population vs black as referent			
South Asian	0.3 (0.2-0.5) [p < 0.001]	0.2 (0.1-0.4) [p < 0.001]	0.6 (0.3-1.0) [p = 0.002]
Among Asians vs Chinese as referent			
Japanese	1.0 (0.9-1.3) [p = 0.99]	1.0 (0.8-1.3) [p = 0.9]	1.0 (0.8-1.2) [p = 0.96]
Filipino	0.7 (0.6-0.8) [p < 0.001]	0.6 (0.5-0.8) [p < 0.001]	0.8 (0.6-0.9) [p = 0.008]
South Asian	0.4 (0.3-0.6) [p < 0.001]	0.3 (0.2-0.5) [p < 0.001]	0.6 (0.4-1.1) [p = 0.1]
Other Asian	0.7 (0.5-0.9) [p = 0.01]	0.8 (0.6-1.2) [p = 0.2]	0.6 (0.4-1.0) [p = 0.04]
Among Asians vs Filipino as referent			
Japanese	1.4 (1.0-1.7) [p < 0.001]	1.6 (1.2-2.0) [p < 0.001]	1.3 (1.0-1.7) [p = 0.04]
South Asian	0.6 (0.4-0.9) [p = 0.005]	0.5 (0.3-1.0) [p = 0.01]	0.8 (0.5-1.5) [p = 0.6]
Other Asian	1.0 (0.8-1.4) [p = 0.9]	1.3 (0.5-1.1) [p = 0.4]	0.8 (0.5-1.3) [p = 0.5]
Among Asians vs Japanese as referent			
South Asian	0.4 (0.3-0.6) [p < 0.001]	0.3 (0.2-0.5) [p < 0.001]	0.6 (0.4-1.1) [p = 0.1]
Other Asian	0.7 (0.5-1.0) [p = 0.02]	0.7 (0.5-1.1) [p = 0.02]	0.6 (0.4-1.0) [p = 0.1]
Among Asians vs other Asian as referent			
South Asian	0.6 (0.4-0.9) [p = 0.002]	0.4 (0.2-0.8) [p = 0.005]	1.0 (0.5-2.0) [p = 1.0]

[a] Cohort has 273,843 persons with 28,013 cancer deaths through 2012. Odds ratios (95% confidence intervals in parentheses) are from logistic models with age, sex, race, smoking, alcohol, body mass index, education, and marital status.

Table 3. Adjusted odds ratios of South Asians vs whites in selected groups[a]

Group	Number of subjects with cancer	OR (95% CI) vs whites[b]	p value
Never smoked	7464	0.6 (0.3-0.9)	0.01
Ex-smokers	4335	0.1 (0.02-0.9)	0.03
Smoke < 1 pack/d	5549	0.6 (0.3-1.4)	0.2
Smoke ≥ 1 pack/d	7972	0.6 (0.2-2.0)	0.4
Baseline age < 40 y	7909	0.7 (0.4-1.0)	0.1
Baseline age 40-49 y	8282	0.1 (0.2-0.7)	0.005
Baseline age 50-59 y	7350	0.2 (01-0.9)	0.03
Baseline age ≥ 60 y	4472	0.2 (0.02-1.9)	0.2
Died in 1964-1979	3795	0.3 (0.1-2.4)	0.5
Died in 1980-1989	6429	0.4 (0.3-1.4)	0.3
Died in 1990-1999	8220	0.4 (0.2-0.9)	0.02
Died in 2000-2012	9569	0.5 (0.3-0.8)	0.005
BMI < 25 kg/m^2	13,909	0.5 (0.3-0.8)	0.005
BMI 25-29 kg/m^2	9563	0.4 (0.2-0.8)	0.02
BMI ≥ 30 kg/m^2	2744	0.8 (0.2-3.8)	0.8
Nonskin cancer[c]	27,635	0.5 (0.4-0.7)	< 0.001

[a] Cohort has 273,843 persons with 28,013 cancer deaths through 2012; because of missing values, sums of cancer subjects in smoking and BMI strata are less than 100%.
[b] OR (95% CI) are from logistic models with age, sex, race, smoking, alcohol, BMI, education, and marital status.
[c] Endpoint is all cancer except 378 cases attributed to skin cancer.
BMI = body mass index; CI = confidence interval; OR = odds ratio.

9 of the 10 South Asian-white or South Asian-Chinese comparisons in men had either an OR below 1.0 or no South Asian cases. Among women, 8 of the 10 cancer types had no cases or an OR below 1.0 for either set of comparisons.

DISCUSSION

Our finding of reduced cancer risk in South Asians aligns with sparse previous reports.[1-6] In a study of cancer incidence among Asian Indians or South Asians in India, Singapore, the UK and the US, the lowest total cancer incidence rates were observed in India and the highest in US whites.[6] Cancer incidence rates among Indians residing outside India were intermediate, leading to the conclusion that overseas South Asians appeared to adopt the cancer patterns of their host country. In another analysis, Mangtani et al[2] compared ethnic South Asian immigrants in England and Wales with non-South Asian first-generation immigrants; all-cancer rates in ethnic South Asians were half those in other immigrant groups. A longer-term study of cancer incidence in South Asian migrants to England from 1986 to 2004 showed that overall, age-adjusted cancer incidence in South Asians was half that in non-South Asians but rose over time.[4] The authors concluded that "although still lower than in non-South Asians, cancer incidence is rising in South Asians, supporting the concept of transition in cancer incidence among South Asians living in England." In a later study, Maringe et al[3] reported that although the survival advantage of South Asians tended to narrow for some cancer types over time, it remained present for colorectal, liver, and lung cancers in men. Comparing Asian Indians/Pakistanis with white Americans, Goggins and Wong[1] reported low cancer incidence and generally above-average survival in South Asians; standardized incidence ratios in men and women were 0.46 (95% CI = 0.44-0.48), and 0.55 (95% CI = 0.53-0.58), respectively. In a report based on racial-ethnic classification from the US 2000 census, Miller et al[5] showed in 7 Asian ethnic groups that cancer incidence and mortality rates were lowest among Asian Indian/Pakistani and Guamanian men and women.

Our 2016 report of cancer incidence in Asian Americans in California showed that adjusted ORs among South Asians vs whites for any cancer were 0.5 (CI = 0.4-0.7, p = 0.002) in men and 0.6 (CI = 0.3-0.9, p = 0.02) in women.[7] That analysis confirmed the established higher Asian/White risk of stomach, liver, and cervical cancer and lung adenocarcinoma.[7] However, South Asians had no significantly increased risk for these cancer types in either the incidence data[7] or the present mortality study. South Asians had slightly increased risk of incident upper airway and digestive tract cancers in men and ovarian cancer in women,[7] but mortality data in Table 4 do not show these associations. In both reports, most Asian groups, including South Asians, had lower risk of melanoma, bladder cancer, and malignant glioma (data not shown). In both analyses, the numbers of South Asian cases were insufficient for stable risk estimates for individual cancer types.

The lower total cancer risk among South Asians (Table 2) included contributions from several common specific cancer types (Table 4). Consistency in strata (Table 3) added to the validity of the finding. Although South Asians in this study population had a relatively low prevalence of smoking,[12] their lowered cancer risk compared with whites in never smokers was similar to that in other smoking subgroups. The persistence of South Asians' lower cancer risk in the later years of follow-up (Table 3) as well as the prior reports across different geographic regions support the validity of our findings.

Hypothetical explanations for low cancer risk in South Asians are all speculative, but an interplay of genetic and environmental factors seems likely. There are reports of distributions favorable to South Asians of genetic mutations associated with decreased risk of certain cancers. Examples are lower prevalence of *BRCA2* than *BRCA1* mutations in several Indian studies[13] for breast cancer and polymorphism at *GSTM1* and *GSTP1* gene loci for prostate cancer.[14] South Asians appear to have a high prevalence of polymorphisms in DNA repair systems XRCC1 and XPD, which aid in DNA repair and reduce cancer susceptibility.[15] Speculation about environmental contributors include low tobacco and alcohol use,[12] plus favorable dietary practices, such as vegetarianism and use of turmeric (curcumin), other spices, and food additives.[16] A relatively high use of screening behaviors and access to care have also been cited.[3,6] In our study population, South Asians were a highly educated and scientifically sophisticated group, making adherence to healthy lifestyle practices a plausible factor in their reduced cancer risk.

In addition to small numbers of cancers in South Asians, limitations of our analyses include an absence of data about diet and other potential lifestyle factors, and use of only baseline measurements. Strengths include the size of the total study cohort, the long follow-up, and control for several potential confounders. Our findings do not point to any specific recommendations for public health measures, but we hope that our report will stimulate research that may lead to interventions that might reduce cancer incidence.

CONCLUSION

In concert with previous studies, the present report strengthens the validity of

Table 4. Adjusted risk of death from the most common cancer types among South Asians[a]

Cancer type	Number of cancers, all/SA	SA vs whites, OR (95% CI)			SA vs Chinese, OR (95% CI)		
		Both sexes	Men	Women	All	Men	Women
Lung	6375/2	0.2 (0.1-0.9) [p = 0.03]	No SA cases	0.8 (0.1-5.9) [p = 0.7]	0.1 (0.03-0.5) [p = 0.003]	No SA cases	0.4 (0.1- 1.8) [p = 0.3]
Colorectal	2903/1	0.2 (0.02-1.0) [p = 0.7]	No SA cases	0.5 (0.1-3.7) [p = 0.2]	0.5 (0.01-0.8) [p = 0.02]	No SA cases	0.5 (0.1-2.7) [p = 0.5]
Breast	2447/3	—	—	0.6 (0.2-1.9) [p = 0.4]	—	—	0.5 (0.02-1.7) [p = 0.3]
Hematologic[b]	2786/7	0.7 (0.4-1.6) [p = 0.4]	1.0 (0.5-2.2) [p = 0.9]	No cases	0.9 (0.4-2.0) [p = 0.8]	1.1 (0.4-1.6) [p = 0.8]	No cases
Prostate	2057/3	—	0.5 (0.2-1.5) [p = 0.2]	Not applicable	—	0.8 (0.2-1.8) [p = 0.7]	Not applicable
Pancreas	1895/3	0.4 (0.1-1.6) [p = 0.2]	0.3 (0.04-1.8) [p = 0.2]	0.8 (0.1-5.9) [p = 0.8]	0.4 (0.1-1.6) [p = 0.2]	0.4 (0.04-2.8) [p = 0.3]	0.5 (0.1-3.8) [p = 0.5]
Upper airway, digestive[c]	1026/2	0.5 (0.1-3.7) [p = 0.5]	0.6 (0.1-4.0) [p = 0.6]	No SA cases	0.4 (0.1-3.1) [p = 0.4]	0.4 (0.1-3.3) [p = 0.4]	No SA cases
Stomach	910/0	No SA cases	No SA cases	No SA cases	No SA cases	No SA cases	No SA cases
Ovary	790/3	—	Not applicable	1.8 (0.6-5.6) [p = 0.3]	—	Not applicable	2.4 (0.7-8.6) [p = 0.2]
Liver	671/2	1.0 (0.2-4.0) [p = 0.99]	0.6 (0.1-4.1) [p = 0.6]	3.5 (0.5-25.9) [p = 0.3]	0.2 (0.05-0.8) [p = 0.2]	0.1 (0.01-0.8) [p = 0.2]	1.6 (0.2-13.4) [p = 0.6]

[a] Logistic models include sex, age, race, education, ethnicity, alcohol, smoking, and marital status.
[b] Includes non-Hodgkin lymphoma, multiple myeloma, myelogenous leukemia, lymphocytic leukemia, Hodgkin lymphoma (n = 73), and 235 other and unspecified leukemia.
[c] Upper airway, digestive: Codes 140-150 except 142, 147, and 161.
CI = confidence interval; SA = South Asians.

the observation that compared with whites and other Asian groups, South Asians, especially South Asian men, have an unexplained lower risk of cancer. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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