The impact of pharmaceutical innovation on longevity

Two econometric studies

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	I	II
Disease	Cancer	All causes of death
Variation	Across diseases	Across regions (states)
Innovation measure	Number of treatments	Mean vintage of treatments
Country	Australia	USA

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The impact of pharmaceutical innovation on Australian cancer mortality rates

Conventional wisdom

"The effect of new treatments for cancer on mortality has been largely disappointing."

Bailar & Gornik (1997), "Cancer undefeated," *New England Journal of Medicine* 336 (22), pp. 1569-74.

" Why have we made so little progress in the War on Cancer?"

Clifton Leaf, "Why we're losing the war on cancer, and how to win it," *Fortune*, March 22, 2004 <http://blog.aperio.com/articles/Fortune_Cancer.pdf>

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My hypothesis

Cancer drugs introduced during the last three decades have yielded significant improvements in cancer survival

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Endogenous technological change

In his model of endogenous technological change, Romer (1990) hypothesized the production function

$$\ln Y = (1 - \alpha) \ln A + (1 - \alpha) \ln L + \alpha \ln K$$

where

Y = output
A = the "stock of ideas"
L = labor used to produce output
K = capital
and $0 < \alpha < 1$

The cumulative number of drugs approved (CUM_DRUG) is analogous to the stock of (FDA-approved) ideas.

Romer, Paul (1990), "Endogenous technical change," *Journal of Political Economy* 98, S71-S102.

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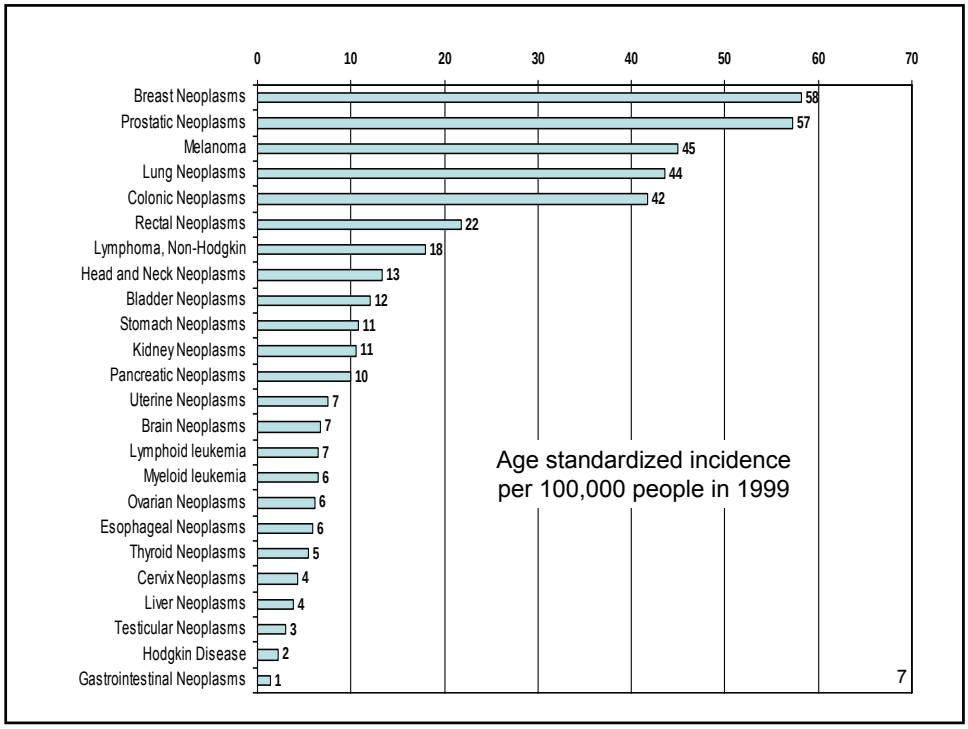
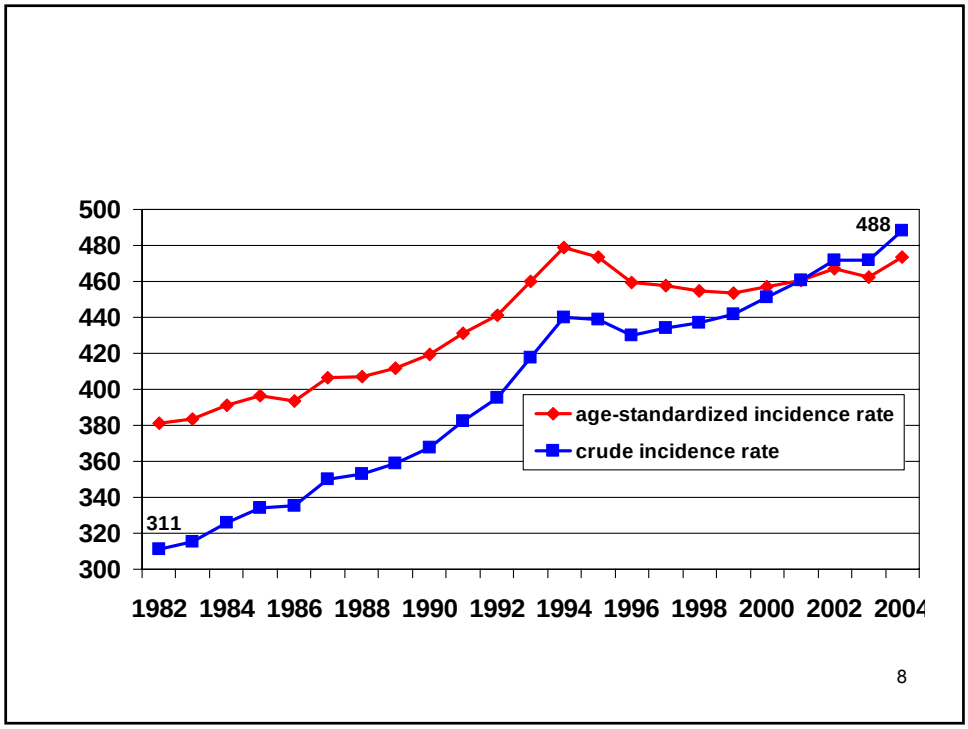

0
10
20
30
40
50
60
70
Breast Neoplasms 58
Prostatic Neoplasms 57
Melanoma 45
Lung Neoplasms 44
Colonic Neoplasms 42
Rectal Neoplasms 22
Lymphoma, Non-Hodgkin 18
Head and Neck Neoplasms 13
Bladder Neoplasms 12
Stomach Neoplasms 11
Kidney Neoplasms 11
Pancreatic Neoplasms 10
Uterine Neoplasms 7
Brain Neoplasms 7
Lymphoid leukemia 7
Myeloid leukemia 6
Ovarian Neoplasms 6
Esophageal Neoplasms 6
Thyroid Neoplasms 5
Cervix Neoplasms 4
Liver Neoplasms 4
Testicular Neoplasms 3
Hodgkin Disease 2
Gastrointestinal Neoplasms 1
Age standardized incidence per 100,000 people in 1999
7


500
480
460
440
420
400
380
360
340
320
300
488
311
age-standardized incidence rate
crude incidence rate
1982 1984 1986 1988 1990 1992 1994 1996 1998 2000 2002 2004
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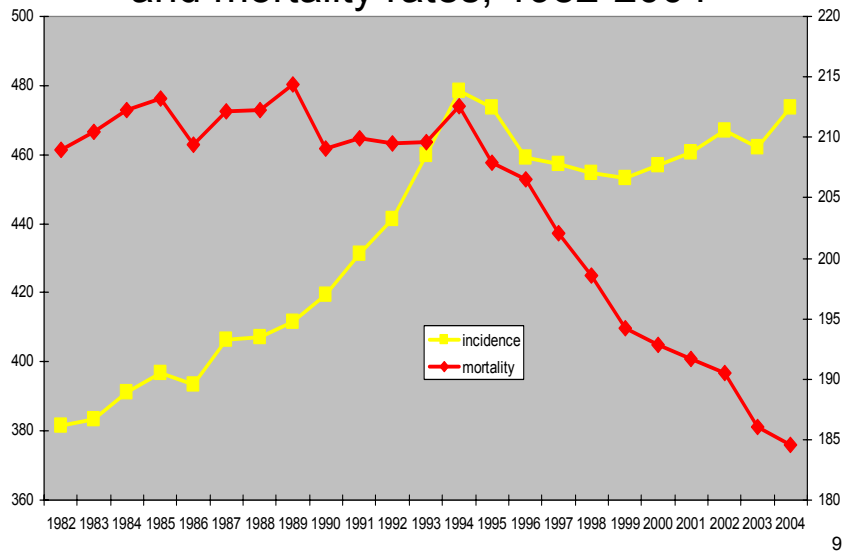
Age-standardized incidence and mortality rates, 1982-2004



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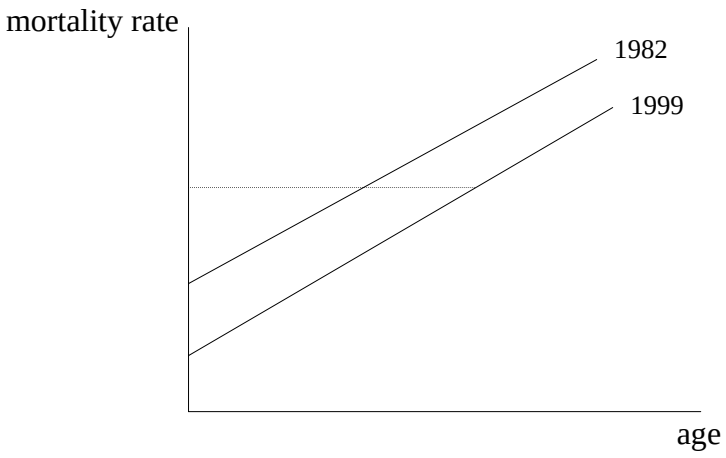

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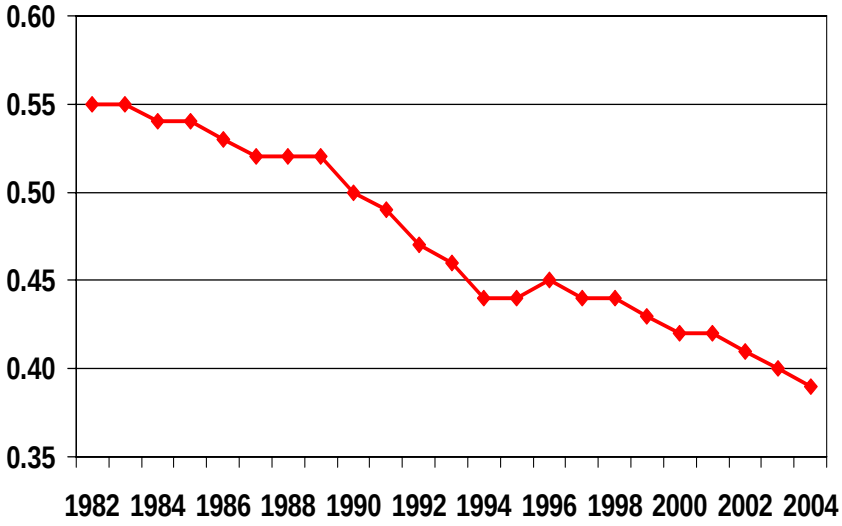
Mortality/incidence ratio



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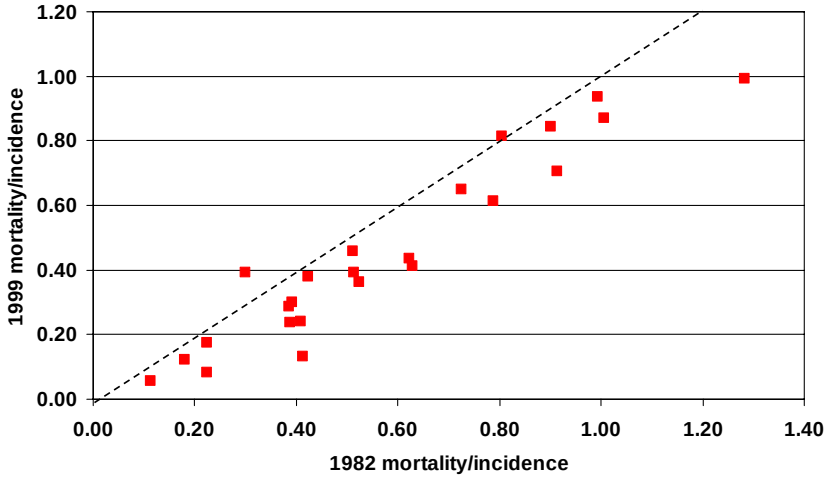

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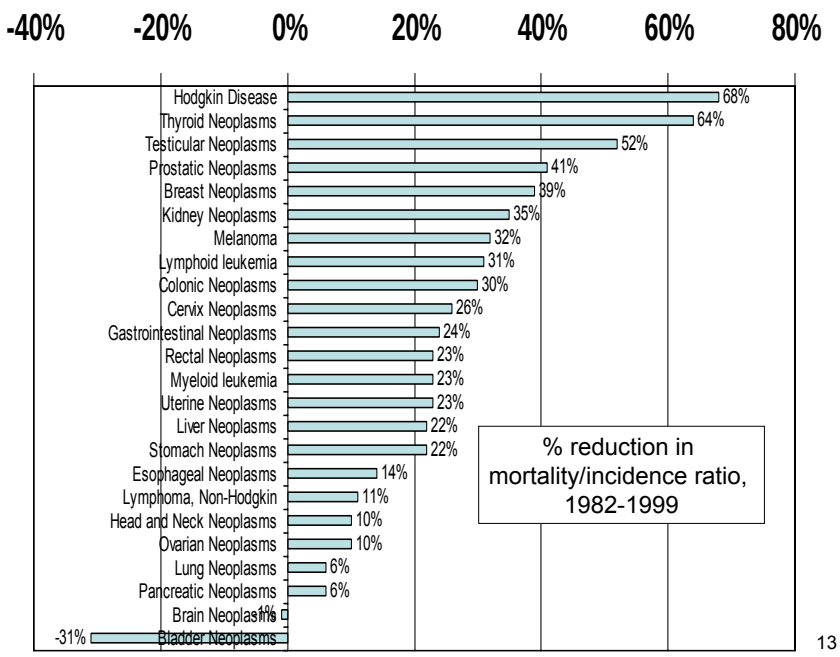

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Data sources

1. Cancer incidence and mortality, by site and year
   Australian Cancer Incidence and Mortality (ACIM) books
   http://www.aihw.gov.au/cancer/data/acim_books/index.cfm
2. Drugs used to treat cancer, by site
   National Drug File - Reference Terminology, 2004_01. Washington, DC: U.S. Department of Veterans Affairs, Veterans Health Administration, January 2004. This file is a source vocabulary of the U.S. National Library of Medicine's Unified Medical Language System Metathesaurus
   http://www.nlm.nih.gov/research/umls/about_umls.html#Metathesaurus
3. FDA approval years of drugs
   Drugs@FDA database
   http://www.fda.gov/cder/drugsatfda/datafiles/

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Lomustine 10 MG Oral Capsule

Alkylating Activity|mechanism_of_action_of| (C0002073)
Brain Neoplasms|may_be_treated_by| (C0006118)
Colonic Neoplasms|may_be_treated_by| (C0009375)
Hodgkin Disease|may_be_treated_by| (C0019829)
Lomustine|ingredient_of| (C0023972)
Lymphoma, Non-Hodgkin|may_be_treated_by| (C0024305)
Decreased Transcription to RNA|physiologic_effect_of| (C1372017)
Decreased DNA Replication|physiologic_effect_of| (C1371554)
Decreased DNA Integrity|physiologic_effect_of| (C1371553)
Oral Capsule|dose_form_of| (C0991533)
Pregnancy|has_contraindicated_drug| (C0032961)
Nitrosourea Compounds|has_contraindication| (C0028210)
Melanoma|may_be_treated_by| (C0025202)
Lung Neoplasms|may_be_treated_by| (C0024121)
Kidney Neoplasms|may_be_treated_by| (C0022665)
Drug Hypersensitivity|has_contraindicated_drug| (C0013182)

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Lymphoma, Non-Hodgkin

CHLORAMBUCIL	**1957**
CYCLOPHOSPHAMIDE	**1959**
URACIL MUSTARD	**1962**
VINCRISTINE SULFATE	**1963**
MANNITOL	**1964**
VINBLASTINE SULFATE	**1965**
PROCARBAZINE HYDROCHLORIDE	**1969**
BLEOMYCIN SULFATE	**1973**
LOMUSTINE	**1976**
CARMUSTINE	**1977**
CISPLATIN	**1978**
INTERFERON ALFA-2B	**1983**
INTERFERON ALFA-2A	**1984**
IFOSFAMIDE	**1988**
MESNA	**1988**
SARGRAMOSTIM	**1991**
FLUDARABINE PHOSPHATE	**1991**
ALDESLEUKIN	**1992**
CLADRIBINE	**1993**
PEGASPARGASE	**1994**

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Melanoma

DACTINOMYCIN	1964
HYDROXYUREA	1967
PROCARBAZINE HYDROCHLORIDE	1969
BLEOMYCIN SULFATE	1973
DACARBAZINE	1975
LOMUSTINE	1976
CARMUSTINE	1977
INTERFERON ALFA-2B	1983
INTERFERON ALFA-2A	1984
ALDESLEUKIN	1992
DOCETAXEL	1996
TEMOZOLOMIDE	1999

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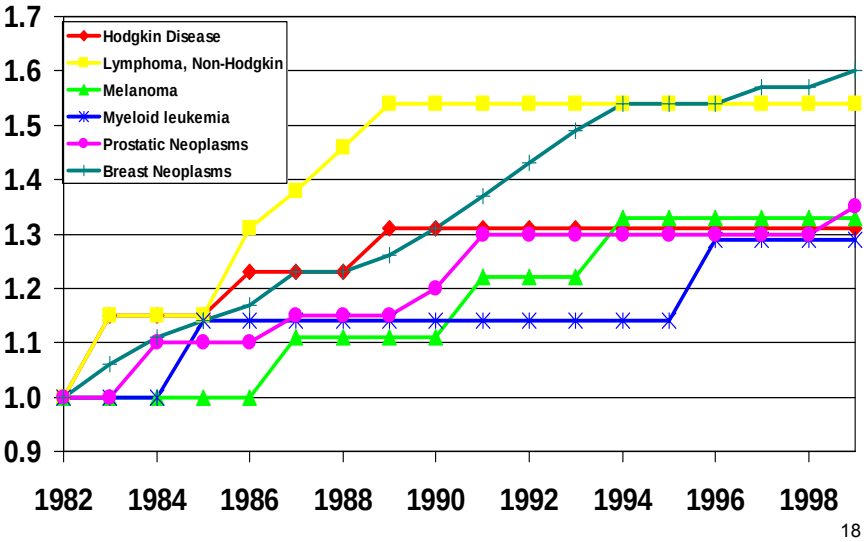
Relative increase in number of drugs approved to treat 6 types of cancer, 1982-1999



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Econometric model

We will investigate the effect of the introduction of new cancer drugs on the age-standardized mortality rate, conditional on the age-standardized incidence rate, by estimating the following model:

$$\ln ASM_{it} = \beta_2 N\_APP_{it+2} + \beta_1 N\_APP_{it+1} + \beta_0 N\_APP_{it} + \beta_{-1} N\_APP_{it-1} + \beta_{-2} N\_APP_{it-2}$$

$$+ \gamma \ln ASI_{it} + \gamma_{-1} \ln ASI_{it-1} + \alpha_i + \delta_t + \varepsilon_{it}$$

(1 = 1,…,24; t = 1985,…,2004)

where:

ASM_{it} = the age-standardized mortality rate from cancer site i in year t

N_DRUG_{it}= the number of drugs that may be used to treat cancer at site i that were approved by the FDA in year t

ASI_{it} = the age-standardized incidence rate of cancer site i in year t

α_i= a fixed effect for cancer site I

δ_t = a fixed effect for year t

ε_{it} = a disturbance

This model is estimated via weighted least squares, where the weight is the mean value of ASM during the period 1985-2004.

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Preliminary estimates

Parameter	Estimate	StdErr	Lower Wald CL	Upper Wald CL	ChiSq	ProbChiSq
n_app_{t+2}	-0.0019	0.0067	-0.0151	0.0113	0.08	0.7771
n_app_{t+1}	-0.0059	0.0065	-0.0186	0.0069	0.81	0.3692
n_app_{t}	-0.0105	0.0065	-0.0231	0.0022	2.62	0.1055
n_app_{t-1}	-0.0136	0.0064	-0.0261	-0.0011	4.58	0.0324
n_app_{t-2}	-0.0141	0.0063	-0.0265	-0.0017	4.97	0.0258
$\ln ASI_t$	0.3388	0.075	0.1917	0.4859	20.39	<.0001
$\ln ASI_{t-1}$	0.1278	0.0742	-0.0176	0.2733	2.97	0.085

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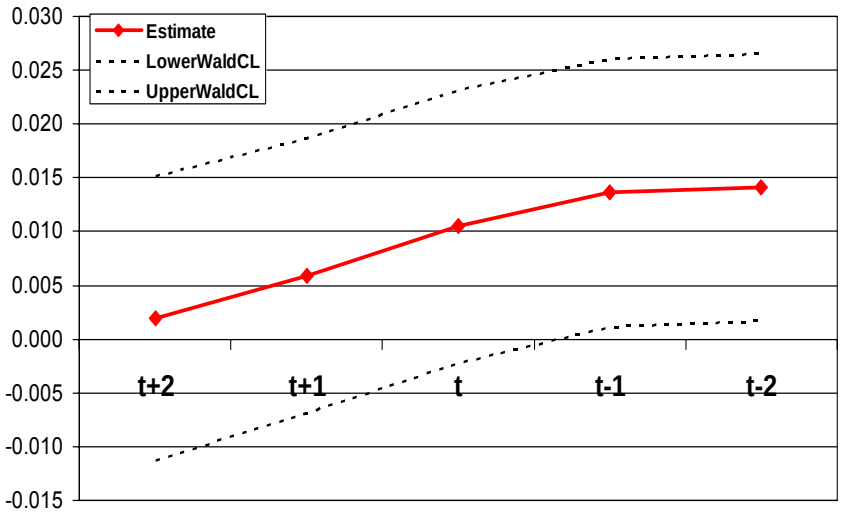
n_app_{t-i} estimates



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Findings

- The age-adjusted cancer mortality rate in year t is inversely related to the number of drugs approved to treat that type of cancer in the years t-1 and t-2, controlling for cancer incidence
- The age-adjusted cancer mortality rate in year t is unrelated to the number of drugs approved to treat that type of cancer in years t, t+1, and t+2

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