Revised Manuscript - Clean Copy

The contribution of pharmaceutical innovation to longevity growth in Germany and France, 2001-2007

Frank R. Lichtenberg

frank.lichtenberg@columbia.edu

Columbia University
and
National Bureau of Economic Research

22 November 2010

Abstract

I investigate the contribution of pharmaceutical innovation to recent longevity growth in Germany and France. First, I examine the effect of the vintage of prescription drugs (and other variables) on the life expectancy and age-adjusted mortality rates of residents of Germany, using longitudinal, annual, state-level data during the period 2001-2007. The estimates imply that about one-third of the 1.4-year increase in German life expectancy during the period 2001-2007 was due to the replacement of older drugs by newer drugs. Next, I examine the effect of the vintage of chemotherapy treatments on age-adjusted cancer mortality rates of residents of France, using longitudinal, annual, cancer-site-level data during the period 2002-2006. The estimates imply that chemotherapy innovation accounted for at least one-sixth of the decline in French cancer mortality rates, and may have accounted for as much as half of the decline.

I. Introduction

Longevity increase is an important part of economic growth and development. Nordhaus (2003) estimated that, "to a first approximation, the economic value of increases in longevity over the twentieth century is about as large as the value of measured growth in non-health goods and services" (p. 17). Murphy and Topel (2006) observed that "the historical gains from increased longevity have been enormous. Over the 20th century, cumulative gains in [U.S.] life expectancy were worth over $1.2 million per person for both men and women. Between 1970 and 2000 increased longevity added about $3.2 trillion per year to national wealth, an uncounted value equal to about half of average annual GDP over the period." In its Human Development Reports, the United Nations Development Program ranks countries by their value of the Human Development Index, which is based on life expectancy at birth as well as on the adult literacy rate and per capita GDP.

Since the 1950s, economists have recognized that, in the long run, the rate of economic growth is determined by (indeed equal to) the rate of technological progress. In neoclassical growth models developed by Nobel laureate Robert Solow (1956, 1957) and colleagues, an economy will always converge towards a steady state rate of growth, which depends only on the rate of technological progress.

In early models of economic growth, the rate of technological progress was assumed to be given, or exogenous: technological progress was regarded as "manna from heaven." Economists began to relax this clearly unrealistic assumption in the 1980s, by developing so-called "endogenous growth models." In Paul Romer's (1990) model, "growth…is driven by technological change that arises from intentional [R&D] investment decisions made by profit-maximizing agents."[1] Jones (1998) argues that "technological progress [is] the ultimate driving force behind sustained economic growth" (p.2), and that "technological progress is driven by research and development (R&D) in the advanced world" (p. 89).

Technological change may be either disembodied or embodied. Suppose firm X invests in R&D, and that this investment results in a valuable discovery. If the technological advance is disembodied, consumers and other firms could benefit from the discovery without purchasing

[1] Growth may also be driven by technological change arising from R&D investment by public organizations, e.g. the National Institutes of Health.

firm X's goods or services; they could benefit just by reading or hearing about the discovery. However, if the technological advance is embodied, consumers and other firms must purchase firm X's goods or services to benefit from its discovery. Solow (1960, p 91): argued that "many if not most innovations need to be embodied in new kinds of durable equipment before they can be made effective. Improvements in technology affect output only to the extent that they are carried into practice either by net capital formation or by the replacement of old-fashioned equipment by the latest models…"[2] Romer also assumes that technological progress is embodied in new goods: "new knowledge is translated into goods with practical value," and "a firm incurs fixed design or research and development costs when it creates a new good. It recovers those costs by selling the new good for a price that is higher than its constant cost of production." Grossman and Helpman (1993) argued that "innovative goods are better than older products simply because they provide more 'product services' in relation to their cost of production." Bresnahan and Gordon (1996) stated simply that "new goods are at the heart of economic progress," and Bils (2004) said that "much of economic growth occurs through growth in quality as new models of consumer goods replace older, sometimes inferior, models."

When technological progress is embodied in new goods, the welfare of consumers (and the productivity of producers) depends on the *vintage* of the goods (or inputs) they purchase. In this context, "vintage" refers to the year in which the good was first produced or sold. For example, the vintage of the drug simvastatin is 1993: that is the year it was approved by the FDA, and first sold. Solow was the first economist to develop a growth model that distinguished between vintages of (capital) goods. In Solow's model, new capital is more valuable than old capital because--since capital is produced based on known technology, and technology improves with time--new capital will be more productive than old capital.[3] A number of econometric studies (Bahk and Gort (1993), Hulten (1992), Sakellaris and Wilson (2004)) have shown that manufacturing firms using later-vintage equipment have higher productivity.

The extent to which the welfare of consumers or the productivity of producers depends on the vintage of the goods they purchase should depend on the research intensity of those goods. The greater the research intensity of the goods, the greater the impact of their vintage on consumer welfare and producer productivity. According to the National Science Foundation, the

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[2] We hypothesize that innovations may be embodied in nondurable goods (e.g. drugs) and services as well as in durable equipment.

[3] http://en.wikipedia.org/wiki/Exogenous_growth_model

pharmaceutical and medical devices industries are the most research intensive industries in the economy.[4]

In the next section, I will investigate the effect of the vintage of prescription drugs (and other variables) on the life expectancy and age-adjusted mortality rates of residents of Germany, using longitudinal, annual, state-level data during the period 2001-2007. The analysis will be based on data on the utilization of over 600 active ingredients in a variety of drug classes, which account for about 250 million prescriptions (43% of all prescriptions in Germany) per year.

In the following section, I will investigate the effect of the vintage of chemotherapy treatments on age-adjusted cancer mortality rates of residents of France, using longitudinal, annual, cancer-site (breast, colon, lung, etc.) -level data during the period 2002-2006.[5] The analysis will be based on data on the utilization of 11 cancer drugs by about 4000 cancer patients per year.

II. Life expectancy in Germany

A. Econometric model

I will estimate models of the following form:

$$OUTCOME_{st} = \beta\ VINTAGE_{st} + \gamma\ X_{st} + \alpha_s + \delta_t + \varepsilon_{st} \quad (1)$$

where

OUTCOME is one of the following variables:

LE_{st} = life expectancy at birth in state s in year t (s = 1,…,16; t = 2001,…,2007)

ln_AAMORT_{st} = the log of the age-adjusted mortality rate in state s in year t[6]

[4] In 1997, "medical substances and devices firms had by far the highest combined R&D intensity at 11.8 percent,…well above the 4.2-percent average for all 500 top 1997 R&D spenders combined. The information and electronics sector ranked second in intensity at 7.0 percent." The pattern of 1997 R&D spending per employee is similar to that for R&D intensity, with medical substances and devices again the highest at $29,095 per employee. Information and electronics is second at $16,381. Combined, the top 500 1997 R&D firms spent $10,457 per employee.

[5] Cancer was the cause of about 30% of deaths in France in 2006.

[6] Age-adjusted death rates are weighted averages of age-specific death rates, where the weights represent a fixed population by age. They are used to compare relative mortality risk among groups and over time. An age-adjusted rate represents the rate that would have existed had the age-specific rates of the particular year prevailed in a population whose age distribution was the same as that of the fixed population.

VINTAGE is one of the following variables:

FDA_YEAR_{st} = the (weighted) mean FDA approval year[7] of ingredients contained in prescriptions consumed in state s in year t

$POST1990\%_{st}$ = the percent of prescriptions consumed in state s in year t that contained ingredients approved by the FDA after 1990

$POST1995\%_{st}$ = the percent of prescriptions consumed in state s in year t that contained ingredients approved by the FDA after 1995

and X includes the following variables:

$ln\_CT\_SCANNERS_{st}$ = the log of the number of CT scanners in hospitals and prevention or rehabilitation facilities per 100,000 persons in state s in year t

ln_GDP_{st} = the log of GDP per person in state s in year t

$UNEMP_{st}$ = the unemployment rate in state s in year t

$ln\_NOTIF\_DISEASES_{st}$ = the log of the number of notifiable diseases per 100,000 persons in state s in year t

ln_AIDS_{st} = the log of the number of new AIDS cases per 100,000 persons in state s in year t

ln_DRUNK_{st} = the log of the number of people injured or killed in road traffic accidents under the influence of alcohol per 100,000 persons in state s in year t

ln_HARD_{st} = the log of the number of users of hard drugs who came to police notice for the first time per 100,000 persons in state s in year t

$ln\_N\_RX_{st}$ = the log of the number of prescriptions per person in state s in year t

ln_BEDS_{st} = the log of the number of hospital beds per 100,000 persons in state s in year t

$ln\_PHYSICIANS_{st}$ = the log of the number of physicians per 100,000 persons in state s in year t

$ln\_PHARMACISTS_{st}$ = the log of the number of pharmacists per 100,000 persons in state s in year t

The first element of X, ln_CT_SCANNERS, is an indicator of an important type of *non-pharmaceutical* medical innovation: diagnostic imaging innovation.

In principle, we would like to control for aspects of "lifestyle" that affect health, such as the fraction of the population that smokes or is obese. Unfortunately, state-level time-series data on these variables are unavailable. Instead, we will include three available measures of "risky behavior": ln_AIDS, ln_DRUNK, and ln_HARD.

[7] As discussed above, in the literature on embodied technical change, "vintage" refers to the year in which a good was first produced or sold (anywhere in the world). The U.S. is the country in which many drugs are first launched. Also, it is difficult to obtain data on the date at which drugs were first launched in Germany.

It might also be desirable to control for health expenditure, although it is not clear whether states with larger increases in health expenditure should have larger or smaller increases in longevity, since people in worse health tend to use more health care. Unfortunately, data on health expenditure, by state, are not available. Instead, we will include four measures of health care resources: ln_N_RX, ln_BEDS, ln_PHYSICIANS, and ln_PHARMACISTS.

In eq. (1), α_s and δ_t represent state fixed effects and year fixed effects, respectively. Due to the inclusion of these effects, eq. (1) is a difference-in-differences model. A significant negative drug vintage coefficient (β) in a model in which the dependent variable is life expectancy would indicate that states that had above-average increases in drug vintage had above-average increases in life expectancy, controlling for other regressors.

Eq. (1) will be estimated by weighted least squares (WLS), weighting by pop_{st}, state s's population in year t. The estimation procedure will account for clustering of disturbances within states.

The drug vintage measure FDA_YEAR will be constructed as follows:

$$FDA\_YEAR_{st} = \frac{\Sigma_d\, N\_RX_{dst}\, APP\_YEAR_d}{\Sigma_d\, N\_RX_{dst}}$$

where

N_RX_{dst} = the number of prescriptions for drug d in state s in year t

APP_YEAR_d = the year in which the active ingredient of drug d was first approved by the FDA[8]

The drug vintage measure POST1990% will be constructed as follows:

$$POST1990\%_{st} = \frac{\Sigma_d\, N\_RX_{dst}\, APP\_YEAR\_GT\_1990_d}{\Sigma_d\, N\_RX_{dst}}$$

[8] If drug d contains 2 or more active ingredients, APP_YEAR_d is the *mean* of the years in which the active ingredients of drug d were first approved by the FDA.

where

$APP\_YEAR\_GT\_1990_d$ = 1 if the active ingredient of drug d was first approved by the FDA after 1990

= 0 otherwise

The drug vintage measure POST1995% will be constructed as follows:

$$POST1995\%_{st} = \frac{\Sigma_d\, N\_RX_{dst}\, APP\_YEAR\_GT\_1995_d}{\Sigma_d\, N\_RX_{dst}}$$

where

$APP\_YEAR\_GT\_1995_d$ = 1 if the active ingredient of drug d was first approved by the FDA after 1995

= 0 otherwise

B. *Data and descriptive statistics*

Pharmaceutical data. Data on the number of prescriptions, by drug, state, and year (N_RX_{dst}) were obtained from the IMS Health National Prescription Analysis database (http://www.imshealth.de/sixcms/detail.php/375), which covers more than 99% of prescriptions reimbursed by German Sick Funds. It does not contain drugs used in a hospital, drugs completely paid out-of-pocket, and drugs prescribed for members of private health insurance companies (approximately 10% of the German population, particularly high-income employees, self-employed persons, military, and government officials). We were unable to obtain data on all drugs sold in Germany. Data were available for drugs included in the following drug classes[9]:

- Cardiovascular (C***)
- Oncology (A04A, L***, B03A, B03C, V03D)
- Parkinson (N04A)
- Alzheimer/Dementia (N07D)
- Antidiabetics (A10*)
- Asthma/COPD (R03*)
- NSAID/Coxibs (M01A)

[9] European Pharmaceutical Market Research Association (EphMRA) drug classification codes are shown in parentheses. The EphMRA classification is a modified modified version of the ATC classification. See http://www.ephmra.org/classification/anatomical-classification.aspx.

Appendix Table 1 compares 2008 data from our sample of drugs to data on all drugs dispensed in the Statutory Health Insurance system. Overall, our dataset provides information on about 250 million prescriptions per year for over 600 active ingredients, which account for 43% of total prescriptions and about 50% of total drug expenditure.

Data on the initial year of FDA approval of active ingredients (APP_YEAR_d) were obtained from the Food and Drug Administration's Drugs@FDA database (http://www.fda.gov/Drugs/InformationOnDrugs/ucm079750.htm). We were able to determine the initial FDA approval year of products accounting for over 80% of the prescriptions in our sample.

Table 1 shows data on the top 25 drugs in our sample, ranked by the number of prescriptions during 2000-2008. Figure 1 shows data on the vintage distribution of prescriptions consumed during the period 2000-2008: it shows the percent of prescriptions consumed during 2000-2008 that were for drugs approved after year t (t = 1940,...,2010). About 75% of prescriptions were for drugs approved after 1975, 50% were for drugs approved after 1986, and 25% were for drugs approved after 1993.

Age-adjusted mortality and life expectancy data. We will analyze two different measures of longevity: the age-adjusted mortality rate, and life expectancy at birth. The Information System of the Federal Health Monitoring (http://www.gbe-bund.de/) provides data on age-adjusted mortality rates, by state and year. It also provides time-series data on life expectancy in Germany as a whole, but not life expectancy by state. However, it provides data on age-specific mortality rates by state and year, from which life expectancy by state and year can be calculated.[10]

Data on life expectancy at birth during 2000-2007 in selected states are shown in Figure 2. The rate of increase of life expectancy varied across states and over time. In 2000, Saarland's life expectancy was higher than Mecklenburg-Vorpommern's; in 2007, it was slightly lower. In 2000, Schleswig-Holstein's life expectancy was slightly higher than Berlin's; in 2007, it was lower.

[10] We verified that population-weighted averages of our state-level life expectancy estimates were very consistent with published estimates for Germany as a whole.

Data on other variables. Data on population, the number of notifiable diseases per 100,000 persons,[11] the number of new AIDS cases per 100,000 persons, the number of CT scanners in hospitals and prevention or rehabilitation facilities, the number of people injured or killed in road traffic accidents under the influence of alcohol, and the number of users of hard drugs who came to police notice for the first time, by state and year, were also obtained from The Information System of the Federal Health Monitoring. Data on GDP per person, the unemployment rate, and the number of hospital beds, physicians, and pharmacists, by state and year, were obtained from Eurostat's regional statistics database (http://epp.eurostat.ec.europa.eu/portal/page/portal/eurostat/home).[12]

Summary statistics, by year, are reported in Table 2. The FDA_YEAR, POST1990%, and POST1995% statistics are weighted means, where the weight is the number of prescriptions. The other statistics (with the exceptions of the number of prescriptions and population) are weighted means, where the weight is the population. The mean FDA approval year increased by 2.1 years between 2001 and 2007. The fraction of prescriptions that contained ingredients approved after 1990 increased from 34% in 2001 to 44% in 2007. Life expectancy at birth increased by 1.4 years between 2001 and 2007.

The complete dataset used for estimation is shown in Appendix Table 2.

C. Empirical results

Estimates of models of life expectancy and the age-adjusted mortality rate are presented in Table 3. We present estimates of six different models, since we use two alternative outcome measures and three alternative drug vintage measures.

In model 1, the dependent variable is life expectancy at birth, and the measure of prescription drug vintage is FDA_YEAR: the (weighted) mean FDA approval year of ingredients contained in prescriptions consumed. The coefficient on this variable is positive and highly significant (p-value = .004). This indicates that states with larger increases in drug vintage had larger increases in life expectancy.

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[11] In the Federal Republic of Germany, health authorities must be informed about cases of certain notifiable diseases, which are listed in the Infection Protection Act. Depending on the disease the suspicion, the disease and/or the death must be reported. (Source: www.rki.de). Data on the incidence and prevalence of other diseases are not available.

[12] Data on educational attainment by state and year were not available.

The only other variable with a coefficient that is statistically significant at the 5% level is ln_NOTIF_DISEASES. As expected, an increase in the number of notifiable diseases per 100,000 persons is associated with a decline in life expectancy. The coefficient on per capita income is insignificant (p-value=.202), and negative: longevity did not increase more in states with high income growth. Some previous investigators have also found evidence of a non-monotonic or even inverse relationship between income and longevity. Uchida et al (1992) found that "for [Japanese] females high income was the factor significantly decreasing life expectancy at 65 years of age in 1980." Hupfeld (2011) theoretically derived a non–monotonic relationship between income and longevity, based on heterogeneous elasticities of labor supply and otherwise standard assumptions. He analyzed this relationship empirically for pensioners in the public pension system in Germany, and find that "the relationship between income and life expectancy is indeed non–monotonic for major sub–groups in the data." And Ruhm (2004) argued that "although health is conventionally believed to deteriorate during macroeconomic downturns, the empirical evidence supporting this view is quite weak and comes from studies containing methodological shortcomings that are difficult to remedy. Recent research that better controls for many sources of omitted variables bias instead suggests that mortality decreases and physical health improves when the economy temporarily weakens. This partially reflects reductions in external sources of death, such as traffic fatalities and other accidents, but changes in lifestyles and health behaviors are also likely to play a role."

The coefficient on ln_PHYSICIANS is *negative* and nearly significant (p-value = .067): states with larger increases in the number of physicians per 100,000 residents had smaller increases in life expectancy. As suggested above, a larger quantity of health resources may be a response to unobserved negative health shocks. The coefficient on ln_HARD is positive and nearly significant (p-value = .086), which is surprising. However, the coefficient on FDA_YEAR is quite insensitive to the inclusion of ln_PHYSICIANS and ln_HARD in the model. When these two variables are excluded, the coefficient on FDA_YEAR is *larger* and more significant: $\beta = .258$ ($Z = 5.01$, p-value $< .001$).

Models 2 and 3 are similar to model 1, but instead of FDA_YEAR, the measure of drug vintage is the fraction of prescriptions containing ingredients approved by the FDA after 1990 or 1995. The estimates of these two models are qualitatively similar to the estimates of models 1. The coefficients on POST1990% and POST1995% are both positive and highly significant.

Models 4-6 are similar to models 1-3, but in these models the dependent variable is the log of the age-adjusted mortality rate. The age-adjusted mortality rate and life expectancy at birth both depend on (are functions of) age-specific mortality rates, but they depend on them in different ways. Model 4 indicates that the age-adjusted mortality rate declined more in states with larger increases in the weighted mean FDA approval year of prescriptions. A one-year increase in mean drug vintage was associated with a 1.8% decline in the age-adjusted mortality rate. The coefficient on ln_CT_SCANNERS is negative and significant in all three mortality-rate models. This is consistent with the hypothesis that longevity has been increased by diagnostic imaging innovation as well as by pharmaceutical innovation.

The parameter estimates can be used to estimate how much of the 1.4-year increase in life expectancy during the period 2001-2007 was attributable to the increase in drug vintage, i.e. to the use of newer drugs. These calculations are shown in the following table.

Model	1	2	3
Vintage measure	FDA_YEAR	POST1990%	POST1995%
2001-2007 change in vintage measure (Δ)	2.1	10%	4%
β	0.21	7.21	5.23
β * Δ	0.43	0.71	0.20

Model 1, based on the FDA_YEAR drug vintage measure, implies that use of newer drugs increased life expectancy at birth by 0.43 years during the period 2001-2007. Model 2, based on the POST1990% drug vintage measure, implies that use of newer drugs increased life expectancy by a larger amount: 0.71 years. Model 3, based on the POST1995% drug vintage measure, implies that use of newer drugs increased life expectancy by a smaller amount: 0.20 years. The mean of these three estimates is 0.45 years, which is about a third (32%) of the increase in life expectancy during the period 2001-2007.

The parameter estimates can also be used to obtain a rough assessment of the overall cost-effectiveness of pharmaceutical innovation. We define the incremental cost-effectiveness ratio (ICER) as follows:

$$\text{ICER} = \frac{\text{change in lifetime drug expenditure due to pharmaceutical innovation}}{\text{change in life expectancy due to pharmaceutical innovation}}$$

The underlying calculations are shown in the following table.

Year	Life expectancy	annual drug expenditure in constant 2000 €[1]	lifetime drug expenditure (= life expectancy * annual drug expenditure)
2001	78.50	€ 300.00	€ 23,550
2007	78.95[2]	€ 364.00	€ 28,737
change	0.45		€ 5,187

1: Source: 2009 OECD Health Database. Data for 2007 are not available, so we use 2000 and 2006 values.
2: "Predicted" life expectancy in 2007 = $LE_{2001} + \beta\ (VINT_{2007} - VINT_{2001})$

German life expectancy at birth was 78.5 years in 2001. The mean of the estimates of β from models 1, 2, and 3 implies that the increase in drug vintage increased life expectancy by 0.45 years between 2001 and 2007. According to the 2009 OECD Health Database, per capita expenditure (in constant 2000 €) on prescription drugs increased from € 300 in 2000 to € 364 in 2006. Assuming that this increase was entirely due to use of newer drugs, pharmaceutical innovation increased lifetime drug expenditure by € 5,187. The implied ICER is € 11,597 (= € 5,187 / 0.45 years), or $16,173 (at the current exchange rate of 1.39 $/€) per life-year. This is a small fraction of leading economists' estimates of the value of (willingness to pay for) an additional year of life.

This rough assessment of the overall cost-effectiveness of pharmaceutical innovation may be compared to evidence from clinical trials as reported in the CEA Registry[13], a comprehensive database of cost-utility analyses on a wide variety of diseases and treatments. A search of the registry found (1) 545 pharmaceutical interventions that decreased cost and improved health (in which case the ICER is negative); (2) 771 pharmaceutical interventions that increased cost and improved health at a cost of less than $16,173 per QALY; and (3) 1481 pharmaceutical interventions that increased cost and improved health at a cost of more than $16,173 per QALY. Therefore, our estimate of the ICER is not very far from the median of the estimates reported in the CEA Registry.

However, evidence about the distribution of ICER estimates from clinical trials may be difficult to interpret, for several reasons. First, clinical trials of some important products may not provide ICER estimates. Johnson et al (2003) reported that "end points other than survival [e.g. reduction in tumor size] were the approval basis for 68% (39 of 57) of oncology drug marketing

[13] The CEA Registry (https://research.tufts-nemc.org/cear4/) is produced by the Center for the Evaluation of Value and Risk in Health, part of the Institute for Clinical Research and Health Policy Studies at Tufts Medical Center in Boston, MA.

applications granted regular approval and for all 14 applications granted accelerated approval from January 1, 1990, to November 1, 2002." Second, more cost-effective interventions may be used more frequently, so that utilization-weighted mean ICER may be lower than unweighted mean ICER. Third, the ICER of a drug is usually calculated using the price of the drug when it was launched, and the average price of a drug 20 years after it was launched[14] is generally much lower than its price when it was launched. Fourth, the ICER calculation may not account for reductions in other medical expenditure attributable to pharmaceutical innovation. For example, the National Institute for Clinical Excellence (2001) acknowledged that its evaluation of the cost-effectiveness of new drug treatments for rheumatoid arthritis did "not include all potential benefits of these agents. For instance no account is taken of the possible reduction in the need for joint replacement surgery, hospitalization or needs for aids and appliances." Lichtenberg (2009) has shown that these "cost offsets" can be large, relative to the direct cost of the intervention.

III. Cancer mortality in France

Now I will investigate the effect of the vintage of chemotherapy treatments on mortality rates of French cancer patients, using longitudinal, annual, cancer-site (breast, colon, lung, etc.) level data during the period 2002-2006.

Two types of statistics are used to measure cancer mortality: survival rates and mortality rates. Survival rates are typically expressed as the proportion of patients alive at some point subsequent to the diagnosis of their cancer. For example, the observed 5-year survival rate is defined as follows:

5-year Survival Rate = Number of people diagnosed with cancer at time t alive at time t+5 / Number of people diagnosed with cancer at time t

= 1 – (Number of people diagnosed with cancer at time t dead at time t+5 / Number of people diagnosed with cancer at time t)

Hence, the survival rate is based on a *conditional* (upon previous diagnosis) mortality rate. The second type of statistic is the *unconditional* cancer mortality rate: the number of deaths, with cancer as the underlying cause of death, occurring during a year per 100,000 population.

[14] As shown in Table 2, the average prescription is for a drug launched about 20 years earlier.

The outcome measure I will analyze is the *unconditional* (age-adjusted) cancer mortality rate. Longitudinal, cancer-site level data on conditional mortality (or survival) are not available during the period for which we have chemotherapy treatment data (2002-2006), although they are available for earlier years.[15] Moreover, Welch et al (2000) argued that "while 5-year survival is a perfectly valid measure to compare cancer therapies in a randomized trial, comparisons of 5-year survival rates across time (or place) may be extremely misleading. If cancer patients in the past always had palpable tumors at the time of diagnosis while current cancer patients include those diagnosed with microscopic abnormalities, then 5-year survival would be expected to increase over time even if new screening and treatment strategies are ineffective." Consequently, Welch et al (2000) concluded that "to avoid the problems introduced by changing patterns of diagnosis…progress against cancer [should] be assessed using [unconditional] population-based mortality rates."

A. *Econometric model*

I will estimate models of the following form:

$$\ln(\text{AAMORT})_{st} = \beta\ \text{VINTAGE}_{st} + \alpha_s + \delta_t + \varepsilon_{st} \quad (2)$$

where

$\ln(\text{AAMORT}_{st})$ = the log of the age-adjusted mortality rate from cancer at site s in year t (s=1,…,24; t=20002,…,2006)

VINTAGE is one of the following variables:

LAUNCH_YEAR_{st} = the (weighted) mean world launch year of chemotherapy treatments for cancer site s in year t

$\text{POST1985\%}_{st}$ = the percent of chemotherapy treatments for cancer site s in year t that contained ingredients launched after 1985

$\text{POST1990\%}_{st}$ = the percent of chemotherapy treatments for cancer site s in year t that contained ingredients launched after 1990

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[15] The Eurocare 3 and Eurocare 4 databases (http://www.eurocare.it/Home/tabid/36/Default.aspx) provide data on survival rates of French cancer patients diagnosed during the following periods: 1983-1985, 1986-1988, 1989-1991, 1992-1994, and 1995-1999.

α_s and δ_t represent cancer-site fixed effects and year fixed effects, respectively. A significant negative drug vintage coefficient (β) in eq. (2) would indicate that cancer sites that had above-average increases in drug vintage had above-average reductions in the age-adjusted mortality rate.

Eq. (2) will be estimated by weighted least squares, weighting by the mean of each cancer site's mortality rate during the entire sample period ($(1 / T) \sum_t AAMORT_{st}$). The estimation procedure will account for clustering of disturbances within cancer sites.

The drug vintage measure LAUNCH_YEAR will be constructed as follows:

$$LAUNCH\_YEAR_{st} = \frac{\Sigma_c\, N\_PATIENTS_{cst}\, INTRO\_YEAR_c}{\Sigma_c\, N\_PATIENTS_{cst}}$$

where

$N\_PATIENTS_{cst}$ = the number of patients with cancer at site s who were treated with chemotherapy agent c in year t

$INTRO\_YEAR_c$ = the year in which chemotherapy agent c was first launched

The drug vintage measure POST1985% will be constructed as follows:

$$POST1985\%_{st} = \frac{\Sigma_c\, N\_PATIENTS_{cst}\, INTRO\_YEAR\_GT\_1985_c}{\Sigma_c\, N\_PATIENTS_{cst}}$$

where

$INTRO\_YEAR\_GT\_1985_c$ = 1 if chemotherapy agent c was first launched after 1985

= 0 otherwise

POST1990% will be constructed in a similar fashion.

The only explanatory variable in eq. (2) (aside from the cancer-site fixed effects and year fixed effects) is chemotherapy vintage. Cancer mortality rates are also likely to depend on other cancer-site-specific, time-varying variables, and these might be correlated with drug vintage. In particular, mortality rates are likely to depend on (1) incidence rates, and (2) non-pharmaceutical innovation. Unfortunately, data on cancer incidence and non-pharmaceutical innovation, by cancer site, are not available for France during the period covered by our chemotherapy data.[16] However, in a recent paper based on U.S. cancer data during the period 1996-2006, Lichtenberg (2010) found that, although pharmaceutical innovation, non-pharmaceutical innovation, and incidence all had significant effects on cancer mortality rates, controlling for the latter two variables had virtually no effect on the pharmaceutical innovation coefficient.

B. Data and descriptive statistics

Pharmaceutical data. Data on the number of patients with cancer at site s who were treated with chemotherapy agent c in year t ($N\_PATIENTS_{cst}$) were obtained from IMS Health's Oncology Analyzer database.[17] IMS collected data on the frequency with which 11 chemotherapy agents were administered to a sample of about 20,000 French cancer patients during the period 2002-2006. As the following table shows, the size of the sample increased over time:

Year	Number of sample patients
2002	2713
2003	3195
2004	3767
2005	5063
2006	5217

The eleven drugs (ranked by frequency of use), and the years in which they were launched, are shown in the following table:

frequency rank	chemotherapy agent	world launch year
1	doxorubicin	1971
2	epirubicin	1984
3	gemcitabine	1995
4	carboplatin	1985
5	docetaxel	1995
6	paclitaxel	1992
7	vinorelbine	1989
8	imatinib	2001
9	capecitabine	1998
10	temozolomide	1999
11	pemetrexed	2004

[16] Data on non-pharmaceutical innovation are not available for any period. According to the European Cancer Observatory, annual data on cancer incidence, by site, are only available during the period 1983-1997 (http://eu-cancer.iarc.fr/16-table.html,en).
[17] If a patient was treated with n chemotherapy agents, that patient would be counted n times.

Table 4 shows the number of sample patients during 2002-2006, by cancer site. The two cancer sites with the largest number of patients were breast and lung. The three chemotherapy agents most frequently used to treat each of the five cancer sites with the largest numbers of patients are shown in Table 5.[18]

Mortality data. Data on age-adjusted[19] mortality rates, by cancer site, were obtained from the Centre d'épidémiologie sur les causes médicales de décès, Institut national de la santé et de la recherche médicale (http://www.cepidc.vesinet.inserm.fr/inserm/html/index2.htm).

The complete dataset used for estimation is shown in Appendix Table 3.

C. Empirical results

Estimates of chemotherapy vintage coefficients (β) from different versions of eq. (2) are shown in Table 6. The first three estimates are based on the full set of cancer sites. In model 1, the vintage measure is the (weighted) mean world launch year of chemotherapy treatments. The coefficient on LAUNCH_YEAR is negative and highly significant (p-value = .008). This indicates that cancer sites for which there were larger increases in chemotherapy vintage had larger reductions in the age-adjusted mortality rate. A 10-year increase in mean drug vintage is estimated to reduce the age-adjusted mortality rate by about 6%. Models 2 and 3 indicate that the change in the age-adjusted mortality rate was also inversely correlated with the other two measures of chemotherapy vintage (POST1985% and POST1990%). Model 2 implies that the mortality rate would be about 12% lower if only post-1985 drugs were used than it would be if only pre-1986 drugs were used.

As noted earlier, these are weighted least-squares estimates, where the weight is the mean of each cancer site's mortality rate during the entire sample period. As shown in Figure 3, the mortality rate for lung cancer is far higher than it is for other types of cancer. Therefore, the estimates of models 1-3 give a great deal of weight to the lung cancer data. Models 4-6 are estimates based on the full set of cancer sites except lung cancer. All three drug vintage coefficients remain negative and highly significant when lung cancer is excluded from the

[18] Only two drugs were used to treat Hodgkin's disease among sample patients.
[19] The age distribution of the French population in 2002 was used to obtain age-adjusted mortality rates.

sample. Excluding lung cancer increases the magnitude of β by about 25% in models 4 and 6, but reduces the magnitude of β by about 25% in model 5.

According to Eurostat,[20] the age-adjusted mortality rate from malignant neoplasms in France declined by 6% between 2002 and 2006. The parameter estimates can be used to estimate how much of this decline was attributable to the increase in drug vintage, i.e. to the use of newer chemotherapy agents. The decline in the age-adjusted mortality rate attributable to the 2002-2006 increase in drug vintage is $\beta * \Delta$, where $\Delta = (V_{2006} - V_{2002})$ and V_t = mean drug vintage in year t.

There are two different data sources from which we can calculate Δ. The first is the IMS Oncology Analyzer database. As noted above, this contains data on the use of 11 cancer drugs by about 4000 patients per year during the period 2002-2006. The second data source is the Groupement pour l 'Elaboration et la Réalisation de Statistiques (GERS, http://www.gie-gers.fr/index.php3). This source provides annual data on the use of all (106) cancer drugs by all cancer patients in France during the period 1998-2007.[21]

Table 7 shows a comparison of chemotherapy vintage measures derived from the IMS Oncology Analyzer and GERS databases.[22] The GERS estimates of the 2002-2006 increase in mean vintage are about three times as large as the IMS estimates. For example, the GERS data imply that mean LAUNCH_YEAR increased by 5.5 years, while the IMS data imply that it increased by only 1.8 years.

Estimates of the decline in the age-adjusted mortality rate attributable to the 2002-2006 increase in drug vintage based on both the IMS data and the GERS data are shown in the following table.

[20] Source: Eurostat hlth_cd_asdr dataset.
[21] GERS provides data on the quantity of each drug, by year, but not by cancer site.
[22] The GERS vintage measures are based on the year each drug was first commercialized in France, rather than the world launch year, which is not available for all drugs. For the 11 drugs for which both dates were available, there is generally a close correspondence between the two dates. For 8 out of the 11 drugs, the year of commercialization in France was 0-2 years after the world launch year.

Model	1	2	3
Vintage measure	LAUNCH_YEAR	POST1985%	POST1990%
β	-0.006	-0.122	-0.107
	IMS Oncology Analyzer database		
2002-2006 change in vintage measure (Δ)	1.8	7%	9%
β ∗ Δ	-0.011	-0.008	-0.010
	GERS database		
2002-2006 change in vintage measure (Δ)	5.5	23%	29%
β ∗ Δ	-0.034	-0.028	-0.031

The estimates of Δ derived from the IMS database imply that the increase in drug vintage reduced the age-adjusted cancer mortality rate by about 1% during 2002-2006, which is about 1/6 of the total decline in the mortality rate. The estimates of Δ derived from the GERS database imply that the increase in drug vintage reduced the age-adjusted cancer mortality rate by about 3% during 2002-2006, which is about half of the total decline in the mortality rate.

IV. Summary

Longevity increase is an important part of economic growth and development. In the long run, the rate of economic growth is determined by the rate of technological progress, which is generated by private and public R&D investment. Most technological progress is embodied in new goods. Therefore, the welfare of consumers (and the productivity of producers) depends on the *vintage* of the goods (or inputs) they purchase, especially when those goods are R&D-intensive. The pharmaceutical and medical devices industries are the most R&D-intensive industries in the economy

In this paper, I have investigated the contribution of pharmaceutical innovation to recent longevity growth in Germany and France. First, I examined the effect of the vintage of prescription drugs (and other variables) on the life expectancy and age-adjusted mortality rates of residents of Germany, using longitudinal, annual, state-level data during the period 2001-2007. Then, I examined the effect of the vintage of chemotherapy treatments on age-adjusted cancer mortality rates of residents of France, using longitudinal, annual, cancer-site-level data during the period 2002-2006.

The analysis of Germany was based on data on the utilization of over 600 active ingredients, which account for about 250 million prescriptions per year. I found that states with larger increases in drug vintage had larger increases in life expectancy, controlling for some other potentially important determinants of life expectancy (diagnostic imaging innovation, per capita *quantity* of drugs consumed, per capita income, the unemployment rate, the notifiable disease rate, the AIDS case rate, the number of physicians, pharmacists, and hospital beds). There was also a highly significant relationship across states between the increase in drug vintage and the decline in the age-adjusted mortality rate.

German life expectancy at birth increased by 1.4 years during the period 2001-2007. The estimates imply that about one-third of this increase was due to the replacement of older drugs by newer drugs. My estimate of the cost per life-year gained from the use of newer drugs is a small fraction of leading economists' estimates of the value of (willingness to pay for) an additional year of life. It is also consistent with estimates from clinical trials.

The analysis of France was based on data on the utilization of 11 cancer drugs by about 4000 cancer patients per year. I found that cancer sites for which there were larger increases in chemotherapy vintage had larger reductions in the age-adjusted mortality rate. A 10-year increase in mean drug vintage was estimated to reduce the age-adjusted mortality rate by about 6%. Changing the measure of drug vintage, and excluding lung cancer—by far the largest cause of cancer deaths in France—had little effect on the relationship between drug vintage and the cancer mortality rate. My estimates implied that chemotherapy innovation accounted for at least one-sixth of the decline in French cancer mortality rates during 2002-2006, and may have accounted for as much as half of the decline.

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Table 1

Top 25 drugs in sample, ranked by number of prescriptions during 2000-2008

Rank	Compound	Number of prescriptions during 2000-2008 (millions)	FDA approval year
1	DICLOFENAC	167.7	1993
2	METOPROLOL	108.0	1978
3	IBUPROFEN	93.8	1974
4	METFORMIN	65.3	1995
5	BISOPROLOL	62.8	1992
6	ENALAPRIL	58.8	1985
7	SIMVASTATIN	55.4	1991
8	FUROSEMIDE	50.8	1966
9	SALBUTAMOL	44.6	1981
10	RAMIPRIL	41.7	1991
11	CAPTOPRIL	40.6	1981
12	AMLODIPINE	40.0	2009
13	VERAPAMIL	36.4	1981
14	THEOPHYLLINE	35.0	1970
15	GLIBENCLAMIDE	32.5	1984
16	TORASEMIDE	32.1	1993
17	LISINOPRIL	29.0	1987
18	INSULIN HUMAN BASE/INSULIN HUMAN ISOPHANE	28.4	.
19	ISOSORBIDE DINITRATE	28.1	1968
20	HYDROCHLOROTHIAZIDE	27.3	1959
21	NIFEDIPINE	26.8	1981
22	HYDROCHLOROTHIAZIDE/TRIAMTERENE	24.4	1961.5
23	HYDROCHLOROTHIAZIDE/RAMIPRIL	24.1	1975
24	NITRENDIPINE	23.5	.
25	ISOSORBIDE MONONITRATE	22.9	1991

Table 2

Sample statistics by year

year	2001	2002	2003	2004	2005	2006	2007
Population (millions)	82	82	83	83	82	82	82
Total no. of prescriptions (millions)	241	251	265	235	241	245	250
No. of prescriptions per person	2.92	3.04	3.20	2.85	2.91	2.96	3.02
FDA_YEAR	1983.5	1983.9	1984.3	1984.7	1984.9	1985.3	1985.6
POST1990%	34.0%	35.4%	36.9%	39.0%	40.2%	42.0%	43.9%
POST1995%	9.7%	10.7%	12.0%	12.9%	11.9%	12.8%	13.5%
Life expectancy at birth	78.5	78.5	78.6	79.2	79.4	79.7	79.9
Age-adjusted mortality rate	857.4	858.3	861.1	811.1	801.0	775.8	766.0
number of CT scanners per 100,000 persons	1.25	1.33	1.38	1.43	1.50	1.55	1.59
Unemployment rate	7.6%	8.4%	9.7%	10.6%	11.0%	10.1%	8.6%
GDP per person (nominal)	€ 25,653	€ 25,978	€ 26,225	€ 26,801	€ 27,215	€ 28,224	€ 29,514
number of new AIDS cases per 100,000 persons	0.95	0.87	0.84	0.92	0.82	0.81	0.73
number of notifiable diseases per 100,000 persons	298.4	347.6	308.8	323.7	353.7	361.7	541.0
number of users of hard drugs who came to police notice for the first time per 100,000 persons	27.7	24.5	21.7	25.4	23.6	22.8	21.9
number of people injured or killed in road traffic accidents under the influence of alcohol per 100,000	41.8	41.1	38.9	35.8	34.5	32.7	32.3
number of hospital beds per 100,000 persons	902.0	887.8	874.4	857.6	846.4	829.0	823.4
number of physicians per 100,000 persons	330.3	333.3	336.7	339.0	341.2	345.5	350.5
number of pharmacists per 100,000 persons	57.8	58.6	58.1	58.0	58.3	59.2	60.2

Table 3

Estimates of models of life expectancy at birth and age-adjusted mortality rate, Germany, 2001-2007

	Dependent variable: Life expectancy at birth										
	Model 1				Model 2				Model 3		
Parm	Estimate	Z	ProbZ		Estimate	Z	ProbZ		Estimate	Z	ProbZ
FDA_YEAR	0.208	2.887	0.004								
POST1990%					7.212	3.479	0.001				
POST1995%									5.230	2.979	0.003
ln_CT_SCANNERS	0.161	1.479	0.139		0.076	0.802	0.422		0.174	1.474	0.140
ln_GDP	-0.929	-1.275	0.202		-1.236	-1.592	0.111		-0.770	-1.145	0.252
UNEMP	-1.489	-1.456	0.145		-0.878	-1.002	0.316		-1.879	-1.579	0.114
ln_NOTIF_DISEASES	-0.251	-2.442	0.015		-0.263	-2.525	0.012		-0.211	-2.289	0.022
ln_AIDS	-0.039	-1.537	0.124		-0.037	-1.401	0.161		-0.033	-1.367	0.172
ln_DRUNK	-0.196	-0.992	0.321		-0.060	-0.270	0.787		-0.240	-1.178	0.239
ln_HARD	0.097	1.718	0.086		0.097	1.805	0.071		0.091	1.521	0.128
ln_N_RX	0.163	0.349	0.727		0.042	0.088	0.930		0.180	0.379	0.705
ln_BEDS	0.009	0.012	0.990		0.603	0.744	0.457		0.108	0.142	0.887
ln_PHYSICIANS	-1.196	-1.831	0.067		-0.808	-1.133	0.257		-1.214	-2.118	0.034
ln_PHARMACISTS	-0.017	-0.036	0.972		-0.014	-0.029	0.977		-0.002	-0.005	0.996
	Dependent variable: Log of age-adjusted mortality rate										
	Model 4				Model 5				Model 6		
FDA_YEAR	-0.018	-2.988	0.003								
POST1990%					-0.565	-3.349	0.001				
POST1995%									-0.474	-4.533	0.000
ln_CT_SCANNERS	-0.021	-2.966	0.003		-0.014	-2.259	0.024		-0.022	-2.900	0.004
ln_GDP	0.023	0.369	0.712		0.043	0.654	0.513		0.012	0.223	0.824
UNEMP	-0.034	-0.388	0.698		-0.078	-0.975	0.330		-0.002	-0.025	0.980
ln_NOTIF_DISEASES	0.016	1.629	0.103		0.017	1.741	0.082		0.012	1.321	0.187
ln_AIDS	0.002	0.904	0.366		0.001	0.728	0.467		0.001	0.663	0.507
ln_DRUNK	-0.001	-0.067	0.947		-0.011	-0.637	0.524		0.002	0.139	0.890
ln_HARD	-0.012	-2.724	0.006		-0.012	-2.850	0.004		-0.011	-2.411	0.016
ln_N_RX	-0.046	-1.109	0.267		-0.039	-0.995	0.320		-0.046	-1.073	0.283
ln_BEDS	0.049	0.756	0.450		0.002	0.022	0.982		0.041	0.619	0.536
ln_PHYSICIANS	0.132	2.264	0.024		0.104	1.761	0.078		0.131	2.647	0.008
ln_PHARMACISTS	0.005	0.119	0.906		0.005	0.125	0.901		0.004	0.084	0.933

The estimates are weighted least-squares estimates, weighting by state population. All equations include fixed state effects and fixed year effects. Standard errors are clustered within states.

Table 4
Number of sample patients during 2002-2006, by cancer site

Cancer site	Number of sample patients, 2002-2006
BREAST	5027
LUNG	4270
NHL	2245
OVARIAN	1534
HODGKINS DISEASE	834
PANCREAS	819
CML	648
BRAIN	461
M.MYELOMA & MALIG PLASMA CELL	401
HEAD & NECK	379
COLORECTAL	332
BLADDER	277
PROSTATE	246
LIVER	243
STOMACH	152
CLL	146
CORPUS UTERI	94
OESOPHAGUS	77
ALL	59
MELANOMA	26
KIDNEY	20
OTHER LEUKAEMIAS	9
AML	4
THYROID	4
CERVIX UTERI	2
MYELOID LEUKAEMIA OTHER/UNSPEC	1
OTHER	1645

Source: IMS Oncology Analyzer

Table 5

Chemotherapy agents most frequently used to treat French cancer patients during 2002-2006, by cancer site

Chemotherapy agent	Rank
BREAST	
EPIRUBICIN	1
DOCETAXEL	2
DOXORUBICIN	3
LUNG	
VINORELBINE	1
GEMCITABINE	2
CARBOPLATIN	3
NHL	
DOXORUBICIN	1
EPIRUBICIN	2
TEMOZOLOMIDE	3
OVARIAN	
CARBOPLATIN	1
PACLITAXEL	2
GEMCITABINE	3
HODGKINS DISEASE	
DOXORUBICIN	1
VINORELBINE	2

Source: IMS Oncology Analyzer

Table 6

Estimates of models of age-adjusted cancer mortality rate, France, 2002-2006

Model	Regressor	Estimate	Stderr	LowerCL	UpperCL	Z	ProbZ
	All cancer sites						
1	Launch_Year	-0.006	0.002	-0.011	-0.002	-2.665	0.008
2	post1985%	-0.122	0.034	-0.187	-0.056	-3.618	0.000
3	post1990%	-0.107	0.029	-0.165	-0.049	-3.644	0.000
	Excluding lung cancer						
4	Launch_Year	-0.008	0.002	-0.011	-0.005	-5.035	0.000
5	post1985%	-0.094	0.028	-0.150	-0.039	-3.328	0.001
6	post1990%	-0.131	0.019	-0.168	-0.094	-6.936	0.000

The estimates are weighted least-squares estimates, weighting by the mean of each cancer site's mortality rate during the entire sample period ($(1 / T) \sum_t AAMORT_{st}$). All equations include fixed cancer-site effects and fixed year effects. Standard errors are clustered within cancer sites.

Table 7

Comparison of chemotherapy vintage measures derived from IMS Oncology Analyzer and GERS databases

year	N		LAUNCH_YEAR		POST1985%		POST1990%	
	IMS	GERS	IMS	GERS	IMS	GERS	IMS	GERS
1998		109,507,687		1978.3		30%		10%
1999		111,235,927		1978.9		32%		15%
2000		115,983,400		1979.6		35%		19%
2001		124,227,347		1980.7		38%		25%
2002	2713	138,344,711	1985.6	1982.1	47%	44%	37%	32%
2003	3195	150,057,851	1986.2	1984.0	50%	53%	39%	41%
2004	3767	156,556,767	1986.3	1985.7	49%	60%	43%	49%
2005	5063	157,138,449	1987.3	1986.8	53%	64%	46%	57%
2006	5217	167,624,451	1987.4	1987.6	53%	67%	46%	61%
2007		175,757,939		1988.1		69%		63%
2006 - 2002			1.8	5.5	7%	23%	9%	29%

Figure 1
% of prescriptions consumed during 2000-2008 that were for drugs approved after year t (t = 1940,...,2010)

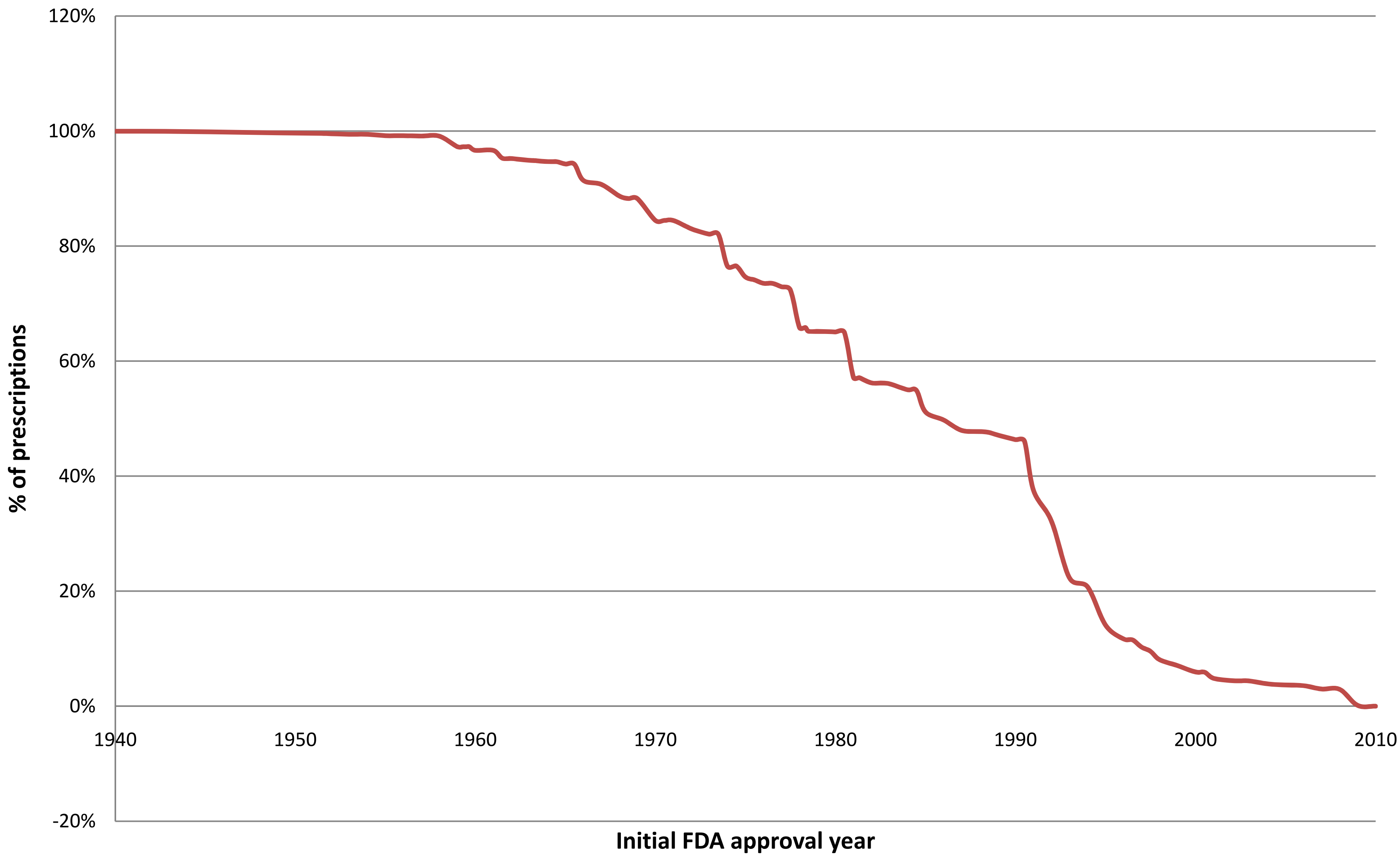


Figure 2
Life expectancy at birth, Germany, 2000-2007, selected states

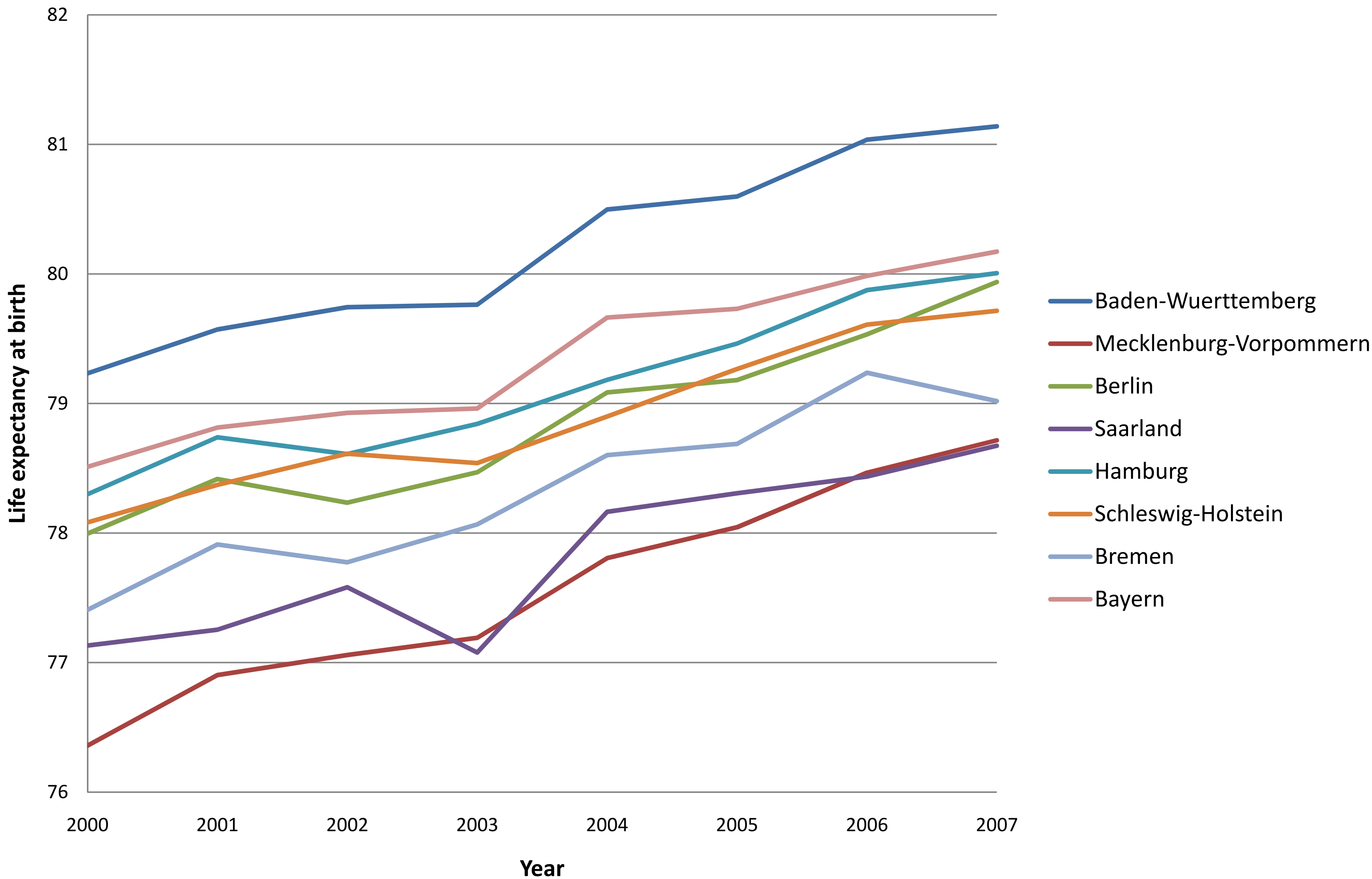
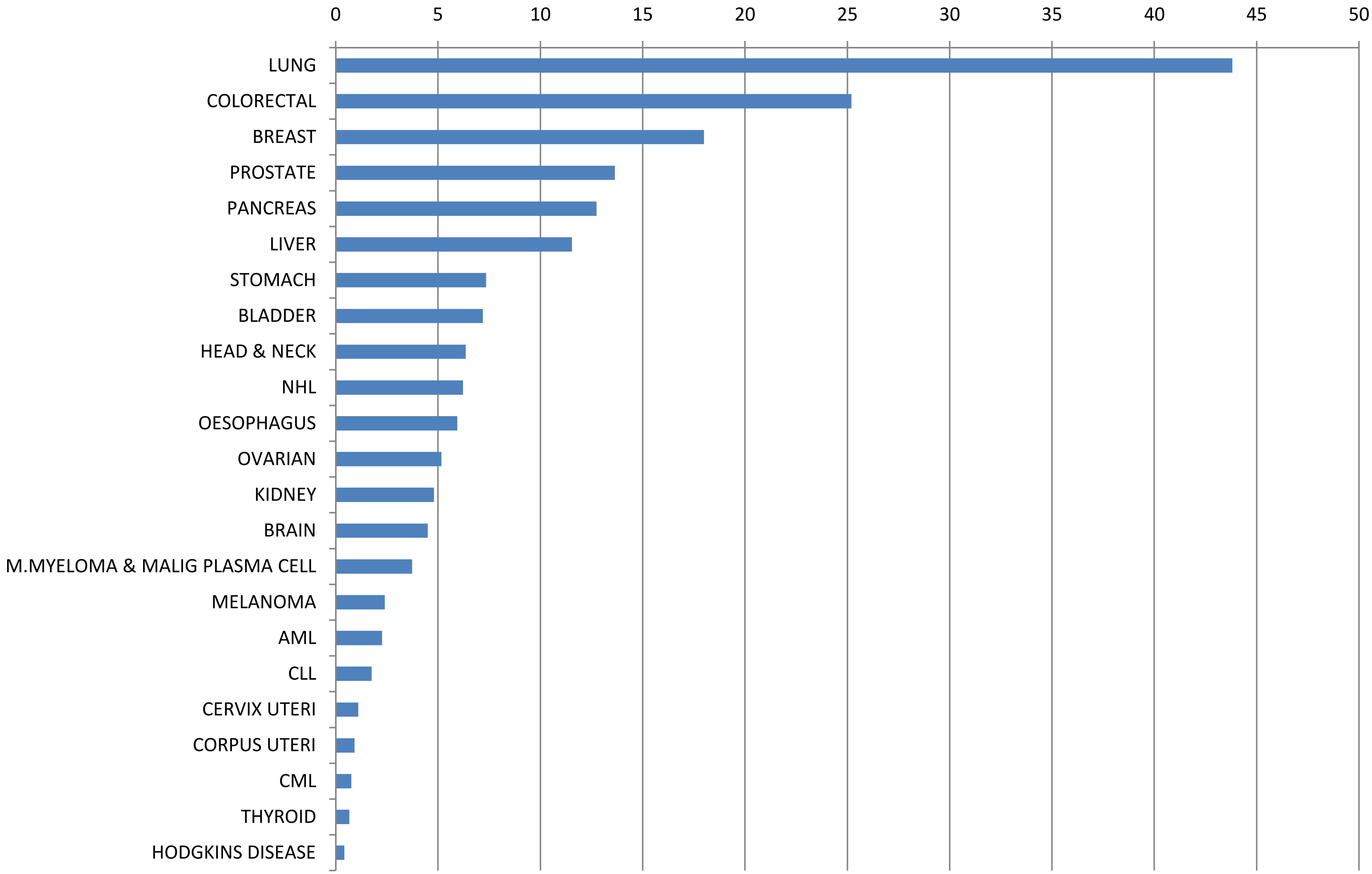


Figure 3

Number of deaths per 100,000 population, by cancer site, France, 2006



Appendix Table 1

Sample coverage of drugs in 2008

	Universe (Statutory Health Insurance)				Sample				Sample/Universe	
ATC-group name	Prescriptions (millions)	Sales (millions)	Average price		Prescriptions (millions)	Sales (millions)	Average price		Prescriptions (millions)	Sales (millions)
Overall market	608.1	26677	44		259	7748	30		43%	29%
A01 Stomalogical preparations	1.2	14	11							
A02 Ulcer therapeutics	25.3	1139	45							
A03 Spasmolytics	8.5	115	14							
A04 Antiemetics and agents for sickness	2.1	73	35		2	43	20		101%	59%
A05 Bilious and liver therapy	0.4	31	76							
A06 Laxatives	2.2	42	19							
A07 Antidiarrheals	4.4	187	42							
A09 Digestives, including enzymes	0.7	58	82							
A10 Antidiabetics	29.5	1691	57		30	1084	37		101%	64%
A11 Vitamins	3.2	76	24							
A12 Minerals	3.1	78	25							
A16 Enzyme substitute	0.1	183	1833							
B01 Antithrombotical agents	15.0	862	57							
B02 Antihemorrhagics	0.3	112	373							
B03 Antianemic combinations	3.6	372	103		1	233	269		24%	63%
B05 Blood substitute drugs and perfusion solutions	3.1	161	52							
C01 Cardiac therapeutics	11.7	279	24		12	132	11		104%	47%
C02 Antihypertensives	4.3	257	60		4	78	18		100%	30%
C03 Diuretics	20.7	399	19		21	151	7		102%	38%
C04 Peripheral vasodilators	1.6	62	39		2	25	14		108%	41%
C05 Vasoprotectives	1.5	30	20		0	1	19		3%	3%
C06 Antihypotonics	0.2	5	25		0	101	1498		34%	2016%
C07 Beta-receptor blocker	35.0	691	20		35	253	7		100%	37%
C08 Calcium antagonists	17.4	331	19		18	135	8		103%	41%
C09 Angiotensin inhibitor	46.2	1889	41		47	1109	24		101%	59%
C10 Antilipemics	16.9	736	44		17	433	25		101%	59%
D01 Antifungals (topical)	4.2	90	21							
D02 Agents for skin protection	0.8	9	11							
D03 Wound treatment agents	0.5	6	12							
D04 Antipruriginous agents	0.8	6	7							
D05 Antipsoriatics	0.8	70	87							
D06 Antiinfectives (dermatological)	2.5	49	20							
D07 Corticosteroids (dermatological)	9.1	163	18							
D08 Antiseptics and disinfective agents	0.8	7	9							

Appendix Table 1

Sample coverage of drugs in 2008

	Universe (Statutory Health Insurance)				Sample				Sample/Universe	
ATC-group name	Prescriptions (millions)	Sales (millions)	Average price		Prescriptions (millions)	Sales (millions)	Average price		Prescriptions (millions)	Sales (millions)
D09 Medical bandages	0.5	19	38							
D10 Anti-acne preparations	1.7	41	24							
D11 Other dermatological preparations	1.4	39	28							
G01 Gynaecological antiinfectivs	1.5	22	15							
G02 Other gynecologicals	0.4	15	38							
G03 Sexual hormones	12.8	424	33							
G04 Urological drugs	6.2	313	51							
H01 Pituitary/hypothalamic hormones	0.4	324	810							
H02 Corticosteroids (systemic)	7.9	155	20							
H03 Thyroids therapeutics	20.0	316	16							
H05 Calcium homoeostasis	0.1	58	583							
J01 Antibiotics	39.1	753	19							
J02 Antifungals	0.6	68	113							
J05 Antivirals	1.6	663	414							
J06 Immune sera and immunoglobulins	0.3	185	617							
J07 Vaccines	1.3	134	103							
L01 Antineoplastic agents	1.0	843	843		1	619	612		101%	73%
L02 Hormone antagonists	1.5	578	385		2	442	285		103%	77%
L03 Immunostimulants	1.2	1156	964		1	787	1163		56%	68%
L04 Immunosuppressants	2.1	1370	652		1	464	310		71%	34%
M01 Antiphlogistics/anti-inflammatory drugs	37.4	607	16		35	163	5		94%	27%
M02 Anti-inflammatory agens (topical)	1.3	16	12							
M03 Muscle relaxants	4.0	134	33							
M04 Gout agents	6.5	94	14							
M05 Osteoporosis agents	3.0	417	139							
N01 Anesthetics	0.3	8	26							
N02 Analgesics	33.9	1398	41							
N03 Antiepileptics	7.9	630	80							
N04 Anti parkinson drugs	5.7	499	87		5	330	64		91%	66%
N05 Psycholeptics	25.4	1103	43							
N06 Psychoanaleptics	20.7	1159	56							
N07 Anti vertiginous and addiction therapeutics	2.7	109	40		1	198	157		47%	182%

Appendix Table 1

Sample coverage of drugs in 2008

	Universe (Statutory Health Insurance)				Sample				Sample/Universe	
ATC-group name	Prescriptions (millions)	Sales (millions)	Average price		Prescriptions (millions)	Sales (millions)	Average price		Prescriptions (millions)	Sales (millions)
P01 Agents againt protozoa	0.7	14	20							
P02 Anthelmintics	0.3	8	25							
P03 Insecticides and repellents	0.7	14	20							
R01 Rhinologic drugs	11.1	85	8							
R02 Throat and pharynx therapeutics	0.6	4	7							
R03 Anti-asthma medication	24.3	1458	60		24	953	40		99%	65%
R04 Chest ointment and other inhalants	0.4	3	7							
R05 Cough and cold preparations	17.5	181	10							
R06 Antihistamines	3.1	73	23							
S01 Ophthalmic drugs	15.6	448	29							
S02 Otologicals	1.3	19	15							
S03 Ophthalmic drugs/otologicals	0.7	12	17							
V01 Allergenes	0.9	300	333							
V03 Antidotes/other agents	0.6	114	190		0	16	157		17%	14%
V10 Therapeutic radiopharmaceuticals	0.0	1								

Sales figures from the Statutory Health Insurance are at the level of public price (pharmacy selling price including VAT), whereas sales figures from IMS in the sample are at the level of ex-factory price. According to the VFA (http://www.vfa.de/en/statistics/pharmaceuticalmarket/), sales at ex-factory price level accounted for 58% of sales at public price level (23.8 bn. EUR of 41 bn. EUR) in the total pharmacy market (=SHI + private insurance + OTC). Therefore the sample covers approx. 50% of SHI pharmaceutical expenditures rather than the directly calculated 29% shown in the table. Also, SHI data are based on the ATC drug classification, while IMS data are based on the EphMRA classification, which may cause some drugs to be classified differently between “universe” and sample.

Pharmaceutical groups in the Statutory Health Insurance (prescriptions in millions, turnover in million €).
Classification: years, Germany, ATC-groups (2. level)
http://www.gbe-bund.de/
Home > Health Care System > Pharmaceutical Supply, Aids and Appliances/Non-medical Therapy > Pharmaceuticals > Table (ad hoc): Pharmaceutical by ATC-groups
Year: 2008

Appendix Table 2: Complete German Dataset

state	year	pop	life expectancy at birth	age-adjusted mortality rate	hard	beds	pharmacists	physicians	gdp	aids	notif	fda_year	post1990%	post1995%	unemp	units_pop	drunk	ct_scanners
Baden-Wurttemberg	2001	10,560,760	79.6	782.9	17.3	920.5	60.7	340.0	€ 29,300	0.36	284.1	1983.9	35.7%	9.9%	3.7%	2.52	43.8	1.07
Baden-Wurttemberg	2002	10,630,962	79.7	778.0	14.1	899.8	60.9	340.0	€ 29,400	0.23	257.9	1984.3	37.1%	11.1%	4.4%	2.58	42.1	1.12
Baden-Wurttemberg	2003	10,678,381	79.8	783.1	9.8	875.5	60.1	341.9	€ 29,500	0.19	229.8	1984.6	38.5%	12.7%	5.7%	2.71	40.5	1.18
Baden-Wurttemberg	2004	10,705,218	80.5	725.9	11.7	851.1	61.1	338.9	€ 29,900	0.27	230.3	1985.1	40.9%	13.7%	6.6%	2.44	39.6	1.28
Baden-Wurttemberg	2005	10,728,313	80.6	721.7	13.0	831.7	61.9	339.9	€ 30,100	0.26	252.4	1985.1	41.9%	12.2%	7.0%	2.48	37.8	1.32
Baden-Wurttemberg	2006	10,738,025	81.0	692.9	13.3	822.6	62.9	343.2	€ 31,700	0.17	279.9	1985.5	43.9%	13.3%	6.3%	2.52	35.2	1.37
Baden-Wurttemberg	2007	10,746,296	81.1	687.0	10.9	808.1	63.0	347.0	€ 33,300	0.15	402.8	1985.9	45.9%	14.3%	4.9%	2.60	33.8	1.40
Bavaria	2001	12,280,404	78.8	833.5	42.9	974.6	63.6	349.7	€ 30,100	0.42	234.4	1983.9	37.1%	10.2%	3.8%	2.59	43.5	1.15
Bavaria	2002	12,358,118	78.9	831.6	37.5	948.7	64.5	350.8	€ 30,700	0.37	255.0	1984.3	38.9%	11.4%	4.5%	2.63	44.4	1.29
Bavaria	2003	12,397,675	79.0	834.5	27.5	926.0	65.4	353.0	€ 30,800	0.30	234.9	1984.6	40.2%	12.3%	6.1%	2.77	40.8	1.37
Bavaria	2004	12,429,229	79.7	783.4	40.9	903.8	64.6	357.4	€ 31,600	0.43	244.1	1985.0	42.6%	13.1%	6.8%	2.46	37.7	1.45
Bavaria	2005	12,455,463	79.7	780.5	28.6	905.7	63.2	360.1	€ 32,100	0.32	292.5	1985.2	43.9%	12.1%	7.0%	2.52	34.3	1.46
Bavaria	2006	12,478,639	80.0	762.8	25.6	861.8	65.3	364.3	€ 33,100	0.27	295.2	1985.6	45.8%	13.0%	6.5%	2.57	31.9	1.53
Bavaria	2007	12,504,647	80.2	744.3	25.8	863.6	65.6	368.4	€ 34,700	0.23	427.3	1985.9	47.6%	13.7%	5.3%	2.61	32.4	1.58
Berlin	2001	3,385,149	78.4	855.2	28.5	677.9	74.9	458.7	€ 23,200	5.11	351.7	1983.3	32.4%	10.1%	15.1%	2.63	29.0	1.39
Berlin	2002	3,390,290	78.2	866.3	25.5	640.7	75.9	462.1	€ 23,200	5.10	417.0	1983.7	33.8%	11.1%	15.6%	2.79	29.3	1.53
Berlin	2003	3,391,515	78.5	857.4	27.5	627.8	74.7	468.4	€ 23,000	5.04	340.2	1984.0	35.2%	12.4%	18.0%	2.99	26.4	1.47
Berlin	2004	3,387,545	79.1	814.7	20.6	615.0	72.8	465.2	€ 22,900	5.79	392.2	1984.3	36.9%	13.0%	19.1%	2.65	24.5	1.51
Berlin	2005	3,391,783	79.2	802.1	21.0	610.4	71.3	439.2	€ 23,400	5.22	465.2	1984.5	38.2%	12.2%	19.2%	2.70	25.6	1.56
Berlin	2006	3,399,895	79.5	774.7	26.1	594.3	71.0	439.7	€ 24,100	5.50	425.3	1985.0	40.4%	13.4%	18.7%	2.77	23.4	1.59
Berlin	2007	3,407,625	79.9	752.6	24.6	586.5	72.2	442.2	€ 24,900	5.05	654.1	1985.5	43.2%	14.2%	16.3%	2.77	24.2	1.64
Brandenburg	2001	2,596,536	77.5	933.5	22.8	837.7	33.4	264.4	€ 17,700	0.27	372.5	1983.7	33.0%	10.2%	16.9%	3.29	52.8	1.12
Brandenburg	2002	2,586,435	77.6	934.1	15.9	839.5	34.3	268.5	€ 18,000	0.54	509.7	1984.2	34.9%	11.4%	16.9%	3.39	50.0	1.20
Brandenburg	2003	2,576,055	77.6	931.5	20.1	824.4	35.9	273.4	€ 18,200	0.43	465.5	1984.7	36.8%	12.8%	18.3%	3.69	44.0	1.24
Brandenburg	2004	2,569,205	78.2	875.5	23.5	820.2	36.6	282.4	€ 18,800	0.54	479.3	1985.2	39.0%	13.8%	19.2%	3.27	39.8	1.28
Brandenburg	2005	2,562,468	78.6	853.9	32.2	817.4	36.8	289.8	€ 19,100	0.23	541.2	1985.3	40.3%	12.6%	18.1%	3.38	38.7	1.44
Brandenburg	2006	2,552,747	78.8	837.9	39.3	810.6	38.2	294.2	€ 20,000	0.74	518.7	1985.6	42.0%	13.1%	16.5%	3.47	35.0	1.45
Brandenburg	2007	2,541,628	79.0	825.3	35.1	810.4	38.2	298.3	€ 21,000	0.90	879.5	1986.0	44.2%	13.5%	13.8%	3.53	35.8	1.53
Bremen	2001	660,327	77.9	849.4	40.6	931.5	71.2	443.4	€ 34,400	1.21	271.8	1982.9	31.8%	8.7%	8.7%	3.05	37.6	1.21
Bremen	2002	660,127	77.8	871.2	36.8	925.0	68.4	447.7	€ 35,300	1.51	429.5	1983.1	32.8%	9.1%	10.0%	3.13	42.9	1.36
Bremen	2003	662,701	78.1	863.3	36.2	901.8	67.6	449.4	€ 35,900	0.45	319.0	1983.2	33.4%	9.2%	11.4%	3.23	42.4	1.51

Appendix Table 2: Complete German Dataset

state	year	pop	life expectancy at birth	age-adjusted mortality rate	hard	beds	pharmacists	physicians	gdp	aids	notif	fda_year	post1990%	post1995%	unemp	units_pop	drunk	ct_scanners
Bremen	2004	662,831	78.6	820.8	41.2	899.8	68.3	451.1	€ 36,600	0.75	332.4	1983.4	34.9%	9.4%	14.6%	2.85	34.7	1.51
Bremen	2005	663,167	78.7	812.7	21.7	867.6	71.9	446.3	€ 37,400	0.60	316.2	1983.7	36.7%	9.1%	16.5%	2.93	36.0	1.51
Bremen	2006	664,275	79.2	777.4	22.7	861.5	69.3	456.8	€ 39,000	1.96	231.8	1984.1	38.4%	9.8%	14.4%	2.96	29.8	1.51
Bremen	2007	663,340	79.0	778.3	12.5	832.0	74.8	467.1	€ 40,400	1.06	444.6	1984.4	40.3%	10.5%	11.9%	3.05	30.5	1.51
Hamburg	2001	1,720,963	78.7	820.7	40.2	742.2	90.4	457.3	€ 44,400	4.13	360.0	1983.5	32.7%	9.6%	7.0%	2.72	36.9	1.57
Hamburg	2002	1,727,445	78.6	841.5	33.7	724.2	88.3	470.2	€ 44,900	4.05	466.2	1983.9	34.2%	11.1%	8.2%	2.81	35.9	1.62
Hamburg	2003	1,732,649	78.8	829.6	32.4	705.5	86.4	478.3	€ 45,000	4.44	357.9	1984.1	34.8%	11.6%	9.6%	2.85	33.8	1.62
Hamburg	2004	1,736,200	79.2	801.6	29.5	683.2	84.7	472.4	€ 45,600	4.55	369.7	1984.3	36.2%	11.9%	10.6%	2.54	36.6	1.56
Hamburg	2005	1,739,454	79.5	782.9	28.6	663.0	83.7	471.4	€ 46,700	3.56	385.3	1984.5	37.2%	11.3%	10.4%	2.52	32.3	1.55
Hamburg	2006	1,748,544	79.9	762.6	27.7	685.6	83.3	474.8	€ 47,600	3.03	509.7	1984.9	39.1%	12.3%	9.8%	2.54	25.9	1.72
Hamburg	2007	1,761,711	80.0	753.2	24.6	685.7	82.8	484.9	€ 49,000	2.72	705.4	1985.3	41.3%	13.3%	8.9%	2.55	24.5	1.70
Hesse	2001	6,072,862	79.0	825.1	21.2	964.1	67.7	336.3	€ 31,200	1.45	224.2	1983.1	33.2%	8.8%	5.5%	2.79	48.8	1.22
Hesse	2002	6,084,909	78.9	828.9	19.4	951.4	67.6	337.4	€ 31,400	1.28	242.0	1983.4	34.4%	9.5%	5.9%	2.86	49.5	1.33
Hesse	2003	6,090,518	78.9	835.8	16.0	936.6	69.3	340.5	€ 32,100	1.10	228.8	1983.8	36.0%	10.8%	7.1%	2.99	46.8	1.38
Hesse	2004	6,089,305	79.6	784.0	12.5	903.5	65.7	338.0	€ 32,700	1.23	224.1	1984.3	38.4%	11.9%	7.9%	2.69	45.8	1.41
Hesse	2005	6,094,315	79.9	762.8	14.1	900.5	64.3	338.1	€ 33,200	1.15	244.4	1984.6	40.1%	11.6%	8.4%	2.74	43.4	1.46
Hesse	2006	6,079,141	80.3	736.5	15.0	865.8	65.5	341.4	€ 34,300	1.00	243.7	1985.1	42.0%	12.6%	8.1%	2.78	45.3	1.51
Hesse	2007	6,072,514	80.3	740.2	14.6	863.3	72.8	344.6	€ 35,500	0.64	425.3	1985.5	44.3%	13.5%	7.3%	2.81	40.2	1.58
Lower Saxony	2001	7,939,556	78.4	860.5	21.3	849.9	57.3	285.8	€ 22,900	0.43	257.0	1983.1	32.3%	8.9%	6.4%	2.91	41.9	1.22
Lower Saxony	2002	7,969,603	78.4	860.7	22.0	836.5	57.6	289.1	€ 22,800	0.43	333.2	1983.5	33.7%	10.0%	7.2%	3.04	41.9	1.18
Lower Saxony	2003	7,987,118	78.3	868.9	19.7	822.7	57.0	295.1	€ 23,000	0.43	277.3	1983.9	35.3%	11.4%	8.5%	3.21	38.2	1.21
Lower Saxony	2004	7,997,717	79.0	815.2	15.0	799.2	55.9	295.6	€ 23,400	0.48	279.3	1984.3	37.3%	12.3%	9.5%	2.82	32.1	1.29
Lower Saxony	2005	7,999,777	79.2	807.7	11.6	774.2	57.5	298.9	€ 24,100	0.43	295.2	1984.5	38.6%	11.2%	10.4%	2.88	34.0	1.36
Lower Saxony	2006	7,989,008	79.5	784.2	10.0	756.9	57.6	303.6	€ 25,000	0.41	311.4	1984.8	40.4%	12.1%	9.7%	2.94	31.9	1.49
Lower Saxony	2007	7,979,442	79.7	771.6	10.3	745.9	58.5	309.0	€ 26,000	0.45	434.3	1985.2	42.4%	12.9%	7.9%	3.03	32.3	1.54
Mecklenburg Western Pomerania	2001	1,767,798	76.9	958.8	26.2	1237.4	39.4	308.5	€ 17,300	0.45	456.7	1983.8	33.7%	10.6%	18.5%	3.74	73.1	1.47
Mecklenburg Western Pomerania	2002	1,752,023	77.1	947.5	14.4	1233.4	39.9	312.8	€ 17,600	0.40	739.0	1984.3	35.5%	11.7%	19.1%	3.89	71.9	1.43
Mecklenburg Western Pomerania	2003	1,737,829	77.2	947.2	6.8	1235.7	40.6	317.6	€ 17,900	0.52	621.9	1985.0	38.0%	13.7%	20.2%	4.19	57.9	1.55

Appendix Table 2: Complete German Dataset

state	year	pop	life expectancy at birth	age-adjusted mortality rate	hard	beds	pharmacists	physicians	gdp	aids	notif	fda_year	post1990%	post1995%	unemp	units_pop	drunk	ct_scanners
Mecklenburg Western Pomerania	2004	1,725,660	77.8	895.9	11.4	1226.9	41.0	327.0	€ 18,400	0.46	681.2	1985.5	40.3%	14.8%	22.1%	3.69	55.6	1.68
Mecklenburg Western Pomerania	2005	1,712,857	78.0	882.1	16.0	1219.1	41.8	331.8	€ 18,700	0.41	664.0	1985.7	41.5%	13.6%	21.3%	3.83	46.9	1.69
Mecklenburg Western Pomerania	2006	1,700,243	78.5	851.5	9.4	1216.8	43.0	338.7	€ 19,400	0.24	707.9	1986.1	43.4%	14.6%	19.2%	3.94	49.0	1.76
Mecklenburg Western Pomerania	2007	1,686,682	78.7	843.5	6.6	1236.4	43.6	341.0	€ 20,700	0.18	981.6	1986.4	45.4%	14.8%	17.4%	3.98	47.6	1.66
North Rhine-Westphalia	2001	18,027,009	78.2	877.1	24.8	866.8	57.3	324.9	€ 25,600	1.20	242.7	1983.4	33.5%	9.6%	6.0%	3.03	30.4	1.29
North Rhine-Westphalia	2002	18,062,938	78.2	880.9	19.2	858.0	58.9	329.8	€ 25,900	1.13	243.4	1983.7	34.7%	10.4%	7.2%	3.12	28.7	1.43
North Rhine-Westphalia	2003	18,075,088	78.2	883.6	16.9	849.5	56.9	331.0	€ 26,100	1.15	232.4	1984.1	35.9%	11.3%	8.8%	3.27	28.8	1.43
North Rhine-Westphalia	2004	18,072,637	78.8	840.3	16.5	834.8	57.9	335.0	€ 26,700	1.00	254.6	1984.5	37.7%	12.0%	9.5%	2.90	25.4	1.47
North Rhine-Westphalia	2005	18,062,870	78.9	828.7	16.5	817.7	58.5	340.0	€ 27,100	1.01	290.9	1984.6	38.9%	11.2%	10.4%	2.97	24.3	1.51
North Rhine-Westphalia	2006	18,041,173	79.4	799.7	16.3	805.4	59.1	345.0	€ 27,900	0.98	311.8	1984.9	40.3%	11.7%	9.8%	2.99	24.3	1.57
North Rhine-Westphalia	2007	18,011,957	79.4	791.4	19.4	799.1	59.1	350.1	€ 29,200	0.92	493.6	1985.3	42.0%	12.4%	8.3%	3.07	24.4	1.60
Rhineland-Palatinate	2001	4,041,175	78.4	867.5	52.4	872.7	60.7	303.1	€ 22,500	0.74	279.7	1983.7	35.3%	9.7%	5.0%	3.03	48.1	1.16
Rhineland-Palatinate	2002	4,051,568	78.5	865.3	55.0	863.5	61.6	308.4	€ 23,000	0.47	345.8	1984.0	36.3%	10.4%	5.6%	3.16	47.1	1.23
Rhineland-Palatinate	2003	4,056,737	78.4	879.7	52.7	844.8	59.3	311.8	€ 23,200	0.35	369.6	1984.2	37.4%	11.4%	6.3%	3.32	49.9	1.31
Rhineland-Palatinate	2004	4,058,894	79.2	819.3	81.1	842.0	60.2	316.4	€ 23,800	0.15	386.6	1984.7	39.3%	12.4%	7.0%	2.94	44.4	1.21
Rhineland-Palatinate	2005	4,059,308	79.2	818.6	63.8	830.6	61.0	321.9	€ 23,900	0.39	388.5	1984.9	40.6%	11.7%	8.7%	3.02	42.1	1.26
Rhineland-Palatinate	2006	4,054,417	79.7	786.9	60.6	831.7	63.6	324.7	€ 24,800	0.44	362.4	1985.3	42.4%	12.8%	8.0%	3.06	38.6	1.36
Rhineland-Palatinate	2007	4,049,459	79.8	774.7	57.5	829.9	63.9	331.1	€ 25,900	0.22	632.6	1985.7	44.5%	13.9%	6.0%	3.14	37.5	1.41
Saarland	2001	1,067,254	77.3	946.2	36.9	1020.7	69.7	357.9	€ 23,600	0.19	230.8	1983.6	34.3%	9.2%	5.9%	2.76	55.7	1.59
Saarland	2002	1,065,390	77.6	937.4	36.6	1011.2	69.7	356.7	€ 23,700	0.38	342.4	1984.0	35.8%	10.4%	7.6%	3.69	55.6	1.78

Appendix Table 2: Complete German Dataset

state	year	pop	life expectancy at birth	age-adjusted mortality rate	hard	beds	pharmacists	physicians	gdp	aids	notif	fda_year	post1990%	post1995%	unemp	units_pop	drunk	ct_scanners
Saarland	2003	1,063,071	77.1	960.9	23.8	1002.7	70.6	366.4	€ 23,900	0.19	281.3	1984.3	37.3%	11.7%	8.3%	3.87	59.6	1.88
Saarland	2004	1,058,853	78.2	886.3	39.6	989.3	74.1	369.9	€ 25,200		291.0	1984.8	39.4%	12.6%	8.7%	3.40	55.5	2.17
Saarland	2005	1,053,000	78.3	886.3	42.1	981.0	75.2	374.6	€ 26,500		335.9	1984.9	40.6%	11.8%	10.8%	3.49	56.4	2.28
Saarland	2006	1,046,775	78.4	867.4	47.6	986.4	65.1	376.4	€ 27,600		300.0	1985.3	42.3%	12.9%	9.5%	3.51	53.5	2.29
Saarland	2007	1,039,965	78.7	852.5	48.6	944.8	72.4	384.0	€ 29,200		475.4	1985.7	44.5%	13.8%	7.3%	3.52	47.8	2.50
Saxony	2001	4,404,708	78.4	860.3	8.6	871.0	33.5	289.7	€ 17,700	0.11	540.8	1983.8	32.9%	10.0%	17.0%	3.67	42.1	1.45
Saxony	2002	4,365,780	78.4	865.9	6.7	872.4	34.1	295.1	€ 18,600	0.14	733.9	1984.4	35.2%	11.6%	17.8%	3.80	41.6	1.56
Saxony	2003	4,334,200	78.4	868.4	6.4	878.4	33.5	299.8	€ 19,200	0.05	645.4	1985.0	37.2%	13.2%	17.8%	4.04	37.1	1.59
Saxony	2004	4,307,838	79.1	812.4	15.2	867.5	33.3	304.3	€ 19,900	0.05	698.9	1985.4	39.3%	14.3%	19.4%	3.61	33.5	1.69
Saxony	2005	4,283,915	79.3	801.3	17.8	851.6	32.9	310.3	€ 20,000	0.28	745.3	1985.7	40.9%	13.7%	18.7%	3.71	31.7	1.77
Saxony	2006	4,261,623	79.7	773.0	19.4	840.2	32.7	315.2	€ 20,900	0.16	716.0	1986.2	42.8%	15.0%	16.6%	3.81	31.8	1.76
Saxony	2007	4,234,377	79.7	772.0	11.6	834.9	33.3	322.5	€ 22,000	0.24	974.7	1986.6	45.0%	15.8%	14.4%	3.81	31.5	1.84
Saxony Anhalt	2001	2,598,379	77.0	965.7	14.0	827.4	38.0	291.4	€ 16,900	0.23	561.9	1983.4	31.9%	10.0%	19.9%	3.83	47.3	1.50
Saxony Anhalt	2002	2,564,828	76.9	972.3	24.3	830.3	39.9	291.1	€ 17,800	0.08	680.5	1983.8	33.5%	11.1%	19.2%	3.98	47.3	1.52
Saxony Anhalt	2003	2,535,413	77.3	945.8	34.6	828.2	40.3	297.4	€ 18,200	0.32	554.6	1984.3	35.6%	13.0%	19.9%	4.30	41.1	1.62
Saxony Anhalt	2004	2,509,790	77.7	907.8	34.9	832.2	37.9	306.5	€ 18,800	0.32	500.2	1984.8	37.5%	14.4%	22.4%	3.83	39.5	1.63
Saxony Anhalt	2005	2,482,447	77.9	894.9	31.9	833.5	41.1	308.4	€ 19,000	0.20	574.8	1985.0	38.5%	13.3%	20.3%	3.95	43.1	1.85
Saxony Anhalt	2006	2,455,784	78.3	870.9	33.0	830.5	44.0	310.1	€ 20,100	0.33	540.2	1985.4	40.2%	14.3%	17.8%	4.03	35.9	1.91
Saxony Anhalt	2007	2,427,602	78.5	862.7	25.6	832.7	46.7	317.4	€ 21,300	0.12	813.1	1985.7	42.2%	15.0%	15.7%	4.14	38.1	1.98
Schleswig-Holstein	2001	2,795,915	78.4	857.1	47.2	1007.4	65.5	331.0	€ 23,800	0.89	265.6	1983.4	34.2%	9.5%	6.4%	2.77	49.6	0.97
Schleswig-Holstein	2002	2,810,106	78.6	848.2	36.6	985.0	64.3	334.1	€ 23,300	0.78	295.8	1983.7	35.2%	10.3%	7.6%	2.83	46.1	1.00
Schleswig-Holstein	2003	2,818,804	78.5	860.1	36.0	979.0	64.1	335.5	€ 23,500	1.10	267.0	1984.1	36.6%	11.4%	8.6%	2.97	47.8	0.99
Schleswig-Holstein	2004	2,825,970	78.9	824.8	26.9	972.3	64.3	339.2	€ 23,900	1.10	248.4	1984.4	38.3%	12.3%	9.7%	2.64	43.5	1.03
Schleswig-Holstein	2005	2,830,112	79.3	799.9	32.0	975.2	65.0	339.2	€ 24,000	0.95	262.5	1984.6	39.6%	11.4%	10.2%	2.70	44.3	1.77
Schleswig-Holstein	2006	2,832,595	79.6	784.2	28.9	946.7	65.9	346.2	€ 24,700	0.95	266.0	1985.0	41.4%	12.4%	9.0%	2.74	37.9	1.13
Schleswig-Holstein	2007	2,835,267	79.7	774.5	24.1	936.5	66.0	349.3	€ 25,400	0.63	378.3	1985.5	43.5%	13.0%	7.9%	2.82	40.2	1.16
Thuringia	2001	2,420,982	77.7	926.1	29.2	983.4	32.7	293.1	€ 17,200		490.5	1983.7	32.6%	9.6%	13.9%	3.20	48.0	1.73
Thuringia	2002	2,401,787	77.8	927.1	30.1	972.5	34.8	295.8	€ 17,700	0.08	662.9	1984.3	34.7%	11.2%	15.1%	3.84	45.3	1.71
Thuringia	2003	2,382,422	77.8	926.3	37.4	970.7	34.8	300.4	€ 18,200	0.04	541.1	1984.9	36.9%	12.9%	16.3%	4.11	42.1	1.80
Thuringia	2004	2,364,382	78.3	872.1	57.8	971.9	36.0	306.5	€ 18,900		661.0	1985.4	38.9%	14.1%	16.3%	3.65	38.7	1.78
Thuringia	2005	2,345,095	78.7	859.7	76.1	970.8	38.7	315.3	€ 19,100	0.04	612.3	1985.7	40.3%	13.4%	17.1%	3.79	38.4	1.83

Appendix Table 2: Complete German Dataset

state	year	pop	life expectancy at birth	age-adjusted mortality rate	hard	beds	pharmacists	physicians	gdp	aids	notif	fda_year	post1990%	post1995%	unemp	units_pop	drunk	ct_scanners
Thuringia	2006	2,322,926	78.8	840.0	59.3	954.6	40.9	322.0	€ 20,100	0.13	677.8	1986.1	42.1%	14.6%	15.6%	3.91	36.2	1.98
Thuringia	2007	2,300,130	79.1	827.0	62.1	957.1	41.8	329.9	€ 21,200		872.6	1986.4	44.1%	15.0%	13.7%	3.92	39.1	2.04

Appendix Table 3
French cancer data

Cancer site	Year	Age-adjusted mortality rate (per 100,000 pop)	Number of patients in IMS sample	Weighted mean world launch year	post1985 %	post1990 %
ALL	2002	0.45	7	1975.3	14%	14%
ALL	2003	0.43	3	2001.0	100%	100%
ALL	2004	0.39	14	1998.9	93%	93%
ALL	2005	0.34	16	1987.9	56%	56%
ALL	2006	0.40	19	1986.8	53%	53%
AML	2003	2.32	1	2001.0	100%	100%
AML	2005	2.40	2	2001.0	100%	100%
AML	2006	2.27	1	2001.0	100%	100%
BLADDER	2002	7.17	32	1993.4	84%	84%
BLADDER	2003	7.53	40	1991.2	63%	63%
BLADDER	2004	7.41	59	1993.1	80%	80%
BLADDER	2005	7.46	71	1992.0	70%	70%
BLADDER	2006	7.19	75	1991.5	65%	65%
BRAIN	2002	4.74	37	1998.8	97%	97%
BRAIN	2003	4.82	46	1997.5	89%	89%
BRAIN	2004	4.58	80	1996.9	85%	85%
BRAIN	2005	4.52	148	1997.1	86%	86%
BRAIN	2006	4.50	150	1997.0	86%	86%
BREAST	2002	19.03	664	1986.2	36%	27%
BREAST	2003	18.68	792	1986.2	37%	28%
BREAST	2004	18.50	926	1986.5	35%	30%
BREAST	2005	18.31	1300	1987.5	42%	38%
BREAST	2006	17.99	1345	1987.8	43%	39%
CERVIX UTERI	2005	1.18	1	1984.0	0%	0%
CERVIX UTERI	2006	1.10	1	1984.0	0%	0%
CLL	2002	1.83	31	1971.0	0%	0%
CLL	2003	1.90	28	1972.1	4%	4%
CLL	2004	1.79	23	1971.0	0%	0%
CLL	2005	1.71	28	1971.0	0%	0%
CLL	2006	1.75	36	1971.0	0%	0%
CML	2002	0.93	89	2001.0	100%	100%
CML	2003	0.95	112	2001.0	100%	100%
CML	2004	0.89	126	2001.0	100%	100%
CML	2005	0.92	163	2001.0	100%	100%
CML	2006	0.76	158	2001.0	100%	100%
COLORECTAL	2002	27.03	22	1998.0	100%	100%
COLORECTAL	2003	27.16	45	1998.0	100%	100%
COLORECTAL	2004	26.68	53	1998.2	100%	100%
COLORECTAL	2005	26.33	108	1998.0	100%	100%
COLORECTAL	2006	25.20	104	1998.1	100%	100%
CORPUS UTERI	2002	0.89	16	1988.5	50%	50%
CORPUS UTERI	2003	0.99	11	1989.5	64%	64%
CORPUS UTERI	2004	0.90	20	1988.2	45%	45%
CORPUS UTERI	2005	1.02	25	1988.6	52%	52%
CORPUS UTERI	2006	0.93	22	1988.5	50%	50%
HEAD & NECK	2002	7.67	49	1987.7	35%	33%

Appendix Table 3
French cancer data

Cancer site	Year	Age-adjusted mortality rate (per 100,000 pop)	Number of patients in IMS sample	Weighted mean world launch year	post1985 %	post1990 %
HEAD & NECK	2003	7.35	62	1987.2	32%	31%
HEAD & NECK	2004	6.95	55	1986.7	22%	18%
HEAD & NECK	2005	6.72	105	1988.7	42%	39%
HEAD & NECK	2006	6.35	108	1988.8	43%	40%
HODGKINS DISEASE	2002	0.46	88	1971.4	2%	0%
HODGKINS DISEASE	2003	0.46	132	1971.4	2%	0%
HODGKINS DISEASE	2004	0.48	201	1971.5	3%	0%
HODGKINS DISEASE	2005	0.44	208	1971.5	3%	0%
HODGKINS DISEASE	2006	0.43	205	1971.9	5%	0%
KIDNEY	2003	5.17	3	1971.0	0%	0%
KIDNEY	2004	4.91	5	1971.0	0%	0%
KIDNEY	2005	4.94	6	1971.0	0%	0%
KIDNEY	2006	4.80	6	1971.0	0%	0%
LIVER	2002	11.63	38	1993.1	92%	92%
LIVER	2003	11.66	47	1993.3	91%	91%
LIVER	2004	11.48	42	1995.3	100%	100%
LIVER	2005	11.65	55	1989.4	71%	71%
LIVER	2006	11.55	61	1990.1	75%	75%
LUNG	2002	41.89	533	1990.6	80%	47%
LUNG	2003	42.98	724	1990.8	79%	48%
LUNG	2004	43.22	739	1991.4	83%	57%
LUNG	2005	44.09	1080	1991.6	78%	56%
LUNG	2006	43.81	1194	1991.5	77%	54%
M.MYELOMA & MALIG PLAS	2002	3.92	85	1971.0	0%	0%
M.MYELOMA & MALIG PLAS	2003	4.07	69	1971.0	0%	0%
M.MYELOMA & MALIG PLAS	2004	3.73	79	1971.0	0%	0%
M.MYELOMA & MALIG PLAS	2005	3.79	83	1971.0	0%	0%
M.MYELOMA & MALIG PLAS	2006	3.73	85	1971.3	1%	1%
MELANOMA	2002	2.32	3	1999.0	100%	100%
MELANOMA	2003	2.36	2	1999.0	100%	100%
MELANOMA	2004	2.32	3	1996.7	100%	100%
MELANOMA	2005	2.41	10	1996.6	100%	90%
MELANOMA	2006	2.41	8	1995.1	100%	88%
NHL	2002	7.19	303	1971.9	0%	0%
NHL	2003	6.81	361	1971.6	1%	1%
NHL	2004	6.65	455	1971.7	0%	0%
NHL	2005	6.56	553	1972.2	2%	2%
NHL	2006	6.22	573	1972.3	3%	2%
OESOPHAGUS	2002	6.99	10	1987.9	50%	10%
OESOPHAGUS	2003	6.59	7	1986.1	29%	0%
OESOPHAGUS	2004	6.23	11	1986.3	18%	9%
OESOPHAGUS	2005	6.22	23	1989.5	61%	39%
OESOPHAGUS	2006	5.94	26	1989.9	62%	42%
OVARIAN	2002	5.53	226	1988.5	48%	48%
OVARIAN	2003	5.35	231	1988.5	48%	48%
OVARIAN	2004	5.23	313	1988.5	50%	50%

Appendix Table 3
French cancer data

Cancer site	Year	Age-adjusted mortality rate (per 100,000 pop)	Number of patients in IMS sample	Weighted mean world launch year	post1985 %	post1990 %
OVARIAN	2005	5.27	398	1988.4	47%	47%
OVARIAN	2006	5.17	366	1988.4	47%	47%
PANCREAS	2002	12.44	106	1995.0	99%	99%
PANCREAS	2003	12.25	130	1995.0	100%	100%
PANCREAS	2004	12.52	180	1994.9	99%	99%
PANCREAS	2005	12.76	200	1995.0	99%	99%
PANCREAS	2006	12.74	203	1994.9	99%	99%
PROSTATE	2002	15.53	23	1994.7	100%	96%
PROSTATE	2003	15.64	36	1993.2	100%	69%
PROSTATE	2004	14.87	58	1993.9	100%	81%
PROSTATE	2005	14.46	60	1994.8	100%	97%
PROSTATE	2006	13.64	69	1994.8	100%	97%
STOMACH	2002	8.57	19	1986.5	21%	21%
STOMACH	2003	8.04	12	1990.1	42%	42%
STOMACH	2004	8.03	18	1993.4	72%	72%
STOMACH	2005	7.69	52	1994.2	75%	75%
STOMACH	2006	7.35	51	1993.2	69%	69%
THYROID	2005	0.62	2	1993.5	100%	100%
THYROID	2006	0.67	2	1993.5	100%	100%