The impact of pharmaceutical innovation on longevity

Two econometric studies

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2008

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
<td>Cancer</td>
<td>All causes of death</td>
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<tr>
<td>Variation</td>
<td>Across diseases</td>
<td>Across regions (states)</td>
</tr>
<tr>
<td>Innovation measure</td>
<td>Number of treatments</td>
<td>Mean vintage of treatments</td>
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<tr>
<td>Country</td>
<td>Australia</td>
<td>USA</td>
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</tbody>
</table>
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.”

“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>
My hypothesis

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

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.

Breast Neoplasms
Prostatic Neoplasms
Melanoma
Lung Neoplasms
Colonic Neoplasms
Rectal Neoplasms
Lymphoma, Non-Hodgkin
Head and Neck Neoplasms
Bladder Neoplasms
Stomach Neoplasms
Kidney Neoplasms
Pancreatic Neoplasms
Uterine Neoplasms
Brain Neoplasms
Lymphoid leukemia
Myeloid leukemia
Ovarian Neoplasms
Esophageal Neoplasms
Thyroid Neoplasms
Cervix Neoplasms
Liver Neoplasms
Testicular Neoplasms
Hodgkin Disease
Gastrointestinal Neoplasms

Age standardized incidence per 100,000 people in 1999

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Age standardized incidence rate
Crude incidence rate

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Age standardized incidence rate
Crude incidence rate
Age-standardized incidence and mortality rates, 1982-2004

Mortality rate

1982
1999

Age
Data sources

1. Cancer incidence and mortality, by site and year
   Australian Cancer Incidence and Mortality (ACIM) books

2. Drugs used to treat cancer, by site
   http://www.nlm.nih.gov/research/umls/about_umls.html#Metathesaurus

3. FDA approval years of drugs
   Drugs@FDA database
   http://www.fda.gov/der/det/detdatafda/datafiles/
Lomustine 10 MG Oral Capsule

Alkylation Activity/mechanism_of_action_of (C0002073)

Brain Neoplasms/may_be_treated_by (C0008118)

Colonic Neoplasms/may_be_treated_by (C0008375)

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 (C0011582)

Lymphoma, Non-Hodgkin

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHLORAMBUCIL</td>
<td>1957</td>
</tr>
<tr>
<td>CYCLOPHOSPHAMIDE</td>
<td>1959</td>
</tr>
<tr>
<td>URACIL MUSTARD</td>
<td>1962</td>
</tr>
<tr>
<td>VINCristine Sulfate</td>
<td>1963</td>
</tr>
<tr>
<td>MANNITOL</td>
<td>1964</td>
</tr>
<tr>
<td>VINBLASTINE SULFATE</td>
<td>1965</td>
</tr>
<tr>
<td>PROCARBazine HYDROCHLORIDE</td>
<td>1969</td>
</tr>
<tr>
<td>BLEOMYCIN SULFATE</td>
<td>1973</td>
</tr>
<tr>
<td>LOMUSTINE</td>
<td>1976</td>
</tr>
<tr>
<td>CARMUSTINE</td>
<td>1977</td>
</tr>
<tr>
<td>CISPLATIN</td>
<td>1978</td>
</tr>
<tr>
<td>INTERFERON ALFA-2B</td>
<td>1983</td>
</tr>
<tr>
<td>INTERFERON ALFA-2A</td>
<td>1984</td>
</tr>
<tr>
<td>IFOSFAMIDE</td>
<td>1988</td>
</tr>
<tr>
<td>MESNA</td>
<td>1988</td>
</tr>
<tr>
<td>SARGRAMOSTIM</td>
<td>1991</td>
</tr>
<tr>
<td>FLUDarabine PHOSPHate</td>
<td>1991</td>
</tr>
<tr>
<td>ALDESLEUKIN</td>
<td>1992</td>
</tr>
<tr>
<td>CLADIRIBINE</td>
<td>1993</td>
</tr>
<tr>
<td>PEGASPARGASE</td>
<td>1994</td>
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Melanoma

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
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</thead>
<tbody>
<tr>
<td>DACTINOMYCIN</td>
<td>1964</td>
</tr>
<tr>
<td>HYDROXYUREA</td>
<td>1967</td>
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<tr>
<td>PROCARBAZINE HYDROCHLORIDE</td>
<td>1969</td>
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<tr>
<td>BLEOMYCIN SULFATE</td>
<td>1973</td>
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<tr>
<td>DACARBAZINE</td>
<td>1975</td>
</tr>
<tr>
<td>LOMUSTINE</td>
<td>1976</td>
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<td>CARMUSTINE</td>
<td>1977</td>
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<tr>
<td>INTERFERON ALFA-2B</td>
<td>1983</td>
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<tr>
<td>INTERFERON ALFA-2A</td>
<td>1984</td>
</tr>
<tr>
<td>ALDESLEUKIN</td>
<td>1992</td>
</tr>
<tr>
<td>DOCETAXEL</td>
<td>1996</td>
</tr>
<tr>
<td>TEMOZOLOMIDE</td>
<td>1999</td>
</tr>
</tbody>
</table>

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

\[
\ln ASM_i = \beta_2 N_{\text{APP}_{i+2}} + \beta_1 N_{\text{APP}_{i+1}} + \beta_0 N_{\text{APP}_i} + \beta_{-1} N_{\text{APP}_{i-1}} + \beta_{-2} N_{\text{APP}_{i-2}} \\
+ \gamma \ln ASI_i + \gamma_{-1} \ln ASI_{i-1} + \alpha_i + \delta_t + \epsilon_{it}
\]

(1 = 1,...,24; t = 1985,...,2004)

where:
- ASM\(_i\) = the age-standardized mortality rate from cancer site \(i\) in year \(t\)
- N\(_{\text{DRUG}}\)_\(i\) = the number of drugs that may be used to treat cancer at site \(i\) that were approved by the FDA in year \(t\)
- ASI\(_i\) = the age-standardized incidence rate of cancer site \(i\) in year \(t\)
- \(\alpha_i\) = a fixed effect for cancer site \(i\)
- \(\delta_t\) = a fixed effect for year \(t\)
- \(\epsilon_{it}\) = a disturbance

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

Preliminary estimates

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>StdErr</th>
<th>Lower Wald CL</th>
<th>Upper Wald CL</th>
<th>ChiSq</th>
<th>ProbChiSq</th>
</tr>
</thead>
<tbody>
<tr>
<td>n_app(+2)</td>
<td>-0.0019</td>
<td>0.0067</td>
<td>-0.0151</td>
<td>0.0113</td>
<td>0.08</td>
<td>0.7771</td>
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<tr>
<td>n_app(+1)</td>
<td>-0.0059</td>
<td>0.0065</td>
<td>-0.0186</td>
<td>0.0069</td>
<td>0.81</td>
<td>0.3692</td>
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<tr>
<td>n_app()</td>
<td>-0.0105</td>
<td>0.0065</td>
<td>-0.0231</td>
<td>0.0022</td>
<td>2.62</td>
<td>0.1055</td>
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<tr>
<td>n_app(-1)</td>
<td>-0.0136</td>
<td>0.0064</td>
<td>-0.0261</td>
<td>-0.0011</td>
<td>4.58</td>
<td>0.0324</td>
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<tr>
<td>n_app(-2)</td>
<td>-0.0141</td>
<td>0.0063</td>
<td>-0.0265</td>
<td>-0.0017</td>
<td>4.97</td>
<td>0.0258</td>
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<tr>
<td>ln ASI(_t)</td>
<td>0.3388</td>
<td>0.075</td>
<td>0.1917</td>
<td>0.4859</td>
<td>20.39</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>ln ASI(_{t-1})</td>
<td>0.1278</td>
<td>0.0742</td>
<td>-0.0176</td>
<td>0.2733</td>
<td>2.97</td>
<td>0.085</td>
</tr>
</tbody>
</table>
### 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 $t+2$.

#### Table: n_app$_{t-i}$ estimates

<table>
<thead>
<tr>
<th>$t$</th>
<th>Estimate</th>
<th>Lower Wald CL</th>
<th>Upper Wald CL</th>
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<tbody>
<tr>
<td>t-2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t+1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>t+2</td>
<td></td>
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