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Sex disparities in cancer incidence by time period and age

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Abstract

Background—Cancer epidemiology manuscripts often point out that cancer rates tend to be higher among males than females, yet rarely is this theme the subject of investigation.

Methods—We used the Surveillance, Epidemiology, and End Results (SEER) program data to compute age-adjusted (2000 US standard population) sex-specific incidence rates and male-to-female incidence rate ratios (IRR) for specific cancer sites and histologies for the period 1975–2004.

Results—The ten cancers with the largest male-to-female IRR were Kaposi sarcoma (28.73), lip (7.16), larynx (5.17), mesothelioma (4.88), hypopharynx (4.13), urinary bladder (3.92), esophagus (3.49), tonsil (3.07), oropharynx (3.06) and other urinary organs (2.92). Only five cancers had a higher incidence in females compared to males: breast (0.01), peritoneum, omentum and mesentery (0.18), thyroid (0.39), gallbladder (0.57), and anus, anal canal and anorectum (0.81). Between 1975 and 2004, the largest consistent increases in male-to-female IRR were for cancers of the tonsil, oropharynx, skin excluding basal and squamous, and esophagus, while the largest consistent decreases in IRR were for cancers of the lip and lung and bronchus. Male-to-female IRRs varied considerably by age, the largest increases of which were for ages 40–59 years for tonsil cancer and hepatocellular carcinoma. The largest decreases in male-to-female IRR by age, meanwhile, were for ages 30–49 years for thyroid cancer, ages ≥ 70 years for esophageal squamous cell carcinoma, and ages ≥ 30 years for lung and bronchus cancer.

Conclusion—These observations emphasize the importance of sex in cancer etiopathogenesis and may suggest novel avenues of investigation.

Keywords

Sex; Male; Female; SEER program; Neoplasms; Incidence; Epidemiology

“Sex, that is, being male or female, is an important basic human variable that should be considered when designing and analyzing studies in all areas and at all levels of biomedical and health-related research. Differences in health and illness are influenced by individual genetic and physiological constitutions, as well as by an individual's interaction with environmental and experimental factors. The incidence and severity of diseases vary between the sexes and may be related to differences in exposures, routes of entry and the processing of a foreign agent, and cellular responses.” (1)

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Introduction

Over the years, many scientific papers have commented that the incidence of a particular cancer is higher in men than women. Other than suggesting that the discrepancies may be due to tobacco and alcohol exposures, relatively little attention has been devoted to exploring the differences in rates. Cancer epidemiology has lacked a strong focus on sex, as many studies have been more concerned with disease etiology than disease heterogeneity. Even in studies with a focus on heterogeneity, sex is usually little more than a covariate in a statistical model. Despite this, sex is one of the most important variables that needs to be considered in the etiology, progression and treatment of disease (1).

Descriptive epidemiology provides a foundation for many disciplines within medical research. In cancer epidemiology, descriptive analyses of incidence trends often promote the formulation of new ideas and hypotheses. Previous descriptive studies have shown that cancer incidence and mortality rates are much higher in males than females at nearly all ages in the majority of countries (2-10). However, few studies have explicitly set out to focus on sex ratios of cancer incidence, and no study has done this using US data.

This study uses data from the Surveillance, Epidemiology, and End Results (SEER) cancer registry program to analyze age-adjusted male-to-female incidence rate ratios (IRR) and sex-specific incidence rates by cancer site, histology, year of diagnosis and age of diagnosis. It is hoped that this exercise will be hypothesis-generating with regards to sex differences in the etiopathogenesis of cancer.

Methods

Data were extracted from the November 2007 submission of the SEER-9 registries database¹. The variables calculated were cancer count, person-years, and incidence rate per 100,000 (age-adjusted to the 2000 US standard population) for each cancer, stratified by sex and age (groupings of 1-9, 10-19 ... 70-79 and 80+ years) for the periods 1975-1984, 1985-1994, 1995-2004 and 1975-2004. Cancer sites and morphologies investigated were non-sex-specific cancers as defined in the SEER standard site recode groupings². The ICD-O-3 codes (11) for the histology-specific analyses were squamous cell carcinoma (8050-8078, 8083-8084); adenocarcinoma (8140-8231, 8250-8551, 8570-8574, 8576); small cell lung cancer (8002, 8040-8045, 8240, 8246); large cell lung cancer (8012); hepatocellular carcinoma (8170-8175); melanoma (8720-8780); soft tissue tumors and sarcoma (8680-8711, 8800-8936, 8980-8981, 8990-8991, 9040-9044, 9120-9133, 9150-9252, 9370-9372, 9490, 9540-9581); transitional cell carcinoma (8120-8139); neuroepithelial tumors (9360-9362, 9381-9421, 9424-9451, 9470-9474, 9490-9501, 9505-9508, 9522-9523); papillary tumors (8050, 8260, 8340-8344, 8350, 8450-8460); and anus, anal canal and anorectum squamous cell carcinoma (8050-8078, 8083-8084, 8124; includes cloacogenic tumors).

Data extraction was restricted to malignant tumors. Male-to-female IRRs were calculated for cancers which had at least 50 cases in each sex by using the male age-adjusted incidence rate as the numerator and the female age-adjusted incidence rate as the denominator. Confidence intervals for the male-to-female IRRs were generated in SEER³. Cancers with consistently increasing or decreasing male-to-female IRRs for the period 1975-2004 and an incidence rate of at least 0.2 per 100,000 for each sex were tabulated and sorted by relative change in male-to-female IRR. Further investigation was considered for cancers which had the highest

¹www.seer.cancer.gov/seerstat

²http://seer.cancer.gov/siterecode/icdo3_d01272003/

³www.seer.cancer.gov/seerstat

incidence in males and/or females, had the highest or lowest male-to-female IRRs, or had the most extreme consistent changes in male-to-female IRR over time. Cancers which qualified for one or more of these groups were not further stratified by histologic group if they had low incidence rates (<0.2 per 100,000) for at least one of the sexes, if further stratification was deemed uninformative or if the cancer site recode grouping was non-specific. Selected cancers had their sex-specific incidence rates and male-to-female IRRs tabulated by subsite and/or predominant histologic group(s) for the years 1975-1984, 1985-1994, 1995-2004 and 1975-2004.

Graphs were produced for each cancer site/histology except for cancers which were non-specific or had low incidence rates in at least one of the sexes. Cancers which had the most extreme consistent changes in male-to-female IRR, an incidence of at least 0.4 per 100,000 and an increasing incidence in at least one of the sexes, are illustrated and discussed herein (graphs for other cancers can be accessed online as supplementary material ⁴). In addition, a graph of total cancer incidence was compiled for the period 1975-2004. All graphs show male-to-female IRRs and sex-specific incidence rates plotted by age of diagnosis for age groups 1-9, 10-19 ... 70-79 and 80+ years. Each data point (age group) of these plots was required to have at least 10 cases for each sex. STATA (StataCorp LP, 2007, Release 10.1) was used for data processing and analysis. Data were graphed using SigmaPlot (SPSS Inc., 2002, Version 11.0).

Results

Table 1 shows sex-specific, age-adjusted incidence rates and male-to-female IRRs stratified by time period for each cancer. During 1975-2004, the ten most common cancers diagnosed among US males were lung and bronchus (93.2 per 100,000 man-years), colon and rectum (70.3), urinary bladder (37.5), non-Hodgkin lymphoma (21.4), skin excluding basal and squamous (19.7), kidney and renal pelvis (14.8), stomach (14.1), pancreas (13.6), lymphocytic leukemia (8.6) and larynx (8.5). For US females, the ten most frequent cancers were breast (126.4 per 100,000 woman-years), colon and rectum (51.2), lung and bronchus (45.2), non-Hodgkin lymphoma (14.4), skin excluding basal and squamous (13.8), pancreas (10.2), urinary bladder (9.6), thyroid (8.9), kidney and renal pelvis (7.2) and stomach (6.4). The ten cancers with the largest male-to-female IRR during 1975-2004 were Kaposi sarcoma (IRR=28.73), lip (7.16), larynx (5.17), mesothelioma (4.88), hypopharynx (4.13), urinary bladder (3.92), esophagus (3.49), tonsil (3.07), oropharynx (3.06) and other urinary organs (2.92). During 1975-2004, only five cancers investigated had a higher incidence in females compared with males: breast (IRR=0.01), peritoneum, omentum and mesentery (0.18), thyroid (0.39), gallbladder (0.57), and anus, anal canal and anorectum (0.81).

Table 2 shows the relative change in male-to-female IRRs and relative change in sex-specific incidence rates for the periods 1985-1994 and 1995-2004 compared with 1975-1984 for cancers showing a consistently increasing or decreasing IRR and incidence rates for each sex of at least 0.2 per 100,000 listed according to percent change in IRR. During 1975-2004, tonsil cancer had the largest increase in male-to-female IRR, and this was the result of an increasing male incidence and decreasing female incidence. Other cancers with rising IRRs were esophagus and mesothelioma, the former due to increases among males not apparent among females, and the latter a female decrease in incidence. Rates for the remaining cancers with rising male-to-female IRRs increased among both sexes, but more so among males than females.

Many cancers had a decline in the male-to-female IRR during 1975-2004. The IRRs for the cancer sites ureter, floor of mouth, retroperitoneum, and lip decreased due to faster declines in male incidence than in female incidence. Reductions in IRR for other cancers - pancreas, nose,

⁴<http://cebp.aacrjournals.org/>

nasal cavity and middle ear, gum and other mouth, Hodgkin lymphoma, and larynx - were solely caused by decreased male incidence, with female rates remaining fairly stable. More rapidly rising rates among females than males reduced the IRRs for cancers of the kidney and renal pelvis, cranial nerves and other nervous system, and thyroid. Perhaps the most notable declining IRR was that for lung and bronchus cancer, which is singular in that it was caused by a simultaneous decrease in male rates and increase in female rates.

Of the cancer sites in Table 2, those with the largest increases in male incidence between the periods 1975-1984 and 1995-2004 were skin excluding basal and squamous (111%), liver and intrahepatic bile duct (103%), anus, anal canal and anorectum (58%), and thyroid (44%). For females, the cancer sites were liver and intrahepatic bile duct (88%), thyroid (76%), skin excluding basal and squamous (69%), and lung and bronchus (59%). Over the same time period, the sites with the largest decreases in incidence have been lip (57%), floor of mouth (48%), larynx (30%), and gum and other mouth (30%) for males, and floor of mouth (41%), tonsil (29%), ureter (15%), and gum and other mouth (14%) for females.

Table 3 shows sex-specific incidence rates and male-to-female IRRs for specific histologic groups of selected cancers. The rates and IRRs for nearly all histologic groups follow the same trends as their parent cancer site. However, this is not true for the two histologic types of esophageal cancer, which trended in opposite directions. The IRR, by 10-year period, for all esophageal cancers combined increased from 3.14, to 3.43 to 3.82 (Table 1), however, this is a combination of increasing IRRs for esophageal adenocarcinoma (6.25, 7.96, and 7.69) and decreasing IRRs for esophageal squamous cell carcinoma (2.93, 2.57, and 2.25) (Table 3). Although the IRRs did not change greatly over time, the IRRs for hepatocellular carcinoma ranged 3.44-3.56, considerably larger than those for intrahepatic bile duct carcinoma which ranged 1.51-1.62, not apparent in the overall IRR for liver and intrahepatic bile duct cancer range of 2.51-2.71. In contrast to the overall lung and bronchus cancer IRR of 2.06, that declined from 3.00 to 1.61 over the decades, the overall IRR ranged from 3.50 for squamous cell carcinoma, to 2.19 for large cell, 1.60 for small cell, and 1.53 for adenocarcinoma; IRRs for each type declined from an early maximum of 5.29 for squamous cell to 1.26 for small cell carcinoma recently.

Incidence rates and male-to-female IRRs are plotted by age of diagnosis for nine cancer sites/histologies (Figs 1a-i) selected because they had the most extreme consistent changes in male-to-female IRR and an incidence of at least 0.4 per 100,000 which was increasing in at least one of the sexes (graphs for other cancers, Supplementary Figures 1-30, can be accessed online⁵). During the earliest decade the male-to-female IRR for tonsil cancer was about 2 at ages less than 70 years and rose to about 4 at older ages; by the recent decade, rising male rates and declining female rates resulted in a male-to-female IRR of more than 5 at ages 40-59 years (Fig. 1a). Rates for the cancer site skin excluding basal and squamous (Fig. 1b) predominated among females at younger ages (<40 years) and among males in the older age groups (≥ 40), and rates rose over time more rapidly among younger women and among older men, resulting in declines in the male-to-female IRR at younger ages and increases at older ages. The incidence of esophageal squamous cell carcinoma among males at all ages and in females less than 70 years of age declined, and the male-to-female IRR decreased at older ages from about 3 to 2 (Fig. 1c). The male-to-female IRR for esophageal adenocarcinoma exceeded 10 at ages 50-59 years and declined with age to 4-5 at the oldest ages (Fig. 1d). Rates for anus, anal canal and anorectal cancers increased comparably in both sexes in nearly all age groups, making the male-to-female IRR fairly stable and less than 1 at ages of more than 50 years (Fig. 1e). The increasing rates of hepatocellular carcinoma in younger age groups (<50 years) has been more rapid among males than females, and the male-to-female IRR rose from less than 3 to more

⁵<http://cebp.aacrjournals.org/>

than 5, in contrast to decreases in the male-to-female IRR at older ages (Fig. 1f). Kidney and renal pelvis cancer IRR were about one at very young ages (Wilms tumors), decreased over the decades at ages 10-39, and rose to a fairly constant two at older ages in spite of rising rates (Fig. 1g). Thyroid cancer male-to-female IRR were around 0.2 at ages 20-29 and rose to at least 0.7 at the oldest ages; rates rose over time more rapidly among younger women and older men, leading to progressively lower IRRs (Fig 1h). Male rates for lung and bronchus malignancies declined slightly at virtually all ages while female rates increased, especially in the age groups of 60 years and older (Fig. 1i), and the male-to-female IRR declined dramatically across all adult age groups, dropping below 1 in recent years among those less than 40 years of age.

Rates during the period 1975-2004 for all cancers combined and for all cancers excluding the sex-specific sites were higher among females than males at adult ages less than 50 years and clearly higher among males than females at ages 60+ years (Fig. 2). When rates for total cancer excluding the sex-specific sites and breast cancer are considered, the male-to-female IRR exceeds one at all ages 30+. Across all ages combined, the cancer burden was higher in males than females for total cancer (male-to-female IRR=1.37, 95%CI: 1.37-1.38), total cancer excluding sex-specific sites (1.14, 95%CI: 1.14-1.14), and total cancer excluding sex-specific sites and breast cancer (1.77, 95%CI: 1.76-1.77).

Discussion

Sex disparities in cancer incidence have often been acknowledged but have rarely been the focus of interest in the epidemiologic literature. This is despite the fact that this variable accounts for considerable differences in carcinogenic exposure and biology. As seen in the results of this study, ratios of incidence by sex and changes in those ratios may be helpful in generating new hypotheses or in substantiating old hypotheses.

Tonsil and oropharyngeal cancers increased in male predominance between 1975 and 2004. These two cancer sites have the strongest and most consistent associations with human papillomavirus (HPV) 16 infection of all the oral cancer sites (12). Although tobacco and alcohol are known to be important risk factors for head and neck malignancies (13,14), historical trends indicate that these exposures are not diverging between the sexes (15)^{6,7}. This suggests that other risk factors, including oral HPV infection, could be driving the increases in male-to-female IRRs of these sites. Evidence to support this is that increased and earlier sexual activity in males, but perhaps not in females, increases the risk of HPV16-associated oral cancer (16). In addition, two studies have shown increased risks of oral HPV-16/18/33 (17) and head and neck cancer (18) in male partners of females diagnosed with various cervical abnormalities. In total, this evidence may support a speculative hypothesis of differential transmission risks between males and females when engaging in opposite sex, genital-oral sexual practices (17,19).

At younger ages, skin excluding basal and squamous (Fig. 1b) exhibited a slow but progressive increased female incidence compared with the relatively stable rates of males. Intermittent exposure to high doses of ultra-violet radiation is the main risk factor for this tumor site (20), and the suggestion that females attempt to tan more than males may explain the increased incidence of melanoma in younger females (21). Alternative explanatory factors include hypotheses of a hormonal etiology (22) and an association with increasing body mass index/body surface area (23). In contrast to the female predominance at younger ages, male incidence rates predominated and increased at a greater pace beyond age 40 years, which caused the IRR

⁶<http://www.niaaa.nih.gov/Resources/DatabaseResources/QuickFacts/AlcoholConsumption/PercentAlcoholGender.htm>

⁷<http://www.niaaa.nih.gov/Resources/DatabaseResources/QuickFacts/AlcoholConsumption/dkpat18.htm>

to inflate. One possible explanation may be the greater lifetime sun exposure in men with outdoor occupations.

The two predominant histologic types of esophageal cancer (Table 3, Figs 1c & 1d) have diverged in both their incidence and male-to-female IRRs. The IRR for esophageal adenocarcinoma increased then stabilized, a pattern unlikely to be accounted for by alcohol and tobacco due to their historical trends and stronger associations with esophageal squamous cell carcinoma relative to esophageal adenocarcinoma (24). Pre-neoplastic states following severe reflux exhibit an increasing male predominance in the step-wise progression to adenocarcinoma (25), which may indicate that the causal exposure(s) of the sex disparity is important at all stages of disease. There is some evidence to suggest that erosive reflux disease may be more prevalent in males at earlier ages compared with females (26,27). Other risk factors, including estrogen exposure (28,29), body mass index (30) and *Helicobacter pylori* infection (31)⁸, have provided no evidence for being the causal agents of the sex ratio imbalance. Putative differences between the sexes that may explain the male predominance of esophageal adenocarcinoma include android obesity (32), production and concentration of gastric acid (33), hiatal hernia (34), defective lower-esophageal sphincter (34), and higher intra-abdominal and intra-gastric pressures (35).

Cancers of the anus, anal canal and anorectum is one of just a few cancers which were more common in females than males at nearly all ages (Fig. 1e). Cloacogenic tumors, a subtype of squamous cell carcinoma which contributes 15% of the malignancies of this site, are more common in females (IRR=0.49, 1975-2004), but this does not fully account for the female predominance of these tumors (IRR=0.77, 1975-2004, for squamous cell carcinoma excluding cloacogenic tumors). A potential reason for the increasing predominance of females may be evolving sexual practices, given the putative association of these cancers with anal HPV infections (36,37).

Hepatocellular carcinoma (HCC) rates rose among both sexes at older ages, but especially among males younger than 60 years of age (Fig. 1f). Major risk factors for HCC in the United States are chronic infection with hepatitis C virus and hepatitis B virus, as well as alcoholic liver disease (38). Chronic hepatitis B and C infections are more common in males than in females (39) and this difference is likely to account for some of the disparity in IRRs. Historical trends of alcohol consumption^{9, 10} imply this to be an unlikely cause of the diverging male-to-female IRRs at younger ages. The strongest hypothesis to date, which may account for the sex disparity in incidence, is the anti-carcinogenic effect of estrogen, which constrains transcription of the pro-inflammatory cytokine interleukin-6 gene, leading to a decrease in HCC (40). Increased body mass index (41) and diabetes (42) have also been associated with increased risk of HCC, although it is not clear that either exposure could account for the increased male-to-female IRR at younger ages (43)¹¹.

The male-to-female IRR for kidney and renal pelvis cancer has not significantly changed (Table 1). Moreover, although the incidence in males and females has been increasing, the IRR for adult malignancies has remained stable at around 2 (Fig. 1g). Therefore, it is unlikely that associated exposures of tobacco (44,45) and obesity (45) are major factors in the male predominance of this cancer site, as these exposures have been changing over time. Reasons for the sex discrepancy of cancer incidence at this site remain unresolved.

⁸L.A. Anderson, 2008, *pers. comm.*

⁹<http://www.niaaa.nih.gov/Resources/DatabaseResources/QuickFacts/AlcoholConsumption/PercentAlcoholGender.htm>

¹⁰<http://www.niaaa.nih.gov/Resources/DatabaseResources/QuickFacts/AlcoholConsumption/dkpat18.htm>

¹¹<http://www.cdc.gov/diabetes/statistics/prev/national/fig2004.htm>

Between 1975 and 2004, thyroid cancer incidence was higher in females than males at all ages (Fig. 1h). The etiology of this cancer is poorly understood (46), but increased female incidence during reproductive ages, suggests a possible hormonal pathogenesis (47). Evidence from autopsy studies indicates that the prevalence of thyroid microcarcinoma is equivalent between the sexes while females account for ~83% of clinical cases (48). This may indicate that females have an increased propensity for diagnostic investigation given their higher rates of thyroid disease, relative to males.

The male-to-female IRRs for lung and bronchus cancer reflect historical exposure to tobacco smoking; as smoking habits have converged between the sexes (15), so has the incidence (Fig. 1i). This pattern is also evident for other cancers for which tobacco smoking is a risk factor, including lip (Supp. Fig. 1) and, at older ages, esophageal squamous cell carcinoma (Fig. 1c), floor of mouth (Supp. Fig. 4) and larynx (Supp. Fig. 16). The dramatic decrease in the IRR in later time periods for cancers of the lung and bronchus exemplifies the effect that a single sex-discrepant exposure can have on cancer incidence.

The vast majority of cancers included in this review have higher incidence rates in males than in females, as accentuated in Figure 2, and this suggests the possibility of universal mechanisms that increase male susceptibility to cancer. Tentative explanatory hypotheses include sex differences in anti-oxidative capacity (49), metal toxicity (50), beliefs and behaviors (51), health care access and utilization (43), sex chromosome complement/aneuploidy/aberrations (52), gene expression (53), hormones (54), immunocompetence (55) and the disposable soma theory of aging (56).

The main strength of male-to-female IRRs, relative to absolute differences in incidence rates, is that they are less likely to be affected by changes in diagnostic techniques, preventative strategies, tumor definitions and coding practices (57); changes in such parameters may not be expected to affect the sexes disproportionately. Male-to-female IRRs, however, are still subject to the effects of sex differences in reporting behavior, illness behavior, health care access and utilization, and physician behavior (9,58). In spite of these unavoidable caveats, the use of a sex-ratio statistic is still advantageous and superior in representing sexual dimorphism in the pathogenesis of cancer. The main limitation of male-to-female IRRs is their dimensionless scale; thus, sex-specific incidence rates have been considered in concert with this measure to provide the reader with both relative and absolute scales. Although it may also be of interest to assess birth cohort effects of male-to-female IRRs, this was not a primary aim of the analyses described herein.

In conclusion, it is clear that the incidence of many different cancers is higher in males than females. Observing how male-to-female IRRs change with age and time period is likely to provide insight for theories of cancer pathogenesis. The pace of these changes alone indicates that the major causes of cancer are environmental. However, the majority of exposures underlying the changes in male-to-female IRRs remain to be elucidated, and are, at best, speculative for most cancers. Future epidemiologic studies should be encouraged to design, analyze and report sex-specific associations to aid our understanding of sex-differences in cancer incidence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig 1.
Male-To-Female Incidence Rate Ratios and Sex-Specific Incidence Rates by Age, 1975-2004:

1. tonsil cancer
2. skin excluding basal and squamous
3. esophageal squamous cell carcinoma
4. esophageal adenocarcinoma
5. anus, anal canal and anorectum
6. hepatocellular carcinoma
7. kidney and renal pelvis
8. thyroid
9. lung and bronchus

Abbreviation: MF IRR, male-to-female incidence rate ratio.

Fig 2.

Male-to-female incidence rate ratios and sex-specific incidence rates by age for total cancer, total cancer excluding sex-specific sites, and total cancer excluding sex-specific sites and breast, 1975-2004

Note that the lines for 'Male incidence, total cancer excluding sex-specific sites' and 'Male incidence, total cancer excluding sex-specific sites and breast' are virtually identical due to the low incidence of breast cancer in males relative to male total cancer incidence.

Incidence Rates and Male-to-Female Incidence Rate Ratios by Cancer, 1975-2004

Table 1

SEER*Stat Database: Incidence - SEER 9 Registries Limited-Use, Nov 2007 Submission (1973-2005). Rates are per 100,000 and age-adjusted to the 2000 US standard population (19 age groups - Census P25-1130). Abbreviations: CI, confidence interval; IRR, incidence rate ratio.

Site	Cancer incidence per 100,000 man/woman years								Male-to-female IRR (95% CI)			
	1975-1984		1985-1994		1995-2004		1975-2004		1975-1984	1985-1994	1995-2004	1975-2004
	male	female	male	female	male	female	male	female				
Lip	4.51	0.43	3.00	0.42	1.93	0.40	2.98	0.42	10.54	7.18	4.77	7.16 (6.77 - 7.57)
Tongue	3.58	1.55	3.71	1.63	3.98	1.64	3.79	1.62	2.31	2.28	2.42	2.34 (2.27 - 2.42)
Salivary Gland	1.38	0.96	1.57	0.92	1.62	1.03	1.54	0.97	1.44	1.71	1.57	1.59 (1.51 - 1.66)
Floor of Mouth	2.36	0.87	1.88	0.70	1.24	0.51	1.76	0.68	2.71	2.69	2.43	2.59 (2.47 - 2.73)
Gum and Other Mouth	2.95	1.72	2.62	1.73	2.07	1.47	2.49	1.63	2.71	1.51	1.41	1.53 (1.47 - 1.58)
Nasopharynx	1.07	0.42	1.05	0.41	1.02	0.43	1.04	0.42	2.53	2.58	2.36	2.48 (2.33 - 2.64)
Tonsil	1.88	0.77	1.92	0.69	2.22	0.55	2.04	0.66	2.43	2.79	4.01	3.07 (2.92 - 3.22)
Oropharynx	0.53	0.20	0.53	0.17	0.50	0.15	0.52	0.17	2.69	3.12	3.37	3.06 (2.79 - 3.37)
Hypopharynx	2.19	0.56	2.11	0.48	1.43	0.35	1.87	0.45	3.89	4.37	4.14	4.13 (3.9 - 4.37)
Other Oral Cavity and Pharynx	0.69	0.24	0.68	0.26	0.45	0.16	0.59	0.22	2.86	2.58	2.76	2.7 (2.48 - 2.94)
Esophagus	6.98	2.22	7.73	2.25	8.20	2.15	7.72	2.21	3.14	3.43	3.82	3.49 (3.4 - 3.59)
Stomach	16.84	7.75	14.59	6.43	11.92	5.56	14.10	6.43	2.17	2.27	2.15	2.19 (2.16 - 2.23)
Small Intestine	1.35	0.97	1.86	1.24	2.22	1.59	1.86	1.30	1.39	1.50	1.39	1.43 (1.38 - 1.49)
Colon and Rectum	75.07	56.02	74.46	52.13	63.99	46.92	70.33	51.16	1.34	1.43	1.36	1.37 (1.37 - 1.38)
Anus, Anal Canal and Anorectum	0.79	1.04	0.95	1.21	1.24	1.47	1.02	1.27	0.76	0.78	0.85	0.81 (0.77 - 0.85)
Liver and Intrahepatic Bile Duct	4.27	1.70	5.98	2.24	8.68	3.20	6.60	2.46	2.51	2.67	2.71	2.69 (2.62 - 2.76)
Gallbladder	1.23	2.21	0.96	1.77	0.88	1.41	1.00	1.74	0.56	0.54	0.63	0.57 (0.55 - 0.6)
Other Biliary	1.97	1.33	1.81	1.23	1.99	1.28	1.93	1.27	1.48	1.47	1.56	1.52 (1.46 - 1.58)
Pancreas	14.53	10.04	13.48	10.27	13.19	10.25	13.65	10.20	1.45	1.31	1.29	1.34 (1.32 - 1.36)
Retropitoneum	0.55	0.43	0.49	0.42	0.44	0.41	0.49	0.42	1.28	1.17	1.08	1.17 (1.09 - 1.26)
Peritoneum, Omentum and Mesentery	0.06	0.07	0.10	0.27	0.09	0.95	0.09	0.47	0.85	0.36	0.10	0.18 (0.16 - 0.21)
Other Digestive Organs	0.47	0.36	0.44	0.31	0.55	0.46	0.49	0.38	1.29	1.41	1.19	1.28 (1.18 - 1.38)
Nose, Nasal Cavity and Middle Ear	1.01	0.52	0.98	0.60	0.86	0.54	0.94	0.56	1.93	1.62	1.61	1.7 (1.6 - 1.8)
Larynx	9.97	1.66	9.15	1.83	6.96	1.51	8.53	1.65	6.00	5.00	4.62	5.17 (5.02 - 5.32)
Lung and Bronchus	98.89	32.97	98.49	47.36	84.28	52.47	93.16	45.18	3.00	2.08	1.61	2.06 (2.05 - 2.07)
Trachea, Mediastinum and Other Respiratory Organs	0.43	0.16	0.36	0.16	0.28	0.12	0.35	0.15	2.64	2.19	2.44	2.4 (2.15 - 2.67)
Bones and Joints	1.01	0.73	1.04	0.75	1.03	0.79	1.03	0.76	1.39	1.40	1.30	1.35 (1.28 - 1.42)
Soft Tissue including Heart	2.75	1.91	2.96	2.10	3.60	2.46	3.15	2.18	1.44	1.41	1.46	1.45 (1.4 - 1.49)
Skin excluding Basal and Squamous	12.07	10.06	18.87	13.26	25.51	16.97	19.70	13.81	1.20	1.42	1.50	1.43 (1.41 - 1.44)
Breast	0.97	107.00	1.09	131.98	1.19	136.11	1.10	126.38	0.01	0.01	0.01	0.01 (0.01 - 0.01)
Urinary Bladder	36.13	9.37	38.15	9.64	37.94	9.71	37.54	9.57	3.85	3.96	3.91	3.92 (3.87 - 3.97)
Kidney and Renal Pelvis	12.04	5.41	14.69	7.13	16.94	8.52	14.84	7.17	2.22	2.06	1.99	2.07 (2.04 - 2.1)
Ureter	1.10	0.43	0.95	0.38	0.85	0.37	0.96	0.35	2.54	2.52	2.30	2.45 (2.29 - 2.61)
Other Urinary Organs	0.67	0.24	0.56	0.21	0.54	0.16	0.58	0.20	2.77	2.70	3.34	2.92 (2.67 - 3.2)
Eye and Orbit	1.01	0.76	0.95	0.64	0.95	0.67	0.97	0.69	1.33	1.48	1.42	1.41 (1.33 - 1.49)
Brain	7.13	4.80	7.88	5.38	7.57	5.18	7.55	5.15	1.48	1.46	1.46	1.47 (1.44 - 1.5)
Cranial Nerves Other Nervous System	0.38	0.30	0.43	0.37	0.43	0.40	0.42	0.36	1.25	1.18	1.07	1.16 (1.07 - 1.25)
Thyroid	2.90	6.61	3.19	7.75	4.18	11.62	3.50	8.93	0.44	0.41	0.36	0.39 (0.38 - 0.4)
Other Endocrine including Thymus	0.58	0.40	0.66	0.52	0.75	0.58	0.67	0.51	1.47	1.28	1.28	1.32 (1.24 - 1.41)

Site	Cancer incidence per 100,000 man/woman years								Male-to-female IRR (95% CI)			
	1975-1984		1985-1994		1995-2004		1975-2004		1975-1984	1985-1994	1995-2004	1975-2004
	male	female	male	female	male	female	male	female				
Hodgkin Lymphoma	3.64	2.38	3.47	2.58	3.15	2.54	3.40	2.51	1.53	1.35	1.24	1.35 (1.32 - 1.39)
Non-Hodgkin Lymphoma	15.14	11.18	22.39	14.50	24.64	16.61	21.35	14.40	1.35	1.54	1.48	1.48 (1.47 - 1.5)
Myeloma	6.38	4.28	7.07	4.75	7.33	4.78	6.98	4.64	1.49	1.49	1.53	1.51 (1.47 - 1.54)
Lymphocytic Leukemia	8.41	4.49	8.80	4.61	8.56	4.57	8.56	4.55	1.88	1.91	1.87	1.88 (1.84 - 1.92)
Myeloid and Monocytic Leukemia	7.70	4.73	7.07	4.55	7.47	4.77	7.38	4.67	1.63	1.56	1.57	1.58 (1.55 - 1.61)
Other Leukemia	1.36	0.77	1.62	0.92	1.13	0.72	1.36	0.80	1.78	1.76	1.56	1.69 (1.61 - 1.78)
Mesothelioma	1.50	0.34	2.05	0.41	2.04	0.41	1.91	0.39	4.42	4.98	5.03	4.88 (4.59 - 5.18)
Kaposi Sarcoma	1.10	0.12	8.14	0.16	2.27	0.13	3.96	0.14	9.29	50.52	17.57	28.73 (26.27 - 31.47)

Rates are per 100,000 and age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130) standard. #CI; confidence interval. The 95% confidence interval is adjusted according to the method by Tiwari et al 2006

Table 2
Male-to-Female Incidence Rate Ratios and Percent Changes for Selected Cancers, 1975-2004

SEER*Stat Database: Incidence - SEER 9 Registries Limited-Use, Nov 2007 Submission (1973-2005). Rates are per 100,000 and age-adjusted to the 2000 US standard population (19 age groups - Census P25-1130). Abbreviation: IRR, incidence rate ratio.

Site	Male-to-female IRR				Relative change in male-to-female IRR		Relative change in male incidence rate		Relative change in female incidence rate	
	1975 - 1984	1985 - 1994	1995 - 2004	1985-94 vs. 1975-84	1995-04 vs. 1975-84	1985-94 vs. 1975-84	1995-04 vs. 1975-84	1985-94 vs. 1975-84	1995-04 vs. 1975-84	1995-04 vs. 1975-84
Tonsil	2.43	2.79	4.01	1.15	1.65	1.02	1.18	0.89	0.71	
Skin excluding Basal and Squamous	1.20	1.42	1.50	1.19	1.25	1.56	2.11	1.32	1.69	
Esophagus	3.14	3.43	3.82	1.09	1.21	1.11	1.17	1.01	0.97	
Mesothelioma	4.42	4.98	5.03	1.13	1.14	1.36	1.36	1.21	1.20	
Anus, Anal Canal and Anorectum	0.76	0.78	0.85	1.03	1.12	1.20	1.58	1.17	1.41	
Liver and Intrahepatic Bile Duct	2.51	2.67	2.71	1.06	1.08	1.40	2.03	1.32	1.88	
Brain	1.48	1.46	1.46	0.99	0.98	1.10	1.06	1.12	1.08	
Ureter	2.54	2.52	2.30	0.99	0.91	0.87	0.77	0.87	0.85	
Floor of Mouth	2.71	2.69	2.43	0.99	0.89	0.79	0.52	0.80	0.59	
Kidney and Renal Pelvis	2.22	2.06	1.99	0.93	0.89	1.22	1.41	1.32	1.57	
Pancreas	1.45	1.31	1.29	0.91	0.89	0.93	0.91	1.02	1.02	
Other Leukemia	1.78	1.76	1.56	0.99	0.88	1.19	0.83	1.20	0.94	
Cranial Nerves Other	1.25	1.18	1.07	0.94	0.86	1.16	1.14	1.23	1.33	
Nervous System	1.28	1.17	1.08	0.91	0.85	0.89	0.81	0.98	0.96	
Retropertoneum	1.93	1.62	1.61	0.84	0.83	0.97	0.85	1.15	1.03	
Nose, Nasal Cavity and Middle Ear	1.72	1.51	1.41	0.88	0.82	0.89	0.70	1.01	0.86	
Gum and Other Mouth	0.44	0.41	0.36	0.94	0.82	1.10	1.44	1.17	1.76	
Thyroid	1.53	1.35	1.24	0.88	0.81	0.95	0.86	1.08	1.07	
Hodgkin Lymphoma	6.00	5.00	4.62	0.83	0.77	0.92	0.70	1.10	0.91	
Larynx	3.00	2.08	1.61	0.69	0.54	1.00	0.85	1.44	1.59	
Lung and Bronchus	10.54	7.18	4.77	0.68	0.45	0.67	0.43	0.98	0.95	
Lip										

Incidence Rates and Male-to-Female Incidence Rate Ratios by Cancer Site and Histology, 1975-2004

SEER*Stat Database: Incidence - SEER 9 Registries Limited-Use, Nov 2007 Submission (1973-2005). Rates are per 100,000 and age-adjusted to the 2000 US standard population (19 age groups - Census P25-1130). Abbreviation: IRR, incidence rate ratio.

Site	Cancer incidence per 100,000 man/woman years									
	1975 - 1984		1985 - 1994		1995 - 2004		1975 - 1984		1985 - 1994	
	male	female	male	female	male	female	male	female	male	female
Lip										
squamous cell carcinoma	4.39	0.38	2.93	0.37	1.85	0.36	2.89	0.37	7.95	5.19
Tonsil										
squamous cell carcinoma	1.75	0.72	1.84	0.66	2.12	0.53	1.94	0.63	2.80	4.01
Hypopharynx										
squamous cell carcinoma	2.08	0.52	2.01	0.46	1.37	0.33	1.78	0.43	4.35	4.17
Esophagus										
squamous cell carcinoma	4.93	1.68	4.21	1.64	2.86	1.27	3.88	1.51	2.57	2.25
adenocarcinoma	1.09	0.17	2.66	0.33	4.57	0.59	2.99	0.39	7.96	7.69
Stomach										
adenocarcinoma	14.27	6.16	12.98	5.44	10.39	4.53	12.29	5.28	2.39	2.30
Colon										
adenocarcinoma	46.98	37.22	49.31	36.59	42.30	33.19	45.83	35.46	1.35	1.27
Rectum & Rectosigmoid Junction										
adenocarcinoma	22.37	13.60	20.80	11.87	17.60	10.18	19.94	11.70	1.75	1.73
Anus, Anal Canal and Anorectum										
squamous cell carcinoma	0.47	0.76	0.57	0.91	0.89	1.14	0.68	0.97	0.63	0.78
Liver and Intrahepatic Bile Duct										
hepatocellular carcinoma	2.92	0.85	4.15	1.20	6.48	1.82	4.75	1.34	3.46	3.56
intrahepatic bile duct	0.22	0.15	0.75	0.46	0.94	0.62	0.69	0.44	1.62	1.51
Gallbladder										
adenocarcinoma	1.02	1.87	0.78	1.51	0.71	1.17	0.81	1.47	0.52	0.61
Pancreas										
adenocarcinoma	8.87	6.20	8.80	6.62	8.99	6.86	8.91	6.59	1.33	1.31
Larynx										
squamous cell carcinoma	9.49	1.57	8.77	1.74	6.67	1.43	8.17	1.57	5.04	4.65
Lung & Bronchus										
squamous cell carcinoma	32.51	6.15	28.34	8.20	19.31	7.74	26.02	7.44	3.46	2.50
adenocarcinoma	21.27	11.15	26.12	16.71	24.60	18.73	24.21	15.84	1.56	1.31
small cell	14.12	6.10	14.87	9.36	11.57	9.19	13.39	8.35	1.59	1.26
large cell	6.39	2.21	7.99	3.73	4.05	2.30	6.00	2.74	2.14	1.76
Skin excluding Basal and Squamous melanoma										
melanoma	11.12	9.34	17.16	12.13	23.20	15.52	17.94	12.67	1.42	1.49
Breast										
adenocarcinoma	0.89	99.24	1.01	125.79	1.12	131.41	1.02	120.36	0.01	0.01
Retropertitoneum										
soft tissue & sarcoma	0.41	0.36	0.39	0.36	0.36	0.34	0.39	0.35	1.09	1.06
Kidney & Renal Pelvis										
adenocarcinoma	9.10	3.94	12.05	5.69	14.48	7.09	12.18	5.72	2.12	2.04
Urinary Bladder										
transitional cell carcinoma	32.51	8.05	35.79	8.66	35.77	8.92	34.91	8.57	4.13	4.01
Ureter										
transitional cell carcinoma	1.01	0.39	0.88	0.35	0.81	0.34	0.89	0.36	2.54	2.39
Thyroid										
papillary	1.95	4.79	2.25	6.12	3.28	9.94	2.58	7.23	0.37	0.33

Site	Cancer incidence per 100,000 man/woman years									
	1975 -1984		1985 - 1994		1995 - 2004		1975 - 1984		1985 - 1994	
	male	female	male	female	male	female	male	female	male	female

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

Anus, Anal Canal and Anorectum squamous cell carcinoma plus cloacogenic tumor

Liver adenocarcinoma excluding klatskin tumor