

THE CANCER PROGRAM FOR REDWOOD MEMORIAL & ST. JOSEPH HOSPITALS

2009 ANNUAL REPORT INCLUDING 2008 STATISTICAL REVIEW

LUNG CANCER

INTRODUCTION

Humboldt County is located on the Redwood Coast of Northern California. U.S census data for 2010 reports county population at 134,623, an increase of 6.4% over the previous census. Humboldt County covers 3,572 square miles, with an average population of 37.7 per square mile, compared to 238.9 per square mile statewide. Nearly thirteen percent of the population was over 65 compared to 11.1% in the state population as a whole; income for 19% of the population was below the poverty level in 2009 versus 14.2% statewide. Median household income in Humboldt County was \$35,985 vs. \$58,925 for the state overall.

Redwood Memorial Hospital (RMH) and St. Joseph Hospital (SJH) are located in Humboldt County. SJH, a 189 bed acute care facility with a co-located inpatient Rehabilitation Unit, is located in Eureka, the largest city and county seat. RMH is a 25 bed Critical Care Access Hospital and full-service, acute care facility located in Fortuna, approximately 20 miles south of Eureka. Each hospital has had an active American College of Surgeons (ACoS) accredited Cancer Program since 1991. Every year, a cancer site is chosen for an in-depth analysis to detect trends and monitor outcomes for each hospital. For this Annual Report Year (ARY) 2009 and Statistical Analysis Year (SAY) 2008, lung cancer was chosen as the tumor site for both hospitals. Because of the relatively small number of cases at RMH and the need to refer cases to SJH for radiation therapy and medical oncology consultation, this report will provide analysis of both individual and combined data for the two facilities.

MATERIALS AND METHODS

Cancer Registry (CR) records for lung cancer cohorts from both 1998 to 2002 and annual data for 2008 from the RMH and SJH were compared with national statistics compiled by the American Cancer Society and other national health agencies and programs. The CR classifies cancer cases as analytic if the case is first diagnosed and/or received all or part of the first course of treatment at either RMH or SJH. Non-analytic cases are diagnosed elsewhere and received their entire first course of treatment elsewhere. Non-analytic cases typically enter the CR by requiring follow-up treatment and care after receiving initial treatment elsewhere. Analytic case statistics are used to study outcomes data using five-year survival rates

Incidence from RMH and SJH are given as absolute numbers while national incidence statistics are given as incidence rates per 100,000 population. Outcome analysis (length of survival by stage) was done by comparing the latest National Cancer Data Base (NCDB) lung cancer survival (1998-2002) with the corresponding 1998-2002 cohort of RMH and SJH data

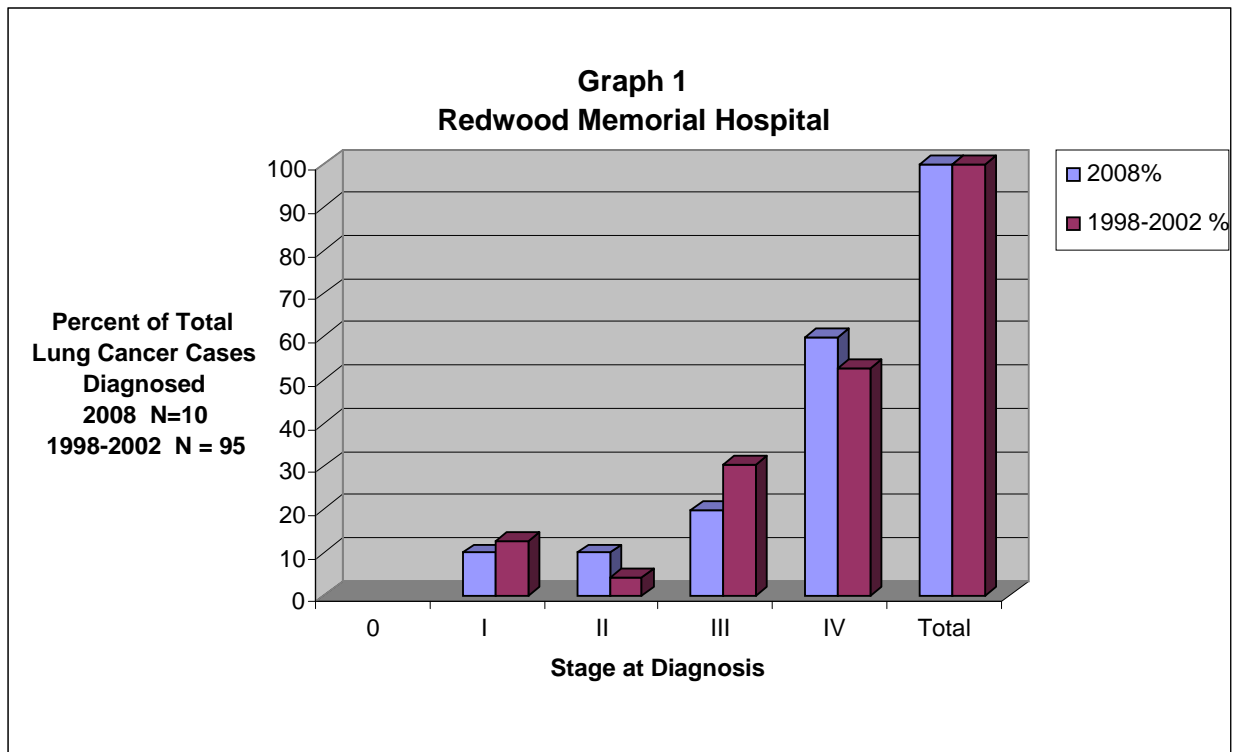
RESULTS

Redwood Memorial Hospital Report

Lung cancer incidence for males in Humboldt County shows a steady incidence from the 1990's to the present and thus does not mirror the decline seen in national statistics, however the numbers are small and do not appear significant. For females, the incidence for RMH patients remains stable while the national statistics show a continued increase in cases.

In 2008, there were 16 AANA (combining analytic and nonanalytic cases) lung cancer cases identified, eight males and eight females. Of the 16 cases, one (6.3%) was small cell lung cancer (SCLC) and 15 cases (93.7%) were nonsmall cell lung cancer (NSCLC). Combined AANA cases from 2000-2008 show 13.5% SCLCs. For comparison to prior years, the 1998 Annual Report shows there were 104 lung cancers at RMH from 1990 to 1996, of which 25% were SCLC. Thus there has been a decline in the percentage of SCLCs from 25% to 13.5% over the last ten to fifteen years.

There were ten RMH 2008 analytic lung cancer cases available for comparative analysis with the 1998-2002 RMH cohort (N=95). The cancer stage distribution for both groups is seen in **Graph 1**. In 2008, 80% of lung cancers were diagnosed in late Stages (III and IV) compared to 83% for the 1998-2002 cohort. There were no significant differences in stage distribution between these two groups for each stage given the small number of cases available.



For comparison, NCDB stage distribution data for nonsmall cell lung cancer 2008 (**Table 1**) show 81% of small cell lung cancer cases and 59% of nonsmall cell cancers presented with Stage III and IV disease.

Table 1			
Stage of Lung, Bronchus - Small Cell Carcinoma Cancer Diagnosed in 2008			
All Diagnosed Cases - All Types Hospitals in All States - Data from 1360 Hospitals			
	Stage	N	%
1.	0	14	0.06%
2.	I	1192	5.5%
3.	II	640	2.95%
4.	III	5751	26.53%
5.	IV	11978	55.25%
6.	OC	31	0.14%
7.	UNK	2072	9.56%
TOTAL		21678	100%

Stage of Lung, Bronchus - Non-Small Cell Carcinoma Cancer Diagnosed in 2008			
All Diagnosed Cases - All Types Hospitals in All States - Data from 1383 Hospitals			
	Stage	N	%
1.	0	214	0.17%
2.	I	31392	25.21%
3.	II	7874	6.32%
4.	III	28927	23.23%
5.	IV	44597	35.82%
6.	OC	243	0.2%
7.	UNK	11256	9.04%
TOTAL		124503	100%

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Tables 2A & 2B show the distribution of treatments by stage performed for the ten 2008 cases. Analysis shows, of the nine NSCLCs, four received radiation only, one had surgery only and 1 had surgery + radiation treatment and three had no treatment. The single SCLC case, which presented with Stage IV disease, received radiation only. Chemotherapy treatment is conspicuously absent. The relatively high proportion of single modality radiation therapy in these advanced-stage patients may well represent palliative treatment (i.e., to bone or brain metastases) rather treatment aimed at disease stabilization. RMH patients requiring radiation and/or chemotherapy treatment are referred, most often to SJH Radiation Oncology Department and to the medical oncologists in Eureka.

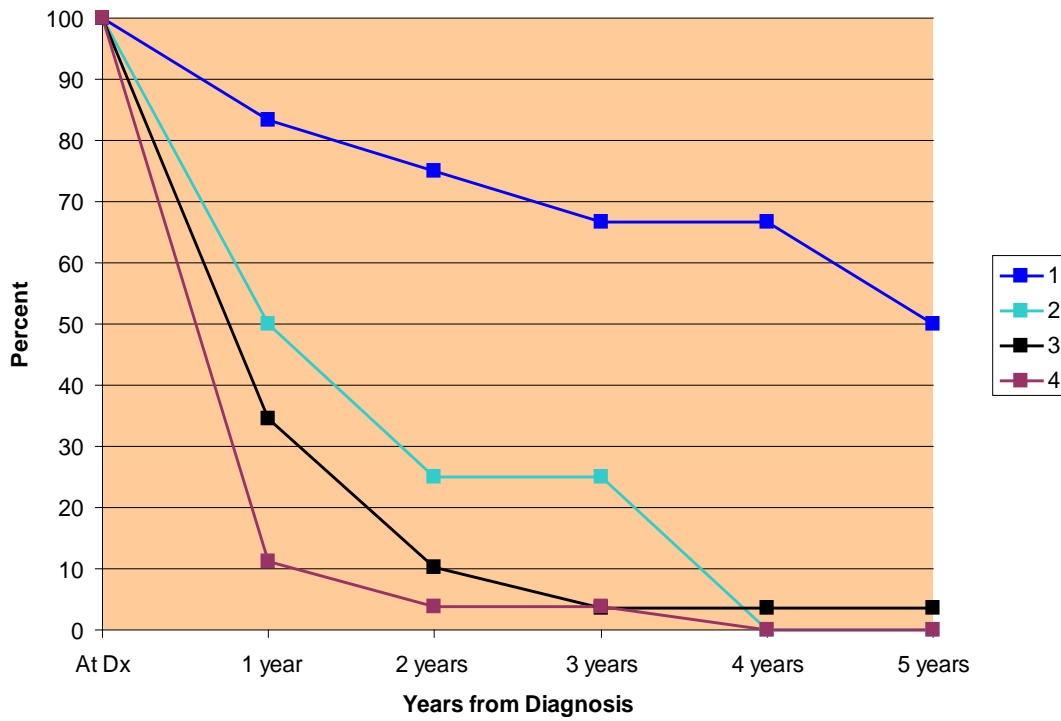
Table 2A Redwood Memorial Hospital, Fortuna CA First Course Treatment by Stage of Lung, Bronchus - Non-Small Cell Carcinoma Cancer Diagnosed in 2008 All Diagnosed Cases							
		Stage				Totals	
		I	II	III	IV	N	%
1.	Radiation Only			2	2	4	44.44%
				50%	50%	100%	
2.	Other Specified Therapy	1				1	11.11%
		100%				100%	
3.	No 1st Course Rx		1		3	4	44.44%
			25%		75%	100%	

Table 2B Redwood Memorial Hospital, Fortuna CA First Course Treatment by Stage of Lung, Bronchus - Small Cell Carcinoma Cancer Diagnosed in 2008 All Diagnosed Cases							
		Stage				Totals	
		I	II	III	IV	N	%
1.	Radiation Only	.			1	1	100%
						100%	
2.	Other Specified Therapy	1				0	N/A

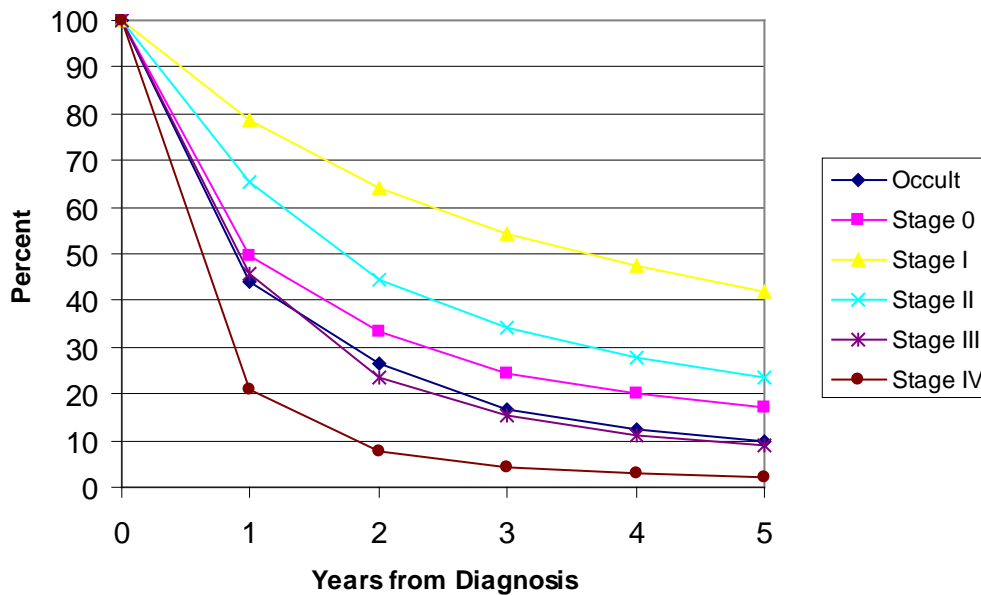
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The most recent actuarial five-year survival curves for RMH analytic cases are constructed utilizing 1998-2002 lung cancer patients for Stages I through IV and are seen in **Graph 2A** and are then compared to 1998-2002 NCDB survival curves for all lung cancer cases by stage in **Graph 2B**. Five-year survival for all RMH patients for all stages for both types is 13.2% and is 0% for the single SCLC case, while NCDB shows a five-year survival of 16.7% for NSCLC and 5.7% for SCLC. The rates do not appear to be significantly different given the small numbers available for evaluation and the relatively high proportion of late stage at diagnosis. For comparison purposes a previous RMH study (the 1990-1996 cohort from the SAY 1997 study) showed 105 analytic cases analyzed showing a five-year survival of 8.6%.

Graph 2A
Observed Survival For Cases Diagnosed in 1998 - 2002 All Lung Cancer Histologies
Redwood Memorial Hospital



Graph 2B
Observed Survival for Lung Cancer Cases, All Histologies
Diagnosed 1998-2002
NCDB Data from 1401 Facilities



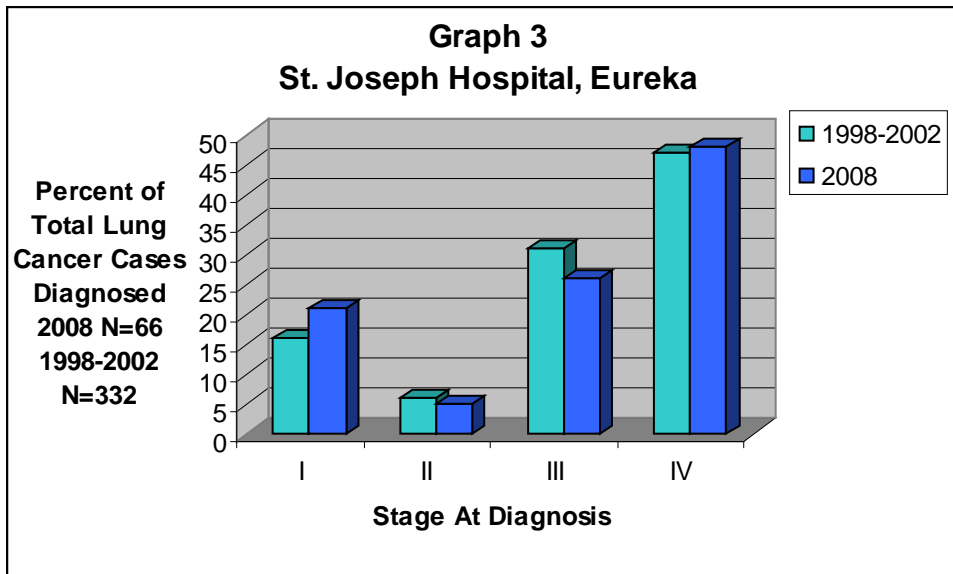
Five-year survival curves by stage for RMH and NCDB lung cancer patients are seen in **Graphs 2a** and **2b**. Survival curves are remarkably similar at each stage, with Stage I RMH patients actually showing higher rates of 5 year survival (50% RMH survival vs. 43.2 % NCDB survival after five years). The greatest negative correlation occurred in Stage II patients with no survivors at 5 years vs. 24.6% survival for the NCDB cohort, however, there were only 4 patients in the RMH cohort available for study. Of note, none of the 50 patients with Stage IV disease survived longer than 4 years.

St. Joseph Hospital Report

The number of diagnosed lung cancers for males at SJH has shown a slow decline which mirrors the decline seen in national data. The NCI State Cancer Profiles report confirms this data, as deaths from lung cancer for men declined in Humboldt County by 2.3 percent annually from 2003 to 2007. The number of lung cancers diagnosed in females shows a slight increase, also similar to national figures, and again mirroring the State Cancer Profile data which showed an increase in deaths from lung cancer for women in Humboldt County of 1.1 percent annually from 2003 to 2007.

In 2008, there were 74 lung cancer cases (combined analytical and non-analytical cases) identified in the SJH Cancer Registry; 35 males and 39 females. Of these 74 lung cancer cases, five were SCLC (6.8%) and 68 were NSCLC (93.2%) with one indeterminate case. For comparison to prior years, the ARY 1998 Report shows there were 520 analytic lung cancer cases collected from 1990-96 showing 15% SCLC and 85% NSCLC. Thus there appears to be a moderate decline in the percentage of SCLC from 15% to 6.8% over the last 10-15 years, corresponding to a reported decline in SCLC nationwide (NCI website monograph on SCLC).

There were 66 SJH 2008 analytic lung cancer cases available for comparative analysis with the 1998-2002 SJH cohort of 583 cases available. The cancer stage distribution for both groups is seen in **Graph 3**. Seventy-five percent of lung cancers were diagnosed in late Stages III & IV compared to 78% for the 1998-2002 cohort, essentially showing no change. There were no significant differences in stage distribution between these two groups. NCDB stage distribution data for NSCLCs shows that between 1998 and 2006, nationwide the majority of patients (63 percent to 67 percent) present with Stage III and IV disease, indicating that RMH and SJH patients are more frequently diagnosed at later stages than the national averages.



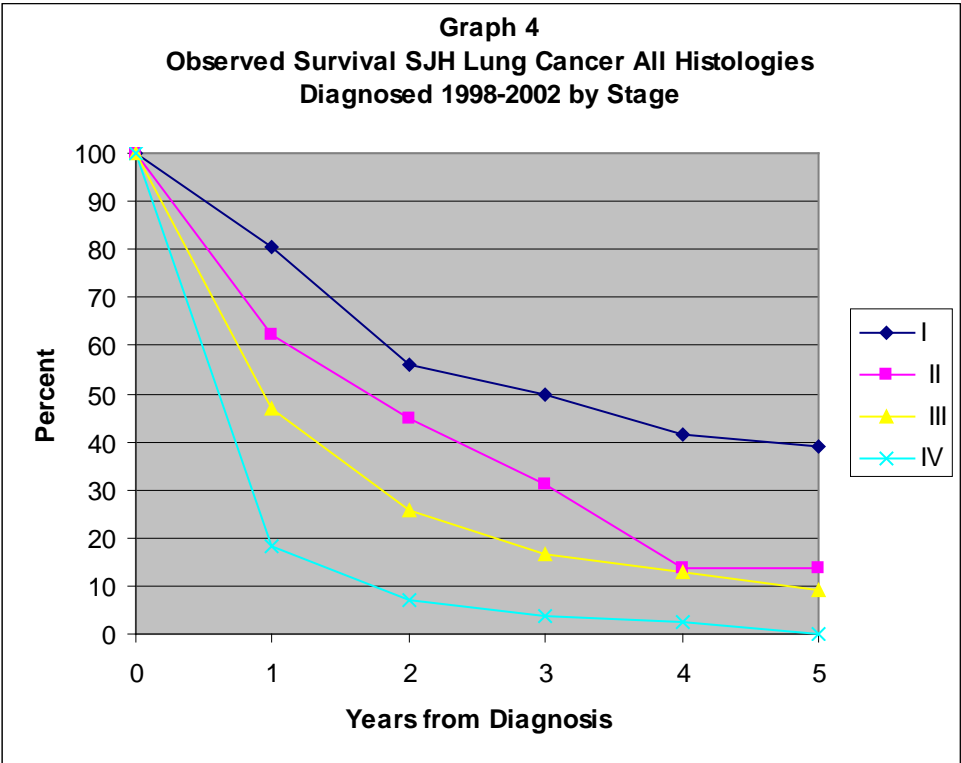
Tables 4A and 4B show the distribution of treatments by stage for the analytic cases for 2008, divided into NSCLC and SCLC types. (Data is from the NCDB data base, case totals differ slightly from the CR data). Treatment is skewed to radiation alone (37%) as it was at RMH, likely representing palliative treatment for metastatic disease, with only 29 percent of patients receiving chemotherapy. NCDB data shows that in 2008 for all NSCLC cases radiation alone for the first course of treatment was only 13 percent while 42 percent of patients received chemotherapy alone or in conjunction with surgery and/or radiation. The NCDB figures are for all stages and as discussed above the SJH analytic cases have consistently represented a higher percentage of Stage III and IV disease.

Treatment Modality	Stage					Totals
	I	II	III	IV	Unk	%
Surgery Only	9	1				17 %
Radiation Only		.	7	14	1	37
Surgery and Chemotherapy	1	2	.	.		5 %
Radiation and Chemotherapy		.	4	4		14
Chemotherapy Only	1		1	1	1	7 %
Surgery, Radiation and Chemotherapy	.		2			3%
Other Specified Therapy	1					2%
No First Course of Treatment			1	6	2	15%

Table 4B St. Joseph Hospital, Eureka California First Course Treatment by Stage of Lung, Bronchus - Small Cell Carcinoma Cancer Diagnosed in 2008 All Analytic Cases						
Treatment Modality	Stage					Totals
	I	II	III	IV	Unk	%
Surgery Only						
Radiation Only				2		40%
Surgery and Chemotherapy						
Radiation and Chemotherapy						
Chemotherapy Only				1		20%
Surgery, Radiation and Chemotherapy						
Other Specified Therapy	1					
No First Course of Treatment				2		40%

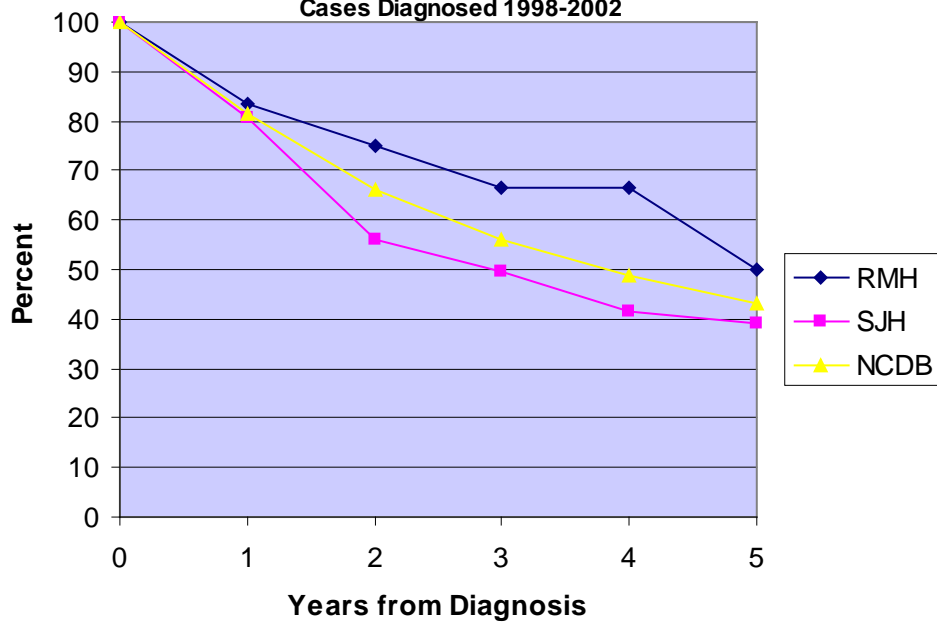
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Five-year survival for all SJH lung cancer cases of all histologies by stage is shown in Graph 4. Graphs 5A through 5D compare SJH and RMH survival results by stage with NCDB data for the 1998-2002 cohorts.

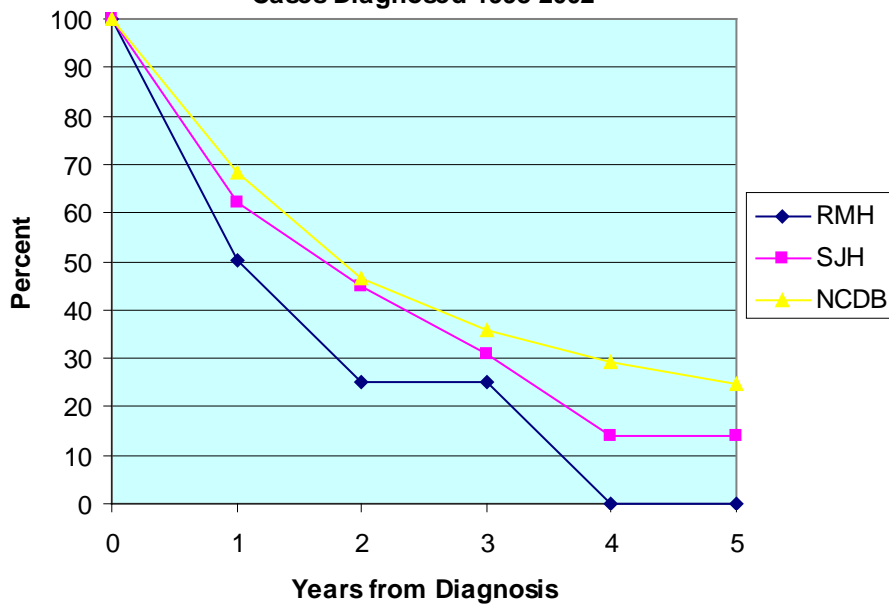


Survival results for SJH are very similar to national statistics. RMH survival is consistently lower than NCDB results, however given the enormous disparity in number of cases, this is not a significant finding.

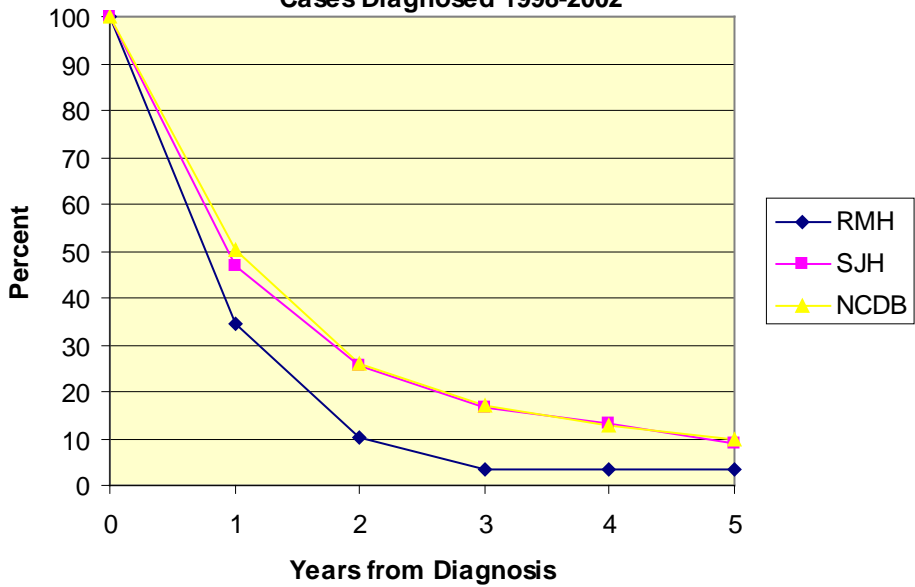
Graph 5A
Lung Cancer Survival Redwood Memorial Hospital and St. Joseph
Hospital Compared to NCDB for
Stage I
Cases Diagnosed 1998-2002



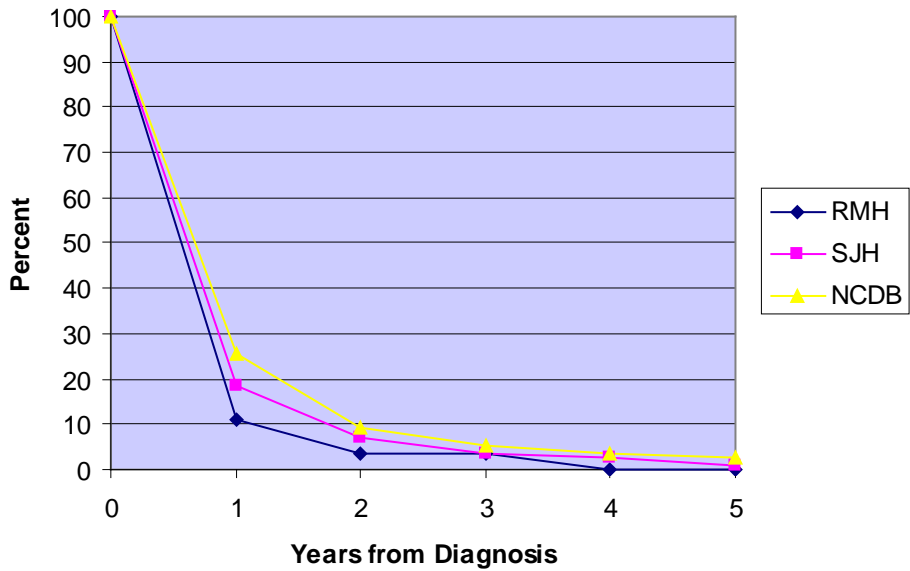
Graph 5B
Lung Cancer Survival Redwood Memorial Hospital and St.
Joseph Hospital Compared to NCDB for
Stage II
Cases Diagnosed 1998-2002



Graph 5C
Lung Cancer Survival Redwood Memorial Hospital and St. Joseph Hospital Compared to NCDB for Stage III
Cases Diagnosed 1998-2002



Graph 5D
Lung Cancer Survival Redwood Memorial Hospital and St. Joseph Hospital Compared to NCDB for Stage IV
Cases Diagnosed 1998-2002



In 2008, there were a total of 90 AANA lung cancer cases identified, which included 43 (47.8%) males and 47 (52.2%) females. National statistics show males slightly predominate at 52.9%. There were 89 lung cancer cases with known histological type. Six were SCLC (6.7%) and 83 were NSCLC (93.3%). National figures show a 13.5% incidence of SCLC. Again, given the relatively small number of cases at SJH and RMH combined, these differences are not significant.

Discussion:

Non-Small Cell Lung Cancer.

Non-Small Cell Lung Cancers are histologically distinguishable from Small Cell Lung Cancer and are resistant to treatment protocols used for treating SCLC. The majority of NSCLC prior to 1970 was squamous cell carcinoma; however the last few decades have seen this type of cancer overtaken by the incidence of adenocarcinoma, potentially due to changes in tobacco blends and use of cigarette filters. Because the majority of smokers do not develop lung cancer, there is speculation that genetic risk factors play a role in the development of lung cancer. Other implicated occupational and environmental risk factors for developing lung cancer include exposure to asbestos and silica fibers, organic compounds such as chloral methyl ether and polycyclic aromatic hydrocarbons (PAHs), diesel fumes, air pollution, a variety of metals such as chromium and nickel, and ionizing radiation.

Adenocarcinomas may be of acinar or papillary types. Broncho-alveolar carcinoma is an adenocarcinoma that spreads along alveolar walls and has a better prognosis than other types of adenocarcinoma. These tumors commonly show Epidermal Growth Factor Receptor (EGFR) mutations leading to effective treatment options with tyrosine kinase inhibitors and other targeted agents. Squamous cell carcinoma arises from areas of squamous dysplasia lining segmental bronchi, leading to squamous cell carcinoma-in-situ and eventually to invasive squamous cell carcinoma.

Large cell carcinoma is a vanishing subcategory that was previously diagnosed because many carcinomas could not be shown to have features of either gland formation or squamous differentiation and were considered “undifferentiated”. Immunohistochemical staining is providing a more accurate method of taking “undifferentiated” carcinomas and categorizing them into squamous cell cancer or adenocarcinomas.

Diagnostic methods commonly performed at SJH and RMH include percutaneous image-guided biopsy, bronchoscopic biopsy with washing and brushing cytologies, mediastinoscopic biopsy and thoracentesis fluid cytology. Many patients are diagnosed with stage IV lung cancer using an image-guided biopsy of a metastatic site. Sputum cytology is rarely used as a diagnostic tool.

Tissue specimens from both facilities are sent to Humboldt Central Laboratory, Eureka, California for pathologic diagnosis. Usual histology methods and stains are augmented by use of immunohistochemical stains which include cytokeratins, P63 (for squamous differentiation), neuroendocrine markers for SCLC and TTF-1 for diagnosing

primary pulmonary carcinoma vs. metastatic carcinomas. Molecular studies for EGFR and BRAF testing are referred to outside reference laboratories.

Surgery provides the best chance for cure of Stage I and II NSCLC. Patients with Stage IIIA N2 disease are potentially surgically curable; national data show 5-year survival rates of 10-30% depending on extent of mediastinal involvement. Stage IIIB with contralateral N3 mediastinal involvement, T4 invasion into surrounding structures, or malignant pleural effusion are inoperable but can be treated with curable intent with combined chemoradiation. Stage IV patients with totally resectable primary tumor and an isolated metastasis to brain or adrenal gland may benefit from metastectomy with occasional long term survivors.

Patients with locally advanced NSCLC may be treated with external beam radiation therapy (RT) to the mediastinum and ipsilateral hilum plus concurrent chemotherapy. Patients with dyspnea, cough, hemoptysis or chest pain may benefit from RT along with patients with bone pain from metastatic disease. Whole brain RT is often used in patients with extensive intracranial disease.

Chemotherapy, when given as adjuvant therapy following surgical treatment for early stage lung cancer, can add to the cure rate and reduce risk of recurrence and death from lung cancer. Chemotherapy, when given concurrently with radiation therapy in locally advanced NSCLC has been shown to improve response rates and prolong disease-free and overall survival. For advanced or recurrent metastatic lung cancer, systemic therapy is given with intent to prolong life. In patients with adequate functional capacity, standard chemotherapy with platinum-based combination chemotherapy has been shown to improve the one-year and two-year overall survival compared to best supportive care alone. Addition of biologic agents such as the VEGF receptor blocker bevacizumab (Avastin) and EGFR blockers such as cetuximab (Erbix) to chemotherapy regimens in certain Stage IV lung cancers has shown to improve median overall survival and progression-free survival. Advances in systemic therapy include access to various targeted biologic agents for management of Stage IV lung cancer and increasing use of molecular testing of tumor tissue for genotyping to select patient-specific tailored treatments. For example, testing for certain mutations such as overexpression of EGFR are useful in predicting response to oral targeted agents such as tarceva (Erlotinib), while presence of a KRAS mutation has shown to predict resistance.

Small Cell Lung Cancer

SCLC has declined from 17% of lung cancers to 13% over the last thirty years. The decrease in SCLC incidence is felt to be due to declining cigarette consumption since cigarette smoke is associated with 95% of SCLC cases. SCLC is a very aggressive and fast growing cancer; the majority of patients present with widespread disease. Pathology features include relatively small cell size compared to other lung cancers, cells with little cytoplasm and inconspicuous nucleoli, "crush artifact" and high mitotic activity. At HCL, immunohistochemical stains such synaptophysin and chromogranin are used to show neuroendocrine differentiation of these tumors and improve accuracy in diagnosis. TTF-1 is a useful marker since 70-80% of these tumors will show positive staining.

Surgical treatment is used for cases when disease is confined to the lung (less than 10% of cases). Approximately one-third of cases will have limited stage disease (cancer involving one hemithorax that can be encompassed in a tolerable radiation field) while two-thirds will have extensive disease. Patients with limited stage are treated with combined chemoradiation modality including prophylactic cranial irradiation in patients with a good response to initial therapy. Those with extensive disease will be considered for chemotherapy, usually with etoposide plus platinum based drugs. The prognosis for patients with SCLC, especially with extensive disease, is dismal with overall five-year survival at 5%.

CONCLUSIONS

Lung cancer was the tumor type analyzed at RMH and SJH for cases collected in 2008. For RMH, lung cancer was the third most common cancer for men and women. There does not appear to be a noticeable change in the total annual number of lung cancer cases when observed over the last twenty years. Eighty percent of cases are diagnosed at Stage III & IV, which is similar to the 83% seen in the 1998-2002 cohort. Overall five-year survival for the 1998-2002 cohort was 13.2%. Stage I patients did relatively well at 50.0% compared to NCDB curves showing 43.2%. All 50 Stage IV patients were dead after four years.

For SJH patients, lung cancer was the second most frequently diagnosed cancer for men and women. Seventy-five percent of lung cancer cases were Stage III and IV at time of diagnosis. Overall five-year survival for the 1998-2002 cohort is 10.5% compared to the national rate of 16.7% for NSLC. Stage for stage, there were no notable differences in survival between the SJH group and NCDB group, however the larger proportion of later-stage diagnosis at SJH results in the lower overall survival.

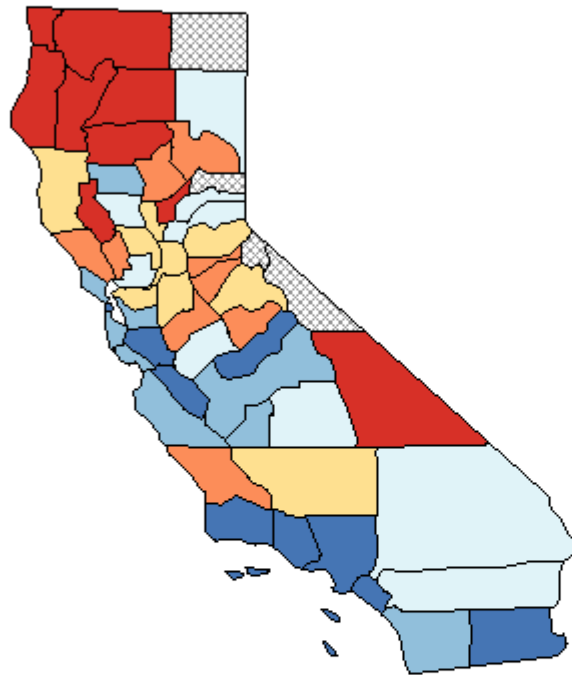
For combined RMH and SJH patients, lung cancer was the second most frequent cancer for men and women. SCLC comprised 6.7% of lung cancer cases while national figures are closer to 13%. Combined five-year survival data were not available for the 2008 cohort.

RMH and SJH in conjunction with Eureka-based Humboldt Central Laboratory/Pathology Department show appropriate capability for diagnosing lung cancer. For early stage lung cancer, RMH and SJH patients are surgically treated at SJH. For late-stage patients and patients with SCLC, appropriate radiation treatment and medical oncology services are provided by SJH Radiation Oncology Department and a Eureka-based medical oncology group, respectively.

Although the incidence of lung cancer nationwide has declined overall, lung cancer remains the leading cause of cancer deaths in the United States. The American Cancer Society estimates for 2010 that 222,520 new cases of lung cancer would be diagnosed, with 157,300 deaths from lung cancer, 28% of all cancer deaths. New cases of lung cancer account for 15% of all new cancer diagnoses in the U.S. In addition, although the national incidence of lung cancer decreased by 1.8% per year from 1991 to 2006 among men, the incidence actually rose 0.4% per year among women during the same period, most likely because the incidence of tobacco use in women declined more slowly.

The death rate from lung cancer for both men and women in Humboldt County remains relatively high at 61.8 to 67.9 per 100,000 for men and 50.5 to 69.0 per 100,000 for women, compared to California's statewide rate of 34.5 deaths per 100,000 overall. (data from NCI State Cancer Profiles). In part, these results may be skewed by the relatively small number of residents in the county (134,623), however, as noted in the introduction, the population in Humboldt County is older than the state average and has a significantly lower median income than statewide averages. Incidence of lung cancer is known to increase with age. The geographic area of the county, relative isolation of many of the county residents, and widespread poverty make access to healthcare a challenge for many residents and create barriers to early detection. The St. Joseph Health System has ongoing programs to assess these barriers and to address identified issues of access to health care for North Coast residents. In addition, the California Center for Rural Policy at Humboldt State University (located in Arcata, a few miles north of Eureka) conducts research aimed at informing policy and promoting the health and well-being of rural communities. As the Cancer Committee moves forward with implementation of the ACoS 2012 standards additional focus will be directed to expanding access to cancer education, screening and care for residents.

Age-Adjusted Death Rates for California, 2003 - 2007
Lung & Bronchus
All Races (includes Hispanic), Female, All Ages



Age-Adjusted Annual Death Rate (Deaths per 100,000)

Quantile Interval

- 50.5 to 69.0
- 42.7 to 50.4
- 38.9 to 42.6
- 36.3 to 38.8
- 32.3 to 36.2
- 21.8 to 32.2
- Suppressed*

United States Rate (95% C.I.)
40.6 (40.4 - 40.7)
California Rate (95% C.I.)
34.5 (34.1 - 34.9)
Healthy People 2010 Goal 03-02
44.9

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State Cancer Registries may provide more current or more local data.

Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries (for more information).

Source: Death data provided by the National Vital Statistics System public use data file. Death rates calculated by the National Cancer Institute using SEER*Stat. Death rates (deaths per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). The Healthy People 2010 goals are based on rates adjusted using different methods but the differences should be minimal. Population counts for denominators are based on the Census 1969-2006 US Population Data File as modified by NCI. The US populations included with the data release have been adjusted for the population shifts due to hurricanes Katrina and Rita for 62 counties and parishes in Alabama, Mississippi, Louisiana, and Texas.

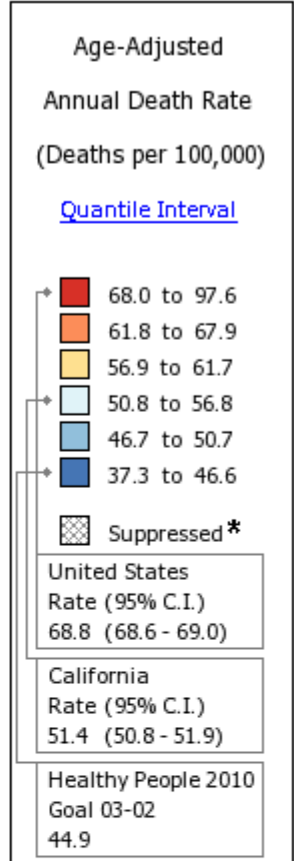
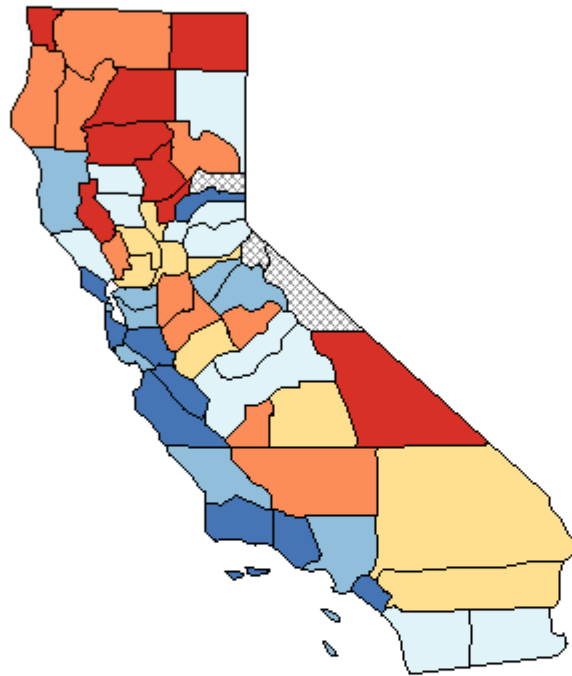
* Data have been suppressed to ensure confidentiality and stability of rate estimates. Counts are suppressed if fewer than 16 cases were reported in a specific area-sex-race category.

** Data have been suppressed for states with a population below 50,000 per sex for American Indian/Alaska Native or Asian/Pacific Islanders because of concerns regarding the relatively small size of these populations in some states.

Healthy People 2010 Goal 03-02 : Reduce the lung cancer death rate to 44.9.

Healthy People 2010 Objectives provided by the Centers for Disease Control and Prevention.

Age-Adjusted Death Rates for California, 2003 - 2007
Lung & Bronchus
All Races (includes Hispanic), Male, All Ages



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Healthy People 2010 Goal 03-02 : Reduce the lung cancer death rate to 44.9.

Healthy People 2010 Objectives provided by the Centers for Disease Control and Prevention .

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