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Frank R. Lichtenberg

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ABSTRACT

Importation of drugs into the U.S. would result in a decline in U.S. drug prices. The purpose of this paper is to assess the consequences of importation for new drug development. A simple theoretical model of drug development suggests that the elasticity of innovation with respect to the expected price of drugs should be at least as great as the elasticity of innovation with respect to expected market size (disease incidence). I examine the cross-sectional relationship between pharmaceutical innovation and market size among a set of diseases (different types of cancer) exhibiting substantial exogenous variation in expected market size. I analyze two different measures of pharmaceutical innovation: the number of distinct chemotherapy regimens for treating a cancer site, and the number of articles published in scientific journals pertaining to drug therapy for that cancer site. Both analyses indicate that the amount of pharmaceutical innovation increases with disease incidence. The elasticity of the number of chemotherapy regimens with respect to the number of cases is 0.53. The elasticity of MEDLINE drug cites with respect to cancer incidence throughout the world is 0.60. In the long run, a 10% decline in drug prices would therefore be likely to cause at least a 5-6% decline in pharmaceutical innovation.

Frank R. Lichtenberg
Graduate School of Business
Columbia University
3022 Broadway, 614 Uris Hall
New York, NY 10027
and NBER
frank.lichtenberg@columbia.edu

Importation of drugs into the U.S. may soon become legal. Since prices of drugs are lower in most other countries than they are in the U.S., importation would result in a decline in U.S. drug prices. The price decline would benefit U.S. consumers in the short run. However, importation may have two other effects that could reduce the welfare of U.S. consumers. First, importation could reduce the quality, or safety, of drugs purchased by Americans, and increase the number of adverse drug events. Second, importation could reduce the number of new drugs developed in the future by reducing the expected profitability of new drug development. In previous papers (Lichtenberg (2005a, 2005b, 2005c)), I have shown that the introduction of new drugs has increased longevity and ability to work, and reduced utilization of hospitals and nursing homes.

Therefore, while importation may yield an increase in static efficiency (lower drug prices), it may also result in reduced dynamic efficiency (fewer new drugs developed). Schumpeter (1947, p. 190, italics in original) suggested that, in general, consumer welfare depends more on dynamic efficiency than it does on static efficiency: "we shall call that system relatively more efficient which we see reason to expect would *in the long run* produce the larger stream of consumers' goods per equal unit of time."

The purpose of this paper is to assess the consequences of importation for new drug development. One way to do this is to estimate the elasticity of drug development with respect to the expected price of drugs.[1, 2] This approach requires substantial exogenous variation in expected drug prices, which may be hard to find. I will pursue an alternative approach: I will attempt to estimate the elasticity of drug development with respect to expected market size. In Section I, I will present a simple theoretical model of drug development which suggests that the elasticity of investment with respect to the expected price of drugs should be at least as great as the elasticity of investment with respect to expected market size. In section II, I will examine the cross-sectional relationship between pharmaceutical innovation and market size among a set of diseases

[1] Abbott and Vernon (2005) review the literature on the linkages between pharmaceutical price regulation, profits, cash flows, and investment in R&D.

[2] Danzon et al (2005) and Kyle (2005) examine the effect of prices, or price controls, on the probability and timing of launch of existing drugs in different countries. Danzon et al (2005) present evidence that countries with lower prices or smaller market size experience longer delays in access to new drugs. Kyle (2005) found that companies delay launch into price-controlled markets, and are less likely to introduce their products in additional markets after entering a country with low prices.

(different types of cancer) exhibiting substantial exogenous variation in expected market size. In section III, I will consider the implications of the estimates, and compare them to estimates from previous studies.

I. A simple theoretical model of drug development

Suppose that the cost function of the pharmaceutical firm is linear, i.e. that there is a fixed cost and that marginal cost is constant:

$$\begin{aligned} C &= C_F + m\,Q \\ &= C_F + C_V \end{aligned} \qquad (1)$$

where

C = total cost
C_F = fixed cost
m = marginal cost
Q = quantity
C_V = variable cost = $m\,Q$

The fixed cost (C_F) is likely to be very large relative to marginal cost. In 2003, the Tufts Center for the Study of Drug Development reported that the fully capitalized cost to develop a new drug, including studies conducted after receiving regulatory approval, averages $897 million.[3] In 2002, the average U.S. price of a generic prescription—which may be close to marginal cost—was $30.

Given this cost function, the firm's profit function is:

$$\begin{aligned} \Pi &= R - C \\ &= P\,Q - (C_F + C_V) \\ &= P\,Q - m\,Q - C_F \\ &= R - C_V - C_F \\ &= \Pi_V - C_F \end{aligned} \qquad (2)$$

where

Π = profit
R = revenue = $P\,Q$

[3] http://csdd.tufts.edu/NewsEvents/RecentNews.asp?newsid=29

P = price
Π_V = variable profit = revenue – variable cost = (P – m) Q

The firm will be willing to invest (incur the fixed cost C_F) if it expects "variable profit" (revenue minus variable cost) to exceed fixed cost. This theory of investment in innovation is quite consistent with Scherer's (2001, p. 220) "virtuous rent-seeking model" of pharmaceutical industry R&D, in which, "as profit opportunities expand, firms compete to exploit them by increasing R&D investments, and perhaps also promotional costs, until the increases in costs dissipate most, if not all, supranormal profit returns."

Suppose we regard both fixed and marginal cost as given. Exogenous changes in price or quantity change variable profit, and therefore may affect whether of not the firm is willing to invest.

If the firm were an unregulated monopolist facing a linear inverse demand curve P = a – b Q, the profit-maximizing price would be P* = (a + m) / 2, and the profit-maximizing quantity would be Q* = (a – m) / 2 b. However, suppose that the firm is prevented, by reimportation or regulation, from charging the profit-maximizing price. The actual price it can charge, P, may be lower than P*. I want to assess the sensitivity of variable profit (hence willingness to invest) to exogenous changes in P, and compare it to the sensitivity of variable profit to exogenous "demand shocks" (e.g., changes in market size).

A change in P has an indirect as well as a direct effect on variable profit, via the demand function. Suppose that the demand function is log-linear rather than linear:

$$Q = N P^{-\beta}$$

or

$$\ln Q = \ln N - \beta \ln P$$

where N is the number of consumers and β is the elasticity of demand. I assume that the elasticity of Q with respect to N is one, e.g. a 10% increase in disease incidence would cause quantity demanded to increase 10%, holding price constant.

Then we may write

$$\ln \Pi_V = \ln(P - m) + \ln Q$$

$$= \ln(P - m) + \ln N - \beta \ln P$$

The elasticity of variable profit with respect to the number of consumers is one. The elasticity of variable profit with respect to price is

$$\frac{\delta \ln \Pi_V}{\delta \ln P} = \frac{P}{P - m} - \beta$$

$$= \frac{1}{1 - (m / P)} - \beta$$

Suppose, for a moment, that the demand for pharmaceuticals were completely inelastic: $\beta = 0$. In this case

$$\frac{\delta \ln \Pi_V}{\delta \ln P} = \frac{1}{1 - (m / P)} > 1 = \frac{\delta \ln \Pi_V}{\delta \ln N}$$

The elasticity of variable profit with respect to price is greater than one, and is therefore greater than the elasticity of variable profit with respect to the number of consumers. *If demand were completely inelastic, variable profit would be more sensitive to price than it is to market size.* A reduction in the number of consumers reduces cost as well as revenue, whereas a reduction in price reduces only revenue.

To calculate the elasticity of variable profit with respect to price when demand is completely inelastic, we require only an estimate of (m / P), the reciprocal of the price-cost margin. Hughes et al (2002, p. 6), citing Grabowski and Vernon (1992, 1996), note that "once multiple generic manufacturers enter [the market following patent expiration], they typically price their drugs at discounts of 70 to 90 percent below the incumbent's price prior to entry. This observation implies that the ratio of price to marginal cost for branded drugs with patent protection is about 6:1." If (m / P) = 1/6, the elasticity of variable profit with respect to price when demand is completely inelastic is 1 / (1–(1/6)) = 1.20.

However, other evidence suggests that the mean ratio of generic price to branded price is much higher. Data from the 2002 Medical Expenditure Panel Survey indicate that the mean price of generic prescriptions was $30 (N = 124,555), and that the mean

price of branded prescriptions was $75 (N = 189,312), so the ratio of mean prices was 0.40. However, this ratio compares prices of different products, e.g. antibiotics and cardiovascular drugs. We can calculate the mean percentage differential of the prices of generic and branded versions of the *same* product by estimating the following model:

$$\ln P_{ij} = \delta \, GENERIC_{ij} + \alpha_j + \varepsilon_{ij}$$

where

P_{ij} = the price of the i^{th} prescription for product j
$GENERIC_{ij}$ = 1 if the i^{th} prescription for product j is a generic prescription
= 0 if the i^{th} prescription for product j is a branded prescription
α_j = a fixed effect for product j, where a product is defined by active ingredient(s), dosage form, strength, and route of administration[4]

The estimate of the within-product price differential δ, based on data on 258,276 prescriptions for 2235 products, is -.317 (t-statistic = 65.3). This implies that the mean ratio of the price of a generic prescription to the price of a branded prescription for the same product is 0.73 (= exp(-.317)). If (m / P) = 0.40, the elasticity of variable profit with respect to price when demand is completely inelastic is 1.68; if (m / P) = 0.73, it is 3.68.

Some evidence indicates that the demand for pharmaceuticals is completely inelastic: a study by Caves, Whinston, and Hurwitz (1991) found that the total amount sold of a drug in both generic and brand-name forms did not increase after generic entry.[5] Moreover, as Folland *et al* (2001) argue, insurance reduces the price elasticity, and prescription drug insurance coverage has been rising. According to an April 2000 Department of Health & Human Services Report to the President[6], in 1998 only 27 cents out of every dollar of pharmaceutical expenditure was paid for out of pocket by households; 53 cents was paid by private insurance and the remainder was paid by Medicaid and other sources (Figure 2-16).

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[4] Product definitions and designation as branded or generic are determined by Multum, Inc.
[5] A choice-modeling experiment performed by Merino-Castelló (2003, p. 31) also provided evidence of low price elasticity of demand for pharmaceuticals.
[6] Department of Health & Human Services (2000), "Report to the President: Prescription Drug Coverage, Spending, Utilization, and Prices," April.

However, evidence from several studies suggests that the elasticity of demand for pharmaceuticals is positive, but not large. One of these was the Health Insurance Experiment (HIE), which randomized people to various insurance plans that differed in their copayments and deductibles. The HIE yielded an elasticity of prescription drug expenditures of 0.27, implying that a 10% reduction in the price of drugs would increase spending by 2.7%. Lillard et al (1999) observed a similar response (0.25) among the elderly.[7] Goldman et al (2002) stated that "overall, the literature suggests elasticities that range between 0.20 and 0.35."

If (m / P) = 1/6, and the demand elasticity is 0.20, the elasticity of variable profit with respect to price happens to be equal to unity, the same as the elasticity of variable profit with respect to the number of consumers:

$$\frac{\delta \ln \Pi_V}{\delta \ln P} = \frac{1}{1-(m/P)} - \beta = \frac{1}{1-(1/6)} - 0.20 = 1$$

If the demand elasticity is 0.35, the elasticity of variable profit with respect to price equals 0.85, which is lower than the elasticity of variable profit with respect to the number of consumers, but not by much. This suggests that the elasticity of variable profit with respect to price is likely to be similar to the elasticity of variable profit with respect to the number of consumers. Hence, an estimate of the effect of the number of consumers on investment may also be considered an approximate estimate, or forecast, of the effect of price on investment.

II. Evidence about the effect of market size on pharmaceutical innovation

To estimate the effect of market size on pharmaceutical innovation, there must be observable, exogenous variation in market size (e.g. disease incidence) that can be linked to innovation measures. Estimates of the incidence (i.e. the annual number of new

[7] The estimated elasticity is based on Goldman et al's (2002) calculations, using the demand response shown in Table 4 of Lillard et al (1999) for elderly with Medicare only. Using information from the Medicare Current Beneficiary Survey (MCBS), they assumed the average coinsurance rate for these elderly is 100% without insurance and 45% with insurance. The 45% average coinsurance rate is based on our calculation of observed coinsurance rates (out-of-pocket expenditures divided by total expenditures) for people with private supplemental drug coverage in the 1995 MCBS.

cases)[8] of 365 conditions have been compiled and posted on the wrongdiagnosis.com website. In most cases, the incidence rates refer to the U.S. or other industrialized nations.[9] Data for the top 25 conditions are shown in Table 1.

Although these data are potentially useful, they may be subject to several limitations. First, they were derived from a variety of sources, covering different regions and time periods, and may not be directly comparable.[10] A second and perhaps greater concern is that reported incidence may not be exogenous with respect to the availability of treatments. An increase in available treatments for a disease may lead to greater public and professional awareness of it (e.g. due to more promotion and advertising by drug companies), and therefore to higher reported incidence.

There is one important set of diseases—different forms of cancer—for which reliable, systematic incidence data are available, and where the potential for "reverse causality" (from treatment availability to incidence) is likely to be quite limited. Reliable data on the incidence of cancer, by cancer site (e.g. breast and prostate) are available from GLOBOCAN. The GLOBOCAN 2002 database provides estimates of the incidence and prevalence of, and mortality from, 27 cancers for all countries in the world in 2002. The database has been built up using the huge amount of data available in the Descriptive Epidemiology Group of the International Agency for Research on Cancer (IARC), part of the World Health Organization. Incidence data are available from cancer registries.

If drugs were the only or primary treatment for cancer, or if drugs were often used to diagnose cancer, as well as to treat it, the possibility of reverse causality would be greater. But drugs are not the only cancer treatment: as noted by the British Columbia Cancer Agency, surgery and radiation therapy, as well as cancer drugs, "are all proven to cure cancer, extend life, or improve quality of life."[11] Also, data contained in the National Library of Medicine's Unified Medical Language System Metathesaurus

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[8] This measure differs from "prevalence", which is the cumulative number of people currently affected.
[9] http://www.wrongdiagnosis.com/lists/incid.htm
[10] Some of the estimates are based on household data (i.e. on self-reported medical conditions), while others are based on surveys of medical providers.
[11] See http://www.bccancer.bc.ca/PPI/CancerTreatment/default.htm. There are also alternative cancer therapies; see http://www.bccancer.bc.ca/HPI/UnconventionalTherapies/default.htm.

indicate that only 0.4% of cancer drugs are used to *diagnose* cancer. The vast majority (98.7%) are used to *treat* cancer; 0.9% are used to *prevent* cancer.

I will examine the relationship, across cancer sites, between cancer incidence and two different measures of pharmaceutical innovation.[12] The first is the number of distinct chemotherapy regimens for treating the cancer site. The second is the number of articles published in scientific journals pertaining to drug therapy for that cancer site.

Cancer Care Ontario (CCO) publishes lists of chemotherapy regimens grouped by disease site. The regimens are categorized according to the recommendations of the respective CCO Disease Site Group. I will use the number of *core* chemotherapy regimens for a disease site. A core therapy is defined as a "standard therapy; a regimen widely used by most Regional Cancer Centres in this disease site."[13] Data on the number of new cases in Canada in 2002, by cancer site, were obtained from GLOBOCAN 2002. Data on the estimated number of new cases in the U.S. in 2000, by cancer site, were obtained from the *SEER Cancer Statistics Review, 1975-2002*.[14]

Data on eighteen cancer sites, listed in descending order of incidence in Canada, are shown in Table 2. In both Canada and the U.S., the top four cancer sites—lung, breast, prostate, and colorectal—account for about two-thirds of all cases. They account for 46% of core chemotherapy regimens. Figure 1 plots the log of the number of core chemotherapy regimens for a site against the log of the number of cases in Canada in 2002. Statistics from the regression of the log of the number of core chemotherapy regimens on the log of the number of cases in Canada in 2002 are:

Regression Statistics	
Multiple R	0.550452
R Square	0.302998
Adjusted R Square	0.259435
Standard Error	0.84812
Observations	18

[12] According to IMS Health, cancer drugs (cytostatics) account for about 5% of global drug expenditure. *IMS Retail Drug Monitor, January 2005*, http://open.imshealth.com/download/jan2005.pdf.

[13] Other categories include "local regimens" (regimens not widely used; used by fewer than four regional cancer centres) and "emergent regimens" (regimens which have not yet been accepted as standard regimens).

[14] See http://seer.cancer.gov/csr/1975_2002/results_merged/sect_01_overview.pdf.

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	5.003104	5.003104	6.955448	0.017927
Residual	16	11.50892	0.719307		
Total	17	16.51202			

	Coefficients	*Standard Error*	*t Stat*	*P-value*
Intercept	-3.06576	1.651987	-1.8558	0.081997
ln(CA cases)	0.525554	0.199276	2.637318	0.017927

The elasticity of the number of chemotherapy regimens with respect to the number of cases is 0.53, and the estimate is significantly different from zero (p-value = .018). A 10% increase in the number of cases in associated with a 5.3% increase in the number of chemotherapy regimens.[15]

Now I will examine the relationship, across cancer sites, between cancer incidence and the number of articles published in scientific journals pertaining to drug therapy for that cancer site. Data on the latter were obtained by searching MEDLINE (Medical Literature Analysis and Retrieval System Online), the U.S. National Library of Medicine's (NLM) premier bibliographic database of biomedical citations and abstracts. The subject scope of MEDLINE is biomedicine and health, broadly defined to encompass those areas of the life sciences, behavioral sciences, chemical sciences, and bioengineering needed by health professionals and others engaged in basic research and clinical care, public health, health policy development, or related educational activities. It contains approximately 13 million references to journal articles that appeared in over 4,800 journals published in the United States and more than 70 other countries primarily from 1966 to the present.[16]

[15] The elasticity is virtually identical when we use the log no. of cases in the U.S. in 2000 instead of the log no. of cases in Canada in 2002. U.S. and Canadian incidence across cancer sites is extremely highly correlated.

[16] The great majority of journals are selected for MEDLINE based on the recommendation of the Literature Selection Technical Review Committee, an NIH-chartered advisory committee of external experts analogous to the committees that review NIH grant applications. The majority of the publications covered in MEDLINE are scholarly journals; a small number of newspapers, magazines, and newsletters considered

References to articles are indexed with terms from NLM's controlled vocabulary, MeSH (Medical Subject Headings). MeSH is the National Library of Medicine's controlled vocabulary thesaurus. It consists of 22,568 descriptors in a hierarchical structure that permit searching at various levels of specificity. The Medical Subject Headings Section staff continually revises and updates the MeSH vocabulary. Staff subject specialists are responsible for areas of the health sciences in which they have knowledge and expertise. In addition to receiving suggestions from indexers and others, the staff collect new terms as they appear in the scientific literature or in emerging areas of research; define these terms within the context of existing vocabulary; and recommend their addition to MeSH.

At the highest (most general) level of the MeSH hierarchical structure are the following 15 headings:

1. Anatomy [A]
2. Organisms [B]
3. Diseases [C]
4. Chemicals and Drugs [D]
5. Analytical, Diagnostic and Therapeutic Techniques and Equipment [E]
6. Psychiatry and Psychology [F]
7. Biological Sciences [G]
8. Physical Sciences [H]
9. Anthropology, Education, Sociology and Social Phenomena [I]
10. Technology and Food and Beverages [J]
11. Humanities [K]
12. Information Science [L]
13. Persons [M]
14. Health Care [N]
15. Geographic Locations [Z]

We can search MEDLINE for all articles pertaining to particular diseases, and for articles specifically pertaining to drug treatment of those diseases. For example, the search string "exp leukemia" identifies all articles in MEDLINE that pertain to any form of leukemia, and the search string "exp leukemia/dt" identifies all articles in the database that pertain to drug therapy for any form of leukemia.

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useful to particular segments of NLM's broad user community are also included. Citations for MEDLINE are created by the NLM, international partners, and collaborating organizations.

The MEDLINE data we have described refer to *publication*; my objective is to measure *innovation*. I think that publication is closely related to, and a good indicator of, innovation. The majority of the publications covered in MEDLINE are scholarly journals, and novelty is generally a necessary (but not sufficient) condition for publication in such journals.[17] However, the novelty criteria used by scholarly journals undoubtedly differ from those used by other authorities (e.g. the U.S. Patent and Trademark Office or Cancer Care Ontario's Disease Site Groups).

Table 3 shows data on incidence in 2002, by region (less vs. more developed), and number of MEDLINE article citations, for 25 cancer sites as defined in GLOBOCAN. I calculated both total and drug-therapy article cites for each cancer site, from which non-drug cites may also be computed:

$TOTAL\_CITE_i$ = the total number of MEDLINE articles pertaining to cancer site i
$DRUG\_CITE_i$ = the number of MEDLINE articles pertaining to drug therapy for cancer site i
$NONDRUG\_CITE_i$ = other MEDLINE articles pertaining to cancer site i
= $TOTAL\_CITE_i - DRUG\_CITE_i$

Using the data in Table 3, I estimated the following four models:

Model 1: $\ln DRUG\_CITES_i = \alpha_1 + \beta_{DW} \ln INC\_WORLD_i + e_i$

Model 2: $\ln NONDRUG\_CITES_i = \alpha_2 + \beta_{NW} \ln INC\_WORLD_i + e_i$

Model 3: $\ln DRUG\_CITES_i = \alpha_3 + \beta_{DM} \ln INC\_MORE_i + \beta_{DL} \ln INC\_LESS_i + e_i$

Model 4: $\ln NONDRUG\_CITES_i = \alpha_4 + \beta_{NM} \ln INC\_MORE_i + \beta_{NL} \ln INC\_LESS_i + e_i$

where:

INC_WORLD_i = the incidence of cancer at site i throughout the world
INC_MORE_i = the incidence of cancer at site i in the more developed region
INC_LESS_i = the incidence of cancer at site i in the less developed region

Estimates of these equations are shown in Table 4. Estimates of model 1 indicate that the elasticity of MEDLINE drug cites with respect to cancer incidence throughout

[17] Novelty is also a necessary condition for *patenting*. A searchable U.S. patents database exists, and some investigators have used patent counts and citations as innovation indicators. However the U.S. patent classification system is much cruder than the MeSH classification system with respect to medical innovation, and is inadequate for our purposes.

the world is 0.60, and is significantly different from zero. Estimates of model 2 indicate that the elasticity of MEDLINE non-drug cites with respect to cancer incidence throughout the world is virtually identical, and is also significantly different from zero. There is more publication (presumably indicating more research and innovation) related to cancers with higher incidence. A 10% increase in cancer incidence is associated with a 6% increase in both the number of drug-therapy publications and non-drug-therapy publications.

Models 3 and 4 distinguish between incidence in the more developed and less developed regions. Model 3 indicates that the number of drug-therapy publications is related to incidence in the more-developed region but not to incidence in the less-developed region. Model 4 indicates that the number of non-drug-therapy publications is also related to incidence in the more-developed region but not to incidence in the less-developed region, although the more- vs. less-developed difference between the sensitivity of the number of drug-therapy publications ($\beta_{DM} - \beta_{DL} = 0.73$) is almost three times as large as the more- vs. less-developed difference between the sensitivity of the number of non-drug-therapy publications ($\beta_{NM} - \beta_{NL} = 0.27$).

I think that the most plausible explanation for the lack of a relationship between the incidence in developing countries and the amount of pharmaceutical innovation has been weak or nonexistent incentives for firms to develop medicines for diseases primarily afflicting people in developing countries. Although the size of the developing-region market is large, the prices manufacturers expect to receive in this market are probably very low.[18]

III. Discussion

I performed two analyses of the relationship, across cancer sites, between cancer incidence and pharmaceutical innovation, using two different measures of the latter: the number of distinct chemotherapy regimens for treating the cancer site, and the number of

[18] Prices of other (non-drug) medical treatments (e.g., hospital care) are also undoubtedly lower in the developing region than they are in the developed region. But the *ratio* of the expected drug price to the price of other medical treatments may be lower in the developing region (due to the low marginal cost of drugs). This could explain why ($\beta_{DM} - \beta_{DL}$) is almost three times as large as ($\beta_{NM} - \beta_{NL}$).

articles published in scientific journals pertaining to drug therapy for that cancer site. Both analyses indicated that the amount of pharmaceutical innovation increases with disease incidence. The elasticity of the number of chemotherapy regimens with respect to the number of cases is 0.53. The elasticity of MEDLINE drug cites with respect to cancer incidence throughout the world is 0.60. These estimates are quite close, despite the fact that the innovation measures used are quite different.

If the ratio of price to marginal cost for branded drugs with patent protection is about 6:1, as some evidence suggests, then the elasticity of variable profit with respect to price is likely to be similar to the elasticity of variable profit with respect to the number of consumers. This suggests that the elasticity of innovation with respect of price is similar to the elasticity of innovation with respect to market size, which I estimate to be in the .53 to .60 range. This estimate is very consistent with Giaccotto, Santerre and Vernon's (2005) estimate (0.583) of the elasticity of pharmaceutical industry R&D with respect to the real price of pharmaceuticals. That study employed time series econometric techniques to explain R&D growth rates using industry-level data from 1952 to 2001.

A recent paper by Abbott and Vernon (2005) suggests that the elasticity of innovation with respect to price may be somewhat higher. Using Monte Carlo techniques, they model how future price controls in the U.S. will impact early-stage product development decisions within the context of a net present value framework that appropriately reflects the uncertainty associated with R&D project technical success, development costs, and future revenues. Using partial-information estimators calibrated with the most contemporary clinical and economic data available, they estimate that cutting prices by 40 to 50 percent in the U.S. will lead to between 30 to 60 percent fewer R&D projects being undertaken (in early-stage development). The elasticity of innovation with respect to price is therefore in the 0.67-1.33 range. Since evidence from the 2002 MEPS suggests that the ratio of price to marginal cost is lower than 6:1, the elasticity of variable profit with respect to price is likely to be greater than the elasticity of variable profit with respect to the number of consumers, so my estimates seem compatible with Abbott and Vernon's.

My estimates, and those obtained by other authors using very different approaches, imply that importation would be likely to significantly reduce the amount of pharmaceutical innovation. It would also be likely to reduce employment in the U.S. pharmaceutical industry. We can get a rough assessment of the employment impact of reduced pharmaceutical innovation by examining the relationship, across pharmaceutical companies, between the number of innovations and the number of employees. I defined the number of innovations by a company as the number of FDA-approved active ingredients contained in products sold by the company that are not contained in any other company's products.[19] Data on the number of innovations by, and number of employees of, 14 selected major pharmaceutical companies are shown in Table 5. Figure 2 plots the log of the number of company employees against the log of the number of innovations. The relationship depicted is highly statistically significant: the elasticity of employment with respect to the number of innovations is 0.71 (p-value < .001).

[19] This measure was constructed from the Multum Lexicon database (http://www.multum.com/Lexicon.htm).

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Table 1
25 conditions with highest U.S. incidence

Condition	Percent	Incidence Rate	US People	Data
1. Diarrhea	100.00%	1 in 1	272 million	almost 100% annually (NIDDK)
2. Common Headache	90.00%	1 in 1	244.8 million	90% approximately; almost everyone gets some each year.
3. Dental caries	55.57%	1 in 2	151.2 million	2,534,161 annual cases in Victoria 1996 (DHS-VIC)
4. Infectious Diarrhea	36.40%	1 in 3	99 million	99 million new cases in the USA 1980 (Digestive diseases in the United States: Epidemiology and Impact – NIH Publication No. 94-1447, NIDDK, 1994)
5. Flu	36.00%	1 in 3	97.9 million	36 per 100 (NHIS96); 35 million annually up to 50 million annually (NIAID/CDC); 10-20% yearly (NIAID)
6. Food poisoning	27.94%	1 in 3	76 million	about 76 million cases annually in USA (NIDDK)
7. Common cold	22.79%	1 in 4	62 million	62 million cases (NIAID); 23.6 per 100 (NHIS96); estimated 1 billion colds in the USA annually; Children get 6-10 yearly, adults 2-4 yearly; over 60's less than 1 a year.
8. Mental illness	22.10%	1 in 4	60.1 million	about 22.1 percent of American adults annually or 44.3 million people (NIMH)
9. Injury	21.69%	1 in 4	59 million	59 million cases (IOM)
10. Hives	15.00%	1 in 6	40.8 million	about 15% Americans each year (NWHIC)
11. Chronic Sinusitis	12.83%	1 in 7	34.9 million	34.9 million cases per year in the USA 1994 (US Government Statistics)
12. Depressive disorders	6.91%	1 in 14	18.8 million	estimated 18.8 million American adults annually (NIMH)
13. Sexually Transmitted Disease	5.62%	1 in 17	15.3 million	15.3 million annual cases (NIAID)
14. Acute Bronchitis	4.60%	1 in 21	12.5 million	4.6 per 100 (NHIS96: acute bronchitis); 14.2 million cases annually
15. Iron deficiency anemia	4.12%	1 in 24	11.2 million	187,979 annual cases in Victoria 1996 (DHS-VIC); 20% women of childbearing age; 2% adult men (NWHIC)
16. Social phobia	3.70%	1 in 27	10.1 million	3.7% adults annually (NIMH)
17. Traveler's diarrhea	3.68%	1 in 27	10 million	estimated 10 million (DBMD)
18. Enteroviruses	3.68%	1 in 27	10 million	estimated 10-15 million cases annually in USA (DVRD)
19. Post-traumatic stress disorde	3.60%	1 in 27	9.8 million	3.6% adults annually (NIMH)
20. Acute urinary conditions	3.09%	1 in 32	8.4 million	8.405 million new conditions (NIDDK)
21. Acute Nonulcer dyspepsia	3.01%	1 in 33	8.2 million	8.2 million new cases (1988/NIDDK)
22. Generalized anxiety disorder	2.80%	1 in 35	7.6 million	2.8% of the adult U.S. population (NIMH)
23. Middle ear infection	2.57%	1 in 38	7 million	7 million annually
24. Occupational Injuries	2.32%	1 in 43	6.3 million	6.3 million workers in 1994 (CDC-OC)
25. Obsessive-compulsive disor	2.30%	1 in 43	6.3 million	2.3% adults annualy (NIMH)

Table 2
Cancer incidence and number of core chemotherapy regimens, by site

Site	Number of cases in Canada in 2002	Number of core chemotherapy regimens	Number of cases in the U.S. in 2000
Lung	20,648	11	164,100
Breast	19,540	21	182,800
Prostate	17,900	11	180,400
Colorectal	17,708	3	130,200
Lymphoma - Non-Hodgkin's	5,671	11	54,900
Renal	3,858	1	31,200
Uterine/Sarcoma	3,643	1	36,100
Leukemia	3,636	16	30,800
Melanoma	3,585	4	47,700
Pancreas	3,277	1	28,300
Gastric	3,132	4	21,500
Ovary	2,661	3	23,100
Central Nervous System	2,356	1	16,500
Myeloma	1,855	3	13,600
Cervix	1,502	2	12,800
Esophagus	1,378	3	12,300
Lymphoma - Hodgkins	838	2	7,400
Testis	775	3	6,900

Table 3

Incidence in 2002, by region, and number of MEDLINE article citations, for 25 cancer sites as defined in GLOBOCAN

Cancer site	ICD10 codes	total number of MEDLINE articles pertaining to cancer site	number of MEDLINE articles pertaining to drug therapy for cancer site	incidence of cancer at site in the less developed region	incidence of cancer at site in the more developed region
Leukaemia	C91-C95	138,971	30,529	175,898	124,202
Lung	C33-C34	98,796	14,341	672,221	676,681
Non-Hodgkin lymphoma	C82-C85,C96	52,485	9,064	149,191	151,096
Colon and rectum	C18-C21	80,738	8,744	355,701	665,731
Ovary etc.	C56,C57.0-4	38,142	7,636	107,541	96,769
Brain, nervous system	C70-C72	106,896	7,435	114,630	74,549
Prostate	C61	44,355	7,015	165,347	513,464
Liver	C22	77,313	6,464	513,060	110,404
Melanoma of skin	C43	46,321	5,039	29,352	130,815
Hodgkin lymphoma	C81	22,973	4,628	34,264	28,033
Stomach	C16	44,298	4,035	619,235	311,154
Bladder	C67	28,574	3,711	130,971	225,242
Multiple myeloma	C90	18,421	3,332	30,473	55,166
Testis	C62	15,731	2,723	20,489	28,103
Pancreas	C25	31,104	2,706	96,650	135,204
Cervix uteri	C53	35,812	2,072	409,404	83,437
Oesophagus	C15	22,324	1,857	386,435	73,875
Oral cavity	C00-C08	36,013	1,683	183,033	91,141
Thyroid	C73	24,347	895	81,656	59,199
Larynx	C32	16,362	694	94,589	64,537
Nasopharynx	C11	7,576	632	72,612	7,189
Other pharynx	C09-C10,C12-C14	4,228	364	81,811	48,459
Breast	C50	118,088	18,959	514,072	636,128
Corpus uteri	C54	27,756	2,891	62,312	136,329
Kidney etc.	C64-C66,C68	38,660	2,848	68,394	139,871

Table 4

Estimates of the relationship between cancer incidence and the number of drug and non-drug MEDLINE citations

Model	1	2	3	4
dep. Var.	ln $DRUG\_CITES_i$	ln $NONDRUG\_CITES_i$	ln $DRUG\_CITES_i$	ln $NONDRUG\_CITES_i$
ln INC_WORLD_i	0.597	0.598		
std. err.	0.210	0.138		
t-stat	2.850	4.330		
p-value	0.009	0.000		
ln INC_MORE_i			0.670	0.433
std. err.			0.209	0.145
t-stat			3.200	3.000
p-value			0.004	0.007
ln INC_LESS_i			-0.065	0.167
std. err.			0.222	0.154
t-stat			-0.290	1.090
p-value			0.774	0.289

Table 5
Number of innovations by, and number of employees of, 14 selected major pharmaceutical companies

Company	Number of active ingredients for which company is sole source	Number of employees in 2003
PFIZER INC	48	122,000
GLAXOSMITHKLINE PLC -AD	18	103,166
NOVARTIS AG -ADR	18	78,541
AVENTIS SA -ADR	10	75,567
ABBOTT LABORATORIES	26	72,181
ROCHE HOLDINGS LTD -ADR	13	65,357
MERCK & CO	26	63,200
ASTRAZENECA PLC -ADR	14	61,900
WYETH	15	52,385
LILLY (ELI) & CO	18	46,100
BRISTOL MYERS SQUIBB	18	44,000
SANOFI-SYNTHELABO -ADR	10	33,086
SCHERING-PLOUGH	8	30,500
NOVO-NORDISK A/S -ADR	5	18,756

Figure 1
The relationship between incidence and innovation

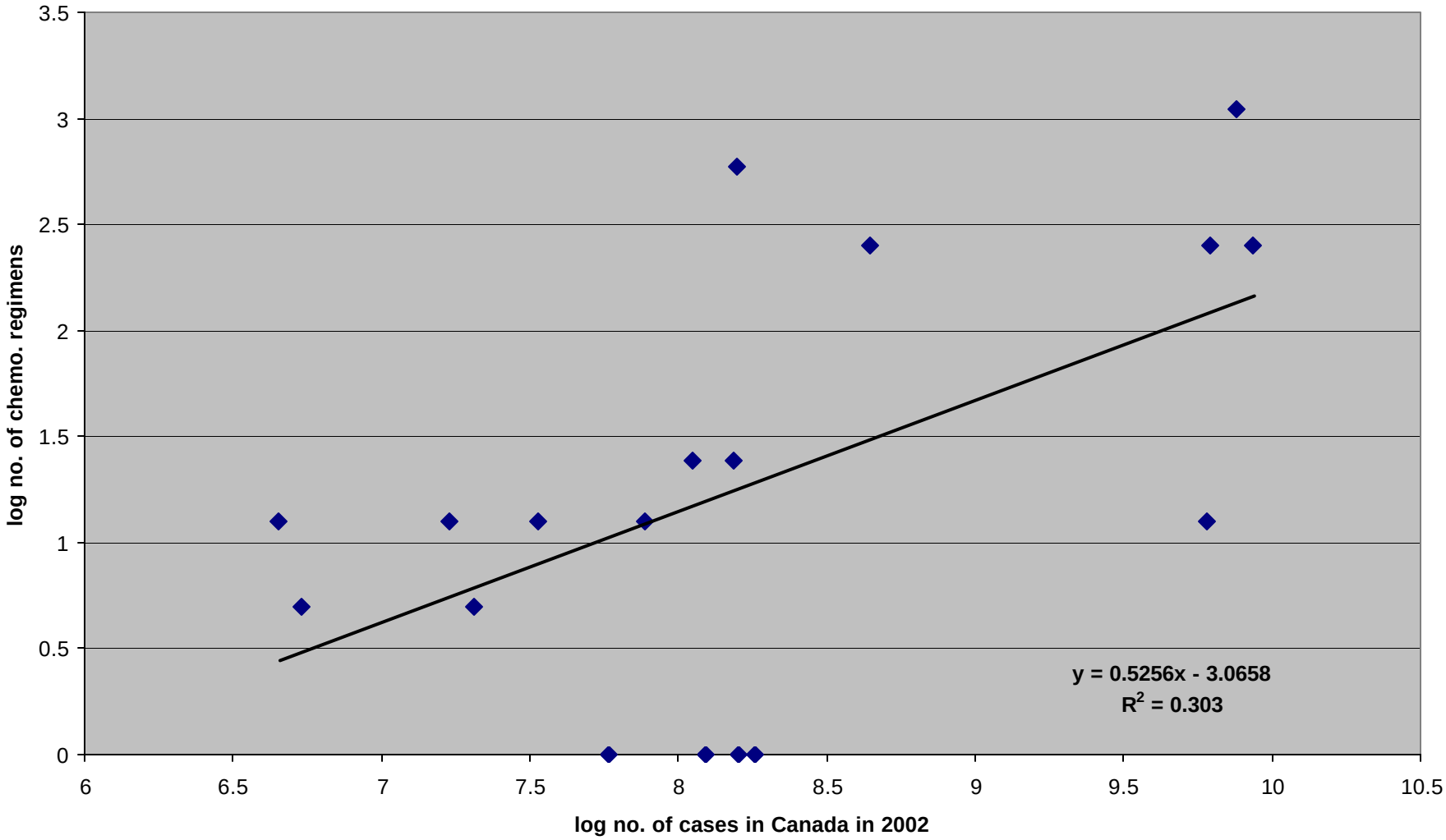

Figure 2
The relationship between innovation and employment