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CESIFO WORKING PAPER NO. 3894
CATEGORY 3: SOCIAL PROTECTION
JULY 2012

CESifo *Working Paper No. 3894*

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Abstract

We use longitudinal, disease-level data to analyze the impact of pharmaceutical innovation on longevity and medical expenditure in Sweden, where mean age at death increased by 1.88 years during the period 1997-2010. Pharmaceutical innovation is estimated to have increased mean age at death by 0.60 years during the period. The estimates indicate that longevity depends on the number of drugs to treat a disease, not the number of drug classes. Pharmaceutical innovation also reduced hospital utilization in Sweden, so the cost per life-year gained from the introduction of new drugs was quite low.

JEL-Code: I120, J110, L650, O330.

Keywords: longevity, pharmaceutical, innovation, drugs, Sweden.

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This research was supported by SNS – Centre for Business and Policy Studies, which placed no restrictions or limitations on data, methods, or conclusions, and had no right of review or control over the outcome of the research.

1. Introduction

Longevity increase is increasingly recognized by economists to be an important part of economic growth and development.[1] Economists have also come to recognize that, in the long run, the rate of economic "growth…is driven by technological change that arises from intentional [research and development (R&D)] investment decisions made by profit-maximizing agents" (Romer (1990)) and by public organizations such as the National Institutes of Health. In principle, technological change could be either disembodied or embodied in new goods. Solow (1960) hypothesized that most technological change is embodied: to benefit from technological progress, one must use newer, or later vintage, goods and services. Bresnahan and Gordon (1996) argued that "new goods are at the heart of economic progress," and Hercowitz (1998, p. 223) also reached the "conclusion…that 'embodiment' is the main transmission mechanism of technological progress to economic growth."

In this paper, we will analyze the impact of pharmaceutical innovation on longevity and medical expenditure in Sweden during the period 1997-2010. According to the National Science Foundation, the pharmaceutical and medical devices industries are the most research intensive industries in the economy. Moreover, new drugs often build on upstream government research (Sampat and Lichtenberg (2011)).

The analysis will be performed using aggregate data, as opposed to patient-level data. Grunfeld and Griliches (1960, p. 1) showed that "aggregation of economic variables can, and in fact frequently does, reduce…specification errors. Hence, aggregation does not only produce an aggregation error, but may also produce an aggregation gain." In particular, patient-level data are surely more subject to selection effects (the sickest patients might get the newest—or oldest—treatments) than aggregate data.

We will use longitudinal, disease-level data to estimate difference-in-differences models of the effect of pharmaceutical innovation on longevity. In essence, we will investigate whether the diseases that experienced more pharmaceutical innovation had larger increases in longevity. Our models will include year and disease fixed effects, so they will control for the overall increase in Swedish longevity and for stable between-disease differences in mortality.

Pharmaceutical innovation can be measured in several different ways, because active substances are divided into different groups according to the organ or system on which they act

[1] See e.g. Nordhaus (2002) and Murphy and Topel (2005).

and their therapeutic, pharmacological and chemical properties. In the Anatomical Therapeutic Chemical (ATC) classification system developed by the World Health Organization Collaborating Centre for Drug Statistics Methodology, drugs are classified in groups at five different levels. The highest (1st) level is the "anatomical main group" level; there are 14 anatomical main groups. The 2nd, 3rd, 4th, and 5th levels are "therapeutic subgroup," "pharmacological subgroup," "chemical subgroup," and "chemical substance," respectively.[2] We will investigate the effects of both new chemical substances and new chemical subgroups on longevity.

Pharmaceutical innovation is likely to have affected medical expenditure as well as longevity. New drugs are generally more expensive than old drugs, so pharmaceutical innovation is likely to have increased pharmaceutical expenditure. We will investigate whether there were larger increases in expenditure on classes of drugs that experienced more pharmaceutical innovation. Previous research has shown that pharmaceutical innovation may also have on impact on other types of medical expenditure, especially expenditure on hospitals and nursing homes. We will investigate whether the diseases that experienced more pharmaceutical innovation had larger declines in hospital utilization. By combining our estimates of the effect of pharmaceutical innovation on longevity, pharmaceutical expenditure, and hospital utilization, we can obtain an estimate of the incremental cost-effectiveness (cost per life-year gained) of pharmaceutical innovation in Sweden during the period 2000-2009.

We will pool data from several rich data sources. Longitudinal disease-level measures of pharmaceutical innovation will be constructed from Läkemedelsverket (Sweden's Medical Products Agency)[3] and from Thériaque.[4] Longitudinal disease-level data on mortality will be obtained from the WHO Mortality Database.[5] Longitudinal disease-level data on hospital

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[2] The complete classification of metformin illustrates the structure of the code:

A	Alimentary tract and metabolism (1st level, anatomical main group)
A10	Drugs used in diabetes (2nd level, therapeutic subgroup)
A10B	Blood glucose lowering drugs, excl. insulins (3rd level, pharmacological subgroup)
A10BA	Biguanides (4th level, chemical subgroup)
A10BA02	Metformin (5th level, chemical substance)

http://www.whocc.no/atc/structure_and_principles/

[3] http://www.lakemedelsverket.se/Sok-efter-lakemedel-och-mediciner-i-Lakemedelsfakta/

[4] Thériaque (http://www.theriaque.org/) is a database of official, regulatory and bibliographic information on all drugs available in France, intended for health professionals. Funding is provided by the Centre National Hospitalier d'Information sur le Médicament.

[5] http://www.who.int/healthinfo/morttables/en/

utilization will be obtained from Eurostat.[6] Longitudinal data on pharmaceutical expenditure and innovation, by drug class, will be obtained from the IMS Health MIDAS database.[7] Some additional data will be obtained from the OECD Health database.

In the next section we develop a model of the impact of pharmaceutical innovation on longevity. Descriptive statistics and estimates of age-at-death models are presented in section 3. The effects of pharmaceutical innovation on hospital utilization and prescription drug expenditure are examined in sections 4 and 5, respectively. The cost-effectiveness of pharmaceutical innovation in Sweden is assessed in section 6. The final section contains a summary and conclusions.

2. Model of the impact of pharmaceutical innovation on longevity

To investigate the impact of pharmaceutical innovation on longevity in Sweden, we will estimate models of the following form:[8]

$$LONGEVITY_{it} = \beta\, Rx\_MEASURE_{it} + \alpha_i + \delta_t + \varepsilon_{it} \qquad (1)$$

$$(i = 1,\ldots, I;\ t = 1997,\ldots,2010)$$

where

$LONGEVITY_{it}$ = a measure of longevity associated with disease i in year t

$Rx\_MEASURE_{it}$ = a measure related to pharmaceutical innovation associated with disease i in year t

α_i = a fixed effect for disease i

δ_t = a fixed effect for year t

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[6] http://epp.eurostat.ec.europa.eu/portal/page/portal/statistics/search_database

[7] IMS describes MIDAS as "a unique data platform for assessing worldwide healthcare markets. It integrates IMS national audits into a globally consistent view of the pharmaceutical market, tracking virtually every product in hundreds of therapeutic classes and providing estimated product volumes, trends and market share through retail and non-retail channels. MIDAS data is updated monthly and retains 12 years of history." IMS Institute for Healthcare Informatics (2011), *The Global Use of Medicines: Outlook Through 2015*, May. http://www.imshealth.com/deployedfiles/ims/Global/Content/Insights/IMS%20Institute%20for%20Healthcare%20Informatics/Global_Use_of_Medicines_Report.pdf

[8] The research design is similar to that used in two studies Lichtenberg (2005, 2009) has done with U.S. data.

ε_{it} = a disturbance

A positive and significant estimate of β in eq. (1) would signify that diseases for which there was more pharmaceutical innovation had larger increases in longevity. Now we will discuss how we will define and measure $LONGEVITY_{it}$ and $Rx\_MEASURE_{it}$, and why we do so.

Measurement of longevity. Life expectancy at birth is probably the most commonly cited measure of longevity. However, this is not the measure of life expectancy we will use. The main reason is that life expectancy at birth (or at higher ages) cannot be measured for specific diseases. A more minor "disadvantage" of this indicator is that it is "hypothetical," rather than "actual": it is based on the period life table, which describes what *would* happen to a hypothetical (or synthetic) cohort if it experienced throughout its entire life the mortality conditions of a particular time period.[9]

The measures of longevity we will use will be based on the age distribution of deaths caused by a disease in a given year. These measures can easily be calculated from data contained in the WHO Mortality Database, which provides data on the number of deaths, by cause, age group, country, and year. The most informative measure is mean age at death.[10] A second measure is the fraction of deaths that occur above a given age, e.g. age 75.[11]

There is a potential pitfall in analyzing the relationship between pharmaceutical innovation related to a disease and the age distribution of deaths from the disease. Suppose that the introduction of a new drug for a disease reduces the number of people who die from the disease; people who would have died from the disease, absent the new drug, die from other diseases instead. Our estimates will not capture between-disease spillover effects. In principle, such between-disease spillover effects could be substantial. However, they appear to be quite modest in practice. Figure 1 shows that if the number of deaths, by cause, in 1997 had prevailed during the entire 1997-2010 period, mean age at death would have increased by almost exactly the same amount as it actually increased. Virtually all of the increase in mean age at death was

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[9] See http://www.cdc.gov/nchs/data/nvsr/nvsr58/nvsr58_21.pdf, p. 1.

[10] Government agencies such as the Australian Institute of Health and Welfare (http://www.aihw.gov.au/national-grim-books/), Statistics Canada (http://www.cbc.ca/news/canada/story/2008/01/14/death-stats.html), and the Arizona Department of Health Services (http://www.azdhs.gov/plan/report/ahs/ahs2010/pdf/2d1.pdf) publish data on mean age at death.

[11] Because mortality data are mostly grouped into 5-year age cells, mean age at death is subject to greater measurement error than the fraction of deaths that occur above a certain age.

due to within-disease increases; almost none was due to a shift in the distribution of causes of death.

Measurement of pharmaceutical innovation. We hypothesize that the health and longevity of a population depends on how technologically advanced the medical goods (including drugs) and services they use are. Furthermore, how technologically advanced a medical good or service is depends on its *vintage*, defined as its year of invention or first use.[12] Many drugs are first launched in the United States, so the vintage of a drug can often be approximated by its initial FDA approval year. For example, atorvastatin might be considered a 1997-vintage drug, because it was first approved by the FDA in 1997.

Therefore, the measure of pharmaceutical innovation we would prefer to use would be based on the (weighted) mean vintage of drugs used to treat a disease. For example, if 20,000 people with a given disease in 2012 were treated with a 1990-vintage drug, and 10,000 people with the same disease in 2012 were treated with a 2005-vintage drug, the weighted mean vintage of drugs used to treat the disease in 2012 would be 2000.

Unfortunately, data on the number of people treated in Sweden by drug, disease, and year are not available, so it is not possible to calculate the weighted mean vintage of drugs, by disease and year. Although we have annual data (from the IMS MIDAS database) on the quantity of each drug sold in Sweden during the period 1999-2010, many drugs may be used to treat multiple diseases, we don't know which diseases these drugs were used to treat, and there is no reasonable way to allocate or assign drugs with multiple indications to specific diseases.[13]

The measure of pharmaceutical innovation we will use instead will be based on the *number* of drugs (chemical substances) previously introduced to treat a condition.[14] We will refer to this as the *stock* of drugs for a condition. The stock of drugs will be computed as follows:

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[12] According to the Merriam Webster dictionary, one definition of vintage is "a period of origin or manufacture (e.g. a piano of 1845 vintage)". http://www.merriam-webster.com/dictionary/vintage. Robert Solow (1960) introduced the concept of vintage into economic analysis. Solow's basic idea was that technical progress is "built into" machines and other goods and that this must be taken into account when making empirical measurements of their roles in production. This was one of the contributions to the theory of economic growth that the Royal Swedish Academy of Sciences cited when it awarded Solow the 1987 Alfred Nobel Memorial Prize in Economic Sciences.

[13] Some datasets on pharmaceutical utilization include information about the diseases the drugs were used to treat. For example, the U.S. Medical Expenditure Panel Survey Prescribed Medicines Files include diagnosis codes, and the IMS Oncology Analyzer database includes diagnosis codes for cancer drugs.

[14] Other measures of pharmaceutical innovation we will consider are the number of *chemical subgroups* (as defined by the World Health Organization Collaborating Centre for Drug Statistics Methodology) previously introduced to treat a condition, and the number of *pharmacological subgroups* previously introduced to treat a condition.

$$N\_CHEM\_SUBSTANCES_{it} = \sum_d IND_{di}\, APP_{dt}$$

where

IND_{di} = 1 if drug d is used to treat (indicated for) disease i

= 0 if drug d is not used to treat (indicated for) disease i

APP_{dt} = 1 if drug d has been commercialized by the beginning of year t

= 0 if drug d has not been commercialized by the beginning of year t

Lichtenberg (2012) showed that, in the case of France, when the number of drugs that can be used to treat a disease increases, the weighted mean vintage of drugs used to treat the disease increases several years later (due to gradual diffusion of new drugs).

The specific versions of eq. (1) we will estimate are:

$$AGE\_DEATH_{it} = \beta\, N\_CHEM\_SUBSTANCES_{i,t-k} + \alpha_i + \delta_t + \varepsilon_{it} \quad (2)$$

$$AGE\_GT75_{it} = \beta\, N\_CHEM\_SUBSTANCES_{i,t-k} + \alpha_i + \delta_t + \varepsilon_{it} \quad (3)$$

$$(i = 1,\ldots, I;\ t = 2000,\ldots,2008)$$

where

AGE_DEATH_{it} = mean age at death from disease i in year t

AGE_GT75_{it} = the fraction of deaths from disease i in year t that occurred after age 75

In his model of endogenous technological change, Romer (1990) hypothesized an aggregate production function such that an economy's output depends on the "stock of ideas" that have previously been developed, as well as on the economy's endowments of labor and capital. Eqs. (2) and (3) may be considered health production functions, in which age at death is an indicator of health output or outcomes, and the cumulative number of drugs approved is analogous to the stock of ideas.

Age at death from a disease may depend on the number of chemical (or pharmacological) *subgroups* that have previously been developed to treat the disease rather than, or in addition to, the number of chemical *substances* (drugs) that have previously been developed to treat the disease. We will investigate this by estimating models like the following:

$$AGE\_DEATH_{it} = \beta\, N\_CHEM\_SUBGROUPS_{i,t-k} + \alpha_i + \delta_t + \varepsilon_{it} \quad (4)$$

where

$N\_CHEM\_SUBGROUPS_{it} = \sum_g IND_{gi} APP_{gt}$

IND_{gi} = 1 if any drugs in chemical subgroup g are used to treat (indicated for) disease i

= 0 if no drugs in chemical subgroup g are used to treat (indicated for) disease i

APP_{gt} = 1 if any drugs in chemical subgroup g had been commercialized by the beginning of year t

= 0 if no drugs in chemical subgroup g had been commercialized by the beginning of year t

Pharmaceutical innovation is not the only type of medical innovation that is likely to contribute to longevity growth. Other medical innovation, such as innovation in diagnostic imaging, surgical procedures, and medical devices, is also likely to affect longevity growth. Therefore, measures of these other types of medical innovation should be included in the longevity model (eq. (1)).[15] Unfortunately, longitudinal disease-level measures of non-pharmaceutical medical innovation are not available for Sweden. However, longitudinal disease-level measures of non-pharmaceutical and pharmaceutical medical innovation are available for the U.S. during the period 1997-2007. Lichtenberg (2012) showed that, in the U.S., the rate of pharmaceutical innovation is not positively correlated with the rate of medical procedure innovation and may be *negatively* correlated with the rate of diagnostic imaging innovation. This suggests that failure to control for other medical innovation is very unlikely to result in overestimation of the effect of pharmaceutical innovation on longevity growth, and may even result in underestimation of this effect.

In section 3 we will report estimates of eq. (2):

$$AGE\_DEATH_{it} = \beta\ N\_CHEM\_SUBSTANCES_{i,t-k} + \alpha_i + \delta_t + \varepsilon_{it} \qquad (5)$$

$$= \beta \sum_d IND_{di}\ APP_{d,t-k} + \alpha_i + \delta_t + \varepsilon_{it}$$

[15] However, the number of people exposed to pharmaceutical innovation tends to be much larger than the number of people exposed to other types of medical innovation. In 2007, 62% of Americans consumed prescription drugs, while only 8% of Americans were admitted to hospitals. (Source: Medical Expenditure Panel Survey, 2007 Full Year Consolidated Data File.)

Data on $APP_{d,t-k}$ were obtained from Läkemedelsverket (Sweden's Medical Products Agency). Data on IND_{di} were obtained from Theriaque. In that database, drug indications are coded using the International Classification of Diseases, Tenth Revision (ICD-10; http://www.who.int/classifications/icd/en/). Sweden began using the ICD-10 system to classify its mortality data in 1997.[16] The most recent year for which mortality data are available for Sweden in the WHO Mortality Database is 2010. Our longevity analysis will therefore cover the period 1997-2010. The ICD-10 contains 12,131 distinct disease codes. These are grouped into 263 "blocks," such as "A00-A09 Intestinal infectious diseases," and "C30-C39 Malignant neoplasms of respiratory and intrathoracic organs."[17] We will perform the analysis using data at the ICD-10 block level.

3. Descriptive statistics and estimates of age-at-death models

Descriptive statistics. Summary statistics on longevity and pharmaceutical innovation in Sweden are shown in Table 1. The average annual number of deaths during 1997-2010 was about 77 thousand. Mean age at death increased by 1.88 years, from 78.40 to 80.28 years, and the fraction of deaths that occurred at an age greater than 75 increased from 69.0% to 72.4%. As of the end of 1990, 191 pharmacological subgroups, 399 chemical subgroups, and 673 chemical substances had been commercialized in Sweden. By the end of 2010, the number of pharmacological subgroups, chemical subgroups, and chemical substances had increased by 32%, 52%, and 128%, respectively. The average annual number of chemical substances commercialized was 43.

To illustrate the nature of the disease-specific data on pharmaceutical innovation, Table 2 lists in chronological order the chemical substances and chemical subgroups with an indication for a particular disease, melanoma and other malignant neoplasms of skin (ICD-10 codes C43-C44). According to the Läkemedelsverket and Theriaque databases, there are currently 19 substances indicated for this disease; nine of these have been commercialized since 1998. These substances fall into 14 chemical subgroups; three of these subgroups have been established (commercialized) since 1998.

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[16] Sweden used the ICD-9 classification from 1987 to 1996. The U.S. Centers for Medicare & Medicaid Services has produced Diagnosis Code Set General Equivalence Mappings for translating ICD-10 codes to ICD-9 codes, and vice versa, but in many cases there is not a one-to-one correspondence between ICD-10 and ICD-9 codes. See http://www.cms.gov/Medicare/Coding/ICD10/2012-ICD-10-CM-and-GEMs.html.

[17] See http://en.wikipedia.org/wiki/ICD-10 and http://apps.who.int/classifications/apps/icd/ClassificationDownload/DLArea/icd102010enMeta.zip.

Figure 2 illustrates the heterogeneity of diseases with respect to their rates of pharmaceutical innovation. In 1997, there were seven diseases for which the number of chemical substances previously commercialized in Sweden was between 31 and 34. For two of these diseases, six or fewer new chemical substances were commercialized during the period 1997-2011. For two others, at least fourteen new chemical substances were commercialized during that period.

Appendix Table 1 shows data on mortality and the number of chemical substances that had been commercialized in 1997 and 2010 for each of the 123 diseases (ICD-10 Blocks) in our sample.

Estimates of age-at-death models. Now we will present estimates of age-at-death models (eqs. (2)-(4) and similar models). All models will be estimated by weighted least squares, weighting by N_DEATHS_{it}, the number of deaths from disease i in year t. This is appropriate because, due to the inclusion of fixed disease effects, we are in essence analyzing within-disease *changes* in age at death, and as shown in Figure 3, the variance of these changes is much larger for diseases causing few deaths than it is for diseases causing many deaths. Also, disturbances will be clustered within diseases.

Estimates of key parameters from 36 different age-at death models are shown in Table 3. Estimates that are significantly different from zero (p-value < 0.05) are shown in bold. In models 1-18, the dependent variable is AGE_DEATH_{it}. In model 1, the regressor is $N\_CHEM\_SUBSTANCES_{i,t}$, the number of chemical substances indicated for disease i that had been commercialized by the end of year t. The coefficient is not statistically significant. In models 2 and 3, the regressors are $N\_CHEM\_SUBSTANCES_{i,t-k}$, where k = 1 and 2, respectively. The coefficients in these models are also insignificant, indicating that mean age at death is not related to the number of substances that had been commercialized up to 2 years before. However, the coefficient on $N\_CHEM\_SUBSTANCES_{i,t-3}$ in model 4 is positive and significant (p-value = 0.0354), indicating that mean age at death *is* related to the number of substances that had been commercialized up to 3 years before. The variable that is most strongly related to AGE_DEATH_{it} (its coefficient has the highest Z value) is $N\_CHEM\_SUBSTANCES_{i,t-6}$ (model 7). Since a new substance generally won't be widely used until a few years after it is commercialized, it is not surprising that the coefficients in models 4-11 are significant, but that the coefficients in models 1-3 aren't significant.

Models 12-18 are similar to models 1-7, but the regressors are the number of chemical *subgroups*, rather than the number of chemical *substances*, that had been commercialized by the end of year t, t-1,…,t-6, respectively. None of the parameters in models 12-18 are significant. Mean age at death is positively related to the number of substances that had been commercialized up to 3 years before, but not to the number of chemical subgroups commercialized.

In the remaining models (models 19-36) in Table 3, the dependent variable is the fraction of deaths that occurred at an age greater than 75. This variable is measured much more precisely than mean age at death, but it is more difficult to interpret. Models 19-29 are analogous to models 1-11. The regressors are the number of chemical *substances* that had been commercialized by the end of year t, t-1,…,t-10, respectively. The parameters in all 11 equations are positive and highly significant (p-value $\leq$ .0263). The coefficient in model 24 has the highest Z value; the number of chemical substances that had been commercialized by the end of year t-5 has the most significant effect on the fraction of deaths that occurred at an age greater than 75.

Models 30-36 are analogous to models 12-18; they examine the effect of the number of chemical subgroups that had been commercialized by the end of year t, t-1,…,t-6, respectively, on the fraction of deaths that occurred at an age greater than 75. None of the parameters in models 12-18 are significant: the change in the fraction of deaths at an age greater than 75 is unrelated to the growth in the number of subgroups.

Overall, the estimates in Table 3 provide support for the hypothesis that an increase in the number of substances that have been commercialized and that may be used to treat a disease causes a rightward shift of the age distribution of deaths from the disease several years later. Now we will estimate the magnitude of the increase in mean age at death that was attributable to growth in the number of substances commercialized. We do this by comparing the estimates of the year fixed effects (δ_t's) in the following two versions of eq. (5):

$$AGE\_DEATH_{it} = \alpha_i + \delta_t + \varepsilon_{it} \quad (6)$$

$$AGE\_DEATH_{it} = \beta\ N\_CHEM\_SUBSTANCES_{i,t-6} + \alpha_i + \delta_t + \varepsilon_{it} \quad (7)$$

Since eq. (6) does not control for the (contemporaneous or lagged) number of chemical substances (β is constrained to equal zero), the year fixed effects in this equation measure the unconditional mean age at death in each year (almost identical to the values reported in Table 1).

Eq. (7) controls for ("holds constant") the number of chemical substances commercialized up to six years earlier, so the year fixed effects in this equation measure the (counterfactual) mean age at death in each year, conditional on no pharmaceutical innovation.

The results of this calculation are shown in Figure 4. As noted above, from 1997 to 2010, mean age at death increased by 1.88 years, from 78.40 to 80.28 years. The estimates of the year fixed effects of eq. (7) indicate that, holding constant the number of chemical substances commercialized up to six years earlier, mean age at death would have increased by 1.29 years, from 78.40 to 79.69 years. We therefore estimate that pharmaceutical innovation increased mean age at death in Sweden by 0.60 years (7.15 months) during the period 1997-2010, and that it accounted for almost 1/3 (31.6%) of the overall increase in mean age at death. It accounted for twice as large a fraction (63%) of the increase in the fraction of deaths that occurred at an age greater than 75.

4. The effect of pharmaceutical innovation on hospital utilization

Now we will examine the effect of pharmaceutical innovation on hospital utilization. Annual data on the number of inpatient hospital days, hospital discharges, and average length of stay (ALOS), by diagnosis during the period 2000-2009, were obtained from Eurostat.[18] Data on the number of hospital days and discharges and average length of stay, for all causes of diseases (ICD-10 codes A00-Z99) excluding external causes of morbidity and mortality (V00-Y98) and liveborn infants (Z38), are shown in Table 4.

Eurostat hospital data, like WHO mortality data, are classified by ICD-10, but the hospital classification is somewhat different from the ICD-10 block classification shown in Appendix Table 1. Appendix Table 2 shows data on the number of hospital discharges, days, and average length of stay, in 2009, by diagnosis as defined in the Eurostat classification.

We estimated relationships between hospital utilization and pharmaceutical innovation, such as the following:

$$\ln(DAYS_{it}) = \beta \ln(N\_CHEM\_SUBSTANCES_{i,t-k}) + \alpha_i + \delta_t + \varepsilon_{it} \quad (8)$$

$$\ln(DAYS_{it}) = \beta \ln(N\_CHEM\_SUBGROUPS_{i,t-k}) + \alpha_i + \delta_t + \varepsilon_{it} \quad (9)$$

[18] The data were obtained from the following Eurostat tables posted at http://epp.eurostat.ec.europa.eu/portal/page/portal/statistics/search_database: hlth_co_disch1, hlth_co_hosday, and hlth_co_inpst.

where

$DAYS_{it}$ = the number of hospital days for disease i in year t (t = 2000,…,2009)

These equations were estimated by weighted least squares, weighting by the total number of hospital days for disease i during the entire period ($DAYS_{i.} = (1/10)\ \Sigma_t\ DAYS_{it}$). We also estimated similar equations in which the dependent variable was $\ln(DISCHARGES_{it})$, where $DISCHARGES_{it}$ = the number of discharges for disease i in year t; in these equations, the weight used was the total number of discharges for disease i during the entire period ($DISCHARGES_{i.}$).

Estimates of the hospital utilization equations are shown in Table 5. Disturbances are clustered within diseases in all models. In models 37-53, the dependent variable is $\ln(DAYS_{it})$. In models 37-47, the regressor is $\ln(N\_CHEM\_SUBSTANCES_{i,t-k})$ for k = 0, 1,…, 10, respectively. The coefficients in the first four models are insignificant, but the coefficients in models 41-47 are negative and significant. This indicates that an increase in the number of drugs commercialized for a disease reduces the number of hospital days due to the disease 4-10 years later. The estimated elasticity when k=8 (when the Z value is largest) is -0.302: a 10% increase in the number of drugs for a disease reduces the number of hospital days due to the disease by 3.0% 8 years later.

In models 48-53, the regressor is $\ln(N\_CHEM\_SUBGROUPS_{i,t-k})$ for k = 0, 1,…, 5, respectively. None of the coefficients are statistically significant. The number of hospital days is inversely related to the lagged number of drugs commercialized, but not the number of chemical subgroups.

Models 54-70 examine the effect of pharmaceutical innovation on the number of discharges. The coefficients in models 54-60 are insignificant, but the coefficients in models 61-63 are negative and significant. This indicates that an increase in the number of drugs commercialized for a disease reduces the number of hospital discharges due to the disease 7-9 years later. The magnitudes of the coefficients in models 61-63 are almost as large as the magnitudes of the coefficients in models 44-46, indicating that most (about 80%) of the reduction in hospital days attributable to pharmaceutical innovation is due to a reduction in the number of discharges, rather than a reduction in length of stay.

Now we will estimate the magnitude of the reduction in hospital days that was attributable to growth in the number of substances commercialized. We do this by comparing the estimates of the year fixed effects (δ_t's) in the following two versions of eq. (8):

$$\ln(DAYS_{it}) = \alpha_i + \delta_t + \varepsilon_{it} \quad (10)$$

$$\ln(DAYS_{it}) = \beta \ln(N\_CHEM\_SUBSTANCES_{i,t-8}) + \alpha_i + \delta_t + \varepsilon_{it} \quad (11)$$

Since eq. (10) does not control for the (contemporaneous or lagged) number of chemical substances (β is constrained to equal zero), the year fixed effects in this equation measure the unconditional log changes in the number of hospital days (almost identical to the values reported in Table 4). Eq. (11) controls for ("holds constant") the number of chemical substances commercialized up to eight years earlier, so the year fixed effects in this equation measure the (counterfactual) log changes in the number of hospital days, conditional on no pharmaceutical innovation.

The results of this calculation are shown in Figure 5. As noted above, from 2000 to 2009, the number of hospital days declined about 6%, from 10.1 million to 9.6 million days. The estimates of the year fixed effects of eq. (11) indicate that, holding constant the number of chemical substances commercialized up to eight years earlier, the number of hospital days would have *increased* by 6.6 percent, from 10.1 million to 10.8 million days. We therefore estimate that if no new drugs had been commercialized during the period 1992-2001, the number of hospital days would have been about 12% higher in 2009.[19]

5. The effect of pharmaceutical innovation on prescription drug expenditure

Now we will assess the impact of pharmaceutical innovation—the expansion of the number of chemical substances—on pharmaceutical expenditure using longitudinal data on about 300 classes of drugs. We have annual data on both the ex-manufacturer value (expressed in US dollars) and quantity (number of "standard units"[20]) of all pharmaceutical products sold to

[19] An alternative way of calculating the effect of no pharmaceutical innovation during 1992-2001 on hospital days in 2009 yields a somewhat larger estimate: 15.8%. At the aggregate level, $\ln(DAYS_t) = \beta \ln(N\_CHEM\_SUBSTANCES_{t-8}) \rightarrow \Delta\ln(DAYS_t) = \beta \Delta\ln(N\_CHEM\_SUBSTANCES_{t-8}) \rightarrow \Delta \ln(DAYS_t) = \ln(N\_CHEM\_SUBSTANCES_{1992}/ N\_CHEM\_SUBSTANCES_{2001}) = -.302 * \ln(723/1175) = .147$. $e^{.147} - 1 = 15.8\%$.

[20] The number of standard 'dose' units sold is determined by taking the number of counting units sold divided by the standard unit factor which is the smallest common dose of a product form as defined by IMS HEALTH. For

pharmacies and hospitals during the period 1999-2010. Each product is assigned to one 3-digit EphMRA Anatomical Therapy Class (ATC3).

We also know the active ingredient(s) ("molecules") contained in each product. The "molecules" identified in the IMS MIDAS database for Sweden do not coincide exactly with "chemical substances" identified in the Läkemedelsverket database. Table 6 provides a comparison of the number of molecules in the IMS MIDAS database for Sweden with the number of chemical substances in the Läkemedelsverket database by the end of each of the years 1999-2010. The number of molecules in the IMS database grew more slowly (38% vs. 43%) during this period.

These data allow us to calculate the following variables:

$MANU\_VALUE_{ct}$ = the ex-manufacturer value (expressed in US dollars) of products in ATC3 sold during year t

$N\_MOLECULE_{ct}$ = the number of molecules in ATC3 at the end of year t

$= \sum_m IN\_CLASS_{mc}\ ON\_MARKET_{mt}$

where

IN_CLASS_{mc} = 1 if any product in ATC class 3 sold during 2000-2010 contains molecule m

= 0 if no product in ATC class 3 sold during 2000-2010 contains molecule m

ON_MARKET_{mt} = 1 if any product containing molecule m is sold by the end of year t

= 0 if no product containing molecule m is sold by the end of year t

By estimating the following model involving these variables, we can assess the impact of the expansion of the number of molecules on pharmaceutical expenditure:

$$\ln(MANU\_VALUE_{ct}) = \beta \ln(N\_MOLECULE_{c,t-k}) + \alpha_c + \delta_t + \varepsilon_{ct} \qquad (12)$$

$$(c=1,\ldots, 303;\ t = 2004,\ldots,2010;\ k = 0,\ldots,5)$$

Eq. (12) was estimated by weighted least squares, weighting by the ex-manufacturer value of the drug class during the entire 2004-2010 period ($MANU\_VALUE_{c.} = (1/6)\ \Sigma_t$

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example, for oral solid forms the standard unit factor is one tablet or capsule whereas for syrup forms the standard unit factor is one teaspoon (5 ml) and injectable forms it is one ampoule or vial. Standard units should be used when the packs or products being compared are different in form.

$MANU\_VALUE_{ct}$). Estimates of eq. (12) are shown in Table 7. The estimates of models 71-76 indicate that the relationship between the growth in expenditure and the growth in the number of molecules 0-5 years earlier is statistically significant. Growth in the number of molecules 3 years earlier has the largest and most significant effect. A 10% increase in the number of molecules in a drug class is associated with an 8.9% increase in expenditure on that class 3 years later.

Earlier in this paper we estimated how much pharmaceutical innovation increased life expectancy and reduced hospital utilization during the period 2000-2009. We also wish to estimate how much pharmaceutical innovation increased pharmaceutical expenditure during the same period. The estimates in Table 7 indicate that the 2000-2009 increase in pharmaceutical expenditure is most closely related to the increase in the number of molecules during 1997-2006. Unfortunately, data on the number of molecules (as defined by IMS) sold in Sweden prior to 1999 are not available. We will therefore use Läkemedelsverket data on the number of chemical substances in 1997 and 2006 instead. As shown in Table 1, the number of chemical substances increased from 962 in 1997 to 1372 in 2006. The estimate of model 74 in Table 7 implies that the 1997-2006 increase in the number of chemical substances increased pharmaceutical expenditure in 2009 by 37.2% (= exp [.891 * ln(1372/962)] – 1). However, the increase in 2009 pharmaceutical expenditure attributable to pharmaceutical innovation during 1997-2006 may have been smaller than that because, as shown in Table 6, during the period 1999-2010 the growth rate of the number of IMS molecules was 12% lower than the growth rate of Läkemedelsverket chemical substances.

6. The cost-effectiveness of pharmaceutical innovation in Sweden

We have presented estimates of the effect of pharmaceutical innovation on age at death (Table 3), hospital utilization (Table 5), and pharmaceutical expenditure (Table 7). Now we will use these estimates to calculate the incremental cost-effectiveness of pharmaceutical innovation,

i.e. the cost per life year gained from the introduction of new drugs. We define the incremental cost-effectiveness ratio (ICER) as follows:[21]

$$ICER = \frac{(LE_{actual} * MedExpend_{actual}) - (LE_{no\_innovation} * MedExpend_{no\_innovation})}{LE_{actual} - LE_{no\_innovation}}$$

where

$MedExpend_{actual}$ = actual per capita medical expenditure in 2009

$MedExpend_{no\_innovation}$ = estimated per capita medical expenditure in 2009 in the absence of 9 prior years of pharmaceutical innovation

LE_{actual} = actual life expectancy in 2009

$LE_{no\_innovation}$ = estimated life expectancy in 2009 in the absence of 9 prior years of pharmaceutical innovation

Table 8 shows a "baseline" calculation of the ICER. After we explain this calculation, we will perform some sensitivity analysis, which will indicate the effect of modifying the assumptions underlying the baseline calculation. Line 1 shows the actual value of life expectancy (mean age at death) in 2009 (80.03 years), and the estimated value (79.56 years, derived from Model 7 in Table 3) if no new chemical substances had been commercialized during 1994-2003. We estimate that life expectancy would have been 0.47 years (5.64 months) lower in 2009 in the absence of pharmaceutical innovation.

Lines 2-4 show three components of medical expenditure, and line 5 shows their sum, total medical expenditure. The 2009 actual values (expressed in USD PPP) were obtained from http://stats.oecd.org/. First we consider (in line 2) pharmaceutical expenditure. Model 74 in Table 7 implied that, if no new chemical substances had been commercialized during 1997-2006, per capita pharmaceutical expenditure in 2008 would have been $91 lower ($245 instead of $336). Next we consider (in line 3) hospital expenditure. Model 45 in Table 5 implied that, if no new chemical substances had been commercialized during 1992-2001, the number of hospital days would have been 12% higher in 2009. If we assume that hospital expenditure is

[21] $LE_{actual} * MedExpend_{actual}$ = actual (undiscounted) lifetime medical expenditure; $LE_{no\_innovation} * MedExpend_{no\_innovation}$ = estimated (undiscounted) lifetime medical expenditure in the absence of 8 prior years of pharmaceutical innovation.

proportional to the number of hospital days, this implies that per capita hospital pharmaceutical expenditure in 2009 would have been $112 higher ($1047 instead of $935). Longitudinal disease-level data on expenditure on or utilization of other medical services are not available, so here we assume (in line 4) that pharmaceutical innovation had no effect on other medical expenditure. As shown in line 5, under these assumptions per capita medical expenditure in 2009 would have been slightly ($21) higher in the absence of prior pharmaceutical innovation, because the estimated increase in hospital expenditure would have been slightly larger than the estimated reduction in pharmaceutical expenditure. Despite this tiny increase in annual medical expenditure, lifetime medical expenditure would have been slightly ($109) lower in the absence of prior pharmaceutical innovation, due to the reduction in life expectancy. The calculations in Table 8 imply that the cost per life-year gained from the introduction of new drugs was $233 (= -$109/ -0.47 years), which is a very small fraction of leading economists' estimates of the value of (or consumers' willingness to pay for) a one-year increase in life expectancy.

Changes in any of the estimates or assumptions documented in Table 8 will, of course, change one's estimate of the ICER. A change that can substantially increase the ICER is reducing the estimate of the hospital cost reduction attributable to pharmaceutical innovation. If we assume that there is *no* hospital cost reduction, the ICER is $19,192. Even this figure is well below the consensus value of a statistical life-year.

Moreover, there are several good reasons to think that the calculations in Table 9 lead to an *overestimate* of the ICER. First, we may have underestimated the increase in life expectancy attributable to pharmaceutical innovation. Recall that pharmaceutical innovation accounted for a larger share (63%) of the increase in the fraction of deaths that occurred at an age greater than 75 than it did of the increase in mean age at death (31.6%). Also, life expectancy at birth (as conventionally defined) increased more than mean age at death between 2000 and 2009 (1.71 years vs. 1.40 years). Second, we may have overestimated the increase in pharmaceutical expenditure attributable to pharmaceutical innovation, because the growth rate of the number of IMS molecules was lower than the growth rate of Läkemedelsverket chemical substances. And third, in Table 8 we assumed that pharmaceutical innovation had no effect on other medical expenditure, but it may have reduced other medical expenditure—especially nursing home expenditure—as it appears to have reduced hospital expenditure. If we assume that the hospital cost reduction is half as large as that implied by model 45 in Table 5—about 6% instead of

12%—and that pharmaceutical innovation also reduced other medical expenditure by 6%, pharmaceutical innovation would be *cost-saving*: the ICER is -$15,189.

7. Summary and conclusions

In this paper, we have used longitudinal, disease-level data to analyze the impact of pharmaceutical innovation on longevity and medical expenditure in Sweden during the period 1997-2010. The measures of longevity we used were based on the age distribution of deaths caused by a disease in a given year. Our estimates do not capture between-disease spillover effects, but these effects appear to be quite modest in practice: almost all of the increase in mean age at death was due to within-disease increases, rather than a shift in the distribution of causes of death. The measure of pharmaceutical innovation we used was based on the number of drugs (chemical substances) previously introduced to treat a condition.

From 1997 to 2010, mean age at death increased by 1.88 years, from 78.40 to 80.28 years. We estimated that, if the number of chemical substances commercialized up to six years earlier had not increased, mean age at death would have increased by 1.29 years, from 78.40 to 79.69 years. Hence pharmaceutical innovation was estimated to have increased mean age at death in Sweden by 0.60 years (7.15 months) during the period 1997-2010—almost 1/3 (31.6%) of the overall increase in mean age at death. It accounted for twice as large a fraction (63%) of the increase in the fraction of deaths that occurred at an age greater than 75. Longevity depends on the number of drugs to treat a disease, not the number of chemical subgroups (drug classes) developed to treat the disease.

We also examined the effect of pharmaceutical innovation on hospital utilization. The estimates indicated that an increase in the number of drugs commercialized for a disease reduces the number of hospital days due to the disease 8 years later. The negative effect of pharmaceutical innovation on the number of hospital days is primarily due to its effect on the number of hospital discharges. We estimated that if no new drugs had been commercialized during the period 1992-2001, the number of hospital days would have been about 12% higher in 2009.

We assessed the impact of pharmaceutical innovation on pharmaceutical expenditure using longitudinal data on about 300 classes of drugs. We estimated that the 1997-2006 increase in the number of chemical substances increased pharmaceutical expenditure in 2009 by 37.2%.

We used our estimates of the effect of pharmaceutical innovation on age at death, hospital utilization, and pharmaceutical expenditure to assess the incremental cost-effectiveness of pharmaceutical innovation, i.e. the cost per life year gained from the introduction of new drugs. First we calculated a "baseline" estimate of the incremental cost-effectiveness ratio (ICER), based on our estimates that, if no new chemical substances had been commercialized during a previous 9-year period, (1) mean age at death in 2009 would have been 0.47 years (5.64 months) lower; (2) per capita pharmaceutical expenditure in 2009 would have been $91 lower; and (3) per capita hospital expenditure in 2009 would have been $112 higher (assuming that hospital expenditure is proportional to the number of hospital days). If we assume that pharmaceutical innovation had no effect on other medical expenditure, lifetime medical expenditure would have been slightly lower in the absence of prior pharmaceutical innovation, due to the reduction in life expectancy. The baseline estimate of the cost per life-year gained from the introduction of new drugs was about $233, which is a very small fraction of leading economists' estimates of the value of (or consumers' willingness to pay for) a one-year increase in life expectancy.

We then performed some sensitivity analysis, which indicated the effect of modifying the assumptions underlying the baseline ICER calculation. If we assume that there is *no* hospital cost reduction from pharmaceutical innovation, the ICER is $19,192. Even this figure is well below the consensus value of a statistical life-year. Moreover, there are several good reasons to think that our baseline calculation *overestimates* the ICER: we may have underestimated the effect of pharmaceutical innovation on life expectancy, and overestimated its effect on pharmaceutical expenditure. If we assume that the hospital cost reduction is half as large as our estimates indicate, and that pharmaceutical innovation also reduced other medical expenditure (e.g. nursing home expenditure) proportionally, pharmaceutical innovation would be *cost-saving*: the ICER is -$15,189.

Pharmaceutical innovation is not the only type of medical innovation that is likely to contribute to longevity growth. Other medical innovation, such as innovation in diagnostic imaging, surgical procedures, and medical devices, is also likely to affect longevity growth. Longitudinal disease-level measures of non-pharmaceutical medical innovation are not available for Sweden, but they are available for the U.S. during the period 1998-2007. But a previous analysis of the U.S. data suggests that failure to control for other medical innovation is very

unlikely to result in overestimation of the effect of pharmaceutical innovation on longevity growth, and may even result in underestimation of this effect.

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Table 1
Summary statistics on longevity and pharmaceutical innovation in Sweden

Year	Number of deaths	Mean age at death	% of deaths at age > 75
1997	78,547	78.40	69.0%
1998	78,649	78.57	69.8%
1999	78,978	78.74	70.4%
2000	77,507	78.87	70.7%
2001	77,620	79.19	71.3%
2002	79,067	79.43	72.0%
2003	78,344	79.40	71.7%
2004	75,858	79.38	71.5%
2005	75,970	79.53	71.7%
2006	76,041	79.74	72.1%
2007	75,940	79.92	72.5%
2008	75,583	80.00	72.2%
2009	74,296	79.97	71.8%
2010	74,146	80.28	72.4%

Year	Number of (3rd level ATC) pharmacological subgroups	Number of (4th level ATC) chemical subgroups	Number of (5th level ATC) chemical substances
1990	191	399	673
1991	192	406	695
1992	194	416	723
1993	198	430	772
1994	200	438	804
1995	206	451	850
1996	209	465	902
1997	218	486	962
1998	227	504	1023
1999	231	518	1074
2000	232	530	1125
2001	234	540	1175
2002	238	550	1224
2003	241	556	1251
2004	242	560	1296
2005	246	568	1326
2006	248	577	1372
2007	250	585	1418
2008	250	588	1454
2009	253	600	1504
2010	253	607	1537

Table 2

Chemical substances (drugs) and chemical subgroups used to treat C43-C44 Melanoma and other malignant neoplasms of skin

Chemical substance (WHO ATC 5th level)	**Year first commercialized in Sweden**
H02AB02 Dexamethasone	1959
H02AB04 Methylprednisolone	1959
H02AB01 Betamethasone	1963
L01AD02 Lomustine	1978
L01AX04 Dacarbazine	1979
V03AF03 Calcium folinate	1984
B01AB04 Dalteparin	1988
B03XA01 Erythropoietin	1989
J02AC01 Fluconazole	1989
V03AF04 Calcium levofolinate	1995
D06BB10 Imiquimod	1998
L03AB04 Interferon alfa-2a	1999
L03AB05 Interferon alfa-2b	2000
B03XA02 Darbepoetin alfa	2001
L01XD03 Methyl aminolevulinate	2001
L01XE01 Imatinib	2001
M05BA08 Zoledronic acid	2001
V09DB06 Technetium Tc-99M rheniumsulfide colloid	2002
L01XC11 Ipilimumab	2011

Chemical subgroup (WHO ATC 4th level)	**Year first commercialized in Sweden**
H02AB Glucocorticoids	1958
L01AD Nitrosoureas	1978
L01AX Other alkylating agents	1979
B01AB Heparin group	1981
V03AF Detoxifying agents for antineoplastic treatment	1984
D06BB Antivirals	1985
M05BA Bisphosphonates	1985
B03XA Other antianemic preparations	1989
J02AC Triazole derivatives	1989
V09DB Technetium Tc-99M, particles and colloids	1990
L03AB Interferons	1993
L01XC Monoclonal antibodies	1998
L01XD Sensitizers used in photodynamic/radiation therapy	2000
L01XE Protein kinase inhibitors	2001

Table 3

Estimates of the relationship between age at death and number of chemical substances and subgroups

Dependent variable: Mean age at death					
Model	**Parameter**	**Estimate**	**Std. Err.**	**Z**	**Pr > |Z|**
1	$N\_CHEM\_SUBSTANCES_{i,t}$	0.0466	0.031	1.50	0.1324
2	$N\_CHEM\_SUBSTANCES_{i,t-1}$	0.0458	0.029	1.58	0.1130
3	$N\_CHEM\_SUBSTANCES_{i,t-2}$	0.0447	0.025	1.77	0.0768
4	**$N\_CHEM\_SUBSTANCES_{i,t-3}$**	**0.0494**	**0.024**	**2.10**	**0.0354**
5	**$N\_CHEM\_SUBSTANCES_{i,t-4}$**	**0.0489**	**0.021**	**2.36**	**0.0182**
6	**$N\_CHEM\_SUBSTANCES_{i,t-5}$**	**0.0498**	**0.018**	**2.85**	**0.0044**
7	**$N\_CHEM\_SUBSTANCES_{i,t-6}$**	**0.0478**	**0.017**	**2.87**	**0.0041**
8	**$N\_CHEM\_SUBSTANCES_{i,t-7}$**	**0.0441**	**0.017**	**2.57**	**0.0101**
9	**$N\_CHEM\_SUBSTANCES_{i,t-8}$**	**0.0414**	**0.016**	**2.56**	**0.0105**
10	**$N\_CHEM\_SUBSTANCES_{i,t-9}$**	**0.0432**	**0.017**	**2.61**	**0.0090**
11	**$N\_CHEM\_SUBSTANCES_{i,t-10}$**	**0.0443**	**0.018**	**2.43**	**0.0151**
12	$N\_CHEM\_SUBGROUPS_{i,t}$	0.0495	0.041	1.22	0.2217
13	$N\_CHEM\_SUBGROUPS_{i,t-1}$	0.0447	0.040	1.13	0.2597
14	$N\_CHEM\_SUBGROUPS_{i,t-2}$	0.0262	0.040	0.65	0.5152
15	$N\_CHEM\_SUBGROUPS_{i,t-3}$	0.0166	0.044	0.38	0.7069
16	$N\_CHEM\_SUBGROUPS_{i,t-4}$	0.0134	0.040	0.34	0.7372
17	$N\_CHEM\_SUBGROUPS_{i,t-5}$	0.0102	0.042	0.24	0.8074
18	$N\_CHEM\_SUBGROUPS_{i,t-6}$	-0.0005	0.046	-0.01	0.9922

Dependent variable: % of deaths at age > 75					
Model	**Parameter**	**Estimate**	**Std. Err.**	**Z**	**Pr > |Z|**
19	**$N\_CHEM\_SUBSTANCES_{i,t}$**	**0.0019**	**0.0009**	**2.25**	**0.0241**
20	**$N\_CHEM\_SUBSTANCES_{i,t-1}$**	**0.0018**	**0.0008**	**2.22**	**0.0263**
21	**$N\_CHEM\_SUBSTANCES_{i,t-2}$**	**0.0016**	**0.0007**	**2.23**	**0.0259**
22	**$N\_CHEM\_SUBSTANCES_{i,t-3}$**	**0.0018**	**0.0007**	**2.54**	**0.0110**
23	**$N\_CHEM\_SUBSTANCES_{i,t-4}$**	**0.0017**	**0.0006**	**2.76**	**0.0058**
24	**$N\_CHEM\_SUBSTANCES_{i,t-5}$**	**0.0018**	**0.0005**	**3.45**	**0.0006**
25	**$N\_CHEM\_SUBSTANCES_{i,t-6}$**	**0.0017**	**0.0005**	**3.32**	**0.0009**
26	**$N\_CHEM\_SUBSTANCES_{i,t-7}$**	**0.0014**	**0.0006**	**2.57**	**0.0102**
27	**$N\_CHEM\_SUBSTANCES_{i,t-8}$**	**0.0013**	**0.0005**	**2.43**	**0.0151**
28	**$N\_CHEM\_SUBSTANCES_{i,t-9}$**	**0.0014**	**0.0005**	**2.73**	**0.0062**
29	**$N\_CHEM\_SUBSTANCES_{i,t-10}$**	**0.0014**	**0.0005**	**2.67**	**0.0077**
30	$N\_CHEM\_SUBGROUPS_{i,t}$	0.0021	0.0015	1.38	0.1687
31	$N\_CHEM\_SUBGROUPS_{i,t-1}$	0.0016	0.0014	1.12	0.2618
32	$N\_CHEM\_SUBGROUPS_{i,t-2}$	0.0005	0.0012	0.46	0.6471
33	$N\_CHEM\_SUBGROUPS_{i,t-3}$	0.0001	0.0012	0.11	0.9161
34	$N\_CHEM\_SUBGROUPS_{i,t-4}$	0.0002	0.0012	0.13	0.8956
35	$N\_CHEM\_SUBGROUPS_{i,t-5}$	0.0000	0.0012	-0.01	0.9946
36	$N\_CHEM\_SUBGROUPS_{i,t-6}$	-0.0004	0.0014	-0.26	0.7972

Table 4

Number of hospital days and discharges and average length of stay, 2000-2009

Year	Number of hospital days	Number of hospital discharges	Average length of stay
2000	10,121,863	1,429,648	7.1
2001	9,892,792	1,413,962	7.0
2002	9,704,398	1,402,318	6.9
2003	9,607,065	1,406,948	6.8
2004	9,431,417	1,416,005	6.7
2005	9,387,429	1,428,401	6.6
2006	9,544,045	1,449,843	6.6
2007	9,552,130	1,473,933	6.5
2008	9,690,826	1,492,115	6.5
2009	9,563,831	1,510,374	6.3

Table 5

Estimates of hospital utilization models

Dependent variable: ln(DAYS)					
Model	**Parameter**	**Estimate**	**Std. Err.**	**Z**	**Pr > |Z|**
37	ln N_CHEM_SUBSTANCES$_{i,t}$	0.012	0.262	0.05	0.9622
38	ln N_CHEM_SUBSTANCES$_{i,t-1}$	0.006	0.208	0.03	0.9785
39	ln N_CHEM_SUBSTANCES$_{i,t-2}$	-0.071	0.162	-0.44	0.6615
40	ln N_CHEM_SUBSTANCES$_{i,t-3}$	-0.236	0.145	-1.63	0.1033
41	**ln N_CHEM_SUBSTANCES$_{i,t-4}$**	**-0.288**	**0.121**	**-2.37**	**0.0178**
42	**ln N_CHEM_SUBSTANCES$_{i,t-5}$**	**-0.299**	**0.106**	**-2.81**	**0.0049**
43	**ln N_CHEM_SUBSTANCES$_{i,t-6}$**	**-0.253**	**0.083**	**-3.07**	**0.0021**
44	**ln N_CHEM_SUBSTANCES$_{i,t-7}$**	**-0.264**	**0.083**	**-3.19**	**0.0014**
45	**ln N_CHEM_SUBSTANCES$_{i,t-8}$**	**-0.302**	**0.087**	**-3.47**	**0.0005**
46	**ln N_CHEM_SUBSTANCES$_{i,t-9}$**	**-0.325**	**0.100**	**-3.27**	**0.0011**
47	**ln N_CHEM_SUBSTANCES$_{i,t-10}$**	**-0.279**	**0.107**	**-2.60**	**0.0092**
48	ln N_CHEM_SUBGROUPS$_{i,t}$	-0.478	0.418	-1.14	0.2528
49	ln N_CHEM_SUBGROUPS$_{i,t-1}$	-0.434	0.332	-1.31	0.1901
50	ln N_CHEM_SUBGROUPS$_{i,t-2}$	-0.375	0.277	-1.35	0.1767
51	ln N_CHEM_SUBGROUPS$_{i,t-3}$	-0.308	0.292	-1.05	0.2915
52	ln N_CHEM_SUBGROUPS$_{i,t-4}$	-0.397	0.252	-1.57	0.1156
53	ln N_CHEM_SUBGROUPS$_{i,t-5}$	-0.287	0.187	-1.54	0.1237

Dependent variable: ln(DISCHARGES)					
Model	**Parameter**	**Estimate**	**Std. Err.**	**Z**	**Pr > |Z|**
54	ln N_CHEM_SUBSTANCES$_{i,t}$	0.176	0.316	0.56	0.5768
55	ln N_CHEM_SUBSTANCES$_{i,t-1}$	0.135	0.236	0.57	0.5667
56	ln N_CHEM_SUBSTANCES$_{i,t-2}$	0.025	0.169	0.15	0.8821
57	ln N_CHEM_SUBSTANCES$_{i,t-3}$	-0.137	0.148	-0.93	0.3539
58	ln N_CHEM_SUBSTANCES$_{i,t-4}$	-0.240	0.153	-1.57	0.1159
59	ln N_CHEM_SUBSTANCES$_{i,t-5}$	-0.238	0.136	-1.75	0.0793
60	ln N_CHEM_SUBSTANCES$_{i,t-6}$	-0.189	0.101	-1.86	0.0623
61	**ln N_CHEM_SUBSTANCES$_{i,t-7}$**	**-0.205**	**0.099**	**-2.07**	**0.0383**
62	**ln N_CHEM_SUBSTANCES$_{i,t-8}$**	**-0.249**	**0.108**	**-2.30**	**0.0216**
63	**ln N_CHEM_SUBSTANCES$_{i,t-9}$**	**-0.245**	**0.124**	**-1.98**	**0.0473**
64	ln N_CHEM_SUBSTANCES$_{i,t-10}$	-0.204	0.128	-1.59	0.1112
65	ln N_CHEM_SUBGROUPS$_{i,t}$	-0.422	0.391	-1.08	0.2806
66	ln N_CHEM_SUBGROUPS$_{i,t-1}$	-0.344	0.377	-0.91	0.3616
67	ln N_CHEM_SUBGROUPS$_{i,t-2}$	-0.171	0.354	-0.48	0.6304
68	ln N_CHEM_SUBGROUPS$_{i,t-3}$	-0.086	0.343	-0.25	0.8020
69	ln N_CHEM_SUBGROUPS$_{i,t-4}$	-0.199	0.283	-0.70	0.4823
70	ln N_CHEM_SUBGROUPS$_{i,t-5}$	-0.183	0.221	-0.83	0.4063

Table 6

Comparison of number of molecules in IMS MIDAS database for Sweden with number of chemical substances in Läkemedelsverket database, 2000-2010

Year	Number of molecules in IMS MIDAS database for Sweden	Number of chemical substances in Läkemedelsverket database
1999	885	1074
2000	930	1125
2001	971	1175
2002	1010	1224
2003	1032	1251
2004	1056	1296
2005	1082	1326
2006	1112	1372
2007	1134	1418
2008	1172	1454
2009	1195	1504
2010	1219	1537

Table 7

Estimates of models of the effect of pharmaceutical innovation on pharmaceutical expenditure (eq. (12))

Model	Parameter	Estimate	Std. Err.	Z	Pr > |Z|
71	**$\ln(N\_MOLECULE_{c,t})$**	0.737	0.302	2.44	0.0147
72	**$\ln(N\_MOLECULE_{c,t-1})$**	0.820	0.287	2.86	0.0042
73	**$\ln(N\_MOLECULE_{c,t-2})$**	0.893	0.206	4.34	<.0001
74	**$\ln(N\_MOLECULE_{c,t-3})$**	0.891	0.177	5.03	<.0001
75	**$\ln(N\_MOLECULE_{c,t-4})$**	0.680	0.191	3.56	0.0004
76	**$\ln(N\_MOLECULE_{c,t-5})$**	0.592	0.157	3.77	0.0002

Table 8

Estimation of incremental cost effectiveness of pharmaceutical innovation: baseline case

Line	Variable	Actual values, 2009 (Y_{actual})	Estimated values in 2009 in the absence of 9 prior years of pharmaceutical innovation ($Y_{no\_innovation}$)	Difference ($Y_{no\_innovation}$ - Y_{actual})	Basis for $Y_{no\_innovation}$ estimate
1	**Life expectancy (Mean age at death)**	80.03	79.56	-0.47	Figure 4
	Per capita medical expenditure in 2009, USD PPP				
2	Prescription drug expenditure	$336	$245	-$91	Y_{actual}* exp[β_{74} ln(N_CHEM_SUBSTANCE$_{1992}$/N_CHEM_SUBSTANCE$_{2001}$)]
3	Hospital expenditure	$935	$1,047	$112	Figure 5
4	Other medical expenditure	$2,450	$2,450	$0	Assumption that pharma. Innovation has no effect on other medical expenditure
5	Total medical expenditure	$3,721	$3,742	$21	Sum of Rx, hospital, and other medical expenditure
6	**Lifetime medical expenditure (= life expectancy * total medical expenditure in 2009)**	$297,792	$297,682	-$109	

Note:

Source for data on actual medical expenditure in 2009: http://stats.oecd.org/

β_{74} = the coefficient on ln(N_MOLECULE$_{c,t-3}$) in ln(MANU_VALUE) Model 74 (Table 7)

Figure 1
Mean age at death:
variable vs. fixed cause of death distribution

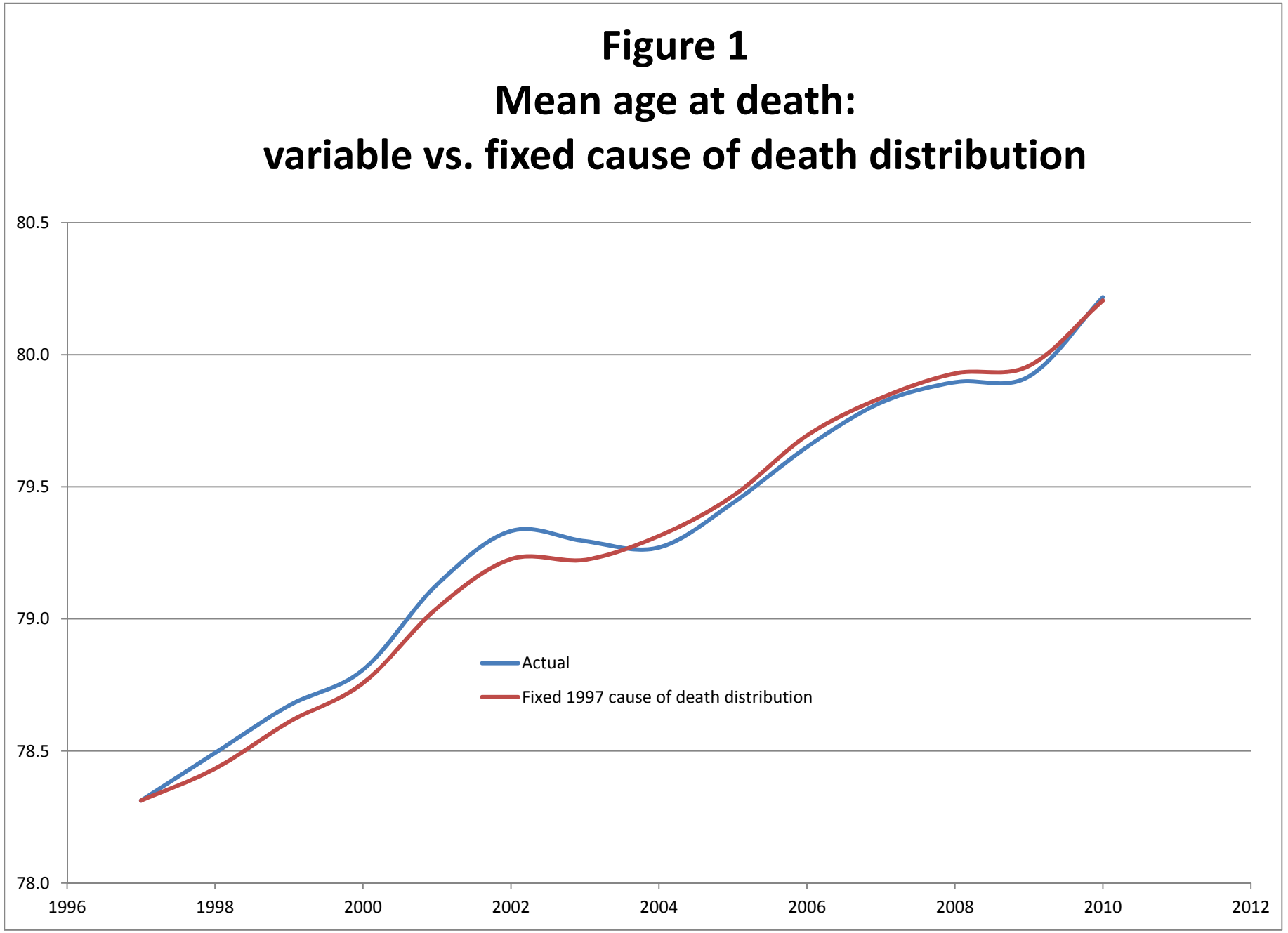


Figure 2
Number of chemical substances previously commercialized in Sweden for selected diseases, 1997-2011

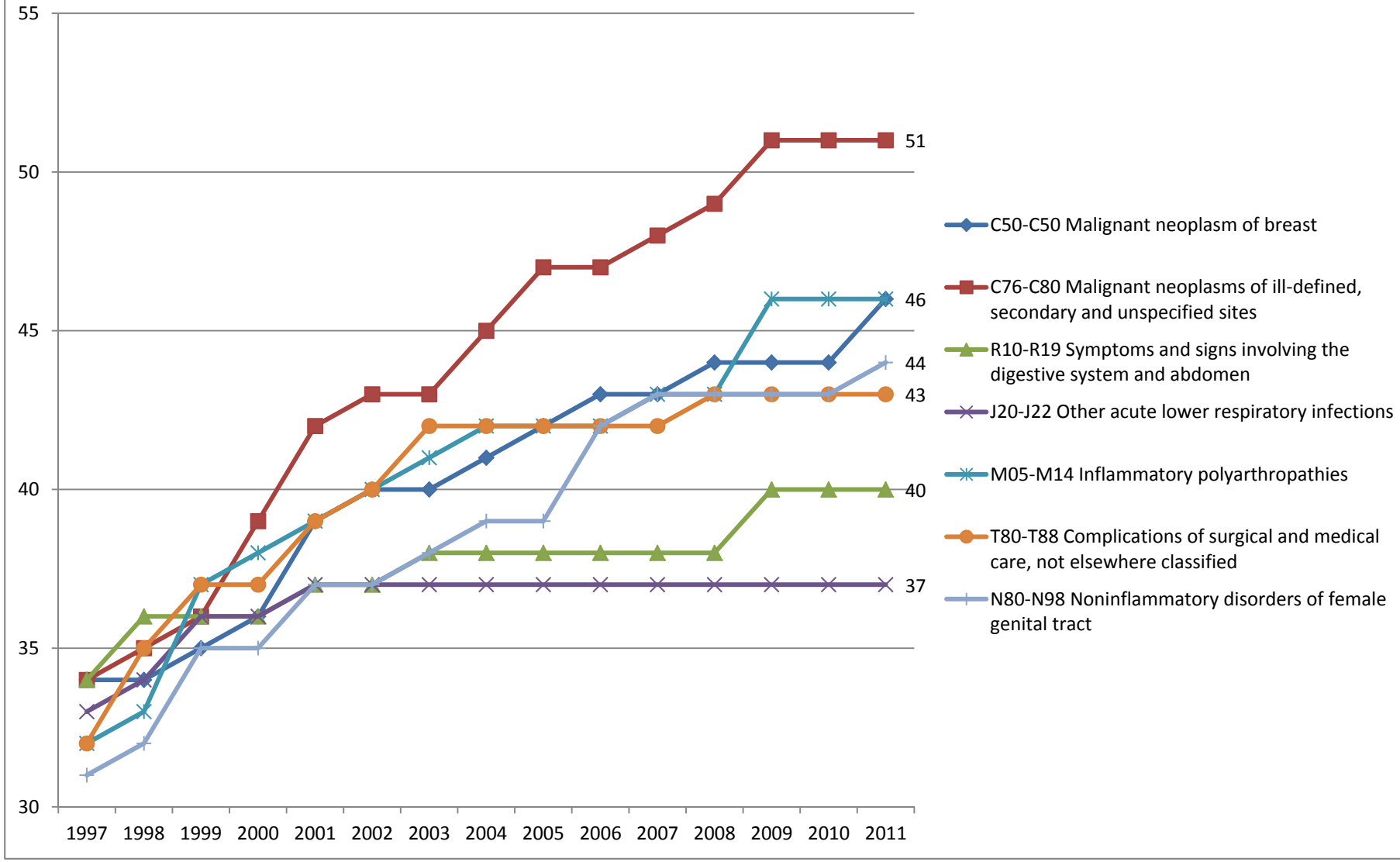


Figure 3
Relationship across diseases between number of deaths in 1997 and 1997-2010 change in mean age at death

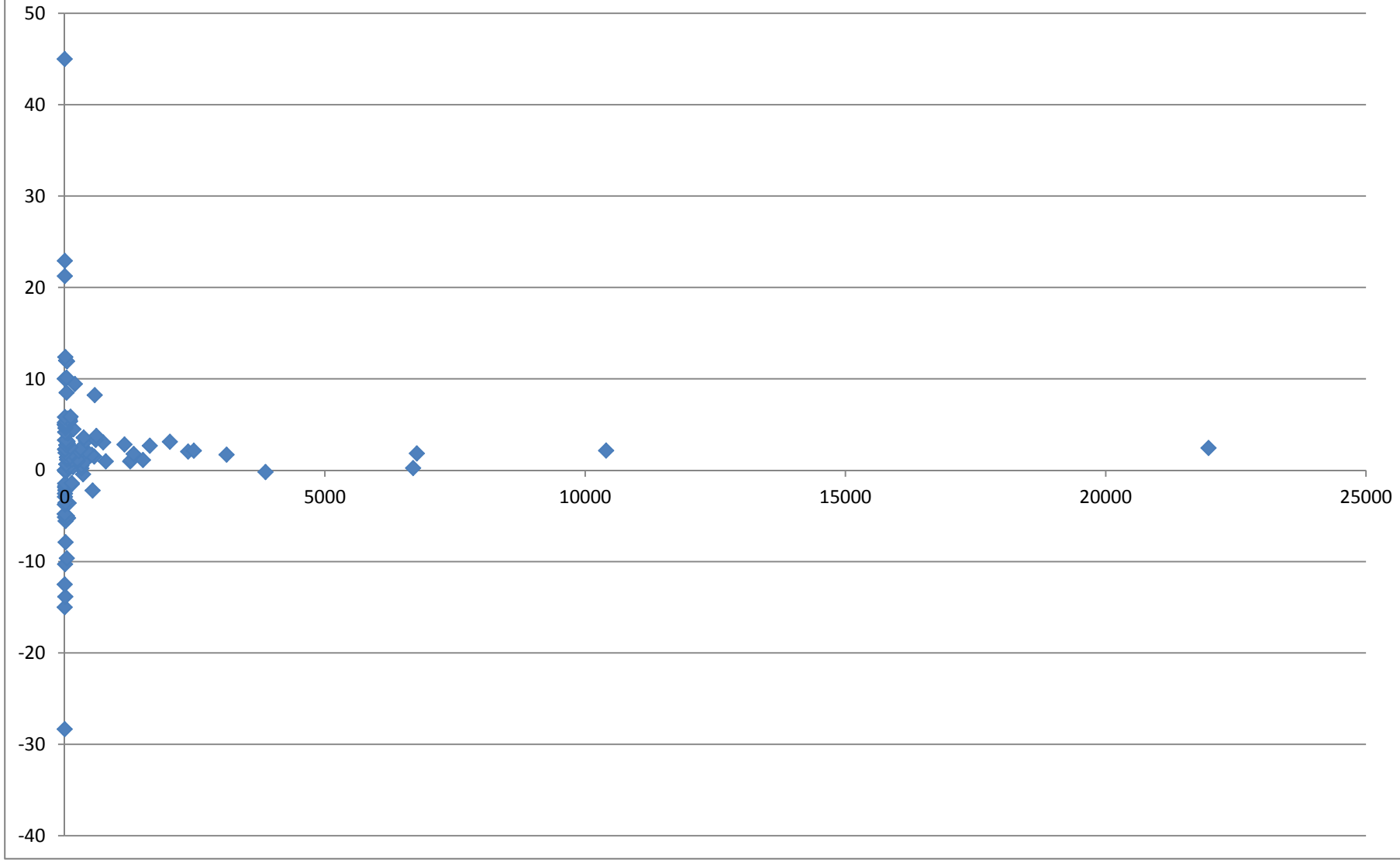
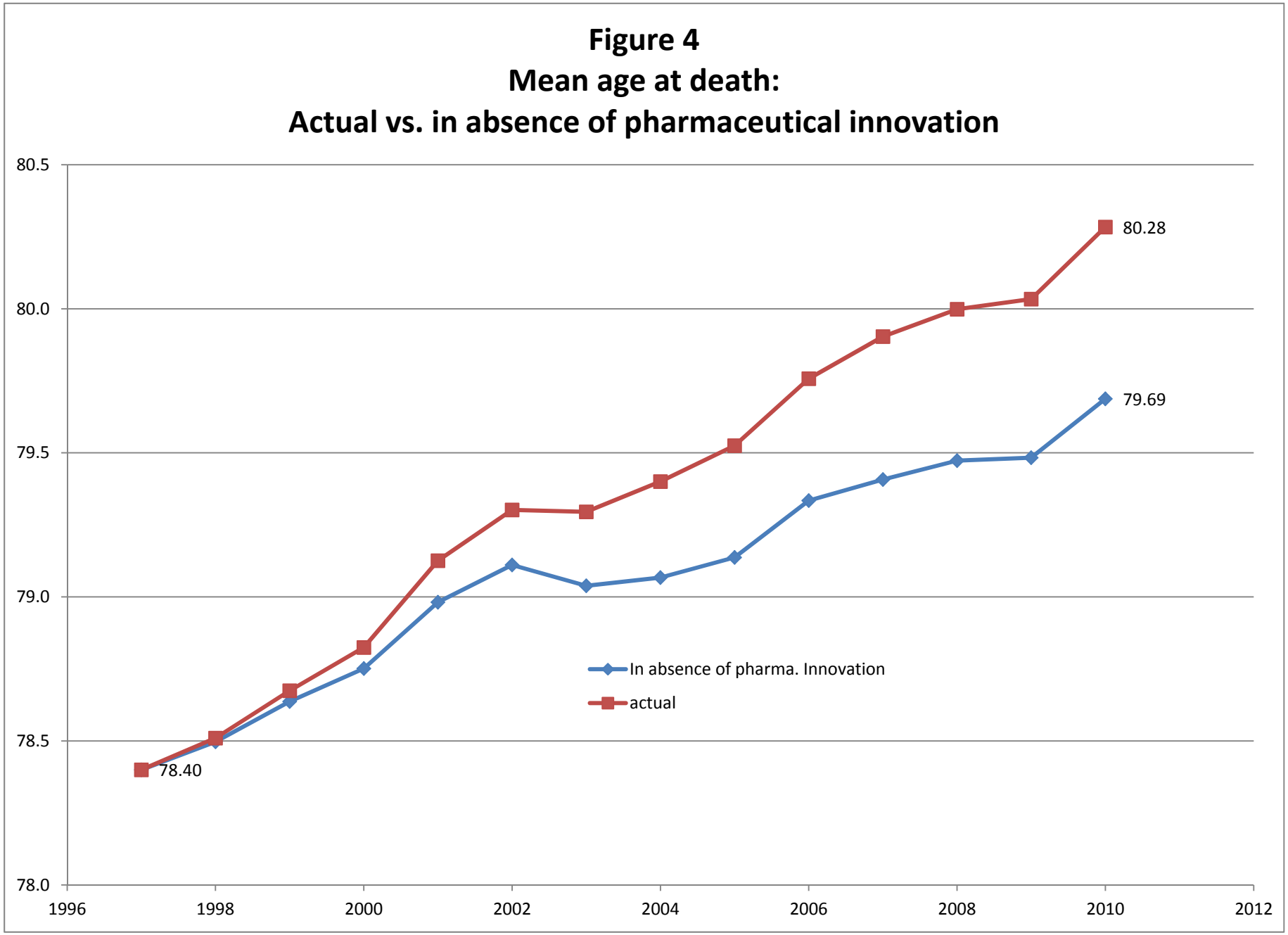


Figure 4
Mean age at death:
Actual vs. in absence of pharmaceutical innovation



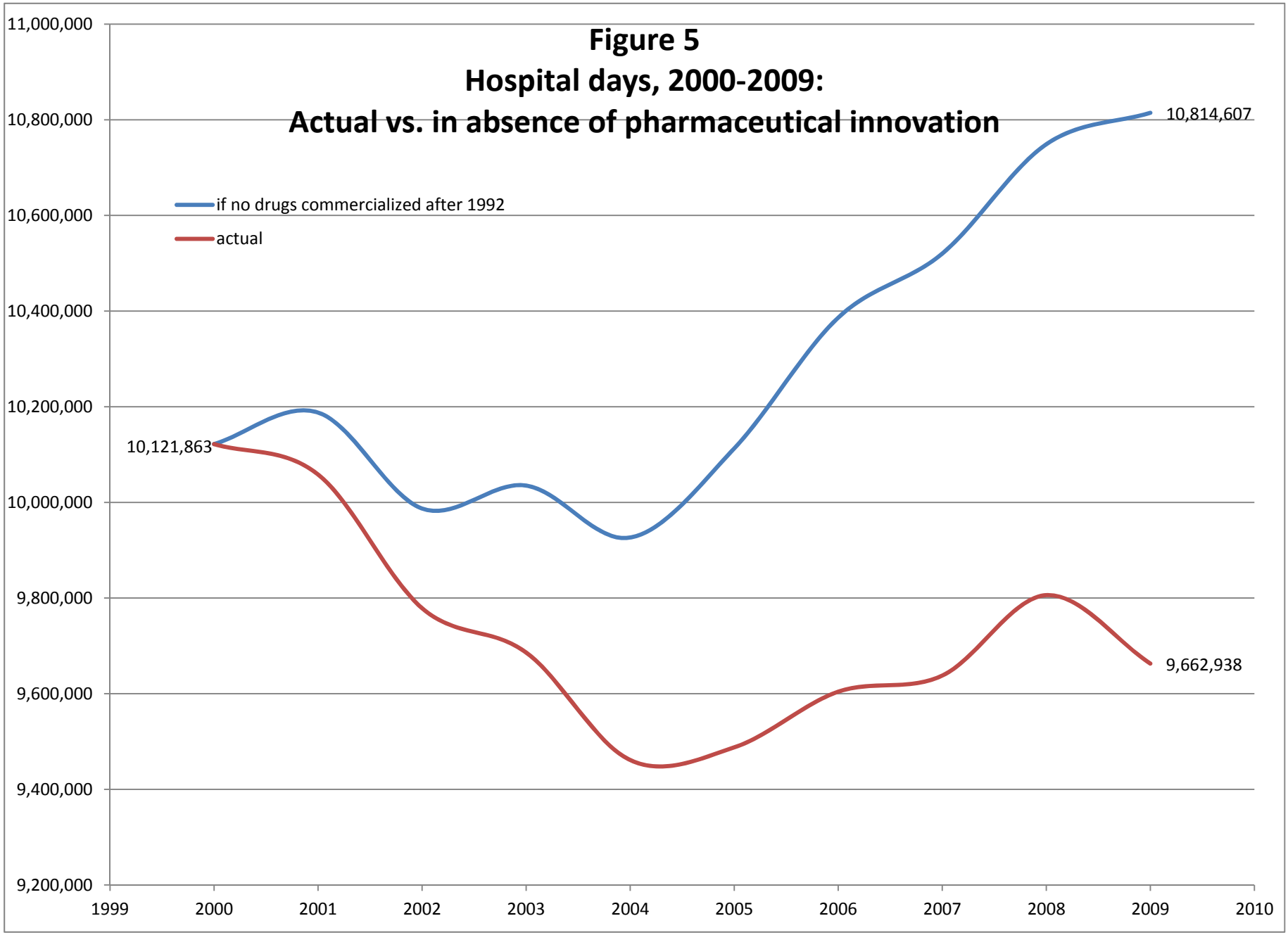


Figure 5
Hospital days, 2000-2009:
Actual vs. in absence of pharmaceutical innovation
if no drugs commercialized after 1992
actual
10,121,863
10,814,607
9,662,938
11,000,000
10,800,000
10,600,000
10,400,000
10,200,000
10,000,000
9,800,000
9,600,000
9,400,000
9,200,000
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010

Appendix Table 1
Data on mortality and DRUG_STOCK, by ICD-10 Block, 1997 and 2010

	Number of deaths		Mean age at death		% of deaths at age > 75		DRUG_STOCK	
ICD-10 Block	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**
A00-A09 Intestinal infectious diseases	36	370	77.2	85.7	75%	92%	20	22
A15-A19 Tuberculosis	39	14	79.4	84.6	79%	93%	10	11
A20-A28 Certain zoonotic bacterial diseases	1	2	87.5	72.5	100%	50%	11	12
A30-A49 Other bacterial diseases	365	977	76.4	79.9	71%	76%	45	54
A50-A64 Infections with a predominantly sexual mode of transmission	.	1	.	72.5	.	0%	.	19
A80-A89 Viral infections of the central nervous system	8	20	66.3	68.5	38%	30%	5	8
B00-B09 Viral infections characterized by skin and mucous membrane lesions	15	18	74.0	72.1	80%	72%	15	17
B15-B19 Viral hepatitis	26	55	54.8	60.1	12%	16%	7	17
B20-B24 Human immunodeficiency virus [HIV] disease	47	11	47.4	59.3	2%	18%	10	32
B25-B34 Other viral diseases	66	30	86.1	80.9	95%	87%	7	8
B35-B49 Mycoses	15	18	75.6	73.4	67%	61%	20	27
B50-B64 Protozoal diseases	2	3	57.5	62.5	0%	33%	18	19
B65-B83 Helminthiases	1	.	37.5	.	0%	.	3	.
B99-B99 Other infectious diseases	137	394	87.2	85.7	99%	92%	8	11
C00-C14 Malignant neoplasms of lip, oral cavity and pharynx	241	287	70.4	71.6	39%	40%	12	14
C15-C26 Malignant neoplasms of digestive organs	6694	6634	74.6	74.8	55%	53%	17	31
C30-C39 Malignant neoplasms of respiratory and intrathoracic organs	3110	3681	70.8	72.5	38%	42%	28	35
C40-C41 Malignant neoplasms of bone and articular cartilage	41	42	67.3	57.6	51%	33%	12	14
C43-C44 Melanoma and other malignant neoplasms of skin	409	537	68.5	71.7	41%	46%	10	18
C45-C49 Malignant neoplasms of mesothelial and soft tissue	303	306	67.5	69.9	33%	43%	21	29
C50-C50 Malignant neoplasm of breast	1504	1401	70.3	71.4	45%	43%	34	44
C51-C58 Malignant neoplasms of female genital organs	1259	1275	71.9	72.8	46%	46%	26	33
C60-C63 Malignant neoplasms of male genital organs	2482	2433	78.5	80.6	70%	76%	25	29
C64-C68 Malignant neoplasms of urinary tract	1326	1285	75.2	77.0	55%	62%	18	23
C69-C72 Malignant neoplasms of eye, brain and other parts of central nervous system	609	606	61.2	65.0	16%	28%	14	17
C73-C75 Malignant neoplasms of thyroid and other endocrine glands	108	84	69.5	72.0	49%	48%	10	15
C76-C80 Malignant neoplasms of ill-defined, secondary and unspecified sites	1151	1039	77.1	79.9	64%	72%	34	51
C81-C96 Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue	2021	1862	72.5	75.6	52%	60%	39	61
C97-C97 Malignant neoplasms of independent (primary) multiple sites	107	174	77.9	78.4	70%	69%	6	8
D50-D53 Nutritional anaemias	15	25	90.5	88.3	100%	92%	9	13
D55-D59 Haemolytic anaemias	19	10	73.3	78.2	63%	90%	9	16
D60-D64 Aplastic and other anaemias	104	147	86.4	87.9	91%	90%	8	13

Appendix Table 1
Data on mortality and DRUG_STOCK, by ICD-10 Block, 1997 and 2010

	Number of deaths		Mean age at death		% of deaths at age > 75		DRUG_STOCK	
ICD-10 Block	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**
D65-D69 Coagulation defects, purpura and other haemorrhagic conditions	14	21	66.8	79.2	50%	71%	22	29
D70-D77 Other diseases of blood and blood-forming organs	13	38	79.4	65.6	69%	39%	12	21
D80-D89 Certain disorders involving the immune mechanism	36	51	62.5	72.6	42%	55%	9	13
E00-E07 Disorders of thyroid gland	38	40	83.3	88.5	92%	93%	12	12
E10-E14 Diabetes mellitus	1636	1936	77.7	80.4	66%	74%	19	44
E20-E35 Disorders of other endocrine glands	17	15	79.9	72.0	82%	73%	22	27
E50-E64 Other nutritional deficiencies	3	16	84.2	89.4	100%	100%	20	26
E70-E90 Metabolic disorders	196	306	67.0	76.4	50%	68%	56	88
F10-F19 Mental and behavioural disorders due to psychoactive substance use	579	288	54.2	62.4	7%	15%	16	22
F20-F29 Schizophrenia, schizotypal and delusional disorders	44	48	79.3	79.3	77%	75%	14	17
F30-F39 Mood [affective] disorders	55	80	83.2	86.4	93%	91%	27	32
F40-F48 Neurotic, stress-related and somatoform disorders	5	7	83.5	86.8	80%	86%	21	25
F50-F59 Behavioural syndromes associated with physiological disturbances and physical factors	19	16	78.6	75.0	79%	63%	27	35
F60-F69 Disorders of adult personality and behaviour	.	2	.	77.5	.	50%	.	11
F70-F79 Mental retardation	7	17	70.4	67.8	43%	24%	7	8
F80-F89 Disorders of psychological development	1	2	12.5	57.5	0%	0%	8	9
F99-F99 Unspecified mental disorder	6	4	84.2	81.3	83%	75%	7	8
G00-G09 Inflammatory diseases of the central nervous system	43	50	60.6	62.0	37%	32%	22	27
G10-G14 Systemic atrophies primarily affecting the central nervous system	273	376	67.8	69.9	39%	40%	1	2
G20-G26 Extrapyramidal and movement disorders	371	575	80.4	81.3	79%	81%	16	24
G30-G32 Other degenerative diseases of the nervous system	596	2085	80.5	83.8	80%	87%	2	5
G35-G37 Demyelinating diseases of the central nervous system	106	150	62.3	67.6	21%	32%	9	12
G40-G47 Episodic and paroxysmal disorders	139	138	57.1	59.0	29%	31%	39	58
G50-G59 Nerve, nerve root and plexus disorders	2	3	85.0	72.5	100%	33%	11	11
G60-G64 Polyneuropathies and other disorders of the peripheral nervous system	16	21	75.0	79.9	56%	76%	7	7
G70-G73 Diseases of myoneural junction and muscle	55	56	55.2	60.8	25%	29%	10	12
H10-H13 Disorders of conjunctiva	.	1	.	97.5	.	100%	.	26
H25-H28 Disorders of lens	1	.	92.5	.	100%	.	1	.
H40-H42 Glaucoma	1	1	82.5	82.5	100%	100%	13	16
H43-H45 Disorders of vitreous body and globe	1	1	87.5	97.5	100%	100%	.	.
H65-H75 Diseases of middle ear and mastoid	1	3	92.5	64.2	100%	33%	18	19
I00-I02 Acute rheumatic fever	1	.	32.5	.	0%	.	9	.

Appendix Table 1
Data on mortality and DRUG_STOCK, by ICD-10 Block, 1997 and 2010

	Number of deaths		Mean age at death		% of deaths at age > 75		DRUG_STOCK	
ICD-10 Block	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**
I05-I09 Chronic rheumatic heart diseases	171	71	78.9	80.7	72%	75%	0	1
I10-I15 Hypertensive diseases	740	1808	82.8	85.9	82%	89%	46	69
I20-I25 Ischaemic heart diseases	21974	15012	79.6	82.1	72%	78%	36	50
I26-I28 Pulmonary heart disease and diseases of pulmonary circulation	790	430	76.9	77.9	67%	68%	8	18
I30-I52 Other forms of heart disease	6766	8684	83.8	85.7	88%	89%	68	79
I60-I69 Cerebrovascular diseases	10402	7602	81.7	83.8	81%	85%	11	17
I70-I79 Diseases of arteries, arterioles and capillaries	3859	2169	82.2	82.0	80%	77%	23	29
I80-I89 Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified	252	135	77.9	78.9	69%	72%	30	40
I95-I99 Other and unspecified disorders of the circulatory system	62	33	86.7	89.6	95%	97%	5	8
J00-J06 Acute upper respiratory infections	45	20	84.5	79.5	93%	70%	51	54
J20-J22 Other acute lower respiratory infections	78	46	87.2	83.6	96%	80%	33	37
J30-J39 Other diseases of upper respiratory tract	12	15	79.6	77.8	83%	80%	47	54
J40-J47 Chronic lower respiratory diseases	2373	2727	78.1	80.1	67%	73%	46	57
J80-J84 Other respiratory diseases principally affecting the interstitium	354	423	79.1	78.6	72%	69%	11	12
K00-K14 Diseases of oral cavity, salivary glands and jaws	9	8	90.8	89.4	100%	100%	17	20
K20-K31 Diseases of oesophagus, stomach and duodenum	537	389	80.6	78.4	76%	62%	16	24
K50-K52 Noninfective enteritis and colitis	138	44	81.4	80.0	79%	75%	11	13
K65-K67 Diseases of peritoneum	46	54	81.5	82.7	78%	78%	4	4
K70-K77 Diseases of liver	569	726	65.5	67.0	27%	25%	13	22
K80-K87 Disorders of gallbladder, biliary tract and pancreas	322	379	79.4	79.6	73%	72%	7	8
K90-K93 Other diseases of the digestive system	324	326	84.3	84.8	88%	86%	21	25
L00-L08 Infections of the skin and subcutaneous tissue	15	31	81.5	81.4	73%	81%	26	32
L10-L14 Bullous disorders	10	9	85.0	89.2	90%	100%	8	9
L20-L30 Dermatitis and eczema	1	.	67.5	.	0%	.	27	.
L40-L45 Papulosquamous disorders	3	4	65.8	88.8	33%	100%	25	34
L50-L54 Urticaria and erythema	2	.	90.0	.	100%	.	16	.
L80-L99 Other disorders of the skin and subcutaneous tissue	139	106	85.1	86.3	88%	92%	26	32
M00-M03 Infectious arthropathies	22	26	77.3	82.3	55%	77%	30	31
M05-M14 Inflammatory polyarthropathies	168	131	76.3	80.8	60%	79%	32	46
M15-M19 Arthrosis	24	18	78.3	81.7	71%	78%	22	27
M20-M25 Other joint disorders	29	12	82.7	85.4	93%	75%	12	13
M30-M36 Systemic connective tissue disorders	113	106	70.3	76.2	54%	68%	15	23
M40-M43 Deforming dorsopathies	7	22	69.6	75.5	57%	68%	3	4
M45-M49 Spondylopathies	27	25	72.5	84.5	52%	88%	13	17
M50-M54 Other dorsopathies	4	4	65.0	86.3	50%	75%	21	22
M60-M63 Disorders of muscles	2	24	85.0	80.2	100%	63%	4	4

Appendix Table 1
Data on mortality and DRUG_STOCK, by ICD-10 Block, 1997 and 2010

	Number of deaths		Mean age at death		% of deaths at age > 75		DRUG_STOCK	
ICD-10 Block	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**
M65-M68 Disorders of synovium and tendon	1	.	57.5	.	0%	.	3	.
M70-M79 Other soft tissue disorders	18	10	78.1	72.5	72%	50%	21	24
M80-M85 Disorders of bone density and structure	30	65	87.0	87.7	93%	92%	17	26
M86-M90 Other osteopathies	17	24	79.6	81.5	76%	75%	17	19
M91-M94 Chondropathies	.	1	.	87.5	.	100%	.	3
M95-M99 Other disorders of the musculoskeletal system and connective tissue	.	1	.	77.5	.	100%	.	3
N00-N08 Glomerular diseases	66	30	73.0	77.1	56%	70%	15	15
N10-N16 Renal tubulo-interstitial diseases	160	78	82.2	82.6	84%	85%	21	24
N17-N19 Renal failure	523	627	82.0	83.7	80%	85%	16	21
N25-N29 Other disorders of kidney and ureter	8	11	81.9	71.6	75%	55%	8	10
N30-N39 Other diseases of urinary system	416	278	85.1	87.2	93%	96%	42	47
N40-N51 Diseases of male genital organs	68	53	84.5	84.9	96%	87%	24	30
N70-N77 Inflammatory diseases of female pelvic organs	8	2	76.9	75.0	75%	50%	18	19
N80-N98 Noninflammatory disorders of female genital tract	11	14	83.4	85.7	82%	86%	31	43
P05-P08 Disorders related to length of gestation and fetal growth	12	14	-0.5	-0.5	0%	0%	4	5
P35-P39 Infections specific to the perinatal period	7	6	4.6	-0.5	0%	0%	.	.
Q20-Q28 Congenital malformations of the circulatory system	94	58	26.1	31.7	7%	10%	0	2
Q80-Q89 Other congenital malformations	15	19	26.9	31.5	7%	11%	4	5
R00-R09 Symptoms and signs involving the circulatory and respiratory systems	28	36	82.1	86.3	93%	86%	19	20
R10-R19 Symptoms and signs involving the digestive system and abdomen	4	4	85.0	81.3	75%	75%	34	40
R25-R29 Symptoms and signs involving the nervous and musculoskeletal systems	.	1	.	92.5	.	100%	.	4
R40-R46 Symptoms and signs involving cognition, perception, emotional state and behaviour	.	1	.	97.5	.	100%	.	14
R50-R69 General symptoms and signs	1279	1560	91.2	92.3	99%	99%	54	68

Appendix Table 2
Hospital discharges, days, and average length of stay, by diagnosis, Sweden, 2009

Diagnosis	discharges	days	alos
A00-A08 - Intestinal infectious diseases except diarrhoea	6,678	34,954	5.2
A09 - Diarrhoea and gastroenteritis of presumed infectious origin	6,537	18,839	2.9
A15-A19_B90 - Tuberculosis	730	9,809	13.4
A40_A41 - Septicaemia	12,390	107,899	8.7
ABORT_OTH - Other pregnancy with abortive outcome (O00-O03,O05-O08)	4,661	7,584	1.6
ARTHROPAT_OTH - Other arthropathies (M00-M15, M18-M22 ,M24-M25)	15,889	76,022	4.8
A_B_OTH - Other infectious and parasitic diseases (remainder of A00-B99)	19,969	109,784	5.5
B20-B24 - Human immunodeficiency virus [HIV] disease	192	2,169	11.3
C18-C21 - Malignant neoplasm of colon, rectosigmoid junction, rectum, anus and anal canal	10,700	115,191	10.8
C33_C34 - Malignant neoplasm of trachea, bronchus and lung	8,869	91,433	10.3
C43_C44 - Malignant neoplasms of skin	2,609	13,600	5.2
C50 - Malignant neoplasm of breast	9,122	42,648	4.7
C53-C55 - Malignant neoplasm of uterus	4,006	25,424	6.3
C56 - Malignant neoplasm of ovary	2,928	25,827	8.8
C61 - Malignant neoplasm of prostate	10,064	65,638	6.5
C67 - Malignant neoplasm of bladder	6,533	33,056	5.1
C_OTH - Other malignant neoplasms (remainder of C00-C97)	45,378	425,207	9.4
D00-D09 - In situ neoplasms	979	2,893	3.0
D00-D48_OTH - Other in situ neoplasms, benign neoplasms and neoplasms of uncertain or unknown behaviour (remainder of D00-D48)	17,221	97,010	5.6
D12 - Benign neoplasm of colon, rectum, anus and anal canal	790	4,415	5.6
D50-D64 - Anaemias	10,841	51,947	4.8
D65-D89 - Other diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	2,982	18,304	6.1
E10-E14 - Diabetes mellitus	15,740	103,086	6.5
E_OTH - Other endocrine, nutritional and metabolic diseases (remainder of E00-E90)	19,554	91,465	4.7
F00-F03 - Dementia	3,218	44,035	13.7
F10 - Mental and behavioural disorders due to use of alcohol	24,121	98,439	4.1
F11-F19 - Mental and behavioural disorders due to psychoactive substance use	10,234	84,180	8.2
F20-F29 - Schizophrenia, schizotypal and delusional disorders	13,217	667,651	50.5
F30-F39 - Mood [affective] disorders	18,599	366,540	19.7
F_OTH - Other mental and behavioural disorders (remainder of F00-F99)	24,093	498,606	20.7
G30 - Alzheimer's disease	1,506	28,059	18.6
G35 - Multiple sclerosis	1,502	11,475	7.6
G40_G41 - Epilepsy, status epilepticus	8,281	34,702	4.2
G45 - Transient cerebral ischaemic attacks and related syndromes	9,061	26,976	3.0
G_OTH - Other diseases of the nervous system (remainder of G00-G99)	20,558	137,060	6.7

Appendix Table 2
Hospital discharges, days, and average length of stay, by diagnosis, Sweden, 2009

Diagnosis	discharges	days	alos
H00-H59_OTH - Other diseases of the eye and adnexa (remainder of H00-H59)	7,734	20,245	2.6
H25_H26_H28 - Cataract	513	1,056	2.1
H60-H95 - Diseases of the ear and mastoid process	8,059	19,452	2.4
I10-I15 - Hypertensive diseases	8,178	37,545	4.6
I20 - Angina pectoris	21,035	73,364	3.5
I21_I22 - Acute myocardial infarction including subsequent myocardial infarction	30,841	147,210	4.8
I23-I25 - Other ischaemic heart disease	5,860	23,179	4.0
I26-I28 - Pulmonary heart disease and diseases of pulmonary circulation	6,941	44,247	6.4
I44-I49 - Conduction disorders and cardiac arrhythmias	38,900	130,837	3.4
I50 - Heart failure	31,204	207,018	6.6
I60-I69 - Cerebrovascular diseases	39,936	438,326	11.0
I70 - Atherosclerosis	7,891	64,117	8.1
I83 - Varicose veins of lower extremities	763	4,689	6.1
INJ_OTH - Other injuries (S10-S51, S53-S71, S73-S81, S83-T14, T79)	38,709	220,091	5.7
INTESTINE_OTH - Other diseases of intestine (K55,K58-K59,K63)	8,453	42,860	5.1
I_OTH - Other diseases of the circulatory system (remainder of I00-I99)	25,524	158,494	6.2
J00-J11 - Acute upper respiratory infections and influenza	9,686	29,480	3.0
J12-J18 - Pneumonia	34,387	223,613	6.5
J20-J22 - Other acute lower respiratory infections	6,688	26,961	4.0
J40-J44_J47 - Chronic obstructive pulmonary disease and bronchiectasis	17,803	111,809	6.3
J45_J46 - Asthma and status asthmaticus	4,341	12,304	2.8
J60-J99 - Other diseases of the respiratory system	11,552	91,594	7.9
K00-K08 - Disorders of teeth and supporting structures	1,519	3,950	2.6
K09-K14 - Other diseases of oral cavity, salivary glands and jaws	1,010	3,433	3.4
K20-K23 - Diseases of oesophagus	3,873	16,822	4.3
K25-K28 - Ulcer of stomach, duodenum and jejunum	5,918	34,627	5.9
K29-K31 - Dyspepsia and other diseases of stomach and duodenum	2,931	11,842	4.0
K50_K51 - Crohn's disease and ulcerative colitis	5,482	34,756	6.3
K52 - Other noninfective gastroenteritis and colitis	2,499	12,272	4.9
K56 - Paralytic ileus and intestinal obstruction without hernia	7,953	47,598	6.0
K60-K62 - Diseases of anus and rectum	4,198	13,891	3.3
K70 - Alcoholic liver disease	1,617	13,965	8.6
K71-K77 - Other diseases of liver	2,386	19,092	8.0
K80 - Cholelithiasis	16,264	59,530	3.7
K81-K83 - Other diseases of gallbladder and biliary tract	4,760	27,404	5.8
K85-K87 - Diseases of pancreas	5,929	40,395	6.8
K_OTH - Other diseases of the digestive system (remainder of K00-K93)	8,355	41,272	4.9
L00-L08 - Infections of the skin and subcutaneous tissue	4,773	25,470	5.3
L20-L45 - Dermatitis, eczema and papulosquamous disorders	1,378	7,674	5.6

Appendix Table 2
Hospital discharges, days, and average length of stay, by diagnosis, Sweden, 2009

Diagnosis	discharges	days	alos
L_OTH - Other diseases of the skin and subcutaneous tissue (remainder of L00-L99)	4,300	36,785	8.6
M16 - Coxarthrosis [arthrosis of hip]	14,316	78,393	5.5
M17 - Gonarthrosis [arthrosis of knee]	13,348	67,780	5.1
M23 - Internal derangement of knee	1,070	1,602	1.5
M30-M36 - Systemic connective tissue disorders	4,223	28,508	6.8
M40-M49 - Deforming dorsopathies and spondylopathies	10,735	74,180	6.9
M50_M51 - Cervical disc disorders, other intervertebral disc disorders	4,678	21,284	4.5
M53_M80-M99 - Other disorders of the musculoskeletal system and connective tissue	6,635	43,595	6.6
M54 - Dorsalgia	7,311	35,079	4.8
M60-M79 - Soft tissue disorders	8,705	30,610	3.5
N00-N16 - Glomerular and renal tubulo-interstitial diseases	10,567	48,370	4.6
N17-N19 - Renal failure	8,659	67,147	7.8
N20-N23 - Urolithiasis	6,330	18,436	2.9
N25-N39 - Other diseases of the urinary system	16,609	84,834	5.1
N40 - Hyperplasia of prostate	4,393	12,453	2.8
N41-N51 - Other diseases of male genital organs	2,023	5,174	2.6
N60-N64 - Disorders of breast	1,313	2,142	1.6
N70-N77 - Inflammatory diseases of female pelvic organs	1,543	4,389	2.8
N91-N95 - Menstrual, menopausal and other female genital conditions	2,330	5,059	2.2
N_OTH - Other diseases of the genitourinary system (remainder of N00-N99)	11,092	27,074	2.4
O04 - Medical abortion	1,698	2,708	1.6
O10-O48 - Complications of pregnancy predominantly in the antenatal period	11,312	33,490	3.0
O60-O75 - Complications of labour and delivery	1,533	4,259	2.8
O80 - Single spontaneous delivery	75,840	179,714	2.4
O81-O84 - Other delivery	27,458	107,858	3.9
O85-O92 - Complications predominantly related to the puerperium	1,447	4,148	2.9
P07 - Disorders related to short gestation and low birth weight, not elsewhere classified	5,581	120,690	21.6
P_OTH - Other conditions originating in the perinatal period (remainder of P00-P96)	9,080	45,597	5.0
Q - Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99)	9,657	56,609	5.9
R07 - Pain in throat and chest	26,202	44,130	1.7
R10 - Abdominal and pelvic pain	25,294	59,403	2.3
R_OTH - Other symptoms, signs and abnormal clinical and laboratory findings (remainder of R00-R99)	70,957	254,689	3.6
S06 - Intracranial injury	12,013	54,970	4.6
S72 - Fracture of femur	24,572	240,033	9.8

Appendix Table 2

Hospital discharges, days, and average length of stay, by diagnosis, Sweden, 2009

Diagnosis	discharges	days	alos
S82 - Fracture of lower leg, including ankle	11,414	59,962	5.3
S_T_OTH - Other and unspecified effects of external causes (remainder of S00-T98)	3,520	7,743	2.2
T20-T32 - Burns and corrosions	1,194	8,730	7.3
T36-T65 - Poisonings by drugs, medicaments and biological substances and toxic effects	8,137	16,304	2.0
T80-T88 - Complications of surgical and medical care, not elsewhere classified	18,542	123,271	6.6
UPRESPIR_OTH - Other diseases of upper respiratory tract (J30-J34, J36-J39)	4,499	9,325	2.1
Z30 - Contraceptive management	118	144	1.2
Z51 - Other medical care	12,399	82,860	6.7
Z_OTH - Other factors influencing health status and contact with health services (remainder of Z00-Z99)	26,970	195,449	7.2