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MORTALITY

Cancer of the Nasal Cavity, Middle Ear and Accessory Sinuses – 15 Year Comparative Survival and Mortality Analysis by Age, Sex, Race, Stage, Grade, Cohort Entry Time-Period, Disease Duration and Topographic Primary Sites: *A Systematic Review of 13,404 Cases for Diagnosis Years 2000-2017: (NCI SEER*Stat 8.3.8)*

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Background.—Sinonasal malignancies are rare, aggressive, deadly and challenging tumors to diagnose and treat. Since 2000, age-adjusted incidence rates average less than 1 case per 100,000 per year, male and female combined, in the United States. For the entire cohort, 2000-2017, overall median age-onset was 62.6 years. Carcinoma constitutes over 90% of these upper respiratory cancers and most cases are advanced, more than 72% (regional or distant stage) when the diagnosis is made. Composite mortality at 5 years was 108 excess deaths/1000/year with a mortality ratio of 558%, and 41% of deaths occurred in this time frame. As a consequence, observed median survival was approximately 6 years with 5-year cumulative observed survival (P) and relative survival rates (SR) 53% and 60%. This mortality and survival update study follows the World Health Organization International Classification of Diseases for Oncology-3rd Edition (ICD-O-3)[1] topographical identification, coding, labeling and listing of 13,404 patient-cases accessible for analysis in the United States National Cancer Institute's Surveillance, Epidemiology and End Results program (NCI SEER Research Data, 18 Registries), 2000-2017 located in 8 primary anatomical sites: *C30.0-Nasal cavity, C30.1-Middle ear, C31.0-Maxillary sinus, C31.1-Ethmoid sinus, C31.2-Frontal sinus, C31.3-Sphenoid sinus, C31.8-Overlapping lesion of accessory sinuses, C31.9-Accessory sinus, NOS.*

Objectives.—1) Utilize national population-based SEER registry data for 2000-2017 to update cancer survival and mortality outcomes for 8 ICD-O-3 topographically coded sinonasal primary sites. 2) Discern similarities and contrasts in NCI-SEER case characteristics. 3) Identify current risk pattern outcomes and shifts in United States citizens, 2000-2017.

Methods.—SEER Research Data, 18 Registries, Nov 2019 Sub (2000-2017)[2,3] are used to examine the risk consequences of 13,404 patients diagnosed with sinonasal malignancies, 2000-2017, in this retrospective population-based study employing prognostic data stratified by topography, age, sex, race, stage, grade, 2 cohort entry time-periods (2000-06 & 2007-17), and disease-duration to 15 years. General methods and standard double decrement life table methodologies for displaying and

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converting SEER site-specific annual survival and mortality data to aggregate average annual data units in durational intervals of 0-1, 0-2, 1-2, 2-5, 0-5, 5-10, and 10-15 years are employed. The reader is referred to the "Registrar Staging Assistant (SEER*RSA)" for local-regional-distant Extent of Disease (EOD) sources used in the development of staging descriptions for the Nasal Cavity and Paranasal Sinuses (maxillary and ethmoid sinuses only) and Summary Stage 2018 Coding Manual v2.0 released September 1, 2020. Cancer staging & grading procedural explanations, statistical significance & 95% confidence levels[4] are described in previous *Journal of Insurance Medicine* articles[5,6] and other publications.[7,8] Poisson confidence intervals at the 95% level based on the number of observed deaths are used in this study but not displayed here to conserve space on the mortality tables. Excluded were all death certificate only and those alive with no survival time.

Results.—In the SEER 18 registries, a total of 13,404 patient cases (2000-2017) were available for analysis with an incidence of less than one patient per 100,000 people. From this group, analysis for survival and mortality totaled 10,624 patients. Males comprised 59.3% of cases and females 40.7%. Whites represented 80.3% of cases and black, others & unknown patients comprised 19.7%. The most common anatomic site of malignancy was the nasal cavity (49.7%); least common was the frontal sinus (1.2%). From diagnosis, across the span of 8 primary sites, first-year mortality rates q ranged from 14.3% (C30.0-nasal cavity) to 30.2% (C31.8-overlapping sinus) with corresponding excess death rates (EDR) of 118/1000/year and 279/1000/year. For single sites, the 5-year cumulative survival ratio (SR) was highest for the nasal cavity (69.5%) and lowest for overlapping lesions of the accessory sinuses (47.2%) with EDRs of 76 and 169 per 1000 per year respectively Overall, 5-year relative survival (SR) for all sinonasal tract malignancies combined was 60.3%, excess mortality (EDR) 108 per 1000 per year and mortality ratio 558%.

Conclusions.—The 8 sinonasal cancer primary sites are characterized by a low percentage of cases in the localized stage (28%). Since excess mortality is high even in the localized stage, overall prognosis is very poor for all patients. Excess mortality persists in cancer of the sinonasal tract as long as 10-15 years after diagnosis and treatment. EDR in the 15-year durational-interval, all sinonasal sites combined remained significant at 27.6 per 1000 per year with continuing decrease in cumulative survival ratio (SR) to 43.9%.

INCIDENCE

Incidence trends are very low for cancer of the upper respiratory tract (defined in the SEER registries as nasal cavity, accessory sinuses and middle ear). *Overall age-adjusted incidence rates* of new cases of invasive cancer of the sinonasal region in the United States, 2000-2017, was 0.7 per 100,000 men and women per year. Chart 1 indicates that incidence rates increase with age and vary by sex and race in the US Incidence is higher in males than in females, higher in whites than in blacks, and higher with increasing age.

Trends in SEER incidence rates age-adjusted to the 2000 US Standard Population by sex & race indicate that the average annual percent change (AAPC) from 1975-2017 was −0.3 per 100,000 per year in all races & both sexes; the percent change (PC) in this time-period was −8.5.

SEER CASE STATISTICS

The 13,404 cases of cancer of the nasal cavity, middle ear and sinuses present in the SEER 18 Registries, 2000-2017, were distributed for the sinonasal group composite by

Chart 1. Nose, Nasal Cavity, Middle Ear, Sinuses, SEER 21 Registries, 2000-2017: *SEER Age-Adjusted Incidence Rates, 2000-2017*[3]

	All Races			Whites			Blacks		
	Total	Males	Females	Total	Males	Females	Total	Males	Females
All ages	0.7	0.9	0.5	0.7	0.9	0.5	0.6	0.9	0.5
Under 65	0.4	0.5	0.3	0.4	0.5	0.3	0.4	0.6	0.3
65 & over	2.8	3.7	2.1	2.9	3.8	2.2	2.2	3	1.7

Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130) standard.

age, sex, race, stage, and grade shown in Chart 2. Data for individual topographical primary sites are presented in Chart 3. The SEER historic stage A selection code is used for staging (local, regional or distant). Overall, there were 8996 staged cases and 2,722 (23.2%) unstaged. Local cases 27.8%, regional 51.5%, distant 20.7%; regional-distant staging 72.2%. A total of 6899 cases were graded and 4247 (38.1%) were of unknown grade. After exclusion of cases with no follow-up data, 10,624 patients remained for survival and mortality analysis. Mean ages for males and females were 61.6 years and 64.2 years, respectively. Ethnic mean ages were whites 63.7, blacks 56.7, other 57.9, and unknown 60.8 years. As shown in the Figure, one-third of female cases were diagnosed at ages 75 and higher. There was a 1.5-to-1 male-to-female ratio by diagnostic frequency with males accounting for 59.3% of cases and females 40.7%. The ethnic distribution of patients with sinonasal region cancer in the SEER frequency database was white 80.3%, black 9.0%, other 9.8%, and unknown 0.9%.

Comparative male and female sinonasal topography group-composite diagnostic frequency with advancing age is illustrated in the Figure. The zenith of male diagnostic frequency (12.4%) occurs at quinquennial ages 60-64; male mean age at diagnosis, 61.6-years. Female diagnostic frequency crests at ages 85+ (12.1%), with approximately one-third of cases diagnosed from age 75 to 85+ years. Female mean age at diagnosis was 64.2 years.

CANCER CASES STUDIED

Overall demographic data are given above for 13,404 patients with cancer of the nasal cavity, sinuses and middle ear in the 2000-2017 database. After the exclusion of patients with no follow-up data, 10,624 patients remained for analysis of mortality and survival. Of these remaining patients, 8404 were white (79%), 2220 were black, and other and unknown patients made up 20.9%. Nasal cavity contained most patient cases (6604), all sinuses combined contained 6473 cases, and least cases (163) were contained in the frontal sinus. The mean age at diagnosis for males and females, all sites combined, was 62.6 years.

FOLLOW-UP

Standard procedures were used by the 18 SEER registries in the follow-up (FU) of patients and in the confirmation of death data. Losses to FU were very low, less than 0.5% of all entrants at 5 years. Losses were higher in Hispanics than in black and white patients.

RESULTS

Because of the small number of cases, results have been confined to 4 tables. *Table 1* presents data for the entire sinonasal cancer group composite, with an age division restricted to those age <65 and those age 65 and up. There is no separation by cohort in Table 1, and data by sex are given only for all ages and stages

Chart 2. SEER: Composite Sinonasal Statistics, 2000-2017

Topography Primary Site Code-Composite: C30.0-1, C31.0-3, C31.8-9 Age x	M&F Number	Percent %	Male Number	Percent %	Female Number	Percent %
<45	1888	14.1	1148	14.4	740	13.6
45-54	1982	14.8	1265	15.9	717	13.1
55-64	2911	21.7	1825	23.0	1086	19.9
65-74	2975	22.2	1840	23.2	1135	20.8
75 up	3648	27.2	1868	23.5	1780	32.6
All ages	13404	100.0	7946	59.3	5458	40.7
Mean x-years	62.6		61.6		64.2	
Race	**White**		**Black**		**Other**	**Unknown**
No. & %	10766	80.3	1202	9.0	1312 9.8%	124 0.9%
Mean x-yrs.	63.7		56.7		57.9	60.8
Entrants	**M&F**	**%**	**Male**	**%**	**Female**	**%**
Freq. 2000-17	13404		7946	59.3	5458	40.7
Surv. 2000-17	10624	79.3	6320	47.2	4304	32.1
Stage	**Local**	**Regional**	**Distant**	**Reg-Dist**	**Unstaged**	**Total Staged**
M&F No,	2499	4632	1865	6497	2722	8996
%	27.8	51.5	20.7	72.2	23.2	
Grade	**I**	**II**	**III**	**IV**	**Unknown**	**All Graded**
M&F No.	1075	2429	2371	1024	4247	6899
%	15.6	35.2	34.3	14.8	38.1	

combined. Annual EDR values (excess death rate) in the first duration interval ranged from 16 per 1000 in localized stage patients under 65, to 394 per 1000 in distant stage patients 65 and up. Excess mortality decreased with duration after diagnosis but was still significantly present from 10 to 15 years afterward. EDRs were also significantly higher in older patients and in males compared with females. Mortality ratios (MRs) were high in patients under 65, but relatively low in the older patients despite the high EDR values. Five-year survival ratios were correspondingly reduced from 88% in the localized stage (patients under <65) to 37% in the distant stage (patients 65 and up).

Table 2 summarizes overall results, all ages, male and female combined, for durations 0-5 and 5-10 years in 2 cohorts of patient-entrants, 2000-06 and 2007-17. Excess mortality increased by stage, and survival ratios decreased as they did in Table 1. When tumor grading is known as in local and regional stages, results by cohort show a consistent improvement from the 2000-06 cohort to the 2007-17 cohort. At duration 0-5 years EDR in patients with local cancer, grades 1&2 (more differentiated, less malignant) were 25 per 1000 per year in the 2000-06 cohort; with higher malignancy, grades 3&4, the EDR was 68 per 1000 per year. The corresponding EDR values in the 2007-2017 cohort were 15 and 65 per 1000, respectively. Cell grading for differentiation/malignancy is relatively less effective in the regional than in the local stage. Grade 1&2 cases predominate in the localized stage, and grades 3&4 in the regional stage. No grading data have been shown for cases in the distant stage. Approximately 38% of the cases had no grading reported (Chart 2). In these cases, the EDR and MR values were intermediate. Data are also shown for the total cases staged and for the unstaged cases. Excess death rates were modestly but consistently improved in the latter cohort

Chart 3. SEER: Individual Sinonasal Primary Site FAMA* Statistics, 2000-2017

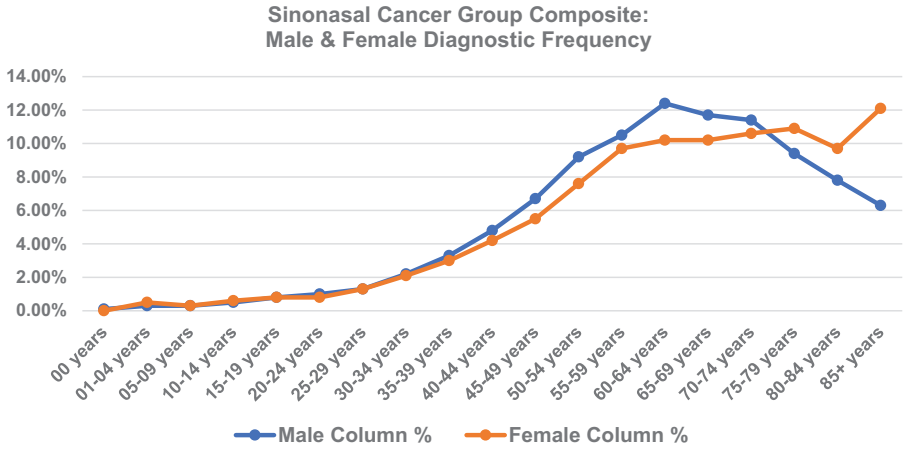
Individual Sinonasal Topographic Primary Sites	M&F	Percent	Male	Percent	Female	Percent
C3.0-Nasal Cavity	**6604**	**49.3**	**3913**	**59.3**	**2691**	**40.7**
Mean x-years	63.0		62.3		64.1	
C30.1-Middle Ear	**327**	**2.4**	**189**	**57.8**	**138**	**42.2**
Mean x-years	59.4		59.8		58.9	
C31.0-Maxillary Sinus	**3851**	**28.7**	**2336**	**60.7**	**1515**	**39.3**
Mean x-years	63.6		61.8		66.5	
C31.1-Ethmoid Sinus	**1058**	**7.9**	**616**	**58.2**	**442**	**41.8**
Mean x-years	59.8		59.2		60.3	
C31.2-Frontal Sinus	**163**	**1.2**	**104**	**63.8**	**59**	**36.2**
Mean x-years	61.7		61.9		61.4	
C31.3-Sphenoid Sinus	**448**	**3.3**	**247**	**55.1**	**201**	**44.9**
Mean x-years	60.7		59.9		61.9	
C31.8-Overlapping Lesion	**259**	**1.9**	**158**	**61.0**	**101**	**39.0**
Mean x-years	60.1		57.7		64.0	
C31.9-Accessory Sinus, NOS	**694**	**5.2**	**383**	**55.2**	**311**	**44.8**
Mean x-years	61.9		61.3		62.9	
C31.0-3, C31.8-9, All Sinuses	**6473**	**48.3**	**3844**	**59.4**	**2629**	**40.6**
Mean x-years	62.5		61.1		64.4	
C30.0-1, C31.0-3, C31.8-9	**13404**	**100.0%**	**7945**	**59.3**	**5458**	**40.7**
Mean x-years	62.6		61.6		64.2	

* FAMA – Frequency and Mean Age.
ICD-O-3 derived codes for sinonasal topographic primary sites.[1]

(2007-17) in both local and regional disease and for both grading groups in the 0-5-year duration but not so in the 5-10-year duration.

Numbers of cases are much reduced at durations 5-10 years because of the attrition due to the high mortality and poor survival. Although comparative mortality showed considerably lower EDR and MR values than in the first 5 years of FU, substantial excess mortality persisted. Ten-year survival ratios ranged from 85% to 31%.

Overall differences by race are shown at the bottom of Table 2. Nonwhite EDR values



Sinonasal Cancer: Diagnostic Frequency, 2000-2017.

Table 1. C30.0-1, C31.0-3, C31.8-9: 2000-2017 Entrants; Sex, Age, Stage, Grade, Duration

Duration Start-End t to t+ch t	No. Alive at Start *l*	Exposure Pt.-Yrs E	Number of Deaths		Mortality Ratio (%) 100d/d'	Mean Ann. Mortality Rate/1,000			Cumul. Surv. Rate		Cum. Surv. Ratio (%) 100P/P'
			Observed d	Expected d'		Observed q	Expected q'	Excess (q-q')	Observed P	Expected P'	
Local, M&F <65											
0-1	993	985.5	22	6.21	354	0.0223	0.0063	16.0	0.9777	0.9937	98.4
1-2	956	955.5	37	6.40	578	0.0387	0.0067	32.0	0.9399	0.9870	95.2
2-5	918	2,351.0	79	17.99	439	0.0336	0.0077	25.9	0.8500	0.9644	88.1
5-10	645	2,393.0	80	23.40	342	0.0334	0.0098	23.7	0.7172	0.9174	78.2
10-15	311	986.5	37	13.16	281	0.0375	0.0133	24.2	0.5896	0.8559	68.9
Median survival time (interval = 12 months): Observed is greater than 20 intervals; Relative is greater than 20 intervals.											
Local, M&F 65 up											
0-1	929	928.5	81	45.22	179	0.0872	0.0487	38.5	0.9128	0.9513	96.0
1-2	847	843.5	97	43.19	225	0.1150	0.0512	63.8	0.8078	0.9026	89.5
2-5	743	1,794.5	186	98.20	189	0.1037	0.0547	48.9	0.5813	0.7619	76.3
5-10	420	1,370.0	154	85.61	180	0.1124	0.0625	49.9	0.3206	0.5483	58.5
10-15	142	410.0	48	35.06	137	0.1171	0.0855	31.6	0.1697	0.3466	49.0
Median survival time (interval = 12 months): Observed = 6.23708 intervals; Relative = 14.0457 intervals.											
Regional, M&F <65											
0-1	2,154	2,138.5	335	12.40	2,701	0.1567	0.0058	150.9	0.8433	0.9942	84.8
1-2	1,788	1,779.5	287	10.68	2,688	0.1613	0.0060	155.3	0.7073	0.9882	71.6
2-5	1,484	3,613.5	298	23.57	1,264	0.0825	0.0065	75.9	0.5510	0.9689	56.9
5-10	907	3,293.0	142	27.00	526	0.0431	0.0082	34.9	0.4419	0.9292	47.6
10-15	433	1,333.0	56	14.61	383	0.0420	0.0110	31.0	0.3529	0.8777	40.2
Median survival time (interval = 12 months): Observed = 7.10548 intervals; Relative = 8.67909 intervals.											
Regional, M&F 65 up											
0-1	1,580	1,575.5	501	73.89	678	0.3180	0.0469	271.1	0.6820	0.9531	71.6
1-2	1,070	1,066.5	243	47.25	514	0.2278	0.0443	183.5	0.5266	0.9109	57.8
2-5	820	1,871.0	271	88.53	306	0.1448	0.0473	97.5	0.3358	0.7869	42.7
5-10	407	1,266.0	141	69.39	203	0.1114	0.0548	56.6	0.1873	0.5894	31.8
10-15	120	362.0	34	25.37	134	0.0939	0.0701	23.8	0.1113	0.4056	27.4
Median survival time (interval = 12 months): Observed = 2.27953 intervals; Relative = 2.95657 intervals.											
Distant, M&F <65											
0-1	995	987.0	242	5.23	4,626	0.2452	0.0053	239.9	0.7548	0.9947	75.9
1-2	737	728.5	137	4.01	3,419	0.1881	0.0055	182.6	0.6128	0.9892	61.9
2-5	583	1,391.5	124	8.58	1,446	0.0891	0.0062	83.0	0.4711	0.9708	48.5
5-10	330	1,138.5	45	8.80	511	0.0395	0.0077	31.8	0.3889	0.9335	41.7
10-15	136	418.0	17	3.98	428	0.0407	0.0095	31.2	0.3259	0.8885	36.7
Median survival time (interval = 12 months): Observed = 3.82563 intervals; Relative = 4.2071 intervals.											

Table 1. Continued

Duration Start-End t to t+ch t	No. Alive at Start *l*	Exposure Pt.-Yrs E	Number of Deaths		Mortality Ratio (%) 100d/d'	Mean Ann. Mortality Rate/1,000			Cumul. Surv. Rate		Cum. Surv. Ratio (%) 100P/P'
			Observed d	Expected d'		Observed q	Expected q'	Excess (q-q')	Observed P	Expected P'	
Distant, M&F 65 up											
0-1	540	538.5	237	25.09	944	0.4401	0.0466	393.5	0.5599	0.9534	58.7
1-2	300	299.5	64	12.40	516	0.2137	0.0414	172.3	0.4402	0.9139	48.2
2-5	235	552.0	69	24.31	284	0.1250	0.0440	81.0	0.2966	0.7978	37.2
5-10	118	357.0	46	18.79	245	0.1289	0.0526	76.2	0.1481	0.6036	24.5
10-15	28	72.0	7	4.66	150	0.0972	0.0647	32.6	0.0856	0.4190	20.4
Median survival time (interval = 12 months): Observed = 1.50056 intervals; Relative = 1.82673 intervals.											
All Ages & Stages K&U, Male											
0-1	6,320	6,100.5	1,237	144.58	856	0.2028	0.0237	179.1	0.7972	0.9763	81.7
1-2	4,644	4,493.0	659	100.64	655	0.1467	0.0224	124.3	0.6803	0.9544	71.3
2-5	3,683	9,005.5	728	210.04	347	0.0808	0.0233	57.5	0.5318	0.8890	59.8
5-10	2,228	7,660.5	470	196.24	240	0.0614	0.0256	35.7	0.3880	0.7799	49.7
10-15	889	2,623.0	166	77.59	214	0.0633	0.0296	33.7	0.2790	0.6686	41.7
Median survival time (interval = 12 months): Observed = 5.91543 intervals; Relative = 9.88503 intervals.											
All Ages & Stages K&U, Female											
0-1	4,304	4,159.0	816	106.05	769	0.1962	0.0255	170.7	0.8038	0.9745	82.5
1-2	3,198	3,091.5	403	71.72	562	0.1304	0.0232	107.2	0.6990	0.9519	73.4
2-5	2,582	6,328.0	536	151.69	353	0.0847	0.0240	60.7	0.5392	0.8851	60.9
5-10	1,574	5,539.5	313	132.11	237	0.0565	0.0238	32.7	0.4077	0.7844	52.0
10-15	694	2,152.5	102	58.35	175	0.0474	0.0271	20.3	0.3187	0.6822	46.7
Median survival time (interval = 12 months): Observed = 6.12194 intervals; Relative = 11.8997 intervals.											

Expected Survival Table: U.S. by SES/geography/race; 1992-2016. Ages 0-99. State-county

were higher at duration 0-5 years, 128 vs 109 extra deaths per 1000 per year, but the difference was much smaller at duration 5-10 years.

Tables 3 & 4 present aggregate average annual mortality and survival prognostic data, 2000-2017, for each sinonasal cancer primary site location. In Chart 4, prognostic results are summarized for each site at the terminal 10-15-year follow-up duration. With cumulative excess death rates (EDR), observed cumulative survival rate (P), and cumulative survival ratio (SR) weighted by exposure as the appropriate indices for primary site differences in excess mortality and survival, maxillary sinus carried the worst long-term prognosis. Maxillary sinus had the highest excess death rate of 37.5 per 1000 persons exposed to the risk of death per year at the end of follow up and the lowest 15-year cumulative observed survival rate (P) of 22.3%. Corresponding expected cumulative survival (P′) was 68.3% with consequently reduced cumulative survival ratio of 32.7% (SR=100P/P′). For all sinuses combined, the EDR was 26.3 per 1000 per year, observed cumulative survival rate (P) of 25.7%, SR 36.9%, and median survival time, approximately 3.7 years. With 4775.5 person-years of exposure (E) and 268 deaths (d), the observed mortality rate for the entire sinonasal tract (100d/NER) for the last interval was 5.6%, EDR 27.6 per 1000, observed cumulative survival (P) 30%, and cumulative survival ratio (SR) 43.9%.

COMMENT

Upper respiratory tract sinonasal malignancies are rare cancers with poor prognosis regardless of anatomic primary site. The tables in this section provide a comprehensive medical-actuarial population-based retrospective analysis of comparative mortality and survival in 8 sinonasal cancers contained in the National Cancer Institute's SEER Research Data, 18 Registries, 2000-2017. Age-adjusted incidence rates are very low, averaging less than 1 case per 100,000 per year, male and female combined. Remarkably, as noted in Tables 3 and 4, diminished numbers of entrants exposed to the risk (E) in some primary sites amounting to 500 person-years or less in the 1st durational interval (C30.1, C31.2-3, C31.8-9), nevertheless, due to extremely high 1st year observed mortality rates (q=100d/E) are linked to very high excess death rates and mortality ratios. For example, C31.8-Overlapping lesion of accessory sinus has 218.5 person-years exposure and 66 deaths in the 1st (0-1 year) interval corresponding to a 30.2% observed interval mortality rate with consequent EDR of 276/1000/year and MR of 1162%, and diminishing to 7.2% in the 3rd (2-5 year) interval with much reduced EDR of 50/1000/year and MR 331%.

Most of the cases, nearly 75%, are advanced (regional or distant) at the time of diagnosis. As a consequence, overall EDR for all sinonasal primary sites combined, 2000-2017, duration 0-5 years, averages 108/1000/year, and the cumulative relative survival rate (survival ratio-SR) is only 60%. Grading of cellular differentiation for malignancy does have a predictive effect on prognosis in local and regional cases. For example, in the 2007-2017 cohort, EDR in regional stage-grade 1&2 cases is 117/1000/year per at duration 0-5 years, but with advanced grades 3&4 differentiation, increases to 160/1000/year.

Excess mortality increases with age, and is higher in males than in females, and in nonwhites than in whites. Although excess mortality decreases with duration, significant excess mortality persists even to duration 10-15 years in all sinonasal sites. Excess death rates were modestly but consistently improved in the latter cohort (2007-17) in both local and regional disease and for both grading groups in the 0–5-year duration but not so in the 5-10-year duration.

Table 2. Cohort, Stage, Grade, Race, Durations 0-5 & 5-10 Years; All Ages, M&F Combined

Stage	Grade	Cohort*	No. Alive at Start *l*	Exposure Pt.-Yrs E	Number of Deaths		Mortality Ratio MR	Excess Death Rate EDR	Cumul. Surv. Rate		Cum. Surv. Ratio (%) Cum SR
					Observed d	Expected d'			Observed P	Expected P'	
Duration 0-5 Years, All Races											
Local	1&2	2000-06	372	1,692.0	89	47.22	188	24.7	0.7608	0.8676	87.7
	1&2	2007-17	518	2,065.0	90	58.60	154	15.2	0.7975	0.8642	92.3
	3&4	2000-06	136	553.0	52	14.40	361	68.0	0.6160	0.8787	70.1
	3&4	2007-17	209	782.0	70	18.94	370	65.3	0.6316	0.8857	71.3
	Unknown	2000-06	302	1,282.0	98	39.18	250	45.9	0.6738	0.8559	78.7
	Unknown	2007-17	385	1,484.5	103	38.54	267	43.4	0.6997	0.8777	79.7
Regional	1&2	2000-06	491	1,689.0	258	39.50	653	129.4	0.4717	0.8891	53.1
	1&2	2007-17	704	2,315.5	324	52.95	612	117.1	0.5111	0.8914	57.3
	3&4	2000-06	595	1,825.0	378	35.66	1,060	187.6	0.3559	0.9086	39.2
	3&4	2007-17	1,007	3,034.5	549	64.44	852	159.7	0.4197	0.8980	46.7
	Unknown	2000-06	466	1,676.0	226	33.58	673	114.8	0.5109	0.9058	56.4
	Unknown	2007-17	661	2,044.0	328	46.71	702	137.6	0.4657	0.8935	52.1
Distant	G&U	2000-06	531	1,612.5	308	26.01	1,184	174.9	0.4136	0.9253	44.7
		2007-17	934	2,632.5	551	48.72	1,131	190.8	0.3776	0.9109	41.4
All Staged	G&U	2000-06	2,893	10,329.5	1,409	235.57	598	113.6	0.5092	0.8916	57.1
	G&U	2007-17	4,228	13,818.5	1,887	312.25	604	114.0	0.5208	0.8918	58.4
Unstaged	Graded	2000-17	191	681.5	89	20.81	428	100.1	0.5173	0.8585	60.3
	Unknown	2000-17	384	1,376.5	163	41.18	396	88.5	0.5629	0.8606	65.4
	G&U	2000-17	575	2,058.0	252	61.98	407	92.3	0.5477	0.8600	63.7
Duration 5-10 Years, All Races											
Local	1&2	2000-06	283	1,218.5	82	37.00	222	36.9	0.5399	0.7429	72.7
	1&2	2007-17	242	668.5	29	21.36	136	11.4	0.6239	0.7338	85.0
	3&4	2000-06	82	375.0	21	9.24	227	31.4	0.4582	0.7756	59.1
	3&4	2007-17	85	213.5	13	5.67	229	34.3	0.4383	0.7695	57.0
	Unknown	2000-06	200	867.5	55	25.63	215	33.9	0.4878	0.7371	66.2
	Unknown	2007-17	173	420.0	34	9.87	345	57.5	0.4650	0.7775	59.8
Regional	1&2	2000-06	227	1,002.0	49	22.52	218	26.4	0.3691	0.7935	46.5
	1&2	2007-17	235	584.5	34	14.50	234	33.4	0.3549	0.7822	45.4
	3&4	2000-06	207	898.0	58	18.16	319	44.4	0.2555	0.8203	31.1
	3&4	2007-17	269	676.0	38	15.36	247	33.5	0.3085	0.7946	38.8
	Unknown	2000-06	228	959.0	80	16.62	481	66.1	0.3315	0.8303	39.9
	Unknown	2007-17	189	535.5	34	11.93	285	41.2	0.3403	0.7934	42.9

Table 2. Continued

Stage	Grade	Cohort*	No. Alive at Start *l*	Exposure Pt.-Yrs E	Number of Deaths		Mortality Ratio MR	Excess Death Rate EDR	Cumul. Surv. Rate		Cum. Surv. Ratio (%) Cum SR
					Observed d	Expected d'			Observed P	Expected P'	
Distant	G&U	2000-06	210	900.5	49	14.13	347	38.7	0.3143	0.8545	36.8
		2007-17	212	554.0	41	11.99	342	52.4	0.2686	0.8168	32.9
All Staged	G&U	2000-06	1,437	6,220.5	394	143.28	275	40.3	0.3685	0.7934	46.4
	G&U	2007-17	1,364	3,556.0	213	87.63	243	35.3	0.3776	0.7840	48.2
Unstaged	Graded	2000-17	85	328.5	16	9.16	175	20.8	0.4111	0.7462	55.1
	Unknown	2000-17	182	685.5	41	19.08	215	32.0	0.4177	0.7472	55.9
	G&U	2000-17	267	1,014.0	57	28.25	202	28.3	0.4157	0.7468	55.7
White Race, Duration 0-5 Years											
All* **	G&U	2000-17	6,156	21,150.5	2,819	524.81	537	108.5	0.5232	0.8821	59.3
White Race, Duration 5-10 Years											
All* **	G&U	2000-17	2,510	8,831.5	549	230.51	238	36.1	0.3812	0.7722	49.4
Black, Other, Unknown Race, Duration 0-5 Years											
All* **	G&U	2000-17	1,540	5,055.5	729	84.67	861	127.5	0.4998	0.9204	54.3
Black, Other, Unknown Race, Duration 5-10 Years											
All* **	G&U	2000-17	558	1,959.0	115	29.15	395	43.8	0.3727	0.8536	43.7

Expected Survival Table: U.S. by SES/geography/race; 1992-2016. Ages 0-99. State-county

Table 3. C30.0-1 and C31.0-3 Entrants, 2000-2017; All Ages, Stages, Grades Combined

Duration Start-End t to t+ch t	No. Alive at Start *l*	Exposure Pt.-Yrs E	Number of Deaths		Mortality Ratio (%) 100d/d'	Mean Ann. Mortality Rate/1,000			Cumul. Surv. Rate		Cum. Surv. Ratio (%) 100P/P'
			Observed d	Expected d'		Observed q	Expected q'	Excess (q-q')	Observed P	Expected P'	
C30.0-Nasal Cavity											
0-1	5,278	5,078.0	726	126.44	574	0.1430	0.0249	118.1	0.8570	0.9751	87.9
1-2	4,152	4,002.5	431	97.26	443	0.1077	0.0243	83.4	0.7647	0.9514	80.4
2-5	3,422	8,400.0	606	210.04	289	0.0721	0.0250	47.1	0.6130	0.8817	69.5
0-5	5,278	17,480.5	1,763	433.74	406	0.1009	0.0248	76.0	0.6130	0.8817	69.5
5-10	2,066	7,178.0	427	189.42	225	0.0595	0.0264	33.1	0.4532	0.7708	58.8
10-15	847	2,512.0	153	81.15	189	0.0609	0.0323	28.6	0.3276	0.6514	50.3
Median survival time (interval = 12 months): Observed = 8.28594 intervals; Relative = 16.0871 intervals.											
C30.1-Middle Ear											
0-1	243	236.5	55	5.20	1,057	0.2326	0.0220	210.6	0.7674	0.9780	78.5
1-2	175	169.0	21	3.33	631	0.1243	0.0197	104.6	0.6720	0.9587	70.1
2-5	142	375.0	21	6.68	315	0.0560	0.0178	38.2	0.5635	0.9083	62.0
0-5	243	780.5	97	15.21	638	0.1243	0.0195	104.8	0.5635	0.9083	62.0
5-10	101	353.0	11	5.69	193	0.0312	0.0161	15.0	0.4838	0.8372	57.8
10-15	44	136.5	6	1.63	367	0.0440	0.0120	32.0	0.4102	0.7949	51.6
Median survival time (interval = 12 months): Observed = 9.20062 intervals; Relative is greater than 20 intervals.											
C31.0-Maxillary Sinus											
0-1	3,033	2,936.0	796	77.22	1,031	0.2711	0.0263	244.8	0.7289	0.9737	74.9
1-2	2,043	1,983.5	382	44.63	856	0.1926	0.0225	170.1	0.5885	0.9518	61.8
2-5	1,542	3,720.0	380	86.22	441	0.1022	0.0232	79.0	0.4308	0.8869	48.6
0-5	3,033	8,639.5	1,558	208.07	749	0.1803	0.0241	156.3	0.4308	0.8869	48.6
5-10	912	3,141.0	208	79.30	262	0.0662	0.0252	41.0	0.3060	0.7794	39.3
10-15	362	1,122.0	71	28.96	245	0.0633	0.0258	37.5	0.2229	0.6825	32.7
Median survival time (interval = 12 months): Observed = 3.26077 intervals; Relative = 4.42013 intervals.											
C31.1-Ethmoid Sinus											
0-1	845	820.5	177	15.84	1,118	0.2157	0.0193	196.4	0.7843	0.9807	80.0
1-2	619	607.5	98	10.57	927	0.1613	0.0174	143.9	0.6578	0.9636	68.3
2-5	498	1,205.0	113	23.06	490	0.0938	0.0191	74.6	0.4955	0.9091	54.5
0-5	845	2,633.0	388	49.47	784	0.1474	0.0188	128.6	0.4955	0.9091	54.5
5-10	309	1,082.5	54	21.84	247	0.0499	0.0202	29.7	0.3911	0.8213	47.6
10-15	142	452.5	15	10.03	150	0.0331	0.0222	11.0	0.3269	0.7327	44.6
Median survival time (interval = 12 months): Observed = 4.86722 intervals; Relative = 7.02396 intervals.											

Table 3. Continued

Duration Start-End t to t+ch t	No. Alive at Start *l*	Exposure Pt.-Yrs E	Number of Deaths		Mortality Ratio (%) 100d/d'	Mean Ann. Mortality Rate/1,000			Cumul. Surv. Rate		Cum. Surv. Ratio (%) 100P/P'
			Observed d	Expected d'		Observed q	Expected q'	Excess (q-q')	Observed P	Expected P'	
C31.2-Frontal Sinus											
0-1	127	122.5	30	2.70	1,113	0.2449	0.0220	222.9	0.7551	0.9780	77.2
1-2	88	84.0	12	1.83	655	0.1429	0.0218	121.1	0.6472	0.9567	67.7
2-5	68	158.0	18	3.48	517	0.1139	0.0221	91.9	0.4633	0.8956	51.7
0-5	127	364.5	60	8.01	749	0.1646	0.0220	142.6	0.4633	0.8956	51.7
5-10	38	121.5	6	3.20	188	0.0494	0.0263	23.1	0.3681	0.7829	47.0
10-15	15	33.5	1	0.87	114	0.0299	0.0261	3.7	0.3398	0.6845	49.6
Median survival time (interval = 12 months): Observed = 3.66764 intervals; Relative = 6.00705 intervals.											
C31.3-Sphenoid Sinus											
0-1	358	347.5	89	6.53	1,362	0.2561	0.0188	237.3	0.7439	0.9812	75.8
1-2	248	239.5	34	4.17	816	0.1420	0.0174	124.6	0.6383	0.9641	66.2
2-5	197	496.0	40	9.99	400	0.0806	0.0201	60.5	0.4998	0.9066	55.1
0-5	358	1,083.0	163	20.69	788	0.1505	0.0191	131.4	0.4998	0.9066	55.1
5-10	127	441.5	36	8.75	411	0.0815	0.0198	61.7	0.3269	0.8197	39.9
10-15	52	167.5	10	4.29	233	0.0597	0.0256	34.1	0.2403	0.7170	33.5
Median survival time (interval = 12 months): Observed = 4.99529 intervals; Relative = 6.34998 intervals.											

Expected Survival Table: U.S. by SES/geography/race; 1992-2016. Ages 0-99. State-county

Table 4. C31.8; C31.9; All Sinuses Combined; All Sinonasal Tract Combined

Duration Start-End t to t+ch t	No. Alive at Start *l*	Exposure Pt.-Yrs E	Number of Deaths		Mortality Ratio (%) 100d/d'	Mean Ann. Mortality Rate/1,000			Cumul. Surv. Rate		Cum. Surv. Ratio (%) 100P/P'
			Observed d	Expected d'		Observed q	Expected q'	Excess (q-q')	Observed P	Expected P'	
C31.8-Overlapping Lesion of Accessory Sinuses											
0-1	224	218.5	66	5.68	1,162	0.3021	0.0260	276.1	0.6979	0.9740	71.7
1-2	147	143.0	35	2.92	1,200	0.2448	0.0204	224.4	0.5271	0.9541	55.2
2-5	104	265.5	19	5.74	331	0.0716	0.0216	49.9	0.4220	0.8935	47.2
0-5	224	627.0	120	14.34	837	0.1914	0.0229	168.5	0.4220	0.8935	47.2
5-10	68	233.5	12	5.01	239	0.0514	0.0215	29.9	0.3255	0.8023	40.6
10-15	29	87.0	2	1.30	154	0.0230	0.0149	8.1	0.2805	0.7410	37.9
Median survival time (interval = 12 months): Observed = 2.64946 intervals; Relative = 4.05166 intervals.											
C31.9-Accessory Sinus, NOS											
0-1	516	500.0	114	10.60	1,075	0.2280	0.0212	206.8	0.7720	0.9788	78.9
1-2	370	355.5	49	7.47	656	0.1378	0.0210	116.8	0.6656	0.9582	69.5
2-5	292	714.0	67	16.39	409	0.0938	0.0230	70.9	0.5016	0.8941	56.1
0-5	516	1,569.5	230	34.46	667	0.1465	0.0220	124.6	0.5016	0.8941	56.1
5-10	181	649.0	29	15.11	192	0.0447	0.0233	21.4	0.4044	0.7950	50.9
10-15	92	264.5	10	7.67	130	0.0378	0.0290	8.8	0.3315	0.6808	48.7
Median survival time (interval = 12 months): Observed = 5.05413 intervals; Relative = 12.1205 intervals.											
C31.0-3; C31.8-9-All Sinuses Combined											
0-1	5,103	4,945.0	1,272	118.68	1,072	0.2572	0.0240	233.2	0.7428	0.9760	76.1
1-2	3,515	3,413.0	610	71.67	851	0.1787	0.0210	157.7	0.6101	0.9555	63.8
2-5	2,701	6,558.5	637	144.75	440	0.0971	0.0221	75.1	0.4541	0.8935	50.8
0-5	5,103	14,916.5	2,519	335.11	752	0.1689	0.0225	146.4	0.4541	0.8935	50.8
5-10	1,635	5,669.0	345	133.36	259	0.0609	0.0235	37.3	0.3341	0.7927	42.1
10-15	692	2,127.0	109	53.15	205	0.0512	0.0250	26.3	0.2570	0.6964	36.9
Median survival time (interval = 12 months): Observed = 3.71867 intervals; Relative = 5.34002 intervals.											
C30.0-1, C31.0-3, C31.8-9, All Sinonasal Tract Sites Combined											
0-1	10,624	10,259.5	2,053	250.33	820	0.2001	0.0244	175.7	0.7999	0.9756	82.0
1-2	7,842	7,584.5	1,062	172.17	617	0.1400	0.0227	117.3	0.6879	0.9535	72.1
2-5	6,265	15,333.5	1,264	361.74	349	0.0824	0.0236	58.8	0.5349	0.8874	60.3
0-5	10,624	33,177.5	4,379	784.24	558	0.1320	0.0236	108.3	0.5349	0.8874	60.3
5-10	3,802	13,200.0	783	328.25	239	0.0593	0.0249	34.5	0.3962	0.7819	50.7
10-15	1,583	4,775.5	268	136.07	197	0.0561	0.0285	27.6	0.2961	0.6746	43.9
Median survival time (interval = 12 months): Observed = 5.99394 intervals; Relative = 10.4741 intervals.											

Expected Survival Table: U.S. by SES/geography/race; 1992-2016. Ages 0-99. State-county

Chart 4. Site-Specific 15-Year Mortality and Survival Outcomes, 2000-2017

ICD-O-3 Code	Site	Exposure NER	MR %	EDR /1000/yr	P %	P'	SR %	MOS years
C30.0	Nasal cavity	2512.0	189	28.6	32.8	65.1	50.3	8.3
C30.1	Middle ear	136.5	367	32.0	41.0	79.5	51.6	9.2
C31.0	Maxillary sinus	1122.0	245	37.5	22.3	68.3	32.7	3.3
C31.1	Ethmoid sinus	452.5	150	11.0	32.7	73.3	44.6	4.9
C31.2	Frontal sinus	33.5	114	3.7	34.0	68.5	49.6	3.7
C31.3	Sphenoid sinus	167.5	233	34.1	24.0	71.7	33.5	5.0
C31.8	Overlapping Sinus	87.0	154	8.1	28.1	74.1	37.9	2.6
C31.9	Accessory sinus NOS	264.5	130	8.8	33.2	68.1	48.7	5.1
C31.0-3; C31.8-9	All Sinuses combined	2127.0	205	26.3	25.7	69.6	36.9	3.7
C30.0; C31.0-3; C31.8-9;	All Sinonasal Sites	4775.5	197	27.6	29.6	67.5	43.9	6.0

Entrants Exposed to Risk of Death (E) – always expressed in person-years.

Number Exposed to Risk of Death (NER) – during an interval that has a duration other than 1 year.

Mortality ratio (MR) – ratio of the number of deaths observed (d) to the number of deaths expected (d'). The ratio is a decimal that is multiplied by 100 to obtain a percent: MR = 100d/d'.

Observed Cumulative Survival Rate (P) – The proportion of those observed to have survived after any duration of follow-up t to those exposed to the risk of death from the beginning of the study.

Expected cumulative survival rate (P') – The proportion of those expected to have survived after any duration of follow-up t to those exposed to the risk of death from the beginning of the study).

Survival Ratio (SR) – The ratio of number of survivors observed to the number of survivors expected. Here calculated as a cumulative ratio (SR = 100P/P').

Median Observed Survival (MOS) – Length of time from date of diagnosis that half the patients in a group of patients are still alive.

Lifetime follow-up is essential, and monitoring of patients must be frequent and meticulous because more than 41% of the deaths, all primary sites combined, occurred within 5 years of diagnosis and most treatment failures occur within this period. Additionally, nearly 33% of patients will develop second primary cancers in the upper aerodigestive tract.

For information on aspects and treatment of cancer of the nasal cavity, middle ear and sinuses the reader is referred to the website of the National Cancer Institute, www.cancer.gov, and to monographs such as editions of *Clinical Oncology*, issued by the American Cancer Society.

In Memoriam: Richard Bunker Singer, M.D., March 22, 1914–February 19, 2010.

Consummate gentleman, dear friend, scholar, colleague, and 'Man for All Seasons.'

REFERENCES

1. World Health Organization. International classification of diseases for oncology (ICD-O), 1st revision, 3rd ed., 2013:37–38. https://apps.who.int/iris/handle/10665/96612
2. Surveillance Research Program, National Cancer Institute SEER*Stat software (www.seer.cancer.gov/seerstat) version 8.3.8.
3. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence Sub - SEER Research Data, 18 Registries, Nov 2019 (2000-2017) - Linked to County Attributes - Time Dependent (1990-2017) Income/Rurality, 1969-2018 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2020, based on the November 2019 submission.
4. Cho H, Howlader N, Mariotto AB, Cronin KA. Estimating relative survival for cancer patients from the SEER Program using expected rates based on Ederer I versus Ederer II method. Surveillance Research Program, National Cancer Institute; 2011. Technical Report #2011-01:1-17. Available at: https://surveillance.cancer.gov/reports/.

5. Pokorski RJ. *Mortality Methodology and Analysis Seminar Text.* Sponsored by the Association of Life Insurance Medical Directors of America. *J Insur Med*. 1988;20:1–45.
6. Milano AF, Singer RB. The Cancer Mortality Risk Project – Cancer Mortality Risks by Anatomic Site: Part I – Introductory Overview; Carcinoma of the Colon: 20-Year Mortality Follow-up Derived from 1973-2013 (NCI) SEER*Stat Survival Database. *J Insur Med*. 2017;47:65–94.
7. Singer RB, Kita MW, Avery JR, eds. *Medical Risks - 1991 Compend of Mortality and Morbidity*. Westport, Conn: Praeger Publishers; 1994.
8. Brackenridge RDC, Croxson RS, Mackenzie R editors. *Medical Selection of Life Risks*, *5th ed*. New York, Palgrave Macmillan; 2006: chaps 3–5.