How cost-effective are new cancer drugs in the U.S.?

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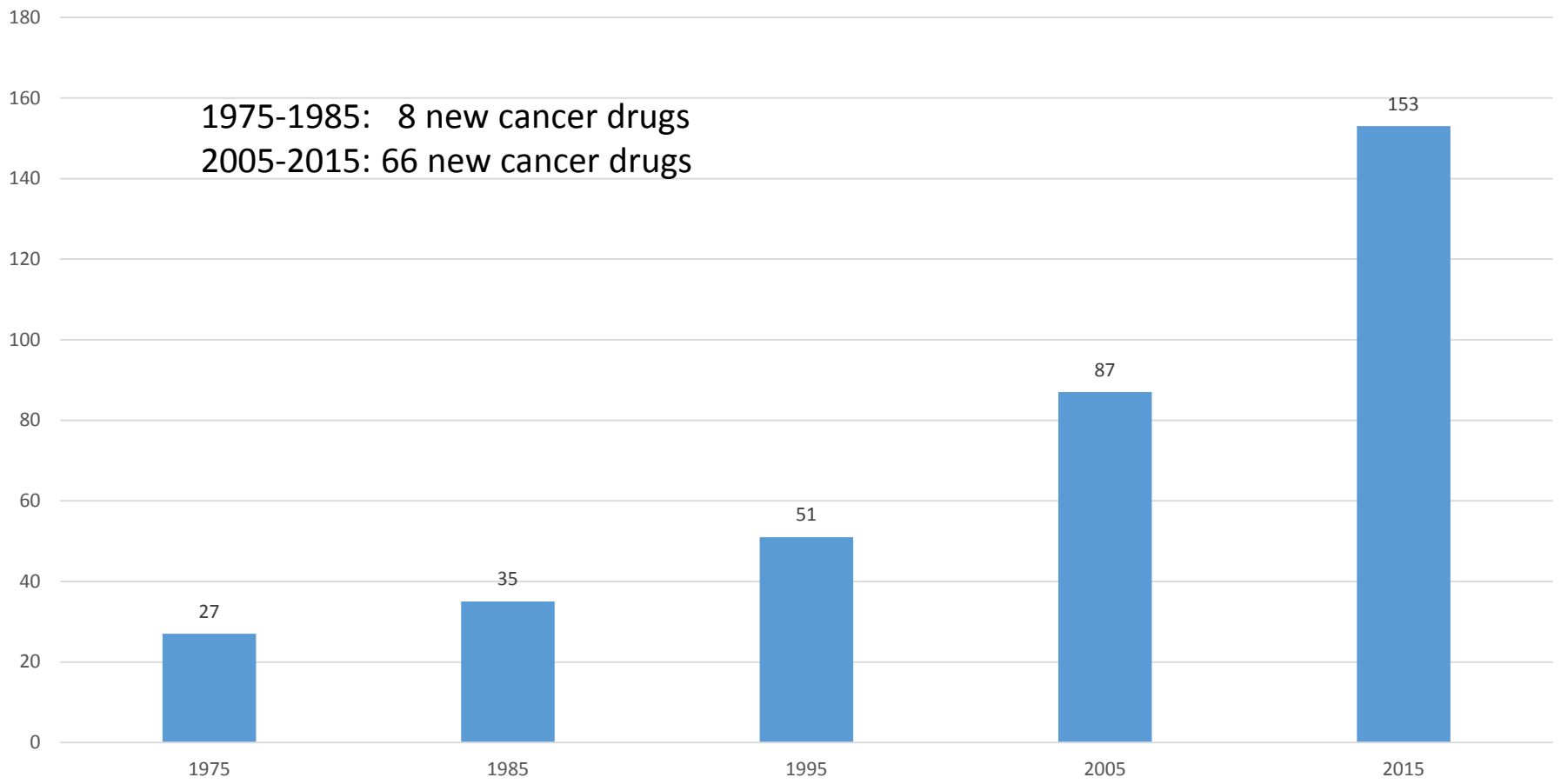
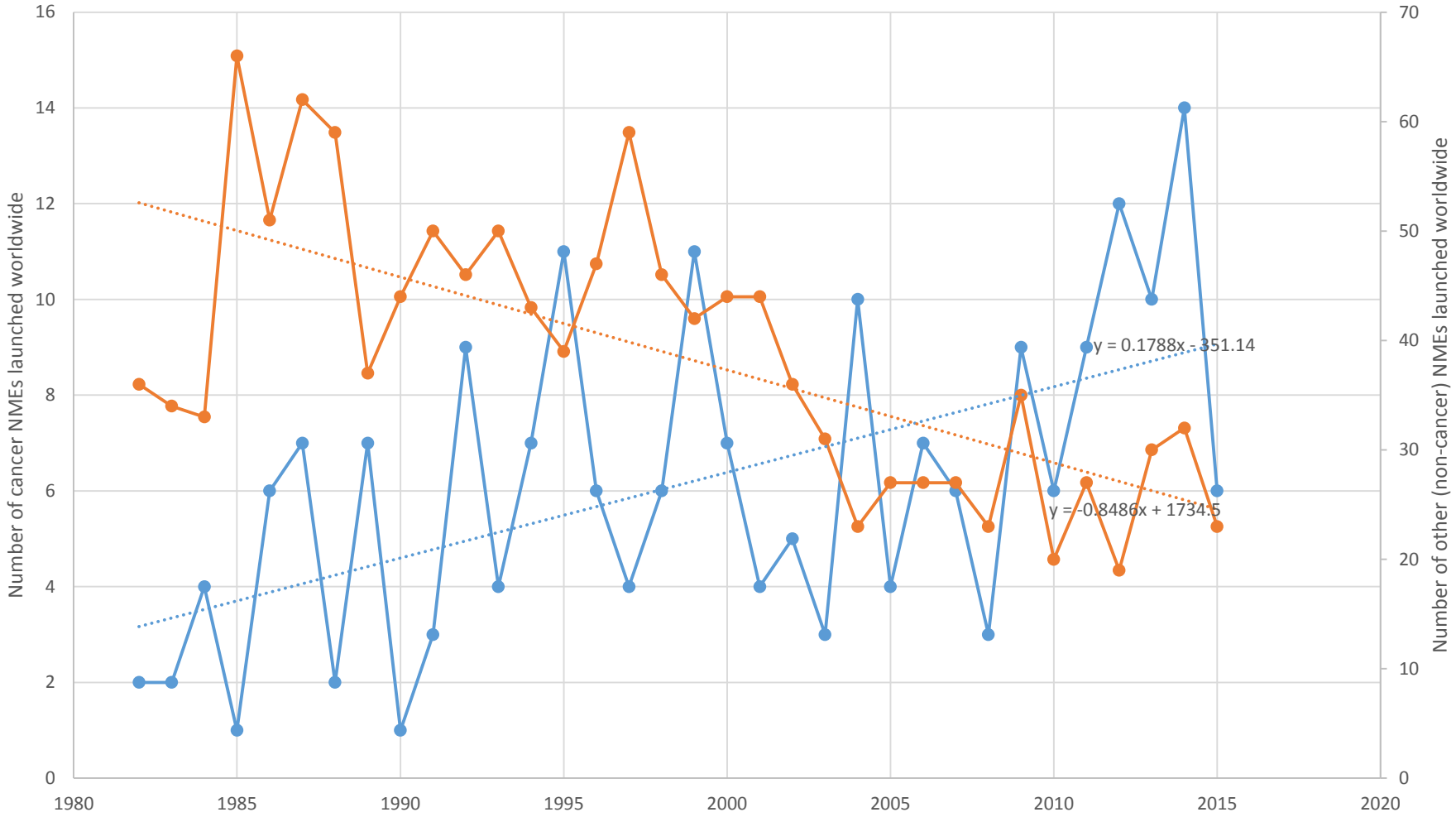
Number of drugs used to treat cancer ever approved by the FDA



Source: Author's calculations based on National Cancer Institute and FDA data:
http://www.cancer.gov/about-cancer/treatment/drugs/cancer-type
http://www.fda.gov/Drugs/InformationOnDrugs/ucm135821.htm

Number of cancer and other new molecular entities launched worldwide, 1982-2015



Source: author's calculations based on IMS Health New Product Focus database
"Cancer NMEs" are NMEs in EphMRA/PBIRG Anatomical Classification L (ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS)

“Historically, NCI [the National Cancer Institute] has played a vital role in cancer drug discovery and development, and, today, that role continues. Frequently, NCI’s drug development efforts focus on unmet needs that are not being adequately addressed by the private sector.”

National Cancer Institute, Enhancing Drug Discovery and Development

US sales of top cancer drugs ($ millions)

Molecule	2010	2011	2012	2013	2014	Change
Total	**21,385**	**22,413**	**23,299**	**24,942**	**28,971**	**7,586**
RITUXIMAB	2,673	2,879	3,037	3,199	3,351	679
BEVACIZUMAB	2,993	2,581	2,543	2,618	2,790	-203
IMATINIB	1,363	1,560	1,674	1,872	2,333	970
DENOSUMAB	27	478	932	1,229	1,552	1,525
ABIRATERONE ACETATE	0	174	454	767	1,010	1,010
LENALIDOMIDE	311	431	537	528	974	663
EVEROLIMUS	108	182	426	714	841	733
DASATINIB	185	291	380	549	725	540
LEUPRORELIN	631	650	639	651	692	62
IPILIMUMAB	0	339	507	541	687	687

Source: IMS Health.
Average annual growth rate of total expenditure = 7.6%

Cost-effectiveness analysis

- Cost-effectiveness is typically expressed as an **incremental cost-effectiveness ratio (ICER)**, a statistic used to summarize the cost-effectiveness of a health care intervention.
- It is defined by the difference in cost between two possible interventions, divided by the difference in their effect:

$$\text{ICER} = \frac{\Delta C}{\Delta E} = \frac{(C_1 - C_0)}{(E_1 - E_0)}$$

where C_1 and E_1 are the cost and effect in the intervention group and where C_0 and E_0 are the cost and effect in the control care group.

- Costs are usually described in monetary units, while effects can be measured in terms of health status or another outcome of interest.
- A common application of the ICER is in cost-utility analysis, in which case the ICER is synonymous with the cost per quality-adjusted life year (QALY) gained.
- ΔE = clinical effectiveness

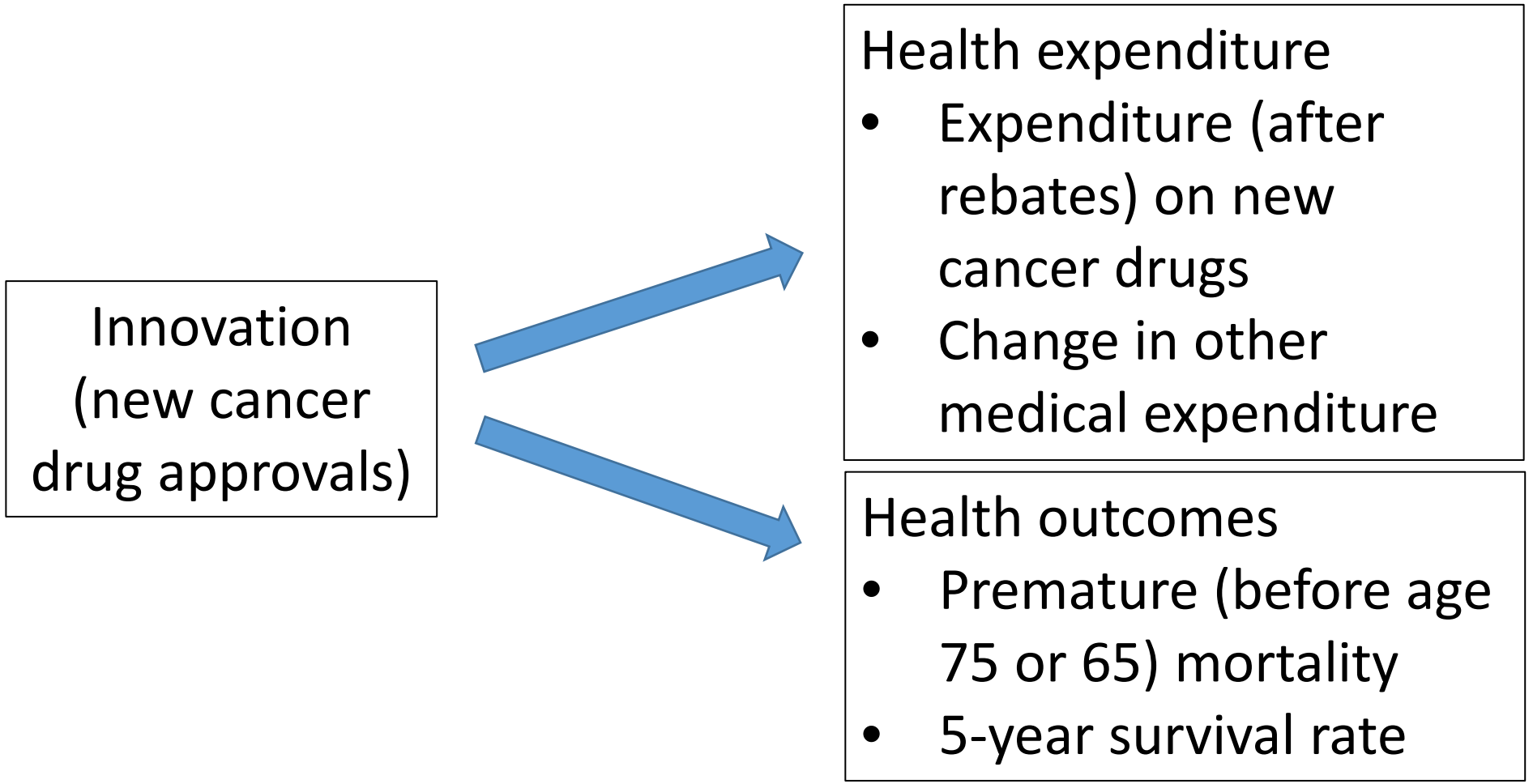
$$\text{ICER} = \frac{(C_1 - C_0)}{(E_1 - E_0)} = \frac{\Delta C}{\Delta E} = \frac{\Delta C \,/\, \Delta \text{CUM\_NCE}}{\Delta E \,/\, \Delta \text{CUM\_NCE}}$$

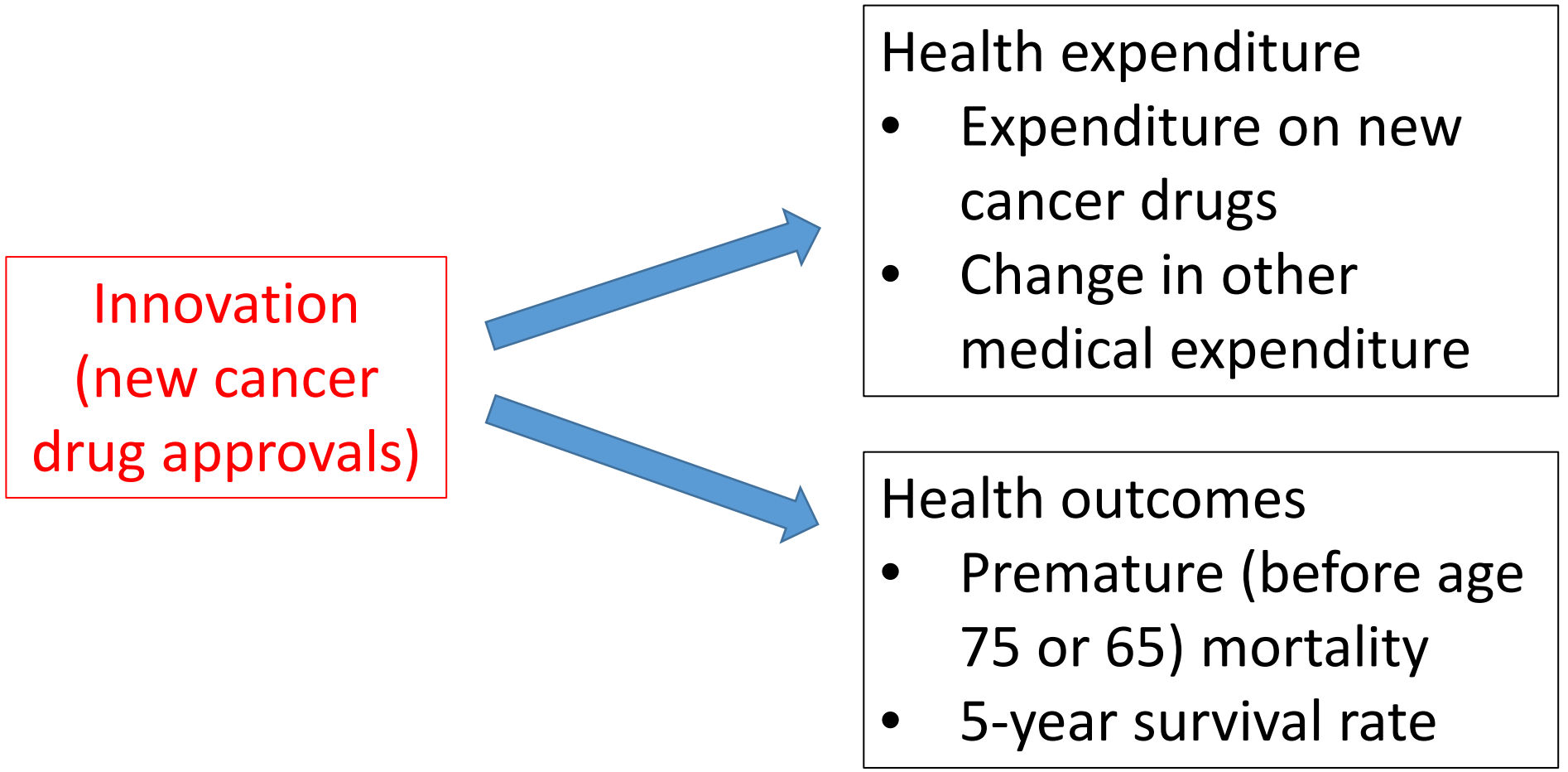
ΔCUM_NCE = increase in number of drugs ever approved

ΔCUM_NCE as an instrument; similar to medical malpractice reform as an instrument in Kessler and McClellan, Do Doctors Practice Defensive Medicine?

Numerator: effect of innovation on treatment cost
Denominator: effect of innovation on treatment outcomes

Analyze these in reverse order: first estimate effect of innovation on treatment outcomes


Innovation (new cancer drug approvals)
Health expenditure
• Expenditure (after rebates) on new cancer drugs
• Change in other medical expenditure
Health outcomes
• Premature (before age 75 or 65) mortality
• 5-year survival rate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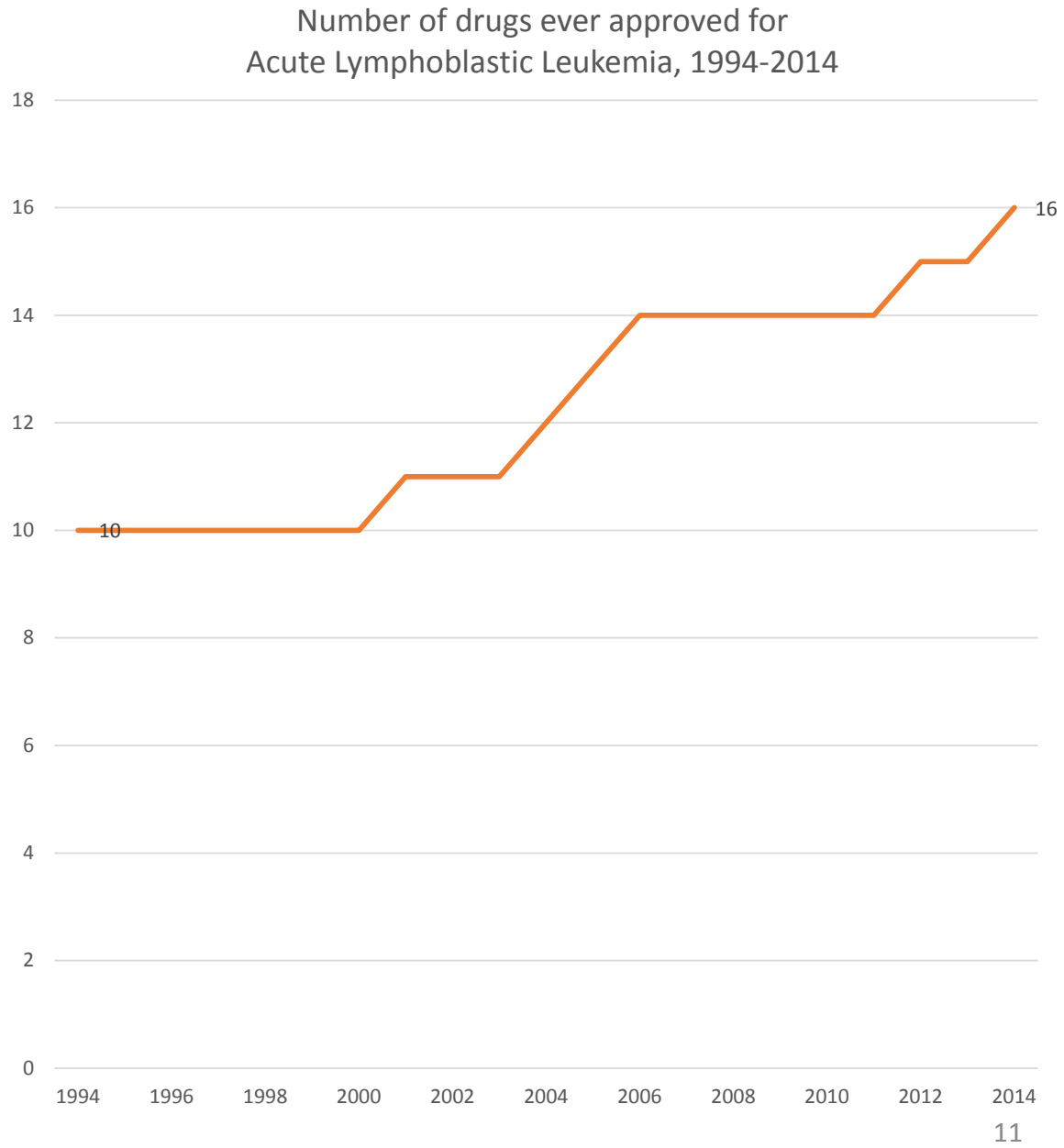
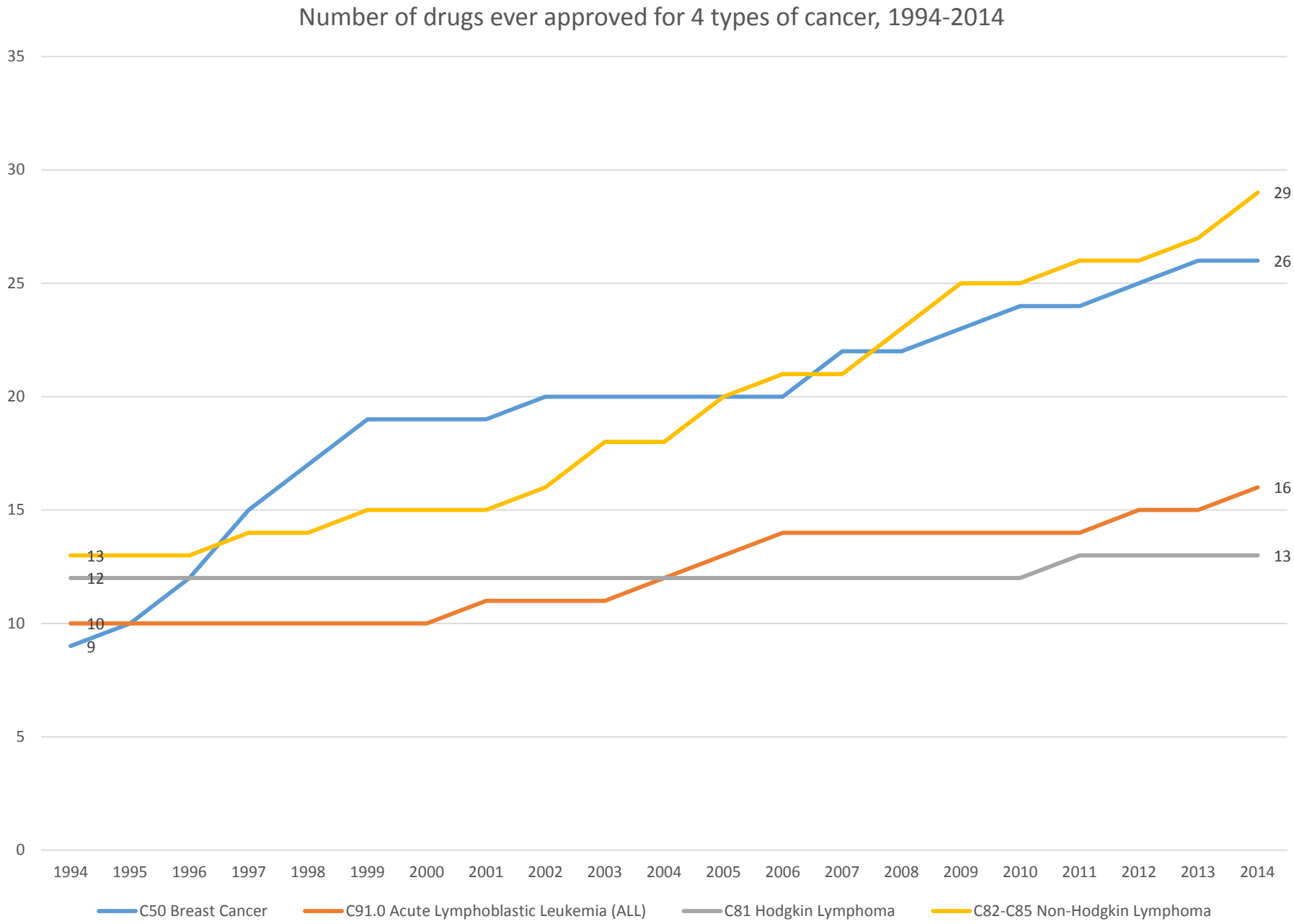
National Cancer Institute: Drugs Approved for Different Types of Cancer

Drugs approved for Acute Lymphoblastic Leukemia

MERCAPTOPURINE	1953
METHOTREXATE SODIUM	1953
PREDNISONE	1955
CYCLOPHOSPHAMIDE	1959
VINCRISTINE SULFATE	1963
CYTARABINE	1969
DOXORUBICIN HYDROCHLORIDE	1974
DAUNORUBICIN HYDROCHLORIDE	1979
ASPARAGINASE	1994
PEGASPARGASE	1994
IMATINIB MESYLATE	2001
CLOFARABINE	2004
NELARABINE	2005
DASATINIB	2006
PONATINIB HYDROCHLORIDE	2012
BLINATUMOMAB	2014




Number of drugs ever approved for 4 types of cancer, 1994-2014
35
30
25
20
15
10
5
0
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
29
26
16
13
13
12
10
9
C50 Breast Cancer
C91.0 Acute Lymphoblastic Leukemia (ALL)
C81 Hodgkin Lymphoma
C82-C85 Non-Hodgkin Lymphoma

Prior to approval, each drug marketed in the United States must go through a detailed FDA review process. In 1992, under the Prescription Drug User Act (PDUFA), FDA agreed to specific goals for improving the drug review time and created a **two-tiered system of review times – *Standard Review* and *Priority Review*.** A Priority Review designation means FDA's goal is to take action on an application within 6 months (compared to 10 months under standard review).

A ***Priority Review* designation** will direct overall attention and resources to the evaluation of applications **for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.**

Significant improvement may be demonstrated by the following examples:

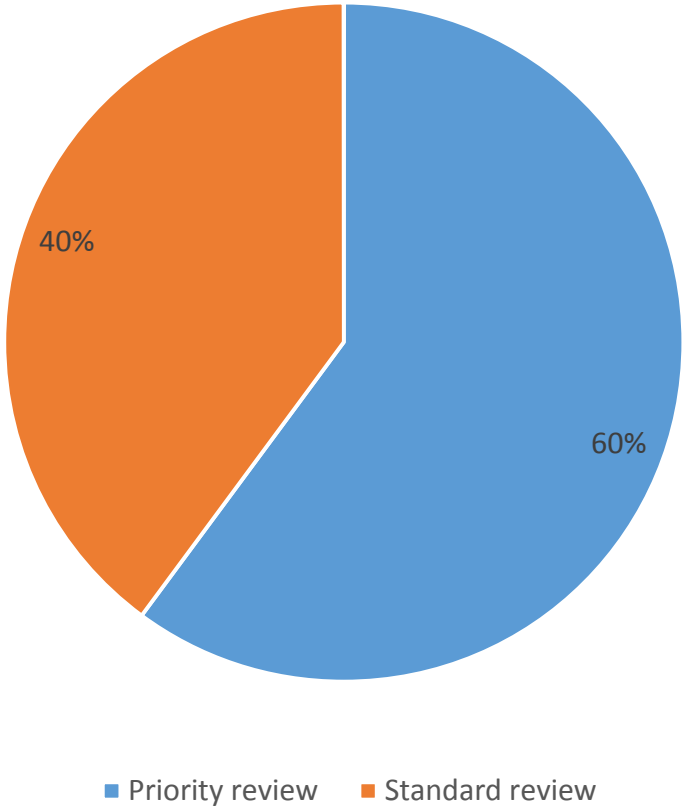
-- evidence of increased effectiveness in treatment, prevention, or diagnosis of condition;

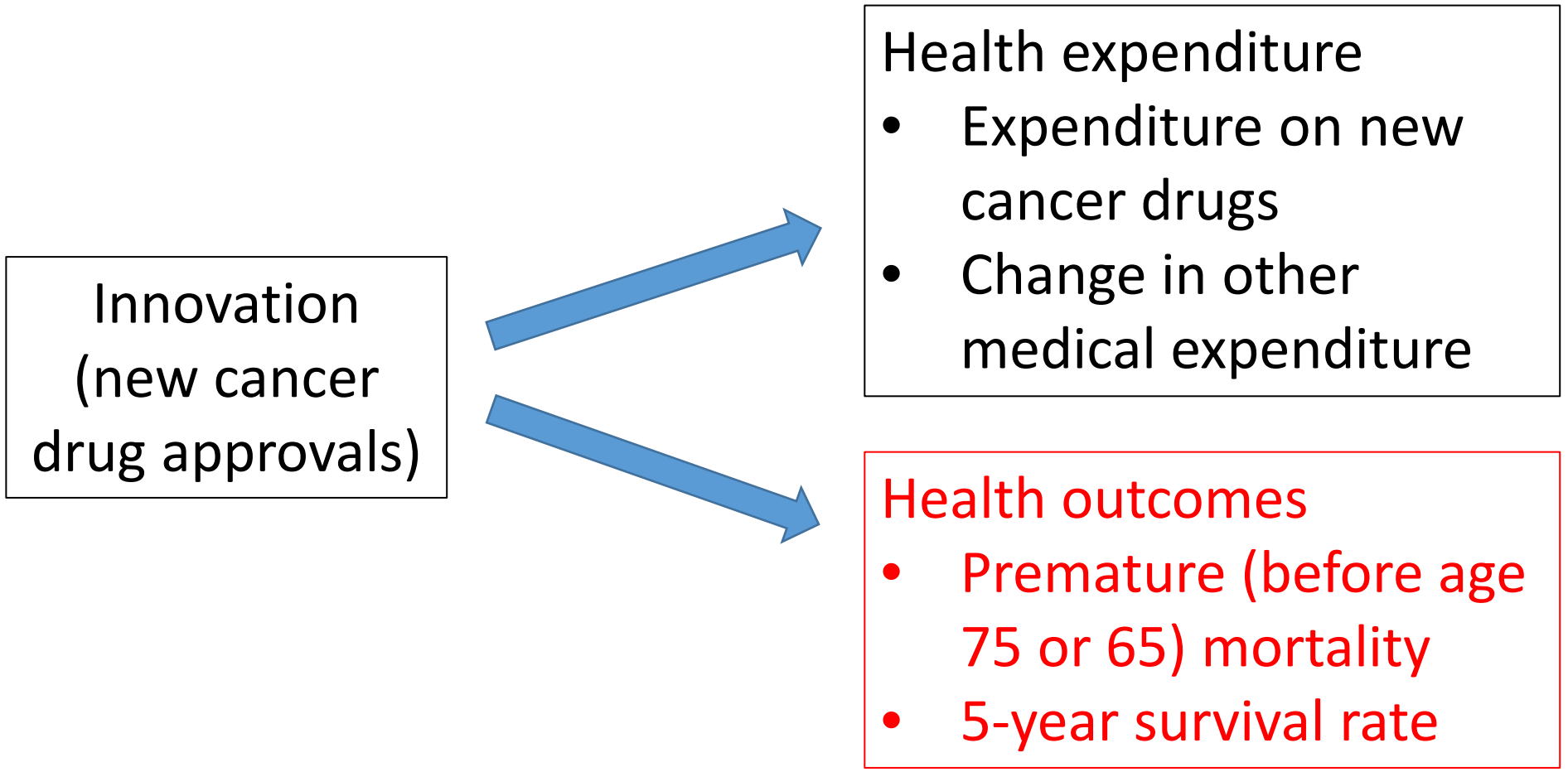
-- elimination or substantial reduction of a treatment-limiting drug reaction;

-- documented enhancement of patient compliance that is expected to lead to an improvement in serious outcomes; or

-- evidence of safety and effectiveness in a new subpopulation.

http://www.fda.gov/ForPatients/Approvals/Fast/ucm405405.htm




Innovation (new cancer drug approvals)
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Effect of innovation on 2 alternative measures of treatment outcomes

Years of potential life lost before age 75

- Not conditional on diagnosis
- "Contemporaneous"
- Patients below age 75
- Control for:
  - Mean age at diagnosis
  - Number of patients diagnosed
- Can measure cost-effectiveness (cost per life-year gained)

5-year observed survival rate

- Conditional on diagnosis
- "Forward-looking"
- All patients
- Control for:
  - 5-year expected survival rate
  - Number of patients diagnosed
- Cannot measure cost-effectiveness (cost per life-year gained)

Centers for Disease Control and Prevention:
Years of Potential Life Lost (YPLL) Reports, 1999 - 2014

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The New York Times - Brea... | Fast Track, Breakthrough T... | WISQARS YPLL Report

webappa.cdc.gov/cgi-bin/broker.exe

ypll

Years of Potential Life Lost (YPLL) Before Age 75

2014 United States
All Races, Both Sexes
All Deaths

Cause of Death	YPLL	Percent
All Causes	20,700,873	100.0%
Malignant Neoplasms	4,416,968	21.3%
Unintentional Injury	**3,146,798**	**15.2%**
Heart Disease	3,130,959	15.1%
Suicide	**1,206,515**	**5.8%**
Perinatal Period	890,645	4.3%
Homicide	**644,476**	**3.1%**
Chronic Low. Respiratory Disease	596,470	2.9%
Liver Disease	581,980	2.8%
Diabetes Mellitus	562,659	2.7%
Cerebrovascular	519,590	2.5%
All Others	5,003,813	24.2%

Download Results in a Spreadsheet (CSV) File

Terms for Causes of Death

Help with Download

Produced By:	**National Center for Injury Prevention and Control, CDC**
Data Source:	**National Center for Health Statistics (NCHS) Vital Statistics System.**

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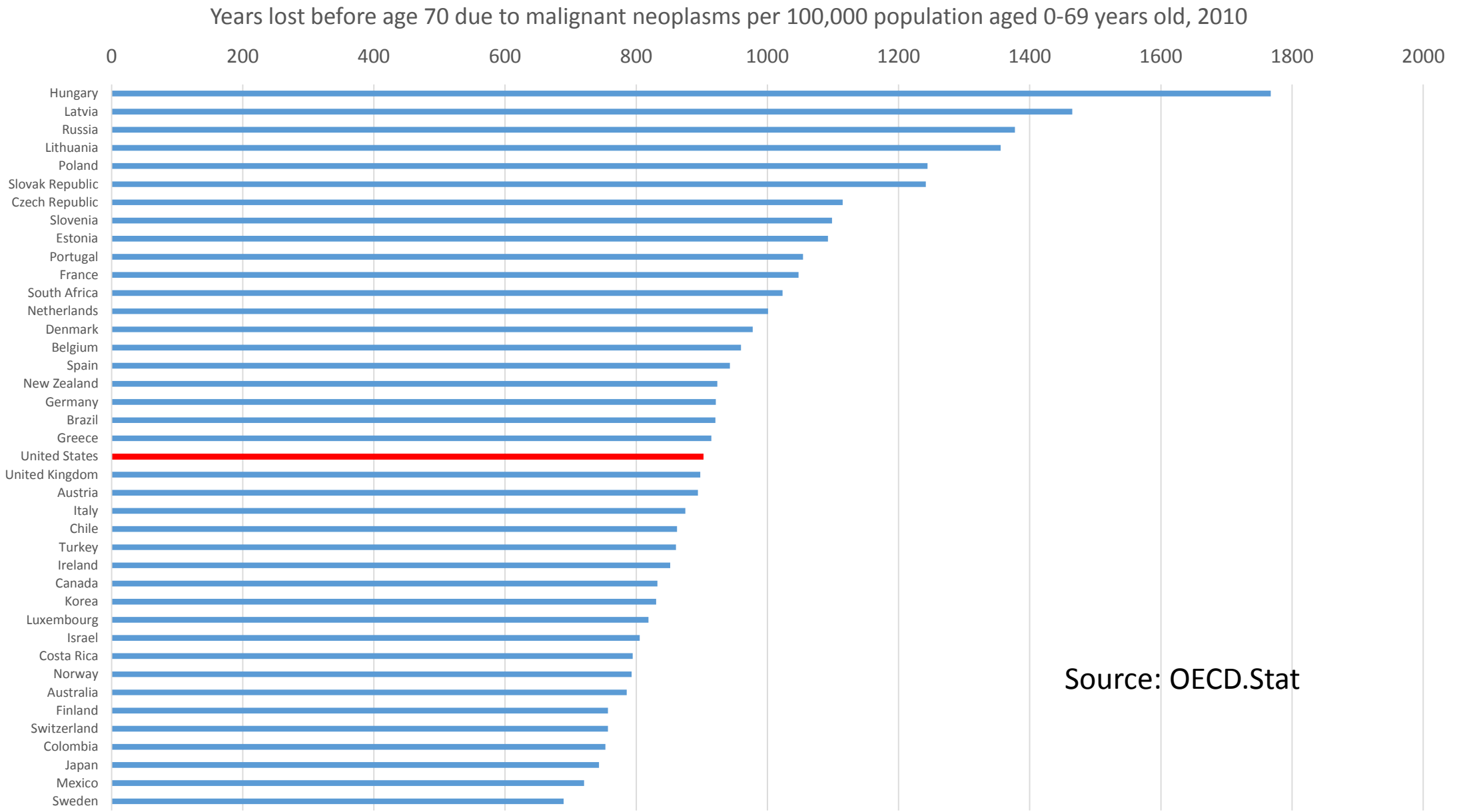


Source: OECD.Stat

The premature (before age 75) cancer mortality rate declined by about 10% between 1999 and 2014,

despite declining competing risk of cardiovascular disease

Year	Years of Potential Life Lost (YPLL) before age 75 due to malignant neoplasms	Population below age 75	Rate per 100,000
1999	4,228,969	256,370,000	1650
2014	4,416,968	299,012,135	1477

Longevity increase is a very important part of economic growth, broadly defined

- Nordhaus (2005) argued that “improvements in health status have been a major contributor to economic welfare over the twentieth century. To a first approximation, the economic value of increases in longevity in the last hundred years is about as large as the value of measured growth in non-health goods and services.”
- The United Nations’ Human Development Index (HDI) is a composite statistic of life expectancy, education, and income per capita indicators, which are used to rank countries into four tiers of human development (United Nations (2016)).

“long-run growth is driven by the discovery of new ideas throughout the world”

- Building on a large collection of previous research by Romer (1990), Grossman and Helpman (1991), Aghion and Howitt (1992), and others, Jones (2002, p. 221) presented a model in which “long-run growth is driven by the discovery of new ideas throughout the world.”
- He postulated an aggregate production function in which total output depends on the total stock of ideas available to this economy as well as on physical and human capital.
- Jones CI (2002). “Sources of U.S. Economic Growth in a World of Ideas,” *American Economic Review* 92 (1): 220-239, March.

Measuring ideas

- In general, measuring the number of ideas is challenging—e.g. because most patents never see the light of day—but due to FDA regulation, measuring pharmaceutical "ideas" is considerably easier than measuring ideas in general.
- The measure of pharmaceutical ideas I will use is the number of new molecular entities approved by the FDA.
- Moreover, the medical substances and devices sector was the most R&D-intensive major industrial sector: almost twice as R&D-intensive as the next-highest sector (information and electronics), and three times as R&D-intensive as the average for all major sectors.
- Since we have precise information about when those ideas reached the market and the diseases to which they apply, we can assess the impact of those ideas on longevity and hospitalization in a difference-in-differences framework.
- I therefore believe that Nordhaus (2005) may have been unduly skeptical when he wrote that "we cannot at this stage attribute the growth in health income to particular investments or expenditures" and that "apply[ing] the techniques of growth accounting to health improvements…is especially challenging."

Fixed-effects model of YPLL75

$$\ln(YPLL75_{s,t}) = \beta\, CUM\_NCE_{s,t} + \gamma \ln(CASES_{s,t-2}) + \pi\, AGE\_DIAG_{s,t-2} + \alpha_s + \delta_t + \varepsilon_{s,t} \qquad (1)$$

$YPLL75_{s,t}$ = years of potential life lost before age 75 from cancer at site s in year t (t = 1999,…,2014)

$CUM\_NCE_{s,t}$ = $\sum_d IND_{d,s}\, APPROVED_{d,t}$ = the number of new chemical entities (drugs) to treat cancer at site s that had been approved by the FDA by the end of year t

$IND_{d,s}$ = 1 if drug d is used to treat (indicated for) cancer at site s

= 0 if drug d is not used to treat (indicated for) cancer at site s

$APPROVED_{d,t}$ = 1 if drug d was approved by the FDA by the end of year t

= 0 if drug d was not approved by the FDA by the end of year t

$CASES_{s,t-2}$ = the number of new cases of cancer at site s diagnosed in year t-2

$AGE\_DIAG_{s,t-2}$ = the mean age at which people who were diagnosed with cancer at site s in year t-2 were diagnosed

α_s = a fixed effect for cancer at site s

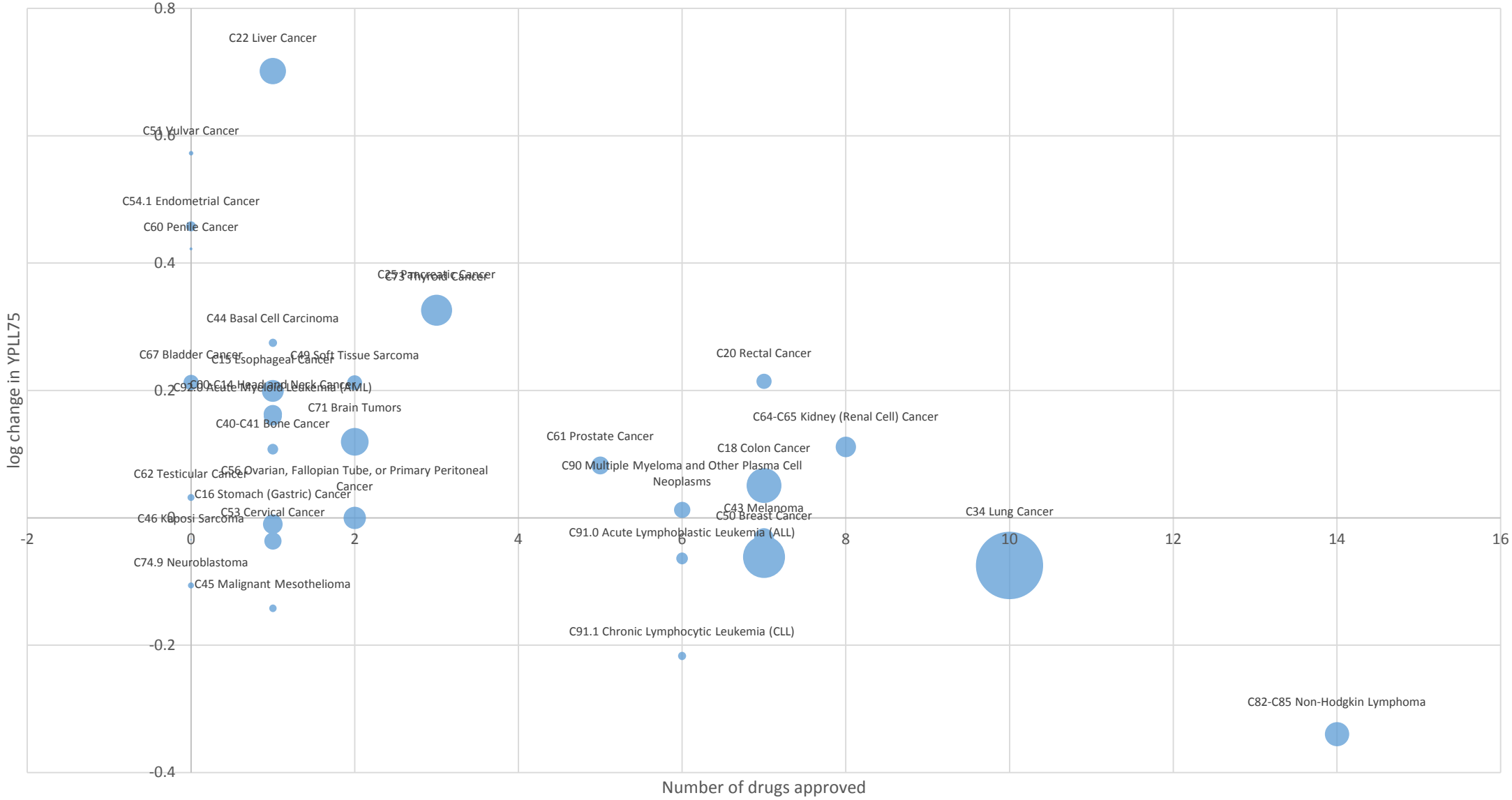
δ_t = a fixed effect for year t

(Simplified) long-difference model

$$\ln(YPLL75_{s,2014}) - \ln(YPLL75_{s,1999}) = \beta\,(CUM\_NCE_{s,2014} - CUM\_NCE_{s,1999}) + (\delta_{2014} - \delta_{1999}) + (\varepsilon_{s,2014} - \varepsilon_{s,1999}) \quad (2)$$

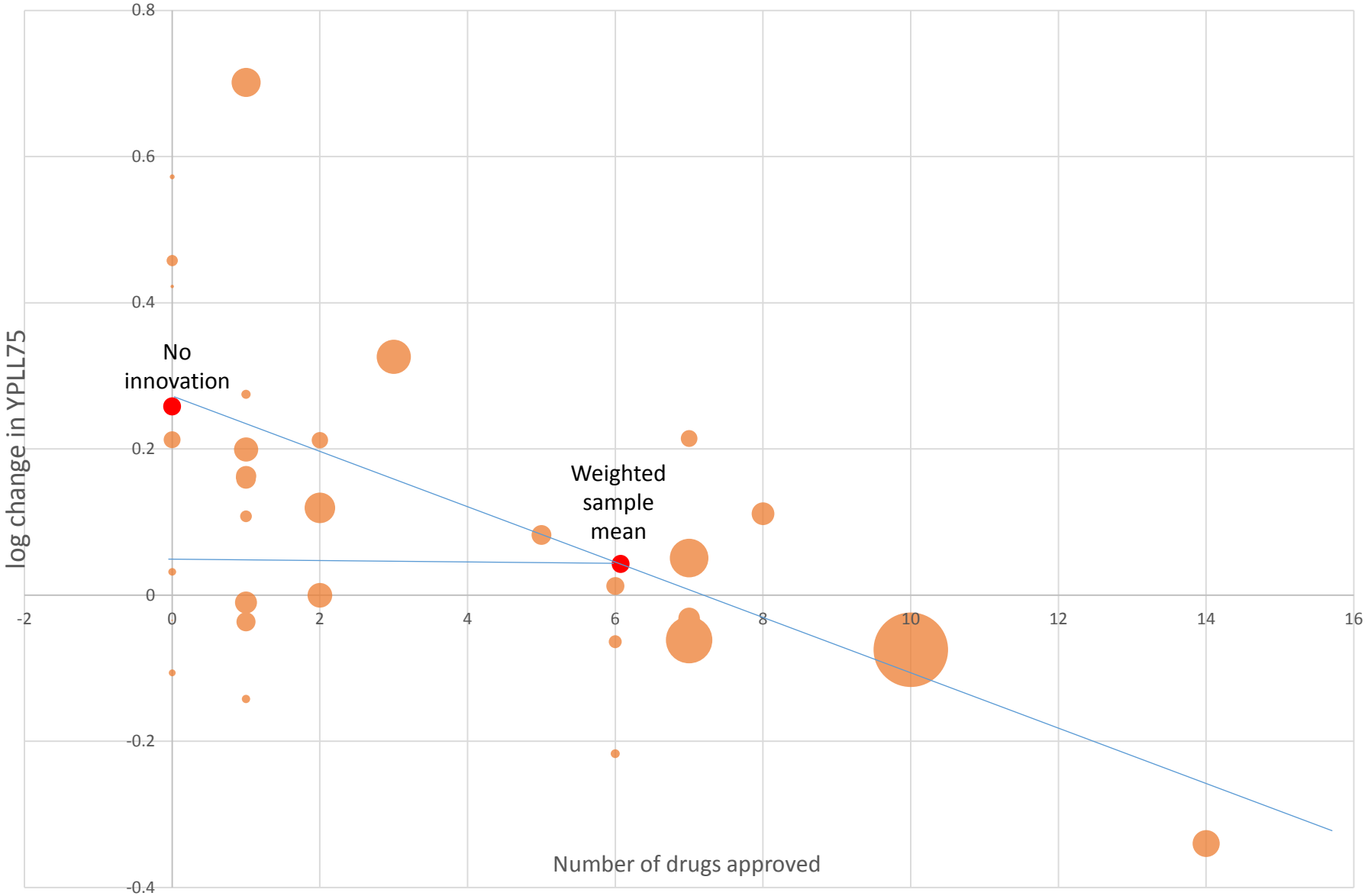
$CUM\_NCE_{s,2014} - CUM\_NCE_{s,1999}$ = the number of new drugs for the treatment of cancer at site s approved between 1999 and 2014.

Correlation across cancer sites between number of drugs approved during 1999-2014 and log change in years of potential life lost before age 75 (YPLL75)

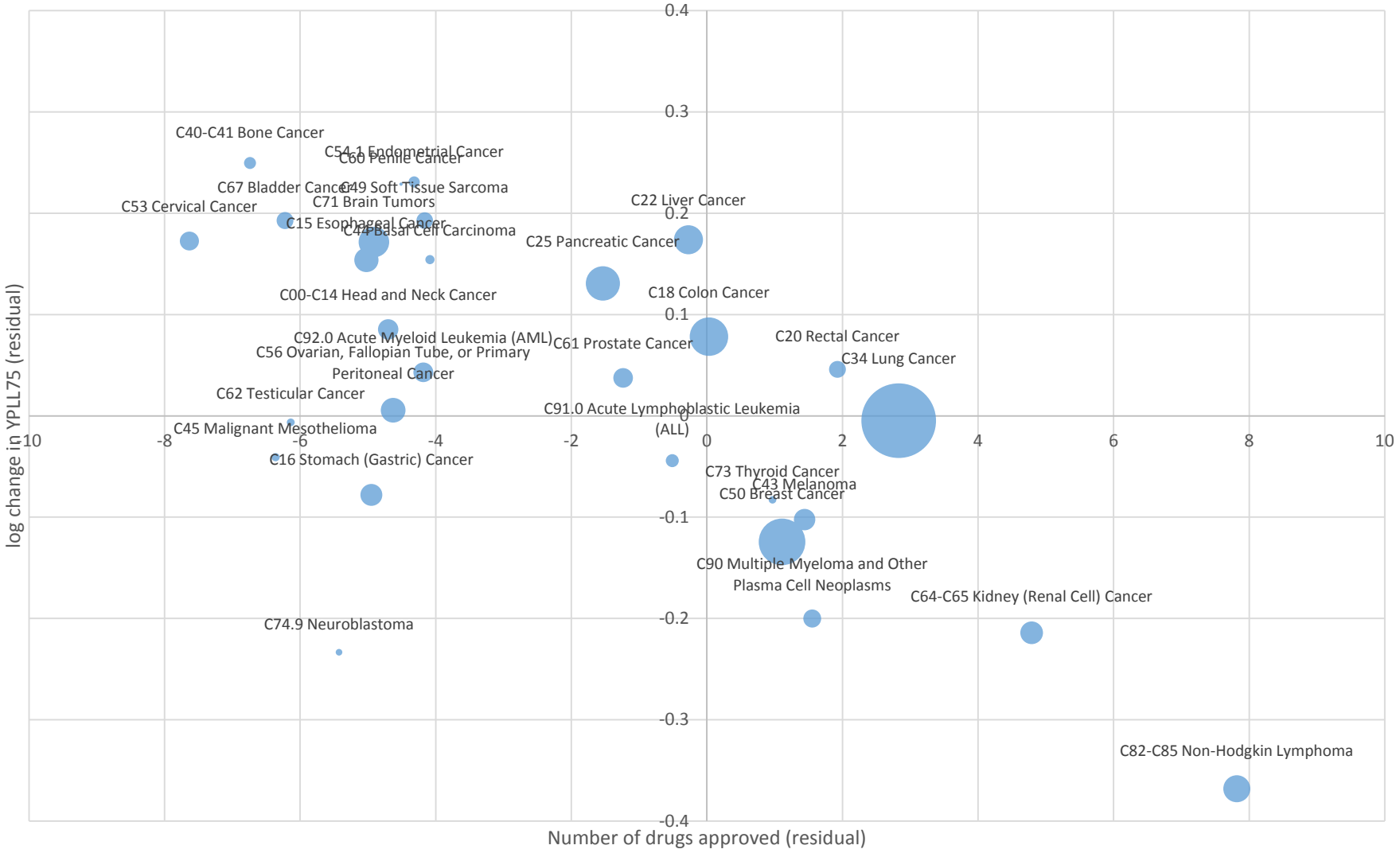


Note: bubble size is proportional to mean level of premature mortality

Correlation across cancer sites between number of drugs approved during 1999-2014 and log change in years of potential life lost before age 75 (YPLL75)



Correlation across cancer sites between number of drugs approved during 1999-2014 and log change in years of potential life lost before age 75 (YPLL75), **controlling for change in incidence and mean age at diagnosis**



More- vs. less-recent approvals

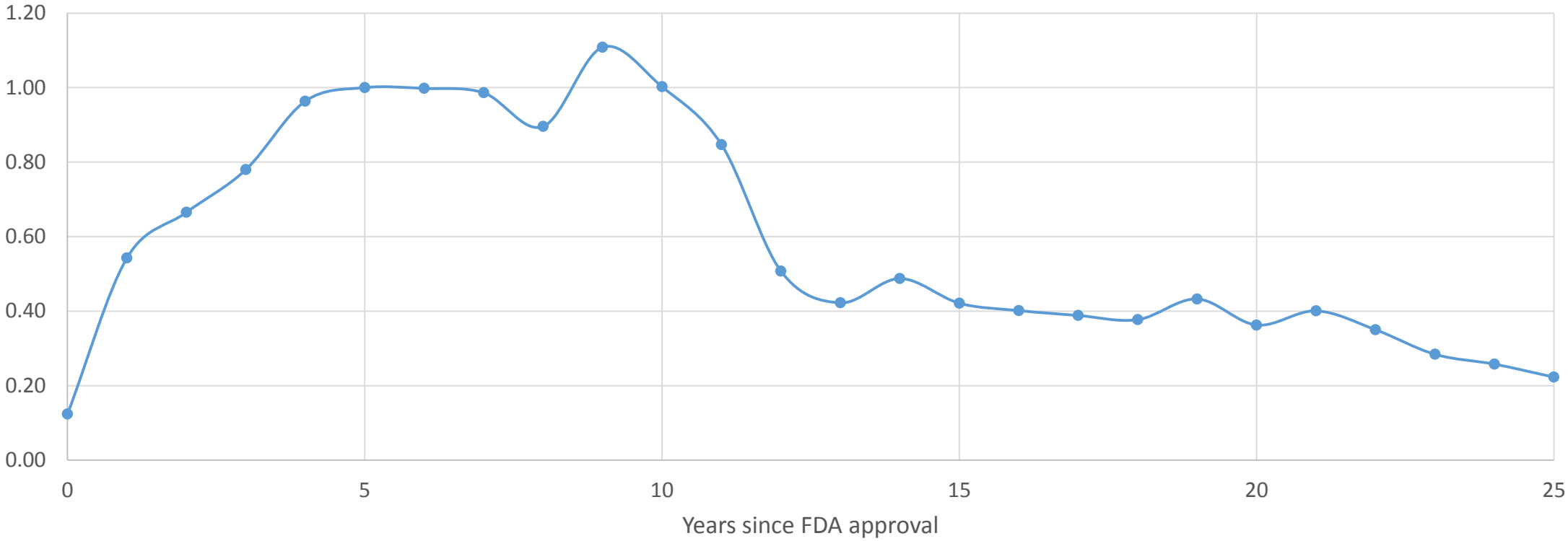
$$\ln(YPLL75_{s,t}) = \beta_{3+} CUM\_NCE_{s,t-3} + \beta_{0-2} (CUM\_NCE_{s,t} - CUM\_NCE_{s,t-3}) + \gamma \ln(CASES_{s,t-2}) + \pi AGE\_DIAG_{s,t-2} + \alpha_s + \delta_t + \varepsilon_{s,t}$$

β_{3+} = marginal effect of an additional drug approved more than 2 years before

β_{0-2} = marginal effect of an additional drug approved 0-2 years before

- Ratio of β_{0-2} to β_{3+} should depend on both relative quantity (utilization) and relative quality of more recent and less recent drug approvals.
- Drugs approved 0-2 years before are used less than drugs approved more than 2 years before

Relative utilization (year 5 = 1.00)



Relative utilization is measured by $\exp(\delta_t - \delta_5)$, where δ_t (t = 0,…,25) are parameters in the equation
$\ln(SU_{am}) = \delta_a + \alpha_m + \varepsilon_{am}$
and SU_{am} is the number of standard units of molecule m sold in the US *a* years after FDA approval.

Future drug approvals?

$$\ln(YPLL75_{s,t}) = \beta_{3+}\, CUM\_NCE_{s,t-3} + \beta_{0-2}\,(CUM\_NCE_{s,t} - CUM\_NCE_{s,t-3})$$
$$\mathbf{+ \beta_{FUTURE}\,(CUM\_NCE_{s,t+3} - CUM\_NCE_{s,t})}$$
$$+ \gamma \ln(CASES_{s,t-2}) + \pi\, AGE\_DIAG_{s,t-2} + \alpha_s + \delta_t + \varepsilon_{s,t}$$

β_{3+} = marginal effect of an additional drug approved more than 2 years before

β_{0-2} = marginal effect of an additional drug approved 0-2 years before

β_{FUTURE} = marginal effect of an additional drug approved 1-3 years after

Mortality in year t is inversely related to drug approvals until year t but unrelated to drug approvals after year t

Model		1	2	3		4	5	6
Dependent variable		LYL75	LYL75	LYL75		LYL65	LYL65	LYL65
N_DRUGS_EVER	Est.	**-0.032**				**-0.033**		
	Z	**-4.65**				**-5.17**		
	Pr > |Z|	**<.0001**				**<.0001**		
N_DRUGS_GT_2	Est.		**-0.0319**	**-0.038**			**-0.033**	**-0.037**
	Z		**-4.70**	**-5.74**			**-5.19**	**-5.74**
	Pr > |Z|		**<.0001**	**<.0001**			**<.0001**	**<.0001**
N_DRUGS_0_2	Est.		**-0.0215**	**-0.0336**			**-0.024**	**-0.033**
	Z		**-2.06**	**-3.20**			**-2.51**	**-3.45**
	Pr > |Z|		**0.0394**	**0.0014**			**0.0122**	**0.0006**
N_DRUGS_AFTER	Est.			0.0159				0.0125
	Z			1.37				0.96
	Pr > |Z|			0.1716				0.3388

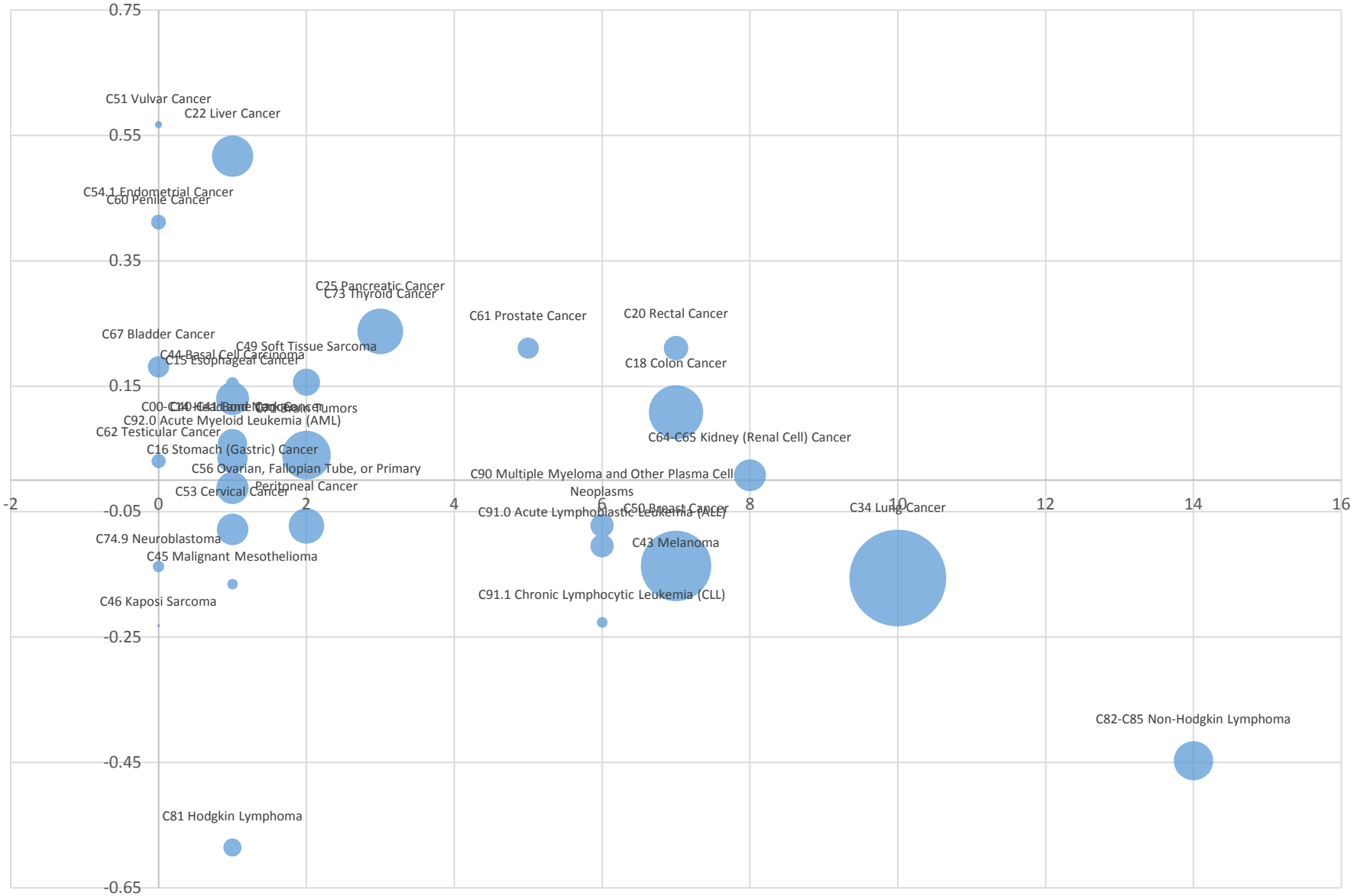
Unexpected finding:
Innovation (increase in number of drugs ever approved) is *negatively* correlated across cancer sites with growth in number of new cases

Chemoprevention?

For example, tamoxifen and raloxifene may reduce breast cancer risk.

If innovation reduces incidence, estimates of the effect of innovation on mortality that control for incidence will be conservative.

Correlation across cancer sites between number of drugs approved during 1999-2014 and log change in **years of potential life lost before age 65 (YPLL65)**



$$\ln(YPLL_{s,t}) = \beta_k \, CUM\_NCE_{s,t-k} + \gamma \ln(CASES_{s,t-2}) + \pi \, AGE\_DIAG_{s,t-2} + \alpha_s + \delta_t + \varepsilon_{s,t} \quad (2)$$

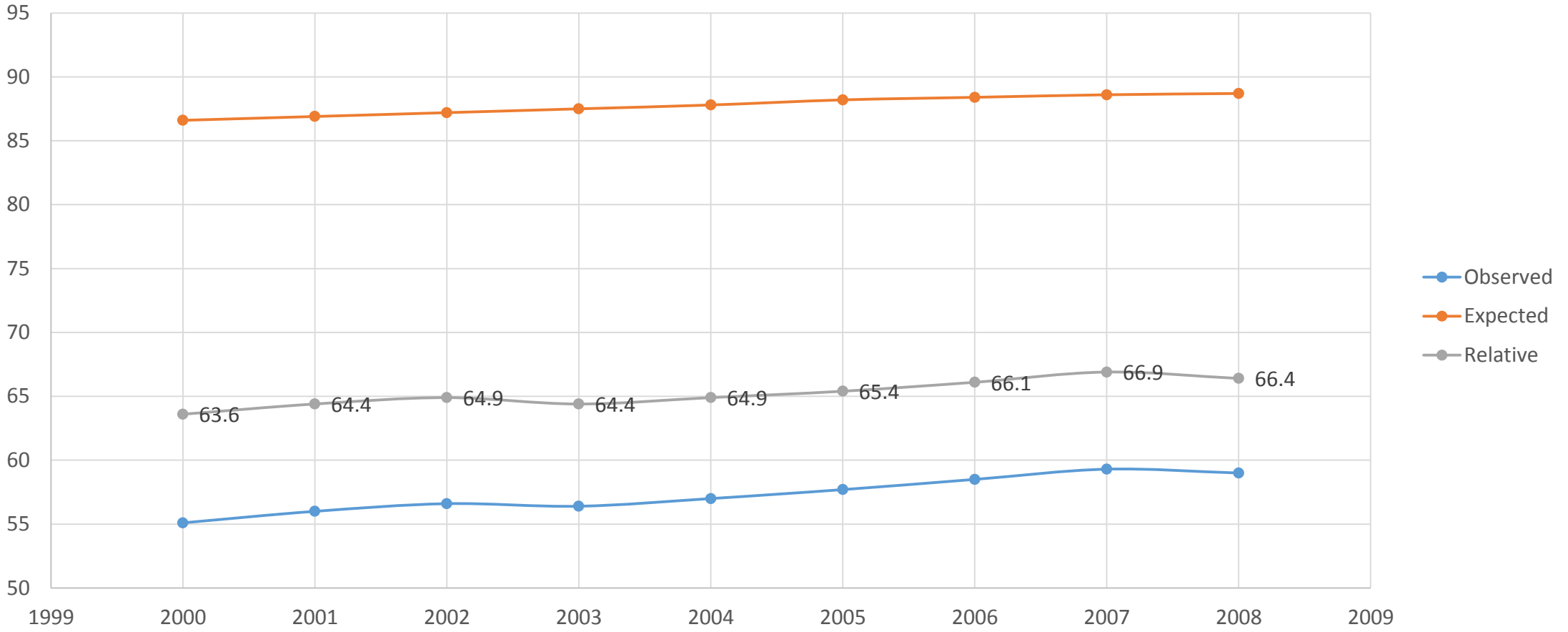
k	β_k	Std. error	Z	Pr > |Z|		mean(ΔCUM_NCE$_{t-k}$)	β_k * mean(ΔCUM_NCE$_{t-k}$)
Dependent variable: ln(YPLL75)							
0	-0.024	0.006	-3.93	<.0001		6.07	-0.145
3	-0.022	0.006	-3.76	0.0002		4.75	-0.104
6	-0.014	0.004	-4.09	<.0001		6.05	-0.085
9	-0.011	0.002	-5.30	<.0001		6.12	-0.070
12	-0.011	0.003	-3.75	0.0002		4.80	-0.051
15	-0.013	0.004	-3.78	0.0002		4.59	-0.061
Dependent variable: ln(YPLL65)							
0	-0.025	0.006	-4.00	<.0001		5.79	-0.146
3	-0.024	0.006	-3.87	0.0001		4.78	-0.113
6	-0.017	0.004	-4.59	<.0001		5.89	-0.099
9	-0.014	0.002	-5.77	<.0001		5.92	-0.082
12	-0.012	0.003	-3.97	<.0001		4.71	-0.056
15	-0.015	0.004	-3.87	0.0001		4.46	-0.067

- First model implies that drugs approved during 1999-2014 reduced YPLL75 in 2014 by 13.5% (= 1 – exp(-0.145)).
- According to the CDC, YPLL75 in 2014 was 4,416,968.
- The estimates imply that if no drugs had been approved during 1999-2014, YPLL in 2014 would have been 5,106,189 (= 4,416,968 / exp(-0.145)).
- Hence the number of life-years before age 75 gained in 2014 from drugs approved during 1999-2014 was 689,222.
- $YPLL_{no\_innov} = YPLL_{actual} * [\{1 / \exp(\beta_k * \text{mean}(\Delta CUM\_NCE_{t-k}))\} – 1]$

Difference between effects of priority- and standard-review drug approvals on premature (before age 75) mortality is not statistically significant

Model	Parameter	Estimate	Std. Error	Z	Pr > |Z|		Chi-Square	Pr > ChiSq
1	cum_drug_0	-0.0239	0.006	-3.93	<.0001			
2	cum_std_0	-0.0256	0.01	-2.64	0.0083			
2	cum_pri_0	-0.0231	0.007	-3.27	0.0011		0.05	0.822
3	cum_drug_3	-0.022	0.006	-3.76	0.0002			
4	cum_std_3	-0.0175	0.016	-1.12	0.264			
4	cum_pri_3	-0.0244	0.006	-3.83	0.0001		0.14	0.706
5	cum_drug_6	-0.0141	0.004	-4.09	<.0001			
6	cum_std_6	-0.0234	0.015	-1.54	0.1236			
6	cum_pri_6	-0.0086	0.007	-1.25	0.2108		0.5	0.478

5-year survival rates, all cancer sites combined, 2000-2008



Fixed-effects model of observed survival rate

$$\ln(SURV\_OBS_{s,t}/(1 - SURV\_OBS_{s,t})) = \beta\, CUM\_NCE_{s,t} + \gamma \ln(CASES_{s,t}) + \pi \ln(SURV\_EXP_{s,t}/(1 - SURV\_EXP_{s,t})) + \alpha_s + \delta_t + \varepsilon_{s,t} \quad (3)$$

$SURV\_OBS_{st}$ = the observed 5-year survival rate of patients diagnosed with cancer at site s in year t (t = 2000,…,2008)

$CUM\_NCE_{s,t-k}$ = $\sum_d IND_{ds}\, APPROVED_{d,t}$ = the number of new chemical entities (drugs) to treat cancer at site s that had been approved by the FDA by the end of year t

IND_{ds} = 1 if drug d is used to treat (indicated for) cancer at site s

= 0 if drug d is not used to treat (indicated for) cancer at site s

$APPROVED_{d,t}$ = 1 if drug d was approved by the FDA by the end of year t

= 0 if drug d was not approved by the FDA by the end of year t

$CASES_{s,t}$ = the number of new cases of cancer at site s diagnosed in year t

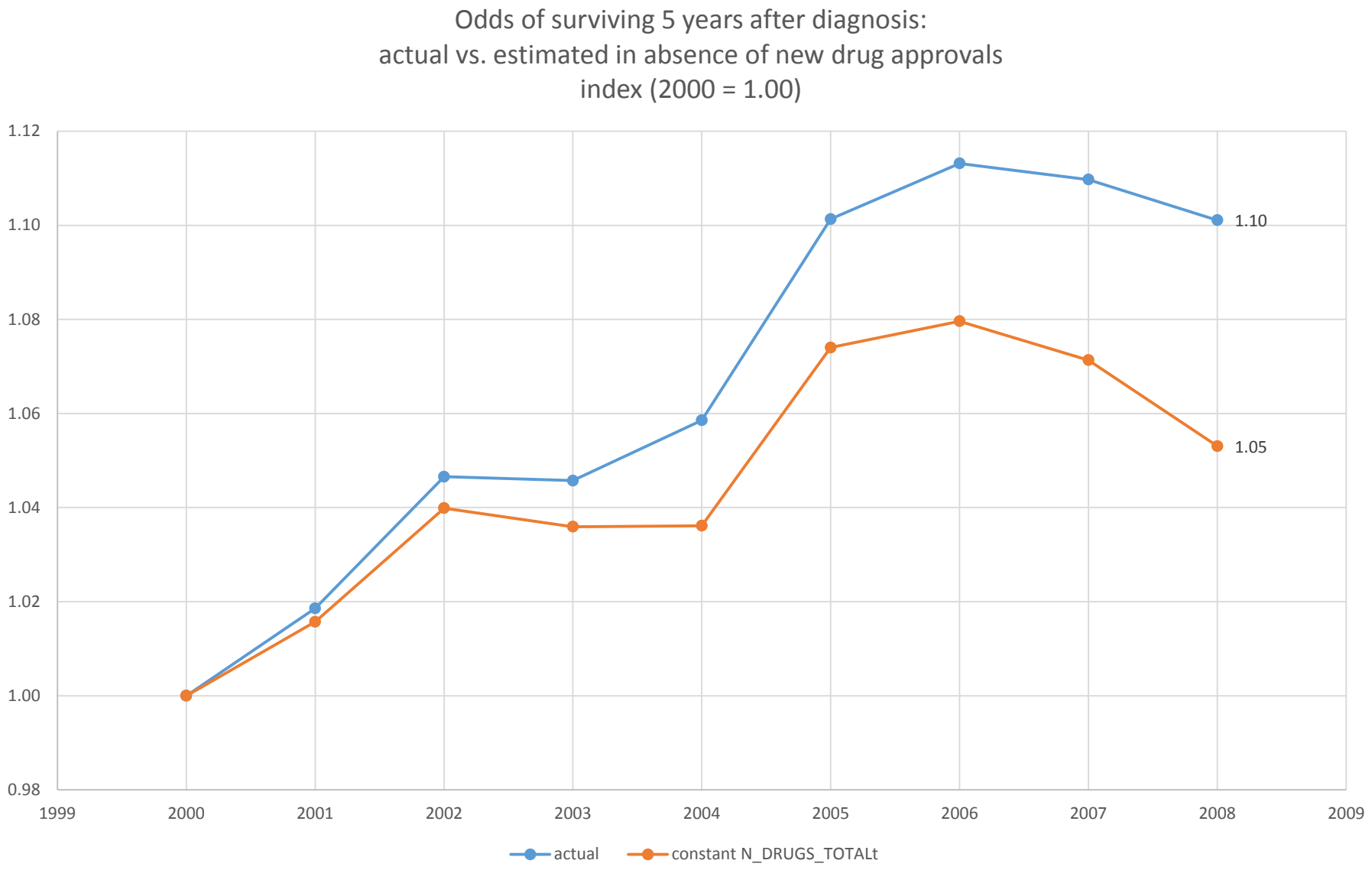
$SURV\_EXP_{s,t}$ = the expected 5-year survival rate of patients diagnosed with cancer at site s in year t

α_s = a fixed effect for cancer at site s

δ_t = a fixed effect for year t

Estimates of eq. (3)

		Including cum_drug_0					Excluding cum_drug_0			
Parameter		Estimate	Std. Error	Z	Pr > |Z|		Estimate	Std. Error	Z	Pr > |Z|
cum_drug_0		0.0175	0.0069	2.54	0.011					
odds_exp		0.4099	0.1105	3.71	0.0002		0.414	0.1116	3.71	0.0002
zn		0.4919	0.1257	3.91	<.0001		0.4645	0.1309	3.55	0.0004
year	2000	-0.0517	0.0447	-1.16	0.2473		-0.0963	0.0428	-2.25	0.0244
year	2001	-0.0361	0.0382	-0.94	0.3451		-0.0779	0.0387	-2.02	0.0439
year	2002	-0.0126	0.0346	-0.37	0.7147		-0.0508	0.0343	-1.48	0.139
year	2003	-0.0164	0.0331	-0.5	0.6193		-0.0516	0.0345	-1.5	0.1346
year	2004	-0.0162	0.0249	-0.65	0.5138		-0.0394	0.0246	-1.6	0.1089
year	2005	0.0197	0.023	0.86	0.3916		0.0002	0.0225	0.01	0.9925
year	2006	0.0249	0.0226	1.1	0.2695		0.0109	0.0218	0.5	0.6154
year	2007	0.0172	0.015	1.15	0.2511		0.0078	0.0156	0.5	0.6179
year	2008	0	0	.	.		0	0	.	.
Intercept		-4.3345	0.9698	-4.47	<.0001		-4.0323	1.0173	-3.96	<.0001

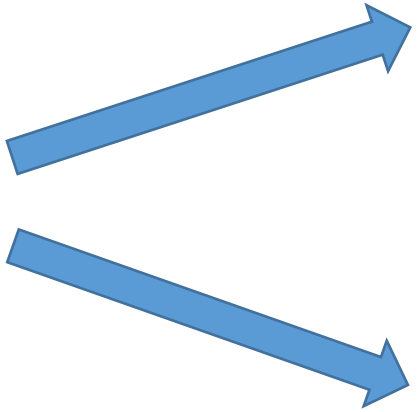


Note: both series control for expected survival and number of patients diagnosed.

Odds of surviving for at least 5 years post diagnosis

Model	Regressor	Estimate	Standard Error	Z	Pr > |Z|		Chi-Square	Pr > ChiSq
1	$N\_DRUGS\_TOTAL_{s,t}$	**0.0175**	**0.0069**	**2.54**	**0.011**			
2	$N\_DRUGS\_PRIORITY_{s,t}$	**0.0279**	**0.0085**	**3.27**	**0.0011**			
2	$N\_DRUGS\_STANDARD_{s,t}$	-0.0043	0.0103	-0.42	0.675		5.17	0.0229
3	$N\_DRUGS\_TOTAL_{s,t-3}$	0.0127	0.0083	1.53	0.1256			
4	$N\_DRUGS\_PRIORITY_{s,t-3}$	**0.0376**	**0.0117**	**3.23**	**0.0012**			
4	$N\_DRUGS\_STANDARD_{s,t-3}$	-0.0155	0.0134	-1.15	0.2488		6.54	0.0106

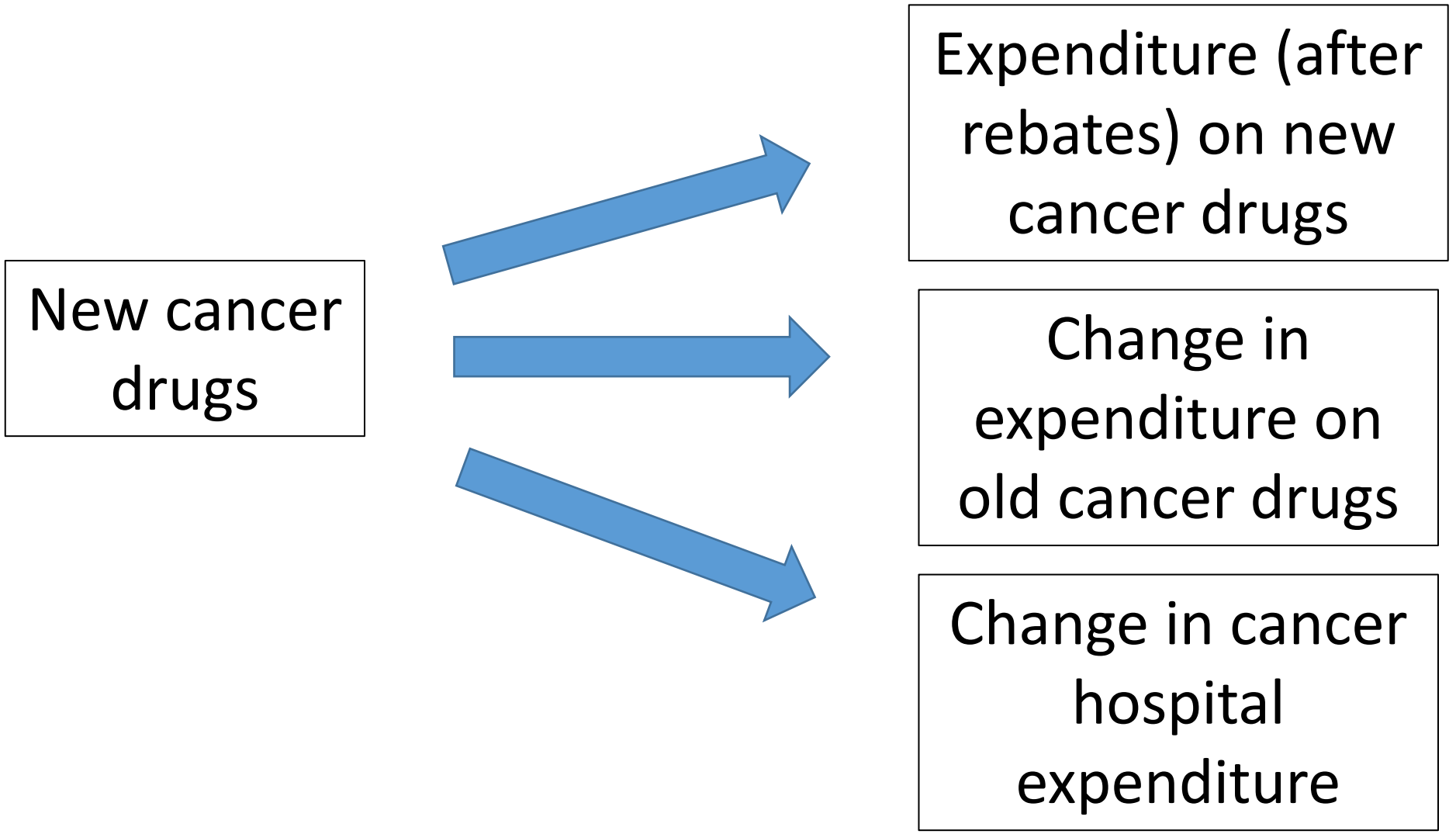
Innovation (new cancer drug approvals)



Health expenditure
- Expenditure on new cancer drugs
- Change in other medical expenditure

Health outcomes
- Premature (before age 75 or 65) mortality
- 5-year survival rate

Effect of new cancer drugs on treatment cost



IMS INSTITUTE FOR HEALTHCARE INFORMATICS

April 2015

Medicines Use and Spending Shifts

A Review of the Use of Medicines in the U.S. in 2014

- Oncologics led all classes in spending in 2014 with $32.3 Bn in spending.
- Estimated expenditure on post-1998 cancer drugs: $20.0 billion

Forbes

Matthew Herper Forbes Staff
I cover science and medicine, and believe this is biology's

PHARMA & HEALTHCARE 5/10/2012 @ 9:54AM | 54,152 views

Inside The Secret World Company Rebates

The free market is alive and well when it comes to drug prices – if you're an insurance company or a government program. But not if you're a consumer.

Top-selling pharmaceuticals, protected by patents, often seem priced in a manner that has

Drug rebates

"the drug industry reports both its gross sales (before the rebates) and net sales (after the rebates are taken out)"

Drug	IMS estimated U.S. sales ($Bil)	Company reported U.S. Sales ($Bil)	Estimated rebates (%)
Lipitor	$7.70	$5.00	35%
Plavix	$6.80	$6.60	3%
Nexium	$6.20	$2.40	61%
Abilify	$5.20	$4.00	24%
Advair	$4.60	$4.00	13%
Seroquel	$4.60	$3.30	27%
Singulair	$4.60	$3.50	23%
Crestor	$4.40	$3.10	30%
Cymbalta	$3.70	$3.20	14%
Humira	$3.50	$3.40	2%
All 10 drugs	$51.30	$38.50	25%

Sources: IMS Health, company statements, analyst reports. According to Pratap Khedkar, a principal at pharma marketing consultancy ZS Associates, "**the size of the rebate average[s] about 30% of a medicines sales**." Herper M (2012). Inside The Secret World Of Drug Company Rebates, *Forbes*, May 10, http://onforb.es/1yu08HG

Rebates

- “Pharmacy benefit managers…get ‘rebates’ from drug manufacturers…The rebates are not publicly disclosed, but they are sizable. Industry analysts estimate that those payments, and other back-room deals, amount to as much as 50 percent of the list price of insulin.”

- Lipska K (2016), Break Up the Insulin Racket, New York Times, February 20.

"about one-fourth of the...increase in new drug cost was offset by a reduction in old drug cost"

Lichtenberg FR (2014), "The impact of pharmaceutical innovation on disability days and the use of medical services in the United States, 1997-2010," *Journal of Human Capital* 8(4): 432-480.

(this statement applies to drugs in general, not just to cancer drugs)

$$\ln(HOSP\_DAYS_{s,t}) = \beta_k\, CUM\_NCE_{s,t-k} + \gamma \ln(CASES_{s,t-2}) + \pi\, AGE\_DIAG_{s,t-2} + \alpha_s + \delta_t + \varepsilon_{s,t} \quad (4)$$

k	β_k	Std. error	Z	Pr > |Z|		Mean(ΔCUM_NCE$_{t-k}$)	β_k * Mean(ΔCUM_NCE$_{t-k}$)
0	-0.014	0.007	-2.21	0.0269		4.76	-0.068
3	-0.017	0.009	-1.84	0.0665		5.28	-0.089
6	-0.019	0.009	-2.06	0.0394		4.91	-0.093
9	-0.019	0.006	-3.16	0.0016		4.61	-0.089
12	-0.023	0.005	-4.92	<.0001		3.30	-0.076
15	-0.027	0.008	-3.52	0.0004		3.11	-0.082

Sample period: 1998-2013

Hospital cost reduction

- First model implies that drugs approved during 1998-2013 reduced the number of hospital days in 2013 by 6.5% (= 1 – exp(-0.068)).
- I will assume that the percentage reduction in hospital cost is also 6.5%
- According to the Agency for Healthcare Research and Quality, in 2013 the cost of hospital care for cancer was $27.9 billion.
- *Charges* were 3.7 times as high as costs: $104 billion.
  - **Costs** tend to reflect the actual costs of production, while charges represent what the hospital billed for the case. Total charges were converted to costs using cost-to-charge ratios based on hospital accounting reports from the Centers for Medicare and Medicaid Services (CMS).
  - **Hospital charges** is the amount the hospital charged for the entire hospital stay. It does not include professional (MD) fees. Charges are not necessarily how much was reimbursed.
- The estimates imply that if no drugs had been approved during 1998-2013, the cost of hospital care for cancer in 2013 would have been $29.9 billion.(= $27.9 billion / exp(-0.068)).
- Hence the reduction in hospital cost in 2013 from drugs approved during 1998-2013 was $1.97 billion.

Cost per life-year gained before age 75

Line	Value	Description
1	$20.0 billion	2014 expenditure (before rebates) on post-1998 drugs (≈ 2/3 of total cancer drug expenditure)
2	$15.0 billion	2014 expenditure (after rebates) on post-1998 drugs, assuming 25% rebate rate
3	$3.7 billion	reduction in old drug cost (assumed to be 25% of new drug cost)
4	$2.0 billion	hospital cost reduction
5	$9.3 billion	net expend--all ages
6	$7.0 billion	net expend--below age 75 (assumed to be 75% of net expenditure for all ages)
7	689,222	life-years before age 75 gained, controlling for incidence and mean age at diagnosis
8	$10,096	cost per life-year gained before age 75

Foreign price is about 55% of U.S. price

(assuming equal rebate %)

Estimate model: $\ln(P_{mr}) = \delta_r + \alpha_m + \varepsilon_{mr}$

where

P_{mr} = manufacturer revenue per standard unit of molecule m in region r (r = USA, ROW)

Estimate by weighted least squares, weighting by number of standard units, using 2014 data on 107 molecules

Parameter	Estimate		Standard Error	t Value	Pr > |t|
$\delta_{ROW} - \delta_{USA}$	-0.591		0.093	6.37	<.0001

exp(-0.591) = 55.4%

World Health Organization (WHO) cost-effectiveness thresholds

- According to the WHO, an intervention is:
  - *cost-effective* if the cost per (quality-adjusted) life year gained is < 3 times per capita GDP
  - *highly cost-effective* if the cost per (quality-adjusted) life year gained is < per capita GDP
- In 2013, U.S. per capita GDP was $53,042