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"The Effects of Pharmaceutical Innovation on Cancer Mortality Rates"

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The Effects of Pharmaceutical Innovation on Cancer Mortality Rates *

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Abstract

Cancer is a leading cause of death in developed countries, and cancer treatments are the top category of pharmaceutical spending in the United States and Europe. This paper assesses whether novel cancer therapies are associated with a reduction in mortality. Using panel data from 11 developed countries, we study the relationship between mortality attributed to a specific cancer site and the availability of pharmaceutical treatments. The cross-country and cross-site variation over time allows us to isolate the decline in mortality attributable to new drugs from that due to changes in lifestyle and environmental factors. We correct for the endogeneity of mortality and the availability of new treatments using instrumental variables. On average, our results show a decline in mortality of 8-9% is associated with the availability of one new treatment for a cancer site. The gains vary across countries and cancer sites. Based on spending from 2000-2011, costs per statistical life saved ranged from $11-12K for bladder and liver cancers to over $150K for cervical, melanoma and stomach cancers. Across countries, Switzerland had the largest spending per statistical life at approximately $66K, while the UK had the lowest with $19K.

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1 Introduction

Health spending and outcomes vary significantly across developed countries. The US ranks 26th among OECD countries in life expectancy, despite spending more per person. Cancer is second only to cardiovascular disease as a cause of death in high income countries, but there is heterogeneity in the overall burden of cancer as well as in specific cancer sites. For example, France has an incidence rate of 34.95 for cancer of the lung and 89.7 for breast cancer, compared to 8.3 and 67.61 in Portugal. In addition, trends in cancer mortality differ across countries and cancer sites. While the war on cancer has produced significant gains for some cancer sites, these gains are not realized equally in all countries.

An important question is the role of national policies, particularly regarding access to new treatments, in driving these outcomes. Recent reports indicate that cancer survival rates in the UK are below those in the rest of Europe (Angelis and the EUROCARE-5 Working Group (2014)). One explanation for this outcome is the reluctance of the UK's National Health Service to reimburse recent cancer therapies. In contrast, France has rates of uptake of new cancer drugs that are comparable to those in the US, while Germany falls somewhere in the middle (Jönsson and Wilking (2007)). In most countries outside the United States, the government plays an important role in determining the price of new pharmaceutical treatments and in promoting access to such treatments. Within the US, government insurance programs such as Medicare as well as private insurers have a clear interest in promoting the appropriate use of the most effective therapies. However, little work exists to pinpoint specific policies that generate the differences in health outcomes, and in cancer survival specifically.

We focus on cancer for several reasons. First, cancer is a leading cause of death. Second, spending on oncology treatments is forecast to exceed $70 billion in developed markets by 2018 (IMS Institute for Healthcare Informatics (2014)), making it the largest category of pharmaceutical spending. Whether this spending results in significant health gains is an important policy issue, particularly since the burden of paying for these treatments generally falls on government programs. After decades of increases, overall cancer mortality has fallen since the early 1990s (Cutler (2008)). This improvement coincides with the introduction of many new treatments have been introduced over the last 20 years, often at controversial price levels (Howard et al. (2015)). The goal of this work is to quantify the extent to which these treatments caused mortality to decline.

We are not the first to tackle this issue. Previous work has documented some gains in the war on cancer, measured either as increased survival or as mortality reduction, and noted differences in these gains across countries. Several papers link these gains to medical innovations and/or

spending on cancer care. The role of pharmaceutical treatments in improving outcomes is the focus of Lichtenberg (2004), Lichtenberg (2010), Lichtenberg (2012) and Lichtenberg (2014), among others. There is some disagreement about whether, for example, the value of the gains fully justifies the higher levels of spending in the US compared to Europe (Philipson et al. (2012), Soneji and Yang (2014)).

We build on these and other papers by exploiting variation in mortality outcomes over time, across cancer sites, and across 11 countries. Innovations in drug development have not been equally spread across all cancer sites, and have occurred at different times. Access to these innovations is not simultaneous across countries, due to regulatory delays and other factors. Our dataset allows us to control for unobserved factors specific to cancer sites and countries, as well as site-specific trends, in order to identify the relationship between increased access to pharmaceutical innovation and changes in cancer mortality. We correct for the endogeneity bias due to unobserved common drivers of mortality shocks and drug innovation using instrumental variables.

On average, our results show a decline in mortality of 8-9% is associated with the availability of one new treatment for a cancer site. The gains vary across countries and cancer sites. Based on spending from 2000-2011, costs per statistical life saved ranged from $11-12K for bladder and liver cancers to over $150K for cervical, melanoma and stomach cancers. Across countries, Switzerland had the largest spending per statistical life at approximately $66K, while the UK had the lowest with $19K. These estimates are at the lower end of the value of statistical life estimated in earlier studies (Viscusi and Aldy (2003)).

2 Econometric Methods

2.1 Evaluating the Benefits of Cancer Drugs

There are several approaches to estimating the benefits of cancer treatments. Health technology assessments (HTAs), often used by payers to determine whether a treatment should be reimbursed, are prospective assessments based on the results of clinical trials. The value of a treatment that yields a median increase in survival of 6 months in a clinical trial can be calculated as half the value of a statistical life-year, for example. However, the use of treatments in practice may differ from the protocol employed in clinical trials. The population of patients receiving the treatment is likely to be different, and doctors may not always adhere to recommended dosing. Thus, the clinical gains observed in randomized controlled trials may not be realized when a treatment is employed more broadly.

Economists often employ a second approach that estimates the benefits to consumers based on the preferences revealed by their consumption decisions. That is, economists estimate demand for a treatment, and these estimates allow the calculation of social welfare (or gains from innovation). Petrin (2002) is an example of this approach in the case of the introduction of the minivan in the automobile market. An application in pharmaceuticals is Dunn (2012), who estimates the welfare gains from innovations in cholesterol drugs. This approach can be problematic in the context of cancer treatments, though. First, patients are unlikely to face the true price of a treatment due to insurance coverage. Prescribers may be unaware of the true price, or insensitive to it, or may act as an imperfect agent for patients. Perhaps most importantly, cancer patients are often close to death. In such situations, assumptions about individual rationality are likely to be inappropriate.

Most economic studies instead look at an outcome measure such as mortality or survival in the general population, and examine how this outcome changes with the availability of new treatments controlling for other factors. Any change in the outcome attributable to cancer therapies can be compared to spending on these treatments to arrive at an estimate of net benefits. Examples of papers using this methodology include Lichtenberg (2010), Lakdawalla et al. (2010), Philipson et al. (2012), and Lichtenberg (2014).

Building on this body of work, we focus on mortality at the cancer site level in a panel of 11 developed countries: Austria, Croatia, the Czech Republic, France, Germany, Ireland, Norway, Sweden, Switzerland, the United Kingdom, and the United States. Two factors motivate our choice of mortality as an outcome measure. The first is the availability of data across countries and time periods. While mortality data is available at an annual frequency, EUROCARE provides recent estimates of country-level survival in Europe only for the entire period of 2000-2007 (but not annually, which limits the ability to study changes in survival over time). The second reason for choosing mortality is that it avoids "lead-time bias" that can affect survival measures. Lead-time bias occurs if, for example, some cancers are diagnosed earlier due to changes in screening or improvements in diagnostic technologies. Even without any change in treatment, survival will appear to increase and to be positively correlated with spending due to longer duration of treatment. [1]

[1] Howard et al. (2016) avoid this problem by restricting their analysis to patients with metastatic cancers in the US, which should not be affected by changes over time in the stage at which cancers are detected. Lichtenberg (2015), Lichtenberg (2016b) and Lichtenberg (2016a) study premature cancer mortality (before 75 or 65 years old) in Canada, Switzerland and Belgium respectively also to avoid the lead-time bias.

2.2 Identifying the Effects of Drug Introductions on Mortality

We are interested in estimating the treatment effect of the availability of new cancer medications on mortality rates. In order to identify a causal effect, we need to control for the variation in other determinants of mortality that could be correlated with the adoption and use of cancer medications. Our outcome data, which we describe in more detail in the following section, include annual observations of mortality rates by cancer sites across countries. Similarly, we have information on the availability and consumption of cancer medications by cancer site, country, and over time.

These multiple sources of variation are critical for identifying the effect of new treatments. A pure cross-country analysis on average mortality rates across all cancers is unlikely to be very informative, given the many country-level healthcare and population characteristics that can affect mortality. The additional variation across cancers within a country allows us to control for country-specific unobserved heterogeneity. Within a cancer, the availability of new treatments occurs at different times in different countries. Unlike some previous work that considers only a single country, we use this additional variation across countries to pin down the effect of a new treatment. Essentially, we use a triple-difference approach that exploits variation across countries, cancer sites and years, and we address the possible endogeneity of the adoption of new drugs with instrumental variables as described below.

To be more precise, let y_{ist} denote the mortality rate by cancer site s for country i at year t and assume that the log rate follows:

$$\ln y_{ist} = \alpha_{is} + \delta_t + \gamma \mathbf{x}_{ist} + \beta d_{ist} + \varepsilon_{ist} \tag{2.1}$$

where α_{is} is a country-cancer site fixed effect, δ_t is a year effect, $\mathbf{x}_{ist}$ are variables such as the incidence of cancer site s in country i in year t, and d_{ist} is a variable characterizing the availability of new drug treatments in year t, such as the number of new drugs approved for cancer site s in country i and prior to year t, or expenditures on new drug treatments for cancer site s in country i and year t.

We include year effects (δ_t) to capture mortality changes over time due to changes in lifestyle or environmental improvements, such as the removal of asbestos, the reduction in air pollution, or a decline in smoking. Country-cancer site specific effects (α_{is}) capture unobserved cancer- and country-specific effects on mortality. For example, a country may have physicians with particular expertise in treating lung cancer, and this expertise may lower mortality from lung cancer in that country. Alternatively, surgical interventions may lower the mortality rate for

certain cancers, and countries may differ in their adoption of such interventions. Controlling for all of these factors, the parameter β identifies the effect of the availability of new cancer treatments on mortality provided the error term ε_{ist} is not correlated with d_{ist}.

However, it is quite possible that the availability of new treatments is correlated with other unobservable factors driving mortality. Pharmaceutical firms could focus more R&D efforts on cancers with an increasing burden, so that new treatments are more likely to be developed for cancers with a positive trend in mortality. A country that anticipates a large burden from cancer in the future may adopt new cancer treatments more quickly. In either case, the availability of treatments is endogenous, and the $\hat{\beta}$ is a biased estimate of the causal effect of drugs on mortality.

To address these endogeneity issues, we instead estimate (2.1) using instrumental variables, our choice of which is described in the next section. We assume that we observe variables in a vector denoted $\mathbf{z}_{ist}$ correlated with d_{ist} but mean independent of ε_{ist} such that

$$E\left(\varepsilon_{ist}\mathbf{z}_{ist}|\alpha_{is},\delta_t,\mathbf{x}_{ist}\right)=0 \tag{2.2}$$

and we then use a two-stages least squares estimation to identify β.

The specification of the availability of new drugs in (2.1) implicitly assumes that take-up of a new treatment is immediate. In practice, innovations may diffuse more slowly as practitioners learn more about them. Previous work (e.g., Lichtenberg (2010)) has allowed for a lag in the adoption of new products. We can do something similar by using $d_{ist-\tau}$, where τ is a lag, instead of d_{ist} in equation (2.1). Note that the 2SLS estimate of β using k years of lags for the instruments and l years of lags for the endogenous right hand side variable is:

$$\hat{\beta}_{lk}=\frac{cov\left(\ln y_{ist},z_{ist-k}\right)}{cov\left(d_{ist-l},z_{ist-k}\right)}$$

which implies that

$$E(\hat{\beta}_{lk})=\beta\frac{cov\left(d_{ist-\tau},z_{ist-k}\right)}{cov\left(d_{ist-l},z_{ist-k}\right)}$$

If $l\neq\tau$, $E(\hat{\beta}_{lk})$ varies over k provided the covariance between d_{ist-l} and z_{ist-k} is not constant over lags k (which is a testable assumption) and, as $E(\hat{\beta}_{\tau k})=\beta$, all $\hat{\beta}_{\tau k}$ are consistent estimates of β for all k provided the instrumental variable condition (2.2) is valid. This means that the estimate of β will not vary significantly with lags of the instruments in the 2SLS estimates only if we use the right number of years as lag for d_{ist-l}. Moreover, if the variables z_{ist} and d_{ist}

always have a maximum correlation when contemporaneous such that

$$|cov\left(d_{ist'}, z_{ist}\right)| \leq |cov\left(d_{ist}, z_{ist}\right)| \text{ for any } t, t'$$

then τ is the number of lag years l that minimizes the absolute value of $E(\hat{\beta}_{l\tau})$, that is $|E(\hat{\beta}_{\tau\tau})| \leq |E(\hat{\beta}_{l\tau})|$ for all l, which is a testable assumption.

While we believe this approach has many advantages, we do not attempt to evaluate the relative contribution of drug innovation compared to other types of changes in health technology, such as imaging or equipment innovation, which is possible with additional data (Lichtenberg (2012) or Lichtenberg (2014)). We only try to identify whether drug treatments have led to cancer mortality reductions, and by how much. In addition, this is a retrospective analysis, which limits its use in pricing decisions going forward.

3 Data and Descriptive Statistics

3.1 Sources of data

3.1.1 Incidence

Our information on cancer incidence is provided by the International Agency from Research on Cancer (IARC) of the World Health Organization (WHO).[2] Incidence is measured as the number of new cases arising in a given period in a specified population, collected routinely by cancer registries. It can be expressed as an absolute number of cases per year or as a rate per 100,000 persons per year, and it approximates the average risk of developing a cancer. The data provide annual measures of the total number of cases and the rate of each of 38 cancer sites by country, sex, and age group.

Because age has powerful influence on risk of cancer and age distributions vary across countries, we calculate age-adjusted standardized rates of incidence (ASIR). The ASIR is a weighted mean of the age-specific rates, where weights are from a selected population distribution, such as the World Standard Population or European standard.[3] These rates allow us to compare incidence rates across countries independent of differences in their age distributions and their demographic changes over time. Throughout this paper, we use the European standard; all results are robust to using the World standard.

[2]Data are available from the IARC database at http://eco.iarc.fr/EUREG/AnalysisT.aspx.
[3]See IARC documentation at http://eco.iarc.fr/EUREG/Glossary.aspx.

Ideally, we would use the stock of patients per cancer site, rather than the flow of newly diagnosed patients. This flow omits the stock of patients who survived from the previous year, and who may continue to consume pharmaceutical treatments. This omission will appear in the error term in our regressions, and may therefore bias our coefficient estimates of β if correlated with the number of new drugs used per cancer site and by country. However, our instrumental variables strategy will also correct for this omitted variable problem of patient stocks, provided the instruments z_{ist} also satisfy condition (2.2) when ε_{ist} includes omitted past stock of patients.

3.1.2 Mortality

We use data on mortality from the WHO.[4] The WHO Mortality Data base comprises deaths registered in national vital registration systems, with underlying cause of death defined as "the disease or injury which initiated the train of morbid events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury" in accordance with the rules of the International Classification of Diseases. The data includes the number of deaths by country, year, sex, age group and cause of death in addition to the population in each one of these categories. Our conversion from ICD9 and ICD10 codes to the cancer sites for which we have incidence data is based on information provided by EUREG.[5]

For a specific tumor site and population (by age and gender), we compute a crude mortality rate by dividing the number of cancer deaths observed during a given year by the corresponding population, expressed as an annual rate per 100,000 persons at risk. We then calculate age-standardized mortality rates (ASMR), using the same method described for incidence.

3.1.3 Pharmaceutical data

We include information on all drugs approved by the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), or other European national regulators that are recommended for at least one cancer site. This set includes treatments with four mechanisms of action. Antineoplastic drugs block the development of neoplasms. Cytostatic drugs, including hormone therapies, block receptors on cancer cells to stop them from growing, but do not kill them. Immunostimulants boost the immune system to help fight cancer. Finally, interferons are biological response modifiers that slow tumor growth by interfering with cancer cell division. These drugs can be used in combination, both with other drugs as well as with radiation and

[4] Data can be downloaded from the WHO Mortality website http://www.who.int/healthinfo/statistics/mortality_rawdata/en/.
[5] See EUREG dictionary at http://eco.iarc.fr/eureg/Dictionary.aspx.

surgery. New treatments in each of these categories have been introduced since 1990, and our analysis focuses on these.[6]

For country-level information on the use of specific cancer drugs, we use the MIDAS dataset from IMS Health. This provides quarterly revenues and the number of units sold for each molecule in each country from 2000 to 2013. We combine revenues and units across all presentations of a drug within a country, and all revenues are converted into 2013 US dollars. In addition, we have the initial launch date for each cancer drug in each of the countries in our dataset, as well as the launch dates of non-cancer drugs.

We match each drug to the specific cancer site(s) it targets using three sources of information. The National Cancer Institute (NCI) provides information on drugs approved by the FDA for each type of cancer.[7] We consulted the Merck Manual to verify the recommended treatments for each cancer site. From the EMA, we record the date at which each drug received approval from the EMA for a specific cancer.

Table 3.1 provides summary statistics for our sample of drugs of the number of cancer sites for which they are approved treatments, where the unit of observation is a single drug. About two-thirds are relatively new, which we define as having an initial global launch date after 1990. On average, the newer drugs are used for just over 2 different cancer sites. Often, additional uses for a drug are discovered over time. In our data, we observe that older drugs treat a larger number of sites, on average, than more recent products. This may reflect the longer period of time for which new uses have been researched, as well as the possibility that older drugs are less likely to be targeted therapies. The drugs that treat the highest number of cancer sites are (for newer drugs) paclitaxel and (for older drugs) fluorouracil; both are on the WHO list of essential medicines.[8]

Table 3.1: *Summary of cancer drugs*

	Number of treated cancer sites				
	N	Mean	SD	Min	Max
Newer drugs	90	2.133	1.973	1	10
Older drugs	48	3.917	3.201	1	15

The available arsenal of drugs to treat cancer varies considerably by site. In Table 3.2, we provide a summary of new drugs by site over the 1990-2013 period. Breast cancer and leukaemia have seen the largest number of treatments introduced. Some cancer sites have had very few

[6] We include only drugs in the ATC "L" category. This excludes recent introductions of HPV vaccines, for example, which reduce the incidence of cervical cancer. The effects on mortality should appear indirectly through the reduction in incidence.

[7] See NCI drug information at http://www.cancer.gov/about-cancer/treatment/drugs/cancer-type.

[8] See WHO Essential Medicines website at http://www.who.int/selection_medicines/list/en/.

new treatments since 1990, including bladder, Hodgkin lymphoma, skin melanoma, soft tissue cancers or liver cancers. The availability of new treatments also varies by country, as we show in Table 3.3. Most newer cancer drugs are eventually launched in our sample of countries, as we would expect given their relatively high income. On average, large markets such as the US, UK and France have more treatments per cancer site-year than smaller countries such as Croatia, Sweden, and Ireland.

Table 3.2: *Summary of new drugs by cancer site across countries/years*

Cancer	Mean	Min	Max
Bladder	0.01	0	1
Breast	6.36	0	13
CNS	2.13	0	5
Cervix uteri	0.81	0	2
Colon	2.70	0	6
Hodgkin lymphoma	0.01	0	1
Kidney	1.03	0	6
Leukaemia	3.87	0	13
Liver	0.23	0	1
Lung	4.32	0	10
Multiple myeloma	0.40	0	3
Non-Hodgkin lymphoma	1.31	0	9
Ovary	2.33	0	4
Pancreas	2.46	0	5
Prostate	1.64	0	5
Rectum	1.36	0	4
Skin melanoma	0.02	0	2
Soft tissue	0.03	0	1
Stomach	2.76	0	5
Testis	0.57	0	1
Thyroid gland	0.23	0	1

Table 3.3: *Summary of new drugs by country across cancer sites/years*

Country	Mean	Min	Max
US	1.13	0	13
Austria	0.95	0	12
Croatia	0.69	0	9
Czech Republic	0.77	0	9
France	1.03	0	11
Germany	1.03	0	12
Ireland	0.83	0	10
Norway	0.89	0	10
Sweden	0.94	0	12
Switzerland	0.94	0	11
UK	0.91	0	11

We use this information to construct measures of the availability of new treatments by cancer, country, and year. The simplest measure is the cumulative number of new treatments for cancer site s launched in country i as of year t, for which we have information from 1990-present.

However, this measure does not capture the intensity of use: a new treatment may be launched, but not widely adopted by oncologists, for example.

We have an alternative measure for the period 2000-2013, which is spending on new and old cancer treatments in country i in year t. However, our data does not distinguish between sales for different cancer sites for treatments that can be used for multiple cancers. We thus allocate sales across cancer sites within a country using the relative incidence for each gender of each cancer site for which a drug may be used. For example, bevacizumab (Avastin®) treats colon cancer as well as lung, renal, and ovarian cancer. If ovarian cancer accounts for 10% of the total cases for women across these four cancers in a particular country, we assign 10% of the sales to ovarian cancer. We do not attempt to allocate sales by gender or age, although access to treatments may vary across both in some countries, depending on health insurance and other aspects of the health care system.[9]

3.1.4 Additional measures

Health outcomes depend on many other factors beyond incidence and pharmaceuticals, of course. Access to physicians, the availability of diagnostic equipment, insurance coverage, and other characteristics of the health system in each country are likely to be important determinants of mortality. While some data is provided by sources such as the OECD, annual observations of these variables are not consistently available for all countries in our study. Our econometric specification includes country-cancer fixed effects, which should absorb most of the variation associated with omitting them.

3.2 Instruments

As explained previously, candidate instruments are variables that are correlated with the availability and usage of new treatments for a specific cancer in a particular country, but which do not otherwise affect mortality from that cancer in that country. One such instrument is provided by the variation in the launch times of a new treatment for each cancer in each country. In the case of Europe, the EMA provides a centralized procedure for approval throughout EU member states. However, the approval date may differ from the launch date for two reasons. While EMA approval gives a pharmaceutical firm the authorization to sell its product throughout the EU, typically the firm must negotiate pricing and reimbursement with each national government. These negotiations may be lengthy and often require additional clinical data to demonstrate

[9] While we also have information on "standard units" (which IMS defines as the smallest common dose of a product formulation, i.e. a tablet, capsule, ampoule, etc.), units do not correspond to doses, and recommended doses vary across treatments (and within treatments across cancers).

cost-effectiveness. This is likely to be correlated with a country's inclination to adopt a new cancer treatment for site s as well as the difficulty of negotiating pricing and reimbursement in that country. We use the average launch delay for non-cancer drugs, i.e. the number of years between a drug's first global launch and its introduction in country i, as an instrument for the availability of new cancer drugs. A second candidate instrument is the cumulative number of new non-cancer drugs approved in a specific country in year t. Note that the availability of non-cancer drugs should have no direct effect on mortality from cancer in a country. These instruments vary across countries and over time, but not across cancer sites within a country.

Finally, we also exploit the fact that countries must import at least some of the pharmaceutical treatments used there. Fluctuations in currency valuations should affect local prices and consumption of imported pharmaceuticals, but have no direct effect on cancer mortality. Our sample of 11 countries includes 8 different currencies: the US dollar, the Euro, the Swiss franc, the British pound, the Swedish krona, the Czech koruna, the Norwegian krone, and the Croatian kuna. We include each country's average annual exchange rate with the Euro and with the US dollar as additional instruments for specifications using spending.

3.3 Descriptive Statistics

Table 3.4 provides an overview of incidence and mortality associated with cancer sites across countries. Both incidence and mortality are presented as age-standardized using the European age distribution. Within our sample of countries, incidence is lowest in France, with an average of 9.25 new cases per 100,000 per year, and highest in Ireland at 15.67. Mortality ranges from 4.35 per 100,000 in Switzerland to 6.65 per 100,000 in the Czech Republic. In most countries, prostate cancer has the highest incidence and lung cancer is the most deadly.

Table 3.4: *Cancer incidence and mortality, by country*

	Mean		Cancer with highest	
Country	Incidence	Mortality	Incidence	Mortality
US	13.30	4.89	Prostate	Lung
Austria	11.41	5.16	Prostate	Lung
Croatia	11.20	5.95	Lung	Lung
Czech Republic	15.37	6.65	Other skin	Lung
France	9.25	5.04	Prostate	Lung
Germany	13.59	5.17	Prostate	Lung
Ireland	15.67	5.57	Other skin	Lung
Norway	11.49	4.90	Prostate	Lung
Sweden	10.88	4.47	Prostate	Prostate
Switzerland	12.42	4.35	Prostate	Lung
UK	12.47	5.19	Breast	Lung

Incidence and mortality rates are per 100,000 and age-adjusted using European weights.

The last two decades have seen an overall drop in cancer mortality, even after controlling for changes in incidence. To show this, in Figure 3.1 we plot the coefficients on year dummy variables from a simple regression of mortality on incidence, i.e. equation (2.1) without any measure of the availability of new treatments. However, the gains against cancer vary greatly by cancer site. For example, mortality from leukaemia shows a notable downward trend (see Figure 3.2). In contrast, we see few improvements in pancreatic cancer (see Figure 3.3). In the regression analysis, our goal is to determine how much change in cancer mortality can be attributed specifically to the availability of new pharmaceutical treatments.

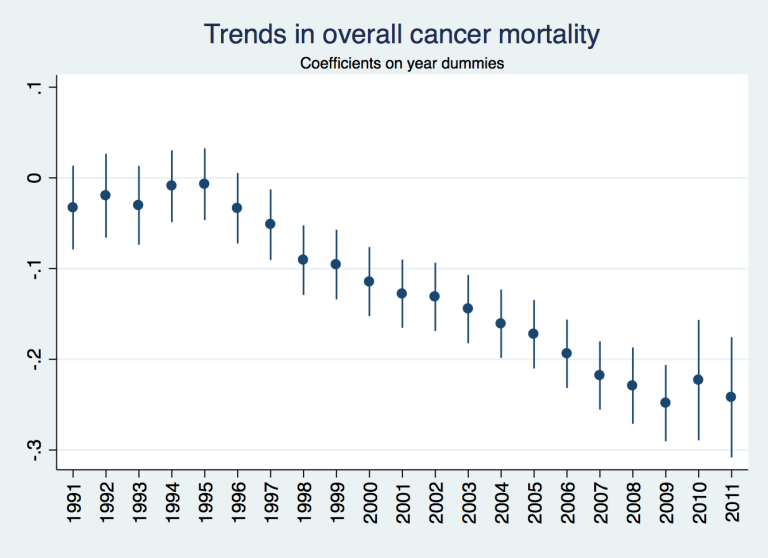

Figure 3.1: *Cancer mortality trend*

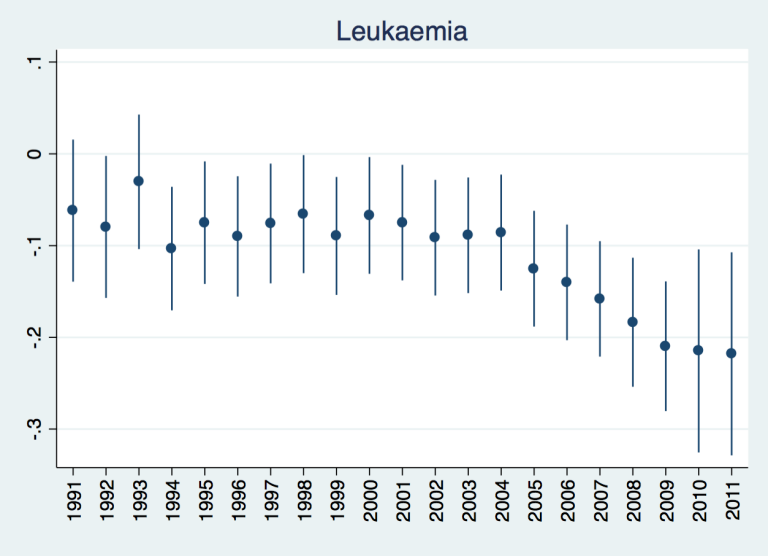

Figure 3.2: *Trend in mortality from leukaemia*

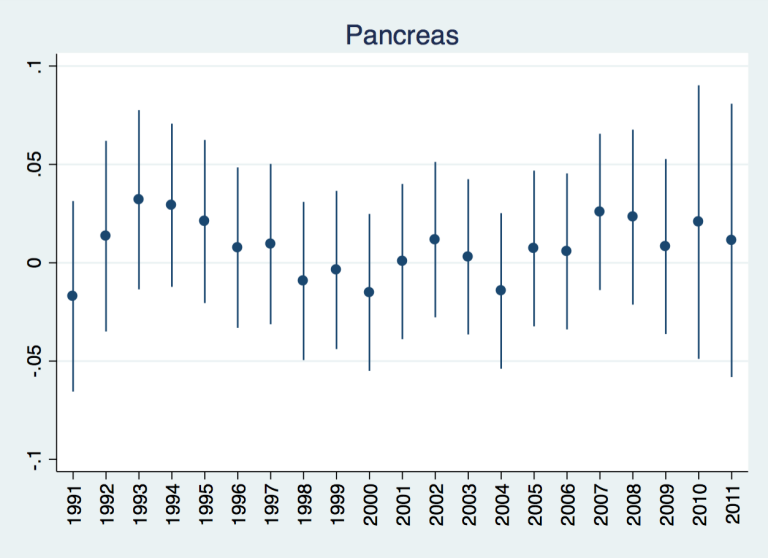

Figure 3.3: *Trend in mortality from pancreatic cancer*

Summary statistics for the variables used in our regression analysis are presented in Table 3.5. In the regressions, we use logs of age-standardized incidence and mortality. In specifications that include spending on treatments sold, we also take logs. We have fewer observations for spending, as our information for these variables begin only in 2000.

Table 3.5: *Summary statistics for regressions*

Variable	Mean	Std. Dev.	Min.	Max.	N
Log mortality rate	0.68	1.78	-5.75	5.88	25900
Log incidence rate	1.67	1.57	-3	6.42	17548
Nb new drugs	1.39	3.97	0	62	26620
Log(spend), new	4.16	5.16	0	17.71	13310
Log(spend), old	4.95	4.03	0	16.02	13310
New non-cancer drugs in country	313.15	218.81	10	1287	26620
Average launch delay for non-cancer drugs (years)	0.49	0.24	0	1.16	26620

4 Results

We first estimate equation (2.1) using the number of new drugs (defined as drugs approved since 1990) as the measure d_{ist} of the usage of new treatments. Appendix A.2 presents empirical results that allow for a lag in the adoption of new drugs. We focus our discussion on specifications with no lags, as they provide a conservative lower bounds of the effects of new drugs on mortality.[10] Table 4.1 contains results for two specifications for each of three samples: men and women

[10]Results with lags yield significant estimates with up to 6 years of lags for the instruments for several variants with lags of the endogenous variables. The preferred number of lag years seems to be 4, but it is not possible to statistically reject 0, 1, 2 or 3 years of lag. The minimum absolute value of the β coefficient is when τ is 0.

combined, men only, and women only. The first specification assumes exogeneity of d_{ist}, and the second instruments for d_{ist} using the instrument variables described in section 3.2. Results from the first stage of the IV specifications are included in the Appendix B. All specifications exploit the panel nature of our data with country-cancer site fixed effects and also include year fixed effects; these are not reported in the tables, but are statistically significant.

Our main focus is on the relationship between the use of new treatments and mortality. We estimate a negative and statistically significant coefficient in all specifications. As expected, the coefficient is larger in magnitude when we use instrumental variables, showing that the error term ε_{ist} is positively correlated with d_{ist} in equation (2.1) and leads to an underestimation of the mortality reduction effect of new drugs when using OLS. The number of older drugs has a statistically insignificant coefficient. Our results suggest that one additional new treatment for a cancer in a country is associated with a decrease in the mortality rate of -12% for both genders, -8% for men, and -9% for women. Because several cancers are gender specific, the average effect is not the average effect on the subset of common cancer sites across genders.

Table 4.1: *Results using count of new drugs as dependent variable*

	Both		Men		Women	
	Panel	Panel IV	Panel	Panel IV	Panel	Panel IV
	b/se	b/se	b/se	b/se	b/se	b/se
Nb new drugs	0.007**	−0.120***	0.012***	−0.082**	0.002	−0.093**
	(0.003)	(0.037)	(0.004)	(0.040)	(0.004)	(0.039)
Incidence x Austria	0.493***	0.427***	0.424***	0.383***	0.434***	0.381***
	(0.045)	(0.054)	(0.050)	(0.055)	(0.049)	(0.056)
Incidence x Croatia	0.100	0.130	0.219**	0.237***	0.153*	0.167**
	(0.083)	(0.093)	(0.086)	(0.092)	(0.080)	(0.084)
Incidence x Czech Republic	0.129	0.070	0.241**	0.204*	0.197**	0.149
	(0.097)	(0.110)	(0.107)	(0.114)	(0.090)	(0.097)
Incidence x France	−0.048	−0.030	0.053	0.077	−0.011	−0.016
	(0.044)	(0.050)	(0.049)	(0.052)	(0.049)	(0.052)
Incidence x Germany	0.455***	0.326*	0.424**	0.317*	0.373***	0.341**
	(0.167)	(0.192)	(0.176)	(0.192)	(0.139)	(0.147)
Incidence x Ireland	0.297***	0.314***	0.307***	0.312***	0.305***	0.304***
	(0.048)	(0.054)	(0.050)	(0.053)	(0.048)	(0.050)
Incidence x Norway	0.337***	0.333***	0.366***	0.333***	0.329***	0.322***
	(0.052)	(0.058)	(0.051)	(0.055)	(0.050)	(0.053)
Incidence x Sweden	0.409***	0.357***	0.410***	0.377***	0.370***	0.327***
	(0.075)	(0.086)	(0.079)	(0.084)	(0.073)	(0.079)
Incidence x Switzerland	0.099	0.084	0.155**	0.134**	0.075	0.084
	(0.070)	(0.079)	(0.063)	(0.067)	(0.056)	(0.059)
Incidence x UK	0.437***	0.272***	0.542***	0.424***	0.253**	0.137
	(0.081)	(0.103)	(0.091)	(0.109)	(0.100)	(0.116)
Incidence x US	0.441***	0.318***	0.471***	0.387***	0.329***	0.299***
	(0.058)	(0.075)	(0.063)	(0.076)	(0.074)	(0.079)
N	6028	6028	5382	5382	5521	5521
Fixed effects	Country*Cancer Year		Country*Cancer Year		Country*Cancer Year	

* p<0.10, ** p<0.05, *** p< .01.

As expected, incidence is an important determinant of cancer mortality. In all specifications, the coefficient on log age-standardized incidence rate is positive and significant. We interact the incidence rate with country dummies in order to allow the elasticity of mortality rate to incidence to be country specific. Taking the IV results as our preferred estimates, on average we find an "elasticity" of cancer mortality to cancer incidence of 0.32 for men, while it is 0.26 for women. The coefficient estimates vary across countries. The US, UK, Sweden, Norway, Ireland, Germany and Austria have the largest elasticities of mortality to incidence. The largest differences in elasticities between men and women are in the US and UK.

As noted previously, mortality rates from cancer have declined, on average, during the two decades of our study. Pharmaceutical innovation is hardly the only change that occurred during this period. For example, changes in lifestyle may have reduced incidence and therefore mortality. To assess the relative importance of the availability of treatments compared to changes in incidence, we compute the average increase in the number of drug treatments and the average change in incidence across all cancers within a country, and calculate the change in the number of deaths implied by our regression results. Table 4.2 presents this summary by country, with the total change in mortality for comparison. Given that the sensitivity of mortality to incidence varies considerably across countries, it is not surprising that the relative importance of innovation and incidence is also heterogeneous. Drug innovation accounted for 10-30% of the total number of lives saved, and is always more important than changes in incidence.

Table 4.2: *Comparison of innovation vs. incidence, Men and Women*

	ASMR		Changes in Lives (1000s)		
	1990	2011	Total	from drugs	from incidence
Austria	6.01	4.19	-153.61	-19.35	-18.27
Croatia	5.84	5.94	5.00	-6.76	-2.52
Czech Republic	7.34	5.21	-224.86	-17.57	-2.23
France	5.76	4.22	-974.45	-161.30	11.22
Germany	5.74	4.52	-1003.38	-211.66	-47.26
Ireland	6.19	5.12	-49.93	-9.08	-7.65
Norway	5.14	4.54	-29.48	-9.82	-8.14
Sweden	4.97	4.09	-82.98	-21.15	-11.58
Switzerland	4.91	3.94	-76.51	-17.46	-2.58
UK	6.09	4.58	-952.78	-137.18	-51.74
US	5.49	4.08	-4427.66	-934.06	-349.39

Notes: Changes in thousands of lives by country between 1990 and 2011.

While the approval and launch of a drug mean that it is a treatment option for a cancer site in a country-year, our measure of the number of new drugs per cancer-country does not

capture differences in the intensity of use. Many factors can affect this. Insurers may restrict the use of new treatments in order to control expenses. Oncologists must be aware of new treatment options and adjust their practice to incorporate their use. It is possible that in some cases, physicians prescribe new treatments even when they are unlikely to be effective, perhaps because dying patients are desperate. To address differences in the use of new treatments across cancers, countries, and years, we estimate regressions using information on expenses. We allow old and new drugs, introduced before or after 1990, to potentially have different effects on mortality.

In Table 4.3, we present the results from specifications using the log of expenditures in country i for cancer site s in year t. We have a shorter time period over which to identify effects, since we only have data on expenditures since 2000. In addition, our data do not allow us to observe which cancer sites a specific drug was prescribed to treat, nor do we know whether use of treatments is the same for both genders. This measurement error is likely to introduce an attenuation bias.

Table 4.3: *Results using Log spending*

	Both		Men		Women	
	Panel	Panel IV	Panel	Panel IV	Panel	Panel IV
	b/se	b/se	b/se	b/se	b/se	b/se
Log(spend), new	0.001	0.092***	0.004*	0.096***	−0.003	0.068**
	(0.002)	(0.029)	(0.003)	(0.034)	(0.003)	(0.033)
Log(spend), old	0.003	−0.073	−0.012	−0.089	0.005	−0.015
	(0.008)	(0.056)	(0.011)	(0.078)	(0.011)	(0.069)
Incidence x Austria	0.569***	0.500***	0.490***	0.440***	0.298***	0.278***
	(0.064)	(0.087)	(0.074)	(0.093)	(0.080)	(0.091)
Incidence x Croatia	0.160	0.105	0.118	0.115	0.182	0.143
	(0.164)	(0.211)	(0.160)	(0.193)	(0.124)	(0.141)
Incidence x Czech Republic	0.110	0.161	0.256**	0.282**	0.110	0.187*
	(0.085)	(0.111)	(0.101)	(0.122)	(0.088)	(0.106)
Incidence x France	0.185***	0.044	0.187**	0.024	0.157*	0.087
	(0.066)	(0.098)	(0.074)	(0.109)	(0.082)	(0.097)
Incidence x Germany	0.449***	0.735***	0.427***	0.637***	0.361***	0.470***
	(0.124)	(0.183)	(0.142)	(0.188)	(0.114)	(0.141)
Incidence x Ireland	0.284*	0.225	0.375***	0.336**	0.388***	0.396***
	(0.160)	(0.208)	(0.139)	(0.168)	(0.130)	(0.146)
Incidence x Norway	0.023	−0.024	0.310***	0.243***	−0.133*	−0.129
	(0.074)	(0.097)	(0.075)	(0.094)	(0.076)	(0.085)
Incidence x Sweden	0.483***	0.315**	0.456***	0.317**	0.318***	0.302***
	(0.084)	(0.124)	(0.091)	(0.126)	(0.085)	(0.103)
Incidence x Switzerland	−0.048	−0.085	0.015	−0.048	0.015	0.022
	(0.072)	(0.094)	(0.075)	(0.097)	(0.056)	(0.062)
Incidence x UK	0.440***	0.304	0.412**	0.342	0.313	0.186
	(0.153)	(0.202)	(0.172)	(0.210)	(0.207)	(0.241)
Incidence x US	0.305***	−0.288	0.295***	−0.190	0.259**	−0.215
	(0.092)	(0.225)	(0.103)	(0.218)	(0.127)	(0.262)
N	3318	3318	2964	2964	3035	3035
Fixed effects	Country*Cancer Year		Country*Cancer Year		Country*Cancer Year	

* p<0.10, ** p<0.05, *** p< .01.

In contrast to our results on the number of approved drugs, we find a positive relationship between spending on new drugs and mortality. Results from the previous specifications suggested that the endogeneity of access to innovation and mortality caused a positive bias in OLS estimates. Our instruments do not perform as well for spending as for the number of approved drugs, so the IV estimates may reflect a similar upward bias. However, there are several additional explanations for why we might not find a negative relationship between spending and mortality.

First, spending reflects both prices and quantities. With the exception of the US, all the countries we examine use some form of price control. If the intensity of use of each new drug were identical across all countries in our sample, spending would still vary across countries due to price differences, but differences driven solely by price would not change mortality.

A second possibility is that differences in efficacy of treatments for different cancers are not reflected in their prices or in treatment guidelines, resulting in a suboptimal mix of products used in practice. Within a country, we might find no relationship between spending and mortality if spending is distorted towards less effective treatments.

Finally, overuse of treatments may be an important factor. Many cancer patients are close to death, and physicians may feel ethically obligated to try treatments that have a very low (but non-zero) chance of helping. This behavior would tend to drive up spending without a significant improvement in mortality rates.

These explanations may vary in salience across countries. Prices and access policies can be very different, and their role in ensuring the appropriate use of treatments merits additional study. While our data do not permit this detailed analysis, the availability of patient and physician level information may allow such studies in the future.

5 Evaluating the Gains from Innovation

5.1 Counterfactual Mortality

We are interested in the mortality a country would have experienced had access to drug innovation been different. The reduced-form nature of our analysis limits our ability to implement a complete counterfactual that would account for changes in the use of substitute treatments, prices, etc. However, we can arrive at a rough estimate of the change in mortality that can be attributed to the availability of new treatments, and compare this to expenditures on those new treatments.

We proceed as follows. For any counterfactual number of new drugs d^*_{ist} instead of d_{ist}, we calculate the predicted mortality rates based on our regression results. That is, we compute the counterfactual mortality rate as

$$\begin{aligned} \ln y^*_{ist} &= \alpha_{is} + \delta_t + \gamma \mathbf{x}_{ist} + \beta d^*_{ist} + \varepsilon_{ist} \\ &= \ln y_{ist} - \beta \left(d_{ist} - d^*_{ist} \right) \end{aligned}$$

This is similar to the approach used in Lichtenberg (2012) to estimate the contribution of drug innovation to mortality reduction in Germany and France. In doing so, we assume that the total population P_{it} does not change due to different mortality rates in all years prior to t in the counterfactual situation. Evaluating such changes in population would require us to account for age-specific competing risks and survival rates that would be observed in the counterfactual scenario. As seen in Appendix A, with this simplifying assumption, we can convert the counterfactual mortality rates into an estimate of the number of deaths z^*_{ist} by cancer site s for each year t and country i as

$$z^*_{ist} = y^*_{ist} * P^*_{it}$$

where P^*_{it} is the total population in country i in year t. Everything else equal, the total number of lives saved in year t is then $z_{ist} - z^*_{ist} = (y_{ist} * P_{it} - y^*_{ist} * P^*_{it})$ and can then be compared to the observed total spending on new drugs.

5.2 Counterfactual 1: No Innovation After 2000

The first counterfactual we consider is a scenario in which no new cancer treatments are launched after 2000 (which is the first year in which we observe drug spending). We compute the average difference in the observed mortality and that predicted using the number of new treatments for each cancer site in each country as of 1999 for all years after 2000 across all countries in our sample, and convert this to a change in the number of lives. Table 5.1 shows the average across countries within cancer sites of these, with the observed ASIR in column 2, the observed and counterfactual ASMR in columns 3 and 4, the number of lives saved in column 5 (in 1000s), and the total expenditures observed for drugs launched after 2000 in column 6 (in 1000s of US dollars). The last column has the cost per life saved as the total expenditures on new drugs divided by the number of lives saved (in 1000s of US dollars). This can also be interpreted as the value of a statistical life that would justify those expenditures.

Table 5.1: *Counterfactual 1 by cancer, Men and Women*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Bladder	14.75	4.40	4.41	0.75	9.10	12.13
Bone	1.06	0.56	0.56	0.00	8.23	.
Breast	53.74	13.77	16.00	219.31	3425.07	15.62
CNS	6.92	5.31	6.24	60.58	1906.90	31.48
Cervix uteri	9.62	2.91	3.02	4.50	893.84	198.69
Colon	30.26	13.71	15.49	171.43	8964.43	52.29
Corpus uteri	17.38	2.43	2.43	0.00	0.00	.
Endocrine glands	0.52	0.30	0.30	0.00	0.00	.
Eye	0.87	0.16	0.16	0.00	0.00	.
Gallbladder	3.35	2.37	2.37	0.00	0.00	.
Hodgkin lymphoma	2.43	0.37	0.37	0.27	14.17	53.30
Kidney	12.86	4.98	6.29	107.35	6160.59	57.39
Larynx	3.85	1.51	1.51	0.00	0.00	.
Leukaemia	10.32	5.55	7.73	291.62	12177.81	41.76
Lip	0.77	0.06	0.06	0.00	0.00	.
Liver	6.35	5.45	5.73	25.10	276.06	11.00
Lung	45.81	37.03	43.44	862.11	22595.70	26.21
Multiple myeloma	4.95	2.97	3.26	32.90	1633.45	49.65
Non-Hodgkin lymphoma	12.79	4.85	5.52	120.15	4686.57	39.01
Nose & sinuses	0.64	0.19	0.19	0.00	0.00	.
Oesophagus	5.50	4.51	4.51	-0.00	0.00	.
Oral cavity	2.35	0.76	0.76	0.00	0.00	.
Other female sites	3.47	3.14	3.14	0.00	0.00	.
Other skin	57.26	0.64	0.64	-0.00	5.74	.
Ovary	13.56	8.93	8.98	2.45	81.01	33.02
Pancreas	10.55	10.28	12.41	129.98	2283.69	17.57
Penis	1.09	0.29	0.29	0.00	0.00	.
Pharynx	4.35	2.08	2.08	0.00	0.00	.
Prostate	110.33	26.50	26.99	31.05	762.63	24.56
Rectum	19.32	7.05	7.85	52.04	4670.00	89.74
Salivary glands	0.86	0.26	0.26	-0.00	0.00	.
Skin melanoma	15.80	2.80	2.82	2.47	391.02	158.36
Small intestine	1.49	0.47	0.47	-0.00	0.00	.
Soft tissue	2.66	0.97	0.98	0.65	30.26	46.56
Stomach	11.47	7.43	8.57	59.48	9466.23	159.14
Testis	7.05	0.38	0.38	0.00	0.00	.
Thyroid gland	5.98	0.53	0.56	2.04	254.22	124.81
Tongue	2.27	0.89	0.89	0.00	0.00	.

We find very large differences across cancer sites. Some cancers had no new drug introductions after 2000, so there is no change in mortality and no spending on new drugs. In a few cases of very low-incidence cancers, the change in lives saved is very small, and we indicate the cost per life saved as missing because the calculation is unlikely to be reliable. Among the others, the highest cost per life saved are for colon, testis, small intestine and tongue cancers, between $100,000 and $200,000. To put these figures into perspective, a report prepared by the Office of Management and Budget in the US in 2003 stated that estimates of the VSL ranged between $1 and $10 million.[11]

Table 5.2 provides a corresponding set of estimates using averages within each country, across cancer sites. Once again, there is substantial heterogeneity, with the UK at the low end (around $19,000) and Switzerland at the high end (around $66,000).

Table 5.2: *Counterfactual 1 by country, Men and Women*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Austria	12.33	4.66	5.28	22.89	1198.72	52.37
Croatia	11.55	5.91	6.21	5.92	197.14	33.29
Czech Republic	16.00	6.09	6.42	15.75	596.02	37.85
France	10.93	4.57	5.39	229.07	10042.25	43.84
Germany	14.17	4.73	5.36	225.73	9685.65	42.91
Ireland	17.02	5.28	5.66	7.58	371.75	49.04
Norway	13.36	4.86	5.20	7.39	277.38	37.55
Sweden	12.44	4.47	4.93	19.29	853.25	44.23
Switzerland	13.37	4.23	4.76	18.28	1210.50	66.22
UK	13.45	4.80	5.33	135.88	2583.57	19.01
US	12.16	4.49	5.58	1488.46	53680.46	36.06

5.3 Counterfactual 2: No Launch Delays After 2000

An alternative counterfactual that we consider removes all launch delays across countries for new cancer drugs post-2000. That is, we take development times for each drug as given, but we assume that a drug is available immediately in all countries following its first introduction anywhere. Launch delays typically result from lengthy pricing and reimbursement negotiations within countries, or differences between the regulatory requirements of the US FDA and the EMA. While the calculation of lives saved is straightforward, as in the previous scenario, we have to make additional assumptions in order to estimate what spending on new drugs would have been. We compute the average spending per new drug, per year, and multiply this by the total number of drug-years in the absence of launch delays. The difference between this figure

[11] See OMB report at https://www.whitehouse.gov/sites/default/files/omb/assets/regulatory_matters_pdf/a-4.pdf.

and the true spending is an approximation of the additional spending a country would have from earlier introductions.

Tables 5.3 and 5.4 contain the estimates of lives saved, spending, and the average cost per life for this scenario. Results are generally similar. Costs per life are somewhat lower at the country level, while at the cancer level they are even more dispersed than in the previous counterfactual. Recall that we assume spending on each additional new drug is "average," which may be very different than true spending on the marginal drug. The marginal additional drug introduced may be much more expensive than the average, while its marginal mortality reduction effect can also be different than the average.

Table 5.3: *Counterfactual 2 by cancer, Men and Women*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Bladder	14.75	4.40	4.33	-4.32	90.96	21.06
Bone	1.06	0.56	0.56	0.00	8.23	.
Breast	53.74	13.77	12.06	-62.76	439.11	7.00
CNS	6.92	5.31	4.94	-15.18	333.71	21.98
Cervix uteri	9.62	2.91	2.76	-2.26	305.21	135.05
Colon	30.26	13.71	12.54	-26.79	1686.05	62.95
Corpus uteri	17.38	2.43	2.43	0.00	0.00	.
Endocrine glands	0.52	0.30	0.30	0.00	0.00	.
Eye	0.87	0.16	0.16	0.00	0.00	.
Gallbladder	3.35	2.37	2.37	0.00	0.00	.
Hodgkin lymphoma	2.43	0.37	0.37	-0.18	141.70	777.86
Kidney	12.86	4.98	4.45	-15.72	3092.67	196.74
Larynx	3.85	1.51	1.51	0.00	0.00	.
Leukaemia	10.32	5.55	3.97	-31.81	6562.13	206.26
Lip	0.77	0.06	0.06	0.00	0.00	.
Liver	6.35	5.45	5.34	-2.20	110.42	50.09
Lung	45.81	37.03	30.51	-172.49	6460.02	37.45
Multiple myeloma	4.95	2.97	2.75	-4.25	1515.57	356.85
Non-Hodgkin lymphoma	12.79	4.85	3.67	-31.99	5985.65	187.11
Nose & sinuses	0.64	0.19	0.19	0.00	0.00	.
Oesophagus	5.50	4.51	4.51	-0.00	0.00	.
Oral cavity	2.35	0.76	0.76	0.00	0.00	.
Other female sites	3.47	3.14	3.14	0.00	0.00	.
Other skin	57.26	0.64	0.64	-0.00	5.74	.
Ovary	13.56	8.93	8.57	-7.91	10.15	1.28
Pancreas	10.55	10.28	9.92	-27.01	211.73	7.84
Penis	1.09	0.29	0.29	0.00	0.00	.
Pharynx	4.35	2.08	2.08	0.00	0.00	.
Prostate	110.33	26.50	25.61	-9.43	114.26	12.12
Rectum	19.32	7.05	6.34	-17.98	1847.09	102.75
Salivary glands	0.86	0.26	0.26	-0.00	0.00	.
Skin melanoma	15.80	2.80	2.76	-1.02	1329.46	1309.11
Small intestine	1.49	0.47	0.47	-0.00	0.00	.
Soft tissue	2.66	0.97	0.94	-2.23	159.93	71.72
Stomach	11.47	7.43	7.27	-1.02	215.90	211.86
Testis	7.05	0.38	0.36	-0.07	0.00	.
Thyroid gland	5.98	0.53	0.52	-0.20	101.69	517.05
Tongue	2.27	0.89	0.89	0.00	0.00	.

Table 5.4: *Counterfactual 2 by country, Men and Women*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Austria	12.33	4.66	4.37	-10.54	284.79	27.01
Croatia	11.55	5.91	4.94	-18.36	166.56	9.07
Czech Republic	16.00	6.09	5.32	-35.14	357.85	10.18
France	10.93	4.57	4.35	-59.58	1375.26	23.08
Germany	14.17	4.73	4.44	-103.96	1485.79	14.29
Ireland	17.02	5.28	4.73	-10.65	162.10	15.22
Norway	13.36	4.86	4.38	-9.82	100.52	10.23
Sweden	12.44	4.47	4.13	-12.97	231.34	17.84
Switzerland	13.37	4.23	3.95	-9.05	316.03	34.91
UK	13.45	4.80	4.32	-117.37	814.29	6.94
US	12.16	4.49	4.45	-49.36	1738.36	35.22

A shortcoming of both counterfactuals is that we do not consider what spending on older drugs would have been, nor do we model how additional competition from new introductions would affect negotiated prices. Our estimates are not directly comparable to those produced in studies with different samples or methodologies. For example, a recent paper examining cancer treatments in the US (Howard et al. (2016)) exploits more detailed patient-level data on treatments and costs. The sample considered is restricted to Medicare recipients who are good candidates for drug treatment. In contrast, our study relies on national-level data by cancer site, corresponding to the entire population.

6 Conclusion

Using time-series data on mortality at the level of cancer site in 11 countries, we find that the availability of relatively novel cancer therapies is associated with a statistically significant, and economically important, reduction in mortality. We also demonstrate that the gains from new drugs vary across cancer sites and across countries. Estimates from two counterfactual scenarios, involving either the removal of all innovation after 2000 or the removal of all launch delays, suggest that the implied VSL from spending on new cancer drugs generally falls in the range of estimates used by many regulatory agencies for policy evaluation. Thus, while the high prices of novel cancer treatments are often criticized as excessive, they are not inconsistent with standards used in other settings.

Our approach is likely to underestimate the "true" benefits or overestimate the cost per life if expensive cancer treatments are frequently used inappropriately. Inappropriate use might arise for many reasons: physician agency issues, marketing efforts that encourage overuse, a lack of diagnostic tests for selecting the best treatment based on a patient's characteristics, a "Hail

Mary" attempt to treat patients near certain death, etc. However, we also cannot exclude that those expenses may improve the quality of lives of many cancer patients without statistically changing their life expectancy and thus without having effects on mortality rate. We noted these and other problems in explaining the lack of a statistically significant change in mortality associated with higher spending on new drugs. Further work to explore these issues is necessary to improve the efficiency of spending on cancer treatments.

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A Mortality reduction and implied cost per statistical life

A.1 Calculation of lives gained

We have estimated a cancer mortality equation as follows:

$$\ln y_{ist} = \alpha_{is} + \delta_t + \gamma \mathbf{x}_{ist} + \beta d_{ist} + \varepsilon_{ist}$$

where y_{ist} denote the age-standardized mortality rate by cancer site s for country i at year t and α_{is} is a country-cancer site fixed effect, δ_t is a year effect, $\mathbf{x}_{ist}$ are observable variables such as the country-cancer site age standardized incidence rate in year t, and d_{ist} is the number of new drugs used and approved for each cancer site, country and year.

For example, if the policy counterfactual starts at date t_0 then the counterfactual population at the beginning of date $t_0 + 1$ will be

$$\begin{aligned} P^*_{it_0+1} &= P_{it_0+1} + \left(z_{ist_0} - z^*_{ist_0}\right) \\ &= P_{it_0+1} + \left(y_{ist_0} - y^*_{ist_0}\right) \times P_{it_0} \\ &= P_{it_0+1} + \left(y_{ist_0} - \exp\left(\ln y_{ist_0} - \beta \Delta^*_{ist_0}\right)\right) \times P_{it_0} \\ &= P_{it_0+1} + y_{ist_0}\left(1 - e^{-\beta \Delta^*_{ist_0}}\right) \times P_{it_0} \end{aligned}$$

where $\Delta^*_{ist_0} = (d_{ist} - d^*_{ist})$.

Then at year $t_0 + 2$, the counterfactual population will depend on the $t_0 + 1$ counterfactual population in the same way if we can assume that the mortality model estimated in the data would be valid for the counterfactual population. This would clearly be valid for the part of the population not affected by the change in cancer mortality rate but is a stronger assumption for the cancer patients.

$$\begin{aligned} P^*_{it_0+2} &= P_{it_0+2} + y_{ist_0+1}\left(1 - e^{-\beta \Delta^*_{ist_0+1}}\right) \times P^*_{it_0+1} \\ &= P_{it_0+2} + y_{ist_0+1}\left(1 - e^{-\beta \Delta^*_{ist_0+1}}\right) \times P_{it_0+1} + y_{ist_0+1} \times y_{ist_0}\left(1 - e^{-\beta \Delta^*_{ist_0+1}}\right)\left(1 - e^{-\beta \Delta^*_{ist_0}}\right) \times P_{it_0} \\ &= P_{it_0+2} + \sum\nolimits_{k=0}^{1} P_{it_0+k} \times \left(\prod\nolimits_{n=0}^{1-k} y_{ist_0+1-n}\left(1 - e^{-\beta \Delta^*_{ist_0+1-n}}\right)\right) \end{aligned}$$

And for any T:

$$\begin{aligned} P^*_{it_0+T} &= P_{it_0+T} + \sum\nolimits_{k=0}^{T-1}\left(\prod\nolimits_{n=0}^{T-k-1} y_{ist_0+T-n-1}\left(1 - e^{-\beta \Delta^*_{ist_0+T-n+1}}\right)\right) P_{it_0+k} \\ &\simeq P_{it_0+T} \end{aligned}$$

if β and Δ^*_{ist} are not too large and y_{ist} is also not too large which is typically the case for cancer mortality and for the counterfactual policy considered.

A.2 Testing the robustness to lags

Table A1 shows the results of the estimates of $\hat{\beta}_{lk}$ for different values of l and k when estimating the effects of the numbers of new drugs on mortality for both genders. With 0 to 4 years of lag for the endogenous variable ($l = 0, 1, 2, 3, 4$), the coefficients $\hat{\beta}_{lk}$ are significantly different from zero for $k = 0$ to 5. In all these cases, we cannot reject the fact that all $\hat{\beta}_{lk}$ for $k = 0$ to 5 are all equal for each given l. We thus cannot reject that the correct number of years of lags τ is 0, 1, 2, 3, 4. For $l = 5$, we have significantly results for $k = 0, 1, 2$ only while results become all insignificant with 6 years of lag for l.

Table A1: *Estimates of coefficient β with different lags, Both*

Incidence Lags (l)	Instrumental variables Lags (k)								
	0	1	2	3	4	5	6	7	8
0	-0.120	-0.117	-0.108	-0.092	-0.077	-0.066	-0.045	-0.018	0.004
	0.037	0.036	0.036	0.034	0.033	0.033	0.032	0.031	0.030
1	-0.136	-0.134	-0.121	-0.106	-0.086	-0.070	-0.052	-0.016	0.002
	0.043	0.043	0.041	0.040	0.038	0.037	0.036	0.035	0.034
2	-0.170	-0.171	-0.162	-0.145	-0.125	-0.103	-0.072	-0.034	-0.018
	0.054	0.055	0.053	0.051	0.049	0.047	0.045	0.044	0.043
3	-0.203	-0.208	-0.197	-0.191	-0.160	-0.146	-0.114	-0.077	-0.054
	0.067	0.068	0.066	0.066	0.061	0.059	0.056	0.053	0.052
4	-0.208	-0.213	-0.209	-0.202	-0.188	-0.166	-0.135	-0.096	-0.057
	0.081	0.083	0.083	0.081	0.079	0.076	0.072	0.068	0.065
5	-0.172	-0.181	-0.177	-0.179	-0.153	-0.142	-0.108	-0.064	-0.058
	0.086	0.089	0.090	0.089	0.085	0.082	0.079	0.077	0.074
6	-0.079	-0.097	-0.090	-0.092	-0.083	-0.056	-0.053	-0.017	-0.016
	0.096	0.099	0.097	0.097	0.094	0.092	0.090	0.089	0.088

Note: Standard errors below coefficients.

Table A2 shows the results of the estimates of $\hat{\beta}_{lk}$ for different values of l and k when estimating the effects of the numbers of new drugs on mortality for males. With 0 to 3 years of lag for the endogenous variable ($l = 0, 1, 2, 3$), the coefficients $\hat{\beta}_{lk}$ are significantly different from zero for $k = 0$ and 1 only when $l \leq 1$ but also for $k = 2$ and 3 when $l = 2$ or 3. In all these cases, we cannot reject the fact that all $\hat{\beta}_{lk}$ for $k = 0$ to 3 are all equal for each given l. We thus cannot reject that the correct number of years of lags τ is 0, 1, 2, 3. For $l = 4, 5, 6$, results become all insignificant.

Table A3 shows the results of the estimates of $\hat{\beta}_{lk}$ for different values of l and k when estimating the effects of the numbers of new drugs on mortality for females. With 0 to 4 years of lag for the endogenous variable ($l = 0, 1, 2, 3, 4$), the coefficients $\hat{\beta}_{lk}$ are significantly different

Table A2: *Estimates of coefficient β with different lags, Male*

Incidence Lags (l)	Instrumental variables Lags (k)								
	0	1	2	3	4	5	6	7	8
0	-0.082	-0.077	-0.069	-0.057	-0.037	-0.022	-0.015	-0.001	0.014
	0.040	0.039	0.038	0.037	0.037	0.036	0.036	0.036	0.035
1	-0.101	-0.094	-0.082	-0.070	-0.046	-0.023	-0.020	-0.004	0.013
	0.046	0.046	0.044	0.044	0.042	0.041	0.041	0.040	0.039
2	-0.129	-0.127	-0.115	-0.103	-0.075	-0.045	-0.033	-0.020	0.002
	0.058	0.058	0.056	0.055	0.052	0.051	0.050	0.049	0.049
3	-0.166	-0.164	-0.152	-0.151	-0.112	-0.088	-0.078	-0.051	-0.035
	0.071	0.071	0.069	0.069	0.064	0.062	0.062	0.059	0.058
4	-0.153	-0.151	-0.145	-0.142	-0.134	-0.094	-0.093	-0.077	-0.040
	0.084	0.084	0.083	0.082	0.081	0.077	0.078	0.075	0.072
5	-0.138	-0.132	-0.124	-0.129	-0.107	-0.102	-0.093	-0.072	-0.062
	0.092	0.091	0.092	0.092	0.089	0.088	0.089	0.087	0.084
6	-0.033	-0.041	-0.038	-0.046	-0.045	-0.017	-0.031	-0.040	-0.039
	0.102	0.102	0.101	0.101	0.101	0.100	0.101	0.101	0.100

Note: Standard errors below coefficients.

from zero for $k = 0, 1, 2$ and for $k = 3$ only when $l = 2, 3, 4$ but also for $k = 4$ when $l = 3$ or 4. In all these cases, we cannot reject the fact that all $\hat{\beta}_{lk}$ significantly different from zero are all equal for each given l. We thus cannot reject that the correct number of years of lags τ is 0, 1, 2, 3, 4. For $l = 5, 6$, results become all insignificant.

Table A3: *Estimates of coefficient β with different lags, Female*

Incidence Lags (l)	Instrumental variables Lags (k)								
	0	1	2	3	4	5	6	7	8
0	-0.093	-0.091	-0.078	-0.062	-0.050	-0.040	-0.013	0.013	0.023
	0.039	0.039	0.038	0.037	0.036	0.036	0.036	0.035	0.036
1	-0.103	-0.107	-0.091	-0.074	-0.058	-0.043	-0.015	0.023	0.024
	0.045	0.045	0.044	0.043	0.041	0.041	0.040	0.040	0.040
2	-0.133	-0.136	-0.134	-0.112	-0.093	-0.078	-0.039	0.011	0.017
	0.056	0.056	0.056	0.054	0.052	0.051	0.050	0.050	0.050
3	-0.165	-0.174	-0.173	-0.160	-0.135	-0.116	-0.071	-0.043	-0.009
	0.068	0.070	0.070	0.068	0.065	0.065	0.060	0.060	0.060
4	-0.191	-0.202	-0.204	-0.192	-0.177	-0.167	-0.102	-0.048	-0.022
	0.086	0.089	0.090	0.088	0.086	0.086	0.078	0.075	0.075
5	-0.174	-0.204	-0.220	-0.212	-0.191	-0.195	-0.109	-0.074	-0.042
	0.101	0.109	0.115	0.113	0.109	0.109	0.095	0.094	0.091
6	-0.208	-0.252	-0.259	-0.247	-0.216	-0.213	-0.106	-0.054	-0.039
	0.145	0.158	0.162	0.158	0.148	0.148	0.123	0.116	0.118

Note: Standard errors below coefficients.

B First Stage Regressions

Table B1: *First stage results using count of new drugs*

	Both	Men	Women
	Nb new drugs	Nb new drugs	Nb new drugs
	b/se	b/se	b/se
Incidence x Austria	-0.510^{***}	-0.426^{**}	-0.559^{***}
	(0.183)	(0.185)	(0.175)
Incidence x Croatia	-0.128	-0.184	-0.074
	(0.356)	(0.341)	(0.294)
Incidence x Czech Republic	-0.282	-0.264	-0.299
	(0.405)	(0.401)	(0.335)
Incidence x France	-0.119	0.080	-0.429^{*}
	(0.215)	(0.207)	(0.221)
Incidence x Germany	-1.055	-1.183^{*}	-0.345
	(0.691)	(0.659)	(0.501)
Incidence x Ireland	0.246	0.108	0.103
	(0.201)	(0.186)	(0.175)
Incidence x Norway	0.073	-0.291	0.003
	(0.219)	(0.191)	(0.184)
Incidence x Sweden	-0.382	-0.339	-0.434
	(0.311)	(0.293)	(0.265)
Incidence x Switzerland	-0.119	-0.225	0.081
	(0.289)	(0.235)	(0.199)
Incidence x UK	-1.327^{***}	-1.285^{***}	-1.210^{***}

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Table B1: *First stage results using count of new drugs*

	Both	Men	Women
	Nb new drugs	Nb new drugs	Nb new drugs
	b/se	b/se	b/se
	(0.344)	(0.349)	(0.369)
Incidence x US	−1.001***	−0.918***	−0.395
	(0.239)	(0.234)	(0.266)
Other new drugs x Austria	0.000	0.000	−0.000
	(0.001)	(0.001)	(0.001)
Other new drugs x Croatia	−0.004**	−0.004**	−0.004**
	(0.002)	(0.002)	(0.002)
Other new drugs x Czech	−0.002	−0.002	−0.002
Republic	(0.001)	(0.001)	(0.001)
Other new drugs x France	0.001	0.000	0.001
	(0.001)	(0.001)	(0.001)
Other new drugs x Germany	−0.000	−0.000	−0.000
	(0.001)	(0.001)	(0.001)
Other new drugs x Ireland	−0.001	−0.001	−0.001
	(0.001)	(0.001)	(0.001)
Other new drugs x Norway	−0.000	−0.000	−0.001
	(0.001)	(0.001)	(0.001)
Other new drugs x Sweden	−0.000	−0.000	−0.000
	(0.001)	(0.001)	(0.001)

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Table B1: *First stage results using count of new drugs*

	Both	Men	Women
	Nb new drugs	Nb new drugs	Nb new drugs
	b/se	b/se	b/se
Other new drugs x	0.000	−0.000	−0.000
Switzerland	(0.001)	(0.001)	(0.001)
Other new drugs x UK	−0.000	−0.000	−0.000
	(0.001)	(0.001)	(0.001)
Other new drugs x US	0.000	0.000	0.000
	(0.001)	(0.001)	(0.001)
Average launch delay for	0.215	0.270	0.203
non-cancer drugs	(0.403)	(0.443)	(0.433)
N	6028	5382	5521
F-stat for under ID	54.90	50.84	55.88
F-stat for weak ID	4.58	4.24	4.67
Sargan statistic	71.11	79.90	21.69

* p<0.10, ** p<0.05, *** p< .01.

Table B2: *First stage results using Log spending*

	Both		Men		Women	
	Log(spend), new	Log(spend), old	Log(spend), new	Log(spend), old	Log(spend), new	Log(spend), old
	b/se	b/se	b/se	b/se	b/se	b/se
Incidence x Austria	0.494	−0.237	0.334	−0.218*	0.208	−0.186
	(0.592)	(0.147)	(0.562)	(0.132)	(0.575)	(0.142)
Incidence x Croatia	0.549	0.126	0.180	0.322	0.385	−0.156
	(1.497)	(0.371)	(1.212)	(0.285)	(0.913)	(0.225)
Incidence x Czech Republic	−0.060	0.087	0.094	0.153	−0.594	−0.176
	(0.791)	(0.196)	(0.762)	(0.179)	(0.665)	(0.164)
Incidence x France	1.683***	0.233	1.867***	0.192	0.839	−0.118
	(0.600)	(0.149)	(0.556)	(0.131)	(0.588)	(0.145)
Incidence x Germany	−2.732**	0.661**	−2.368**	0.105	−1.515*	0.474**
	(1.120)	(0.278)	(1.071)	(0.252)	(0.818)	(0.202)
Incidence x Ireland	0.266	−0.361	0.371	−0.029	−0.170	−0.207
	(1.474)	(0.366)	(1.050)	(0.247)	(0.936)	(0.231)
Incidence x Norway	0.616	−0.141	0.794	−0.009	0.046	−0.095
	(0.678)	(0.168)	(0.564)	(0.133)	(0.553)	(0.136)
Incidence x Sweden	1.205	−0.801***	1.095	−0.545***	0.085	−0.581***
	(0.760)	(0.189)	(0.679)	(0.159)	(0.613)	(0.151)
Incidence x Switzerland	0.179	−0.297*	0.412	−0.350***	−0.115	−0.010
	(0.650)	(0.161)	(0.564)	(0.132)	(0.400)	(0.098)
Incidence x UK	1.290	−0.703**	0.625	−0.365	2.072	−0.616

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Table B2: *First stage results using Log spending*

	Both		Men		Women	
	Log(spend), new	Log(spend), old	Log(spend), new	Log(spend), old	Log(spend), new	Log(spend), old
	b/se	b/se	b/se	b/se	b/se	b/se
	(1.441)	(0.358)	(1.320)	(0.310)	(1.563)	(0.385)
Incidence x US	6.807***	0.436**	5.404***	0.189	6.753***	0.415*
	(0.825)	(0.205)	(0.768)	(0.180)	(0.902)	(0.222)
Other new drugs x Austria	−0.001	0.002	−0.000	0.003*	−0.000	0.003
	(0.006)	(0.002)	(0.007)	(0.002)	(0.007)	(0.002)
Other new drugs x Croatia	−0.008	0.004*	−0.007	0.004	−0.008	0.004
	(0.009)	(0.002)	(0.010)	(0.002)	(0.010)	(0.002)
Other new drugs x Czech	−0.006	−0.000	−0.006	−0.000	−0.004	−0.000
Republic	(0.008)	(0.002)	(0.008)	(0.002)	(0.008)	(0.002)
Other new drugs x France	0.001	0.002	0.002	0.003	0.002	0.002
	(0.006)	(0.002)	(0.007)	(0.002)	(0.007)	(0.002)
Other new drugs x Germany	−0.000	0.002	0.001	0.002*	0.000	0.002
	(0.005)	(0.001)	(0.006)	(0.001)	(0.006)	(0.001)
Other new drugs x Ireland	−0.000	0.001	0.001	0.001	0.001	0.000
	(0.009)	(0.002)	(0.010)	(0.002)	(0.010)	(0.002)
Other new drugs x Norway	−0.006	0.001	−0.005	0.001	−0.005	0.001
	(0.005)	(0.001)	(0.006)	(0.001)	(0.006)	(0.001)
Other new drugs x Sweden	−0.003	−0.001	−0.002	−0.001	−0.002	−0.001
	(0.006)	(0.002)	(0.007)	(0.002)	(0.007)	(0.002)

Continued on next page

Table B2: *First stage results using Log spending*

	Both		Men		Women	
	Log(spend), new	Log(spend), old	Log(spend), new	Log(spend), old	Log(spend), new	Log(spend), old
	b/se	b/se	b/se	b/se	b/se	b/se
Other new drugs x	−0.002	−0.001	−0.002	−0.000	−0.001	−0.001
Switzerland	(0.006)	(0.001)	(0.006)	(0.002)	(0.006)	(0.002)
Other new drugs x UK	−0.001	0.002	−0.000	0.002	−0.001	0.002
	(0.007)	(0.002)	(0.007)	(0.002)	(0.007)	(0.002)
Other new drugs x US	−0.000	−0.001	0.000	−0.000	0.000	−0.001
	(0.002)	(0.000)	(0.002)	(0.000)	(0.002)	(0.000)
Average launch delay for	2.190	−0.783**	2.145	−0.681*	2.378	−0.687
non-cancer drugs	(1.591)	(0.395)	(1.757)	(0.413)	(1.729)	(0.426)
Exchange rate, €	0.066	0.024	0.065	0.019	0.086	0.026
	(0.095)	(0.024)	(0.105)	(0.025)	(0.103)	(0.025)
Exchange rate, USD	−0.587	−0.603***	−0.657	−0.642***	−0.472	−0.633**
	(0.929)	(0.231)	(1.025)	(0.241)	(1.008)	(0.248)
N	3318	3318	2964	2964	3035	3035
F-stat for under ID	25.19		23.22		22.50	
F-stat for weak ID	1.79		1.65		1.60	
Sargan statistic	22.57		28.86		13.56	

* p<0.10, ** p<0.05, *** p< .01.

C Age-standardized mortality rates

Table C1: *Average ASMR (per 100,000) by Country and Cancer Site, Men and Women*

	Austria	Croatia	Czech Republic	France	Germany	Ireland	Norway	Sweden	Switzerland	UK	US
All but skin	175.81	206.77	230.71	183.84	182.40	200.47	171.45	155.41	152.53	193.16	176.27
Bladder	4.18	4.83	5.66	5.18	4.67	4.15	5.01	4.01	4.12	5.67	3.60
Bone	0.43	1.28	0.91	0.85	0.47	0.67	0.38	0.39	0.42	0.41	0.42
Breast	15.49	15.14	15.83	14.76	16.09	17.95	12.81	12.09	14.10	17.49	14.12
CNS	4.59	6.64	5.91	4.19	5.02	6.25	5.18	5.25	4.96	4.97	4.38
Cervix uteri	3.10	3.72	6.14	2.03	3.42	4.07	3.80	2.52	1.76	3.48	2.79
Colon	14.66	14.09	19.49	13.98	16.03	16.61	16.56	12.11	10.87	13.32	14.48
Corpus uteri	4.35	3.15	5.11	3.17	2.78	3.20	3.15	2.61	2.76	2.89	2.64
Endocrine glands	0.21	0.39	0.31	0.29	0.29	0.37	0.27	0.25	0.39	0.28	0.25
Eye	0.13	0.18	0.22	0.17	0.14	0.26	0.20	0.11	0.20	0.14	0.08
Gallbladder	3.48	3.69	6.91	1.74	3.54	1.30	1.41	3.98	1.80	0.83	1.12
Hodgkin lymphoma	0.73	0.55	0.88	0.41	0.49	0.59	0.32	0.32	0.32	0.47	0.46
Kidney	5.14	4.41	10.11	4.39	5.78	4.21	4.75	5.21	3.85	4.29	4.03
Larynx	1.79	4.47	2.50	2.90	1.53	1.64	0.70	0.44	0.95	1.16	1.32
Leukaemia	5.83	5.75	6.98	6.07	5.90	6.03	4.81	5.14	4.90	5.18	6.53
Lip	0.04	0.21	0.11	0.05	0.04	0.17	0.07	0.04	0.04	0.03	0.02
Liver	6.53	7.06	7.32	8.80	4.86	4.05	2.03	4.51	5.49	3.22	4.49
Lung	32.91	45.13	47.49	35.46	35.10	41.96	32.52	24.85	29.90	44.63	51.49
Multiple myeloma	2.56	2.13	2.67	2.75	2.78	3.69	3.83	3.32	3.01	3.05	3.35
Non-Hodgkin lymphoma	4.25	3.72	4.04	4.89	4.32	5.95	4.26	5.30	4.90	5.56	6.55
Nose & sinuses	0.17	0.20	0.32	2.13	0.17	0.23	0.26	0.14	0.19	0.18	0.16
Oesophagus	2.91	3.85	3.50	5.99	4.06	8.20	2.78	2.83	4.10	8.65	4.11
Oral cavity	0.97	1.25	1.07	0.99	1.10	0.72	0.72	0.54	0.65	0.63	0.48
Other female sites	4.60	5.55	4.78	4.55	3.48	1.62	2.06	3.60	1.67	2.19	2.76
Other skin	0.61	0.97	1.01	0.49	0.38	1.19	0.44	0.37	0.54	0.54	0.74
Ovary	9.02	8.48	10.70	7.70	9.16	12.21	10.58	9.62	7.65	10.81	8.35
Pancreas	11.45	9.27	13.25	9.01	10.57	10.15	9.79	10.71	9.12	8.68	9.59
Penis	0.31	0.37	0.51	0.22	0.32	0.42	0.27	0.30	0.25	0.34	0.17
Pharynx	2.21	3.79	2.41	4.36	2.62	1.51	1.03	0.93	2.37	1.23	1.36
Prostate	26.72	24.15	26.86	25.50	25.51	30.67	37.50	35.52	28.32	26.86	22.70
Rectum	7.45	11.10	14.83	4.95	7.47	7.67	7.90	5.83	4.77	7.15	2.90
Salivary glands	0.27	0.36	0.43	0.24	0.23	0.37	0.24	0.23	0.21	0.24	0.22
Skin melanoma	2.80	2.76	2.88	1.82	2.04	2.18	4.31	3.18	2.74	2.32	2.53
Small intestine	0.37	0.41	0.54	0.38	0.31	0.43	0.73	0.70	0.45	0.39	0.35
Soft tissue	1.07	0.68	0.85	1.02	1.03	1.12	0.81	1.21	1.02	1.05	1.31
Stomach	11.47	17.10	12.98	6.46	11.12	9.73	7.96	6.47	5.54	8.19	4.02
Testis	0.42	0.62	0.89	0.35	0.50	0.36	0.40	0.21	0.36	0.30	0.25
Thyroid gland	0.84	0.61	0.79	0.52	0.72	0.61	0.58	0.54	0.61	0.41	0.42
Tongue	1.23	1.73	1.26	1.40	0.83	0.85	0.60	0.50	0.75	0.67	0.64

Table C2: *Average ASMR (per 100,000) by Country and Cancer Site, Men Only*

	Austria	Croatia	Czech Republic	France	Germany	Ireland	Norway	Sweden	Switzerland	UK	US
All but skin	231.52	297.61	314.11	261.65	239.63	243.35	212.50	183.35	200.00	235.70	214.21
Bladder	7.80	9.65	10.70	9.84	8.73	6.76	8.65	6.75	7.10	9.51	6.13
Bone	0.56	1.75	1.18	1.21	0.59	0.90	0.47	0.49	0.52	0.52	0.51
Breast	0.35	0.67	0.35	0.44	0.38	0.28	0.17	0.18	0.19	0.25	0.28
CNS	5.57	8.17	7.00	5.13	6.00	7.64	6.29	6.25	6.10	6.15	5.30
Cervix uteri	.	.	.	.	.	.	.	.	.	.	.
Colon	19.37	19.65	26.77	18.04	19.40	20.71	18.64	13.65	14.14	15.92	17.25
Corpus uteri	.	.	.	.	.	.	.	.	.	.	.
Endocrine glands	0.23	0.47	0.38	0.35	0.34	0.43	0.26	0.27	0.44	0.31	0.27
Eye	0.15	0.25	0.25	0.19	0.16	0.29	0.24	0.12	0.25	0.15	0.10
Gallbladder	3.06	3.18	5.63	1.66	2.95	1.04	1.41	3.06	1.58	0.71	1.00
Hodgkin lymphoma	0.93	0.70	1.11	0.54	0.61	0.73	0.40	0.39	0.38	0.59	0.57
Kidney	7.39	6.91	15.08	6.76	8.71	6.15	6.74	6.85	5.62	6.04	5.77
Larynx	3.66	9.70	5.24	5.86	3.09	3.01	1.31	0.82	1.88	2.08	2.35
Leukaemia	7.67	7.67	9.36	8.02	7.74	8.17	6.13	6.41	6.43	6.73	8.57
Lip	0.07	0.39	0.20	0.09	0.08	0.36	0.14	0.07	0.07	0.05	0.04
Liver	10.65	10.70	10.79	15.42	7.47	5.28	2.63	5.96	8.95	4.39	6.59
Lung	55.84	86.17	87.48	64.30	61.81	59.48	45.66	31.75	47.65	63.49	69.30
Multiple myeloma	2.99	2.53	3.21	3.40	3.43	4.71	4.87	4.13	3.75	3.75	4.12
Non-Hodgkin lymphoma	5.35	4.79	5.16	6.26	5.48	7.07	5.31	6.61	6.13	6.87	8.17
Nose & sinuses	0.24	0.29	0.46	4.10	0.26	0.28	0.36	0.19	0.28	0.24	0.21
Oesophagus	5.47	7.42	6.70	11.23	7.22	11.70	4.66	4.53	7.12	12.99	7.18
Oral cavity	1.66	2.39	1.87	1.72	1.85	1.07	1.01	0.69	1.02	0.88	0.66
Other female sites	.	.	.	.	.	.	.	.	.	.	.
Other skin	0.88	1.23	1.45	0.71	0.58	1.90	0.68	0.55	0.82	0.83	1.25
Ovary	.	.	.	.	.	.	.	.	.	.	.
Pancreas	13.70	12.02	16.45	11.43	12.72	11.85	11.06	11.51	10.57	10.03	11.14
Penis	0.31	0.37	0.51	0.22	0.32	0.42	0.27	0.30	0.25	0.34	0.17
Pharynx	3.95	7.59	4.45	8.22	4.64	2.46	1.68	1.51	4.11	1.90	2.20
Prostate	26.72	24.15	26.86	25.50	25.51	30.67	37.50	35.52	28.32	26.86	22.70
Rectum	10.47	16.00	22.19	6.74	10.05	10.95	10.47	7.48	6.34	9.85	3.69
Salivary glands	0.39	0.55	0.67	0.37	0.35	0.59	0.30	0.29	0.31	0.34	0.33
Skin melanoma	3.62	3.51	3.85	2.18	2.58	2.44	5.63	4.07	3.63	2.73	3.61
Small intestine	0.48	0.59	0.73	0.49	0.38	0.50	0.80	0.81	0.59	0.47	0.43
Soft tissue	1.36	0.88	1.07	1.28	1.25	1.33	0.96	1.34	1.19	1.25	1.50
Stomach	16.23	26.41	18.78	9.84	15.57	13.55	11.27	8.91	8.02	12.23	5.64
Testis	0.42	0.62	0.89	0.35	0.50	0.36	0.40	0.21	0.36	0.30	0.25
Thyroid gland	0.79	0.49	0.59	0.46	0.66	0.50	0.50	0.47	0.55	0.34	0.40
Tongue	2.15	3.46	2.27	2.49	1.37	1.35	0.89	0.67	1.17	0.97	0.96

Table C3: *Average ASMR (per 100,000) by Country and Cancer Site, Women Only*

	Austria	Croatia	Czech Republic	France	Germany	Ireland	Norway	Sweden	Switzerland	UK	US
All but skin	140.32	143.96	172.79	124.60	145.67	169.82	144.54	137.00	119.67	164.64	149.58
Bladder	2.13	1.98	2.51	1.90	2.41	2.31	2.59	2.02	2.14	3.10	1.87
Bone	0.32	0.90	0.69	0.54	0.38	0.47	0.30	0.30	0.33	0.31	0.33
Breast	26.87	25.96	27.22	26.73	28.39	33.39	23.64	22.54	25.56	31.76	25.57
CNS	3.77	5.40	4.98	3.35	4.18	4.96	4.17	4.32	3.94	3.91	3.59
Cervix uteri	3.10	3.72	6.14	2.03	3.42	4.07	3.80	2.52	1.76	3.48	2.79
Colon	11.59	10.55	14.64	11.06	13.73	13.32	15.15	10.99	8.52	11.36	12.38
Corpus uteri	4.35	3.15	5.11	3.17	2.78	3.20	3.15	2.61	2.76	2.89	2.64
Endocrine glands	0.19	0.35	0.27	0.24	0.26	0.32	0.28	0.23	0.35	0.25	0.23
Eye	0.11	0.15	0.19	0.15	0.12	0.24	0.19	0.09	0.16	0.13	0.07
Gallbladder	3.74	4.02	7.75	1.79	3.92	1.52	1.42	4.78	1.97	0.94	1.22
Hodgkin lymphoma	0.58	0.43	0.70	0.29	0.39	0.46	0.25	0.25	0.28	0.37	0.37
Kidney	3.60	2.60	6.52	2.58	3.72	2.61	3.14	3.88	2.49	2.89	2.65
Larynx	0.33	0.49	0.31	0.39	0.30	0.47	0.21	0.12	0.21	0.42	0.50
Leukaemia	4.62	4.49	5.40	4.69	4.72	4.39	3.80	4.16	3.82	4.01	5.00
Lip	0.03	0.11	0.06	0.02	0.01	0.04	0.03	0.02	0.02	0.01	0.01
Liver	3.46	4.37	4.77	3.42	2.90	3.03	1.53	3.29	2.69	2.26	2.73
Lung	16.52	14.77	17.76	11.68	16.01	27.81	22.29	19.56	16.20	30.77	37.87
Multiple myeloma	2.28	1.90	2.30	2.30	2.35	2.90	3.05	2.69	2.49	2.53	2.78
Non-Hodgkin lymphoma	3.47	2.93	3.21	3.83	3.50	5.02	3.42	4.20	3.98	4.50	5.27
Nose & sinuses	0.12	0.13	0.22	0.38	0.10	0.18	0.19	0.09	0.11	0.13	0.11
Oesophagus	0.87	1.04	0.96	1.56	1.47	5.17	1.21	1.36	1.64	5.06	1.59
Oral cavity	0.36	0.31	0.37	0.33	0.42	0.40	0.45	0.40	0.32	0.41	0.32
Other female sites	4.60	5.55	4.78	4.55	3.48	1.62	2.06	3.60	1.67	2.19	2.76
Other skin	0.42	0.82	0.75	0.35	0.27	0.70	0.29	0.23	0.37	0.35	0.36
Ovary	9.02	8.48	10.70	7.70	9.16	12.21	10.58	9.62	7.65	10.81	8.35
Pancreas	9.69	7.19	10.73	6.94	8.83	8.66	8.70	10.00	7.91	7.57	8.29
Penis	.	.	.	.	.	.	.	.	.	.	.
Pharynx	0.69	0.64	0.65	0.88	0.81	0.67	0.46	0.41	0.86	0.64	0.65
Prostate	.	.	.	.	.	.	.	.	.	.	.
Rectum	5.38	7.84	9.71	3.62	5.62	5.04	5.97	4.52	3.61	5.06	2.26
Salivary glands	0.20	0.22	0.26	0.15	0.16	0.20	0.20	0.19	0.14	0.16	0.14
Skin melanoma	2.20	2.22	2.19	1.53	1.64	1.96	3.20	2.43	2.06	1.97	1.67
Small intestine	0.30	0.28	0.41	0.30	0.26	0.36	0.69	0.61	0.34	0.33	0.29
Soft tissue	0.86	0.52	0.69	0.81	0.89	0.96	0.69	1.12	0.89	0.90	1.16
Stomach	8.51	10.73	9.09	3.91	8.23	6.64	5.49	4.61	3.68	5.17	2.77
Testis	.	.	.	.	.	.	.	.	.	.	.
Thyroid gland	0.84	0.67	0.89	0.55	0.75	0.70	0.63	0.59	0.64	0.45	0.42
Tongue	0.45	0.30	0.37	0.42	0.35	0.41	0.33	0.34	0.38	0.41	0.37

D Counterfactuals by gender

Table D1: *Counterfactual 1 by cancer, Men Only*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Bladder	23.77	7.79	7.79	0.42	9.98	23.63
Bone	1.22	0.73	0.73	0.00	8.23	.
Breast	0.92	0.31	0.35	1.64	2980.33	1817.72
CNS	8.11	6.43	7.16	23.57	2102.04	89.17
Cervix uteri	.	.	.	.	.	.
Colon	35.66	17.36	18.83	65.99	8514.62	129.04
Corpus uteri	.	.	.	.	.	.
Endocrine glands	0.54	0.32	0.32	-0.00	0.00	.
Eye	0.97	0.19	0.19	0.00	0.00	.
Gallbladder	3.13	2.07	2.07	-0.00	0.00	.
Hodgkin lymphoma	2.73	0.46	0.46	0.11	14.42	127.98
Kidney	17.40	7.34	8.55	48.04	7454.87	155.18
Larynx	6.91	3.00	3.00	-0.00	0.00	.
Leukaemia	12.88	7.33	9.10	113.06	11905.18	105.30
Lip	1.20	0.11	0.11	0.00	0.00	.
Liver	9.56	8.27	8.55	12.56	350.27	27.89
Lung	64.24	55.98	61.93	356.35	23735.17	66.61
Multiple myeloma	5.98	3.69	3.93	13.25	1585.90	119.69
Non-Hodgkin lymphoma	14.99	6.08	6.63	46.70	4692.69	100.48
Nose & sinuses	0.85	0.27	0.27	-0.00	0.00	.
Oesophagus	8.77	7.59	7.59	-0.00	0.00	.
Oral cavity	3.39	1.19	1.19	0.00	0.00	.
Other female sites	.	.	.	.	.	.
Other skin	68.39	0.97	0.97	-0.00	5.74	.
Ovary	.	.	.	.	.	.
Pancreas	12.19	12.07	13.67	48.24	2256.38	46.78
Penis	1.14	0.29	0.29	0.00	0.00	.
Pharynx	7.23	3.70	3.70	-0.00	0.00	.
Prostate	121.07	26.50	26.82	20.30	762.63	37.57
Rectum	24.92	9.83	10.54	21.77	4874.93	223.88
Salivary glands	1.06	0.39	0.39	0.00	0.00	.
Skin melanoma	16.54	3.63	3.64	1.15	391.02	339.40
Small intestine	1.80	0.58	0.58	-0.00	0.00	.
Soft tissue	3.03	1.13	1.14	0.24	111.27	458.56
Stomach	15.59	10.63	11.70	27.10	9811.36	362.01
Testis	7.41	0.38	0.38	0.00	0.00	.
Thyroid gland	3.14	0.48	0.50	0.66	115.98	175.24
Tongue	3.40	1.46	1.46	-0.00	0.00	.

Table D2: *Counterfactual 1 by country, Men Only*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Austria	13.30	5.88	6.40	8.59	1211.94	141.11
Croatia	13.52	8.43	8.75	2.77	199.41	71.99
Czech Republic	18.46	8.12	8.45	6.86	603.63	87.97
France	12.29	6.20	6.90	86.32	10122.53	117.26
Germany	15.76	5.99	6.55	89.95	9770.82	108.63
Ireland	18.48	6.17	6.50	3.00	375.22	125.18
Norway	13.26	5.59	5.87	2.72	280.74	103.21
Sweden	12.08	4.87	5.21	6.51	855.26	131.39
Switzerland	14.29	5.25	5.73	7.24	1226.46	169.34
UK	14.16	5.60	6.03	49.17	2591.43	52.71
US	15.69	5.35	6.22	538.04	54445.57	101.19

Table D3: *Counterfactual 1 by cancer, Women Only*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Bladder	6.11	2.18	2.18	0.16	7.39	47.48
Bone	0.90	0.42	0.42	0.00	8.23	.
Breast	105.64	24.81	27.84	150.34	3553.98	23.64
CNS	5.74	4.31	4.88	18.68	1762.95	94.39
Cervix uteri	10.06	2.91	2.99	3.44	1881.77	546.93
Colon	24.93	11.10	12.20	54.55	9525.27	174.61
Corpus uteri	18.83	2.43	2.43	0.00	0.00	.
Endocrine glands	0.50	0.27	0.27	-0.00	0.00	.
Eye	0.78	0.14	0.14	-0.00	0.00	.
Gallbladder	3.58	2.60	2.60	0.00	0.00	.
Hodgkin lymphoma	2.13	0.30	0.30	0.08	13.88	177.69
Kidney	8.42	3.17	3.77	24.83	4935.63	198.80
Larynx	0.85	0.31	0.31	-0.00	0.00	.
Leukaemia	7.85	4.28	5.48	79.56	12583.86	158.18
Lip	0.36	0.03	0.03	-0.00	0.00	.
Liver	3.20	3.19	3.31	5.43	176.20	32.46
Lung	27.71	22.41	25.56	240.75	21082.53	87.57
Multiple myeloma	3.96	2.45	2.62	10.24	1692.71	165.26
Non-Hodgkin lymphoma	10.66	3.89	4.29	34.42	4678.85	135.93
Nose & sinuses	0.44	0.13	0.13	-0.00	0.00	.
Oesophagus	2.30	1.92	1.92	0.00	0.00	.
Oral cavity	1.33	0.38	0.38	0.00	0.00	.
Other female sites	3.63	3.14	3.14	0.00	0.00	.
Other skin	46.13	0.42	0.42	0.00	5.74	.
Ovary	14.34	8.93	8.97	1.88	95.72	51.01
Pancreas	8.93	8.78	10.15	42.18	2545.96	60.36
Penis	.	.	.	.	.	.
Pharynx	1.51	0.66	0.66	-0.00	0.00	.
Prostate	.	.	.	.	.	.
Rectum	13.79	4.98	5.41	14.92	4479.35	300.22
Salivary glands	0.67	0.17	0.17	-0.00	0.00	.
Skin melanoma	15.22	2.15	2.16	0.61	391.02	636.25
Small intestine	1.20	0.38	0.38	-0.00	0.00	.
Soft tissue	2.30	0.85	0.86	0.23	15.54	68.16
Stomach	7.41	5.07	5.67	15.80	8994.46	569.15
Testis	.	.	.	.	.	.
Thyroid gland	8.80	0.56	0.58	0.79	433.68	549.84
Tongue	1.15	0.39	0.39	-0.00	0.00	.

Table D4: *Counterfactual 1 by country, Women Only*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Austria	8.85	3.56	3.98	7.54	1178.06	156.32
Croatia	8.56	3.95	4.11	1.53	194.03	127.04
Czech Republic	12.39	4.37	4.57	4.52	586.06	129.78
France	7.23	3.11	3.64	72.06	9907.71	137.49
Germany	10.86	3.62	4.02	69.15	9471.11	136.96
Ireland	13.63	4.27	4.54	2.38	367.37	154.07
Norway	10.31	3.82	4.08	2.53	272.11	107.53
Sweden	9.37	3.60	3.97	7.06	846.53	119.89
Switzerland	10.04	3.18	3.52	5.64	1187.08	210.40
UK	11.19	3.92	4.30	46.57	2564.79	55.08
US	11.76	3.74	4.49	479.90	52289.87	108.96

Table D5: *Counterfactual 2 by cancer, Men Only*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Bladder	23.77	7.79	7.70	-2.53	99.84	39.49
Bone	1.22	0.73	0.73	0.00	8.23	.
Breast	0.92	0.31	0.28	-0.48	382.09	802.69
CNS	8.11	6.43	6.12	-6.35	367.86	57.96
Cervix uteri	.	.	.	.	.	.
Colon	35.66	17.36	16.30	-11.53	1601.45	138.86
Corpus uteri	.	.	.	.	.	.
Endocrine glands	0.54	0.32	0.32	-0.00	0.00	.
Eye	0.97	0.19	0.19	0.00	0.00	.
Gallbladder	3.13	2.07	2.07	-0.00	0.00	.
Hodgkin lymphoma	2.73	0.46	0.46	-0.08	144.16	1879.21
Kidney	17.40	7.34	6.77	-7.97	3742.40	469.31
Larynx	6.91	3.00	3.00	-0.00	0.00	.
Leukaemia	12.88	7.33	5.78	-14.81	6415.23	433.19
Lip	1.20	0.11	0.11	0.00	0.00	.
Liver	9.56	8.27	8.15	-1.17	140.11	119.81
Lung	64.24	55.98	48.65	-90.79	6785.79	74.74
Multiple myeloma	5.98	3.69	3.51	-1.79	1471.46	822.73
Non-Hodgkin lymphoma	14.99	6.08	4.99	-14.42	5993.47	415.73
Nose & sinuses	0.85	0.27	0.27	-0.00	0.00	.
Oesophagus	8.77	7.59	7.59	-0.00	0.00	.
Oral cavity	3.39	1.19	1.19	0.00	0.00	.
Other female sites	.	.	.	.	.	.
Other skin	68.39	0.97	0.97	-0.00	5.74	.
Ovary	.	.	.	.	.	.
Pancreas	12.19	12.07	11.76	-10.82	209.20	19.34
Penis	1.14	0.29	0.29	0.00	0.00	.
Pharynx	7.23	3.70	3.70	-0.00	0.00	.
Prostate	121.07	26.50	25.87	-6.62	114.26	17.25
Rectum	24.92	9.83	9.11	-8.54	1928.14	225.81
Salivary glands	1.06	0.39	0.39	0.00	0.00	.
Skin melanoma	16.54	3.63	3.59	-0.45	1329.46	2933.81
Small intestine	1.80	0.58	0.58	-0.00	0.00	.
Soft tissue	3.03	1.13	1.11	-0.87	588.12	675.98
Stomach	15.59	10.63	10.47	-0.51	223.77	436.15
Testis	7.41	0.38	0.37	-0.05	0.00	.
Thyroid gland	3.14	0.48	0.48	-0.06	46.39	799.29
Tongue	3.40	1.46	1.46	-0.00	0.00	.

Table D6: *Counterfactual 2 by country, Men Only*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Austria	13.30	5.88	5.59	-4.81	304.53	63.29
Croatia	13.52	8.43	7.32	-9.48	164.37	17.33
Czech Republic	18.46	8.12	7.27	-17.54	384.98	21.94
France	12.29	6.20	5.98	-27.63	1479.81	53.56
Germany	15.76	5.99	5.73	-43.33	1498.50	34.58
Ireland	18.48	6.17	5.69	-4.31	176.75	41.05
Norway	13.26	5.59	5.17	-4.10	104.56	25.52
Sweden	12.08	4.87	4.59	-5.20	242.87	46.73
Switzerland	14.29	5.25	5.01	-3.66	340.09	92.84
UK	14.16	5.60	5.19	-46.23	831.30	17.98
US	15.69	5.35	5.32	-13.54	1596.87	117.92

Table D7: *Counterfactual 2 by cancer, Women Only*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Bladder	6.11	2.18	2.15	-0.84	73.88	88.23
Bone	0.90	0.42	0.42	0.00	8.23	.
Breast	105.64	24.81	22.36	-45.83	455.64	9.94
CNS	5.74	4.31	4.07	-4.92	308.52	62.77
Cervix uteri	10.06	2.91	2.79	-1.78	642.56	361.75
Colon	24.93	11.10	10.36	-8.83	1791.53	202.81
Corpus uteri	18.83	2.43	2.43	0.00	0.00	.
Endocrine glands	0.50	0.27	0.27	-0.00	0.00	.
Eye	0.78	0.14	0.14	-0.00	0.00	.
Gallbladder	3.58	2.60	2.60	0.00	0.00	.
Hodgkin lymphoma	2.13	0.30	0.30	-0.06	138.78	2399.83
Kidney	8.42	3.17	2.91	-4.06	2477.73	610.68
Larynx	0.85	0.31	0.31	-0.00	0.00	.
Leukaemia	7.85	4.28	3.28	-10.09	6780.94	672.24
Lip	0.36	0.03	0.03	-0.00	0.00	.
Liver	3.20	3.19	3.14	-0.49	70.48	142.98
Lung	27.71	22.41	19.41	-42.18	6027.41	142.89
Multiple myeloma	3.96	2.45	2.30	-1.42	1570.55	1106.30
Non-Hodgkin lymphoma	10.66	3.89	3.12	-10.47	5975.79	570.52
Nose & sinuses	0.44	0.13	0.13	-0.00	0.00	.
Oesophagus	2.30	1.92	1.92	0.00	0.00	.
Oral cavity	1.33	0.38	0.38	0.00	0.00	.
Other female sites	3.63	3.14	3.14	0.00	0.00	.
Other skin	46.13	0.42	0.42	0.00	5.74	.
Ovary	14.34	8.93	8.65	-6.22	12.00	1.93
Pancreas	8.93	8.78	8.54	-9.31	236.05	25.36
Penis	.	.	.	.	.	.
Pharynx	1.51	0.66	0.66	-0.00	0.00	.
Prostate	.	.	.	.	.	.
Rectum	13.79	4.98	4.58	-5.12	1771.68	345.82
Salivary glands	0.67	0.17	0.17	-0.00	0.00	.
Skin melanoma	15.22	2.15	2.12	-0.31	1329.46	4258.87
Small intestine	1.20	0.38	0.38	-0.00	0.00	.
Soft tissue	2.30	0.85	0.83	-0.80	82.15	103.31
Stomach	7.41	5.07	5.00	-0.27	205.14	755.29
Testis	.	.	.	.	.	.
Thyroid gland	8.80	0.56	0.55	-0.08	173.47	2043.25
Tongue	1.15	0.39	0.39	-0.00	0.00	.

Table D8: *Counterfactual 2 by country, Women Only*

		ASMR		Change in	Spending	Cost per
	ASIR	Observed	Counterfactual	lives (1000s)	(millions)	Life (1000s)
Austria	8.85	3.56	3.37	-3.34	292.08	87.54
Croatia	8.56	3.95	3.42	-5.05	165.02	32.68
Czech Republic	12.39	4.37	3.92	-10.08	347.43	34.47
France	7.23	3.11	2.98	-17.18	1391.87	81.00
Germany	10.86	3.62	3.41	-35.87	1529.95	42.66
Ireland	13.63	4.27	3.87	-3.85	167.05	43.43
Norway	10.31	3.82	3.47	-3.45	103.47	29.96
Sweden	9.37	3.60	3.36	-4.68	236.74	50.59
Switzerland	10.04	3.18	2.97	-3.26	319.21	97.92
UK	11.19	3.92	3.56	-42.98	844.39	19.65
US	11.76	3.74	3.71	-23.35	1790.75	76.70