The long-run impact of changes in prescription drug sales on mortality and hospital utilization in Belgium, 1998-2019

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Abstract

Objectives

We investigate the long-run impact of changes in prescription drug sales on mortality and hospital utilization in Belgium during the first two decades of the 21st century.

Methods

We analyze the correlation across diseases between changes in the drugs used to treat the disease and changes in mortality or hospital utilization from that disease. We employ two different measures of changes in the drugs used to treat a disease: changes in the *number* of drugs and changes in the mean *vintage* (Belgian authorization year) of drugs.

Results

The 1998-2018 increase in drug vintage is estimated to have reduced the number of years of life lost before ages 85, 75, and 65 in 2018 by about 401 thousand (30%), 237 thousand (32%), and 146 thousand (38%), respectively. The 1991-2010 increase in drug vintage is estimated to have reduced the number of hospital days and discharges in 2019 by 4.71 million (30%) and 501 thousand (22%), respectively.

Conclusions

Even if we ignore the reduction in hospital utilization attributable to changes in pharmaceutical consumption, a conservative estimate of the 2018 cost per life-year before age 85 gained is €11,324. We estimate that previous changes in pharmaceutical consumption reduced 2019 expenditure on inpatient curative and rehabilitative care by at least €5004 million, which is higher than total expenditure on prescribed medicines in 2019: €4893.7 million.

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Extended abstract

We investigate the long-run impact of changes in prescription drug sales on mortality and hospital utilization in Belgium during the first two decades of the 21st century, by analyzing the correlation across diseases between changes in the drugs used to treat the disease and changes in mortality or hospital utilization from that disease. This "difference-in-differences" approach controls for the effects of aggregate macroeconomic and demographic trends, to the extent that those trends have similar effects on mortality or hospital utilization from different diseases.

We employ two different measures of changes in the drugs used to treat a disease: changes in the *number* of drugs and changes in the mean *vintage* (Belgian authorization year) of drugs. These changes are not positively correlated across diseases with indicators of nonpharmaceutical medical innovation.

The 1998-2018 growth of the number of deaths and the number of years of life lost before ages 85, 75, and 65 is significantly inversely related across diseases to the growth in the number of drugs sold and to the change in the vintage of drugs sold. The 1998-2018 increase in the number of drugs sold is estimated to have reduced the number of years of life lost before ages 85, 75, and 65 in 2018 by about 264 thousand (22%), 147 thousand (23%), and 87 thousand (26%), respectively, and the 1998-2018 increase in drug vintage is estimated to have reduced the number of years of life lost before ages 85, 75, and 65 in 2018 by about 401 thousand (30%), 237 thousand (32%), and 146 thousand (38%), respectively.

Even if we ignore the reduction in hospital utilization attributable to changes in pharmaceutical consumption, a conservative estimate of the 2018 cost per life-year before age 85 gained is €11,324. This figure is 28% of Belgium's 2018 per capita income; authors writing on behalf of the WHO-CHOICE project suggested in 2005 that "interventions that avert one disability-adjusted life-year (DALY) for less than average per capita income for a given country or region are considered very cost–effective."

The 2000-2019 growth of the number of hospital days is highly significantly inversely related to both the growth of the number of drugs and the change in drug vintage 4-11 years earlier. The 1991-2010 increase in the number of drugs sold is estimated to have reduced the number of hospital days and discharges in 2019 by 3.75 million (26%) and 372 thousand (17%), respectively, and the 1991-2010 increase in drug vintage is estimated to have reduced the number of hospital days and discharges in 2019 by 4.71 million (30%) and 501 thousand (22%), respectively.

We estimate that previous changes in pharmaceutical consumption reduced 2019 expenditure on inpatient curative and rehabilitative care by between €5004 and €6283 million. Even the lower estimate of hospital cost reduction is higher than total expenditure on prescribed medicines in 2019: €4893.7 million. Our estimates imply that the long-run change in pharmaceutical consumption was cost-saving, i.e., that its net cost per life-year gained was negative.

Keywords: pharmaceutical; innovation; mortality; hospitalization; Belgium; cost-effectiveness

I. Introduction

During the last few decades, there have been substantial changes in the prescription drugs sold in Belgium. According to data provided by IQVIA, the number of drugs (WHO ATC5 chemical substances[1]) sold in Belgium increased from 1212 in 1989 to 1450 in 2019. 51% of the drugs sold in 1989 were not sold in 2019; 60% of the drugs sold in 2019 had not been sold in 1989. 25% of 1989 Defined Daily Doses (DDDs) were for drugs that were not sold in 2019; 51% of 2019 DDDs were for drugs that were not sold in 1989. The top 20 (ranked by DDD) antineoplastic and immunomodulating agents (ATC anatomical main group L) in 1989 and 2019 are shown in Appendix Table 1.[2]

The fact that there have been substantial changes in the prescription drug market is not surprising, since the pharmaceutical industry is one of the most research-intensive industries. In Europe in 2021, the pharmaceutical industry's ratio of R&D to sales (13.72%) was 3.46 times as high as it was for all industries (European Commission (2022)).

Many leading economists believe that economic growth is primarily driven by technological progress, which is generated by R&D investment. Jones (1998, pp. 89-90) argued that "technological progress is driven by research and development (R&D) in the advanced world." Jones (2002) presented a model in which long-run growth is driven by the discovery (via research effort) of new ideas throughout the world. His model built upon a large collection of previous research, including Romer (1990), Grossman and Helpman (1991), and Aghion and Howitt (1992), as well as earlier contributions by Phelps (1966), Shell (1966), Nordhaus (1969), and Simon (1986).

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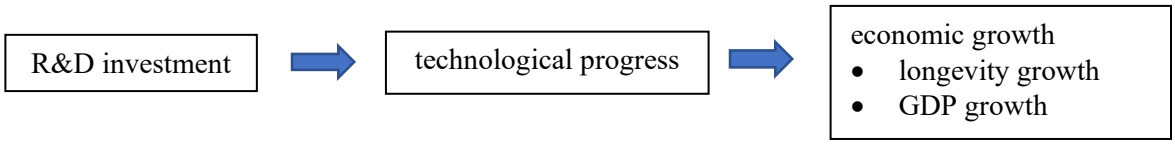
[1] See World Health Organization (2023a). In the WHO Anatomical Therapeutic Chemical (ATC) classification system, the active substances are classified in a hierarchy with five different levels. The system has fourteen main anatomical/pharmacological groups or 1st levels. Each ATC main group is divided into 2nd levels which could be either pharmacological or therapeutic groups. The 3rd and 4th levels are chemical, pharmacological or therapeutic subgroups and the 5th level is the chemical substance. The 2nd, 3rd and 4th levels are often used to identify pharmacological subgroups when that is considered more appropriate than therapeutic or chemical subgroups. 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)

[2] The number of antineoplastic and immunomodulating agents sold increased from 49 in 1989 to 202 in 2019.

Economists also recognize that mortality reduction is an important component of economic growth, broadly defined. Nordhaus (2003) argued that "to a first approximation, the economic value of increases in longevity in the last hundred years is about as large as the value of measured growth in non-health goods and services." Cutler, Deaton and Lleras-Muney (2006) concluded that "knowledge, science, and technology are the keys to any coherent explanation" of mortality.

In a nutshell:



The purpose of this study is to investigate the long-run impact of changes in prescription drug sales on mortality and hospital utilization in Belgium during the periods 1998-2018 and 2000-2019, respectively.[3] To perform this assessment, we will analyze the correlation across diseases between changes in the drugs used to treat the disease and changes in mortality or hospital utilization from that disease. This "difference-in-differences" approach controls for the effects of aggregate macroeconomic and demographic trends, to the extent that those trends have similar effects on mortality or hospital utilization from different diseases.[4]

We will measure changes in the drugs used to treat a disease in two different ways. One measure is the change in the *number* of drugs used to treat a disease.[5] Data on the number of drugs used to treat 6 diseases that were sold during the period 1999-2019 are shown in Figure 1. Similar numbers (between 31 and 38) of drugs were sold to treat the 6 diseases in 1999. The 1999-2019 change in the number of drugs sold—29 for diabetes, 14 for acute myocardial infarction, 1 for septicemia—varied considerably across diseases. We will test the hypothesis that the diseases for which there were larger percentage increases in the number of drugs sold had smaller percentage increases (or larger declines) in mortality and hospital utilization.

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[3] Due to the disruptive impact on public health of the Covid pandemic, which began in 2020, post-2019 data will not be included in our analysis. Also, post-2018 data on mortality by detailed cause are not yet available.

[4] Some of those trends—e.g., the increase, from 10.8% in 1997 to 15.9% in 2018, in the fraction of the population that was obese (self-reported)—may have increased mortality and hospital utilization, while others—e.g., the decline from, 25.5% in 1997 to 15.4% in 2018%, in the percentage of the adult population who are daily smokers—may have reduced them.

[5] Some models of economic growth (including those developed by Nobel laureate Paul Romer (see Jones (2019)) postulate that economic growth depends on the growth in the *number* of ideas (e.g., the *number* of drugs).

The second measure of the change in drug sales is the change in the mean *vintage* of drugs.[6] A drug's vintage will be measured as the first year in which that drug was authorized for sale in Belgium by the Agence Fédérale des Médicaments et des Produits de Santé. We hypothesize that, in general, newer (later vintage) drugs tend to be of higher quality (more effective) than older (earlier vintage) drugs.

The hypothesis that later vintage goods tend to be of higher quality than earlier vintage goods has been advocated by many economists since it was first formulated in the 1950s. Johansen (1959) developed a theoretical model of vintage capital in which there are technological improvements in capital in later vintages. Intriligator (1992, p. S77) said that "the newer capital is more productive than the older capital as a result of technological improvements in the later vintages." Bresnahan and Gordon (1996) said that "new goods are at the heart of economic progress." As noted by Jovanovic and Yatsenko (2012), in "the Spence–Dixit–Stiglitz tradition…new goods [are] of higher quality than old goods." Bohlman, Golder, and Debanjan (2002, p. 1177) said that "technology improves over time…As technology advances, later entrants can utilize a more recent and efficient vintage of technology than an earlier entrant who has committed to older technology…vintage effects will benefit later entrants…We refer to 'vintage effects' as any technology shift that results in lower costs for a later entrant, enabling it to achieve higher product quality." In 1987, the Royal Swedish Academy of Sciences awarded the Alfred Nobel Memorial Prize in Economic Sciences to Robert Solow for his contributions to the theory of economic growth. The Academy cited Solow's 1960 article, *Investment and Technical Progress,* in which he presented a

> new method of studying the role played by capital formation in economic growth. His basic assumption was that technical progress is "built into" machines and other capital goods and that this must be taken into account when making empirical measurements of the role played by capital. This idea then gave birth to the "vintage approach" (a similar idea was discussed by Leif Johansen in Norway at about the same time)…The most important aspect of Solow's article was not so much the empirical outcome, but the method of analyzing "vintage capital." Nowadays, the vintage capital concept has many other applications and is no longer solely employed in analyses of the factors underlying economic growth…The vintage approach has proved invaluable, both from the theoretical point of view and in applications such as the analysis of the development of industrial structures.

[6] The change in the number of drugs is very strongly positively correlated across diseases with the change in the mean vintage of drugs.

Data on the mean "vintage" (Belgian authorization year) of drugs sold during the period 1989-2019 are shown in Figure 2. Between 1989 and 2019, the weighted (by DDD) mean vintage of drugs sold in Belgium increased by 13.9 years, from 1975.4 to 1989.2. The average DDD consumed in 2019 had been authorized about 30 years earlier. The unweighted mean vintage increased by a similar amount: 13.2 years, from 1979.9 to 1993.1.[7] Data on the (unweighted[8]) mean vintage of drugs used to treat 5 diseases sold during the period 1999-2019 are shown in Figure 3. The vintages of drugs for the 5 diseases were very similar (about 1981.5) in 1999. During the next 20 years, the mean vintage of drugs for malignant neoplasm of larynx increased by 7.8 years, but there was no increase in the mean vintage of drugs for cholelithiasis and other disorders of gallbladder.

In the next section, we will describe the econometric models that we will estimate. In Section III, we will explain how the variables included in those models were constructed using data from a number of reliable sources. Estimates of the models will be presented in Section IV. Major implications of the estimates will be discussed in Section V. The final section provides a summary and conclusions.

II. Econometric model of mortality and hospital utilization

Our estimates of the effect of (current or lagged) attributes of drugs sold on mortality and hospital utilization will be based on the following model:

$$\ln(\text{outcome}_{dt}) = \beta_k \, \text{rx_measure}_{d,t-k} + \alpha_d + \delta_t + \varepsilon_{dt} \qquad (1)$$

where outcome_{dt} is one of the following variables:

n_deaths_{dt} = the number of deaths due to disease d in year t

yll85_{dt} = the number of years of life lost before age 85 due to disease d in year t

yll75_{dt} = the number of years of life lost before age 75 due to disease d in year t

[7] The fact that weighted vintage is lower than unweighted vintage indicates that there tend to be fewer DDDs of new drugs than of old drugs.

[8] We cannot compute the weighted (by DDD) vintage of drugs for a disease. Many drugs are used to treat multiple diseases. We have data on total DDDs of each drug in each year, but data on DDDs by drug, disease, and year are not available. Although we cannot compute utilization-weighted vintage by *disease* and year, we can compute utilization-weighted (and unweighted) vintage by *country* and year for 41 countries. Both the 2017 levels of, and long-run (2007–2017) changes in, weighted and unweighted vintage are significantly positively correlated across countries.

$yll65_{dt}$ = the number of years of life lost before age 65 due to disease d in year t[9]

$hosp_days_{dt}$ = the total number of hospital days due to disease d in year t

$discharges_{dt}$ = the number of hospital discharges due to disease d in year t

los_{dt} = the average length (in days) of hospital discharges due to disease d in year t

and $rx_measure_{d,t-k}$ is one of the following variables:

$\ln(n_drug_{d,t-k})$ = the log of the number of WHO ATC5 chemical substances used to treat disease d sold in year t-k

$vintage_{d,t-k}$ = the (unweighted) mean vintage (Belgian authorization year) of WHO ATC5 chemical substances used to treat disease d sold in year t-k

$n_drug_{d,t-k}$ is computed as follows:

$$n_drug_{d,t-k} = \sum_s treat_{sd}\ sold_{s,t-k}$$

where

$treat_{sd}$ = 1 if chemical substance s is used to treat (indicated for) disease d[10]
= 0 if chemical substance s is not used to treat (indicated for) disease d

$sold_{s,t-k}$ = 1 if chemical substance s was sold in year t-k
= 0 if chemical substance s was not sold in year t-k

$vintage_{d,t-k}$ is computed as follows:

$$vintage_{d,t-k} = \sum_s treat_{sd}\ sold_{s,t-k}\ year_auth_s \ / \ \sum_s treat_{sd}\ sold_{s,t-k}$$

where

$year_auth_s$ = the year in which chemical substance s was first authorized in Belgium.

In eq. (1), α_d is a fixed effect for disease d, and δ_t is a fixed effect for year t. The year fixed effects (δ_t's) in eq. (1) control for the effects of changes in aggregate demographic and macroeconomic variables (e.g. population size and age structure, GDP, educational attainment),

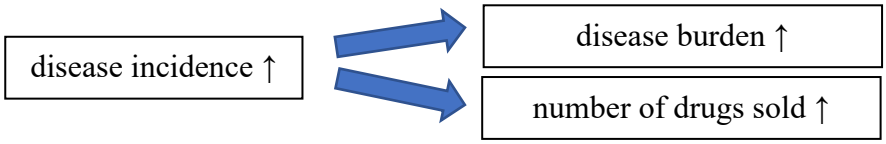
[9] The U.S. CDC's WISQARS Years of Potential Life Lost (YPLL) Report website permits one to specify age thresholds of 65, 70, 75, 80, and 85. The World Health Organization has used YPLL to measure disease burden in its Global Burden of Disease (GBD) and Global Health Estimates (GHE) reports for many years. In the 2010 GBD, the WHO used an age threshold of 86.01 years for all persons. In the current GHE, the WHO uses an age threshold of 91.93 years for all persons.

[10] Many drugs have multiple indications: 50% of drugs have 2 or more indications (causes of disease in the WHO Global Health Estimates disease classification), and 7% of drugs have 5 or more indications.

to the extent that those variables have similar effects on mortality and hospital utilization from different diseases.

Eq. (1) allows the effect of the number or mean vintage of drugs sold on mortality and hospital utilization to be subject to a lag. Some drugs may have to be utilized for several years to have their maximum impact those outcomes. We will present estimates of mortality models with lags of 0-5 years, and of hospital utilization models with lags of 0-11 years.

$rx_measure_{d,t-k}$ is the only disease-specific, time-varying regressor in eq. (1). If the data were available, we would control for disease incidence. Failure to control for incidence is unlikely to result in overestimation of the magnitude of β_k; exclusion of incidence may even result in *underestimation* of the magnitude of β_k. Higher disease incidence is likely to result in both higher disease burden and a larger number of drugs sold:



Previous studies (Acemoglu and Linn (2004), Danzon et al (2005)) have shown that both innovation (the number of drugs developed) and diffusion (the number of drugs launched in a country) depend on *market size*.

Annual mortality data are available for the years 1998-2018. From eq. (1) (a model of the *level* of an outcome), we can derive the following model of the long-run (1998-2018) *growth* of a mortality outcome:

$$\Delta\ln(outcome_d) = \beta_k \, \Delta rx_measure_k_d + \delta' + \varepsilon'_d \qquad (2)$$

where

$\Delta\ln(outcome_d)$ = $\ln(outcome_{d,2018}) - \ln(outcome_{d,1998})$ = the log-change from 1998 to 2018 of a mortality outcome from disease d

$\Delta rx_measure_k_d$ = $rx_measure_{d,2018-k} - rx_measure_{d,1998-k}$ = the change from 1998-k to 2018-k in the rx_measure of disease d

δ' = $\delta_{2018} - \delta_{1998}$

ε'_d = $\varepsilon_{d,2018} - \varepsilon_{d,1998}$

We will estimate eq. (2) by weighted least squares, weighting by $(outcome_{d,1998} + outcome_{d,2018})/2$. The analysis will be performed on about 70 diseases included in the U.S.

National Center for Health Statistics List of 113 Selected Causes of Death (New Jersey Department of Health (2023)). We exclude deaths from external causes.

The estimate of δ' in eq. (2) is an estimate of mortality growth in the *absence* of changes in drug sales, i.e., if mean(Δrx_measure_k_d) = 0. This can be compared with mortality growth in the *presence* of changes in drug sales: mean(Δln(outcome$_d$)).

The validity of estimates of the parameters of eq. (2) is predicated on the assumption of "parallel trends", i.e., on the assumption that outcomes of diseases with different values of Δrx_measure_k_d were changing at similar rates prior to 1998. To assess the validity of this assumption, we will also estimate 2 versions of the following model, one excluding and the other including (ln(outcome$_{d,2003}$) - ln(outcome$_{d,1998}$)):

$$\ln(\text{outcome}_{d,2018}) - \ln(\text{outcome}_{d,2003}) = \beta_k (\text{vintage}_{d,2018-k} - \text{vintage}_{d,2003-k}) + \gamma (\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})) + \varepsilon_d \quad (3)$$

The finding that controlling for 1998-2003 mortality growth has little effect on estimates of β_k in eq. (3) would provide support for the assumption of parallel trends.

Annual hospital utilization data are available for the years 2000-2019. We will estimate the following model of the long-run (2000-2019) growth of a hospital outcome:

$$\Delta\ln(\text{outcome}_d) = \beta_k \Delta\text{rx_measure_}k_d + \delta' + \varepsilon'_d \quad (4)$$

where

$\Delta\ln(\text{outcome}_d)$ = $\ln(\text{outcome}_{d,2019}) - \ln(\text{outcome}_{d,2000})$ = the log-change from 2000 to 2019 of a hospital outcome from disease d

Δrx_measure_k_d = $\text{rx_measure}_{d,2019-k} - \text{rx_measure}_{d,2000-k}$ = the change from 2000-k to 2019-k in the rx_measure of disease d

$\delta' = \delta_{2019} - \delta_{2000}$

$\varepsilon'_d = \varepsilon_{d,2019} - \varepsilon_{d,2000}$

We will estimate eq. (4) by weighted least squares. For the first measure of hospital utilization, the weight will be ($\text{hosp_days}_{d,2000} + \text{hosp_days}_{d,2019}$)/2. For the second and third measures, the weight will be ($\text{discharges}_{d,2000} + \text{discharges}_{d,2019}$)/2. The analysis of hospital outcomes will be performed on about 115 diseases included in the OECD Health Statistics database.

The long-run change in the number or mean vintage of chemical substances sold (Δrx_measure_k_d) might be correlated across diseases with other changes in disease treatment. Belgian data on treatment methods, by disease and year, are not available. However, U.S. data on methods of treatment by office-based medical providers, by disease and year, are available from U.S. Medical Expenditure Panel Survey Office-Based Medical Provider Visits Event Files (Agency for Healthcare Research and Quality (2023)). The 1998 and 2015 files contain records of 104,740 and 172,388 patient visits, respectively. Each record indicates the patient's diagnosis (coded by modified clinical classification code (CCS)), and whether the patient received each of the following: lab tests, a sonogram or ultrasound, x-rays, a mammogram, an mri/ctscan, an EKG or ECG, an EEG, a vaccination, anesthesia, other diagnostic tests or exams, or any of them. The fraction of visits in which at least one of those treatments was performed increased from 32% in 1998 to 40% in 2015. We computed the 1998-2015 change in the fraction of visits for each disease (157 CCS codes) in which *any* of those procedures were performed: Δany_procedure%$_{CCS}$ = any_ procedure%$_{CCS,2015}$ - any_ procedure%$_{CCS,1998}$, where any_ procedure%$_{CCS,t}$ = the fraction of visits with patient diagnosis CCS in year t in which any procedure was performed. We also computed the 1998-2015 change in the log of the number of and mean vintage of drugs sold using this disease classification: Δrx_measure_0$_{CCS}$ = rx_measure_0$_{CCS,2015}$ – rx_measure_0$_{CCS,1998}$. Then we estimated the following simple regression by weighted least-squares, weighting by the mean number of patient visits in 1998 and 2015: Δany_ procedure%$_{CCS}$ = $\alpha + \pi$ Δrx_measure_0$_{CCS}$ + ε. When Δrx_measure_0$_{CCS}$ = Δln(n_drug$_{CCS,t}$), the estimate of π (= -.117; t-value = -2.95; p-value = 0.0036). When Δrx_measure_0$_{CCS}$ = Δvintage$_{CCS,t}$, the estimate of π (= -.0066; t-value = -2.79; p-value = 0.0059). Diseases for which there were larger 1998-2015 increases in the number and vintage of drugs sold had significantly *smaller* 1998-2015 increases in the fraction of U.S. office-based medical provider visits in which any procedure was performed. This suggests that, to the extent that use of those procedures reduces mortality and hospital utilization, failure to control for them may bias estimates of β_k in eqs. (2) and (3) towards zero.

III. Data sources

Pharmaceutical sales data. Data on the number of DDDs (if any) of drugs sold in each year (1989-2019) were provided by IQVIA.

Drug indications. Data on the approved indications of each drug ($treat_{sd}$) were obtained by combining data from two sources. The first source is the Thériaque database, produced by the Centre National Hospitalier d'Information sur le Médicament (2023). This database contains information on over 30,000 drug products sold in France. For each product, the database provides (1) the WHO ATC code(s) of the substance(s) contained in the product, and (2) the ICD-10 codes of the product's approved indications. This enabled us to compute the approved indications of each ATC code.

The second source is the Medication Reference Terminology (MED-RT) database produced by the U.S. Department of Veterans Affairs, Veterans Health Administration (2023). This database provides lists of diseases that each drug "may treat."

Neither of these databases is complete. Thériaque provides information about 2552 ATC codes, 1211 of which are not included in MED-RT. MED-RT provides information about 2156 ATC codes, 815 of which are not included in Thériaque. Information about 1341 ATC codes is available from both sources. We considered drug s to have indication d ($treat_{sd} = 1$) if either database said that was the case.

Drug vintage. Data on the first year in which each drug was authorized for sale in Belgium was obtained from the Agence Fédérale des Médicaments et des Produits de Santé (2023).

Mortality and population data were obtained from the WHO Mortality Database (World Health Organization (2023b)).

Hospital utilization data were obtained from the OECD Health Statistics database (OECD (2023a)). The disease classification is the International Shortlist for Hospital Morbidity Tabulation (OECD (2023b)).

Aggregate mortality and population data for 1998 and 2018 and aggregate hospital utilization data for 2000 and 2019 are shown in Appendix Table 2.

Appendix Table 3 contains a subset of the data used in the mortality analysis. Appendix Table 4 contains a subset of the data used in the hospital utilization analysis.

IV. Estimates of models of mortality and hospital utilization

A. Mortality growth estimates

Estimates of β_k from eq. (2) for mortality outcomes are presented in Table 1 and plotted in Figure 4. Each estimate shown is from a separate regression. In rows 1-6 of the table, the dependent variable is the 1998-2018 change in the log of the number of deaths. The assumed lag from rx_measure to outcome ranges between 0 years (row 1) to 5 years (row 6). The columns on the left in Table 1 and the charts on the left in Figure 4 show estimates when $rx_measure_{d,t-k} = \ln(n_drug_{d,t-k})$. The columns and charts on the right show estimates when $rx_measure_{d,t-k} = vintage_{d,t-k}$.

The estimates in rows 1-6 indicate that the 1998-2018 growth in the number of deaths is significantly inversely related across diseases to the growth in the number of drugs sold 0-2 years earlier, and to the change in the vintage of drugs sold 0-1 years earlier. It is most significantly inversely related to the contemporaneous (k = 0) changes in both regressors. The estimates in row 1 indicate that a 10% increase in the number of drugs is associated with a 9.4% reduction in the number of deaths, and that a one-year increase in mean drug vintage is associated with a 7.7% reduction in the number of deaths.

In rows 7-12 of the table, the dependent variable is the 1998-2018 change in the log of the number of years of life lost before age 85 (YLL85). The 1998-2018 growth in YLL85 is significantly inversely related across diseases to the contemporaneous growth in the number of drugs sold, and to the change in the vintage of drugs sold 0-1 years earlier.

In rows 13-18 of the table, the dependent variable is the 1998-2018 change in the log of the number of years of life lost before age 75 (YLL75). The 1998-2018 growth in YLL75 is significantly inversely related across diseases to the growth in the number of drugs sold 0-2 years earlier, and to the change in the vintage of drugs sold 0-1 years earlier. It is most significantly inversely related to the contemporaneous (k = 0) changes in both regressors.

In rows 19-24 of the table, the dependent variable is the 1998-2018 change in the log of the number of years of life lost before age 65 (YLL65). The 1998-2018 growth in YLL65 is significantly inversely related across diseases to the growth in the number of drugs sold 0-5 years earlier, and to the change in the vintage of drugs sold 0-3 years earlier.

As discussed above, the estimate of δ' in eq. (2) is an estimate of mortality growth in the *absence* of changes in drug sales, i.e., if mean(Δrx_measure_k_d) = 0. This can be compared with mortality growth in the *presence* of changes in drug sales: mean(Δln(outcome$_d$)). These calculations, based on estimates where k = 0 (no lag), are shown in Figure 5.

Panel A of Figure 5 shows the calculations when the outcome measure is the number of deaths. The actual 1998-2018 decline in the number of deaths per 100,000 population was 6.0% (this decline is not statistically significantly different from zero). The estimates in row 1 of Table 1 indicate that, if the number of drugs sold had not increased between 1998 and 2018, the number of deaths per 100,000 population would have increased by 35.4%, and that if the vintage of drugs sold had not increased between 1998 and 2018, the number of deaths per 100,000 population would have increased by 62.6%. We don't think those estimates are implausible: the population by age figures in Appendix Table 2 indicate that the fraction of the population over age 74 increased from 6.9% to 8.9%, and the fraction of the population over age 84 increased from 1.8% to 2.8%.

Panel B of Figure 5 shows the calculations when the outcome measure is YLL85. The number of years of life lost before age 85 per 100,000 population below age 85 (POP_LT_85) declined by 27.7%. The estimates in row 7 of Table 1 indicate that, if the number of drugs sold had not increased between 1998 and 2018, YLL85/POP_LT_85 would have declined by only 7.8%, and that if the vintage of drugs sold had not increased, YLL85/POP_LT_85 would have increased by 2.5%, but neither of those estimates are significantly different from zero.

Panel C of Figure 5 shows the calculations when the outcome measure is YLL75. The number of years of life lost before age 75 per 100,000 population below age 85 (POP_LT_75) declined by 26.3%. The estimates in row 13 of Table 1 indicate that, if the number of drugs sold had not increased between 1998 and 2018, YLL75/POP_LT_75 would have declined by only 4.4%, and that if the vintage of drugs sold had not increased, YLL75/POP_LT_75 would have increased by 8.9%, but neither of those estimates are significantly different from zero.

Panel D of Figure 5 shows the calculations when the outcome measure is YLL65. The number of years of life lost before age 65 per 100,000 population below age 85 (POP_LT_65) declined by 29.0%. The estimates in row 19 of Table 1 indicate that, if the number of drugs sold had not increased between 1998 and 2018, YLL65/POP_LT_65 would have declined by only

3.7%, and that if the vintage of drugs sold had not increased, YLL65/POP_LT_65 would have increased by 13.6%, but neither of those estimates are significantly different from zero.

As discussed above, the validity of these estimates is predicated on the assumption of "parallel trends", and that assumption can be assessed by investigating whether estimates of β_k in the model of 2003-2018 mortality growth (eq. (3)) are sensitive to whether or not we control for 1998-2003 mortality growth. Estimates of two versions of eq. (3) are presented in Appendix Table 5. The estimates indicate that controlling for 1998-2003 mortality growth has little effect on estimates of β_k in eq. (3), which provides support for the assumption of parallel trends.

B. Hospital utilization growth estimates

Estimates of β_k from eq. (4) for hospital utilization outcomes are presented in Table 2 and plotted in Figure 6. Each estimate shown is from a separate regression. In rows 1-12 of the table, the dependent variable is the 2000-2019 change in the log of the number of hospital days. The assumed lag from rx_measure to outcome ranges between 0 years (row 1) to 11 years (row 12). The columns on the left in Table 2 and the charts on the left in Figure 6 show estimates when $rx_measure_{d,t-k} = \ln(n_drug_{d,t-k})$. The columns and charts on the right show estimates when $rx_measure_{d,t-k} = vintage_{d,t-k}$.

The estimates in rows 1-12 of Table 2 indicate that the 2000-2019 change in the log of the number of hospital days is not significantly related to either the growth in the number of drugs or the change in drug vintage 0-3 years earlier, but it is highly significantly inversely related to both the growth in the number of drugs and the change in drug vintage 4-11 years earlier. The estimates in row 10 indicate that a 10% increase in the number of drugs is associated with an 8.0% reduction in the number of hospital days 9 years later, and that a one-year increase in mean drug vintage is associated with a 6.4% reduction in the number of hospital days 9 years later.

The estimates in rows 13-24 of Table 2 indicate that the 2000-2019 change in the log of the number of hospital discharges is not significantly related to the growth in the number of

drugs 0-11 years earlier; it is significantly inversely related to the change in drug vintage 4-11 years earlier.[11]

The estimates in rows 25-36 of Table 2 indicate that the 2000-2019 change in the log of the average length of hospital stays is significantly inversely related to the growth in the number of drugs 2-11 years earlier, and significantly inversely related to the change in drug vintage 1-11 years earlier.

Comparisons of hospital utilization growth in the presence of changes in drug sales to hospital utilization growth in the absence of changes in drug sales, based on estimates where k = 9, are shown in Figure 7. As shown in Panel A, between 2000 and 2019 the number of hospital days per 100,000 population declined by 24.6%. The estimates in row 10 of Table 2 imply that if the number of drugs had not increased between 1991 and 2010, the number of hospital days per 100,000 population would have increased by 1.4% between 2000 and 2019, and that if the mean vintage of drugs had not increased between 1991 and 2010, the number of hospital days per 100,000 population would have increased by 8.0% between 2000 and 2019, but neither of those estimates are statistically significantly different from zero.

As shown in Panel B, between 2000 and 2019 the number of hospital discharges per 100,000 population declined by 2.4%. The estimates in row 22 of Table 2 imply that if the number of drugs had not increased between 1991 and 2010, the number of hospital discharges per 100,000 population would have increased by 17.5% between 2000 and 2019 (although this estimate is not statistically significantly different from zero), and that if the mean vintage of drugs had not increased between 1991 and 2010, the number of hospital discharges per 100,000 population would have increased by 24.3% between 2000 and 2019.

As shown in Panel C, between 2000 and 2019 the average length of hospital stays declined by 26.9%. The estimates in row 34 of Table 2 imply that if the number of drugs had not increased between 1991 and 2010, the average length of hospital stays would have declined by only 15.4% between 2000 and 2019, and that if the mean vintage of drugs had not increased between 1991 and 2010, the average length of hospital stays would have declined by only 16.2% between 2000 and 2019.

[11] It is significantly *positively* related to the contemporaneous change in drug vintage, which is surprising.

V. Discussion

The estimates shown in Figures 5 and 7 indicate the estimated effects of changes in pharmaceutical consumption on the long-run (1998-2018 or 2000-2019) *growth* in mortality and hospital utilization. Now we will use these estimates to calculate the percentage and absolute differences in the *levels* of mortality in 2018 and hospital utilization in 2019 attributable to changes in pharmaceutical consumption. These calculations are shown in Table 3.

The number of deaths per 100,000 population was 1023 in 1998. It declined, by 6.0%, to 961 by 2018. The estimates in Figure 5 imply that if n_drug had remained constant, the number of deaths per 100,000 population would have increased by 35.4%, to 1385, in 2018, and the number of deaths per 100,000 population would have been 44% (= (1 + 35.4%)/(1 – 6.0%)) higher. If vintage had remained constant, the number of deaths per 100,000 population in 2018 would have been 73% (= (1 + 62.6%)/(1 – 6.0%)) higher. As shown in column 1 of Table 3, the 1998-2018 increase in n_drug is estimated to have reduced the number of deaths in 2018 by 48,379 (31%), and the 1998-2018 increase in vintage is estimated to have reduced the number of deaths in 2018 by 80,235 (42%).

As shown in columns 2-4 of Table 3, the 1998-2018 increase in n_drug is estimated to have reduced the number of years of life lost before ages 85, 75, and 65 in 2018 by about 264 thousand (22%), 147 thousand (23%), and 87 thousand (26%), respectively, and the 1998-2018 increase in vintage is estimated to have reduced the number of years of life lost before ages 85, 75, and 65 in 2018 by about 401 thousand (30%), 237 thousand (32%), and 146 thousand (38%), respectively.

Data from the marketing research firm IQVIA and from Agence Fédérale des Médicaments et des Produits de Santé (2023) indicate that 2018 expenditure on drugs that were authorized during the period 1998-2018 was €2.99 billion (62% of total drug expenditure). This implies that, even if we ignore the reduction in hospital utilization attributable to changes in pharmaceutical consumption, a conservative estimate of the cost per life-year before age 85 gained is €11,324 (= €2.99 billion / 263,746 life-years). As noted by Bertram et al (2016), authors writing on behalf of the WHO's Choosing Interventions that are Cost–Effective project (WHO-CHOICE) suggested in 2005 that "interventions that avert one disability-adjusted life-year (DALY) for less than average per capita income for a given country or region are

considered very cost–effective; interventions that cost less than three times average per capita income per DALY averted are still considered cost–effective." Belgium's per capita GDP in 2018 was €40,260.

Moreover, as shown in columns 5-6 of Table 3, the 1991-2010 increase in n_drug is estimated to have reduced the number of hospital days and discharges in 2019 by 3.75 million (26%) and 372 thousand (17%), respectively, and the 1991-2010 increase in drug vintage is estimated to have reduced the number of hospital days and discharges in 2019 by 4.71 million (30%) and 501 thousand (22%), respectively.

We estimate that, in the absence of previous changes in pharmaceutical consumption, the number of hospital days in 2019 would have been 35-43% higher than it actually was. It is reasonable to assume that expenditure on inpatient curative and rehabilitative care would have increased proportionately, by 35-43%. According to the OECD, expenditure on inpatient curative and rehabilitative care in 2019 was €14,499.3 million. Hence, we estimate that previous changes in pharmaceutical consumption reduced 2019 expenditure on inpatient curative and rehabilitative care by an amount between €5004 million (= 35% * €14,499.3 million) and €6283 million (= 43% * €14,499.3 million). Even the lower estimate of hospital cost reduction is higher than total expenditure on prescribed medicines in 2019: €4893.7 million.[12]

VI. Summary and conclusions

We have investigated the long-run impact of changes in prescription drug sales on mortality and hospital utilization in Belgium during the first two decades of the 21st century, by analyzing the correlation across diseases between changes in the drugs used to treat the disease and changes in mortality or hospital utilization from that disease. This "difference-in-differences" approach controls for the effects of aggregate macroeconomic and demographic

[12] Using data on 67 medical conditions in 15 OECD Countries, Lichtenberg (2019) showed that the number of hospital discharges and days of care in 2015 were significantly inversely related to the number of drugs launched during 1982–2005, and that the estimated reduction in 2015 hospital expenditure that may have been attributable to post-1981 drug launches was 5.3 times as large as 2015 expenditure on those drugs. And using data on about 200 diseases in the U.S., Lichtenberg (2023) estimated that the drugs approved during 1984-1997 reduced 2014 hospital cost by at least $45 billion. IQVIA data indicate that gross (before rebates) expenditure in 2014 on drugs approved during 1984-1997 was $42 billion.

trends, to the extent that those trends have similar effects on mortality or hospital utilization from different diseases.

We employed two different measures of changes in the drugs used to treat a disease: changes in the *number* of drugs and changes in the mean *vintage* (Belgian authorization year) of drugs. These changes are not positively correlated across diseases with indicators of nonpharmaceutical medical innovation.

The 1998-2018 growth of the number of deaths and the number of years of life lost before ages 85, 75, and 65 is significantly inversely related across diseases to the growth in the number of drugs sold and to the change in the vintage of drugs sold. The 1998-2018 increase in the number of drugs sold is estimated to have reduced the number of years of life lost before ages 85, 75, and 65 in 2018 by about 264 thousand (22%), 147 thousand (23%), and 87 thousand (26%), respectively, and the 1998-2018 increase in drug vintage is estimated to have reduced the number of years of life lost before ages 85, 75, and 65 in 2018 by about 401 thousand (30%), 237 thousand (32%), and 146 thousand (38%), respectively. Even if we ignore the reduction in hospital utilization attributable to changes in pharmaceutical consumption, a conservative estimate of the 2018 cost per life-year before age 85 gained is €11,324. This figure is 28% of Belgium's 2018 per capita income; authors writing on behalf of the WHO-CHOICE project suggested in 2005 that "interventions that avert one disability-adjusted life-year (DALY) for less than average per capita income for a given country or region are considered very cost–effective."

Moreover, the 2000-2019 growth of the number of hospital days is highly significantly inversely related to both the growth of the number of drugs and the change in drug vintage 4-11 years earlier. The 1991-2010 increase in the number of drugs sold is estimated to have reduced the number of hospital days and discharges in 2019 by 3.75 million (26%) and 372 thousand (17%), respectively, and the 1991-2010 increase in drug vintage is estimated to have reduced the number of hospital days and discharges in 2019 by 4.71 million (30%) and 501 thousand (22%), respectively.

We estimated that previous changes in pharmaceutical consumption reduced 2019 expenditure on inpatient curative and rehabilitative care by between €5004 and €6283 million. Even the lower estimate of hospital cost reduction is higher than total expenditure on prescribed medicines in 2019: €4893.7 million (OECD (2023a)). Our estimates imply that the long-run

change in pharmaceutical consumption was *cost-saving*, i.e., that its net cost per life-year gained was *negative*.

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Figure 1
Number of drugs used to treat 6 diseases sold, 1999-2019

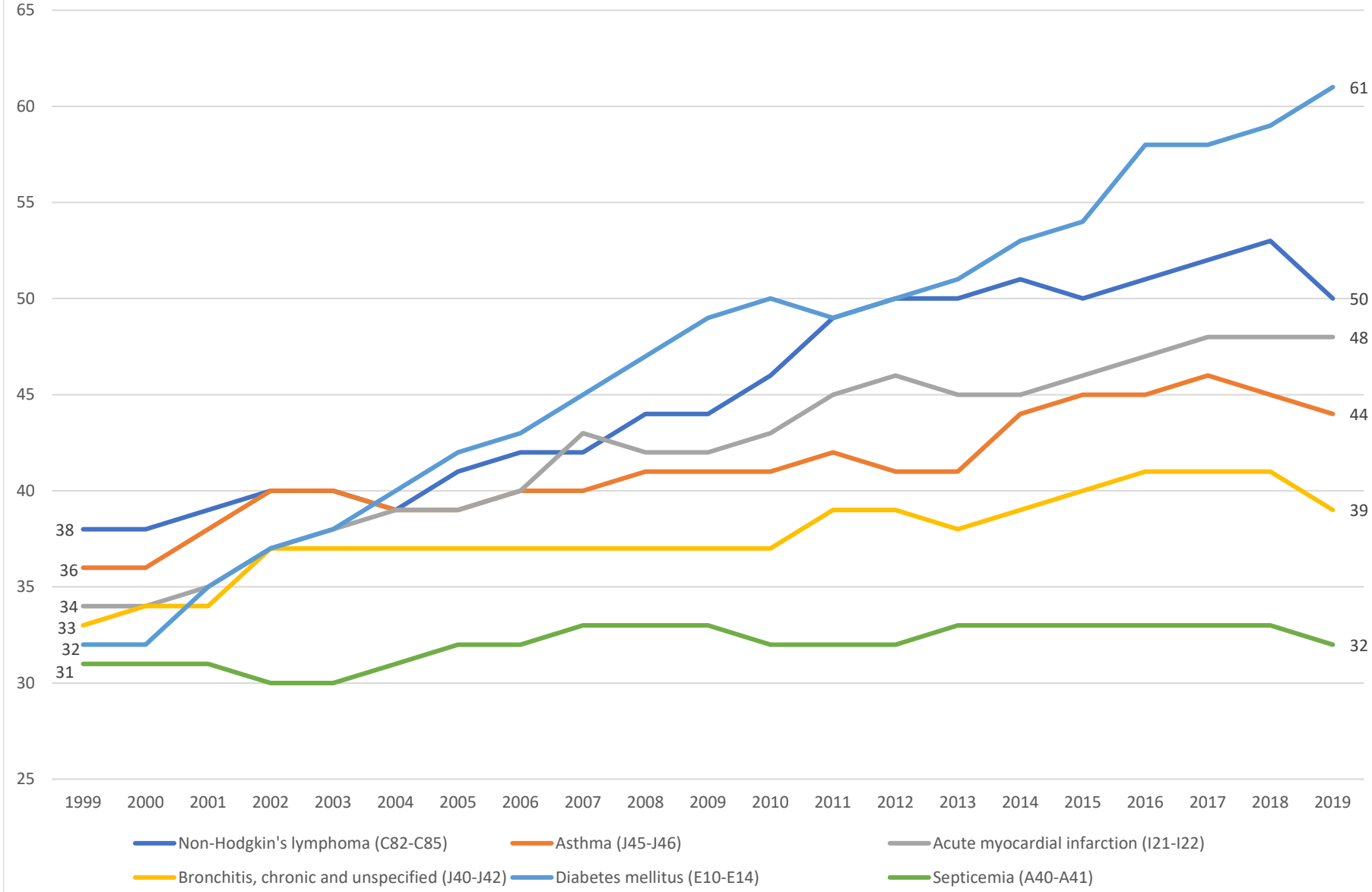


Figure 2
Mean vintage (Belgian authorization year) of drugs sold, 1989-2019

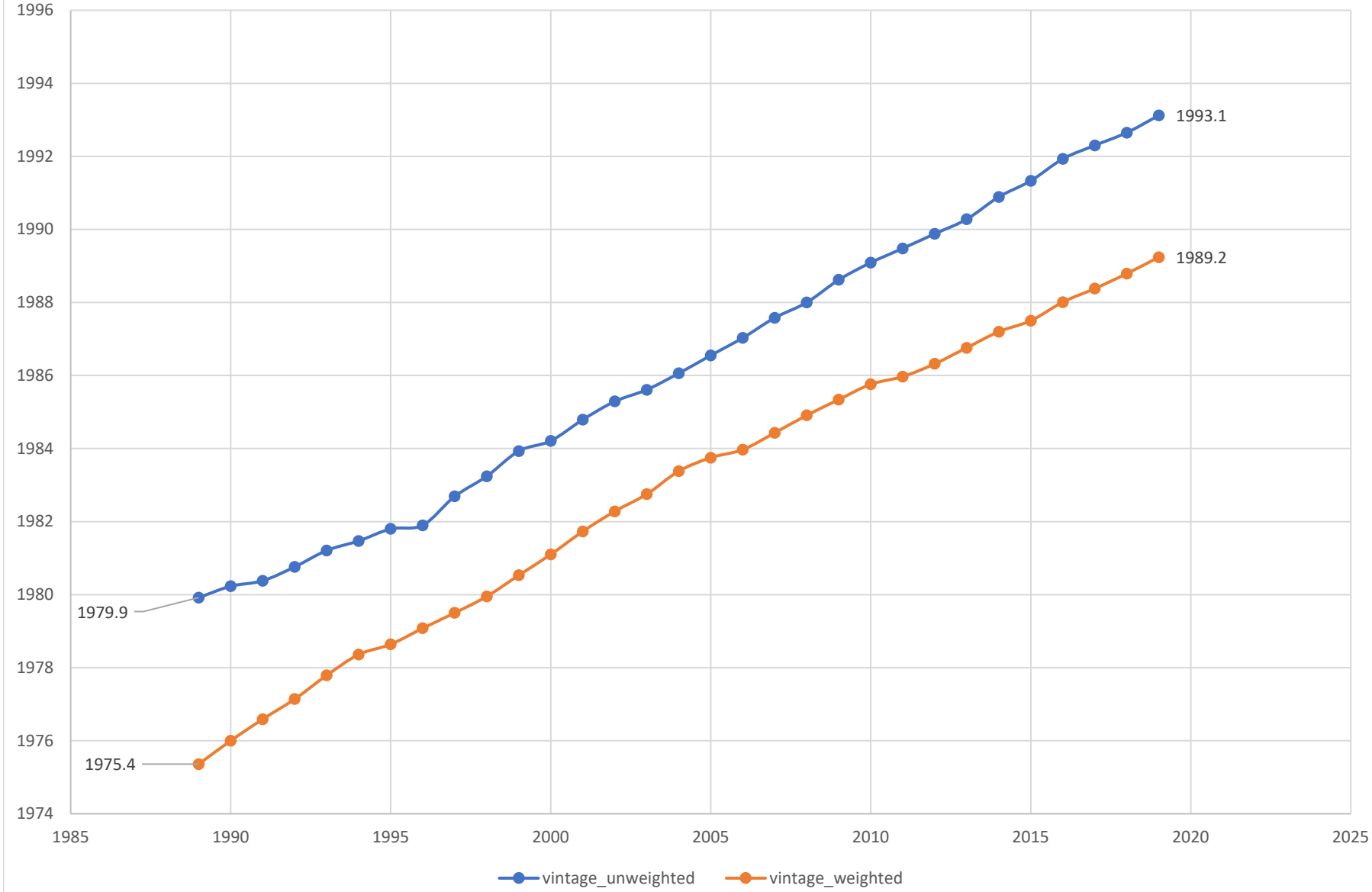


Figure 3
(Unweighted) mean vintage (Belgian authorization year) of drugs used to treat 5 diseases sold, 1999-2019

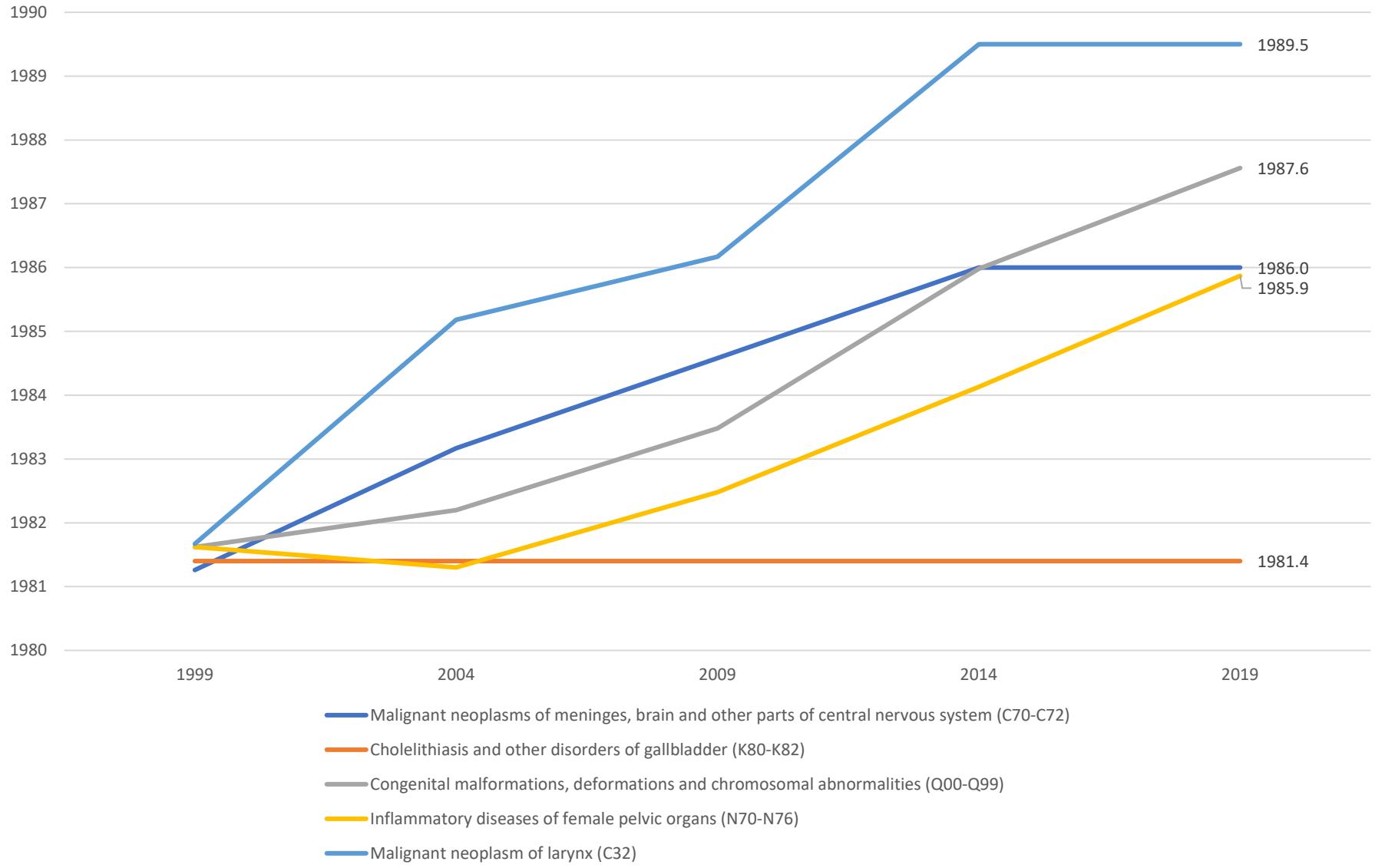
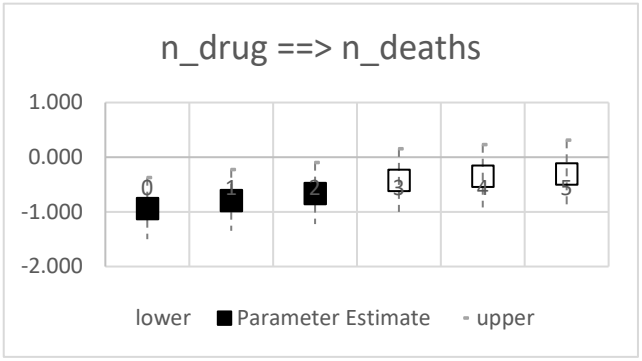
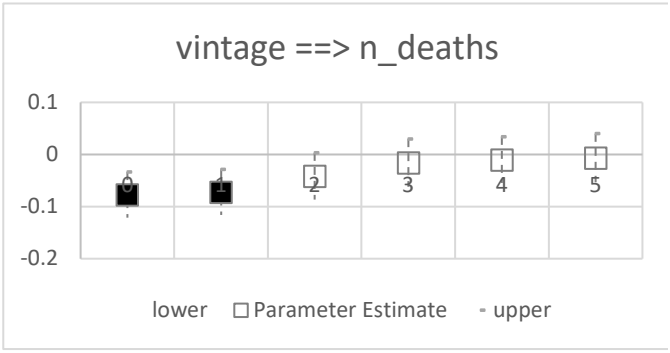


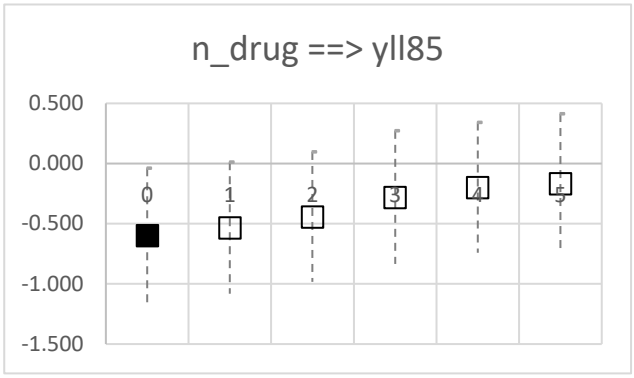
Figure 4

Estimates of β_k from eq. (2) for mortality outcomes:

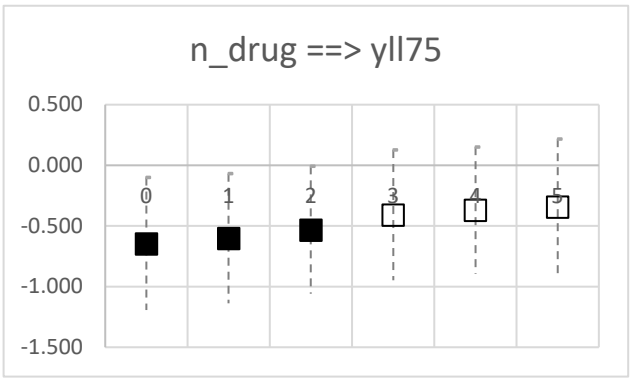
$$\ln(\text{outcome}_{d,2018}) - \ln(\text{outcome}_{d,1998}) = \beta_k\,(\text{rx_measure}_{d,2018\text{-}k} - \text{rx_measure}_{d,1998\text{-}k}) + \delta' + \varepsilon'_d$$



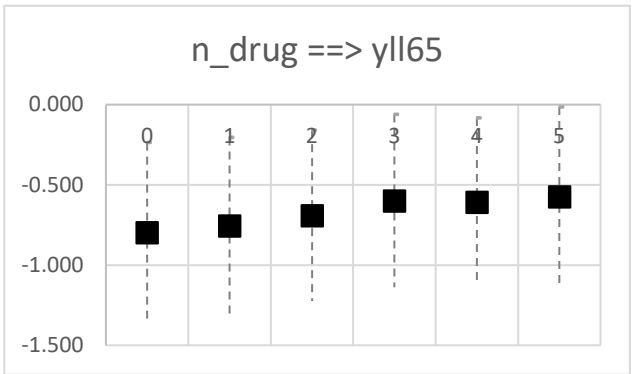










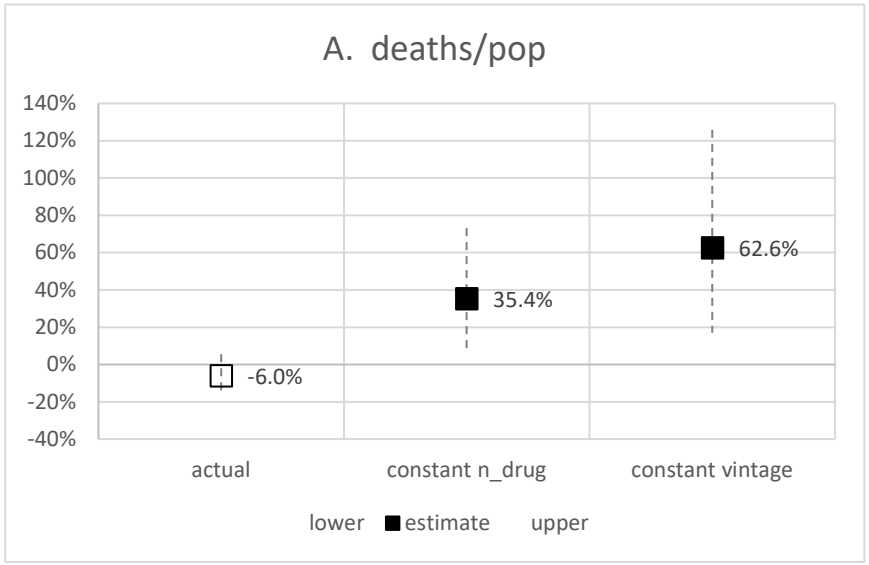


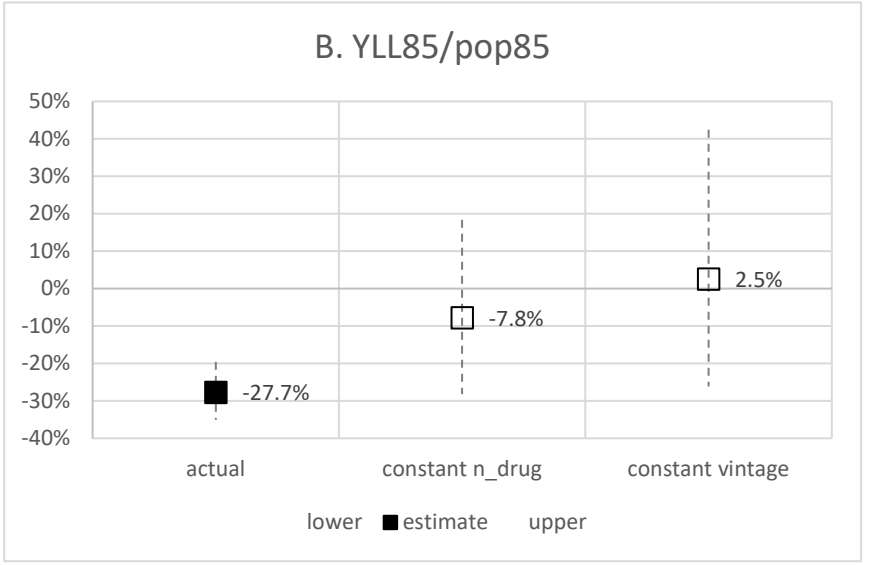


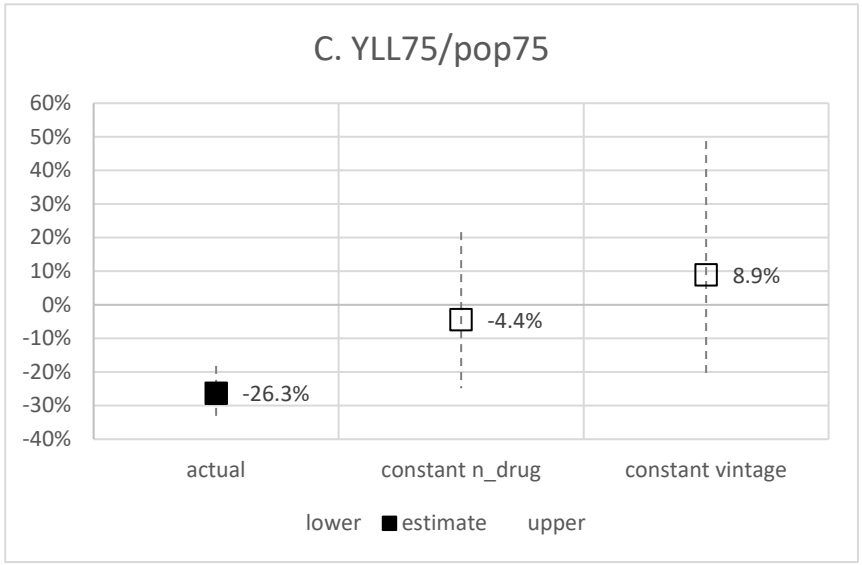
Solid squares denote significant (p-value < .05) estimates; hollow squares denote insignificant estimates.

Figure 5

1998-2018 % increase in mortality rates: actual versus estimated, in absence of change in pharmaceutical consumption







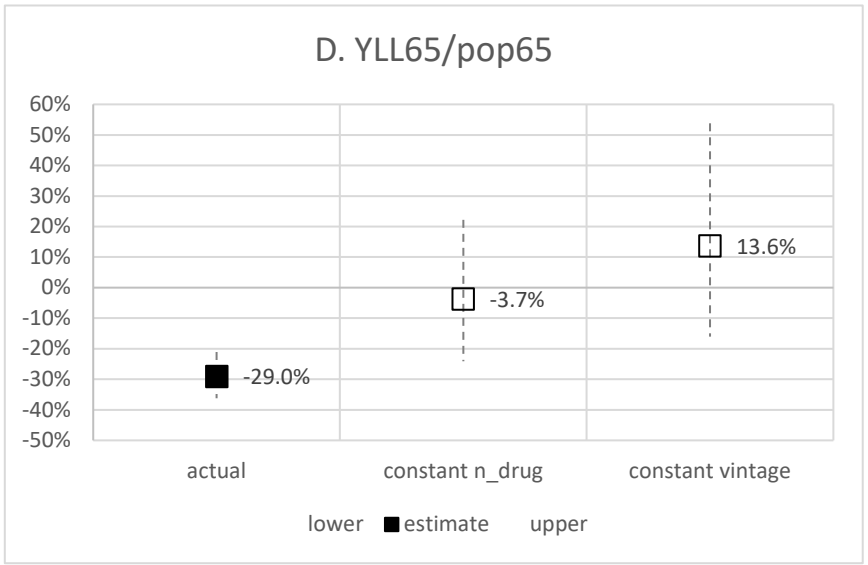
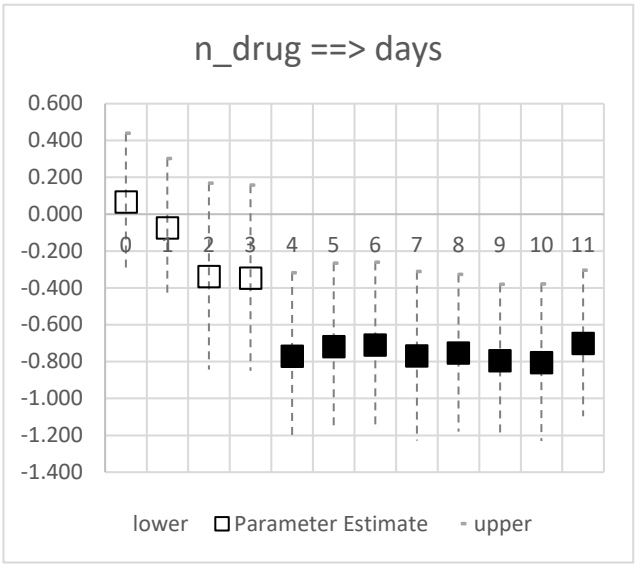
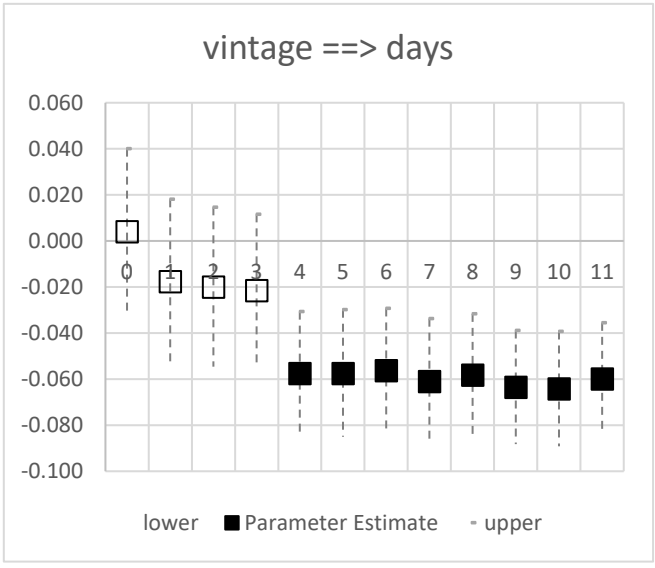


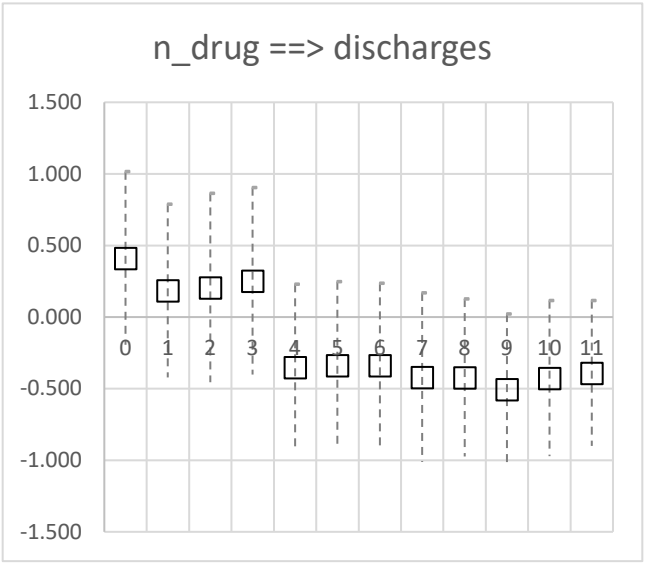
Figure 6

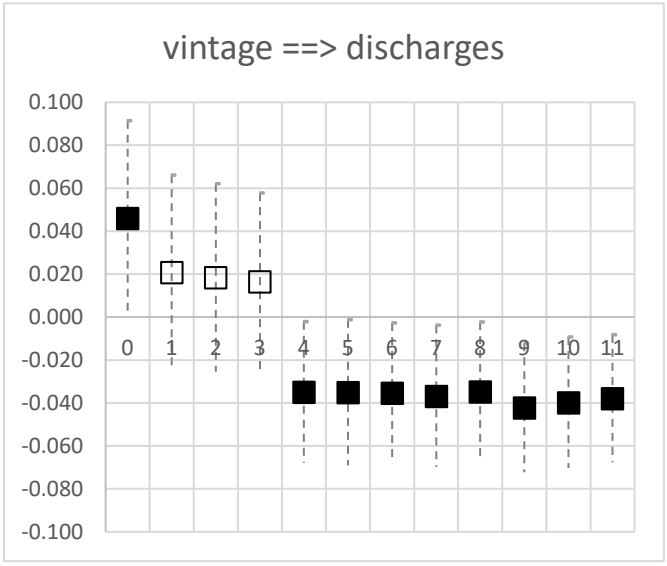
Estimates of β_k from eq. (4) for hospital utilization outcomes:

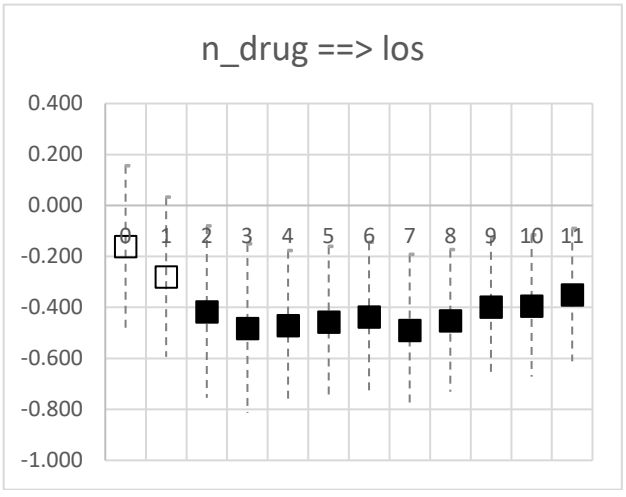
$$\ln(\text{outcome}_{d,2019}) - \ln(\text{outcome}_{d,2000}) = \beta_k\,(\text{rx_measure}_{d,2019-k} - \text{rx_measure}_{d,2000-k}) + \delta' + \varepsilon'_d$$











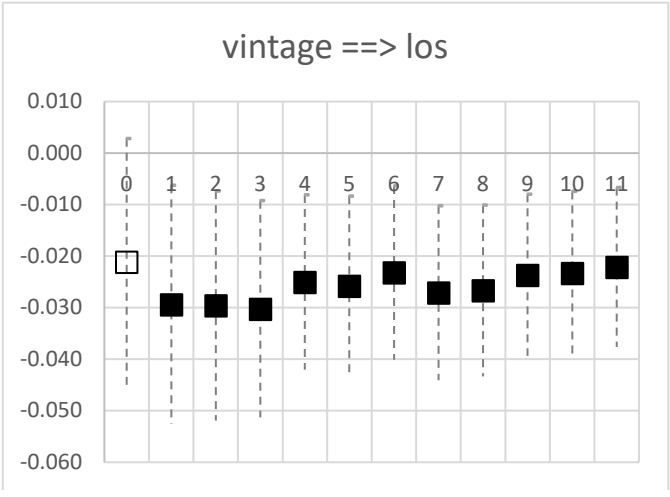


Figure 7

2000-2019 % increase in hospital utilization: actual versus estimated, in absence of change in pharmaceutical consumption

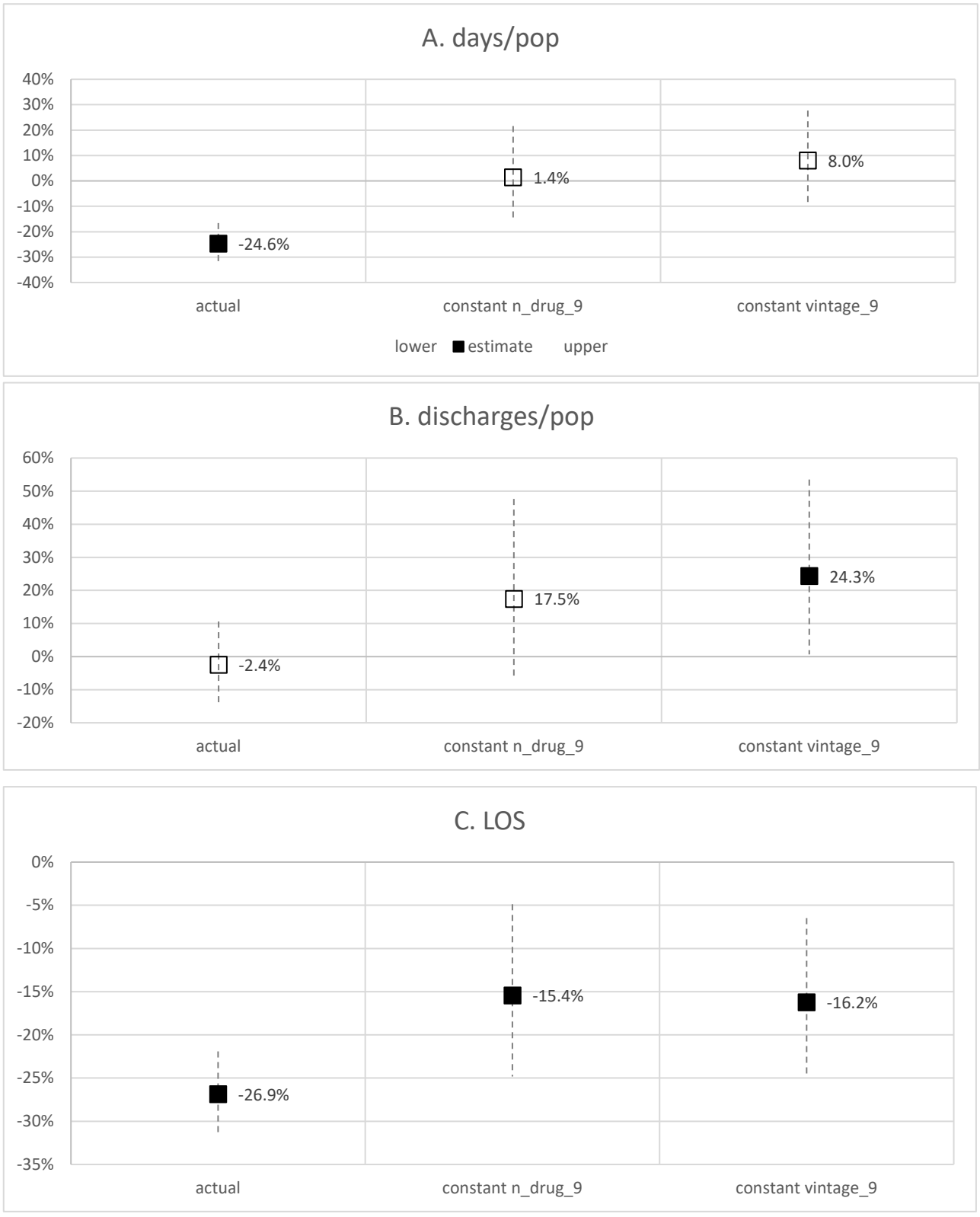


Table 1

Estimates of β_k from eq. (2) for mortality outcomes:

$$\ln(\text{outcome}_{d,2018}) - \ln(\text{outcome}_{d,1998}) = \beta_k\,(\text{rx_measure}_{d,2018\text{-}k} - \text{rx_measure}_{d,1998\text{-}k}) + \delta' + \varepsilon'_d$$

		Regressor: Δln(n_drug_k)					Regressor: Δvintage_k			
row	**k (lag)**	**Estimate**	**Std. Err.**	**t Value**	**Pr > |t|**		**Estimate**	**Std. Err.**	**t Value**	**Pr > |t|**
		Dep. Var.: Δln(n_deaths)					**Dep. Var.: Δln(n_deaths)**			
1	0	**-0.936**	**0.282**	**-3.32**	**0.001**		**-0.077**	**0.022**	**-3.54**	**0.001**
2	1	**-0.789**	**0.280**	**-2.82**	**0.006**		**-0.073**	**0.022**	**-3.34**	**0.001**
3	2	**-0.662**	**0.281**	**-2.36**	**0.021**		-0.042	0.022	-1.87	0.065
4	3	-0.425	0.288	-1.48	0.144		-0.016	0.023	-0.70	0.484
5	4	-0.346	0.288	-1.20	0.233		-0.011	0.022	-0.48	0.633
6	5	-0.307	0.308	-1.00	0.321		-0.007	0.023	-0.29	0.772
		Dep. Var.: Δln(yll85)					**Dep. Var.: Δln(yll85)**			
7	0	**-0.599**	**0.279**	**-2.15**	**0.035**		**-0.047**	**0.021**	**-2.24**	**0.027**
8	1	-0.536	0.274	-1.96	0.054		**-0.044**	**0.021**	**-2.14**	**0.035**
9	2	-0.443	0.270	-1.64	0.104		-0.019	0.021	-0.88	0.381
10	3	-0.282	0.277	-1.02	0.311		-0.002	0.022	-0.10	0.921
11	4	-0.201	0.271	-0.74	0.460		0.001	0.020	0.03	0.977
12	5	-0.168	0.290	-0.58	0.563		0.004	0.021	0.18	0.861
		Dep. Var.: Δln(yll75)					**Dep. Var.: Δln(yll75)**			
13	0	**-0.647**	**0.273**	**-2.37**	**0.020**		**-0.053**	**0.020**	**-2.65**	**0.010**
14	1	**-0.603**	**0.267**	**-2.25**	**0.027**		**-0.050**	**0.020**	**-2.50**	**0.014**
15	2	**-0.534**	**0.263**	**-2.03**	**0.045**		-0.029	0.020	-1.44	0.154
16	3	-0.411	0.268	-1.53	0.129		-0.016	0.021	-0.75	0.456
17	4	-0.372	0.261	-1.43	0.158		-0.015	0.020	-0.74	0.459
18	5	-0.344	0.280	-1.23	0.222		-0.011	0.021	-0.56	0.579
		Dep. Var.: Δln(yll65)					**Dep. Var.: Δln(yll65)**			
19	0	**-0.797**	**0.281**	**-2.84**	**0.006**		**-0.066**	**0.020**	**-3.30**	**0.002**
20	1	**-0.756**	**0.276**	**-2.74**	**0.008**		**-0.060**	**0.020**	**-3.02**	**0.003**
21	2	**-0.691**	**0.267**	**-2.59**	**0.011**		**-0.044**	**0.021**	**-2.15**	**0.035**
22	3	**-0.599**	**0.269**	**-2.22**	**0.029**		-0.034	0.021	-1.59	0.116
23	4	**-0.607**	**0.262**	**-2.32**	**0.023**		-0.034	0.020	-1.72	0.089
24	5	**-0.575**	**0.280**	**-2.05**	**0.043**		-0.030	0.021	-1.44	0.154

Note: each estimate is from a separate regression.

Estimates in bold are statistically significant (p-value < .05).

Table 2

Estimates of β_k from eq. (4) for hospital utilization outcomes:

$$\ln(\text{outcome}_{d,2019}) - \ln(\text{outcome}_{d,2000}) = \beta_k\,(\text{rx_measure}_{d,2019-k} - \text{rx_measure}_{d,2000-k}) + \delta' + \varepsilon'_d$$

		Regressor: Δln(n_drug_k)					Regressor: Δvintage_k			
row	k (lag)	Estimate	Std. Err.	t Value	Pr > |t|		Estimate	Std. Err.	t Value	Pr > |t|
		Dep. Var.: Δln(days)					Dep. Var.: Δln(days)			
1	0	0.068	0.185	0.36	0.716		0.004	0.018	0.22	0.824
2	1	-0.074	0.188	-0.39	0.696		-0.018	0.018	-0.99	0.324
3	2	-0.338	0.253	-1.34	0.184		-0.020	0.017	-1.16	0.250
4	3	-0.347	0.252	-1.38	0.171		-0.022	0.017	-1.30	0.195
5	4	**-0.772**	**0.227**	**-3.40**	**0.001**		**-0.058**	**0.013**	**-4.28**	**<.0001**
6	5	**-0.720**	**0.226**	**-3.18**	**0.002**		**-0.057**	**0.014**	**-4.17**	**<.0001**
7	6	**-0.710**	**0.225**	**-3.16**	**0.002**		**-0.056**	**0.013**	**-4.18**	**<.0001**
8	7	**-0.770**	**0.229**	**-3.36**	**0.001**		**-0.061**	**0.014**	**-4.48**	**<.0001**
9	8	**-0.753**	**0.213**	**-3.53**	**0.001**		**-0.058**	**0.013**	**-4.39**	**<.0001**
10	9	**-0.796**	**0.207**	**-3.84**	**0.000**		**-0.064**	**0.012**	**-5.16**	**<.0001**
11	10	**-0.805**	**0.213**	**-3.78**	**0.000**		**-0.064**	**0.012**	**-5.15**	**<.0001**
12	11	**-0.701**	**0.198**	**-3.54**	**0.001**		**-0.060**	**0.012**	**-4.92**	**<.0001**
		Dep. Var.: Δln(discharges)					Dep. Var.: Δln(discharges)			
13	0	0.411	0.302	1.36	0.177		**0.046**	**0.023**	**2.01**	**0.047**
14	1	0.183	0.302	0.61	0.545		0.021	0.023	0.92	0.361
15	2	0.203	0.330	0.62	0.538		0.018	0.022	0.84	0.404
16	3	0.250	0.327	0.77	0.445		0.016	0.021	0.79	0.432
17	4	-0.353	0.291	-1.21	0.228		**-0.035**	**0.016**	**-2.13**	**0.035**
18	5	-0.339	0.293	-1.16	0.249		**-0.035**	**0.017**	**-2.08**	**0.040**
19	6	-0.340	0.287	-1.18	0.240		**-0.035**	**0.016**	**-2.17**	**0.032**
20	7	-0.421	0.295	-1.43	0.156		**-0.037**	**0.016**	**-2.24**	**0.027**
21	8	-0.424	0.275	-1.54	0.126		**-0.035**	**0.016**	**-2.15**	**0.034**
22	9	-0.508	0.264	-1.92	0.057		**-0.042**	**0.015**	**-2.81**	**0.006**
23	10	-0.429	0.272	-1.58	0.117		**-0.040**	**0.015**	**-2.62**	**0.010**
24	11	-0.392	0.254	-1.54	0.125		**-0.038**	**0.015**	**-2.56**	**0.012**
		Dep. Var.: Δln(los)					Dep. Var.: Δln(los)			
25	0	-0.162	0.159	-1.02	0.310		-0.021	0.012	-1.77	0.080
26	1	-0.281	0.157	-1.80	0.075		**-0.029**	**0.012**	**-2.54**	**0.013**
27	2	**-0.418**	**0.169**	**-2.48**	**0.015**		**-0.030**	**0.011**	**-2.66**	**0.009**
28	3	**-0.483**	**0.166**	**-2.92**	**0.004**		**-0.030**	**0.011**	**-2.88**	**0.005**
29	4	**-0.471**	**0.147**	**-3.20**	**0.002**		**-0.025**	**0.008**	**-2.96**	**0.004**
30	5	**-0.458**	**0.148**	**-3.09**	**0.003**		**-0.026**	**0.009**	**-2.96**	**0.004**
31	6	**-0.437**	**0.146**	**-3.00**	**0.003**		**-0.023**	**0.008**	**-2.75**	**0.007**
32	7	**-0.490**	**0.149**	**-3.29**	**0.001**		**-0.027**	**0.008**	**-3.21**	**0.002**
33	8	**-0.453**	**0.139**	**-3.25**	**0.002**		**-0.027**	**0.008**	**-3.22**	**0.002**
34	9	**-0.398**	**0.136**	**-2.94**	**0.004**		**-0.024**	**0.008**	**-3.03**	**0.003**
35	10	**-0.394**	**0.139**	**-2.83**	**0.006**		**-0.023**	**0.008**	**-2.94**	**0.004**
36	11	**-0.351**	**0.130**	**-2.69**	**0.008**		**-0.022**	**0.008**	**-2.87**	**0.005**

Table 3

Estimated percentage and absolute differences in levels of mortality in 2018 and hospital utilization in 2019 attributable to changes in pharmaceutical consumption

column	1	2	3	4	5	6
	2018 deaths	2018 YLL85	2018 YLL75	2018 YLL65	2019 days	2019 discharges
actual or estimated values in 2018 or 2019						
actual	109,853	957,772	495,759	242,255	10,869,130	1,827,788
estimated, if constant n_drug	158,233	1,221,518	642,637	328,830	14,620,091	2,200,174
estimated, if constant vintage	190,088	1,358,586	732,416	387,964	15,579,356	2,328,901
estimated % reduction in 2018 or 2019, due to change in n_drug or vintage						
n_drug change	31%	22%	23%	26%	26%	17%
vintage change	42%	30%	32%	38%	30%	22%
estimated reduction in 2018 or 2019, due to change in n_drug or vintage						
n_drug change	48,379	263,746	146,878	86,575	3,750,961	372,386
vintage change	80,235	400,814	236,658	145,709	4,710,225	501,113

Appendix Table 1

Top 20 (ranked by DDD) ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS in 1989 and 2019

Top 20 (ranked by DDD) drugs in 1989			
ATC	**MOLECULE**	**year authorized**	**ddd1989**
L01XX11	ESTRAMUSTINE	1978	58,327,163
L01BC02	FLUOROURACIL	1973	50,894,135
L02BB01	FLUTAMIDE	2000	29,799,702
L02BA01	TAMOXIFENE	1975	8,073,000
L01AA02	CHLORAMBUCIL	2001	6,483,074
L04AX01	AZATHIOPRINE	1971	6,239,931
L02AE03	GOSERELINE	1987	3,544,189
L01BB02	MERCAPTOPURINE	1962	1,971,468
L01AD02	LOMUSTINE		1,436,264
L01DB03	EPIRUBICINE	1985	948,384
L01DB01	DOXORUBICINE	1989	899,964
L01BA01	METHOTREXATE	1968	801,600
L02AB01	MEGESTROL	1987	703,125
L04AD01	CICLOSPORINE	1983	635,000
L02AA02	POLYESTRADIOL PHOSPHATE	1961	579,997
L01AA01	CYCLOPHOSPHAMIDE	1962	525,625
L01BB03	TIOGUANINE	1974	506,692
L01CB01	ETOPOSIDE	1981	491,447
L01AA06	IFOSFAMIDE	1981	314,281
L02AB02	MEDROXYPROGESTERONE		292,500

Top 20 (ranked by DDD) drugs in 2019			
ATC	**MOLECULE**	**year authorized**	**ddd2019**
L04AB02	INFLIXIMAB	1999	800,380,242
L04AB04	ADALIMUMAB	2003	448,143,808
L01BC02	FLUOROURACIL	1973	355,386,483
L02AE04	TRIPTORELINE	1988	346,310,425
L04AX01	AZATHIOPRINE	1971	284,342,157
L04AC05	USTEKINUMAB	2009	216,678,846
L04AA06	ACIDE MYCOPHENOLIQUE	1996	210,640,204
L02AE02	LEUPRORELINE	2005	161,205,049
L02AE03	GOSERELINE	1987	134,882,903
L03AB07	INTERFERON BETA-1A	1998	130,015,687
L02BX02	DEGARELIX	2009	104,666,264
L02BG06	EXEMESTANE	2000	98,671,022
L04AB06	GOLIMUMAB	2009	86,281,752
L01XA01	CISPLATINE	1998	80,811,504
L02BA03	FULVESTRANT	2004	79,692,819
L04AX07	DIMETHYL FUMARATE	2017	65,453,981
L01FF01	NIVOLUMAB		64,716,505
L04AX05	PIRFENIDONE	2011	63,343,778
L01AA01	CYCLOPHOSPHAMIDE	1962	63,264,313
L04AB05	CERTOLIZUMAB PEGOL	2009	56,911,341

Appendix Table 2

A. Aggregate mortality and population data for 1998 and 2018

		Years of life lost (YLL)		
Year	**No. of deaths**	**before age 85**	**before age 75**	**before age 65**
1998	104,382	1,196,074	613,414	313,316
2018	110,693	946,467	469,792	218,460
% change	6.0%	-20.9%	-23.4%	-30.3%
	Population			
	total	**below age 85**	**below age 75**	**below age 65**
1998	10,203,008	10,023,391	9,500,058	8,514,986
2018	11,427,068	11,102,874	10,413,740	9,279,006
% change	12.0%	10.8%	9.6%	9.0%
	Rates per 100,000 population			
	Deaths	**YLL85**	**YLL75**	**YLL65**
1998	1023	11933	6457	3680
2018	969	8525	4511	2354
% change	-5.3%	-28.6%	-30.1%	-36.0%

B. Aggregate hospital utilization data for 2000 and 2019

	days	**discharges**	**los**	**population**
2000	12,867,139	1,671,057	7.7	10,250,000
2019	11,525,244	1,920,874	6.0	11,490,000
% change	-10.4%	14.9%	-22.1%	12.1%

	Rates per 100,000 population	
	days	discharges
2000	125,533	16,303
2019	100,307	16,718
% change	-20.1%	2.5%

Appendix Table 3
Subset of data used in mortality analysis

	deaths		YLL85		YLL75		YLL65		n_sold			year_auth		
Cause of death/Year	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1990**	**2006**	**2018**	**1990**	**2006**	**2018**
Salmonella infections (A01-A02)	19	4	170	58	73	35	28	23	6	9	9	1973.5	1981.1	1986.4
Certain other intestinal infections (A04,A07-A09)	94	477	876	1,837	526	732	369	334	18	21	22	1979.5	1981.2	1982.2
Respiratory tuberculosis (A16)	63	14	925	128	468	53	208	10	8	8	10	1973.3	1970.4	1979.6
Other tuberculosis (A17-A19)	12	12	224	219	134	154	81	104	15	14	17	1976.9	1972.5	1982.0
Meningococcal infection (A39)	24	8	1,753	232	1,513	177	1,273	137	8	11	12	1970.1	1978.6	1985.7
Septicemia (A40-A41)	696	825	6,338	6,154	2,750	2,586	1,233	991	27	30	31	1982.2	1983.8	1985.0
Syphilis (A50-A53)	4	2	80	23	45	13	28	3	9	9	9	1968.8	1968.8	1968.8
Viral hepatitis (B15-B19)	169	1	2,567	33	1,259	23	552	13	4	1	1	2001.8	2002.0	2002.0
Human immunodeficiency virus (HIV) disease (B20-B24)	57	53	2,376	678	1,813	358	1,283	160	6	13	22	1983.7	2000.5	2006.7
Malaria (B50-B54)	4	25	180	848	140	598	100	355	5	33	45	1973.0	1996.0	2000.2
Other and unspecified infectious and parasitic diseases and their sequelae (A00,A05,A20-A36,A42-A44,A48-A49,A54-A79,A81-A82,A85.0-A85.1,A85.8,A86-B04,B06-B09,B25-	223	910	2,926	4,995	1,544	2,063	824	775	101	138	150	1978.5	1983.2	1986.5
Malignant neoplasms of lip, oral cavity and pharynx (C00-C14)	566	522	11,968	8,880	7,163	4,653	3,445	1,623	11	17	20	1979.7	1984.7	1988.4
Malignant neoplasm of esophagus (C15)	621	739	10,770	10,115	5,690	4,645	2,335	1,410	12	18	22	1981.8	1985.3	1990.4
Malignant neoplasm of stomach (C16)	1,115	641	12,864	7,575	5,814	3,825	2,204	1,593	14	22	28	1980.8	1985.6	1991.4
Malignant neoplasms of colon, rectum and anus (C18-C21)	3,138	2,628	36,128	25,295	15,768	11,180	5,523	3,878	10	23	31	1978.0	1990.1	1995.7
Malignant neoplasms of liver and intrahepatic bile ducts (C22)	619	938	8,328	11,685	3,628	5,288	1,215	1,763	7	14	17	1977.6	1987.7	1992.2

Appendix Table 3
Subset of data used in mortality analysis

	deaths		YLL85		YLL75		YLL65		n_sold			year_auth		
Cause of death/Year	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1990**	**2006**	**2018**	**1990**	**2006**	**2018**
Malignant neoplasm of pancreas (C25)	1,310	1,849	16,868	21,170	7,348	9,265	2,553	3,008	14	24	29	1978.9	1987.0	1991.2
Malignant neoplasm of larynx (C32)	314	160	5,760	2,363	3,140	1,118	1,358	338	6	12	14	1976.3	1986.2	1989.5
Malignant neoplasms of trachea, bronchus and lung (C33-C34)	6,379	5,861	99,083	78,020	46,055	34,943	15,413	10,163	22	34	42	1983.4	1988.3	1993.6
Malignant melanoma of skin (C43)	220	355	4,600	5,193	2,768	2,915	1,473	1,365	12	22	25	1981.7	1988.6	1991.8
Malignant neoplasm of breast (C50)	2,540	2,237	42,195	28,613	23,068	14,798	10,515	6,163	31	48	59	1980.9	1986.5	1991.4
Malignant neoplasm of cervix uteri (C53)	178	174	3,493	3,440	2,060	2,108	1,088	1,068	10	18	22	1979.5	1987.4	1992.6
Malignant neoplasms of corpus uteri and uterus, part unspecified (C54-C55)	388	382	4,648	3,365	2,068	1,348	748	358	14	21	24	1976.3	1983.3	1986.9
Malignant neoplasm of ovary (C56)	695	574	9,770	6,678	4,760	3,083	1,973	1,103	22	32	37	1983.3	1987.1	1990.9
Malignant neoplasm of prostate (C61)	1,646	1,598	12,408	8,933	3,608	2,473	590	395	16	26	33	1981.5	1987.3	1992.3
Malignant neoplasms of kidney and renal pelvis (C64-C65)	602	522	7,712	4,891	3,482	2,004	1,275	589	12	19	25	1978.9	1985.4	1991.8
Malignant neoplasm of bladder (C67)	876	798	8,863	5,590	3,350	2,033	865	558	15	22	25	1981.3	1985.7	1988.6
Malignant neoplasms of meninges, brain and other parts of central nervous system (C70-C72)	706	636	15,269	13,355	9,259	8,062	5,126	4,355	22	30	32	1981.6	1984.8	1986.3
Hodgkin's disease (C81)	61	41	1,473	650	983	380	620	215	19	25	29	1984.0	1986.0	1989.3
Non-Hodgkin's lymphoma (C82-C85)	657	662	10,020	6,113	5,103	2,623	2,298	1,093	32	41	52	1985.9	1987.0	1992.2
Leukemia (C91-C95)	892	972	12,522	9,494	6,442	4,501	3,274	2,144	31	44	66	1983.0	1986.4	1994.8

Appendix Table 3
Subset of data used in mortality analysis

	deaths		YLL85		YLL75		YLL65		n_sold			year_auth		
Cause of death/Year	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1990**	**2006**	**2018**	**1990**	**2006**	**2018**
Multiple myeloma and immunoproliferative neoplasms (C88,C90)	420	517	4,923	3,960	2,140	1,385	735	380	16	24	30	1984.7	1989.0	1993.0
Other and unspecified malignant neoplasms of lymphoid, hematopoietic and related tissue (C96)	4	38	70	385	33	175	5	83	6	12	18	1978.5	1987.3	1995.3
All other and unspecified malignant neoplasms (C17,C23-C24,C26-C31,C37-C41,C44-C49,C51-C52,C57-C60,C62-C63,C66,C68-C69,C73-C80,C97)	3,531	3,293	44,699	35,962	21,509	17,407	9,129	7,092	41	65	85	1983.7	1988.8	1994.6
In situ neoplasms, benign neoplasms and neoplasms of uncertain or unknown behavior (D00-D48)	447	1,477	4,223	11,929	1,936	5,421	918	2,256	30	51	68	1980.2	1987.3	1993.4
Anemias (D50-D64)	122	201	765	823	308	398	143	225	26	29	40	1977.2	1978.5	1986.6
Diabetes mellitus (E10-E14)	1,671	1,499	14,828	9,295	5,930	3,573	2,188	1,128	20	43	59	1990.2	1994.6	1998.6
Malnutrition (E40-E46)	25	176	180	475	100	160	63	25	1	2	2	1978.0	1987.5	1987.5
Other nutritional deficiencies (E50-E64)	3	5	20	80	8	40	0	10	41	55	60	1978.0	1982.4	1984.8
Meningitis (G00,G03)	24	29	547	680	369	475	249	323	24	32	36	1980.8	1985.0	1989.1
Parkinson's disease (G20-G21)	643	1,333	3,648	5,513	785	1,108	110	183	7	17	20	1973.4	1987.7	1990.7
Alzheimer's disease (G30)	1,002	2,345	4,920	5,553	1,005	855	120	128	4	9	9	1979.8	1990.0	1990.0
Acute rheumatic fever and chronic rheumatic heart diseases (I00-I09)	211	255	1,400	1,358	403	515	85	200	10	9	10	1972.4	1967.2	1972.4
Hypertensive heart disease (I11)	345	290	2,023	748	823	265	308	93	34	47	46	1983.0	1986.0	1987.6

Appendix Table 3
Subset of data used in mortality analysis

	deaths		YLL85		YLL75		YLL65		n_sold			year_auth		
Cause of death/Year	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1990**	**2006**	**2018**	**1990**	**2006**	**2018**
Hypertensive heart and renal disease (I13)	56	204	245	308	55	30	13	0	34	47	46	1983.0	1986.0	1987.6
Acute myocardial infarction (I21-I22)	7,735	3,879	83,040	34,370	36,103	15,408	13,378	5,535	26	40	48	1981.0	1987.2	1992.1
Other acute ischemic heart diseases (I24)	437	324	3,083	2,520	1,003	1,148	268	415	1	4	6	1990.0	1997.8	2002.2
Atherosclerotic cardiovascular disease, so described (I25.0)	4,742	2,717	36,153	15,605	12,125	5,705	3,243	1,773	22	32	35	1981.5	1987.0	1990.0
All other forms of chronic ischemic heart disease (I20,I25.1-I25.9)	5,070	2,770	38,428	15,965	12,925	5,880	3,453	1,828	33	48	56	1983.7	1988.5	1992.3
Acute and subacute endocarditis (I33)	18	59	240	675	85	300	18	135	21	22	21	1985.7	1984.8	1983.4
Diseases of pericardium and acute myocarditis (I30-I31,I40)	34	43	408	323	183	128	90	38	3	3	3	1992.7	1992.7	1992.7
Heart failure (I50)	4,513	5,043	18,733	14,575	5,805	5,063	1,820	1,710	30	46	52	1981.7	1986.5	1989.6
All other forms of heart disease (I26-I28,I34-I38,I42-I49,I51)	7,571	7,497	55,873	39,823	23,178	16,923	9,455	6,718	49	71	79	1979.1	1984.8	1988.7
Essential hypertension and hypertensive renal disease (I10,I12,I15)	499	423	4,180	2,230	1,625	915	603	288	43	71	81	1984.0	1988.7	1992.2
Cerebrovascular diseases (I60-I69)	8,627	6,478	57,479	34,635	20,719	13,377	7,619	4,842	17	20	25	1983.7	1984.6	1989.8
Atherosclerosis (I70)	918	111	4,195	410	1,273	143	313	43	3	6	11	1985.7	1991.7	2000.2
Aortic aneurysm and dissection (I71)	637	488	6,275	3,610	2,375	1,430	723	463	1	1	1	1990.0	1990.0	1990.0
Other diseases of arteries, arterioles and capillaries (I72-I78)	503	581	4,543	4,230	1,920	1,815	690	633	26	32	37	1981.1	1983.6	1987.0

Appendix Table 3
Subset of data used in mortality analysis

	deaths		YLL85		YLL75		YLL65		n_sold			year_auth		
Cause of death/Year	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1990**	**2006**	**2018**	**1990**	**2006**	**2018**
Other disorders of circulatory system (I80-I99)	397	210	3,470	1,948	1,520	938	645	375	36	47	52	1977.4	1981.5	1986.0
Influenza (J09-J11)	368	543	1,443	3,918	513	2,053	188	1,141	4	6	5	1977.8	1985.3	1982.6
Pneumonia (J12-J18)	3,913	4,718	21,770	17,455	8,145	6,318	3,440	2,318	41	55	59	1978.3	1983.5	1986.2
Acute bronchitis and bronchiolitis (J20-J21)	109	192	785	452	442	195	310	105	25	36	39	1978.9	1984.7	1986.4
Other and unspecified acute lower respiratory infections (J22,U04)	19	538	65	1,601	13	531	0	204	21	23	23	1984.5	1986.0	1986.0
Bronchitis, chronic and unspecified (J40-J42)	534	272	2,623	720	815	223	265	45	27	36	40	1980.0	1984.2	1986.9
Emphysema (J43)	702	231	7,960	2,195	2,978	813	678	213	6	7	11	1991.3	1992.9	1999.3
Asthma (J45-J46)	344	109	5,718	1,013	3,138	500	1,560	218	28	39	44	1982.3	1985.9	1989.4
Other chronic lower respiratory diseases (J44,J47)	3,715	3,935	32,063	31,845	10,610	11,648	2,365	2,665	16	25	37	1983.6	1988.2	1996.5
Pneumoconioses and chemical effects (J60-J66,J68)	327	55	3,255	180	880	55	115	15	5	5	8	1978.4	1973.0	1986.6
Pneumonitis due to solids and liquids (J69)	491	923	3,218	3,740	1,290	1,253	573	368	.	.	.	.	.	.
Other diseases of respiratory system (J00-J06,J30- J39,J67,J70-J98)	1,398	1,400	11,191	9,707	4,214	3,787	1,534	1,302	97	130	140	1980.5	1984.3	1987.0
Peptic ulcer (K25-K28)	414	195	3,229	1,258	1,279	545	499	178	10	17	18	1979.3	1986.9	1988.3
Diseases of appendix (K35-K38)	14	11	103	58	33	30	18	13	4	4	6	1982.8	1977.3	1989.2
Hernia (K40-K46)	88	111	473	413	143	133	25	48	.	.	.	.	.	.
Alcoholic liver disease (K70)	849	686	22,600	15,693	14,570	9,263	7,733	4,100	4	8	10	1977.3	1986.4	1991.6
Other chronic liver disease and cirrhosis (K73-K74)	425	644	7,780	10,833	4,328	5,700	2,038	2,183	11	17	22	1982.0	1986.2	1992.5

Appendix Table 3
Subset of data used in mortality analysis

	deaths		YLL85		YLL75		YLL65		n_sold			year_auth		
Cause of death/Year	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1990**	**2006**	**2018**	**1990**	**2006**	**2018**
Cholelithiasis and other disorders of gallbladder (K80-K82)	267	252	1,455	788	453	218	125	33	3	5	5	1969.3	1981.4	1981.4
Acute and rapidly progressive nephritic and nephrotic syndrome (N00-N01,N04)	4	8	33	130	8	93	0	63	21	22	26	1979.3	1978.4	1983.4
Chronic glomerulonephritis, nephritis and nephropathy not specified as acute or chronic, and renal sclerosis unspecified (N02-N03,N05-N07,N26)	29	16	310	128	175	40	90	5	8	8	11	1982.1	1979.8	1988.6
Renal failure (N17-N19)	961	1,508	6,069	4,985	2,129	1,580	707	488	18	23	31	1979.6	1983.2	1989.7
Other disorders of kidney (N25,N27)	2	3	8	43	0	18	0	8	8	8	11	1980.0	1977.6	1987.3
Infections of kidney (N10-N12,N13.6,N15.1)	113	433	680	1,505	230	423	78	100	15	26	29	1983.9	1990.1	1992.3
Hyperplasia of prostate (N40)	25	22	118	50	23	8	3	0	2	10	12	1978.0	1994.3	1996.9
Inflammatory diseases of female pelvic organs (N70-N76)	7	12	55	198	33	125	23	83	16	19	22	1978.2	1979.9	1984.9
Pregnancy with abortive outcome (O00-O07)	1	1	58	48	48	38	38	28	7	7	10	1972.7	1968.4	1980.9
Other complications of pregnancy, childbirth and the puerperium (O10-O99)	12	3	640	143	520	113	400	83	43	56	65	1980.4	1983.6	1987.2
Certain conditions originating in the perinatal period (P00-P96)	152	186	12,785	15,717	11,265	13,857	9,745	11,997	146	200	219	1979.4	1983.9	1986.9
Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99)	287	296	20,170	16,733	17,390	13,871	14,663	11,233	53	69	85	1979.3	1982.4	1987.8

Appendix Table 3
Subset of data used in mortality analysis

	deaths		YLL85		YLL75		YLL65		n_sold			year_auth		
Cause of death/Year	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1998**	**2018**	**1990**	**2006**	**2018**	**1990**	**2006**	**2018**
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00-R99)	3,392	7,722	29,948	59,598	16,623	31,985	9,306	15,878	190	242	266	1979.7	1983.2	1985.7
All other diseases (Residual)	8,333	13,712	77,264	91,924	40,837	43,577	22,717	19,929	382	581	703	1979.7	1985.7	1990.5
Other and unspecified nontransport accidents and their sequelae (W20-W31,W35-W64,W75-W99,X10-X39,X50-X59,Y86)	703	2,000	7,417	14,657	4,592	8,067	3,009	4,615	3	3	3	1973.7	1973.7	1973.7
Complications of medical and surgical care (Y40-Y84,Y88)	91	554	1,070	5,305	558	2,358	305	915	5	10	11	1976.8	1988.4	1990.8

Appendix Table 4
Subset of data used in hospital utilization analysis

	days		discharges		los		n_sold			year_auth		
	2000	2019	2000	2019	2000	2019	1989	2008	2019	1989	2008	2019
101 Intestinal infectious diseases except diarrhoea	68,350	60,643	13,670	14,791	5.0	4.1	24	31	31	1976.0	1980.6	1980.5
102 Diarrhoea and gastroenteritis of presumed infectious origin	19,289	15,464	4,104	3,682	4.7	4.2	7	10	8	1983.4	1985.4	1984.4
103 Tuberculosis	24,869	15,514	1,256	929	19.8	16.7	19	22	25	1976.4	1977.2	1982.5
104 Septicaemia	61,537	211,935	4,130	14,925	14.9	14.2	26	31	30	1982.0	1984.6	1985.0
105 Human immunodeficiency virus [HIV] disease	6,380	5,039	417	442	15.3	11.4	5	36	46	1982.0	1996.9	2001.4
106 Other infectious and parasitic diseases	146,676	164,723	21,570	25,738	6.8	6.4	126	197	220	1980.1	1986.5	1990.3
201 Malignant neoplasm of colon, rectum and anus	157,474	105,074	9,661	9,820	16.3	10.7	9	25	31	1976.9	1991.9	1995.7
202 Malignant neoplasms of trachea, bronchus and lung	125,939	101,521	11,449	9,953	11.0	10.2	21	35	42	1983.1	1989.2	1993.6
203 Malignant neoplasms of skin	12,946	9,326	2,232	2,743	5.8	3.4	16	29	36	1983.4	1989.1	1993.5
204 Malignant neoplasm of breast	90,368	48,107	11,439	12,335	7.9	3.9	29	50	59	1980.4	1987.5	1991.4
205 Malignant neoplasm of uterus	27,695	13,530	2,978	2,460	9.3	5.5	16	28	31	1976.2	1986.3	1989.4
206 Malignant neoplasm of ovary	24,162	12,968	1,873	1,425	12.9	9.1	21	33	37	1983.1	1988.0	1990.9
207 Malignant neoplasm of prostate	72,597	34,887	6,914	6,709	10.5	5.2	14	26	33	1980.6	1987.3	1992.3
208 Malignant neoplasm of bladder	46,178	36,743	5,701	6,335	8.1	5.8	14	22	25	1980.9	1985.7	1988.6
209 Other malignant neoplasms	509,189	467,168	39,472	44,920	12.9	10.4	55	98	128	1982.2	1990.1	1995.5
210 Carcinoma in situ	11,830	14,737	2,232	4,754	5.3	3.1	7	18	21	1973.4	1993.1	1996.1
211 Benign neoplasm of colon, rectum and anus	14,063	11,612	3,430	4,004	4.1	2.9	2	6	6	1964.0	1986.7	1986.7
212 Leiomyoma of uterus	45,589	12,803	7,353	4,742	6.2	2.7	2	6	6	1964.0	1987.5	1987.5

Appendix Table 4
Subset of data used in hospital utilization analysis

	days		discharges		los		n_sold			year_auth		
	2000	2019	2000	2019	2000	2019	1989	2008	2019	1989	2008	2019
213 Other benign neoplasms and neoplasms of uncertain or unknown behaviour	101,486	67,830	17,201	15,416	5.9	4.4	24	49	58	1980.5	1990.6	1994.3
301 Anaemias	70,832	88,870	8,638	12,174	8.2	7.3	26	33	39	1978.5	1981.9	1985.7
302 Other diseases of the blood and bloodforming organs and certain disorders involving the immune mechanism	33,696	37,012	5,265	5,213	6.4	7.1	39	70	79	1980.9	1988.3	1991.7
401 Diabetes mellitus	196,032	129,049	17,348	15,363	11.3	8.4	16	47	61	1990.1	1995.6	1999.2
402 Other endocrine, nutritional and metabolic diseases	194,691	203,615	26,670	40,723	7.3	5.0	138	209	232	1980.2	1985.5	1989.0
501 Dementia	133,692	60,602	5,641	3,503	23.7	17.3	9	18	18	1973.9	1985.7	1985.7
502 Mental and behavioural disorders due to alcohol	75,215	73,135	11,061	11,081	6.8	6.6	19	25	26	1973.1	1979.0	1980.0
503 Mental and behavioural disorders due to use of other psychoactive subst.	16,446	13,798	2,164	2,379	7.6	5.8	18	27	28	1971.8	1981.0	1981.8
504 Schizophrenia, schizotypal and delusional disorders	22,955	18,192	1,739	1,895	13.2	9.6	17	28	32	1971.7	1981.4	1984.6
505 Mood [affective] disorders	178,522	72,095	13,947	4,938	12.8	14.6	23	35	38	1975.8	1982.9	1985.1
506 Other mental and behavioural disorders	146,198	74,176	15,229	11,071	9.6	6.7	78	114	125	1977.8	1984.0	1986.4
601 Alzheimer's disease	47,752	85,500	2,221	4,750	21.5	18.0	4	9	9	1979.8	1990.0	1990.0
602 Multiple sclerosis	13,083	14,097	1,869	1,905	7.0	7.4	13	22	31	1975.9	1984.3	1992.3
603 Epilepsy	81,619	73,922	12,182	16,070	6.7	4.6	23	32	39	1973.2	1979.2	1984.6
604 Transient cerebral ischaemic attacks and related syndromes	82,895	42,437	8,127	8,161	10.2	5.2	5	7	10	1990.4	1990.6	1996.1

Appendix Table 4
Subset of data used in hospital utilization analysis

	days		discharges		los		n_sold			year_auth		
	2000	2019	2000	2019	2000	2019	1989	2008	2019	1989	2008	2019
605 Other diseases of the nervous system	217,241	331,607	21,509	106,970	10.1	3.1	94	133	152	1977.2	1983.0	1987.1
701 Cataract	32,137	3,466	16,914	2,666	1.9	1.3	2	2	2	2000.0	2000.0	2001.0
702 Other diseases of the eye and adnexa	36,593	20,782	10,455	9,896	3.5	2.1	85	126	130	1979.7	1985.2	1988.1
800 Diseases of the ear and mastoid process	50,504	36,045	12,318	12,015	4.1	3.0	26	32	30	1975.0	1978.1	1980.9
901 Hypertensive diseases	64,031	225,194	6,885	21,447	9.3	10.5	36	73	81	1982.7	1989.3	1992.4
902 Angina pectoris	40,091	6,507	8,909	2,324	4.5	2.8	23	40	42	1982.0	1989.6	1992.0
903 Acute myocardial infarction	150,604	111,507	15,853	17,423	9.5	6.4	23	42	48	1979.8	1988.6	1992.1
904 Other ischaemic heart disease	307,562	116,464	50,420	35,292	6.1	3.3	22	38	39	1982.4	1989.3	1990.6
905 Pulmonary heart disease & diseases of pulmonary circulation	69,714	55,902	5,126	6,655	13.6	8.4	10	20	29	1976.9	1988.0	1995.0
906 Conduction disorders and cardiac arrhythmias	203,266	156,702	28,629	40,180	7.1	3.9	30	37	36	1976.9	1980.3	1983.4
907 Heart failure	264,786	161,424	18,136	14,160	14.6	11.4	26	47	51	1980.4	1987.1	1989.9
908 Cerebrovascular diseases	497,162	379,870	30,131	28,778	16.5	13.2	15	20	25	1982.7	1984.6	1989.8
909 Atherosclerosis	119,354	92,518	12,179	17,792	9.8	5.2	3	6	11	1985.7	1991.7	2000.2
910 Varicose veins of lower extremities	39,758	6,550	14,725	2,047	2.7	3.2	4	5	5	1974.3	1978.4	1978.4
911 Other diseases of the circulatory system	347,319	254,325	38,591	32,193	9.0	7.9	79	114	118	1980.0	1984.3	1986.8
1001 Acute upper respiratory infections and influenza	47,309	98,482	11,002	24,020	4.3	4.1	49	61	61	1979.5	1982.7	1983.0
1002 Pneumonia	406,654	364,934	32,020	36,862	12.7	9.9	39	58	59	1977.7	1984.1	1986.1
1003 Other acute lower respiratory infections	140,760	107,210	17,595	21,442	8.0	5.0	34	48	50	1981.6	1986.3	1987.2

Appendix Table 4
Subset of data used in hospital utilization analysis

	days		discharges		los		n_sold			year_auth		
	2000	2019	2000	2019	2000	2019	1989	2008	2019	1989	2008	2019
1005 Other diseases of upper respiratory tract	50,853	25,400	20,341	14,111	2.5	1.8	54	75	79	1980.0	1984.7	1987.3
1006 Chronic obstructive pulmonary disease and bronchiectasis	365,719	381,498	27,706	35,654	13.2	10.7	32	48	58	1978.9	1984.5	1990.0
1007 Asthma	52,483	24,374	7,392	5,078	7.1	4.8	28	40	43	1982.3	1986.4	1988.7
1008 Other diseases of the respiratory system	215,490	163,333	16,325	16,013	13.2	10.2	42	52	60	1979.9	1981.7	1985.5
1101 Disorders of teeth and supporting structures	17,569	6,670	9,247	2,668	1.9	2.5	25	29	30	1973.9	1976.3	1977.1
1102 Other diseases of oral cavity, salivary glands and jaws	12,250	10,526	3,141	2,339	3.9	4.5	28	32	32	1975.6	1977.8	1980.3
1103 Diseases of oesophagus	79,438	37,556	13,464	8,942	5.9	4.2	8	13	13	1983.4	1988.5	1988.5
1104 Peptic ulcer	91,321	33,314	8,953	4,217	10.2	7.9	10	17	18	1979.3	1986.9	1988.3
1105 Dyspepsia and other diseases of stomach and duodenum	39,001	31,920	5,821	6,650	6.7	4.8	11	11	12	1977.1	1976.6	1979.1
1109 Crohn's disease and ulcerative colitis	33,997	29,471	3,434	4,534	9.9	6.5	21	22	31	1976.2	1974.3	1985.1
1110 Other noninfective gastroenteritis and colitis	44,706	49,358	9,512	11,752	4.7	4.2	7	10	11	1987.1	1988.4	1990.5
1111 Paralytic ileus and intestinal obstruction without hernia	99,900	94,160	9,250	11,919	10.8	7.9	2	2	2	1977.5	1977.5	1977.5
1113 Diseases of anus and rectum	32,432	20,920	7,371	6,153	4.4	3.4	9	9	11	1977.0	1976.0	1985.6
1114 Other diseases of intestine	75,460	55,395	9,316	9,389	8.1	5.9	34	40	43	1976.6	1978.6	1982.7
1115 Alcoholic liver disease	52,877	55,740	4,099	4,645	12.9	12.0	4	9	9	1977.3	1988.6	1988.6
1116 Other diseases of liver	39,708	30,015	3,514	3,335	11.3	9.0	15	23	28	1985.0	1988.7	1994.0
1117 Cholelithiasis	123,157	101,946	19,864	27,553	6.2	3.7	2	4	4	1970.5	1985.0	1985.0

Appendix Table 4
Subset of data used in hospital utilization analysis

	days		discharges		los		n_sold			year_auth		
	2000	2019	2000	2019	2000	2019	1989	2008	2019	1989	2008	2019
1118 Other diseases of gall bladder and biliary tract	47,510	36,320	5,001	6,262	9.5	5.8	4	5	5	1977.0	1981.8	1981.8
1119 Diseases of pancreas	65,792	60,378	6,036	8,271	10.9	7.3	3	3	4	1984.7	1984.7	1991.5
1120 Other diseases of the digestive system	45,075	89,802	4,553	16,036	9.9	5.6	25	33	35	1981.2	1982.7	1984.5
1201 Infections of the skin and subcutaneous tissue	49,620	52,240	7,406	8,564	6.7	6.1	42	59	58	1979.0	1984.2	1985.9
1202 Dermatitis, eczema and papulosquamous disorders	13,598	6,985	1,478	1,145	9.2	6.1	44	56	65	1980.4	1982.5	1989.2
1203 Other diseases of the skin and subcutaneous tissue	106,814	60,754	7,854	8,438	13.6	7.2	64	85	94	1974.8	1980.4	1985.1
1301 Coxarthrosis [arthrosis of hip]	174,496	147,200	11,556	21,647	15.1	6.8	18	23	22	1975.2	1980.0	1978.5
1302 Gonarthrosis [arthrosis of knee]	155,805	195,456	10,599	26,413	14.7	7.4	18	25	24	1975.2	1981.6	1980.3
1303 Internal derangement of knee	30,769	3,590	13,378	2,112	2.3	1.7	9	10	10	1967.1	1970.1	1970.1
1304 Other arthropathies	96,528	106,690	13,223	29,636	7.3	3.6	62	85	104	1979.0	1983.3	1989.4
1305 Systemic connective tissue disorders	22,963	19,509	2,208	2,192	10.4	8.9	27	33	41	1977.7	1980.4	1988.4
1306 Deforming dorsopathies and spondylopathies	85,815	142,319	9,535	18,246	9.0	7.8	23	33	39	1979.9	1985.1	1989.0
1307 Intervertebral disc disorders	153,289	100,321	22,879	23,886	6.7	4.2	4	6	5	1962.5	1974.8	1969.4
1308 Dorsalgia	58,053	23,214	10,555	4,380	5.5	5.3	17	21	22	1978.9	1981.5	1982.1
1309 Soft tissue disorders	24,191	67,109	4,244	21,648	5.7	3.1	50	65	71	1976.6	1980.9	1983.7
1310 Other disorders of the musculoskeletal system and connective tissue	267,794	162,996	41,199	18,953	6.5	8.6	30	48	47	1979.2	1985.2	1985.7
1401 Glomerular and renal tubulo-interstitial diseases	74,570	98,974	10,215	22,494	7.3	4.4	33	43	49	1980.4	1983.4	1986.7

Appendix Table 4
Subset of data used in hospital utilization analysis

	days		discharges		los		n_sold			year_auth		
	2000	2019	2000	2019	2000	2019	1989	2008	2019	1989	2008	2019
1402 Renal failure	64,963	40,105	4,848	3,518	13.4	11.4	14	24	28	1979.9	1987.2	1990.6
1403 Urolithiasis	62,099	24,478	18,818	12,883	3.3	1.9	4	5	6	1972.3	1978.0	1981.3
1404 Other diseases of the urinary system	114,270	188,402	15,236	26,167	7.5	7.2	51	77	82	1980.1	1984.8	1987.2
1405 Hyperplasia of prostate	84,037	36,758	10,774	9,425	7.8	3.9	2	10	11	1978.0	1994.3	1998.5
1406 Other diseases of male genital organs	25,782	25,766	8,057	5,992	3.2	4.3	25	35	35	1979.0	1983.4	1984.5
1407 Disorders of breast	18,773	7,778	6,953	4,575	2.7	1.7	4	6	5	1969.8	1974.7	1976.2
1408 Inflammatory diseases of female pelvic organs	14,551	6,198	3,307	1,675	4.4	3.7	19	26	28	1978.8	1981.3	1984.1
1409 Menstrual, menopausal and other female genital conditions	21,347	4,770	6,099	1,908	3.5	2.5	25	46	51	1975.6	1985.8	1988.8
1410 Other disorders of the genitourinary system	105,106	46,165	21,897	17,098	4.8	2.7	6	10	10	1966.5	1976.1	1981.3
1501 Medical abortion	1,600	316	842	186	1.9	1.7	3	3	4	1971.0	1971.0	1978.0
1502 Other pregnancy with abortive outcome	11,472	4,622	6,038	3,081	1.9	1.5	7	7	9	1972.7	1968.4	1977.3
1503 Complications of pregnancy predominantly in the antenatal period	324,429	294,986	50,692	77,628	6.4	3.8	15	18	19	1982.9	1985.5	1987.2
1504 Complications of pregnancy predominantly during labour and delivery	145,228	132,318	26,405	36,755	5.5	3.6	6	10	10	1976.2	1984.4	1988.4
1505 Single spontaneous delivery	202,630	14,445	41,353	4,815	4.9	3.0	1	3	3	1961.0	1985.3	1985.3
1506 Other delivery	40,456	672	6,224	160	6.5	4.2	2	4	4	1967.0	1982.3	1982.3
1507 Complications predominantly related to the puerperium	12,740	6,683	2,498	2,025	5.1	3.3	3	6	4	1984.7	1985.2	1979.0

Appendix Table 4
Subset of data used in hospital utilization analysis

	days		discharges		los		n_sold			year_auth		
	2000	2019	2000	2019	2000	2019	1989	2008	2019	1989	2008	2019
1601 Disorders related to short gestation and low birth weight	14,388	21,532	723	1,321	19.9	16.3	6	8	8	1984.3	1990.6	1990.6
1602 Other conditions originating in the perinatal period	22,967	19,828	3,281	3,605	7.0	5.5	80	107	110	1978.0	1982.0	1984.5
1700 Congenital malformations, deformations and chromosomal abnormalities	58,919	43,065	10,911	9,570	5.4	4.5	40	49	57	1977.1	1979.8	1985.5
1801 Pain in throat and chest	29,755	19,414	8,042	8,089	3.7	2.4	39	54	57	1979.4	1983.3	1985.8
1802 Abdominal and pelvic pain	26,347	16,621	7,749	6,156	3.4	2.7	35	53	56	1978.2	1983.0	1985.6
1804 Other symptoms, signs and abnormal clinical and laboratory findings	317,655	327,257	58,825	64,168	5.4	5.1	175	240	253	1978.4	1983.3	1985.8
1901 Intracranial injury	100,723	93,632	20,984	13,376	4.8	7.0	4	4	4	1967.8	1967.8	1967.8
1904 Fracture of femur	387,258	381,486	16,340	20,510	23.7	18.6	0	4	4	.	2001.0	2001.0
1905 Fracture of lower leg, including ankle	100,013	95,303	10,418	13,423	9.6	7.1	0	1	0	.	2002.0	.
1906 Other injuries	459,480	503,055	61,264	60,609	7.5	8.3	18	21	21	1977.6	1980.6	1980.7
1907 Burns and corrosions	18,042	10,922	1,841	1,126	9.8	9.7	18	19	18	1980.9	1981.0	1981.6
1908 Poisonings by drugs, medicaments and biological substances and toxic effects of substances chiefly nonmedicinal as to source	46,855	68,775	11,428	13,226	4.1	5.2	30	43	46	1980.1	1986.6	1988.5
1909 Complications of surgical and medical care, not elsewhere classified	245,731	288,708	23,628	35,643	10.4	8.1	53	66	79	1980.1	1982.0	1986.7
1911 Other and unspecified effects of external causes	15,535	21,533	2,390	4,141	6.5	5.2	25	30	33	1974.8	1976.9	1981.0

Appendix Table 4
Subset of data used in hospital utilization analysis

	days		discharges		los		n_sold			year_auth		
	2000	**2019**	**2000**	**2019**	**2000**	**2019**	**1989**	**2008**	**2019**	**1989**	**2008**	**2019**
2102 Contraceptive management	4,120	560	2,575	467	1.6	1.2	9	17	19	1979.6	1988.5	1992.4
2104 Other medical care (including radiotherapy and chemotherapy sessions)	130,191	192,654	30,277	14,595	4.3	13.2	3	3	3	1998.3	1998.3	1998.3
2105 Other factors influencing health status and contact with health services	281,418	254,280	34,743	50,856	8.1	5.0	14	28	30	1984.9	1990.0	1992.3

Appendix Table 5: Estimates of models of 2003-2018 mortality growth, not controlling and controlling for 1998-2003 mortality growth

$\ln(\text{outcome}_{d,2018}) - \ln(\text{outcome}_{d,2003}) = \beta_k (\text{vintage}_{d,2018\text{-}k} - \text{vintage}_{d,2003\text{-}k}) + \gamma (\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})) + \varepsilon_d$

Variable	Estimate	Std. Err.	t Value	Pr > |t|		Estimate	Std. Err.	t Value	Pr > |t|
	outcome = deaths								
$\text{vintage}_{d,2018} - \text{vintage}_{d,2003}$	**-0.055**	**0.027**	**-2.06**	**0.0423**		-0.051	0.028	-1.84	0.069
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						0.137	0.177	0.77	0.443
$\text{vintage}_{d,2017} - \text{vintage}_{d,2002}$	**-0.073**	**0.026**	**-2.83**	**0.0058**		**-0.070**	**0.027**	**-2.59**	**0.0114**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						0.086	0.176	0.48	0.6293
$\text{vintage}_{d,2016} - \text{vintage}_{d,2001}$	-0.028	0.022	-1.27	0.2067		-0.022	0.023	-0.97	0.3346
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						0.156	0.184	0.85	0.399
$\text{vintage}_{d,2015} - \text{vintage}_{d,2000}$	-0.029	0.022	-1.28	0.2028		-0.023	0.023	-1.00	0.3195
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						0.158	0.182	0.87	0.3881
$\text{vintage}_{d,2014} - \text{vintage}_{d,1999}$	-0.023	0.024	-0.96	0.3381		-0.017	0.025	-0.69	0.4913
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						0.176	0.182	0.97	0.3367
$\text{vintage}_{d,2013} - \text{vintage}_{d,1998}$	-0.034	0.023	-1.52	0.1333		-0.029	0.024	-1.21	0.2306
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						0.139	0.184	0.76	0.4518
	outcome = yll85								
$\text{vintage}_{2018} - \text{vintage}_{2003}$	-0.046	0.029	-1.57	0.1202		-0.048	0.029	-1.66	0.1015
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.210	0.200	-1.05	0.2978
$\text{vintage}_{2017} - \text{vintage}_{2002}$	-0.052	0.026	-1.95	0.0547		**-0.056**	**0.027**	**-2.11**	**0.0379**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.242	0.200	-1.21	0.2283
$\text{vintage}_{2016} - \text{vintage}_{2001}$	-0.008	0.022	-0.38	0.7026		-0.012	0.022	-0.55	0.5828
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.201	0.206	-0.98	0.3308
$\text{vintage}_{2015} - \text{vintage}_{2000}$	-0.009	0.023	-0.41	0.6812		-0.013	0.023	-0.56	0.5759
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.199	0.205	-0.97	0.3338
$\text{vintage}_{2014} - \text{vintage}_{1999}$	-0.004	0.024	-0.18	0.8587		-0.008	0.024	-0.32	0.7523
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.191	0.205	-0.93	0.3547
$\text{vintage}_{2013} - \text{vintage}_{1998}$	-0.019	0.023	-0.82	0.4128		-0.024	0.023	-1.01	0.3152
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.220	0.205	-1.07	0.2868

Appendix Table 5: Estimates of models of 2003-2018 mortality growth, not controlling and controlling for 1998-2003 mortality growth

$\ln(\text{outcome}_{d,2018}) - \ln(\text{outcome}_{d,2003}) = \beta_k (\text{vintage}_{d,2018\text{-}k} - \text{vintage}_{d,2003\text{-}k}) + \gamma (\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})) + \varepsilon_d$

Variable	Estimate	Std. Err.	t Value	Pr > |t|		Estimate	Std. Err.	t Value	Pr > |t|
	outcome = yll75								
$\text{vintage}_{2018} - \text{vintage}_{2003}$	**-0.067**	**0.029**	**-2.29**	**0.0244**		**-0.070**	**0.028**	**-2.45**	**0.0163**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.425	0.184	-2.31	0.0233
$\text{vintage}_{2017} - \text{vintage}_{2002}$	**-0.066**	**0.026**	**-2.57**	**0.0119**		**-0.072**	**0.025**	**-2.88**	**0.005**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.456	0.182	-2.50	0.0144
$\text{vintage}_{2016} - \text{vintage}_{2001}$	-0.023	0.022	-1.05	0.2945		-0.029	0.021	-1.37	0.1749
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.438	0.190	-2.31	0.0234
$\text{vintage}_{2015} - \text{vintage}_{2000}$	-0.025	0.023	-1.09	0.2809		-0.030	0.022	-1.36	0.1766
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.434	0.189	-2.29	0.0245
$\text{vintage}_{2014} - \text{vintage}_{1999}$	-0.021	0.024	-0.86	0.3937		-0.027	0.024	-1.14	0.2596
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.430	0.190	-2.26	0.0264
$\text{vintage}_{2013} - \text{vintage}_{1998}$	-0.033	0.023	-1.44	0.1527		-0.041	0.023	-1.82	0.0731
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.454	0.189	-2.41	0.0183
	outcome = yll65								
$\text{vintage}_{2018} - \text{vintage}_{2003}$	**-0.099**	**0.031**	**-3.23**	**0.0018**		**-0.096**	**0.028**	**-3.37**	**0.0012**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.760	0.185	-4.12	<.0001
$\text{vintage}_{2017} - \text{vintage}_{2002}$	**-0.089**	**0.027**	**-3.36**	**0.0012**		**-0.094**	**0.024**	**-3.83**	**0.0003**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.803	0.181	-4.43	<.0001
$\text{vintage}_{2016} - \text{vintage}_{2001}$	-0.046	0.024	-1.96	0.0535		**-0.050**	**0.022**	**-2.29**	**0.0248**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.794	0.191	-4.15	<.0001
$\text{vintage}_{2015} - \text{vintage}_{2000}$	**-0.049**	**0.025**	**-2.01**	**0.0473**		**-0.052**	**0.023**	**-2.28**	**0.0251**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.788	0.191	-4.12	<.0001
$\text{vintage}_{2014} - \text{vintage}_{1999}$	-0.045	0.026	-1.70	0.0933		**-0.049**	**0.024**	**-2.01**	**0.0476**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.793	0.193	-4.11	<.0001
$\text{vintage}_{2013} - \text{vintage}_{1998}$	**-0.051**	**0.025**	**-2.07**	**0.0421**		**-0.056**	**0.023**	**-2.44**	**0.0171**
$\ln(\text{outcome}_{d,2003}) - \ln(\text{outcome}_{d,1998})$						-0.799	0.191	-4.19	<.0001