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HAS MEDICAL INNOVATION REDUCED CANCER MORTALITY?

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ABSTRACT

We examine the effects of two important types of medical innovation—diagnostic imaging innovation and pharmaceutical innovation—and cancer incidence rates on U.S. cancer mortality rates during the period 1996-2006. The outcome measure we use is not subject to lead-time bias, and our measures of medical innovation are based on extensive data on treatments given to large numbers of patients with different types of cancer.

We estimate difference-in-difference models of the age-adjusted cancer mortality rate using longitudinal, annual, cancer-site-level data on over 60 cancer sites. There is a significant inverse relationship between the cancer mortality rate and both lagged imaging innovation and contemporaneous drug innovation, and a significant positive relationship between the cancer mortality rate and the lagged incidence rate. Imaging innovation, drug innovation, and declining incidence jointly explain about three-fourths of the decline in cancer mortality.

Only 7% of the mortality decline is attributable to the decline in (lagged) incidence. About one-fourth of the mortality decline is attributable to drug innovation, and 40% of the decline is attributable to (lagged) imaging innovation. Life expectancy at birth may have been increased by almost three months between 1996 and 2006 by the combined effects of cancer imaging and cancer drug innovation.

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Introduction

The war on cancer began with the National Cancer Act of 1971. The act was intended "to amend the Public Health Service Act so as to strengthen the National Cancer Institute in order to more effectively carry out the national effort against cancer."

Two types of statistics are often used to assess progress in the war on cancer: survival rates and mortality rates. Survival rates are typically expressed as the proportion of patients alive at some point subsequent to the diagnosis of their cancer. For example, the observed 5-year survival rate is defined as follows:

5-year Survival Rate = Number of people diagnosed with cancer at time t alive at time t+5 / Number of people diagnosed with cancer at time t
= 1 – (Number of people diagnosed with cancer at time t dead at time t+5 / Number of people diagnosed with cancer at time t)

Hence, the survival rate is based on a *conditional* (upon previous diagnosis) mortality rate. The second type of statistic is the *unconditional* cancer mortality rate: the number of deaths, with cancer as the underlying cause of death, occurring during a year per 100,000 population.

As shown in Figure 1a, the 5-year relative survival rate from cancer has increased steadily since the mid 1970s.[1] Although this increase suggests that there has been significant progress in the war against cancer, it might simply be a reflection of (increasing) lead-time bias. Lead time bias is the bias that occurs when two tests for a disease are compared, and one test (the new, experimental one) diagnoses the disease earlier, but there is no effect on the outcome of the disease--it may appear that the test prolonged survival, when in fact it only resulted in earlier diagnosis when compared to traditional methods.[2] Welch et al (2000) argued that "while 5-year survival is a perfectly valid measure to compare cancer therapies in a randomized trial, comparisons of 5-year survival rates across time (or place) may be extremely misleading. If cancer patients in the past always had palpable tumors at the time of diagnosis while current cancer patients

[1] Relative survival is defined as the ratio of the proportion of observed survivors (all causes of death) in a cohort of cancer patients to the proportion of expected survivors in a comparable cohort of cancer-free individuals. The formulation is based on the assumption of independent competing causes of death. Since a cohort of cancer-free individuals is difficult to obtain, expected life tables are used, i.e. it is assumed that cancer deaths are a negligible proportion of all deaths. Ederer et al (1961).
[2] See American College of Physicians (1999).

include those diagnosed with microscopic abnormalities, then 5-year survival would be expected to increase over time even if new screening and treatment strategies are ineffective." Welch et al (2000) found no correlation across cancer sites between the long-run (40-year) change in the (conditional) survival rate and the unconditional mortality rate.[3] They concluded from this that "improving 5-year survival over time…should not be taken as evidence of improved prevention, screening, or therapy," and "to avoid the problems introduced by changing patterns of diagnosis…progress against cancer [should] be assessed using population-based mortality rates."

Bailar and Gornik (1997) assessed overall progress against cancer in the United States from 1970 through 1994 by analyzing changes in (unconditional) age-adjusted cancer mortality rates. They concluded that "observed changes in mortality due to cancer primarily reflect changing incidence or early detection. The effect of new treatments for cancer on mortality has been largely disappointing."

Bailar and Gornik's assessment may have been unduly pessimistic: as shown in Figures 1b and 1c, during the period 1973-1994, the age-adjusted mortality rate increased 6.4%, while the age-adjusted incidence rate increased 22.6%. Although part of the relatively rapid growth of measured cancer incidence may have been due to improved detection, an important part may have been rapid growth in true incidence, due to a decline in competing mortality risks, especially from cardiovascular disease. More people developed cancer because they had survived heart attacks.

In the early 1990s, there was a marked change in U.S. cancer mortality and incidence. After rising steadily for 15 years, the age-adjusted mortality rate declined steadily, falling 17.2% between 1991 and 2006. During the same period, the age-adjusted incidence rate declined 9.7%.

[3] However, Welch et al did not control for changes in cancer incidence. Lichtenberg (2009) showed that, when incidence growth is controlled for, there is a highly significant correlation across cancer sites, in both the U.S. and Australia, between the change in 5-year survival for a specific tumor and the change in tumor-related mortality.

In this paper, I will analyze the effects of two important types of medical innovation—diagnostic imaging innovation and pharmaceutical innovation—and cancer incidence rates on unconditional cancer mortality rates since the early to mid 1990s.[4]

Methodology

The unconditional cancer mortality rate is essentially the unconditional probability of death from cancer (P(death from cancer)). The law of total probability implies the following:

$$P(\text{death from cancer}) = P(\text{death from cancer} \mid \text{cancer diagnosis}) * P(\text{cancer diagnosis}) + P(\text{death from cancer} \mid \text{no cancer diagnosis}) * (1 - P(\text{cancer diagnosis})) \quad (1)$$

If the probability that a person who has never been diagnosed with cancer dies from cancer is quite small ($P(\text{death from cancer} \mid \text{no cancer diagnosis}) \approx 0$), which seems plausible, this reduces to

$$P(\text{death from cancer}) \approx P(\text{death from cancer} \mid \text{cancer diagnosis}) * P(\text{cancer diagnosis}) \quad (2)$$

Hence

$$\ln P(\text{death from cancer}) \approx \ln P(\text{death from cancer} \mid \text{cancer diagnosis}) + \ln P(\text{cancer diagnosis}) \quad (3)$$

I hypothesize that the conditional mortality rate ($P(\text{death from cancer} \mid \text{cancer diagnosis})$) depends upon the average quality of imaging and pharmaceutical procedures:[5]

$$\ln P(\text{death from cancer} \mid \text{cancer diagnosis}) = \beta_1 \text{ image\_quality} + \beta_2 \text{ drug\_quality} \quad (4)$$

Substituting (4) into (3),

$$\ln P(\text{death from cancer}) \approx \beta_1 \text{ image\_quality} + \beta_2 \text{ drug\_quality} + \ln P(\text{cancer diagnosis}) \quad (5)$$

[4] In previous studies (Lichtenberg 2008, 2009a, 2009b), I have examined the effect of pharmaceutical innovation on relative cancer survival rates, controlling for variables likely to reflect changes in probability of diagnosis (e.g. age at diagnosis, cancer stage of diagnosis, and number of people diagnosed).

[5] The average quality of imaging procedures may also affect the probability of diagnosis.

I will estimate difference-in-difference (DD) versions of eq. (5) using longitudinal, cancer-site-level data on over 60 cancer sites.[6] The equations will be of the following form:

$$\ln(\text{mort\_rate}_{st}) = \beta_1 \text{adv\_imag\%}_{s,t-k} + \beta_2 \text{new\_drug\%}_{s,t-k} + \beta_3 \ln(\text{inc\_rate}_{s,t-k}) + \alpha_s + \delta_t + \varepsilon_{st} \quad (6)$$

where

mort_rate_{st}	= the age-adjusted mortality rate from cancer at site s (s = 1,…, 60) in year t (t=1991,…,2006)
$\text{adv\_imag\%}_{s,t-k}$	= advanced imaging procedures as % of total imaging procedures associated with cancer at site s in year t-k (k=0,1,…)
$\text{new\_drug\%}_{s,t-k}$	= "new" (e.g. post-1990) drug procedures as % of all drug procedures associated with cancer at site s in year t-k (k=0,1,…)
$\text{inc\_rate}_{s,t-k}$	= the age-adjusted incidence rate of cancer at site s in year t-k
α_s	= a fixed effect for cancer site s
δ_t	= a fixed effect for year t
ε_{st}	= a disturbance

If the replacement of standard imaging procedures by advanced imaging procedures has reduced the age-adjusted mortality rate, conditional on cancer drug innovation and cancer incidence, cancer sites that have had above-average increases in adv_imag% would have had above-average reductions in the age-adjusted mortality rate. This hypothesis may be tested by testing whether $\beta_1 < 0$ in eq. (6). Similarly, if the replacement of old drug procedures by new drug procedures has reduced the age-adjusted mortality rate, conditional on diagnostic imaging innovation and cancer incidence, cancer sites that have had above-average increases in new_drug% would have had above-average reductions in the age-adjusted mortality rate. This hypothesis may be tested by testing whether $\beta_2 < 0$ in eq. (6).

This equation will be estimated via weighted least-squares, weighting by the mean mortality rate of cancer site s during the entire sample period ($(1 / T) \sum_t \text{mort\_rate}_{st}$). The estimation procedure will account for clustering of disturbances within cancer sites. Eq.

[6] The cancer sites are those included in the National Cancer Institute's SEER Cause of Death Recode shown in Appendix Table 1.

(6) includes *lagged* values of adv_imag% and the other explanatory variables, since it may take several years for advanced imaging procedure utilization to have its peak effect on mortality rates.

The imaging procedure innovation measure will be constructed as follows:

$$\text{adv\_imag\%}_{st} = \frac{\Sigma_p \, \text{n\_proc}_{pst} \, \text{adv}_p}{\Sigma_p \, \text{n\_proc}_{pst}}$$

where

n_proc_{pst} = the number of times diagnostic imaging procedure p was performed in connection with cancer diagnosed at site s in year t

adv_p = 1 if procedure p is an advanced imaging procedure

= 0 if procedure p is a standard imaging procedure

The drug procedure innovation measure will be constructed as follows:

$$\text{new\_drug\%}_{st} = \frac{\Sigma_p \, \text{n\_proc}_{pst} \, \text{post\_year}_p}{\Sigma_p \, \text{n\_proc}_{pst}}$$

where

n_proc_{pst} = the number of times drug procedure p[7] was performed in connection with cancer diagnosed at site s in year t

post_year_p = 1 if the active ingredient of drug procedure p was approved by the FDA after year y[8]

= 0 if the active ingredient of drug procedure p was approved by the FDA before year y+1

[7] Drug procedures are procedures listed on MEDSTAT outpatient and inpatient claims with the following service types (STDSVC): chemotherapy (STDSVC=111), drugs (NEC) (STDSVC=155), or injectable medications (STDSVC=158).

[8] I will define y in two different ways: y=1990 and y=1995.

Data and descriptive statistics

Cancer incidence and mortality rates. Data on age-adjusted cancer incidence and mortality rates, by cancer site and year, were obtained from the National Cancer Institute's Cancer Query Systems (http://seer.cancer.gov/canques/index.html). Mortality data are based on a complete census of death certificates and are therefore not subject to sampling error, although they are subject to other errors, i.e. errors in reporting cause of death and age at death.[9] Cancer incidence rates are based on data collected from population-based cancer registries, which currently cover approximately 26 percent of the US population; incidence rates are therefore subject to sampling error.

Diagnostic imaging innovation. Data on the number of diagnostic imaging procedures, by CPT code[10], principal diagnosis (ICD9) code, and year (n_proc_{pst}) were obtained from MEDSTAT MarketScan Commercial Claims and Encounters Database produced by Thomson Medstat (Ann Arbor, MI).[11] Each claim in this database includes information about the procedure performed (CPT code), the patient's diagnosis (ICD9 code), and the date of service.

I used Berenson-Eggers Type of Service (BETOS) codes developed by CMS to determine whether each imaging procedure was a standard or advanced procedure ($adv_p = 0$ or $adv_p = 1$).[12] The BETOS coding system was developed primarily for analyzing the growth in Medicare expenditures. The coding system covers all HCPCS (including CPT) codes; assigns a HCPCS code to only one BETOS code; consists of readily understood

[9] During the period 1979-1998, cause of death was coded using ICD9 codes. Since 1999, cause of death has been coded using ICD10 codes. An advantage of the National Cancer Institute's Cancer Query Systems is that the mortality data from the two periods have been linked together.
[10] According to the American Medical Association's *CPT Assistant Archives,* procedures with CPT codes between 70010 and 75893 are diagnostic imaging procedures.
[11] The MarketScan Databases capture person-specific clinical utilization, expenditures, and enrollment across inpatient, outpatient, prescription drug, and carve-out services from a selection of large employers, health plans, and government and public organizations. The MarketScan Databases link paid claims and encounter data to detailed patient information across sites and types of providers, and over time. The annual medical databases include private sector health data from approximately 100 payers. Historically, more than 500 million claim records are available in the MarketScan Databases. The Commercial Claims and Encounters Database provides data on the medical experience of active employees, early retirees, COBRA continues, and their dependents insured by employer-sponsored plans (i.e., non-Medicare eligibles).
[12] See the Centers for Medicare & Medicaid Services Berenson-Eggers Type of Service (BETOS) code database (http://www.cms.hhs.gov/HCPCSReleaseCodeSets/20_BETOS.asp#TopOfPage)

clinical categories (as opposed to statistical or financial categories); consists of categories that permit objective assignment; is stable over time; and is relatively immune to minor changes in technology or practice patterns. Advanced imaging procedures (with a BETOS code beginning with I2) involve either a computed tomography (CT) scan or magnetic resonance imaging (MRI). Standard imaging procedures have BETOS codes beginning with I1. According to the 2006 BETOS Public Use File, 544 HCPCS codes correspond to standard imaging procedures, and 152 HCPCS codes correspond to advanced imaging procedures. For example, code 71010 (Radiologic examination, chest; single view, frontal) is a standard imaging procedure, and code 70450 (Computed tomography, head or brain; without contrast material) is an advanced imaging procedure.

The MEDSTAT Marketscan data are available during the period 1991-2007. The coverage of the database expanded over time. As shown in Figure 2, during the period 1991-1995, the average annual number of imaging procedures associated with a cancer diagnosis was about 46,000. During the period 1996-2001, the average annual number was about 90,000. In 2007, the number of imaging procedures associated with a cancer diagnosis was about 771,000.

Figure 2 also shows that the fraction of imaging procedures that were advanced procedures increased from 38% in 1991 to 70% in 2006. Below we will show that the magnitude of the increase varied significantly across cancer sites. Figure 3 illustrates the shift between 1991 and 2007 in the distribution of imaging procedures used on cancer patients: it shows the percent of 1991 and 2007 imaging procedures accounted for by the top 15 procedures in 2007. The top two procedures in 2007 were CT scans. They accounted for less than 6% of procedures in 1991, and over 20% of procedures in 2007.

Although the MEDSTAT Marketscan database contains a large number of claims, it is not based on a nationally representative sample of Americans. Moreover, the database I use contains data on medical care used by active employees, early retirees, COBRA continues, and their dependents insured by employer-sponsored plans. Medical care used by people eligible for Medicare is not covered.[13] The majority of cancer patients are enrolled in Medicare. Nevertheless, there is likely to be a strong positive

[13] I do not have access to a separate MEDSTAT database that covers Medicare-eligible retirees with employer-sponsored Medicare Supplemental plans.

correlation across cancer sites between innovations in treatment of nonelderly and elderly patients. If there was more treatment innovation for cancer type A than for cancer type B among nonelderly patients, there was likely to have been more treatment innovation for cancer type A than for cancer type B among elderly patients.

Pharmaceutical innovation. It is worth distinguishing between two types of drugs: self-administered drugs, and drugs administered by physicians and other medical providers (e.g., chemotherapy). Utilization of self-administered drugs is reported in outpatient prescription records (claims). These records generally don't include any information about the patient's diagnosis. In contrast, drugs that are administered by physicians and other medical providers are reported as outpatient and inpatient services (procedures). These records include information about the patient's diagnosis.

For most diseases other than cancer, most drug expenditure is on self-administered drugs, and determining the diagnosis associated with a particular drug's use (hence measuring n_proc_{pst}) can be difficult. But the following table, based on 2007 MEDSTAT data, shows that over two-thirds of cancer drug expenditure is on drugs administered by providers.

	2007 payments (millions)			
Therapeutic Group	provider-administered	self-administered	total	provider-administered as % of total
Antineoplastic Agents	$1,179	$537	$1,717	69%
Other drugs	$1,611	$14,958	$16,570	10%
TOTAL	$2,791	$15,495	$18,286	15%

Data from IMS Health's National Sales Perspectives are consistent with this: in 2004, clinics and hospitals accounted for 72% of U.S. expenditure on oncology drugs. Moreover some self-administered drugs contain the same active ingredients as provider-administered drugs. During the sample period (i.e. prior to Medicare Part D), a self-administered drug was covered by Medicare only if there was a provider-administered drug with the same active ingredient. We will use data on provider-administered drugs only, since the number of times provider-administered drug p was used to treat cancer originating at site s in year t can be measured precisely.

Data on the number of drug procedures, by HCPCS code, principal diagnosis (ICD9) code, and year, were also obtained from MEDSTAT MarketScan Commercial Claims and Encounters Database. No drug procedure data are available for 1991, and as shown in Figure 4, during the period 1992-1998, the average annual number of drug procedures associated with a cancer diagnosis was about 10,000. The number of drug procedures associated with a cancer diagnosis increased rapidly after 1998, from 83,000 in 1999 to 2.2 million in 2007.

Data on the active ingredient(s) contained in each drug procedure were obtained from Multum's Lexicon database (http://www.multum.com/Lexicon.htm). Data on the initial year of FDA approval of active ingredients were obtained from the Food and Drug Administration's Drugs@FDA database (http://www.fda.gov/Drugs/InformationOnDrugs/ucm079750.htm).

Due to delays in the establishment by CMS of procedure codes for new chemotherapy procedures, our measure of chemotherapy vintage (pharmaceutical innovation) is likely to be a "lagging indicator" of the true increase in chemotherapy treatment vintage. The following table shows the FDA approval dates and HCPCS code establishment dates for five cancer drugs approved by the FDA in 1996.

Drug	FDA approval date	HCPCS code establishment date	Lag (months)
daunorubicin liposomal	4/8/1996	1/1/1999	33
docetaxel	5/14/1996	1/1/1998	20
gemcitabine	5/15/1996	1/1/1998	20
topotecan	5/28/1996	1/1/1998	19
irinotecan	6/14/1996	1/1/1998	19

FDA, Listing of Approved Oncology Drugs with Approved Indications, http://www.fda.gov/cder/cancer/druglistframe.htm
CMS, 2007 Alpha-Numeric HCPCS File, http://www.cms.hhs.gov/HCPCSReleaseCodeSets/downloads/anweb07.zip

HCPCS codes for these five drugs were established 19-33 months after FDA approval. These drugs were administered to patients prior to the establishment of their HCPCS codes. The following table shows unpublished IMS Health data for four of these drugs

on the number of "standard units" sold in the U.S. via retail and hospital channels in the years 1996-1998.

	1996	1997	1998
docetaxel	36,962	115,191	211,728
gemcitabine	185,237	508,379	763,405
topotecan	88,987	150,492	170,665
irinotecan	117,510	371,832	439,420

According to one Medicare carrier, "J9999 [not otherwise classified, antineoplastic drugs] is the code that should be used for chemotherapy drugs that do not already have an assigned code."[14] 16% of chemotherapy treatments for patients with colorectal cancer used code J9999 in 2004.

Figure 4 shows that post-1990 drug procedures as a percent of total drug procedures increased from below 10% in 1992-1995 to over 36% in 2006-2007. The mean fraction of total drug procedures that were post-1995 procedures increased from about 4% in 1992-1995 to 26% in 2006-2007.[15] Figure 5 illustrates the shift between 1999 and 2007 in the distribution of drug procedures used on cancer patients: it shows the percent of 1999 and 2007 drug procedures accounted for by the top 15 procedures in 2007. The fifth most common procedure in 2007 (palonosetron) accounted for 3.8% of 2007 drug procedures and 0.0% of 1999 drug procedures. The FDA approved this drug in 2003. The tenth most common procedure in 2007 (trastuzumab) accounted for 2.4% of 2007 drug procedures and 0.0% of 1999 drug procedures. The FDA approved this drug in 1998.

Table 1 shows statistics on mortality, incidence, diagnostic imaging procedures, and drug procedures, by cancer site in 1996 and 2006.

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[14] http://www.palmettogba.com/palmetto/providers.nsf/44197232fa8516898525719600693 9dd/85256d580043e75485256db3004fe953

[15] One might expect the number of post-1995 procedures to be zero before 1996. There may be a few errors in my procedure for determining the initial year of FDA approval of active ingredients. Also, patients may have access to investigational drugs prior to their approval by the FDA.

Empirical results

Estimates of the model of the age-adjusted mortality rate (eq. (6)) are presented in Table 2. Since the mortality rate may depend on lagged as well as contemporaneous values of incidence and innovation, there are many possible specifications (corresponding to different lag structures) of eq. (6). To reduce the number of specifications, we will proceed as follows. First, we will analyze the effect of just one variable—incidence in year t-k—on mortality in year t, for different values of k. Next, we will analyze the effect of imaging innovation in year t-k on mortality in year t, for different values of k, conditional on the appropriate incidence lag and drug innovation in year t. Finally, we will analyze the effect of drug innovation (measured in two different ways) in year t-k on mortality in year t, for different values of k, conditional on the appropriate incidence and imaging innovation lags.

Models 1 through 9 are fixed-effect regressions of mortality in year t on incidence in year t-k (k = 0,1,…,8). The coefficients and 95% confidence limits from these models are plotted in Figure 6. The coefficients of the first eight models are positive and significant at the 5% level. The largest coefficient is for k = 5, suggesting that an increase in incidence has its largest impact on mortality with a five-year lag.

The fact that changes in incidence have a significant effect on mortality suggests that at least part of the changes in incidence are "real"; changes in measured incidence are not purely a result of changes in measurement or screening. Although the elasticity of mortality with respect to incidence is positive and significant, the largest estimate is substantially less than one: the coefficient on $\ln(\text{inc\_rate}_{s,t-5})$ in model 6 is .351. This may be due to several factors: sampling error, changes in screening practices, and "learning by doing" or scale economies in cancer treatment: an increase in the number of patients with a given type of cancer may increase average treatment quality.

Models 10 through 15 explore the imaging innovation lag structure: they are regressions of $\ln(\text{mort\_rate}_{st})$ on $\text{adv\_imag\%}_{s,t-k}$ for different values of k (k= 0,1,…,5), controlling for $\text{new\_drug\%}_{s,t}$ and $\ln(\text{inc\_rate}_{s,t-5})$. The imaging innovation coefficients and their 95% confidence limits are plotted (on an inverted scale) in Figure 7. When k equals 0, 1, or 2, the imaging innovation coefficient is not statistically significant. However, when k equals 3, 4, or 5, the imaging innovation coefficient is negative and

significant. This indicates that use of more advanced imaging procedures reduces cancer mortality rates 3-5 years later.

Models 16 through 18 explore the drug innovation lag structure, using one measure of drug innovation: drug treatments involving ingredients approved by the FDA after 1990 as a fraction of total drug treatments (post1990%). They are regressions of $\ln(\text{mort\_rate}_{st})$ on $\text{post1990\%}_{s,t-k}$ for different values of k (k= 0,1,2), controlling for $\text{adv\_imag\%}_{s,t-5}$ and $\ln(\text{inc\_rate}_{s,t-5})$. The coefficient on the contemporaneous drug innovation measure ($\text{post1990\%}_{s,t}$) in model 16 is negative and significant; the coefficients on lagged drug innovation in models 17 and 18 are not significant. This may be due, in part, to the fact that post1990% is likely to be a "lagging indicator" of the true increase in chemotherapy treatment vintage, due to delays in the establishment by CMS of procedure codes for new chemotherapy procedures. Also, the number of drug treatments early in the sample period was quite small.

Models 19 through 21 explore the drug innovation lag structure, using an alternative measure of drug innovation: drug treatments involving ingredients approved by the FDA after 1995 as a fraction of total drug treatments (post1995%). They are regressions of $\ln(\text{mort\_rate}_{st})$ on $\text{post1995\%}_{s,t-k}$ for different values of k (k= 0,1,2), controlling for $\text{adv\_imag\%}_{s,t-5}$ and $\ln(\text{inc\_rate}_{s,t-5})$. Once again, the coefficient on the contemporaneous drug innovation measure ($\text{post1995\%}_{s,t}$) in model 19 is negative and significant; the coefficients on lagged drug innovation in models 20 and 21 are not significant.

Models 16 and 19 both indicate that there is a significant inverse relationship between the age-adjusted cancer mortality rate and both lagged imaging innovation and contemporaneous drug innovation, and a significant positive relationship between the age-adjusted cancer mortality rate and the lagged incidence rate. While there is some correlation across cancer sites between changes in imaging innovation, drug innovation, and incidence, Table 3 shows that we obtain similar estimates of the effects of imaging and drug innovation on the cancer mortality rate, whether or not we control for the other factors.

During the sample period (1996-2006), the age-adjusted cancer mortality rate declined 13.4%, from 207.0 to 181.1 deaths per 100,000 population. We can use our

estimates to assess the contributions of imaging innovation, drug innovation, and declining cancer incidence to this decline in the cancer mortality rate. For example, the estimated contribution of imaging innovation is β_1 (adv_imag%$_{.,1991}$ - adv_imag%$_{.,2001}$), where adv_imag%$_{.,t}$ is the (weighted) average value of adv_imag% across all cancer sites in year t. Using the estimates of β_1, β_2, and β_3 from model 16 in Table 2, we obtain the following decomposition of the 1996-2006 decline in cancer mortality:

Factor	**Contribution to the 1996-2006 decline in the age-adjusted cancer mortality rate**
imaging innovation	5.3%
drug innovation	3.7%
decline in age-adjusted incidence	1.0%
other factors	3.4%
TOTAL	13.4%

Imaging innovation, drug innovation, and declining incidence jointly explain about three-fourths of the decline in cancer mortality. Only 7% of the mortality decline is attributable to the decline in (lagged) incidence. About one-fourth (27%) of the mortality decline is attributable to drug innovation, and 40% of the decline is attributable to (lagged) imaging innovation.

If we assume that the decline in cancer mortality had no effect on (did not increase) mortality from other causes of death, we can also estimate how much cancer imaging and drug innovation increased life expectancy at birth in the U.S. between 1996 and 2006. The calculations above imply that cancer imaging innovation and drug innovation reduced the cancer mortality rate by 10.2 (= 40% * 25.9) and 7.1 (= 27% * 25.9) deaths per 100,000 population, respectively. During this period, the age-adjusted mortality rate from *all causes* of death declined by 119.4 deaths per 100,000 population, from 894.5 to 775.1, and life expectancy at birth increased by 1.6 years, from 76.1 to 77.7 years.[16] If the decline in cancer mortality had no effect on mortality from other causes of death, about 9% (= 10.2 / 119.4) of the decline in the mortality rate from *all causes* of death is attributable to cancer imaging innovation, and about 6% is attributable to cancer drug innovation. Life expectancy at birth may have been increased by just under three

[16] Life expectancy at birth and the age-adjusted mortality rate from all causes of death are both calculated from age-specific rates of mortality from all causes of death.

months (= (9% + 6%) * 1.6 years) between 1996 and 2006 by the combined effects of cancer imaging and cancer drug innovation. Research by Nordhaus (2003), Viscusi (2004), and Murphy and Topel (2006) indicates that Americans place a high value on increased life expectancy.

Summary

Several previous studies have examined the overall impact of medical innovation on cancer mortality. These studies may have been subject to several limitations. First, the outcome measure in all of these studies was the cancer survival rate—the proportion of patients alive at some point subsequent to the diagnosis of their cancer—and this measure may be subject to lead-time bias. Second, only one kind of medical innovation—chemotherapy innovation—was usually analyzed, and this was usually measured by the number of drugs potentially available to cancer patients, rather than by the drugs actually used by them.

This paper builds upon previous research in several ways. First, the outcome measure we use—the *unconditional* cancer mortality rate (the number of deaths, with cancer as the underlying cause of death, occurring during a year per 100,000 population)—is not subject to lead-time bias. Second, we analyze the effects of two important types of medical innovation—diagnostic imaging innovation and pharmaceutical innovation—and cancer incidence rates on cancer mortality rates. Third, our measures of medical innovation are based on extensive data on treatments given to large numbers of patients with different types of cancer.

We estimated difference-in-difference models of the age-adjusted cancer mortality rate using longitudinal, annual, cancer-site-level data on over 60 cancer sites during the period 1996-2006. There was a significant inverse relationship between the cancer mortality rate and both lagged imaging innovation and contemporaneous drug innovation, and a significant positive relationship between the cancer mortality rate and the lagged incidence rate. Imaging innovation, drug innovation, and declining incidence jointly explain about three-fourths of the decline in cancer mortality. Only 7% of the mortality decline is attributable to the decline in (lagged) incidence. About one-fourth

(27%) of the mortality decline is attributable to drug innovation, and 40% of the decline is attributable to (lagged) imaging innovation. Our findings do not support the conclusions of a 1997 article assessing progress in the war on cancer: "observed changes in mortality due to cancer primarily reflect changing incidence or early detection. The effect of new treatments for cancer on mortality has been largely disappointing." Our findings also imply that the statement by Black and Welch (1993) that "the increasing use of sophisticated diagnostic imaging promotes a cycle of increasing intervention that often confers little or no benefit" does not apply to cancer.

If the decline in cancer mortality had no effect on mortality from other causes of death, about 9% of the decline in the mortality rate from *all causes* of death is attributable to cancer imaging innovation, and about 6% is attributable to cancer drug innovation. Life expectancy at birth may have been increased by just under three months between 1996 and 2006 by the combined effects of cancer imaging and cancer drug innovation.

References

American College of Physicians (1999), "Effective Clinical Practice: Primer on Lead Time, Length and Overdiagnosis Bias," March/April, http://www.acponline.org/clinical_information/journals_publications/ecp/primers/marapr99.htm

Bailar JC 3rd, Gornik HL (1997). "Cancer undefeated," *N Engl J Med.* 336(22), 1569-74, May 29, http://content.nejm.org/cgi/content/full/336/22/1569

Black, William C., and H. Gilbert Welch (1993), "Advances in Diagnostic Imaging and Overestimations of Disease Prevalence and the Benefits of Therapy," *N Engl J Med.* 328 (17), 1237-1243, April 29.

Ederer, F., Axtell, L. M. and Cutler, S. J. (1961). The relative survival rate. A statistical methodology. In End Results and Mortality Trends in Cancer. National Cancer Institute Monograph 6 101-121. U.S. Department of Health Education and Welfare, Public Health Service, National Institutes of Health, National Cancer Institute, Bethesda, MD. http://srab.cancer.gov/documents/survival/ederer.pdf

Lichtenberg, Frank R. (2008), "Pharmaceutical Innovation and U.S. Cancer Survival, 1992-2003: Evidence from Linked SEER-MEDSTAT Data," *Forum for Health Economics & Policy* 10 (1) (Frontiers in Health Policy Research), Article 1. http://www.bepress.com/fhep/10/1/1

Lichtenberg, Frank R. (2009a), "The effect of new cancer drug approvals on the life expectancy of American cancer patients, 1978-2004," *Economics of Innovation and New Technology* 18 (5), 407-28.

Lichtenberg, Frank R. (2009b), "International differences in cancer survival rates: the role of new drug launches," *International Journal of Healthcare Technology and Management* 10 (3), 138-55.

Lichtenberg, Frank R. (2009c), "Are Increasing 5-Year Survival Rates Evidence of Success Against Cancer? A reexamination using data from the U.S. and Australia," working paper.

Murphy, Kevin M. and Robert H. Topel (2006). "The Value of Health and Longevity," *Journal of Political Economy* 114 (4), August, 871-904.

National Cancer Institute, Overview of Population-based Cancer Survival Statistics, http://srab.cancer.gov/survival/

Nordhaus, William D. (2003). "The Health of Nations: The Contribution of Improved Health to Living Standards," in *Measuring the Gains from Medical Research: An*

Economic Approach, eds. Kevin Murphy and Robert Topel. Chicago: University of Chicago Press.

SEER Cancer Statistics, http://seer.cancer.gov/statistics/

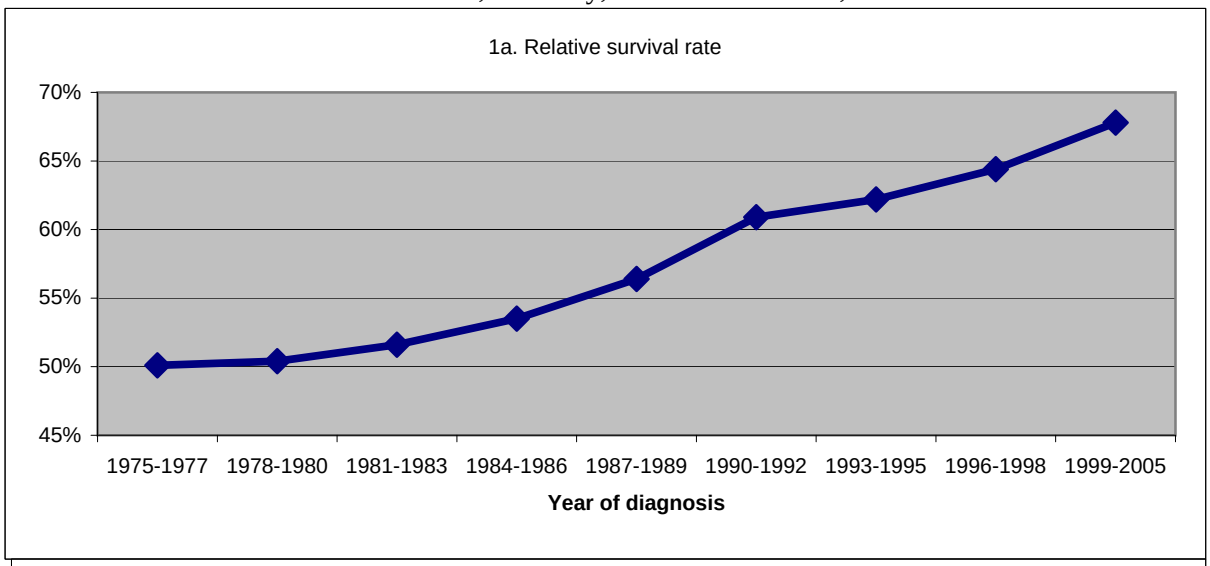
Welch, H. Gilbert, Lisa M. Schwartz, and Steven Woloshin (2000), "Are Increasing 5-Year Survival Rates Evidence of Success Against Cancer?," *JAMA* 283 (22). 2975-2978 http://jama.ama-assn.org/cgi/content/abstract/283/22/2975?ck=nck

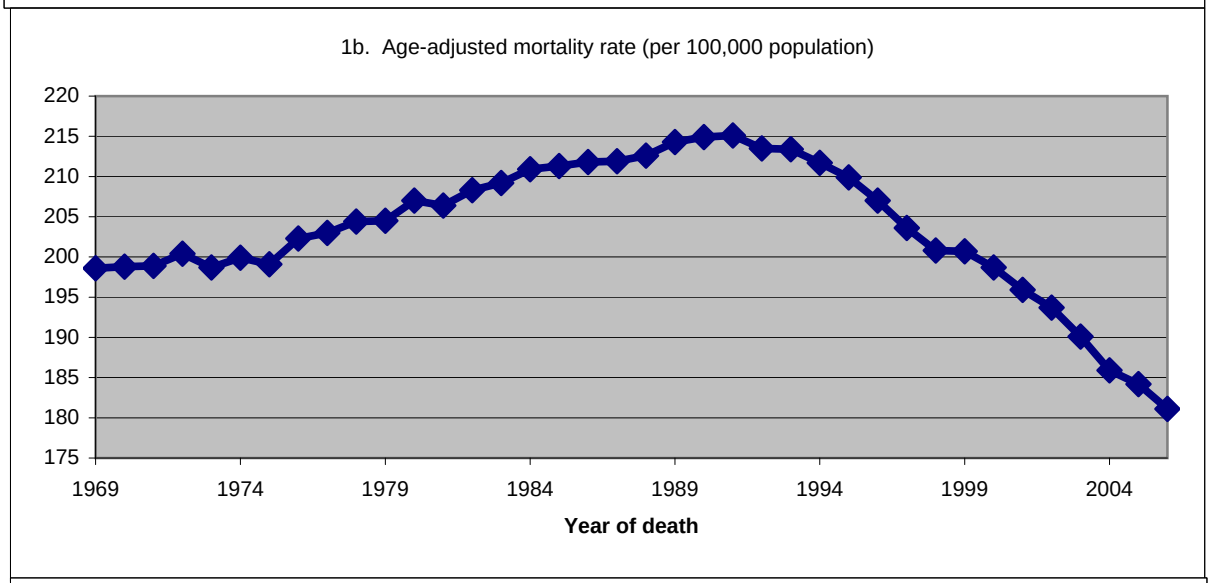
United States Government Accountability Office (2008), Medicare Part B Imaging Services, Rapid Spending Growth and Shift to Physician Offices Indicate Need for CMS to Consider Additional Management Practices, June, Report GAO-08-452**,** http://www.gao.gov/new.items/d08452.pdf

Viscusi, W. Kip (2004), "The Value of Life: Estimates with Risks by Occupation and Industry," *Economic Inquiry* 2004 42 (1), January, pp. 29–48).

Wikipedia, Lead-time bias, http://en.wikipedia.org/wiki/Lead_time_bias

Figure 1
U.S. cancer survival, mortality, and incidence rates, 1970s-2006





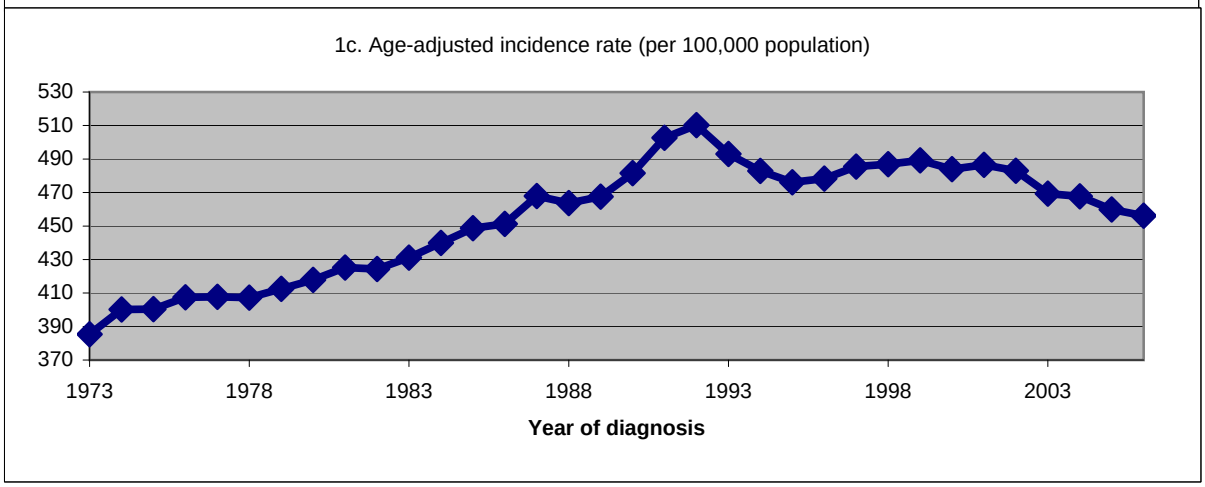


Figure 2
Cancer imaging procedures

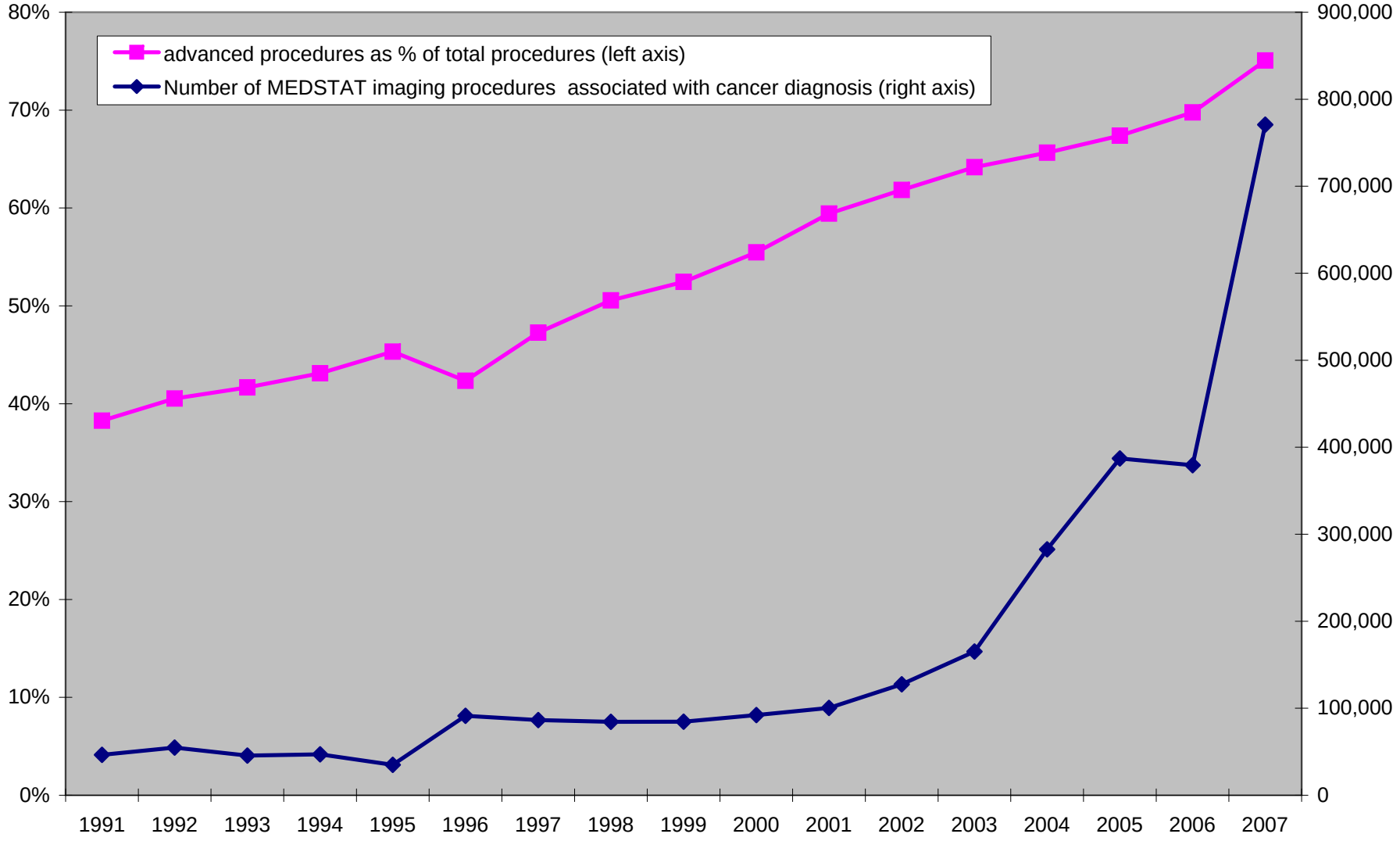


Figure 3
Percent of 1991 and 2007 imaging procedures accounted for by top 15 procedures in 2007

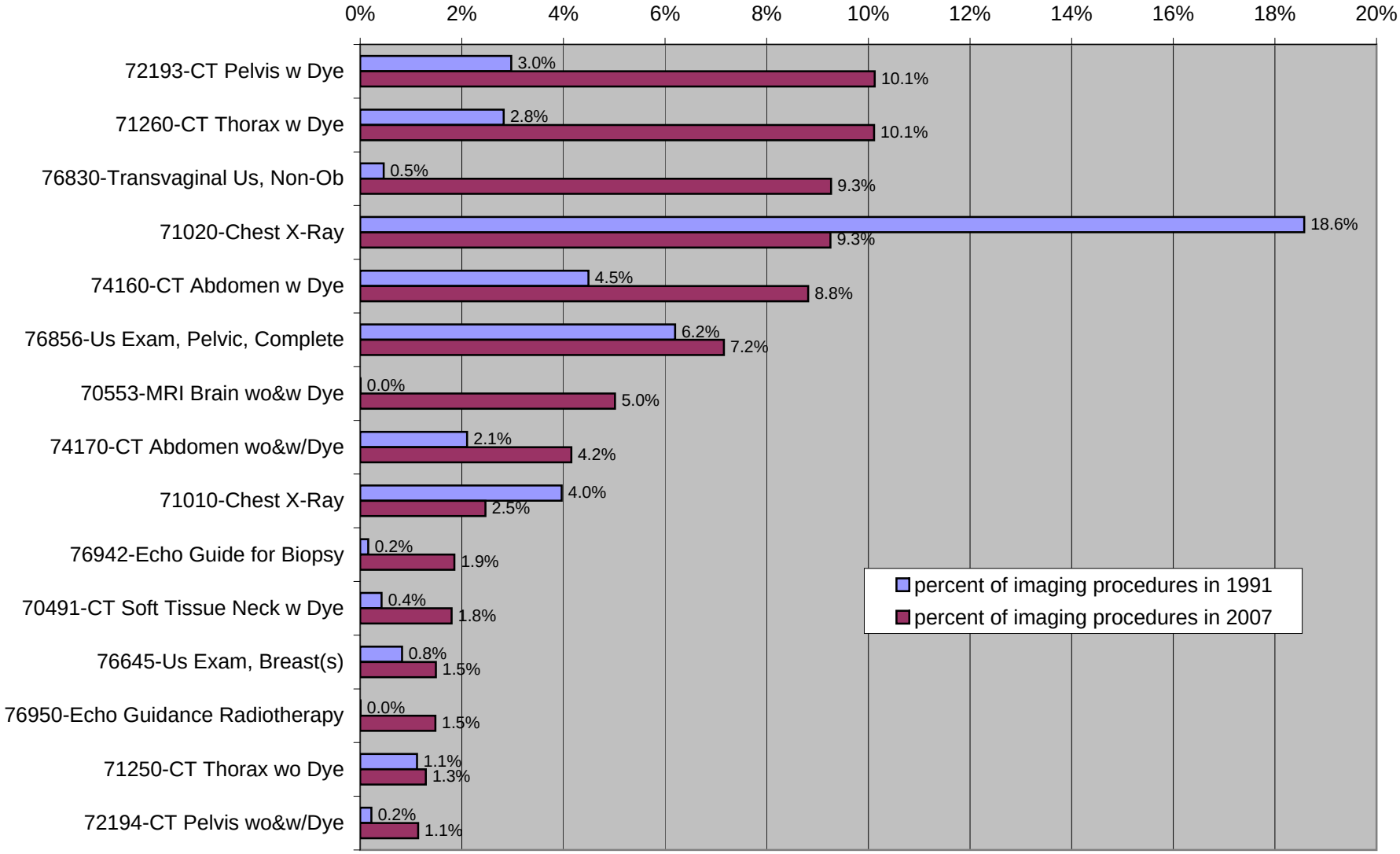


Figure 4
Cancer drug procedures

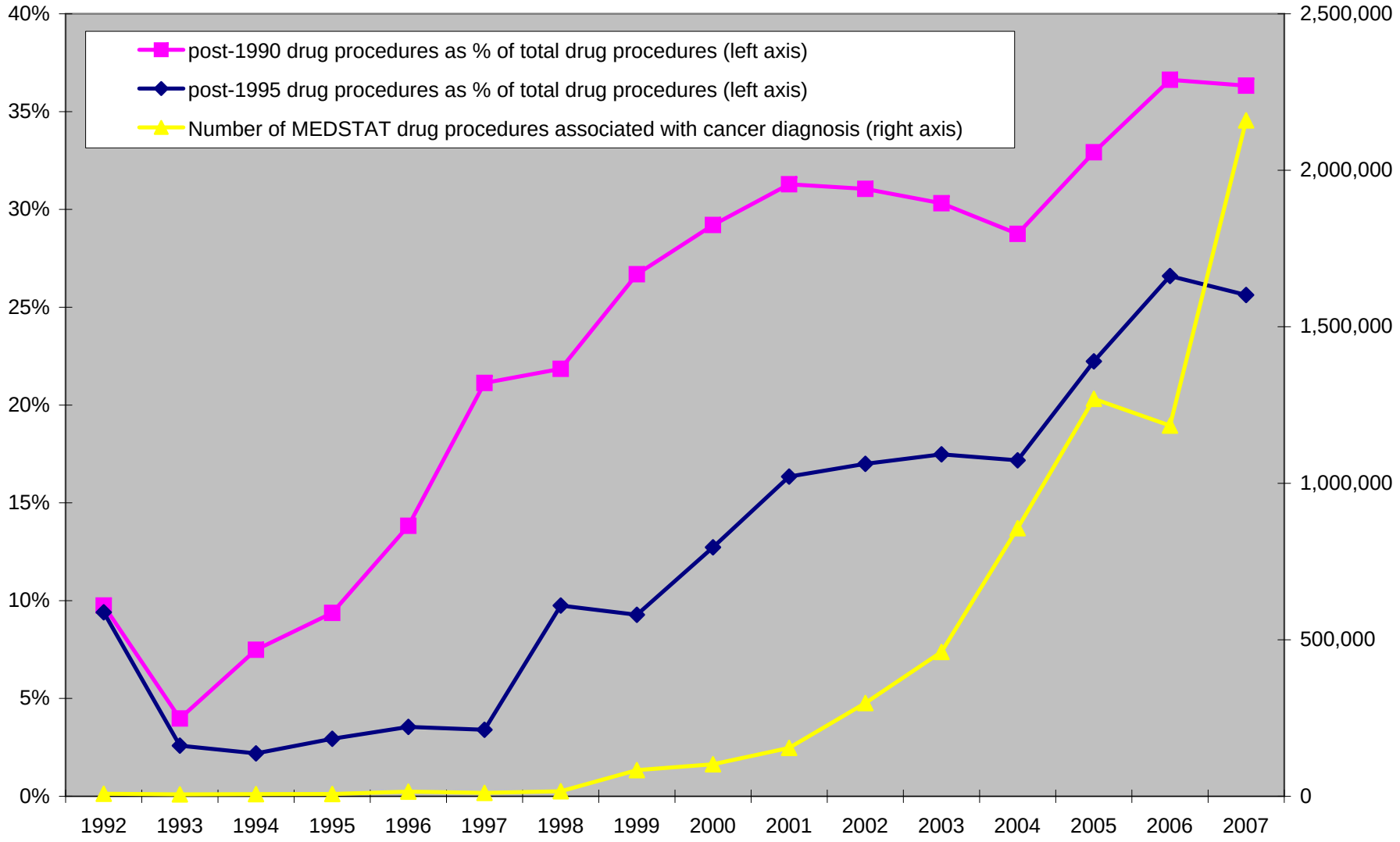


Figure 5
Percent of 1999 and 2007 drug procedures accounted for by top 15 procedures in 2007

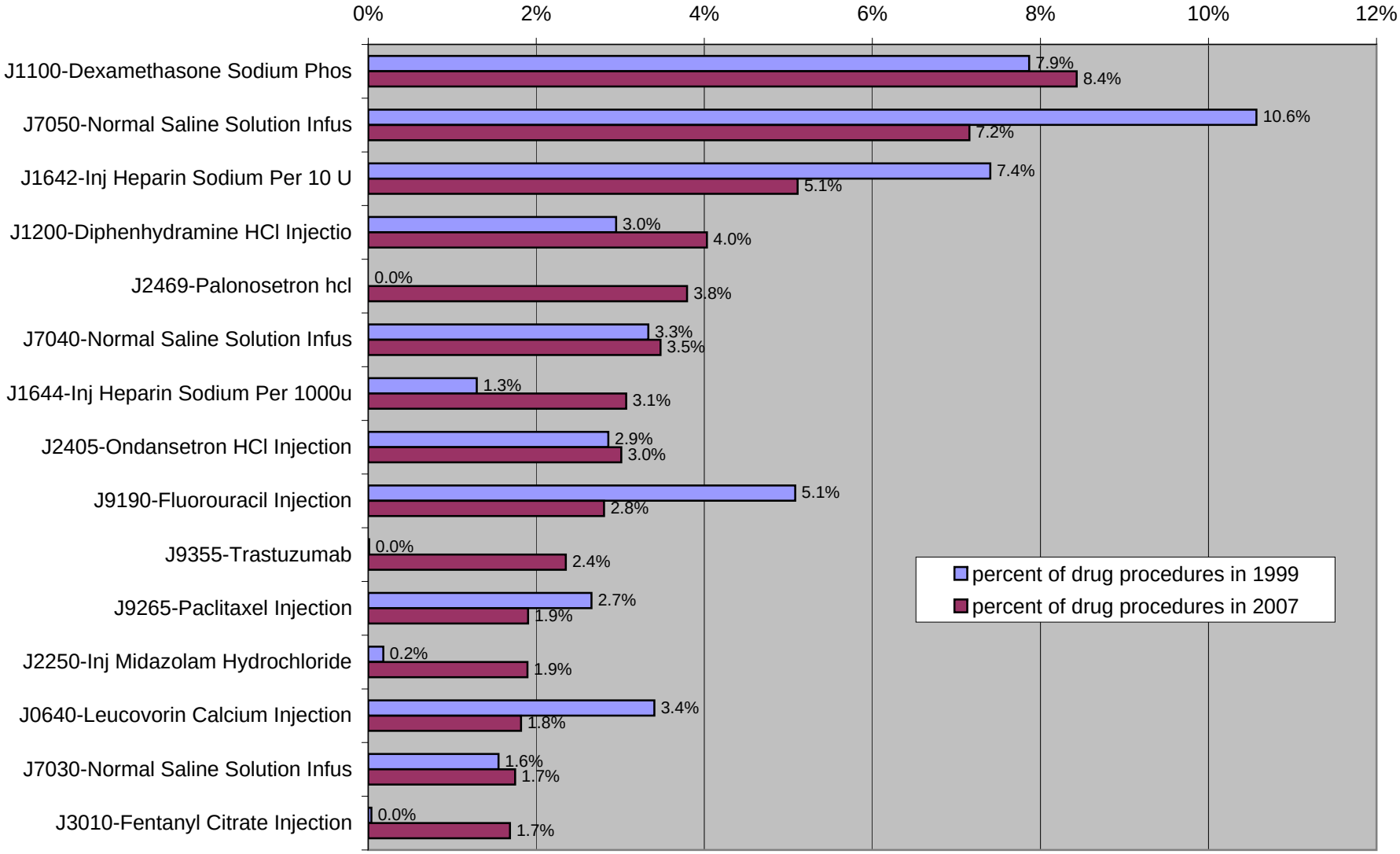


Figure 6
Effect of incidence in year t-k on mortality in year t, k=0,1,…,8

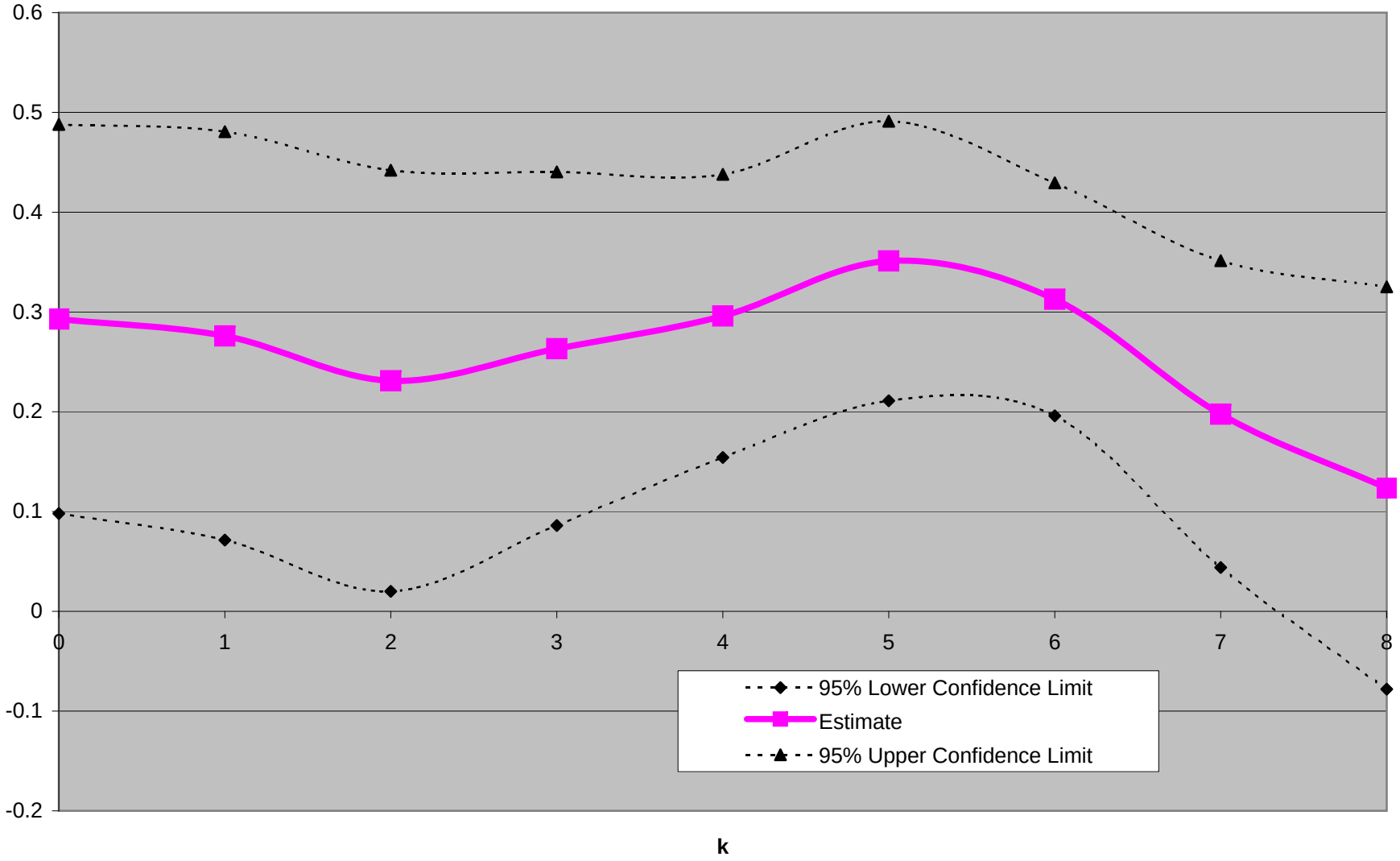


Figure 7
Effect of adv_image% in year t-k on mortality in year t, k=0,1,…,5

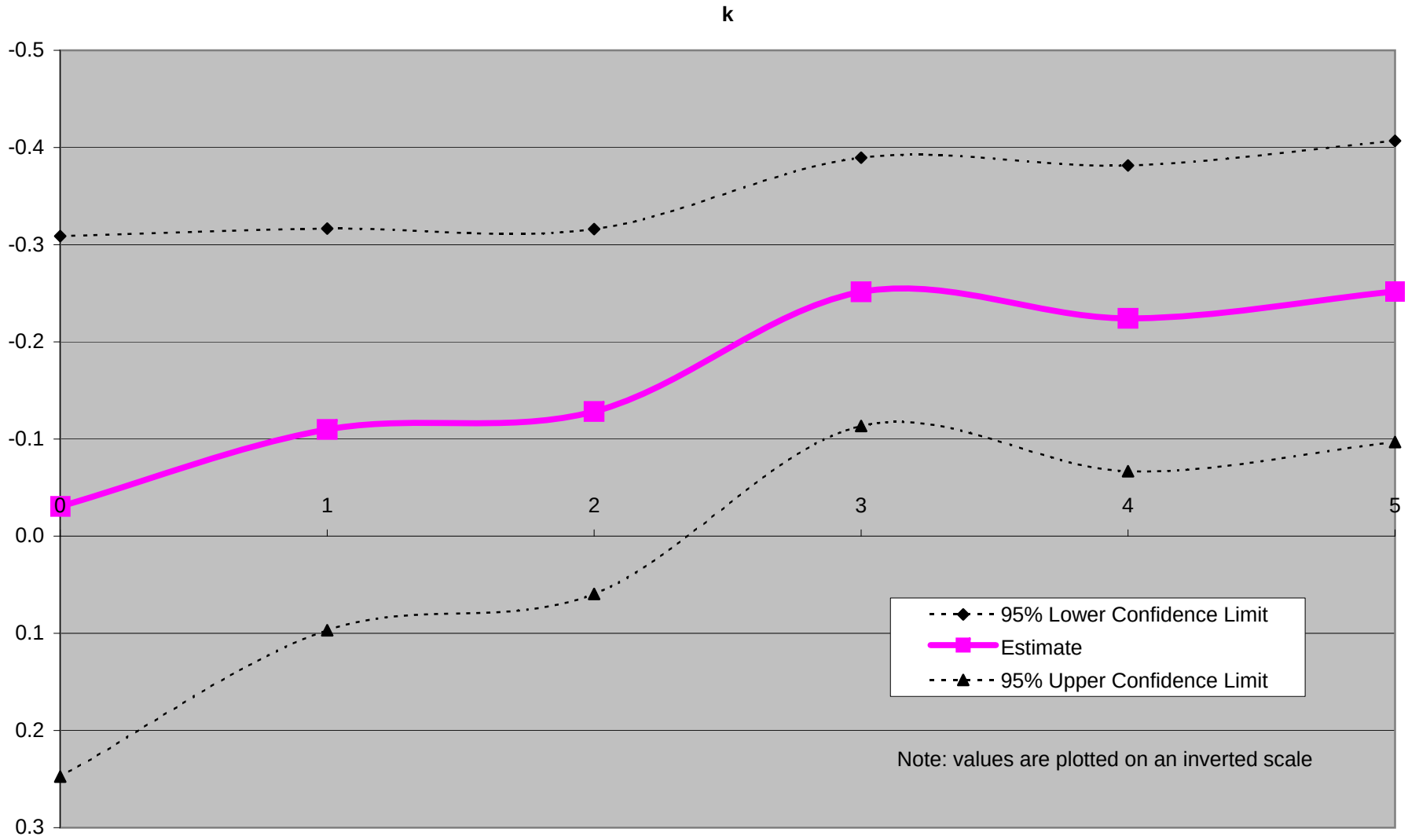


Table 1
Mortality, incidence, diagnostic imaging procedures, and drug procedures, by cancer site in 1996 and 2006

		mortality rate		incidence rate		no. of imaging procs.		advanced imaging %		no. of drug procs.		post-1990 drug procs. %		post-1995 drug procs. %	
Recode	Site	1996	2006	1996	2006	1,996	2,006	1996	2006	1,996	2,006	1996	2006	1996	2006
20010	Lip	0.0	0.0	1.3	0.7	10	73	20%	70%	.	34	.	18%	.	15%
20020	Tongue	0.7	0.6	2.6	2.9	307	1,926	40%	74%	35	7,885	0%	34%	0%	15%
20030	Salivary Gland	0.2	0.2	1.3	1.3	205	649	78%	81%	.	881	.	36%	.	21%
20040	Floor of Mouth	0.1	0.0	1.1	0.5	37	154	22%	68%	.	189	.	49%	.	12%
20050	Gum and Other Mouth	0.5	0.4	1.8	1.6	169	582	44%	65%	5	455	0%	35%	0%	17%
20060	Nasopharynx	0.3	0.2	0.8	0.6	138	731	54%	79%	41	3,138	15%	25%	0%	10%
20070	Tonsil	0.2	0.2	1.2	1.5	117	1,410	41%	77%	.	4,013	.	31%	.	16%
20080	Oropharynx	0.2	0.2	0.3	0.3	32	423	50%	80%	1	1,142	0%	30%	0%	15%
20090	Hypopharynx	0.2	0.1	0.9	0.6	35	175	49%	70%	.	1,012	.	37%	.	22%
20100	Other Oral Cavity and Pharynx	0.6	0.5	0.4	0.2	81	358	46%	73%	11	627	0%	38%	0%	13%
21010	Esophagus	4.3	4.4	4.8	4.6	1,082	5,336	34%	69%	66	17,599	6%	28%	0%	19%
21020	Stomach	5.1	3.7	8.5	7.3	648	3,089	46%	79%	151	12,184	7%	27%	7%	20%
21030	Small Intestine	0.4	0.4	1.7	2.0	128	766	45%	83%	19	2,754	0%	29%	0%	25%
21040	Colon excluding Rectum	18.7	14.3	39.3	32.9	3,296	22,609	51%	84%	1,635	163,182	2%	31%	0%	27%
21050	Rectum and Rectosigmoid Junction	3.1	2.8	15.4	12.5	2,003	10,749	56%	83%	1,124	64,513	1%	31%	0%	25%
21060	Anus, Anal Canal and Anorectum	0.2	0.2	1.3	1.4	111	1,243	55%	86%	38	4,833	0%	28%	0%	21%
21071	Liver	3.6	4.1	4.6	6.1	370	1,927	61%	79%	11	2,160	0%	28%	0%	21%
21072	Intrahepatic Bile Duct	0.9	1.2	0.9	0.6	196	1,085	84%	85%	.	1,167	.	42%	.	36%
21080	Gallbladder	0.8	0.6	1.1	1.1	90	437	54%	82%	34	1,911	0%	40%	0%	31%
21090	Other Biliary	0.6	0.5	1.3	1.7	81	503	31%	72%	.	1,382	.	38%	.	30%
21100	Pancreas	10.5	10.8	11.3	12.0	1,033	6,621	58%	83%	108	22,778	0%	44%	0%	36%
21110	Retroperitoneum	0.1	0.1	0.4	0.4	88	488	86%	87%	.	344	.	36%	.	26%
21120	Peritoneum, Omentum and Mesentery	0.2	0.3	0.5	0.7	72	525	65%	76%	60	1,135	12%	35%	0%	22%
21130	Other Digestive Organs	0.2	0.3	0.4	0.6	78	226	50%	92%	.	173	.	34%	.	23%
22010	Nose, Nasal Cavity and Middle Ear	0.2	0.1	0.7	0.6	253	509	69%	86%	.	800	.	33%	.	26%
22020	Larynx	1.5	1.2	4.3	3.2	349	1,555	39%	73%	30	4,120	0%	35%	0%	18%
22030	Lung and Bronchus	57.9	51.7	66.4	60.0	10,425	39,897	39%	70%	2,301	142,887	26%	40%	9%	27%
22050	Pleura	0.2	0.1	0.0	0.0	51	122	39%	57%	1	385	0%	35%	0%	27%
22060	Trachea, Mediastinum and Other Respiratory Organs	0.1	0.1	0.2	0.2	769	350	40%	76%	66	1,103	14%	27%	0%	16%
23000	Bones and Joints	0.5	0.4	0.8	0.9	912	2,572	54%	47%	3	1,767	0%	29%	0%	14%
24000	Soft Tissue including Heart	1.5	1.3	2.8	3.0	1,502	7,304	53%	74%	85	10,183	20%	34%	20%	21%
25010	Melanoma of the Skin	2.8	2.7	17.3	21.1	2,267	10,823	38%	60%	333	13,647	8%	17%	1%	6%

Table 1 (continued)

Mortality, incidence, diagnostic imaging procedures, and drug procedures, by cancer site in 1996 and 2006

		mortality rate		incidence rate		no. of imaging procs.		advanced imaging %		no. of drug procs.		post-1990 drug procs. %		post-1995 drug procs. %	
Recode	Site	1996	2006	1996	2006	1,996	2,006	1996	2006	1,996	2,006	1996	2006	1996	2006
25020	Other Non-Epithelial Skin	0.8	0.8	1.9	1.7	339	1,153	23%	64%	39	3,033	3%	19%	3%	10%
26000	Breast	16.8	13.2	73.2	66.4	27,894	93,405	16%	48%	3,836	361,396	13%	43%	3%	32%
27010	Cervix Uteri	1.6	1.2	4.8	3.4	651	3,018	44%	79%	15	9,870	0%	26%	0%	15%
27020	Corpus Uteri	1.1	1.0	12.2	11.8	558	4,635	47%	79%	27	9,232	22%	32%	7%	18%
27030	Uterus, NOS	1.0	1.1	0.3	0.3	270	1,577	55%	84%	8	1,410	0%	38%	0%	23%
27040	Ovary	4.5	4.3	7.1	6.3	1,915	10,863	59%	85%	566	50,287	30%	37%	0%	23%
27050	Vagina	0.2	0.1	0.3	0.4	53	267	45%	86%	.	625	.	39%	.	35%
27060	Vulva	0.2	0.3	1.2	1.2	95	397	41%	67%	.	1,821	.	22%	.	10%
27070	Other Female Genital Organs	0.1	0.1	0.4	0.4	181	281	54%	81%	26	897	8%	28%	0%	14%
28010	Prostate	18.0	11.8	84.5	81.6	3,132	17,389	46%	74%	636	17,728	3%	35%	1%	26%
28020	Testis	0.2	0.1	2.7	2.8	1,125	8,923	54%	74%	96	10,754	23%	22%	23%	13%
28030	Penis	0.1	0.1	0.3	0.3	25	131	60%	88%	.	49	.	55%	.	51%
28040	Other Male Genital Organs	0.0	0.0	0.2	0.2	78	151	72%	79%	.	36	.	0%	.	0%
29010	Urinary Bladder	4.4	4.3	20.8	20.5	1,256	6,148	34%	63%	291	16,316	4%	23%	1%	17%
29020	Kidney and Renal Pelvis	4.3	4.0	11.4	13.9	1,766	14,392	50%	77%	441	4,309	18%	41%	1%	29%
29030	Ureter	0.1	0.1	0.6	0.7	94	197	26%	52%	1	312	0%	36%	0%	26%
29040	Other Urinary Organs	0.1	0.1	0.3	0.3	150	319	59%	81%	5	359	0%	35%	0%	27%
30000	Eye and Orbit	0.1	0.1	0.9	0.8	244	599	73%	76%	.	379	.	22%	.	8%
31010	Brain and Other Nervous System	4.7	4.2	6.6	6.1	4,225	10,766	90%	93%	73	6,624	15%	38%	0%	27%
32010	Thyroid	0.5	0.5	6.5	11.0	463	3,117	36%	63%	.	2,935	.	58%	.	51%
32020	Other Endocrine including Thymus	0.3	0.3	0.7	0.8	545	2,309	69%	86%	.	3,189	.	28%	.	17%
33010	Hodgkin Lymphoma	0.5	0.4	2.8	2.9	2,517	9,188	60%	82%	443	20,361	7%	20%	5%	14%
33040	Non-Hodgkin Lymphoma	8.8	6.7	19.4	19.5	7,807	38,616	69%	89%	1,376	84,503	28%	33%	5%	24%
34000	Myeloma	3.9	3.5	5.8	5.4	1,324	6,661	32%	49%	166	26,099	6%	55%	2%	39%
35011	Acute Lymphocytic Leukemia	0.5	0.5	1.4	1.4	192	1,373	24%	43%	117	7,641	0%	17%	0%	5%
35012	Chronic Lymphocytic Leukemia	1.7	1.4	4.6	4.3	228	2,278	39%	82%	73	16,319	59%	46%	0%	25%
35013	Other Lymphocytic Leukemia	0.2	0.1	0.5	0.3	80	241	50%	81%	1	906	0%	39%	0%	18%
35022	Chronic Myeloid Leukemia	0.9	0.3	1.8	1.5	205	375	17%	45%	71	1,069	4%	38%	0%	31%
35023	Other Myeloid/Monocytic Leukemia	0.1	0.2	0.2	0.1	36	124	11%	68%	18	381	0%	29%	0%	25%
35031	Acute Monocytic Leukemia	0.1	0.0	0.2	0.2	26	48	8%	33%	.	110	.	23%	.	8%
35041	Other Acute Leukemia	1.0	0.7	0.5	0.2	253	841	38%	54%	11	6,979	0%	51%	0%	43%
37000	Miscellaneous Malignant Cancer	14.4	13.7	.	.	5,435	11,020	64%	75%	304	20,906	13%	35%	3%	21%

Table 2
Estimates of eq. (6)

Model	Regressor	Estimate	Standard Error	95% Lower Confidence Limit	95% Upper Confidence Limit	Z	Pr > |Z|
Incidence lag structure							
1	$\ln(inc\_rate_{s,t})$	0.293	0.100	0.098	0.488	2.95	0.0032
2	$\ln(inc\_rate_{s,t-1})$	0.276	0.104	0.071	0.481	2.64	0.0082
3	$\ln(inc\_rate_{s,t-2})$	0.231	0.108	0.020	0.442	2.15	0.0319
4	$\ln(inc\_rate_{s,t-3})$	0.263	0.090	0.086	0.440	2.91	0.0036
5	$\ln(inc\_rate_{s,t-4})$	0.296	0.072	0.154	0.438	4.09	<.0001
6	$\ln(inc\_rate_{s,t-5})$	0.351	0.072	0.211	0.491	4.91	<.0001
7	$\ln(inc\_rate_{s,t-6})$	0.313	0.060	0.196	0.429	5.25	<.0001
8	$\ln(inc\_rate_{s,t-7})$	0.198	0.078	0.044	0.351	2.52	0.0118
9	$\ln(inc\_rate_{s,t-8})$	0.124	0.103	-0.078	0.325	1.20	0.2298
Advanced imaging lag structure							
10	$adv\_imag\%_{s,t}$	-0.031	0.142	-0.309	0.248	-0.22	0.829
10	$post1990\%_{s,t}$	-0.152	0.072	-0.292	-0.011	-2.11	0.0348
10	$\ln(inc\_rate_{s,t-5})$	0.321	0.070	0.183	0.459	4.56	<.0001
11	$adv\_imag\%_{s,t-1}$	-0.110	0.106	-0.317	0.097	-1.04	0.2979
11	$post1990\%_{s,t}$	-0.155	0.072	-0.295	-0.015	-2.16	0.0305
11	$\ln(inc\_rate_{s,t-5})$	0.313	0.070	0.176	0.450	4.49	<.0001
12	$adv\_imag\%_{s,t-2}$	-0.128	0.096	-0.316	0.060	-1.34	0.1806
12	$post1990\%_{s,t}$	-0.150	0.071	-0.289	-0.011	-2.11	0.0345
12	$\ln(inc\_rate_{s,t-5})$	0.308	0.071	0.170	0.447	4.36	<.0001
13	$adv\_imag\%_{s,t-3}$	-0.252	0.070	-0.390	-0.113	-3.57	0.0004
13	$post1990\%_{s,t}$	-0.159	0.068	-0.293	-0.025	-2.33	0.0198
13	$\ln(inc\_rate_{s,t-5})$	0.299	0.068	0.165	0.433	4.37	<.0001

Note: The dependent variable is $\ln(mort\_rate_{st})$. The equations were estimated via weighted least-squares, weighting by the mean mortality rate of cancer site s during the entire sample period ($(1 / T) \sum_t mort\_rate_{st}$). The estimation procedure accounts for clustering of disturbances within cancer sites.

Table 2 (continued)
Estimates of eq. (6)

Model	Regressor	Estimate	Standard Error	95% Lower Confidence Limit	95% Upper Confidence Limit	Z	Pr > |Z|
Advanced imaging lag structure							
14	$adv\_imag\%_{s,t-4}$	-0.224	0.080	-0.382	-0.067	-2.79	0.0052
14	$post1990\%_{s,t}$	-0.157	0.069	-0.291	-0.022	-2.29	0.0222
14	$ln(inc\_rate_{s,t-5})$	0.294	0.074	0.149	0.439	3.98	<.0001
15	$adv\_imag\%_{s,t-5}$	-0.252	0.079	-0.407	-0.097	-3.18	0.0015
15	$post1990\%_{s,t}$	-0.161	0.066	-0.290	-0.032	-2.44	0.0145
15	$ln(inc\_rate_{s,t-5})$	0.296	0.071	0.156	0.436	4.14	<.0001
Post-1990 drug lag structure							
16	$adv\_imag\%_{s,t-5}$	-0.252	0.079	-0.407	-0.097	-3.18	0.0015
16	$post1990\%_{s,t}$	-0.161	0.066	-0.290	-0.032	-2.44	0.0145
16	$ln(inc\_rate_{s,t-5})$	0.296	0.071	0.156	0.436	4.14	<.0001
17	$adv\_imag\%_{s,t-5}$	-0.231	0.089	-0.404	-0.057	-2.61	0.0091
17	$post1990\%_{s,t-1}$	-0.107	0.065	-0.234	0.019	-1.66	0.0962
17	$ln(inc\_rate_{s,t-5})$	0.318	0.085	0.152	0.485	3.75	0.0002
18	$adv\_imag\%_{s,t-5}$	-0.231	0.086	-0.399	-0.062	-2.68	0.0074
18	$post1990\%_{s,t-2}$	-0.055	0.049	-0.150	0.040	-1.14	0.2562
18	$ln(inc\_rate_{s,t-5})$	0.328	0.085	0.161	0.495	3.84	0.0001
Post-1995 drug lag structure							
19	$adv\_imag\%_{s,t-5}$	-0.229	0.085	-0.397	-0.062	-2.69	0.0072
19	$post1995\%_{s,t}$	-0.161	0.074	-0.305	-0.016	-2.18	0.0294
19	$ln(inc\_rate_{s,t-5})$	0.307	0.076	0.158	0.455	4.04	<.0001
20	$adv\_imag\%_{s,t-5}$	-0.215	0.095	-0.401	-0.030	-2.28	0.0228
20	$post1995\%_{s,t-1}$	-0.083	0.087	-0.253	0.088	-0.95	0.3433
20	$ln(inc\_rate_{s,t-5})$	0.319	0.085	0.152	0.487	3.75	0.0002
21	$adv\_imag\%_{s,t-5}$	-0.221	0.088	-0.394	-0.048	-2.51	0.0122
21	$post1995\%_{s,t-2}$	-0.037	0.070	-0.173	0.100	-0.52	0.6003
21	$ln(inc\_rate_{s,t-5})$	0.328	0.085	0.163	0.494	3.88	0.0001

Table 3

Estimates of effects of imaging and drug innovation on cancer mortality rate, controlling and not controlling for other factors

Regressor	Covariates	Estimate	Standard Error	95% Lower Confidence Limit	95% Upper Confidence Limit	Z	Pr > |Z|
$adv\_imag\%_{s,t-5}$	$post1990\%_{s,t}$, $ln(inc\_rate_{s,t-5})$	-0.252	0.079	-0.407	-0.097	-3.18	0.0015
$adv\_imag\%_{s,t-5}$	none	-0.286	0.098	-0.478	-0.093	-2.90	0.0037
$post1990\%_{s,t}$	$adv\_imag\%_{s,t}$, $ln(inc\_rate_{s,t-5})$	-0.161	0.066	-0.290	-0.032	-2.44	0.0145
$post1990\%_{s,t}$	none	-0.164	0.073	-0.306	-0.022	-2.26	0.0239
$post1995\%_{s,t}$	$adv\_imag\%_{s,t}$, $ln(inc\_rate_{s,t-5})$	-0.161	0.074	-0.305	-0.016	-2.18	0.0294
$post1995\%_{s,t}$	none	-0.205	0.089	-0.380	-0.030	-2.30	0.0216

Appendix Table 1
SEER Cause of Death Recode 1969+ (9/17/2004)

Cancer Causes of Death	**ICD-9**	**Recode**
All Malignant Cancers	140-208, 238.6	--
Oral Cavity and Pharynx		
Lip	140	20010
Tongue	141	20020
Salivary Gland	142	20030
Floor of Mouth	144	20040
Gum and Other Mouth	143, 145	20050
Nasopharynx	147	20060
Tonsil	146.0-146.2	20070
Oropharynx	146.3-146.9	20080
Hypopharynx	148	20090
Other Oral Cavity and Pharynx	149	20100
Digestive System		
Esophagus	150	21010
Stomach	151	21020
Small Intestine	152	21030
Colon and Rectum		
Colon excluding Rectum	153, 159.0	21040
Rectum and Rectosigmoid Junction	154.0-154.1	21050
Anus, Anal Canal and Anorectum	154.2-154.3, 154.8	21060
Liver and Intrahepatic Bile Duct		
Liver	155.0, 155.2	21071
Intrahepatic Bile Duct	155.1	21072
Gallbladder	156.0	21080
Other Biliary	156.1-156.2, 156.8-156.9	21090
Pancreas	157	21100
Retroperitoneum	158.0	21110
Peritoneum, Omentum and Mesentery	158.8-158.9	21120
Other Digestive Organs	159.8-159.9	21130
Respiratory System		
Nose, Nasal Cavity and Middle Ear	160	22010
Larynx	161	22020
Lung and Bronchus	162.2-162.5, 162.8-162.9	22030
Pleura	163	22050
Trachea, Mediastinum and Other Respiratory Organs	162.0, 164.2-164.3, 164.8-164.9, 165	22060
Bones and Joints	170	23000
Soft Tissue including Heart$	164.1, 171	24000
Skin excluding Basal and Squamous		
Melanoma of the Skin	172	25010
Other Non-Epithelial Skin	173	25020
Breast	174-175	26000
Female Genital System		
Cervix Uteri	180	27010
Corpus and Uterus, NOS		
Corpus Uteri	182	27020
Uterus, NOS	179	27030
Ovary	183.0	27040

Appendix Table 1 (continued)
SEER Cause of Death Recode 1969+ (9/17/2004)

Cancer Causes of Death	**ICD-9 (1979-1998)**	**Recode**
Vagina	184.0	27050
Vulva	184.1-184.4	27060
Other Female Genital Organs	181, 183.2-183.5, 183.8-183.9, 184.8-184.9	27070
Male Genital System		
Prostate	185	28010
Testis	186	28020
Penis	187.1-187.4	28030
Other Male Genital Organs	187.5-187.9	28040
Urinary System		
Urinary Bladder	188	29010
Kidney and Renal Pelvis	189.0-189.1	29020
Ureter	189.2	29030
Other Urinary Organs	189.3-189.4, 189.8-189.9	29040
Eye and Orbit	190	30000
Brain and Other Nervous System	191, 192	31010
Endocrine System		
Thyroid	193	32010
Other Endocrine including Thymus$	164.0, 194	32020
Lymphoma		
Hodgkin Lymphoma	201	33010
Non-Hodgkin Lymphoma	200, 202.0-202.2, 202.8-202.9	33040
Myeloma	203.0, 238.6	34000
Leukemia		
Lymphocytic Leukemia		
Acute Lymphocytic Leukemia	204.0	35011
Chronic Lymphocytic Leukemia	204.1	35012
Other Lymphocytic Leukemia	202.4, 204.2, 204.8-204.9	35013
Myeloid and Monocytic Leukemia		
Acute myeloid	205.0, 207.0, 207.2	35021
Acute Monocytic Leukemia	206.0	35031
Chronic Myeloid Leukemia	205.1	35022
Other Myeloid/Monocytic Leukemia	205.2-205.3, 205.8-205.9, 206.1-206.2, 206.8-206.9	35023
Other Leukemia		
Other Acute Leukemia	208.0	35041
Aleukemic, subleukemic and NOS	203.1, 207.1, 207.8, 208.1-208.2, 208.8-208.9	35043
Mesothelioma (ICD-10 only)+	N/A	36010
Kaposi Sarcoma (ICD-10 only)+	N/A	36020
Miscellaneous Malignant Cancer	159.1, 195-199, 202.3, 202.5-202.6, 203.8	37000