Has medical innovation reduced cancer mortality?

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Two questions

- Are we making progress in the war on cancer?
- If so, how much of this progress is attributable to medical innovation—the development and use of new medical goods and services?

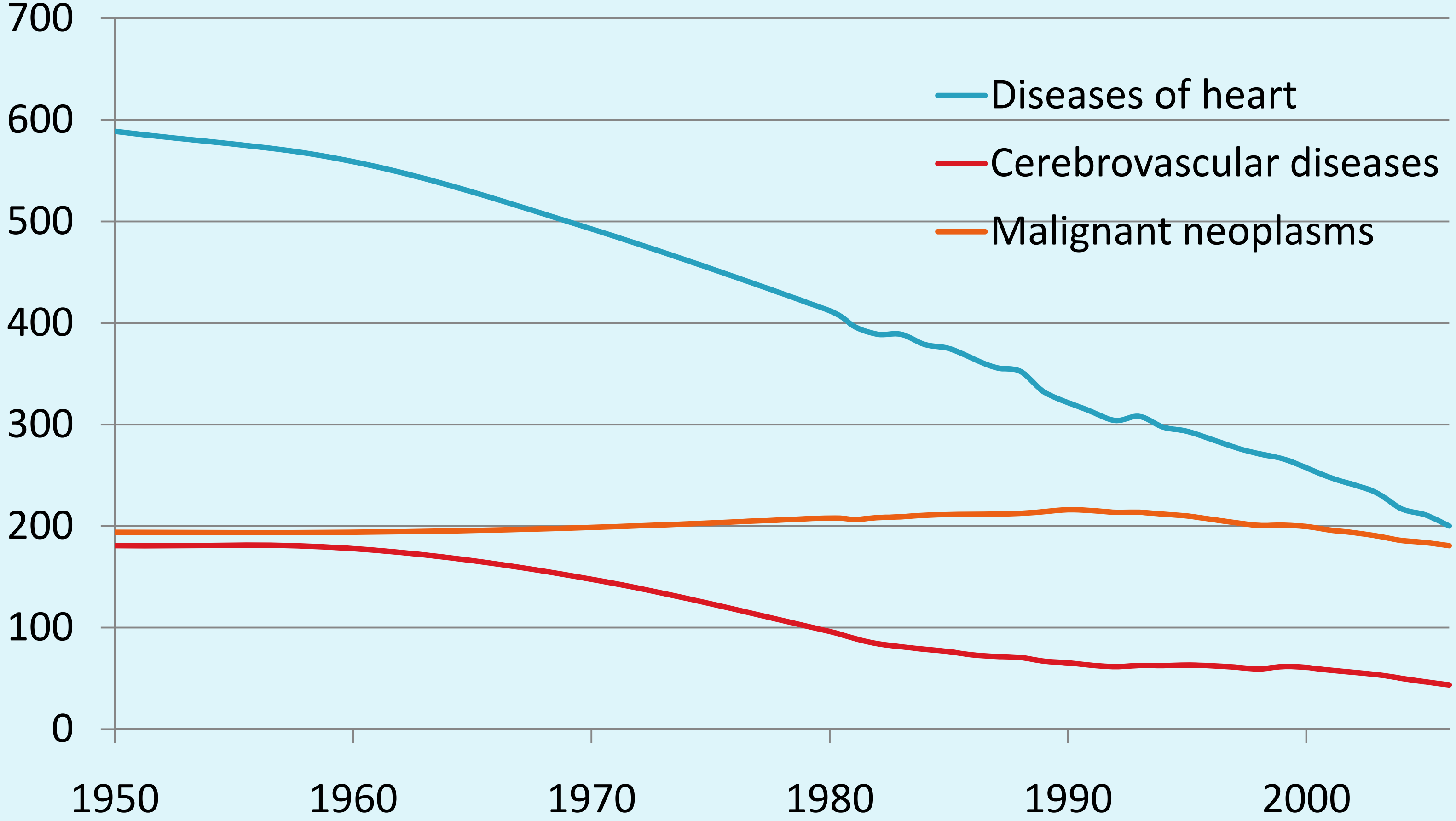
- Bailar and Gornik (1997): “The effect of new treatments for cancer on mortality has been largely disappointing.”

  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 and Welch (1993): “The increasing use of sophisticated diagnostic imaging promotes a cycle of increasing intervention that often confers little or no benefit.”

  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.

Age-adjusted mortality rates, 1950-2006

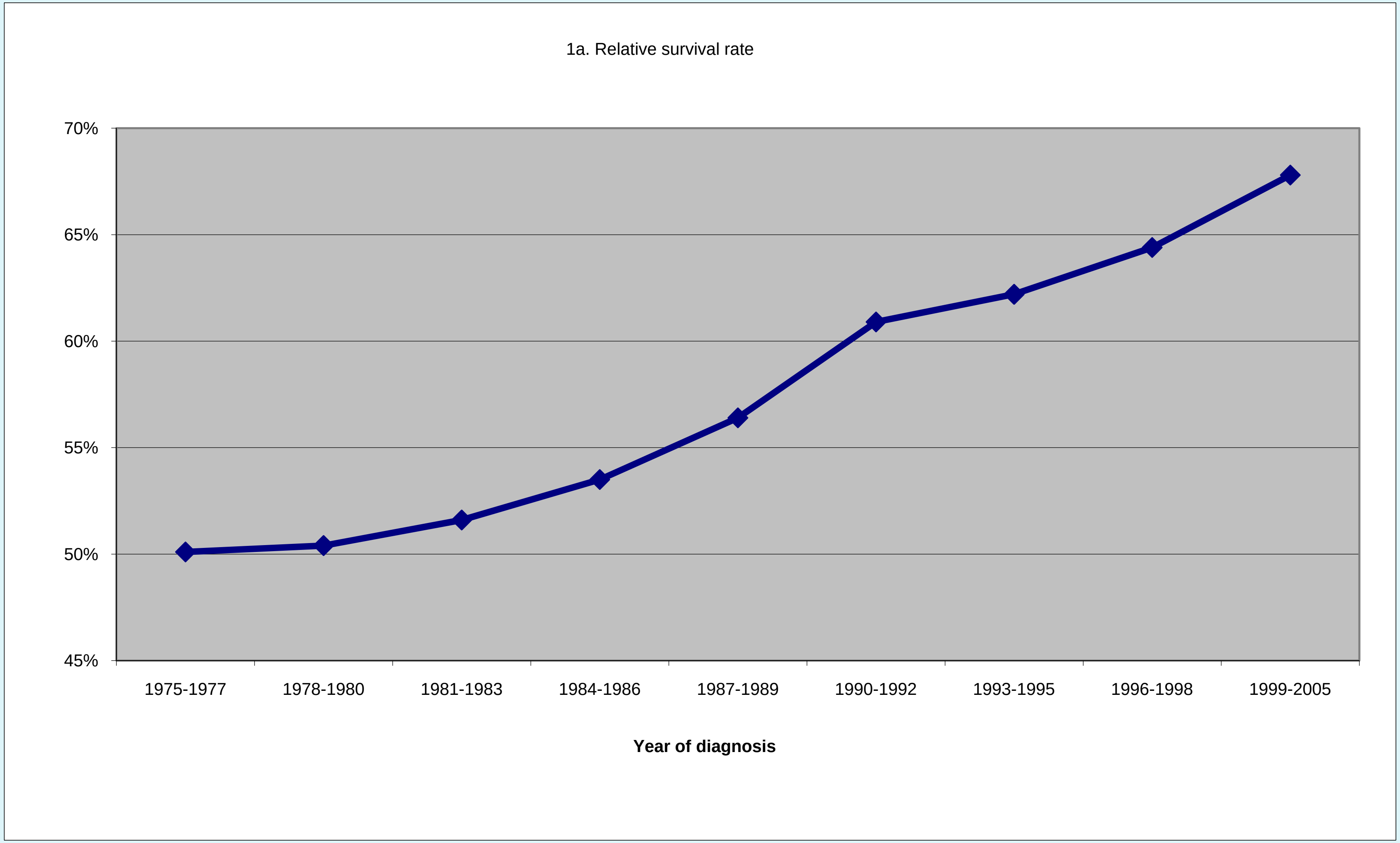


Source: Health, United States, 2009, Table 26

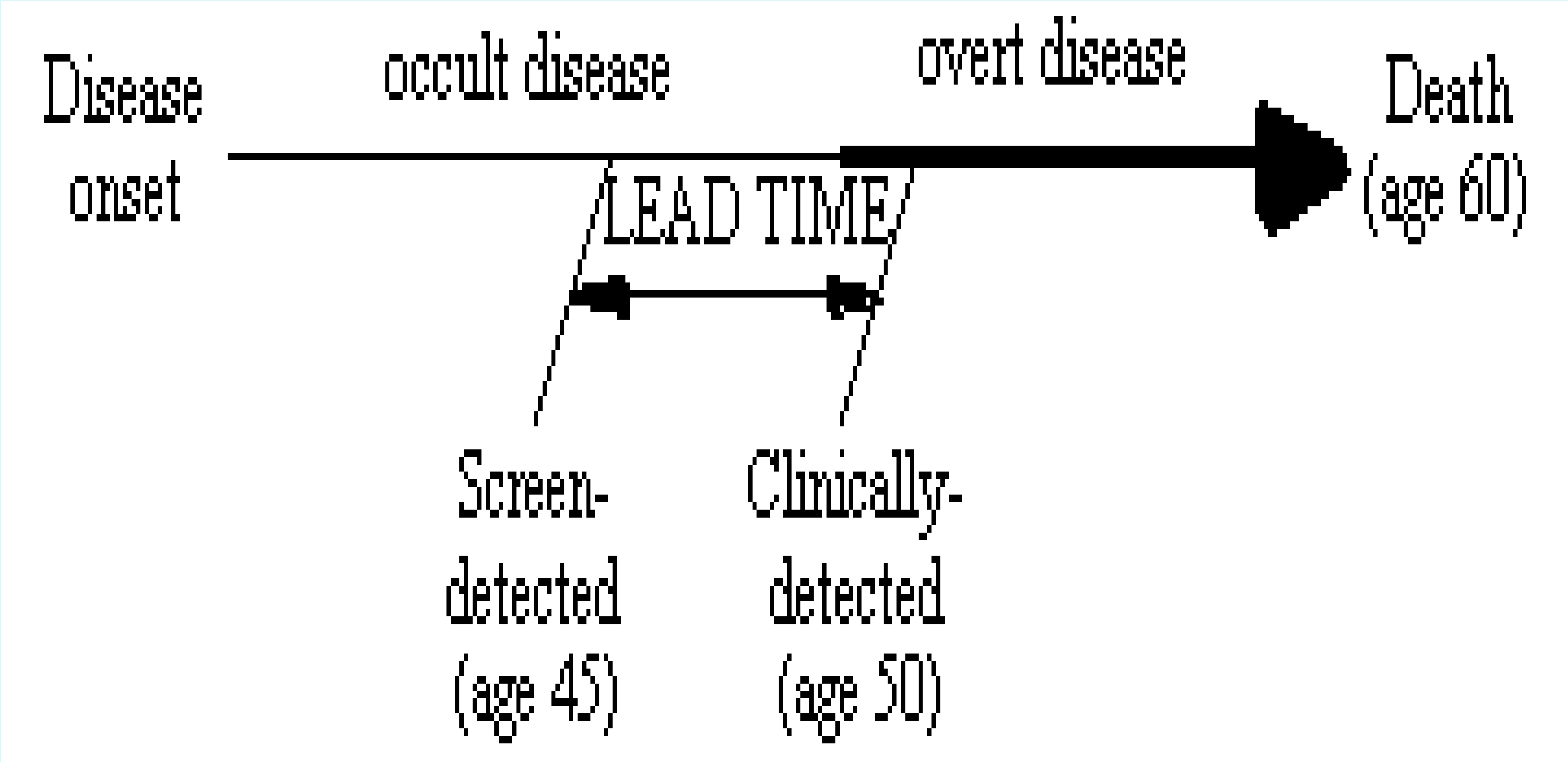
Survival rates vs. mortality rates

- 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.

Relative survival rate



Lead-time bias



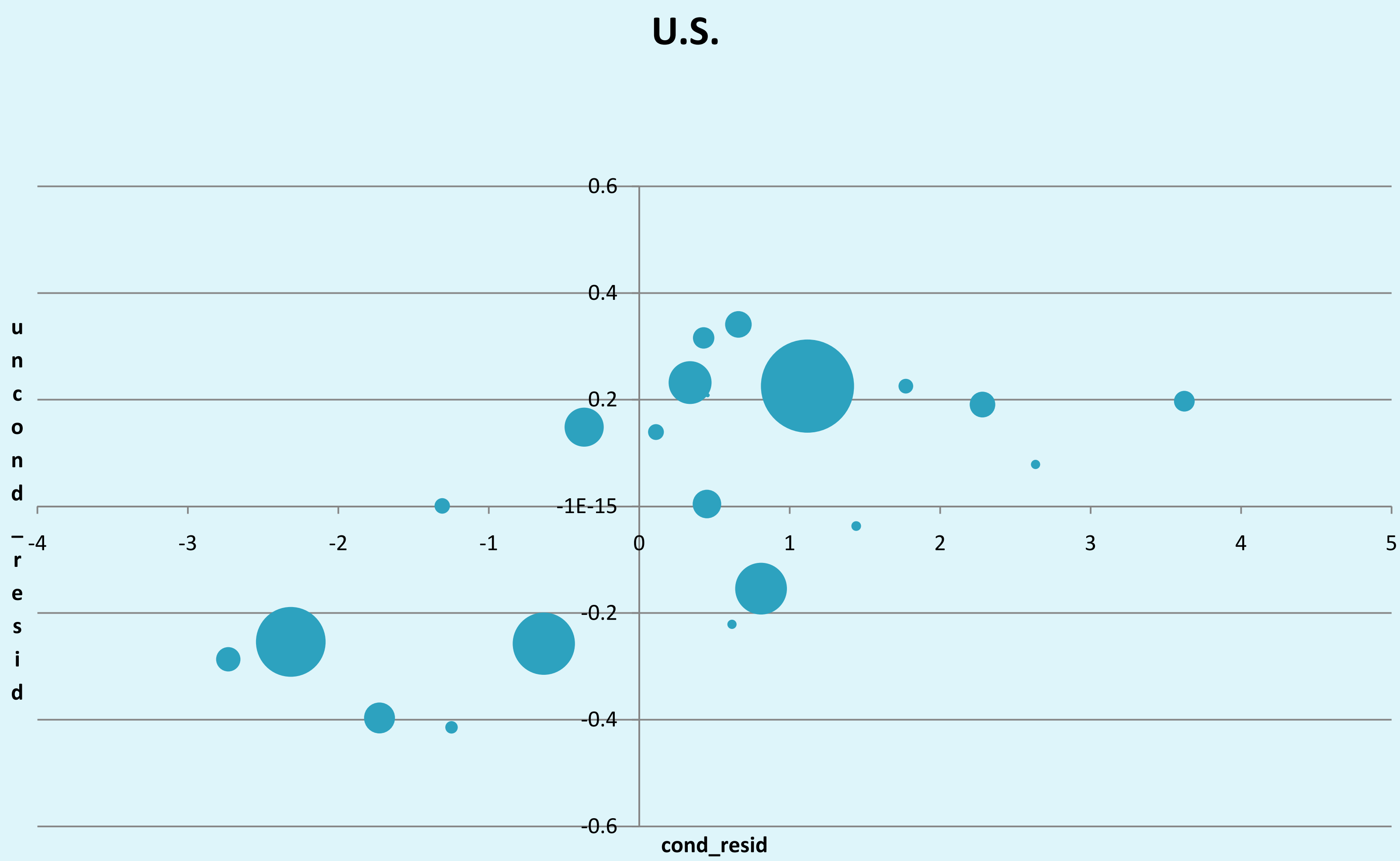
- Welch et al (2000) argued that “while 5-year survival is a perfectly valid measure to compare cancer therapies in a randomized trial, comparisons of 5-year survival rates across time (or place) may be extremely misleading. If cancer patients in the past always had palpable tumors at the time of diagnosis while current cancer patients 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.

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

- Welch et al 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**."

- 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.

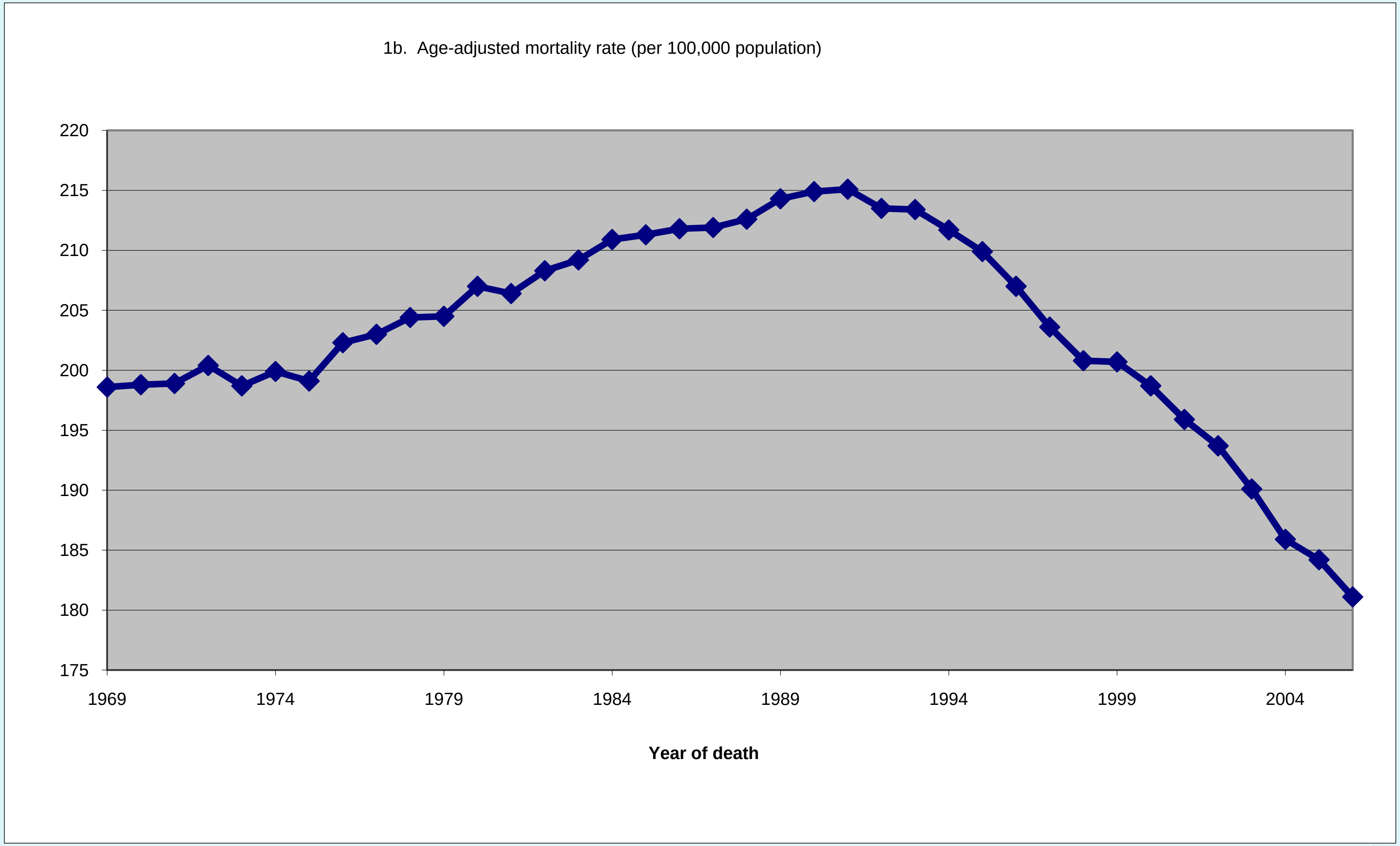
Correlation across cancer sites between growth in unconditional mortality and growth in conditional mortality, controlling for growth in incidence



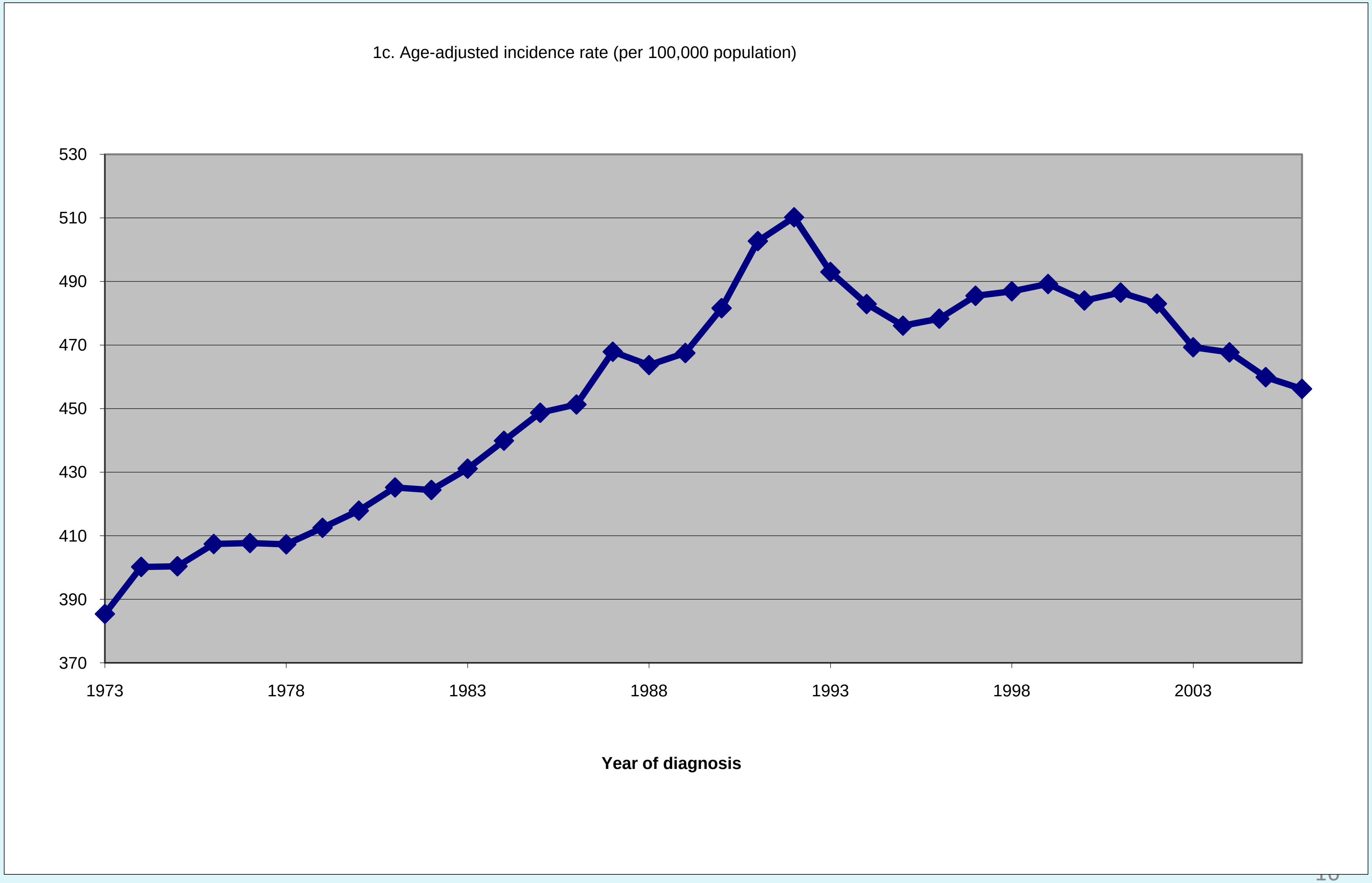
Correlation across cancer sites between growth in unconditional mortality and growth in conditional mortality, controlling for growth in incidence

- 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 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

Cancer mortality rate



Cancer incidence rate



- In this paper, I 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.

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(death from cancer) =

P(death from cancer | cancer diagnosis) * P(cancer diagnosis) +

P(death from cancer | no cancer diagnosis) * (1 – P(cancer diagnosis))

If the probability that a person who has never been diagnosed with cancer dies from cancer is quite small (P(death from cancer | no cancer diagnosis) ≈ 0), which seems plausible, this reduces to

P(death from cancer) ≈

P(death from cancer | cancer diagnosis) * P(cancer diagnosis)

Hence

ln P(death from cancer) ≈
ln P(death from cancer | cancer diagnosis) + ln P(cancer diagnosis) (3)

I hypothesize that the conditional mortality rate (P(death from cancer | cancer diagnosis)) depends (inversely) upon the average quality of imaging and pharmaceutical procedures:

ln P(death from cancer | cancer diagnosis) =
β_1 image_quality + β_2 drug_quality (4)

Substituting (4) into (3),

ln P(death from cancer) ≈
β_1 image_quality + β_2 drug_quality + ln P(cancer diagnosis) (5)

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

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

where

$mort\_rate_{st}$ = the age-adjusted mortality rate from cancer at site s (s = 1,…, 60) in year t (t=1991,…,2006)

$adv\_imag\%_{s,t-k}$ = advanced imaging procedures as % of total imaging procedures associated with cancer at site s in year t-k (k=0,1,…)

$new\_drug\%_{s,t-k}$ = "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,…)

$inc\_rate_{s,t-k}$ = 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 cancer sites that have had above-average increases in adv_imag% had above-average reductions in the age-adjusted mortality rate, then $\beta_1 < 0$ in eq. (6).
- Eq. (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.

Imaging procedure innovation measure

$$adv\_imag\%_{st} = \frac{\Sigma_p\ n\_proc_{pst}\ adv_p}{\Sigma_p\ n\_proc_{pst}}$$

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

Drug procedure innovation measure

$$new\_drug\%_{st} = \frac{\Sigma_p \, n\_proc_{pst} \, post\_year_p}{\Sigma_p \, n\_proc_{pst}}$$

where

n_proc_{pst} = the number of times drug procedure p 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

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

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).
- *Diagnostic imaging innovation.* Data on the number of diagnostic imaging procedures, by CPT code, 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). Each claim in this database includes information about the procedure performed (CPT code), the patient's diagnosis (ICD9 code), and the date of service.
- Advanced imaging procedures involve either a computed tomography (CT) scan or magnetic resonance imaging (MRI).

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	1996	2006	1996	2006	1996	2006	1996	2006	1996	2006
22030	Lung and Bronchus	57.9	51.7	66.4	60.0	10,425	39,897	39%	70%	2,301	######	26%	40%	9%	27%
21040	Colon excluding Rectum	18.7	14.3	39.3	32.9	3,296	22,609	51%	84%	1,635	######	2%	31%	0%	27%
28010	Prostate	18.0	11.8	84.5	81.6	3,132	17,389	46%	74%	636	17,728	3%	35%	1%	26%
26000	Breast	16.8	13.2	73.2	66.4	27,894	93,405	16%	48%	3,836	######	13%	43%	3%	32%

Figure 2
Cancer imaging procedures

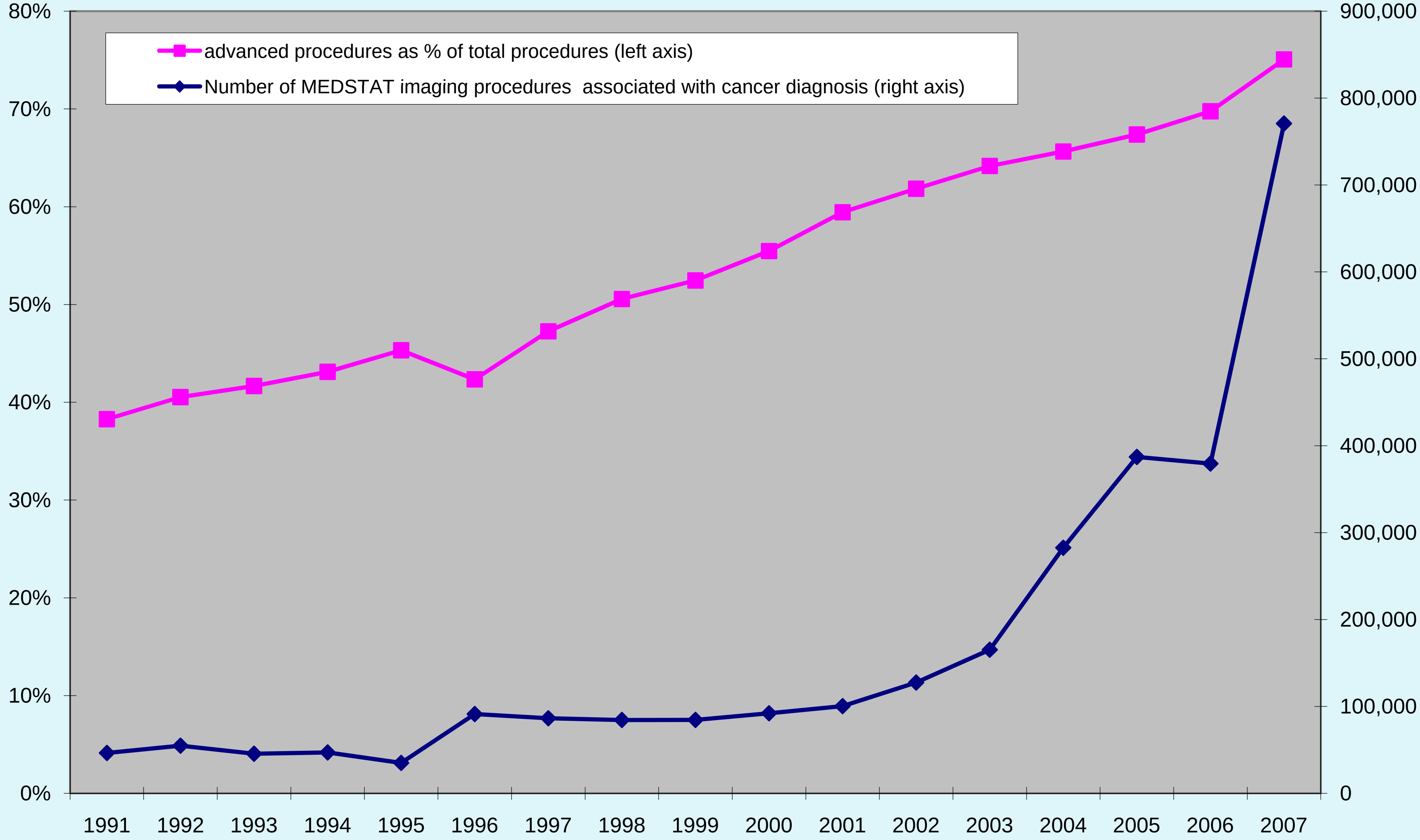


Figure 3
Percent of 1991 and 2007 imaging procedures accounted for by top 15 procedures in 2007

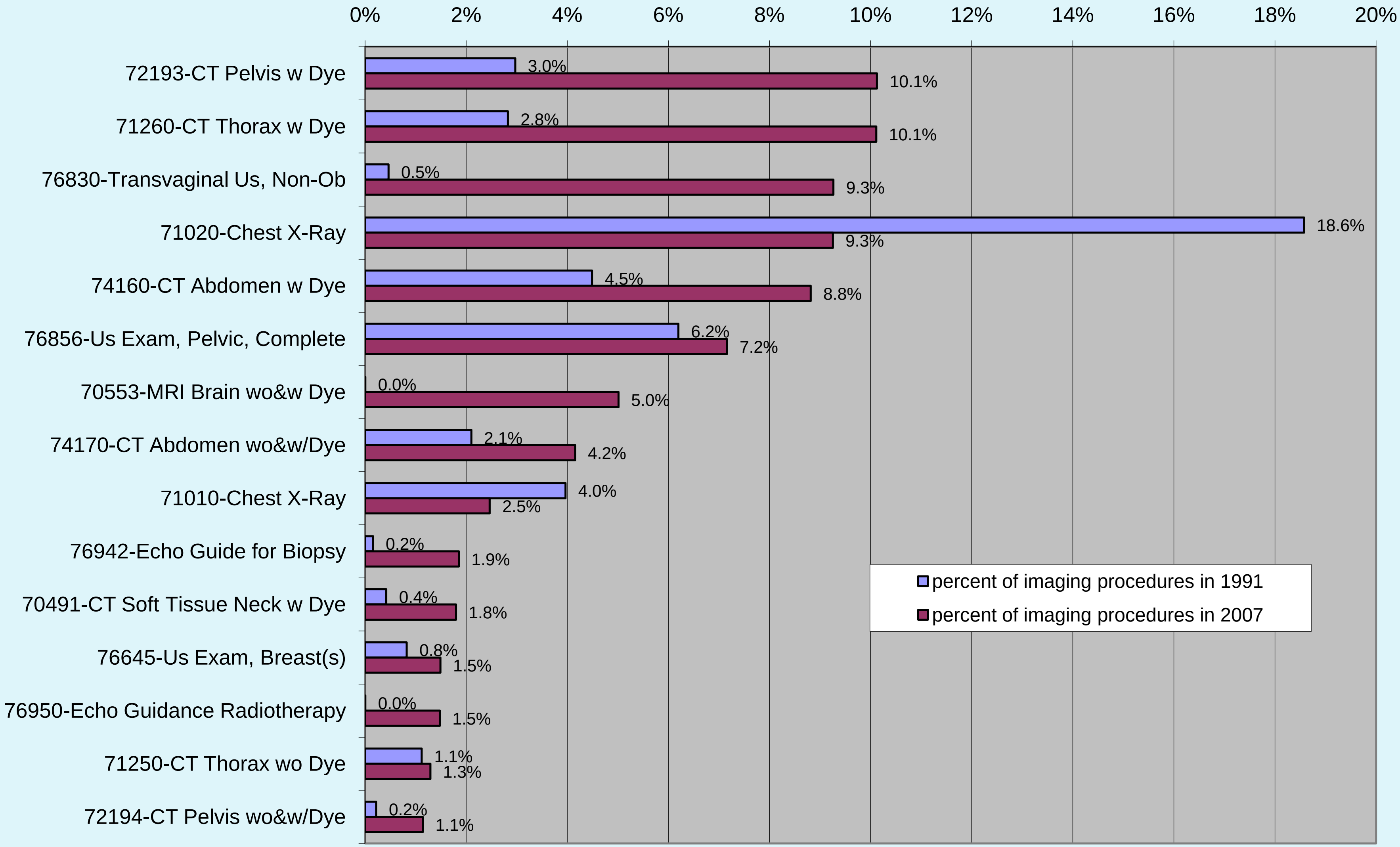


Figure 4
Cancer drug procedures

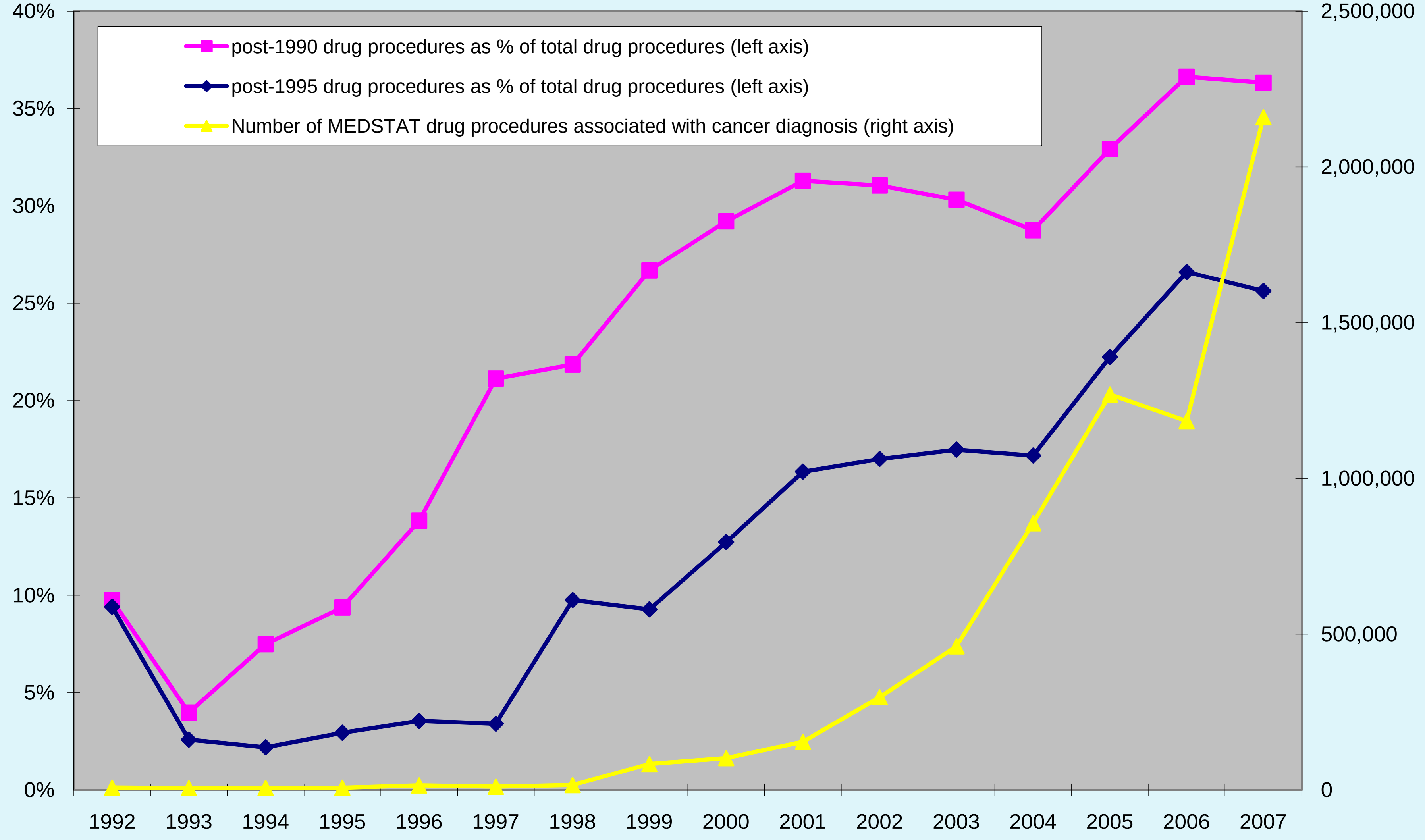


Figure 5
Percent of 1999 and 2007 drug procedures accounted for by top 15 procedures in 2007

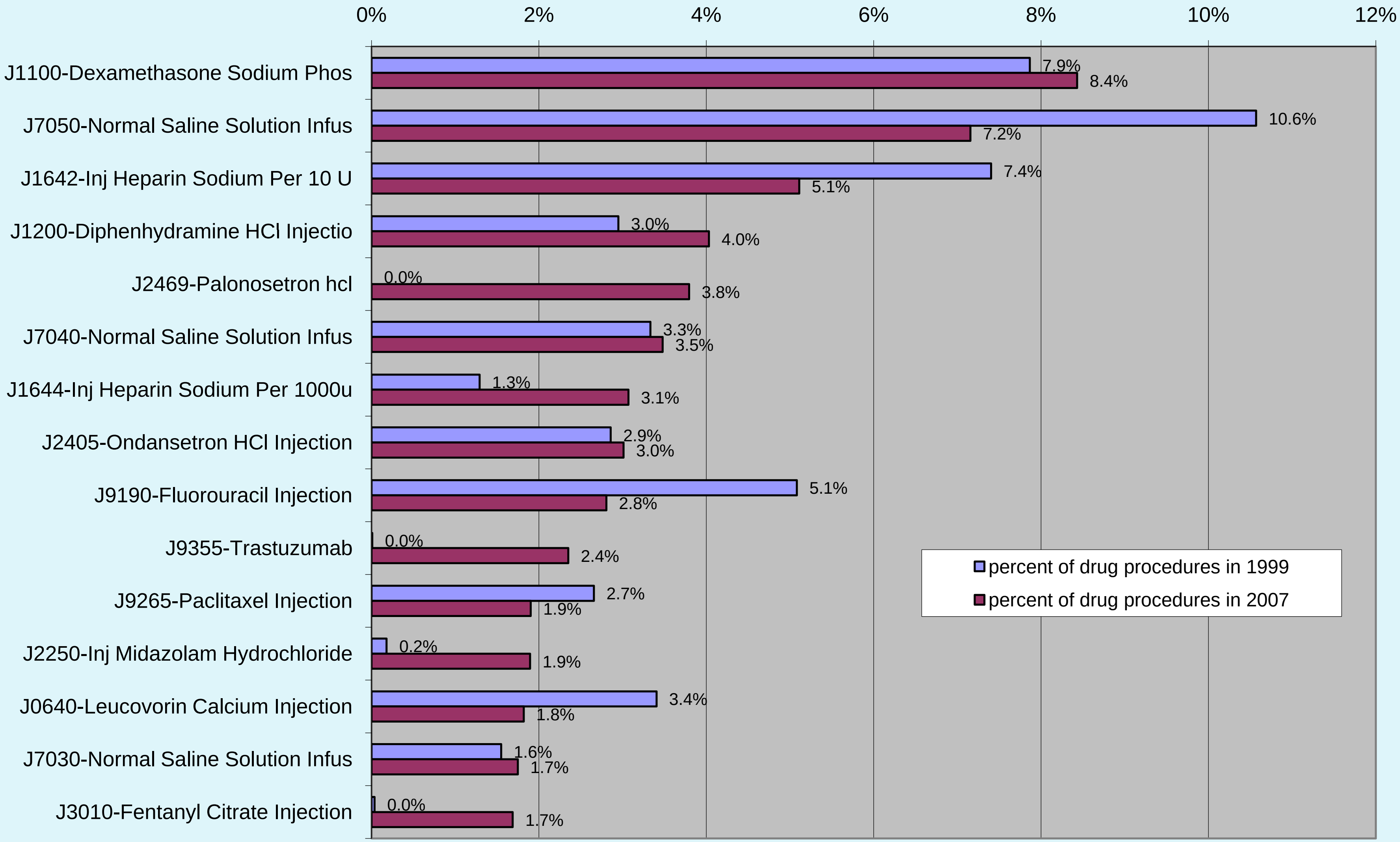


Figure 6
Effect of incidence in year t-k on mortality in year t, k=0,1,…,8

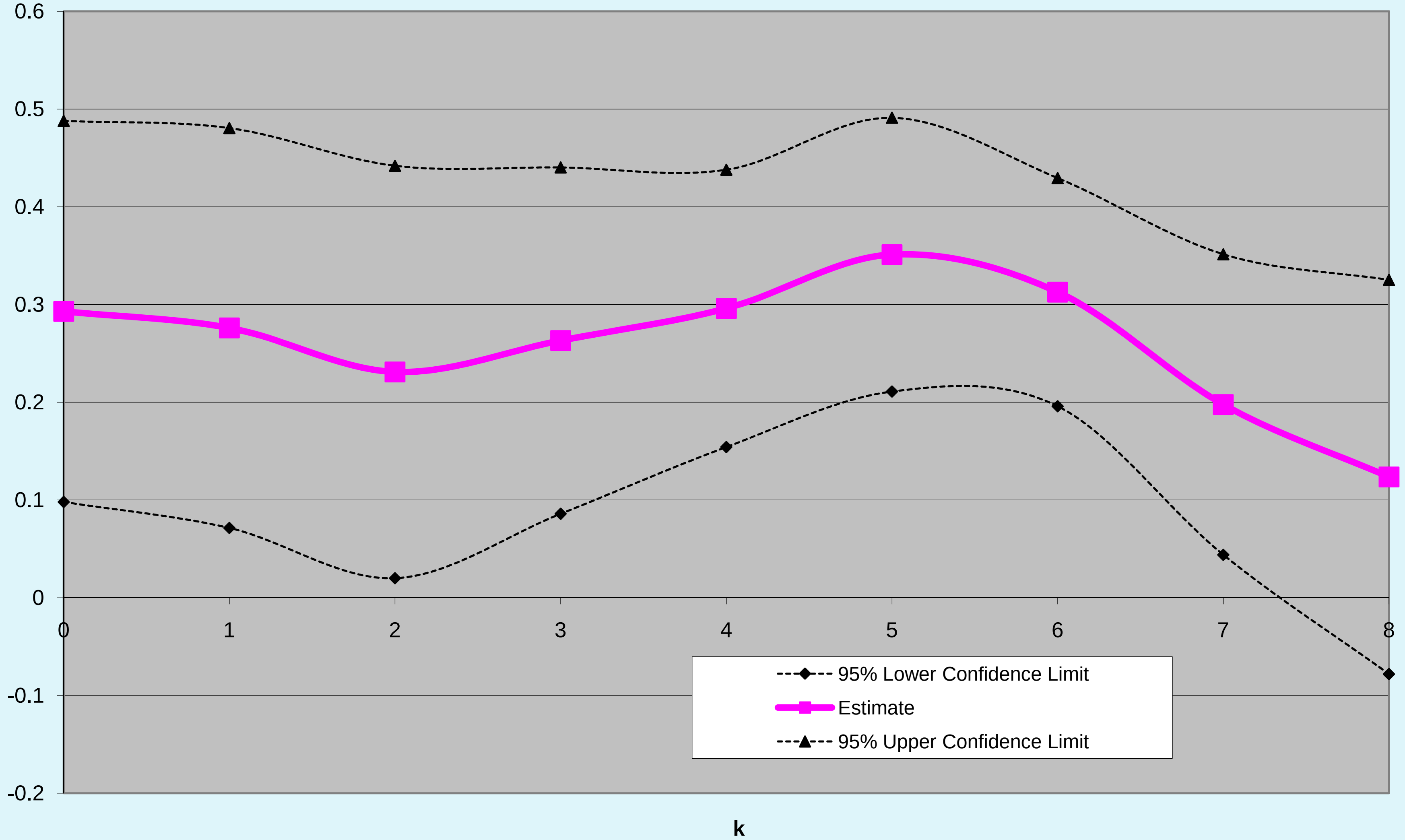


Figure 7
Effect of adv_image% in year t-k on mortality in year t, k=0,1,…,5

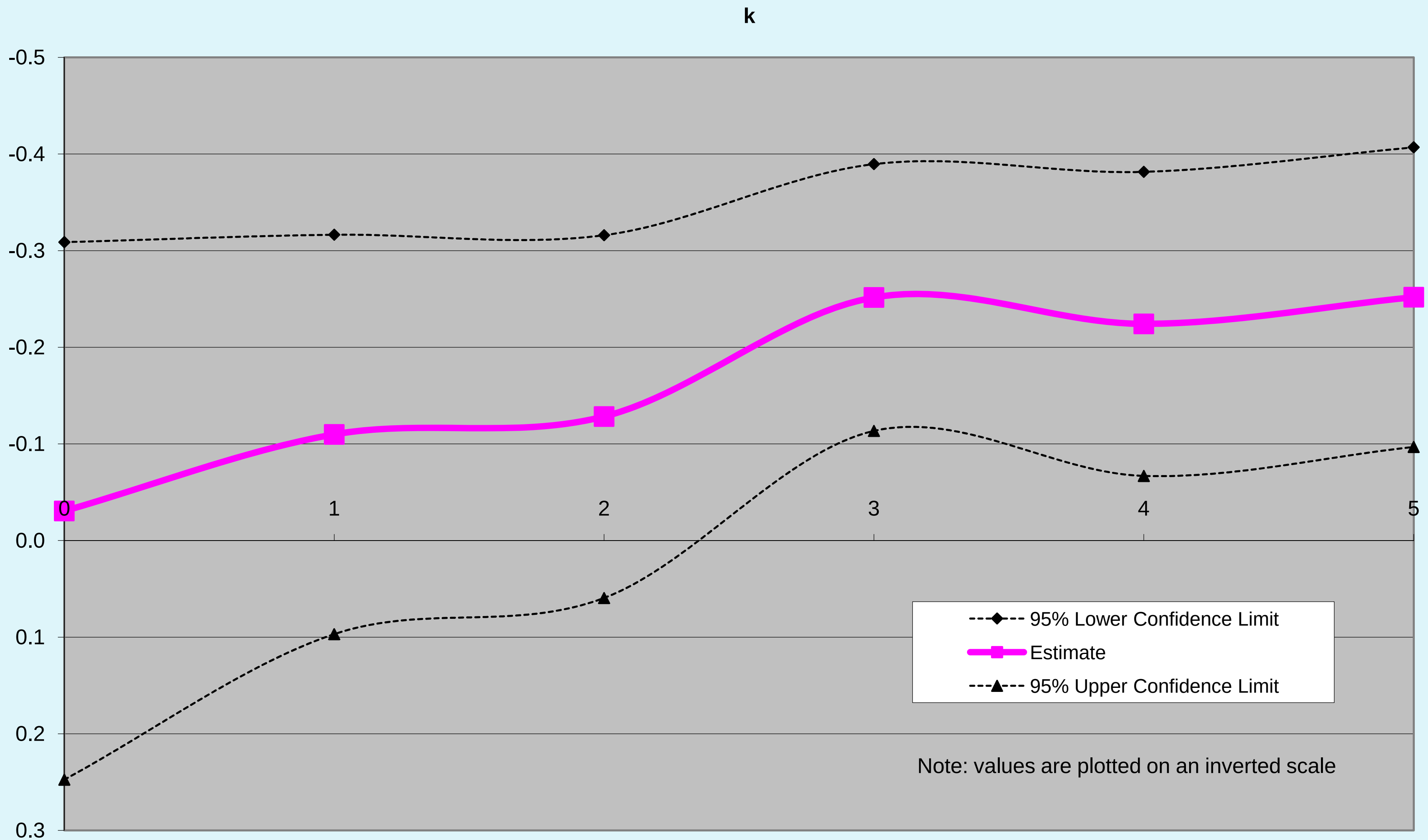


Table 3

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

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%

- A 1 percent reduction in cancer mortality is worth nearly $500 billion.
- Kevin M. Murphy and Robert H. Topel, The Value of Health and Longevity**,** *Journal of Political Economy*, 2006, vol. 114, no. 5

Impact on U.S. life expectancy

- 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.
- 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 months (= (9% + 6%) * 1.6 years) between 1996 and 2006 by the combined effects of cancer imaging and cancer drug innovation.