Innovation and the Production of Health

Estimates of the Impact of New Cancer Drugs

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Background and context

- Outcome in populations
  - Improvements in (quality adjusted) life expectancy
  - Sources of improved health
    - Environmental changes
    - Innovations in health care
- Impact of new cancer drugs on survival and mortality
  - Statistical analysis of longitudinal and cross sectional variation
- Supporting evidence
  - Early detection versus treatment
  - Disease specific studies (breast cancer as example)

Statistical analysis of contribution of new cancer drugs

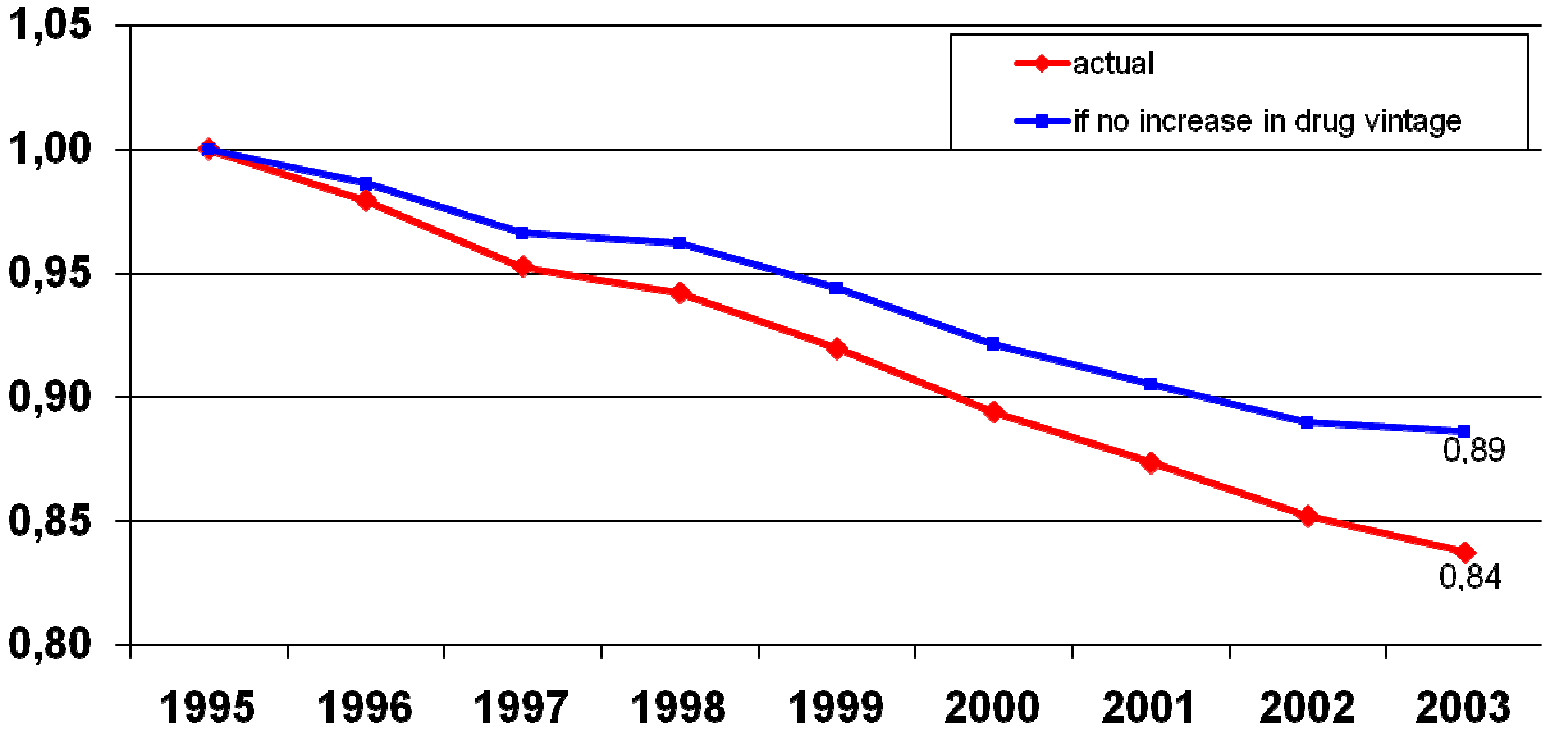
IMPACT OF INNOVATION ON SURVIVAL

Jönsson, Lichtenberg and Wilking

Three studies in 2007 report

- US longitudinal study
  - Nearly half (44%) of the observed improvement in the two-year cancer survival rate between 1992 and 2000 at 50 USA cancer centres could be attributed to the use of newer cancer drugs.
- European cross section study
  - Around one sixth (14% – 19%) of the inter-country differences in 5-year cancer survival rates across 5 major European countries is due to differences in the uptake of newer drugs (post-1985) in each country.
- International longitudinal mortality study
  - Nearly one third (30%) of the decline in cancer mortality rates seen in 20 countries (including the US and Europe) during the period 1995 - 2003, could be accounted for by the use of newer drugs. The observed decrease in mortality of 16% would have been only 11% if newer drugs had not been used.

Contribution of the increase in cancer drug vintage to the decline in the age-adjusted cancer mortality rate



Increase in drug vintage accounts for 30% of the 1995-2003 decline in the age-adjusted cancer mortality rate.

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Lichtenberg 2009 publications

- US data 1978-2004
  - Innovation measured as FDA approvals of cancer drugs had a positive effect on survival rates, controlling for cancer stage distribution, mean age at diagnosis, and incidence
    - *Economics of Innovation and Technology 18(5), 407-28*
- International differences
  - 17 types of cancer in 38 countries
  - Controlling for all other determinants of survival
  - Availability of drugs is associated with increased survival
    - *International Journal of Healthcare Technology and Management 10(3),138-55*

MATTIAS BERNOW, BENGT JÖNSSON, NILS WILKING

DOES CANCER DRUG VINTAGE AFFECT CANCER SURVIVAL?

NEW DATA AND MODELS

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Basic research questions

- **Hypothesis**
  - **Mean cancer drug vintage has a positive effect on cancer survival**
- **Definition of vintage**
  - **Vintageijk = Σd [Ndijk * *YEARd]* / Σd Ndijk**
  - Ndijk = the sales of cancer drug d used to treat patients with cancer site i, in country j, in year k.
  - (1) YEARd = the year of initial launch
  - (2) YEARd =1 if YEARd > limit year;= 0 if YEARd ≤ limit year
- **Definition of control variables**
  - **Dummies for disease, country and year**

Control variables

- Diseases (6)
  - Survival varies between cancer sites
  - Dummies have value 1 if they refer to the same pair of drugs/disease; otherwise zero
    - Breast cancer used as reference
- Countries (9)
  - Survival varies between countries
  - Dummies has value 1 if the pair of drug/disease refer t o a specific country; otherwise zero
    - Finland used as reference
- Year (9)
  - 1996 (base year) - 2004
  - Value of 1 if the pair of survival and drug vintage refer to a certain year, otherwise zero

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Models

- *Model 1 - two dimensions: cancer site and country*
- *Model 2 - three dimensions: cancer site, country and year*

Data

- Cancers
  - colorectal, lung, breast, ovarian, non-Hodgkin lymphoma and leukaemia
- Countries
  - Finland, Germany, the Netherlands,Norway, Slovenia, Switzerland, UK, Poland and USA
- Survival data
  - Dr Brenner and Dr Gondos, German Cancer research Centre,Heidelberg
- Data on sales of 21 cancer drugs
  - IMS Health

Descriptive statistics

- 480 data points
- More variations in survival between cancers than between countries, and over time
- Differences in both survival and drug vintage between countries for the different cancers
- A positive trend in both survival and drug vintage.
  - This poses no problem as the model is a difference-in-difference model (Stock and Watson 2003, pp. 385-388 and 419-420).

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RESULTS

Table 5.1.1: Results from model 1

Dependent variable	Survival	Survival
Intercept	-456.551	78.754
	(<0.001)***	(<0.001)***
Vintage	0.269	0.068
	(<0.001)***	(<0.001)***
Colorectal	-25.360	-25.17
	(<0.001)***	(<0.001)***
Leukemia	-36.791	-37.765
	(<0.001)***	(<0.001)***
Lung	-64.934	-64.243
	(<0.001)***	(<0.001)***
Non-Hodgkin Lymphoma	-24.984	-28.945
	(<0.001)***	(<0.001)***
Ovarian	-39.882	-39.401
	(<0.001)***	(<0.001)***
Germany	2.659	2.243
	(0.001)***	(0.020)**
Netherlands	0.239	-0.076
	(0.775)	(0.918)
Norway	1.639	1.444
	(0.033)**	(<0.050)**
Poland	-9.966	-10.614
	(<0.001)***	(<0.001)***
Slovenia	-3.609	-3.725
	(<0.001)***	(<0.001)***
Switzerland	4.984	4.242
	(<0.001)***	(<0.001)***
United Kingdom	-1.801	-2.268
	(0.019)**	(0.020)**
USA	3.457	3.200
	(<0.001)***	(<0.001)***
Cancer site	All	All
Country	All	All
Years	All	All
Vintage	Year	>1995
Adjusted R^2	0.963	0.966

*** significance at the one percent level
** significance at the five percent level
* significance at the ten percent level

Table 5.2.1: Results from model 2

Dependent variable	Survival	Survival
Intercept	-35.529	77.514
	(0.701)	(<0.001)***
Vintage	0.057	0.038
	(0.223)	(<0.001)***
1997	0.311	0.244
	(0.677)	(0.739)
1998	0.973	0.813
	(0.202	(0.270)
1999	1.660	1.442
	(0.032)**	(0.052)*
2000	2.346	2.038
	(0.003)***	(0.006)***
2001	2.976	2.400
	(<0.001)***	(0.002)***
2002	3.576	2.568
	(<0.001)***	(0.002)***
2003	4.232	3.070
	(<0.001)***	(<0.001)***
2004	4.860	3.576
	(<0.001)***	(<0.001)***
Colorectal	-24.899	-25.020
	(<0.001)***	(<0.001)***
Leukemia	-37.090	-37.503
	(<0.001)***	(<0.001)***
Lung	-65.344	-64.776
	(<0.001)***	(<0.001)***
Non-Hodgkin Lymphoma	-26.695	-28.156
	(<0.001)***	(<0.001)***
Ovarian	-40.216	-39.799
	(<0.001)***	(<0.001)***
Germany	2.761	2.495
	(0.001)***	(0.001)***
Netherlands	-0.159	-0.159
	(0.829)	(0.824)
Norway	1.763	1.589
	(0.017)**	(0.026)**
Poland	-10.660	-10.726
	(<0.001)***	(<0.001)***
Slovenia	-4.001	-3.902
	(<0.001)***	(<0.001)***
Switzerland	4.990	4.563
	(<0.001)***	(<0.001)***
United Kingdom	-2.183	-2.276
	(0.003)***	(0.002)***
USA	3.704	3.451
	(<0.001)***	(<0.001)***
Cancer site	All	All
Country	All	All
Years	All	All
Vintage	Year	>1995
Adjusted R^2	0.967	0.966

*** significance at the one percent level
** significance at the five percent level
* significance at the ten percent level

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Summary of results

- New estimates give similar results as previous studies
  - Improvements in data on number of treated patients
  - Improvements in survival data
- Result sensitive to the definition of vintage
  - Problems when using it for calculating absolute improvements in outcome (survival)

SUPPORTING EVIDENCE

Treatment or early detection?

Two studies support impact of new treatments

- Lichtenberg 2010
  - Control for increased incidence
  - Data from US 1976-2002 and AUS 1984-2002
  - 15% increase in unconditional mortality
- Sun, Jena et al 2010
  - Control for probability of detection
  - SEER US 1988-2000
  - The majority (> 75%) of all gain in survival is due to improved treatment

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The NEW ENGLAND JOURNAL of MEDICINE

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Effect of Screening Mammography on Breast-Cancer Mortality in Norway

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ABSTRACT

BACKGROUND

A challenge in quantifying the effect of screening mammography on breast-cancer mortality is to provide valid comparison groups. The use of historical control subjects does not take into account chronologic trends associated with advances in breast-cancer awareness and treatment.

METHODS

The Norwegian breast-cancer screening program was started in 1996 and expanded geographically during the subsequent 9 years. Women between the ages of 50 and 69 years were offered screening mammography every 2 years. We compared the incidence-based rates of death from breast cancer in four groups: two groups of women who from 1996 through 2005 were living in counties with screening (screening group) or without screening (nonscreening group); and two historical-comparison groups that from 1986 through 1995 mirrored the current groups.

RESULTS

We analyzed data from 40,075 women with breast cancer. The rate of death was reduced by 7.2 deaths per 100,000 person-years in the screening group as compared with the historical screening group (rate ratio, 0.72; 95% confidence interval [CI], 0.63 to 0.81) and by 4.8 deaths per 100,000 person-years in the nonscreening group as compared with the historical nonscreening group (rate ratio, 0.82; 95% CI, 0.71 to 0.93; $P<0.001$ for both comparisons), for a relative reduction in mortality of 10% in the screening group ($P=0.13$). Thus, the difference in the reduction in mortality between the current and historical groups that could be attributed to screening alone was 2.4 deaths per 100,000 person-years, or a third of the total reduction of 7.2 deaths.

CONCLUSIONS

The availability of screening mammography was associated with a reduction in the rate of death from breast cancer, but the screening itself accounted for only about a third of the total reduction. (Funded by the Cancer Registry of Norway and the Research Council of Norway.)

From the Cancer Registry of Norway, Oslo (M.K., F.L., H.-O.A.); the Departments of Epidemiology (M.K., H.-O.A.) and Biostatistics (M.Z.), Harvard School of Public Health; and the Dana–Farber Cancer Institute and Harvard Medical School (M.Z., H.-O.A.) — all in Boston; and the Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm (H.-O.A.). Address reprint requests to Dr. Kalager at Oslo University Hospital, Department of Surgery, Montebello, 0310 Oslo, Norway, or at mkalager@hsph.harvard.edu.

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CONCLUSIONS AND FURTHER RESEARCH

Conclusions

- Impact of new cancer drugs on survival has been established in a number of studies
- While this can be related to lead time, controlling for this indicate that treatment rather than early detection is the main explanatory factor for improvements in survival
- Further studies are important to answer import questions about the value of innovation
  - Relative effectiveness
  - Cost-effectiveness

Further research

- More exact data on number of treated patients of all patients diagnosed with the disease
  - Sales data are only a proxy for treatment
- Improved survival data
  - Still limited data for most countries
- How do we get individual patient data which links treatment and effect
  - Registry studies in different countries
  - Account of all relevant treatments and diagnostics
  - Costs and Quality of life data