

Multiple Primary Cancers in the United States, 2007-2011

NAACCR's Data Quality Assessment Workgroup

INTRODUCTION

Background: Cancer survival has improved significantly over time because of advances in earlier cancer diagnoses and treatments. However, with prolonged survival after an initial cancer, cancer survivors also face about a 14% increased risk of developing subsequent multiple primary cancers compared to the general population. Even though multiple primary cancers have been counted in cancer incidence statistics, they have been traditionally excluded from population-based cancer survival analyses. Several recent studies brought this practice into question, and reported that excluding multiple primary cancers from survival calculations could result in selection bias and consequently affect the comparability of survival estimates across registries.

Objectives: In this study, we examined characteristics of multiple primary cancers in the United States in attempt to further explore the implications of excluding multiple primary cancers from survival analyses.

METHODS

Source of data

- ◆ The Cancer in North American (CINA) Analytic File 1995-2011 obtained from the North American Association of Central Cancer Registries (NAACCR) was used for the study.
- ◆ Data from the 47 states and the District of Columbia (covering 97% of U.S population) that met the NAACCR high quality data standards were included in the analyses.
- ◆ Malignant cancer cases (including *in situ* bladder cancers) diagnosed from 2007 to 2011 were the primary interest of our evaluations.
- ◆ Sequence number central (NAACCR data item #380) was used to define first vs. multiple primary cancers. Cancer cases with a sequence number value of 00 or 01 were classified as the first primary cancers, while cancer cases with a sequence number value of 02 or higher were classified as multiple primary cancers.

Data analyses

- ◆ Percent of tumors classified as multiple primary cancers was calculated by gender, age (<=39, 40-49, 50-59, 60-69, 70-79, and 80+), race/ethnicity (non-Hispanic white, non-Hispanic black, non-Hispanic other, and Hispanic), cancer site, and diagnosis year, respectively.
- ◆ Percent of multiple primary cancers by cancer site was also calculated for individual cancer registries. Summary statistics, including the minimum, maximum, and mean across registries, are provided.
- ◆ To evaluate how the length of registry operations affected ascertainment of multiple primary cancers, we obtained the reference year information of each cancer registry from the NAACCR's CINA publication. The association between percent of multiple primary cancers and the reference year of registry operations was evaluated by Spearman's correlation coefficient.
- ◆ To evaluate whether cancers registered as multiple primary cancers were more likely to be diagnosed at an early stage, percent of local-staged tumors among multiple primary cancers was compared with that among first primary cancers.

RESULTS

- ◆ During 2007 and 2011, a total of 7,426,337 malignant cancer cases (including *in situ* bladder cancers) were reported to the 48 central cancer registries in the United States. Among these, 17.4% were registered as multiple primary cancers (17.1% among males and 17.7% among females).
- ◆ Percent of cancers registered as multiple primaries varied considerably by cancer site and among registries (Table 1).

Table 1. Summary statistics of percent of cancers registered as multiple primaries among 48 registries

Cancer Site	Minimum (%)	Maximum (%)	Mean (%)
All Sites	11.1	20.6	16.9
Oral Cavity and Pharynx	9.6	27.6	20.0
Esophagus	10.8	23.5	18.9
Stomach	11.8	26.7	18.7
Colon and Rectum	12.0	23.7	18.6
Liver and Intrahepatic Bile Duct	6.2	21.2	13.0
Pancreas	9.7	21.2	16.8
Larynx	9.0	23.8	18.2
Lung and Bronchus	13.6	26.6	21.7
Melanoma of the Skin	14.0	26.8	20.7
Breast	10.3	21.3	17.0
Cervix Uteri	3.0	14.4	6.9
Corpus and Uterus, NOS	8.5	17.9	12.5
Ovary	8.6	19.8	14.2
Prostate	5.3	10.5	8.3
Testis	1.0	9.1	4.2
Urinary Bladder	17.2	29.7	24.2
Kidney and Renal Pelvis	14.1	25.4	20.5
Brain and Other Nervous System	7.4	15.3	11.3
Thyroid	8.0	15.9	12.5
Hodgkin Lymphoma	1.7	11.9	7.4
Non-Hodgkin Lymphoma	11.8	23.8	18.1
Myeloma	8.7	24.2	16.8
Leukemia	10.8	25.4	18.1

- ◆ Percent of cancers registered as multiple primaries also varied by age (Figure 1) and race/ethnicity (Figure 2).

Figure 1. Percent of cancers registered as multiple primaries by age at diagnosis

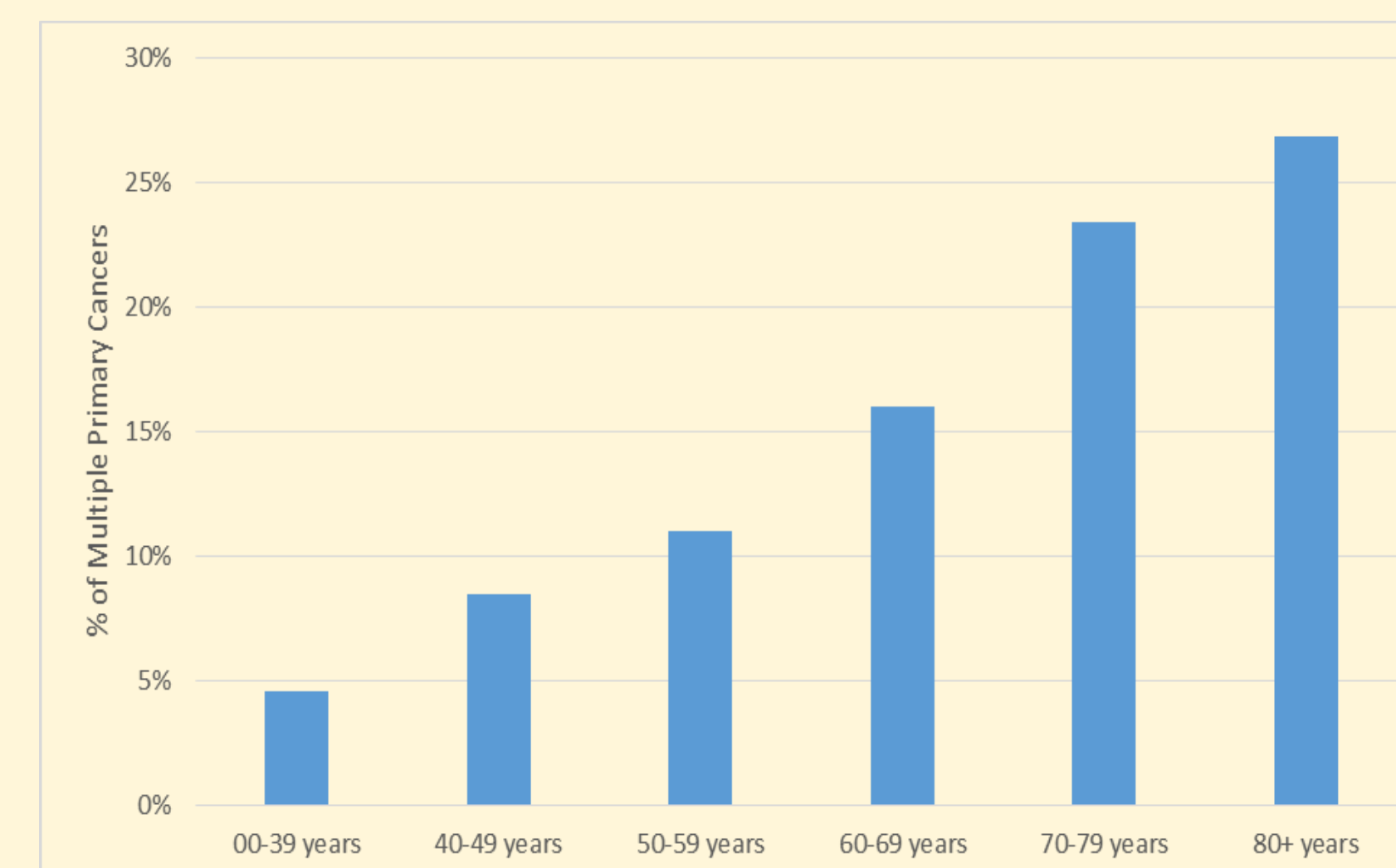
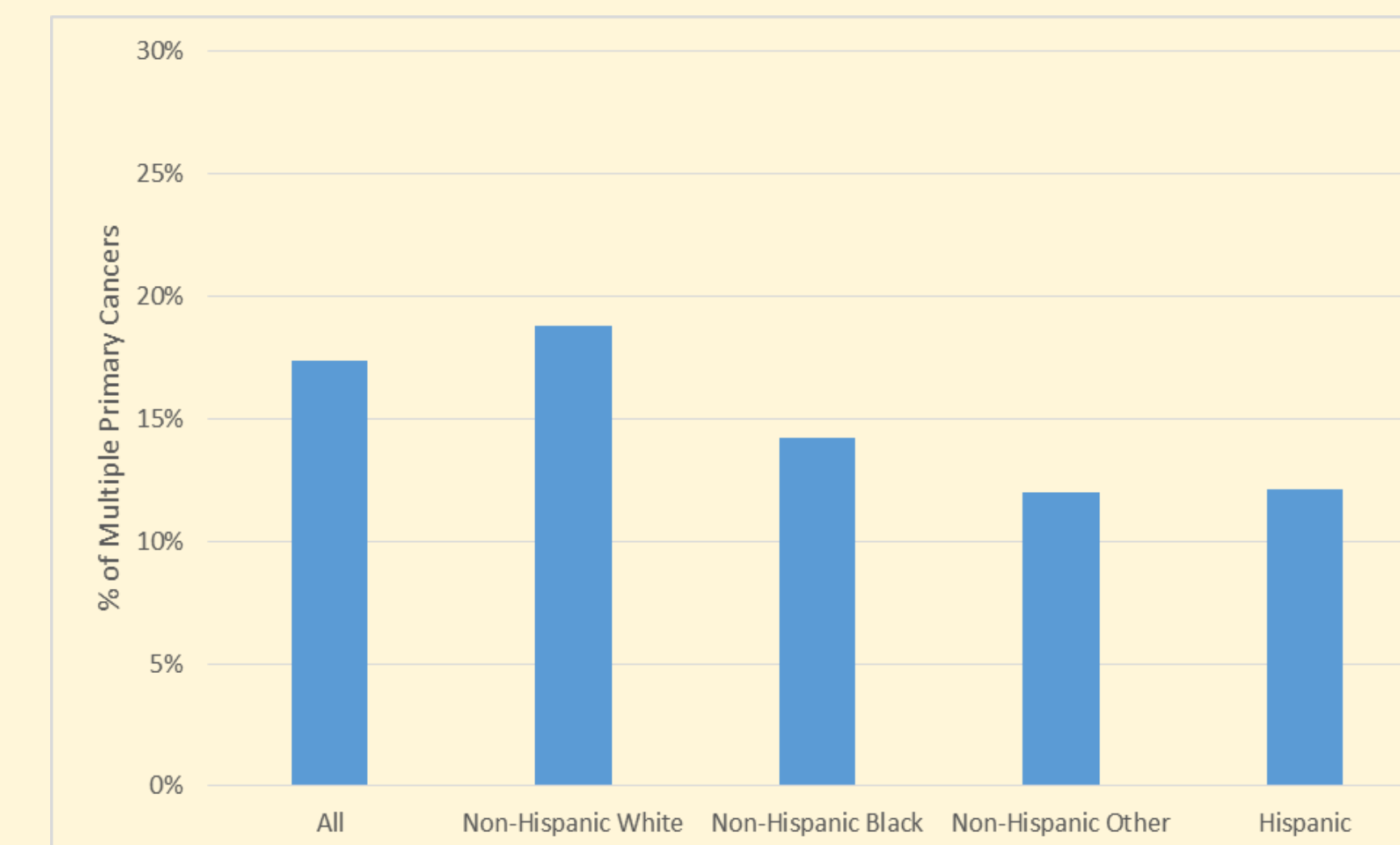


Figure 2. Percent of cancers registered as multiple primaries by race/ethnicity group



- ◆ Figure 3 shows the scatter plot of percent of cancers registered as multiple primaries during 2007-2011 vs. registry's reference year for 48 cancer registries. Spearman's correlation coefficient between these two was -0.43 (p value = 0.0026), indicating newer registries were associated with a lower percent of multiple primary cancers.

RESULTS (CONTINUED)

- ◆ Percent of cancers registered as multiple primaries increased over time (i.e. by diagnosis year) (Figure 4).

Figure 3. Scatter plot of percent of cancers registered as multiple primaries vs. reference year of registry operations

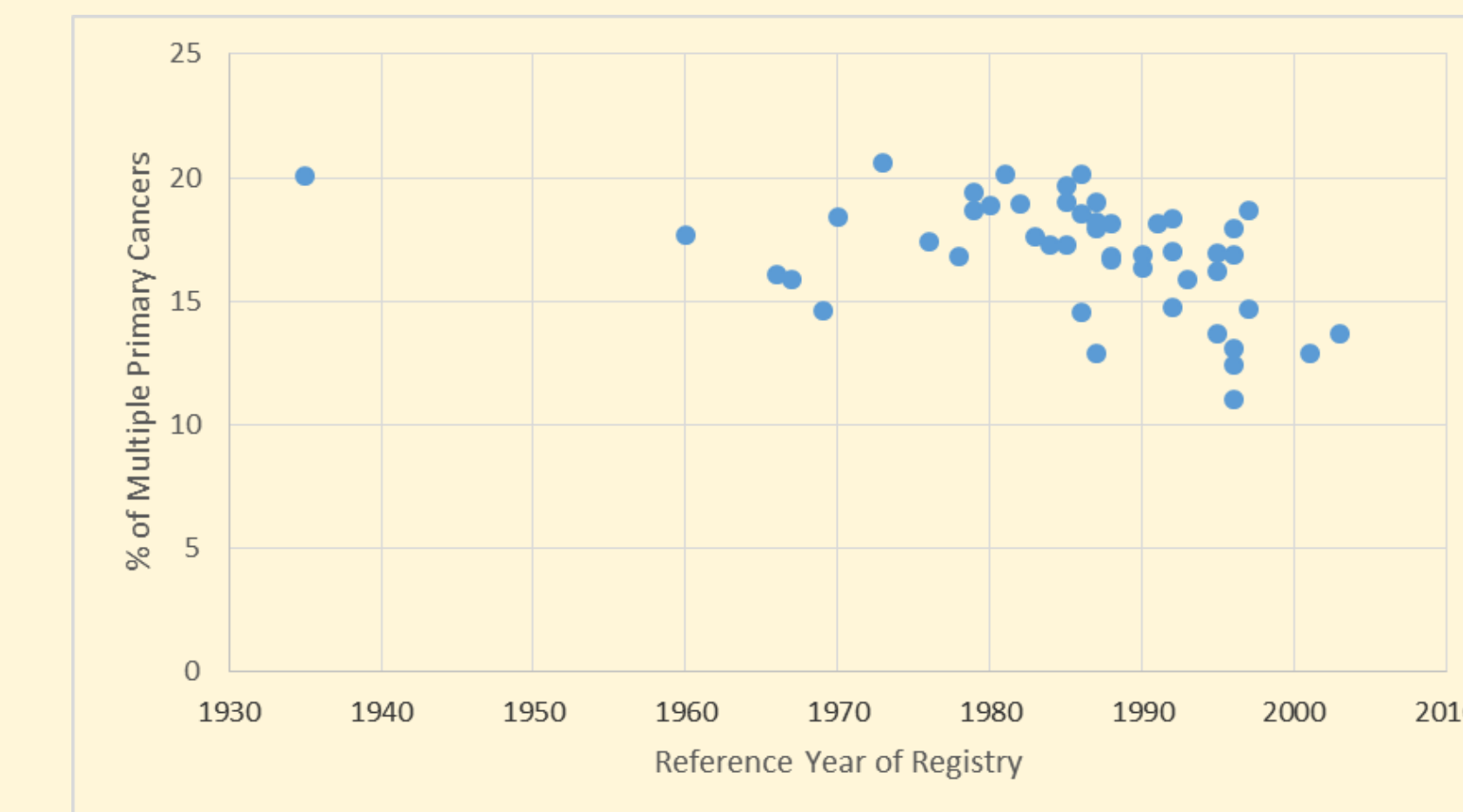
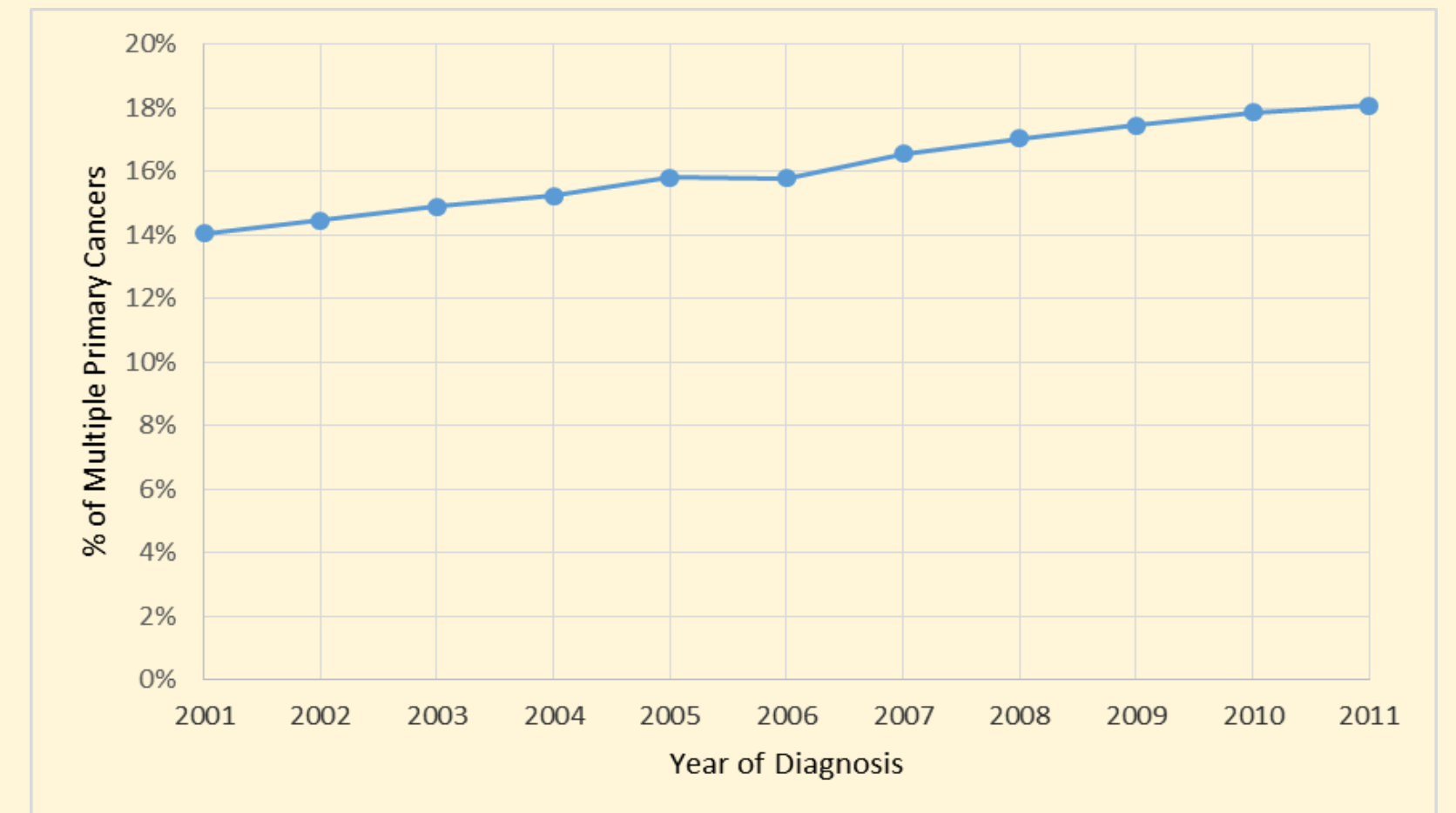


Figure 4. Percent of cancers registered as multiple primaries by year of diagnosis, 2001-2011



- ◆ Cancers registered as multiple primaries were more likely to be diagnosed at an early stage than cancers registered as the first primary for most of cancer sites evaluated (Table 2)

Table 2. Percent of cancers diagnosed at local stage by cancer site and primary status (first primary vs. multiple primary)

Cancer Sites	% of Local Stage among First Primaries (A)	% of Local Stage among Multiple Primaries (B)	Ratio (B/A)
All Sites	46.7	47.3	1.01
Oral Cavity and Pharynx	29.2	40.5	1.39
Esophagus	18.6	25.6	1.37
Stomach	25.6	32.1	1.25
Colon and Rectum	38.4	43.7	1.14
Liver and Intrahepatic Bile Duct	38.7	45.9	1.19
Pancreas	8.5	12.1	1.42
Larynx	53.2	58.6	1.10
Lung and Bronchus	15.9	27.5	1.73
Melanoma of the Skin	77.4	76.0	0.98
Breast	60.3	67.9	1.13
Cervix Uteri	44.1	40.5	0.92
Corpus and Uterus, NOS	67.1	62.6	0.93
Ovary	14.2	15.2	1.07
Prostate	78.5	79.5	1.01
Testis	67.1	67.9	1.01
Urinary Bladder	84.2	84.2	1.00
Kidney and Renal Pelvis	64.2	68.2	1.06
Thyroid	69.6	68.4	0.98

DISCUSSION AND LIMITATIONS

Discussion: The current study reveals that a significant proportion of cancer cases in the United States were registered as multiple primary cancers and the frequency of multiple primary cancers also varied widely by race/ethnicity, age, year of diagnosis, cancer site, stage, and registry. Excluding multiple primary cancers from survival analyses means excluding a significant proportion of cases, and this exclusion will be disproportionate across registries and patients with different demographic and/or tumor characteristics. This selection bias can consequently affect the comparability of survival estimates.

Limitations: Other factors, such as multiple primary rules, affect ascertainment of multiple primary cancers, but were not evaluated in the study.