UNIVERSITY OF SOUTHERN CALIFORNIA

Keck School of Medicine

Department of Preventive Medicine
USC Cancer Surveillance Program

Community Cancer Assessment Regarding Beverly Hills, California

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The University of Southern California Cancer Surveillance Program (USC-CSP) is the population-based cancer registry for Los Angeles County that was begun in 1972. By law, all cancers diagnosed in California since January 1, 1988 are reported to one of the regional registries that form the California Cancer Registry (CCR), the legally mandated cancer reporting system of California. The USC-CSP serves as Region 9 of the CCR, and is also one of the registries participating in the National Cancer Institute's Surveillance, Epidemiology and End-Results Program. Cancer surveillance in the USC-CSP is funded by the California Department of Health Services, the Centers for Disease Control and Prevention, and the National Cancer Institute. Data is collected on all new cancer patients inAngeles County since 1972 and includes information on age, race/ethnicity, address at diagnosis, gender and specific type of cancer. All invasive cancers, excluding non-melanoma skin cancers, are reported, along with in situ breast and bladder cancer, and benign brain tumors. Completeness of the reporting to the registry is estimated at over 95%.

This report is in response to concerns expressed by parents regarding an alleged excess of different types of cancers among alumni of Beverly Hills High School who attended during the period 1975-1997. In order to address this particular concern, the cases would have to be validated by examination of pathology reports, the case definition standardized to the definition of the population at risk (for example, if the cases include persons who attended Beverly Hills High School for less than one year, then the population at risk must include the same number of people), and ideally the exact number of persons in each class should be known. The case definition should exclude persons with benign tumors or conditions other than invasive malignancies (except non-melanoma skin cancer, which is not a reportable cancer). In addition, the denominator must include years of follow-up for all persons at risk (approximately 230,000 person-years for an average class size of 500 followed during the period 1975-1997, and 322,000 person-years for an average class size of 700), in order to be comparable to incidence rates per 100,000 person-years. Finally, the annual incidence rate of Hodgkin's disease cannot be used as a comparison to the number cases accumulating over many years, (which is a cumulative risk or prevalence), a completely different measure. Because all of this information has not been provided to the Los Angeles County Department of Health Services or the USC Cancer Surveillance Program, the risk among the alumni cannot be directly assessed.

Instead, we can evaluate the risk among residents of Beverly Hills of roughly the same age group, 15-44, by comparing the observed numbers of cases in this age group to that expected based on incidence rates of similar people in Los Angeles (of the same age, race, gender and socioeconomic status). Whenever possible, we examined the occurrence of cancer by gender, race/ethnicity and socioeconomic status strata; otherwise we used expected numbers based on all socioeconomic status groups combined using age-adjusted LAC-wide incidence rates. If the expected or observed number of cancers in the census tract for any given comparison is 10 or less, the analysis is

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suppressed, since results would be difficult to interpret. In the attached tables we report the 95% confidence interval around the expected number, the observed number and the relative risk (risk in Beverly Hills compared to elsewhere in Los Angeles), when the relative risk was greater than 1.5 and the p value was less than 0.05. We use these cut-off points because they are epidemiological standards when interpreting possible causal associations. We assessed the neighborhood risks of non-Hodgkin's lymphoma, Hodgkin's lymphoma, and thyroid cancer because those were the cancers that parents were concerned about.

Results:
The observed numbers of Hodgkin's lymphoma, non-Hodgkin's lymphoma and thyroid cancer among white residents were within the expected range compared to other whites of similar socioeconomic status, gender and age, although at the upper limits of normal. Results could not be computed for any cancers occurring in non-whites because there were too few cases.

When examined by subtype, most of the thyroid cancer consisted of the papillary subtype. Young white men residing in Beverly Hills had a 3-fold increased risk of papillary thyroid cancer compared to other similar Los Angeles residents, however this is based on very small numbers so the estimate may be unstable and hard to distinguish from chance, and is therefore not included in the tables below. The number of observed cases of papillary thyroid cancer among young women in Beverly Hills was within the expected range. Of note, we observe a similar increase in this type of thyroid cancer among men and women living in other areas near Beverly Hills. The cause of this general increase is not known but initial descriptive studies are underway to address the issue and will be completed later this year.

This type of neighborhood analysis has some limitations. It is possible that residents moved out of Beverly Hills and were diagnosed with cancer while living in other areas, and that persons now residing in Beverly Hills in that age group never attended the high school. This problem of misclassification of residence makes it somewhat difficult to draw inferences about the Beverly Hills High School alumni. If it is ultimately concluded that there is an excess of certain types of cancer among BHHS alumni by qualified academic or public health experts, any determination regarding a purported cause should incorporate known risk factors for those types of cancer. Each type of cancer has a specific set of causes and there has been much learned about these causes for some cancers.

Thyroid cancer (especially the papillary type) has been increasing in Los Angeles and elsewhere over the past decade (see figure below). It is also more common among persons of higher socioeconomic status (Haselkorn T, Cancer, Causes and Control, 11: 2000). Part of the increase could be explained by better diagnosis of smaller lesions. The main risk factor for this type of thyroid cancer is radiation, either ionizing (as in x-rays) or atomic (as in radioactive material). Again, there is no evidence linking petroleum or petroleum products to an increased risk of this cancer.

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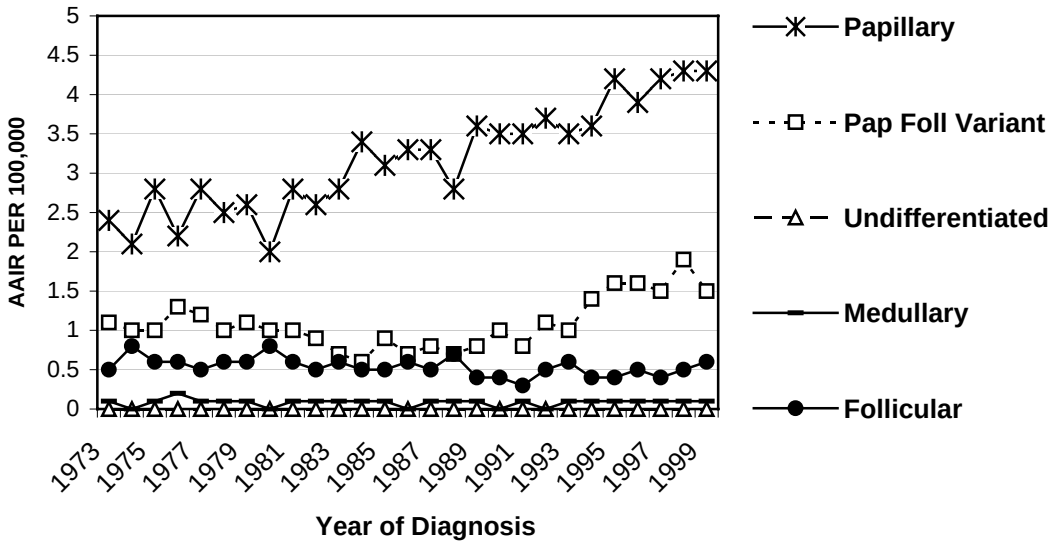
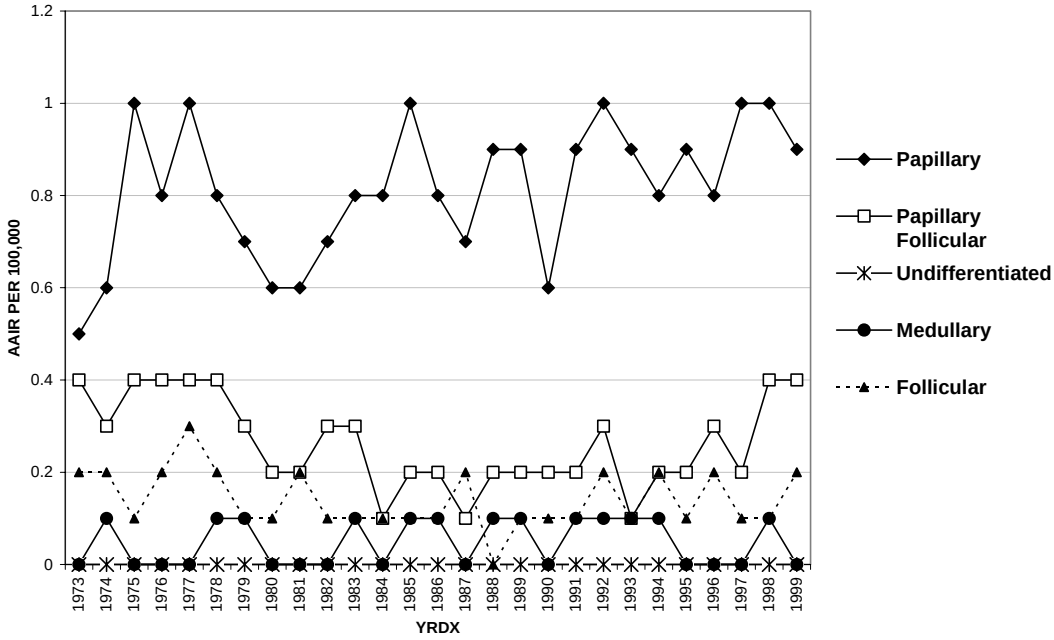
THYROID CANCER AGE ADJUSTED INCIDENCE RATE (AAIR)/ 100,000
IN U.S. FEMALES 0-39 YEARS OF AGE
1973-1999, SEER 9 REGIONS, US2000STANDARD



INVASIVE THYROID CANCER IN US MALES 0-39
1973-1999 US2000STANDARD, SEER 9 REGIONS



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Hodgkin's lymphoma in young adults peaks around age 20-24 and consists mainly of the nodular sclerosing type (Figure 3). It has long been thought to be host response to a delayed infection with a common childhood virus. Persons with 6 or more siblings have 44% less risk of young adult Hodgkin's disease compared to persons with 1-2 siblings (Gutensohn, 1981), and higher socioeconomic status is associated with a 1.5- 2 fold increased risk (Figure 4). The hypothesis states that if children are raised in a protected environment with fewer siblings and very clean surroundings, they are less likely to get exposed to many childhood infections when they are young. Instead they acquire some of these infections when they start high school or college, where they come into more close contact with their peers, and Hodgkin's lymphoma is thought to be the occasional consequence of one of these viruses, as yet unknown. Other diseases with a similar natural history of more severe consequences when contracted at a later age include chickenpox (pneumonia and encephalitis), Epstein-Barr virus (infectious mononucleosis), and pre-vaccine-era polio (paralysis).

Hodgkin's lymphoma has been observed to cluster in space and time (Alexander, 1989), which supports the hypothesis of an underlying infectious cause. As Nancy Mueller, Ph.D., Harvard School of Public Health states in her review of young adult Hodgkin's disease, "In summary, there is evidence that risk of HL in young adults is associated with higher education, higher social class, fewer siblings, less crowded housing, early birth position. All of those factors foster susceptibility to late infections with the common childhood infections... For both young adults and middle-aged persons, there is evidence that HL may be the result of an age-related host response to a common infection. Among older Americans, risk appears to be independent of factors associated with age at infection." (Mueller, N, Hodgkin's Disease in Cancer Epidemiology and Prevention, editors David Schottenfeld and Joseph F. Fraumeni, Jr., 1996, Oxford University Press, page 899-900).

In Los Angeles County, there have been concerns about an excess of young adult Hodgkin's lymphoma at two other high schools over the past 15 years in La Canada and Palos Verdes. These high schools, along with Beverly Hills High School, are in the highest socioeconomic status areas of the county. Because of what we know about the causation of young adult Hodgkin's lymphoma, we would expect an excess of this type of cancer among students at these particular localities.

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Figure 3.

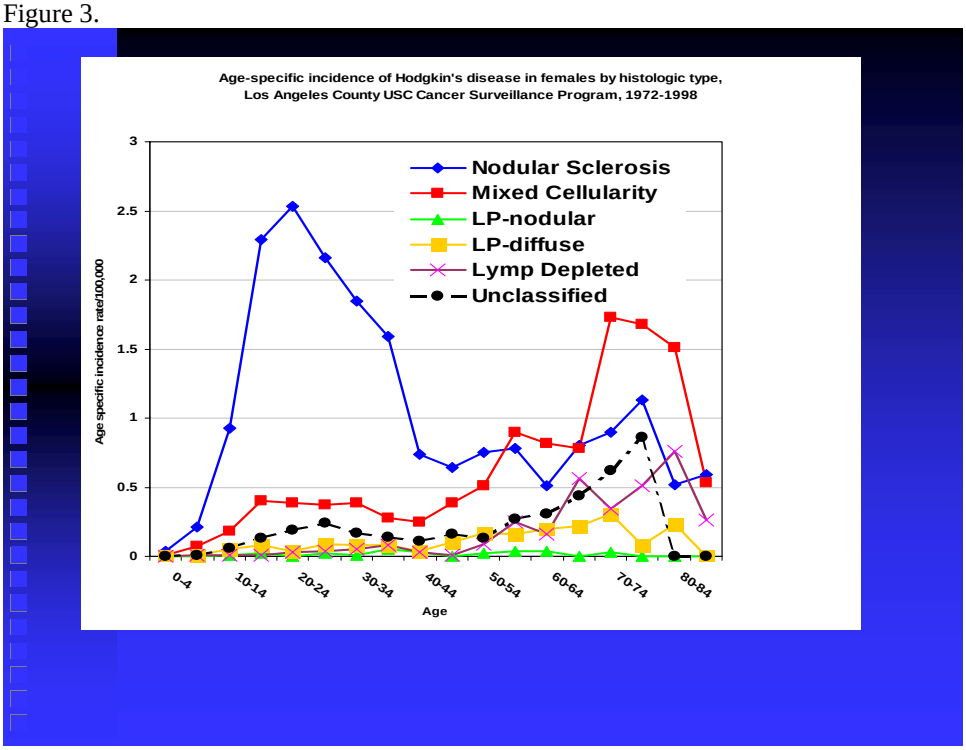
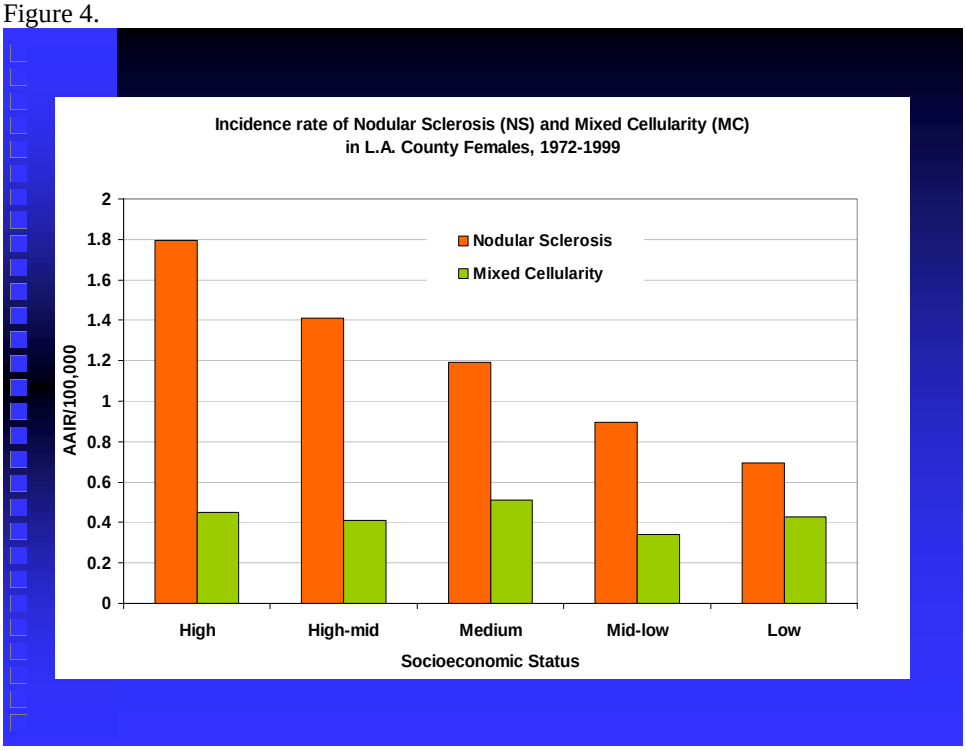


Figure 4.



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Non-Hodgkin's lymphoma is difficult to study because there are many sub-types probably representing many different diseases. Risk factors for non-Hodgkin's lymphoma include immunodeficiency, including acquired (HIV or immunosuppressive therapy associated with transplants), or inherited conditions; exposures associated with agriculture, Helicobacter pylori infection (for gastric lymphoma), and use of black hair dye. Some medical conditions have been associated with NHL including scleroderma and rheumatoid arthritis, and there is recent evidence suggesting that Hepatitis C and blood transfusions may increase risk. But for the most part, risk factors are unknown. There is little evidence linking NHL to exposure to petroleum products. Interested readers are referred to a recent review (Bernstein L and Cozen W, The Epidemiology of Non-Hodgkin's Lymphoma and Multiple Myeloma, in Bertino's Encyclopedia of Cancer).

Oil workers exposed to petroleum and petroleum products have been studied many times. A meta-analysis performed on 9 cohorts of petroleum workers in the U.S. and Britain (over 208,000 workers) confirmed the link between this occupational exposure and a specific type of leukemia (acute myelocytic leukemia), but not other types (Wong, 1995).

A few studies have linked Hodgkin's lymphoma or non-Hodgkin's lymphoma to areas of high traffic density or oil refineries, but these studies are ecological (not based on individual data), based on cancers in different age groups, and the authors themselves have stated that the findings are likely to be due to chance. Many more studies have been published showing no link between oil refineries or petroleum products and these types of cancers. We are continually monitoring cancer incidence in Los Angeles County and have not observed increases in these types of cancers in areas close to active oil wells

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Analysis of thyroid cancer, Hodgkin's lymphoma and non-Hodgkin's lymphoma in Beverly Hills and adjacent areas.

Table 1. Expected and observed numbers of Hodgkin's disease patients ages 15-44 residing in census tracts 700600, 700800, 700901, 700902, and 70100 (Beverly Hills) from 1972-1999, USC Cancer Surveillance Program.

Race/Gender	SES[1]	No. Expected[2]	No. Observed	Relative Risk[3]
Males White	All levels	1-12	11	ns
Female White	Al levels	1-12	10	ns

[1]Socioeconomic status assigned according to characteristics of the census tract of residence at the time of diagnosis (Liu, 1999) SES groups combined if number of cases is < 10).
[2] 95% confidence intervals around the expected number of cancers, based on the gender/race/SES/age specific incidence of that cancer in Los Angeles County applied to the specific population.
3 Not significant (relative risk less than 1.5 or $p > 0.05$).

Table 2. Expected and observed numbers of non-Hodgkin's lymphoma patients ages 15-44 residing in census tracts 700600, 700800, 700901, 700902, and 70100 (Beverly Hills) from 1972-1999, USC Cancer Surveillance Program.

Race/Gender	SES1	No. Expected2	No. Observed	Relative Risk3
Males White	All levels	4-18	15	ns
Females White	All levels	0-11	10	ns

[1]Socioeconomic status assigned according to characteristics of the census tract of residence at the time of diagnosis (Liu, 1999) (SES groups combined if number of cases is < 10).
[2] 95% confidence intervals around the expected number of cancers, based on the gender/race/SES/age specific incidence of that cancer in Los Angeles County applied to the specific population
[3]Not significant (relative risk less than 1.5 or $p > 0.05$).

Table 3. Expected and observed numbers of thyroid cancer patients ages 15-44 residing in census tracts 700600, 700800, 700901, 700902, and 70100 (Beverly Hills) from 1972-1999, USC Cancer Surveillance Program.

Race/Gender	SES1	No. Expected2	No. Observed	Relative Risk3
Males White	All levels	-	<10	ns
Females White	High	3-17	16	ns
	Middle-High	2-14	14	ns

[1]Socioeconomic status assigned according to characteristics of the census tract of residence at the time of diagnosis (Liu, 1999) (SES groups combined if number of cases is < 10).
[2]95% confidence intervals around the expected number of cancers, based on the gender/race/SES/age specific incidence of that cancer in Los Angeles County applied to the specific population.
[3]Not significant (relative risk less than 1.5 or $p > 0.05$).

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