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MORTALITY

Thyroid Cancer: 20-Year Comparative Mortality and Survival Analysis of Six Thyroid Cancer Histologic Subtypes by Age, Sex, Race, Stage, Cohort Entry Time-Period and Disease Duration (SEER*Stat 8.3.2)

A Systematic Review of 145,457 Cases for Diagnosis Years 1993–2013

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Background.—Incidence and prognosis of cancers of the endocrine glands vary greatly by stage and histologic type, and, thyroid cancer accounts for most (92%) of the cancers of the endocrine glands. It is the 8th most common of cancers and has been rising in incidence since 1975. It remains a formidable health threat in the United States in 2016 with estimated cases of 64,300 and 1980 deaths.
Objective.—Provide 20-year comparative mortality analysis of thyroid cancer in a recent group of 145,457 staged cases (97.5%) of a total of 149,202 patients during the 1993-2013 entry time-period in six histologic subtypes by age, sex, race, stage and disease duration.
Methods.—Population-based data from SEER registries,[1] 1973-2013, (SEER*Stat 8.3.2.) were analyzed.
Results.—Tables 1-8 provide basic SEER epidemiologic, demographic, case-statistics, and comparative mortality follow-up data of 4 principal and 2 supplementary thyroid cancer oncotypes by age, sex, race, stage and disease duration of patients in the 1993-2013 time-period.
Conclusions.—Thyroid cancer when localized has a very good prognosis, with no significant excess mortality after diagnosis in papillary and papillary follicular variant cancers (PFV). Because nearly two thirds of thyroid cancers are localized, and excess death rate (EDR) is small in patients with regional cancer under age 50, overall excess mortality for all ages also virtually disappeared after 10 years in papillary and follicular cancer. Overall, the 5-year survival rate is greater than 90% for papillary and follicular carcinomas. Nevertheless, because of the marked predominance of papillary carcinoma, the continued increase in its relative frequency and annual projected deaths, thyroid carcinoma remains a significant health concern in the current era.

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INTRODUCTION

From 1974-2013, the overall incidence of thyroid cancer has increased 3% annually. The incidence and mortality rates for advanced stage papillary thyroid cancer has also expanded. These findings are consistent with

a true increase in the occurrence of thyroid cancer in the United States.[2] According to the National Cancer Institute (NCI)-Thyroid Cancer Treatment (PDQ) – Health Professional Version (December 15, 2016), there are 4 main histologic types of thyroid cancer: papillary, follicular, medullary & anaplastic. However, according to the *International Classification of Diseases for Oncology, Third Edition*, topography code C739 for thyroid cancer in the SEER Site/Validation List (September 18, 2015), nearly 60 oncologic histology variants for the thyroid gland are enumerated. Also, the thyroid gland may occasionally be the site of other primary tumors, including sarcomas, lymphomas, epidermoid carcinomas, and teratomas. Moreover, the thyroid may also be the site of metastasis from other cancers, particularly of the lung, breast, and kidney.

METHODS

Data Sources

Population-based data from SEER Registries Research Data, 1973-2013, were analyzed.

Life Table Methodology

The application of life table methodology to risk appraisal has been well described by Singer,[3,4] Pokorski[5] and others.[6]

Thyroid Site Code (TSC)

The site code is taken from the coding system utilized for all diseases in *A Descriptive Index of Mortality Studies from Selected Sources, 1991-1995.*[7] In this Index, the 3-digit code for thyroid cancer is 174; the first digit indicates malignant tumor and is omitted for this cancer publication, hence the index site code – IC74, for thyroid cancer.

Demographics Characteristics

This analysis included sex, race, age and mean age at diagnosis.

Case Characteristics

Thyroid cancer cases (*International Classification of Diseases for Oncology, Third Edition*; topography code C739) were classified according to histologic type. Four principle histologic oncotypes and 2 other commonly considered subtypes were selected for mortality analysis including: 1) Papillary adenocarcinoma, NOS (8260), 2) Follicular adenocarcinoma, NOS (8330), 3) Medullary carcinoma, NOS (8510), 4) Undifferentiated and anaplastic carcinoma (8020-8021), 5) Oxyphilic adenocarcinoma-Hurthle cell (8290), and 6) Papillary carcinoma, follicular variant-PFV (8340).

Incidence-Based Mortality Rates (IBM)

The 6 thyroid cancer histologic subtypes in this report (see Table 2) were selected for long-term comparative mortality analysis after determining case statistics by performing frequency & mean age (FAMA) queries, and distribution analysis by age, sex, race and stage from the SEER database to aid in the selection of age-related durational-interval groupings for mortality analysis, and to ascertain distribution data by age, sex, race, tumor stage, cohort-entry period and other case-statistic properties. Therefore, unlike traditional mortality rates, IBM rates for this report were examined according to site selection variables recorded at diagnosis (eg, histology, stage, grade, etc) and available in the SEER*Stat program.

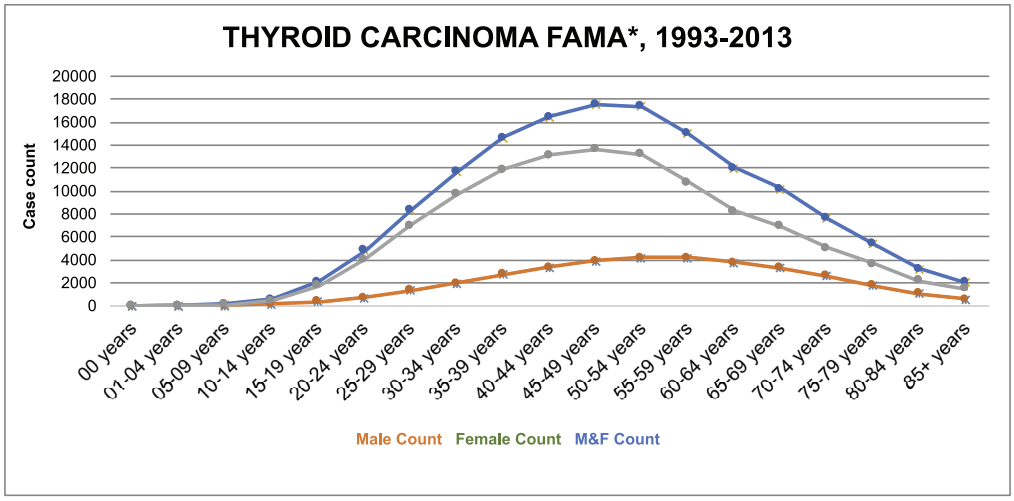
Cancer Stage

The SEER Stage LRD "Historic Stage Recode A" was used to classify thyroid cancer cases by stage as *localized* (confined within the thyroid capsule), *regional* (tumor extension beyond the limits of the thyroid gland or spread by more than 1 lymphatic or vascular supply

Table 1. Thyroid Cancer Overview: Epidemiologic & Demographic Characteristics: SEER 1993-2013

CASE STATISTICS OVERVIEW

SEER*Stat 8.3.2: (1973-2013)



	M&F	Male	Female	All Races	White	Black	Other**	Unknown
All:	149,202	36,092	113,110	149,202	121,960	9,691	15,806	1,745
Percent %:		24.2	75.8		81.7	7.9	10.6	1.2
Mean Age:	49.64	53.24	48.34	49.64	49.62	50.5	44.84	44.36

Stage:	**Total**	**Local**	**Regional**	**Distant**	**Unstaged**
Count:	145,457	89,868	49,076	6,513	3,745
Percent %:	97.50%	61.80%	33.70%	4.50%	2.50%

Survival Database No: 130,028 **Frequency Database No:** 149,202

Median Survival: >20 years

5-Yr Rel. Cum. Survival: 97.60% **5-Yr Obs. Cum. Survival:** 93.72%

**Other (American Indian/Alaska Native, Asian/Pacific Islander)

route to tissues adjacent to the thyroid gland or to regional lymph nodes), or *distant* (further direct extension or extracervical metastasis to other organs) in order to utilize cases coded and entered as far back as 1973. Parenthetically, many revisions have been made in SEER coding since 1973, but cases so coded have survival data only from the year in which the new code was put into use. For instance, the Stage I-IV, or, TNM codes of the American Joint Committee on Cancer (AJCC) were not used by SEER until 1988 and have undergone further revisions in 2004 and again in 2010.

Histologic Grade

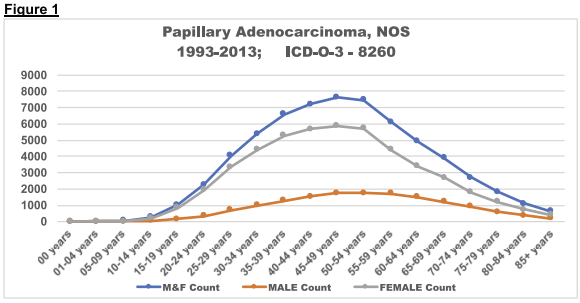
Grading of malignancy is excluded because only a small proportion of cases were graded (21.5% since 1973). Only microscopically confirmed cases are included. Thyroid cancer cases were excluded if the diagnosis was made in a death certificate or by autopsy, if the case was unstaged, and if there was a previous or current additional cancer. Patients have been subdivided by age, sex, stage and histological type into the combinations that appeared to be most informative in a limit of six pages of mortality tables (Tables 3-8) and 2 tables illustrating descriptive epidemiologic and demographic case statistics (Tables 1 & 2).

Statistical Significance

Standard errors are shown for the survival rates in the SEER survival tables. In the SEER program, the actuarial method: Ederer II method is used for cumulative

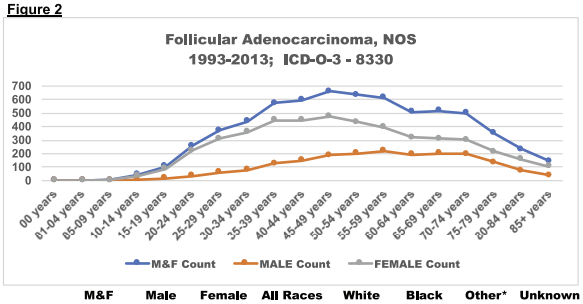
Table 2. Thyroid Cancer: Six Histologic Subtypes; Epidemiologic & Demographic Case Statistics, SEER 1993-2013

Figure 1



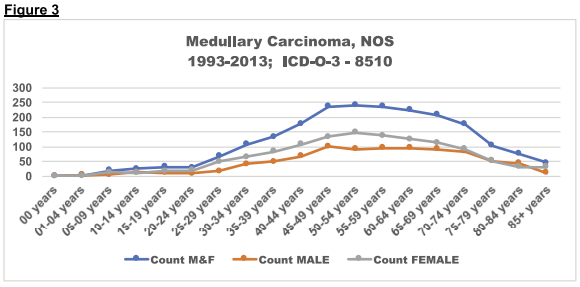
	M&F	Male	Female	All Races	White	Black	Other*	Unknown
All:	63,198	15,145	48,053	63,198	51,262	3,181	7,950	805
Mean Age:	48.16	51.59	47.04	48.15	48.17	49.45	47.8	43.48
Stage:	Local	Regional	Distant	Unstaged				
Count:	35,590	24,008	2,254	1,346	63,198			
Percent %:	56.3%	38.0%	3.6%	2.1%	100%			

Figure 2



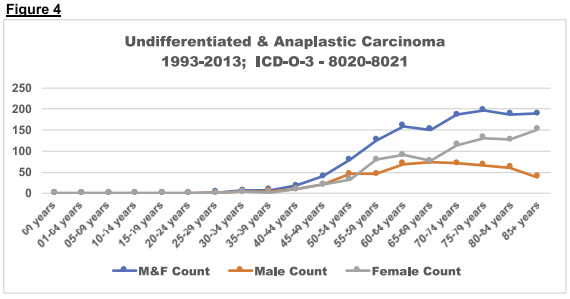
	M&F	Male	Female	All Races	White	Black	Other*	Unknown
All:	6,553	1,925	4,628	6,553	5,054	792	627	80
Mean Age:	51.63	55.89	49.90	51.59	51.97	51.75	50.75	42.15
Stage:	Local	Regional	Distant	Unstaged				
Count:	3,348	2,426	562	217	6,553			
Percent %:	51.09%	37.02%	8.58%	3.31%	100%			

Figure 3



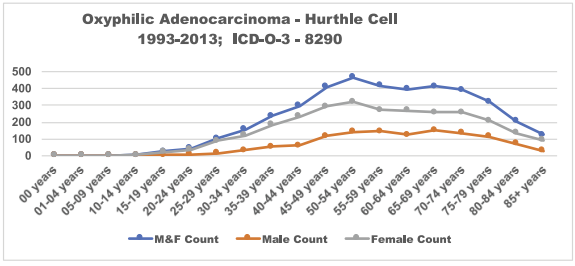
	M&F	Male	Female	All Races	White	Black	Other*	Unknown
All:	2,156	903	1,253	2,156	1,829	173	128	76
Mean Age:	53.56	54.84	52.7	55.53	54.18	51.18	50.43	43.24
Stage:	Local	Regional	Distant	Unstaged		(Blacks: Survival Database:145)		
Count:	1,071	722	299	64	2,156			
Percent %:	49.68%	33.49%	13.87	2.97%	100%			

Figure 4



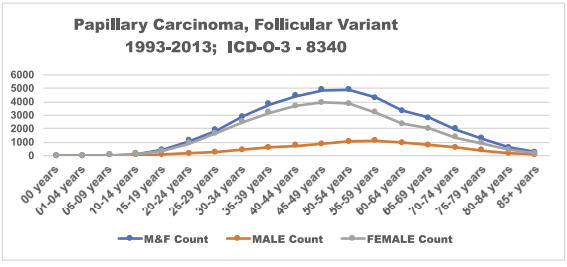
	M&F	Male	Female	All Races	White	Black	Other*	Unknown
All:	1,349	509	840	1,349	1,081	103	162	3
Mean Age:	70.65	67.7	72.58	70.44	70.64	68.64	70.44	70.26
Stage:	Local	Regional	Distant	Unstaged				
Count:	8020-8021 ICD-O-3 histology types all considered distant stage							

Figure 5



	M&F	Male	Female	All Races	White	Black	Other*	Unknown
All:	4,006	1,209	2,797	4,006	3,395	317	253	41
Mean Age:	59.58	59.86	56.53	57.53	57.67	56.05	57.23	48.47
Stage:	Local	Regional	Distant	Unstaged				
Count:	2,128	1,625	156	97	4,006			
Percent %:	53.12%	40.56%	3.89%	2.42%	100%			

Figure 6



	M&F	Male	Female	All Races	White	Black	Other*	Unknown
All:	38,980	8,328	30,652	38,980	32,063	3,157	3,399	361
Mean Age:	49.67	53.55	48.67	49.66	49.75	49.68	48.55	46.13
Stage:	Local	Regional	Distant	Unstaged				
Count:	27,838	10,039	805	298	38,980			
Percent %:	71.42%	25.75%	2.07%	0.76%	100%			

*Other (American Indian/Alaska Native, Asian/Pacific Islander)
Expected Survival Table: U.S. 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspec 1991&U

expected survival. Ederer II method calculates the expected survival rates for patients under observation at each point of follow-up. So, the matched individuals are considered to be at risk until the corresponding cancer patient dies or is censored. Also, confidence interval: Log (-Log ()) Transformation; the level is 95% is adhered to. Poisson confidence intervals at the 95% level based on the number of observed deaths in this study are not displayed here to conserve space on mortality tables.

RESULTS

Incidence & Mortality Rates

According to the SEER Cancer Statistics Review 1975-2012,[8] age-adjusted incidence rates

in 2008-2012 were 20.0 per 100,000 in women, but only 6.2 per 100,000 in men. Annual delay-adjusted SEER incidence rates increased from 4.85 per 100,000 in 1975 to 15.24 per 100,00 in 2012. In 2012, delay-adjusted incidence was 22.15 per 100,000 in females and 8.20 per 100,000 in males (CSR Table 26.4). Age variation in overall incidence is smaller than in most cancers. In the 2008-12 time-period, the rate per 100,000 is just 8.9 in persons 10-24 years, 9.8 in young adults 25-29, increasing gradually to 24.4 at ages 60-64, then decreasing to 11.3 at ages 85 and up. By race the lowest rate was in blacks (8.0), and the highest in white non-Hispanics (15.1). The trend in overall SEER incidence was upward from 2008-12, with an Average Annual Percent Change (AAPC) of +2.8%. Age adjusted US mortality rates, 2008-12: All ages 0.5 deaths per 100,000, under 65 (0.1), 65 and over (3.0).

Case Statistics & Main Epidemiologic Characteristics

The epidemiology and case distribution characteristics of the 1993-2013 study population is shown in Tables 1 & 2. Table 1 is an overview summary of incidence rates and trends by age & mean age at diagnosis, sex, race, stage distribution and 5-year survival rates in a total of 149,202 cases of invasive thyroid carcinoma in the SEER frequency database, all histologic subsites combined. Table 2, Figures 1-6 illustrates the statistical distributions of frequency & mean age, sex, race and stage for each thyroid cancer oncotype studied. Both similar and different demographic, epidemiologic and biostatistical trends and patterns reflect differing biologic entities except for the PFV variant. The total of 149,202 cases is higher than the total of 130,028 in the survival database due to the routine exclusion of cases lacking follow-up (FU) or due to lack of staging. Incidence by quinquennial age from birth is displayed in graphic form and indicates that thyroid cancer in males & females begins early in life. Incidence in females reaches its zenith at 45-49 years, then smoothly declines to age 85+ years. Male incidence reaches a plateau at 50-59 years and then gradually diminishes to age 85+ years.

Of patients with thyroid cancer, 51.2% are under 50 years of age. Younger patients under 35 constitute 18.5% of the total, subdivided into 13.4% by age 25-34, 4.7% age 15 to 24, and about 0.5% in children under age 15. Females (113,110; 75.8%) outnumbered males (36,092; 24.2%) by more than 3 to 1. Whites (121,960; 81.7%) outnumbered blacks (9,691; 7.9%) by a wide margin. Mean ages in males 53.24 years, females 48.34, whites 49.62, blacks 50.5, other including American Indian/Alaska Native, Asian/Pacific Islander 44.84, and unknown 44.36. A very small number of in-situ cases were from the total.

By stage, almost two thirds of the cases were localized, one third regional, 4.5% distant, and 2.5% unstaged. These characteristics differ sharply from those of the typical major cancer site, with few patients under 45, a more even sex distribution, and a minority of patients in the localized stage. Median survival was more than 20-years, 5-year relative cumulative survival (100P/P′) was 97.6% and 5-year observed cumulative survival (P) was 93.7%.

Mortality Analysis by Histologic Oncotype

Prior to accomplishing long-term thyroid cancer comparative mortality analysis on 6 histologic subsets, 130,028 cases of invasive thyroid cancer (all histologic subtypes, age, sex and race combined in the SEER*Stat 8.3.2 survival database utilizing the cohort entry-period 1993-2013) were first examined to obtain an overview understanding of the nature and magnitude of the risk, the mathematical burden of excess mortality, and projected observed, expected and relative cumulative survival. Aggregate average annual mortality and survival results (all sites combined) are displayed below for the following durational intervals: 0-1, 1-2, 2-5, 5-10, 10-15 and 15-20 years. (See Chart 1).

Observed (actual) deaths exceeded expected deaths by more than 3 to 1 in the first duration and is reflected in a mortality ratio (MR) of 332% and excess death rate (EDR) of 17.9 per 1000. Observed deaths are higher than expected deaths in virtually all durational intervals and mortality ratios are high for the first 5 years of follow-up, but then drop to almost normal levels. Five-year observed cumulative survival (P) is >90% but drops to 77% in 20 years. However, relative cumulative survival (100P/P′) remains above 95% in all durations. Interval expected cumulative survival (P′) is displayed.

Papillary Carcinoma (ICD-O-3, 8260)

Papillary carcinoma is the most common type of invasive thyroid cancer, accounting for 42.4% of total cases in the SEER*Stat frequency database for the 1993-2013 cohort entry-period period. Table 2-Figure 1 case statistics indicate that this histologic tumor accounted for 76.0% in females, 81.1% in whites but only 5.0% in blacks. Of patients with papillary thyroid cancer, 56.3% have localized disease at the time of diagnosis, 38.0% have regional involvement, 3.6% have distant metastasis, and 2.1% are unstaged. Mean age at diagnosis for whites and blacks was 48.47 and 49.45 years, respectively. Mean age was higher by more than 4.5 years in males vs females, 51.59 and 47.04, respectively.

Prognosis of papillary carcinoma is excellent. Comparative mortality for localized papillary carcinoma is shown in Tables 3 & 7. There is no excess mortality by sex or race for local stage disease and the relative cumulative survival ratio is 100% or above in both sexes and by race. Mortality at 20 years is not statistically significant due to minimal exposures and deaths. Excess mortality for regional disease continued to be modest in white males at 5 and 10 years with mortality ratios of 145 & 135, respectively, and respective EDRs of 4.7 and 4.2 deaths per 1000. For both durations, relative cumulative survival ratios were above 95%. Excess mortality in white females for regional disease was modest with mortality ratios at 5 and 10 years of 132 & 107 with respective EDRs of 1.8 and 0.5 per 1000. Relative survival at these intervals remained at 99% or above. In black males, excess mortality in regional disease was quite high with a mortality ratio of 353 and EDR of 32.1 per 1000 in the first duration but at 5 and 10 years dropped to an MR of 159 & 98 and EDR of 7.0 & -0.3 per 1000 respectively. Excess mortality for regional disease in black females was similar to that in black males with an initial high MR and EDR in the first interval of 330 & 16.8 per 1000 but dropping to an MR of 136 and EDR of 2.7 per 1000 by 5 years. Relative survival remained above 95% at 10 years.

Only 2254 cases of papillary carcinoma with distant extension or metastasis were contained in the 1993-2013 SEER database, 3.6% of the total of 63,198 cases of invasive cancer in this site. In the source database queries (not displayed here), excess mortality was very high by sex and race, decreased progressively with duration, but was still present in both sexes and all races at duration 15-20 years. For instance, the initial 0-1-year duration MR and EDR for distant disease in white females was 1026 & 106.5 per 1000, respectively, but progressively diminished to 174 and 5.2 per 1000 at duration 15-20 years. At the 15-20-year duration, observed survival was 62.4%, and relative survival ratio was 71.9%. Expected cumulative survival was 86.7%.

Follicular Carcinoma (ICD-O-3, 8330)

Follicular carcinoma (ICD-O-3, 8330) (papillary carcinoma-follicular variant aside) is the second most common type of invasive thyroid cancer, accounting for 4.4% of total cases in the SEER*Stat frequency database for the 1993-2013 cohort entry-period. Table 2-Figure 2 case statistics indicate that this histologic tumor accounted for 77.1% of follicular cancers in whites but only 12.1% in blacks. Similar to papillary carcinoma, almost two and a half-fold excess female preponderance, is observed for follicular carcinoma. At all ages,

Table 3. Papillary Adenocarcinoma, NOS, (ICD-O-3, 8260), 1993-2013, Age, Stage

Duration Start-End	No. Alive at Start	Exposure Pt.-Yrs	Number of Deaths		Mortality Ratio (%)	Mean Ann. Mortality Rate/1,000			Cumul. Surv. Rate		Cum. Surv. Ratio (%)
			Observed	Expected		Observed	Expected	Excess	Observed	Expected	
t to t+ch t	***l***	**E**	**d**	**d′**	**100d/d′**	**q**	**q′**	**(q-q′)**	**P**	**P′**	**100P/P′**
					Age <50, Localized						
0-1	17,414	16,355.5	20	24.53	82	0.0012	0.0015	− 0.3	0.9988	0.9985	100.0
1-2	15,277	14,436.0	23	23.10	100	0.0016	0.0016	0.0	0.9972	0.9969	100.0
2-5	13,572	33,513.0	53	62.08	85	0.0016	0.0019	− 0.3	0.9924	0.9913	100.1
5-10	8,769	27,824.0	61	67.66	90	0.0022	0.0024	− 0.2	0.9817	0.9790	100.3
10-15	2,822	6,137.0	19	19.99	95	0.0031	0.0033	− 0.2	0.9675	0.9624	100.5
15-20	425	1,263.5	8	5.76	139	0.0063	0.0046	1.8	0.9387	0.9397	99.9
					Ages 50 up, Localized						
0-1	13,507	12,623.5	122	150.22	81	0.0097	0.0119	− 2.2	0.9903	0.9881	100.2
1-2	11,618	10,886.5	104	140.44	74	0.0096	0.0129	− 3.3	0.9808	0.9754	100.6
2-5	10,051	23,856.5	258	350.92	74	0.0108	0.0147	− 3.9	0.9487	0.9326	101.7
5-10	5,836	16,995.5	251	319.32	79	0.0148	0.0188	− 4.0	0.8783	0.8457	103.8
10-15	1,506	2,849.0	63	69.07	91	0.0221	0.0242	− 2.1	0.7627	0.7431	102.6
15-20	131	355.5	16	12.55	128	0.0450	0.0353	9.7	0.6286	0.6154	102.1
					All Ages, Localized						
0-1	30,921	28,979.0	142	173.87	82	0.0049	0.0060	− 1.1	0.9951	0.9940	100.1
1-2	26,895	25,322.5	127	164.60	77	0.0050	0.0065	− 1.5	0.9901	0.9875	100.3
2-5	23,623	57,369.5	311	416.41	75	0.0054	0.0073	− 1.8	0.9738	0.9661	100.8
5-10	14,605	44,819.5	312	388.45	80	0.0070	0.0087	− 1.7	0.9400	0.9242	101.7
10-15	4,328	8,986.0	82	90.34	91	0.0091	0.0101	− 0.9	0.8943	0.8786	101.8
15-20	556	1,619.0	24	18.38	131	0.0148	0.0114	3.5	0.8373	0.8284	101.1
					Age <50, Regional						
0-1	13,495	12,619.0	19	16.40	116	0.0015	0.0013	0.2	0.9985	0.9987	100.0
1-2	11,724	10,985.0	17	16.48	103	0.0015	0.0015	0.0	0.9970	0.9972	100.0
2-5	10,229	24,975.0	60	42.21	142	0.0024	0.0017	0.7	0.9897	0.9921	99.8
5-10	6,471	20,496.0	51	45.44	112	0.0025	0.0022	0.3	0.9771	0.9809	99.6
10-15	2,106	4,749.0	18	14.47	124	0.0038	0.0030	0.7	0.9596	0.9653	99.4
15-20	342	1,020.5	10	4.16	240	0.0098	0.0041	5.7	0.9133	0.9453	96.6
					Ages 50 up, Regional						
0-1	7,809	7,298.0	194	102.90	189	0.0266	0.0141	12.5	0.9734	0.9859	98.7
1-2	6,593	6,174.5	131	91.38	143	0.0212	0.0148	6.4	0.9528	0.9713	98.1
2-5	5,625	13,128.5	265	219.14	121	0.0202	0.0167	3.5	0.8944	0.9231	96.9
5-10	3,087	8,867.5	248	189.59	131	0.0280	0.0214	6.6	0.7745	0.8255	93.8
10-15	780	1,628.5	66	42.67	155	0.0405	0.0262	14.3	0.6251	0.7197	86.9
15-20	93	253.5	13	9.32	139	0.0513	0.0368	14.5	0.4675	0.5851	79.9
					All Ages, Regional						
0-1	21,304	19,917.0	213	119.50	178	0.0107	0.0060	4.7	0.9893	0.9940	99.5
1-2	18,317	17,159.5	148	108.10	137	0.0086	0.0063	2.3	0.9808	0.9877	99.3
2-5	15,854	38,103.5	325	263.99	123	0.0085	0.0069	1.6	0.9554	0.9672	98.8
5-10	9,558	29,363.5	299	236.69	126	0.0102	0.0081	2.1	0.9077	0.9283	97.8
10-15	2,886	6,377.5	84	57.25	147	0.0132	0.0090	4.2	0.8502	0.8869	95.9
15-20	435	1,274.0	23	13.56	170	0.0181	0.0106	7.4	0.7744	0.8393	92.3

Expected Survival Table: U.S. 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspec 1991&U.

incidence rates are higher for females than for males in both whites and blacks. Mean age at diagnosis was similar for whites and blacks, 51.97 vs. 51.75, respectively, but higher by 6 years in males than females.

Of patients with follicular thyroid cancer, 51% have localized cancer at the time of diagnosis, 37% have regional involvement, and 8.6% have distant metastasis while 3.3% were unstaged. Table 7 and 8 indicate that similar to papillary cancer, men are *proportionally* more likely than women to be diagnosed with nonlocalized disease. Excess in advanced stages is also found in blacks, contrasting with the pattern of papillary cancer. The proportion of black patients with follicular thyroid cancer spread to distant organs is less than that of whites (3.53% vs 4.96%)

Table 4. Follicular Adenocarcinoma, NOS, (ICD-O-3, 8330), 1993-2013, Age, Stage

Duration Start-End	No. Alive at Start	Exposure Pt.-Yrs	Number of Deaths		Mortality Ratio (%)	Mean Ann. Mortality Rate/1,000			Cumul. Surv. Rate		Cum. Surv. Ratio (%)
			Observed	Expected		Observed	Expected	Excess	Observed	Expected	
t to t+ch t	***l***	**E**	**d**	**d′**	**100d/d′**	**q**	**q′**	**(q-q′)**	**P**	**P′**	**100P/P′**
Age <50, Localized											
0-1	1,642	1,589.0	9	2.38	378	0.0057	0.0015	4.2	0.9943	0.9985	99.6
1-2	1,527	1,483.5	6	2.37	253	0.0040	0.0016	2.4	0.9903	0.9969	99.3
2-5	1,434	3,869.0	4	6.94	58	0.0010	0.0018	– 0.8	0.9874	0.9915	99.6
5-10	1,144	4,530.5	11	10.90	101	0.0024	0.0024	0.0	0.9746	0.9795	99.5
10-15	664	2,214.5	14	7.57	185	0.0063	0.0034	2.9	0.9450	0.9624	98.2
15-20	247	661.0	4	3.06	131	0.0061	0.0046	1.4	0.9242	0.9391	98.4
Ages 50 up, Localized											
0-1	1,320	1,269.0	30	22.46	134	0.0236	0.0177	5.9	0.9764	0.9823	99.4
1-2	1,188	1,154.5	15	21.59	69	0.0130	0.0187	– 5.7	0.9637	0.9639	100.0
2-5	1,106	2,821.5	58	61.04	95	0.0206	0.0216	– 1.1	0.9052	0.9023	100.3
5-10	767	2,694.0	79	69.91	113	0.0293	0.0259	3.4	0.7731	0.7899	97.9
10-15	324	1,002.5	30	32.33	93	0.0299	0.0323	– 2.3	0.6631	0.6663	99.5
15-20	99	285.5	10	12.75	78	0.0350	0.0447	– 9.6	0.5413	0.5232	103.5
All Ages, Localized											
0-1	2,962	2,858.0	39	24.86	157	0.0136	0.0087	4.9	0.9864	0.9913	99.5
1-2	2,715	2,638.0	21	24.01	87	0.0080	0.0091	– 1.1	0.9785	0.9823	99.6
2-5	2,540	6,690.5	62	68.46	91	0.0093	0.0102	– 1.0	0.9516	0.9523	99.9
5-10	1,911	7,224.5	90	81.39	111	0.0125	0.0113	1.2	0.8914	0.8997	99.1
10-15	988	3,217.0	44	40.08	110	0.0137	0.0125	1.2	0.8327	0.8439	98.7
15-20	346	946.5	14	15.54	90	0.0148	0.0164	– 1.6	0.7671	0.7704	99.6
Age <50, Regional											
0-1	1,136	1,096.0	3	1.75	171	0.0027	0.0016	1.1	0.9973	0.9984	99.9
1-2	1,053	1,018.0	3	1.73	173	0.0029	0.0017	1.2	0.9944	0.9967	99.8
2-5	980	2,630.5	15	5.15	291	0.0057	0.0020	3.7	0.9782	0.9908	98.7
5-10	770	2,981.5	8	7.76	103	0.0027	0.0026	0.1	0.9661	0.9778	98.8
10-15	435	1,513.0	7	5.56	126	0.0046	0.0037	0.9	0.9422	0.9595	98.2
15-20	178	538.5	2	2.84	70	0.0037	0.0053	– 1.6	0.9191	0.9334	98.5
Ages 50 up, Regional											
0-1	1,040	1,001.0	41	18.72	219	0.0410	0.0187	22.3	0.9590	0.9813	97.7
1-2	921	880.5	19	16.64	114	0.0216	0.0189	2.7	0.9383	0.9628	97.5
2-5	821	2,168.5	46	46.27	99	0.0212	0.0213	– 0.1	0.8789	0.9023	97.4
5-10	608	2,123.0	84	54.55	154	0.0396	0.0257	13.9	0.7198	0.7907	91.0
10-15	262	833.0	35	28.72	122	0.0420	0.0345	7.5	0.5690	0.6598	86.2
15-20	81	247.5	9	13.17	68	0.0364	0.0532	– 16.8	0.4615	0.4929	93.6
All Ages, Regional											
0-1	2,176	2,097.0	44	20.34	216	0.0210	0.0097	11.3	0.9790	0.9903	98.9
1-2	1,974	1,898.5	22	18.42	119	0.0116	0.0097	1.9	0.9676	0.9807	98.7
2-5	1,801	4,799.0	61	51.54	118	0.0127	0.0107	2.0	0.9312	0.9494	98.1
5-10	1,378	5,104.5	92	62.51	147	0.0180	0.0122	5.8	0.8522	0.8924	95.5
10-15	697	2,346.0	42	34.30	122	0.0179	0.0146	3.3	0.7738	0.8281	93.4
15-20	259	786.0	11	16.00	69	0.0140	0.0204	– 6.4	0.7139	0.7442	95.9

Expected Survival Table: U.S. 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspec 1991&U.

perhaps indicating more expeditious diagnosis and treatment in blacks in recent years.

In localized follicular cancer, all ages combined (Table 4), the notable finding is that excess mortality is seen *only* in the first year of follow-up with a mortality ratio (MR) of 157% and EDR of 4.9 per 1000, both sexes combined. There was no significant excess mortality in any of the 5 duration intervals from 1 to 20 years, the MR ranging between 87% and 111%, all ages combined. Observed (actual) mortality rates, q, were consistently lower than the matched population rates, q′, at durations 1-2 and 2-5 years. In the last three 5-year duration intervals, there were only minor, apparently random variations from an MR of 100%.

Excess mortality in regional follicular thyroid cancer continued to be minimal in patients under 50 years, male and female combined. The MR ranged between 171% & 173%,

and the EDR from 1.1 to 1.2 per 1000 per year (Table 4). However, EDR rose sharply with age in the first year, from 1.1 in those under 50 to 22.3 in those over 50. When all ages were combined, the pattern of progressive decrease of EDR from 0-1 year to 10-15 years is notable. The EDR decrease to -6.4 at the 15-20 duration is based on a small exposure with 11 deaths (95% CL 5.5 to 19.7), a change that is not statistically significant.

The total 1973-2013 SEER *survival* database was used to garner sufficient cases by age, sex, race and stage for detailed mortality analysis. Five and 10-year comparative mortality and cumulative survival indices by sex and race, all stages combined noted in Tables 7 & 8 for follicular carcinoma are shown in Chart 2.

In Table 7, mortality ratios and excess death rates are similar in white males and females at 0-5 & 5-10 year durations and cumulative survival ratios are 90% or above. The 5-year relative survival rate in white males of 41.6% for distant follicular carcinoma is only about half that for distant papillary carcinoma (72.9%), suggesting a different natural history in these histologic types. The prognosis for white males, and females is similar when compared within stage. In black males and females at the 0-5-year duration, EDRs were much higher and observed and relative survival lower than in their white male and female counterparts.

Medullary Carcinoma (ICD-O-3, 8510)

Medullary carcinoma of the thyroid is uncommon. It is so named because a specialized cell in the thyroid gland, the perifollicular calcitonin-producing C cell, which regulates calcium metabolism may become malignant. Tumors from these cells are called "medullary" carcinomas. It accounts for only 2156 (1.4%) of all invasive thyroid cancer cases in the 1993-2013 SEER frequency database, and 1827 total cases in the SEER survival database. The proportions tend to be higher in women (58.1%), than in men (41.9%). A preponderance in medullary carcinoma in the SEER frequency database is observed for whites, 1829 – 84.8%, but not for blacks, 173 – 8.0% (Table 2, Figure 3). This compares with the patterns of papillary and follicular carcinomas; papillary – whites >81.1% higher than blacks, and follicular – whites >77.1% higher than blacks. The mean age at diagnosis is lower in females than in males, 52.7 years vs 54.84 years. The mean age in whites is much higher than the mean age in blacks, 54.18 vs 51.18. Rates in females begin to rise at ages 15-19, 10 years earlier than in males at ages 25-29, and reach a higher peak at age 50-54. During the entire 1993-2013 period, only 145 cases all stages combined and a total of 31 deaths in blacks are reported in the SEER survival database (black survival & mortality tables not displayed). The small number precludes detailed analysis by race.

About half the cases are localized at diagnosis, 33.5% have regional involvement, and 13.9% show distant metastasis (Table 2, Figure 3). For *localized* disease (Table 8), mortality and survival at 5-years are: MR 92%, EDR -0.9 per 1000, and cumulative observed survival and relative survival 94.9% and 100.7%, respectively). For *regional* disease, mortality and survival are less favorable with median observed and relative survival just slightly more than 14 years. At the 0-5 and 5-10 year durations, MR is 345% and 280%, and EDR is 25.7 & 20.6 per 1000, respectively. In these durations, cumulative survival ratios decline to 87.8% and 77.9%, respectively. Prognosis worsens with *distant* metastasis. At 5-years, the MR and EDR are 1314% and 158.7 per 1000, respectively. At 10-years, the relative survival falls to 27.2% (Table 8). When all stages are combined, mortality ratios do not decline below 250% until after 10 years.

Undifferentiated & Anaplastic Carcinoma (ICD-O-3, 8020-8021)

Table 2-Figure 4 case statistics indicate that anaplastic, or undifferentiated carcinoma, is a very rare histologic type of thyroid cancer,

Table 5. Papillary Carcinoma, Follicular Variant (ICD-O-3, 8340) Compared With Pap. & Foll

Duration Start-End	No. Alive at Start	Exposure Pt.-Yrs	Number of Deaths		Mortality Ratio (%)	Mean Ann. Mortality Rate/1,000			Cumul. Surv. Rate		Cum. Surv. Ratio (%)
			Observed	Expected		Observed	Expected	Excess	Observed	Expected	
t to t+ch t	***l***	**E**	**d**	**d′**	**100d/d′**	**q**	**q′**	**(q-q′)**	**P**	**P′**	**100P/P′**
(PFV) 8340, Male, All Ages, Local Stage											
0-1	4,518	4,260.5	44	48.14	91	0.0103	0.0113	– 1.0	0.9897	0.9887	100.1
1-2	3,959	3,749.0	45	44.61	101	0.0120	0.0119	0.1	0.9778	0.9769	100.1
2-5	3,494	8,782.0	91	116.18	78	0.0104	0.0132	– 2.9	0.9480	0.9385	101.0
5-10	2,347	8,484.0	119	136.45	87	0.0140	0.0161	– 2.1	0.8820	0.8645	102.0
10-15	1,080	2,971.0	47	60.38	78	0.0158	0.0203	– 4.5	0.8146	0.7784	104.6
15-20	249	682.0	21	16.32	129	0.0308	0.0239	6.9	0.7073	0.6894	100.5
(PFV) 8340, Female, All Ages, Local Stage											
0-1	20,057	18,947.5	70	108.00	65	0.0037	0.0057	– 2.0	0.9963	0.9943	100.2
1-2	17,768	16,853.0	62	102.80	60	0.0037	0.0061	– 2.4	0.9926	0.9882	100.4
2-5	15,876	40,092.0	195	278.01	70	0.0049	0.0069	– 2.1	0.9783	0.9677	101.1
5-10	11,017	39,807.5	288	341.57	84	0.0072	0.0086	– 1.3	0.9428	0.9264	101.8
10-15	5,138	14,787.0	147	161.16	91	0.0099	0.0109	– 1.0	0.8939	0.8761	102.0
15-20	1,341	3,544.5	44	46.46	95	0.0124	0.0131	– 0.7	0.8283	0.8180	101.3
(PAP) 8260, Male, All Ages, Local Stage											
0-1	5,784	5,436.0	51	53.27	96	0.0094	0.0098	– 0.4	0.9906	0.9902	100.0
1-2	5,037	4,733.0	36	49.70	72	0.0076	0.0105	– 2.9	0.9831	0.9798	100.3
2-5	4,393	10,628.0	102	123.03	83	0.0096	0.0116	– 2.0	0.9545	0.9460	100.9
5-10	2,707	8,284.0	96	112.87	85	0.0116	0.0136	– 2.0	0.8986	0.8823	101.8
10-15	793	1,678.0	27	24.96	108	0.0161	0.0149	1.2	0.8334	0.8186	101.8
15-20	104	290.0	6	5.49	109	0.0207	0.0189	1.8	0.7509	0.7417	101.2
(PAP) 8260, Female, All Ages, Local Stage											
0-1	25,137	23,543.0	91	122.42	74	0.0039	0.0052	– 1.3	0.9961	0.9948	100.1
1-2	21,858	20,589.5	91	113.24	80	0.0044	0.0055	– 1.1	0.9917	0.9893	100.2
2-5	19,230	46,741.5	209	292.53	71	0.0045	0.0063	– 1.8	0.9784	0.9707	100.8
5-10	11,898	36,535.5	216	275.36	78	0.0059	0.0075	– 1.6	0.9497	0.9340	101.7
10-15	3,535	7,308.0	55	65.52	84	0.0075	0.0090	– 1.4	0.9088	0.8928	101.8
15-20	452	1,329.0	18	12.89	140	0.0135	0.0097	3.8	0.8577	0.8491	101.0
(FOLL) 8330, Male, All Ages, Local Stage											
0-1	778	756.5	13	10.67	122	0.0172	0.0141	3.1	0.9828	0.9859	99.7
1-2	722	702.0	3	10.32	29	0.0043	0.0147	– 10.4	0.9786	0.9714	100.7
2-5	679	1,772.5	37	29.15	127	0.0209	0.0164	4.4	0.9173	0.9241	99.3
5-10	493	1,836.5	35	30.86	113	0.0191	0.0168	2.3	0.8313	0.8489	97.9
10-15	241	800.0	14	15.27	92	0.0175	0.0191	– 1.6	0.7633	0.7696	99.2
15-20	89	258.0	5	6.20	81	0.0194	0.0240	– 4.6	0.6606	0.6742	98.0
(FOLL) 8330, Female, All Ages, Local Stage											
0-1	2,184	2,101.5	26	14.29	182	0.0124	0.0068	5.6	0.9876	0.9932	99.4
1-2	1,993	1,936.0	18	13.75	131	0.0093	0.0071	2.2	0.9784	0.9861	99.2
2-5	1,861	4,918.0	25	39.37	63	0.0051	0.0080	– 2.9	0.9639	0.9626	100.1
5-10	1,418	5,388.0	55	50.46	109	0.0102	0.0094	0.8	0.9132	0.9182	99.5
10-15	747	2,417.0	30	24.83	121	0.0124	0.0103	2.1	0.8578	0.8711	98.5
15-20	257	688.5	9	9.37	96	0.0131	0.0136	– 0.5	0.8104	0.8077	100.3

Expected Survival Table: U.S. 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspec 1991&U.

accounting for approximately1349 (0.9%) of total cases in the SEER frequency database in the 1993-2013 time-period. Tumors of follicular cell origin may fail to differentiate, in which case they give rise to the "anaplastic" or "undifferentiated" carcinomas. Table 2-Figure 4 case statistics also indicate that this histologic type of tumor rises substantially only after the sixth decade of life. After age 50, age-specific incidence curves in females continues to increase with age reaching a high point at 85+ years, whereas in males it reaches a plateau at age 65 and then begins a slow steady decline. Mean age at advanced diagnostic ages is less in males than in females, 67.7 & 72.6, respectively. For all races, mean ages are: whites 70.6, blacks 68.6, other 70.4, and unknown 70.3. In general, the anaplastic carcinomas are advanced at the time of diagnosis.

Table 6. Medullary, Papillary & Follicular Carcinoma 1993-13 Compared; All Stages Combined

Duration Start-End	No. Alive at Start	Exposure Pt.-Yrs	Number of Deaths		Mortality Ratio (%)	Mean Ann. Mortality Rate/1,000			Cumul. Surv. Rate		Cum. Surv. Ratio (%)
			Observed	Expected		Observed	Expected	Excess	Observed	Expected	
t to t+ch t	***l***	**E**	**d**	**d′**	**100d/d′**	**q**	**q′**	**(q-q′)**	**P**	**P′**	**100P/P′**
Medullary (8510), All Ages											
0-1	1,772	1,679.5	96	18.98	506	0.0572	0.0113	45.9	0.9428	0.9887	95.4
1-2	1,491	1,422.0	52	15.93	327	0.0366	0.0112	25.4	0.9083	0.9776	92.9
2-5	1,301	3,085.0	89	35.55	250	0.0288	0.0115	17.3	0.8334	0.9441	88.3
5-10	756	2,216.5	64	28.20	227	0.0289	0.0127	16.2	0.7110	0.8844	80.4
10-15	197	340.0	14	5.11	274	0.0412	0.0150	26.1	0.5463	0.8236	66.3
15-20	7	16.5	1	0.11	921	0.0606	0.0066	54.0	0.3642	0.7969	45.7
Papillary (8260), All Ages											
0-1	54,145	50,725.0	591	319.57	185	0.0117	0.0063	5.4	0.9883	0.9937	99.5
1-2	46,714	43,900.5	347	285.35	122	0.0079	0.0065	1.4	0.9805	0.9872	99.3
2-5	40,740	98,483.5	757	704.88	107	0.0077	0.0072	0.5	0.9577	0.9661	99.1
5-10	24,882	76,388.0	692	644.82	107	0.0091	0.0084	0.6	0.9150	0.9253	98.9
10-15	7,434	15,858.0	180	153.28	117	0.0114	0.0097	1.7	0.8619	0.8811	97.8
15-20	1,028	3,005.0	51	32.82	155	0.0170	0.0109	6.0	0.7949	0.8327	95.5
Follicular (8330), All Ages											
0-1	5,607	5,412.5	205	59.00	347	0.0379	0.0109	27.0	0.9621	0.9891	97.3
1-2	5,013	4,851.5	81	50.94	159	0.0167	0.0105	6.2	0.9460	0.9787	96.7
2-5	4,609	12,114.5	204	136.97	149	0.0168	0.0113	5.5	0.8993	0.9458	95.1
5-10	3,424	12,761.0	229	155.46	147	0.0179	0.0122	5.8	0.8217	0.8895	92.4
10-15	1,727	5,671.0	104	77.28	135	0.0183	0.0136	4.7	0.7470	0.8296	90.0
15-20	611	1,745.5	27	31.77	85	0.0155	0.0182	− 2.7	0.6856	0.7521	91.2
Undifferentiated & Anaplastic (8020-8021), All Ages, (1973-2013)*											
0-1	1,239	1,223.0	999	43.78	2,282	0.8168	0.0358	781.0	0.1832	0.9642	19.0
1-2	208	204.5	73	5.11	1,428	0.3570	0.0250	332.0	0.1178	0.9401	12.5
2-5	128	309.5	39	7.49	520	0.1260	0.0242	101.8	0.0797	0.8731	9.1
5-10	68	263.5	8	9.02	89	0.0304	0.0342	− 3.9	0.0686	0.7319	9.4
10-15	37	133.5	3	5.55	54	0.0225	0.0416	− 19.1	0.0602	0.5922	10.2
15-20	19	69.0	6	2.27	264	0.0870	0.0329	54.1	0.0340	0.4990	6.8
Oxyphilic - Hurthle Cell (8290), All Ages (1973-2013)*											
0-1	3,678	3,575.5	112	54.71	205	0.0313	0.0153	16.0	0.9687	0.9847	98.4
1-2	3,361	3,245.5	72	50.95	141	0.0222	0.0157	6.5	0.9472	0.9692	97.7
2-5	3,058	8,076.5	183	138.64	132	0.0227	0.0172	5.5	0.8849	0.9201	96.2
5-10	2,256	8,623.0	190	169.16	112	0.0220	0.0196	2.4	0.7927	0.8325	95.2
10-15	1,152	3,763.0	97	91.61	106	0.0258	0.0243	1.4	0.6937	0.7346	94.4
15-20	445	1,563.0	51	39.15	130	0.0326	0.0251	7.6	0.5892	0.6471	91.1
Papillary-Follicular Variant (8340), All Ages											
0-1	34,133	32,257.5	243	222.58	109	0.0075	0.0069	0.6	0.9925	0.9931	99.9
1-2	30,139	28,588.5	195	208.70	93	0.0068	0.0073	− 0.5	0.9858	0.9859	100.0
2-5	26,843	67,902.0	492	549.79	89	0.0072	0.0081	− 0.9	0.9644	0.9620	100.3
5-10	18,599	67,737.5	683	665.74	103	0.0101	0.0098	0.3	0.9162	0.9151	100.1
10-15	8,815	25,929.5	322	313.62	103	0.0124	0.0121	0.3	0.8583	0.8601	99.8
15-20	2,422	6,446.0	95	93.20	102	0.0147	0.0145	0.3	0.7895	0.7978	99.0

* 1973-2013; for the purposes of garnering >case volume.

Expected Survival Table: U.S. 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspec 1991&U.

Only 1239 cases were available in the SEER survival database from 1973-2013 for a comparative mortality analysis (Table 6). Prognosis for anaplastic carcinoma is extremely poor. Initial excess mortality is extremely high, but decreases progressively with duration. MR and EDR at the 0-1 duration are 2282 and 781 per 1000. MR and EDR at the 1-2 year follow-up duration are 1428 and 332 per 1000. At the 5-year follow-up duration, MR, EDR and relative cumulative survival are 520%, 101.8 per 1000, and 9.1%, respectively, contrasting with the superior comparative mortality and survival indices for papillary, follicular and medullary carcinomas (Table 6). Mortality is not statistically significant

Table 7. Thyroid Carcinoma, 1973-2013, Histology, All Ages, Race, Sex, Stage, Durations 0-5 & 5-10 Yrs

		e-links to source file	No. Alive at Start	Exposure Pt.-Yrs	Number of Deaths		Mortality Ratio	Excess Death Rate	Cumul. Surv. Rate		Cum. Surv. Ratio (%)
					Observed	Expected			Observed	Expected	
Stage	**Race-Sex**	**Duration**	***l***	**E**	**d**	**d′**	**MR**	**EDR**	**P**	**P′**	**Cum SR**
					Papillary, ICD-0-3-8260						
Local	**White-Male**	0-5	5,166	19,189.5	169	211.71	80	– 2.2	0.9568	0.9453	101.2
Local		5-10	2,636	8,668.0	101	119.67	84	– 2.2	0.8988	0.8811	102.0
Regional	W-M	0-5	5,166	18,721.5	283	195.02	145	4.7	0.9267	0.9484	97.7
Regional		5-10	2,454	8,085.0	133	98.75	135	4.2	0.8525	0.8915	95.6
Distant	W-M	0-5	709	2,292.0	191	35.33	541	67.9	0.6755	0.9270	72.9
Distant		5-10	264	851.0	33	12.73	259	23.8	0.5615	0.8592	65.4
All	W-M	0-5	11,041	40,203.0	643	442.77	145	5.0	0.9244	0.9456	97.8
All		5-10	5,354	17,604.0	267	231.39	115	2.0	0.8549	0.8845	96.7
					Papillary, ICD-0-3-8260						
Local	**White-Female**	0-5	21,584	80,285.5	347	480.27	72	– 1.7	0.9782	0.9700	100.8
Local		5-10	11,000	35,988.0	222	280.27	79	– 1.6	0.9482	0.9322	101.7
Regional	W-F	0-5	13,052	47,079.5	346	261.15	132	1.8	0.9643	0.9722	99.2
Regional		5-10	6,259	20,500.5	153	143.47	107	0.5	0.9278	0.9381	98.9
Distant	W-F	0-5	1,008	3,432.5	196	29.07	674	48.6	0.7745	0.9606	80.6
Distant		5-10	429	1,487.5	27	8.96	301	12.1	0.7074	0.9317	75.9
All	W-F	0-5	35,644	130,797.5	889	768.68	116	0.9	0.9672	0.9706	99.7
All		5-10	17,688	57,976.0	402	433.51	93	– 0.5	0.9338	0.9342	99.9
					Papillary, ICD-0-3-8260						
Local	**Black-Male**	0-5	281	1,035.0	15	15.60	96	– 0.6	0.9247	0.9258	99.9
Local		5-10	132	437.5	6	7.83	77	– 4.2	0.8592	0.8449	101.7
Regional	B-M	0-5	141	530.5	10	6.28	159	7.0	0.9196	0.9423	97.6
Regional		5-10	80	290.5	4	4.09	98	– 0.3	0.8642	0.8764	98.6
Distant	B-M	0-5	28	92.5	9	1.60	563	80.0	0.6513	0.9179	71.0
Distant		5-10	12	33.5	4	0.67	596	99.4	0.2512	0.8383	30.0
All	B-M	0-5	450	1,658.0	34	23.48	145	6.3	0.9064	0.9306	97.4
All		5-10	224	761.5	14	12.59	111	1.9	0.8255	0.8552	96.5
					Papillary, ICD-0-3-8260						
Local	**Black-Female**	0-5	1,683	6,078.5	42	49.26	85	– 1.2	0.9653	0.9597	100.6
Local		5-10	790	2,589.0	24	25.35	95	– 0.5	0.9225	0.9132	101.0
Regional	B-F	0-5	614	2,264.0	31	16.61	187	6.4	0.9348	0.9636	97.0
Regional		5-10	309	991.0	12	8.83	136	3.2	0.8791	0.9206	95.5
Distant	B-F	0-5	61	180.0	18	1.59	1,134	91.2	0.6584	0.9583	68.7
Distant		5-10	23	69.5	6	0.54	1,109	78.5	0.4159	0.9236	45.0
All	B-F	0-5	2,358	8,522.5	91	67.38	135	2.8	0.9491	0.9607	98.8
All		5-10	1,122	3,649.5	42	34.69	121	2.0	0.8966	0.9154	97.9
					Follicular, ICD-0-3-8330						
Local	**White-Male**	0-5	881	3,861.0	59	57.71	102	0.3	0.9243	0.9270	99.7
Local		5-10	640	2,614.0	45	43.94	102	0.4	0.8487	0.8514	99.7
Regional	W-M	0-5	715	2,983.5	64	48.37	132	5.2	0.8976	0.9211	97.5
Regional		5-10	482	1,886.0	64	38.23	167	13.7	0.7527	0.8307	90.6
Distant	W-M	0-5	155	417.5	93	13.87	671	189.5	0.3530	0.8476	41.6
Distant		5-10	41	150.5	17	5.48	310	76.5	0.1876	0.7029	26.7
All	W-M	0-5	1,751	7,262.0	216	119.86	180	13.2	0.8634	0.9199	93.9
All		5-10	1,163	4,650.5	126	87.59	144	8.3	0.7523	0.8360	90.0

Expected Survival Table: U.S. 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspec 1991&U.

after 5-years due to minimal exposures and deaths.

Oxyphilic Adenocarcinoma – Hurthle cell (ICD-O-3, 8290)

Oncocytic or oxyphilic carcinomas (also called *Hurthle cell carcinoma)* is a relatively rare variant of follicular carcinoma and behave as a slightly more aggressive form of follicular cancer but present similarly. It is an uncommon invasive thyroid cancer, accounting for 4006 (2.7%) of total cases in the 1993-2013 SEER frequency database. There were 3307 cases in the SEER survival database in the 1993-2013 time-period and a moderate

Table 8. Thyroid Carcinoma, 1973-2013, Histology, All Ages, Race, Sex, Stage, Durations 0-5 & 5-10 Yrs

		e-links to source file	No. Alive at Start	Exposure Pt.-Yrs	Number of Deaths		Mortality Ratio	Excess Death Rate	Cumul. Surv. Rate		Cum. Surv. Ratio (%)
					Observed	Expected			Observed	Expected	
Stage	**Race-Sex**	**Duration**	***l***	**E**	**d**	**d′**	**MR**	**EDR**	**P**	**P′**	**Cum SR**
					Follicular, ICD-0-3-8330						
Local	**White-Female**	0-5	2,414	10,545.5	90	87.85	102	0.2	0.9589	0.9588	100.0
Local		5-10	1,805	7,637.5	86	81.47	106	0.6	0.9044	0.9085	99.6
Regional	W-F	0-5	1,551	6,543.5	124	63.61	195	9.2	0.9114	0.9521	95.7
Regional		5-10	1,090	4,428.5	73	48.19	151	5.6	0.8412	0.9014	93.3
Distant	W-F	0-5	255	789.5	128	24.15	530	131.5	0.4569	0.8574	53.3
Distant		5-10	84	278.5	34	6.42	530	99.0	0.2516	0.7664	32.8
All	W-F	0-5	4,220	17,878.5	342	175.82	195	9.3	0.9113	0.9517	95.8
All		5-10	2,979	12,344.5	193	136.13	142	4.6	0.8427	0.9002	93.6
					Follicular, ICD-0-3-8330						
Local	**Black-Male**	0-5	92	373.5	13	7.87	165	13.7	0.8352	0.8983	93.0
Local		5-10	54	214.0	7	4.75	147	10.5	0.7101	0.8030	88.4
Regional	B-M	0-5	78	324.0	10	6.45	155	10.9	0.8604	0.9041	95.2
Regional		5-10	50	202.5	4	4.95	81	− 4.7	0.7808	0.7982	97.8
Distant	B-M	0-5	25	77.0	13	2.97	438	130.3	0.4103	0.8193	50.1
Distant		5-10	8	27.0	3	0.74	404	83.6	0.2564	0.7182	35.7
All	B-M	0-5	195	774.5	36	17.28	208	24.2	0.7926	0.8930	88.8
All		5-10	112	443.5	14	10.45	134	8.0	0.6797	0.7925	85.8
					Follicular, ICD-0-3-8330						
Local	**Black-Female**	0-5	362	1,504.0	14	16.37	86	− 1.6	0.9553	0.9463	100.9
Local		5-10	246	995.5	19	13.10	145	5.9	0.8673	0.8853	98.0
Regional	B-F	0-5	245	988.5	13	10.07	129	3.0	0.9403	0.9497	99.0
Regional		5-10	155	595.0	14	7.85	178	10.3	0.8345	0.8882	93.9
Distant	B-F	0-5	75	231.0	42	6.20	678	155.0	0.4050	0.8736	46.4
Distant		5-10	23	71.5	8	1.66	482	88.7	0.2222	0.7793	28.5
All	B-F	0-5	682	2,723.5	69	32.59	212	13.4	0.8862	0.9413	94.1
All		5-10	424	1,662.0	41	22.63	181	11.1	0.7821	0.8787	89.0
					Medullary, ICD-O-3-8510						
Local	**All Races**	0-5	886	3,244.0	35	37.88	92	− 0.9	0.9485	0.9421	100.7
Local		5-10	417	1,224.0	22	16.90	130	4.2	0.8605	0.8772	98.1
Regional	All Races	0-5	628	2,238.0	81	23.49	345	27.4	0.8246	0.9486	86.9
Regional		5-10	283	841.0	27	9.64	280	21.8	0.6913	0.8973	77.0
Distant	All Races	0-5	258	704.5	121	9.21	1,314	158.7	0.4491	0.9391	47.8
Distant		5-10	56	151.5	15	1.65	911	88.1	0.2413	0.8873	27.2
All	All Races	0-5	1,772	6,186.5	237	70.46	336	26.9	0.8334	0.9441	88.3
All		5-10	756	2,216.5	64	28.20	227	16.2	0.7110	0.8844	80.4
					Hurthle Cell, ICD-O-3-8290						
Local	**All Races**	0-5	1,976	8,259.0	110	126.80	87	− 2.0	0.9335	0.9249	100.9
Local		5-10	1,288	4,992.0	90	95.56	94	− 1.1	0.8525	0.8389	101.6
Regional	All Races	0-5	628	2,238.0	81	23.49	345	25.7	0.8329	0.9489	87.8
Regional		5-10	283	841.0	27	9.64	280	20.6	0.6975	0.8955	77.9
Distant	All Races	0-5	151	389.5	88	12.68	694	193.4	0.3549	0.8499	41.8
Distant		5-10	32	97.0	10	3.08	325	71.3	0.2248	0.7181	31.3
All	All Races	0-5	3,678	14,897.5	367	244.30	150	8.2	0.8849	0.9201	96.2
All		5-10	2,256	8,623.0	190	169.16	112	2.4	0.7927	0.8325	95.2

Expected Survival Table: U.S. 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspec 1991&U.

female preponderance (2797 cases – 69.8%). Male and female mean ages are 59.9 and 56.5 years, respectively. Mean age in whites and blacks are 57.7 and 56.1, respectively. Female incidence reaches its zenith at 50-54 years, plateaus and then sharply declines at 70-74 years. Male incidence reaches its zenith 5 years later, plateaus and then begins a slower decline at 70-74 years. 53.1% are local stage at diagnosis, 40.6% are regional stage, 3.9% are distant and 2.2% are unstaged. Aggregate average annual mortality and survival results, 1993-2013, are displayed below for the following durational intervals: 0-1, 1-2, 2-5, 5-10, 10-15 and 15-20 years, all ages, races and stages combined (See Chart 3).

Chart 1. Thyroid Carcinoma (All Sites Combined) 1993-2013, SEER*Stat 8.3.2

Duration	Lives	Exposure	Deaths	Deaths'	MR	EDR	P	P'	100P/P'
0-1	130,028	123,467.5	3,157	950.70	332	17.9	0.9744	0.9923	98.2
1-2	113,750	108,253.0	1,130	811.90	139	2.9	0.9643	0.9849	97.9
2-5	191,626	257,091.0	2,412	2,125.33	113	1.1	0.9372	0.9605	97.6
0-5	130,028	488,811.5	6,699	3,887.93	172	5.8	0.9372	0.9605	97.6
5-10	69,628	247,047.0	2,766	2,414.81	115	1.4	0.8854	0.9141	96.9
10-15	31,364	93,510.5	1,227	1,080.40	114	1.6	0.8270	0.8618	96.0
15-20	9,160	24,808.0	335	329.68	102	0.2	0.7703	0.8043	95.8

Expected Survival Table: US 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspecified 1991 & Unknown.

Observed (actual) deaths exceeded expected deaths by 2 to 1 in the first interval and is reflected in a mortality ratio (MR) of 188% and excess death rate (EDR) of 12.9 per 1000. Mortality in the second duration (1-2 years) declined to 144% and an EDR of 6.6 per 1000. Thereafter, there was virtually no excess mortality, and relative cumulative survival at 15 years was 95.6%. However, in the last interval, there were only 19 deaths with tiny exposure; therefore, mortality was not statistically significant. There was no significant excess mortality in any of the last 3 duration intervals from 5 to 15 years (sixth duration is not statistically significant), the MR ranging between 117% and 105%, all ages combined. Observed mortality rates, q, were consistently about the same as the matched population rates, q', in forth through sixth durations. In the last three 5-year duration intervals, there were only minor, apparently random variations from an MR of 100%, and the MR was not statistically significant in the 15-20-year durational interval.

Papillary Carcinoma, Follicular Variant-PFV (ICD-O-3, 8340)

The term *mixed papillary and follicular carcinoma* is no longer used, having been superseded simply by *papillary carcinoma.*[9] Nevertheless, there are a total of 38,980 cases in the SEER frequency database from 1993-2013 with designated ICD-O-3, 8340, (topography code C739 for thyroid cancer in the SEER Site/Validation List, September 18, 2015), and therefore, a brief overview of current information is warranted to compare this histologic variant with the invasive thyroid cancer oncotypes in this report. Table 2-Figure 6 case statistics indicate that this histologic tumor accounted for 30,652 cases in females (78.6%), 82.3% in whites, 8.1% in blacks, 8.7% in other races, and only about 0.9% unknown. Mean age at diagnosis for whites and blacks was 49.75 and 49.66 years, respectively. Mean age was higher by about 4 years in males (53.55). Of patients with PCFV thyroid cancer, 71.4% have localized disease at time of

Chart 2. Follicular Carcinoma (All Stages Combined) 1993-2013, SEER*Stat 8.3.2 Five & Ten-Year Comparative Mortality and Cumulative Survival Indices by Sex and Race

Race-Sex	Duration (Years)	MR %	EDR Per 1000	Observed Survival (P)	Expected Survival (P')	Cum SR (%)
White-Male	0-5	180	13.2	86.3%	92.0%	93.9
	5-10	144	8.3	75.2%	83.6%	90.0
White-Female	0-5	195	9.3	91.1%	95.2%	95.8
	5-10	142	4.6	84.3%	90.0%	93.6
Black-Male	0-5	208	24.2	79.3%	89.3%	88.8
	5-10	134	8.0	68.0%	79.3%	85.8
Black-Female	0-5	212	13.4	88.6%	94.1%	94.1
	5-10	181	11.1	78.2%	87.9%	89.0

Chart 3. Oxyphilic Adenocarcinoma – Hurthle Cell (SEER*Stat 8.3.2)

Duration	Lives	Exposure	Deaths	Deaths'	MR	EDR	P	P'	100P/P'
0-1	3,307	3,204.5	88	46.79	188	12.9	0.9725	0.9854	98.7
1-2	3,014	2,898.5	63	43.77	144	6.6	0.9514	0.9705	98.0
2-5	2,720	7,119.0	140	119.24	117	2.9	0.8967	0.9224	97.2
5-10	1,962	7,259.0	148	141.35	105	0.9	0.8110	0.8352	97.0
10-15	904	2,588.0	68	63.77	107	1.6	0.7023	0.7344	95.6
15-20	226	437.5	19	13.43	141	10.4	0.6048	0.6462	93,6

Expected Survival Table: US 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspecified 1991 & Unknown.

diagnosis, 25.8% have regional involvement, 2.1% have distant metastasis, and 0.8% are unstaged. Female incidence begins at ages 1-4 years (3 cases), continues to its highpoint at 45-49 years, and then gradually slopes downward with 181 cases at 85+ years. Male incidence begins at age 5-9 years (13 cases), then slowly rises to its zenith 10 years later (55-59) and then gradually declines to 85+ years with 70 cases. Aggregate average annual mortality and survival results, 1993-2013, are displayed in Chart 4 for the following durational intervals: 0-1, 1-2, 2-5, 5-10, 10-15 and 15-20 years, all ages, races and stages combined.

In Chart 5, expected deaths-d' exceeded actual or observed deaths-d in all durational intervals and is reflected in mortality ratios of 101% or less. In the Chart 4, EDRs are all basically negative integers and relative survival never dips below 100% at any duration. Mortality and survival in the 15-20-year durational interval is not statistically significant due to the extremely small exposure and number of deaths. Outcomes are quite sim-

Chart 5. PFV Thyroid Carcinoma – Observed vs Expected

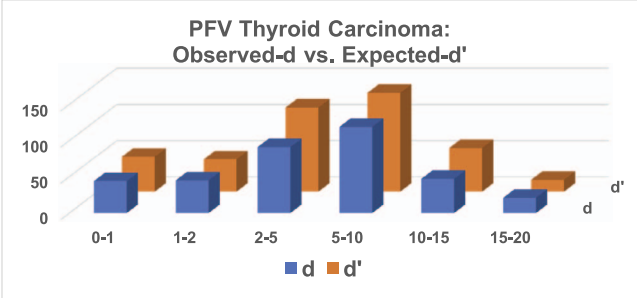


Chart 4. PFV Thyroid Carcinoma, SEER*Stat 8.3.2

Duration	Lives	Exposure	Deaths	Deaths'	MR	EDR	P	P'	100P/P'
0-1	4,518	4,260.5	44	48.14	91	− 1.0	0.9897	0.9887	100.1
1-2	3,595	3,749.0	45	44.61	101	0.1	0.9778	0.9769	100.1
2-5	3,494	8,782.0	91	116.18	78	− 2.9	0.9480	0.9385	100.0
5-10	2,437	8,484.0	119	136.45	87	− 2.1	0.8820	0.8645	102.0
10-15	1,080	2,971.0	47	60.38	78	− 4.5	0.8146	0.7784	102.6
15-20	249	682.0	21	16.32	129	6.9	0.7073	0.6894	104.6

Expected Survival Table: US 1970-2011 by individual year (White, Black, Other [AI/API], Ages 0-99, All races for Other Unspecified 1991 & Unknown.

ilar to 20-year follow-up mortality and survival associated with thyroid papillary cancer (ICD-O-3, 8260) noted in Table 6.

COMMENTS AND CONCLUSIONS

Descriptive epidemiologic characteristics for both papillary and follicular thyroid cancer indicate that it is remarkable to observe a considerable female patient (3 to 1) preponderance to male patients. For papillary and papillary follicular variant (PFV) cancer, incidence for women exceeds that for men by more than 3 to 1. For follicular cancer, incidence in women exceeds that in men by a factor of 2.4. The male-female mean age at diagnosis is a bit earlier for papillary carcinoma (48.2 yrs) than for follicular carcinoma (51.6 yrs). Localized disease in papillary and PFV carcinoma with no significant excess mortality after diagnosis has a very good prognosis. Because nearly two thirds of thyroid cancers are localized, and excess death rate (EDR) is small in patients with regional cancer under age 50, overall excess mortality for all ages also virtually disappeared after 10 years in papillary and follicular cancer. Oxyphilic carcinoma (also called Hurthle cell carcinoma) behave as a slightly more aggressive form of follicular cancer but present similarly. Medullary thyroid carcinoma (MTC) is uncommon, has a large white predominance and a poorer prognosis with non-localized disease than follicular cancer. Anaplastic or undifferentiated carcinoma, which is rare, afflicts those in later decades in life. It is quite deadly in the early durations of follow-up. Nevertheless overall, thyroid cancer remains a formidable health concern in the United States in 2016 with estimated cases of 64,300 and 1980 deaths.

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