The association between pharmaceutical innovation and both premature mortality and hospital utilization in Switzerland, 1996–2019

Frank R. Lichtenberg¹,²,³*

Abstract

We analyze the association that pharmaceutical innovation had with premature mortality from all diseases in Switzerland during the period 1996–2018, and its association with hospital utilization for all diseases in Switzerland during the period 2002–2019. The analysis is performed by investigating whether the diseases that experienced more pharmaceutical innovation had larger subsequent declines in premature mortality and hospitalization. Pharmaceutical innovation is measured by the growth in the number of drugs used to treat a disease ever registered in Switzerland. Utilization of a chemical substance reaches a peak 9–12 years after it was first launched, and then declines. Our estimates indicate that the number of years of potential life lost before ages 85, 75, and 65 is significantly inversely related to the number of chemical substances ever registered 6–9, 3–9, and 0–9 years earlier, respectively. The new chemical substances that were registered during the period 1990–2011 are associated with reductions in the number of years of potential life lost before ages 85, 75, and 65 in 2018 of 257 thousand, 163 thousand, and 102 thousand, respectively. The number of hospital days is significantly inversely related to the number of chemical substances ever registered 8–10 years earlier. The new chemical substances that were registered during the period 1994–2010 are associated with reductions in the number of hospital days in 2019 of 2.07 million. Average length of inpatient hospital stays is significantly inversely related to the number of chemical substances ever registered 2–10 years earlier. The new chemical substances that were registered during the period 1999–2015 are associated with reductions in the average length of stays in 2019 of 0.4 days. Under the assumption that pharmaceutical innovation is exogenous with respect to premature mortality and hospitalization, and that it is uncorrelated with other potential determinants of health outcomes, if we ignore the reduction in hospital utilization associated with previous pharmaceutical innovation, a rough estimate of the cost per life-year before age 85 gained in 2018 is €14,310. However, about 85% of the 2018 expenditure on drugs registered during the period 1990–2011 may have been offset by the reduction in expenditure on inpatient curative and rehabilitative care. The net cost per life-year before age 85 gained in 2018 may therefore have been €2,201.

Keywords: Prescription drugs, Hospitalization, Longevity, Innovation, Switzerland

1 Introduction

A previous study (Lichtenberg, 2016) analyzed the association that pharmaceutical innovation had with premature mortality from cancer in Switzerland during the period 1995–2012, by investigating whether the cancer sites that experienced more pharmaceutical innovation...
had larger declines in premature mortality, controlling for the number of people diagnosed and mean age at diagnosis. That study found that premature cancer mortality before ages 75 and 65 was significantly inversely related to the cumulative number of drugs registered 5, 10, and 15 years earlier.

Cancer accounts for only about one-third of the years of potential life lost (YPLL) before age 75 in Switzerland.\(^1\) In the present study, we will use similar methods to analyze the association that pharmaceutical innovation had with premature mortality from all diseases in Switzerland during a period that includes more recent years: 1996–2018. There was considerable variation across diseases in the growth in the number of drugs used to treat the diseases ever registered in Switzerland. This is illustrated by Fig. 1, which shows data for 5 diseases, for which fairly similar (between 27 and 31) numbers of drugs had been registered by 1993. During the next 25 years, 16 or fewer drugs were registered for 3 diseases, 21 drugs were registered for “other lower respiratory diseases,” and 47 drugs were registered for “other malignant neoplasms.”

We will extend the analysis performed in the previous study in two additional ways. We will analyze an additional measure of premature mortality: the number of years of potential life lost before age 85 (as well as before 75 and 65).\(^2\) And, we will analyze the association that pharmaceutical innovation had with hospital utilization for all diseases in Switzerland during the period 2002–2019. In 2018, expenditure on inpatient curative and rehabilitative care was almost three times as great as expenditure on prescribed medicines: €18.0 billion vs. €6.3 billion.

In the next section, we will describe the econometric model that we will use to analyze the association that pharmaceutical innovation had with premature mortality and hospitalization due to all diseases in Switzerland during the period 1996–2019. The data sources used to estimate this model are discussed on Sect. 3. Empirical results are presented in Sect. 4. Some implications of the estimates are discussed on Sect. 5. Section 6 provides a summary.

---

\(^1\) Association of Public Health Epidemiologists in Ontario (2006) describes the calculation of YPLL.

\(^2\) In 2018, Swiss life expectancy at birth was 83.75 years. The U.S. Centers for Disease Control’s WISQARS Years of Potential Life Lost (YPLL) Report website (Centers for Disease Control, 2021) allows the user to calculate YPLL before ages 65, 70, 75, 80, and 85.
2 Econometric model of premature mortality and hospital utilization

We begin with the following general model of the association between health outcomes and the history of pharmaceutical innovation:

\[ \ln(Y_{ct}) = \beta \ln(N_{NEW_{ct}} + \frac{\gamma_1}{\gamma_2} N_{NEW_{ct-1}} + \frac{\gamma_2}{\gamma_3} N_{NEW_{ct-2}} + \cdots) + \alpha_c + \delta_t + \varepsilon_{ct} \]  

(1)

where

- \( Y_{ct} \) is a measure of premature mortality or hospital utilization due to medical condition \( c \) in year \( t \)
- \( N_{NEW_{ct-k}} \) is the number of new drugs used to treat medical condition \( c \) that were approved in year \( t - k \) \( (k = 0, 1, 2, \ldots) \);
- \( \alpha_c \) is a fixed effect for medical condition \( c \);
- \( \delta_t \) is a fixed effect for year \( t \).

According to Eq. (1), premature mortality and hospitalization due to a medical condition depends on the logarithm of a distributed lag function of the number of new drugs approved to treat the disease, controlling for fixed medical condition and year effects. This specification allows the effect of a new drug approval on outcomes to depend upon how long ago the drug was approved. For example, \((\gamma_2/\gamma_1) = 2\) would imply that a drug approved 2 years ago has twice as great an impact as a drug approved one year ago.

The lag structure of Eq. (1)—in particular, whether recently approved drugs have a smaller or larger impact than drugs approved longer ago—is likely to depend on several factors. Two considerations suggest that recently approved drugs should have a smaller impact. First, utilization of recently-launched drugs tends to be lower than utilization of drugs launched many years earlier. Evidence about the shape of the age (number of years since launch)-utilization profile can be obtained by estimating the following equation:

\[ \ln(N_{SU_{mn}}) = \rho_m + \delta_n + \varepsilon_{mn} \]  

(2)

where

- \( N_{SU_{mn}} \) is the number of standard units of chemical substance \( m \) sold \( n \) years after it was first launched \( (n = 0, 1, \ldots, 20) \);
- \( \rho_m \) is a fixed effect for chemical substance \( m \);
- \( \delta_n \) is a fixed effect for age \( n \).
The expression \( \exp(\delta_c - \delta_{c,t}) \) is a “relative utilization index”; it is the mean ratio of the quantity of a drug sold \( n \) years after it was launched to the quantity of the same drug sold 12 years after it was launched. We estimated Eq. (2), using annual data for the period 2010–2020 on 1015 chemical substances. Estimates of the “relative utilization index” are shown in Fig. 2. These estimates indicate that utilization of a chemical substance reaches a peak 9–12 years after it was first launched, and then declines. It is used about twice as much 9 years after a peak 9–12 years after it was first launched, and then indicate that utilization of a chemical substance reaches a utilization index” are shown in Fig. 2. These estimates are one of the following variables:

\[
Y_{PLL85_{ct}} = \text{the number of years of potential life lost before age 85 due to cause } c \text{ in year } t \ (t=1996, 1997, \ldots, 2018);
\]

\[
Y_{PLL75_{ct}} = \text{the number of years of potential life lost before age 75 due to cause } c \text{ in year } t \ (t=1996, 1997, \ldots, 2018);
\]

\[
Y_{PLL65_{ct}} = \text{the number of years of potential life lost before age 65 due to cause } c \text{ in year } t \ (t=1996, 1997, \ldots, 2018);
\]

\[
\text{HOSP\_DAYS}_{ct} = \text{the number of hospital days due to cause } c \text{ in year } t \ (t=2002, 2003, \ldots, 2019);
\]

\[
\text{ALOS}_{ct} = \text{the average length of hospital stays due to cause } c \text{ in year } t \ (t=2002, 2003, \ldots, 2019)
\]

and

\[
\text{CUM\_DRUG}_{c,t-k} = \sum_{m} \text{IND}_{mc} \text{ LAUNCHED}_{m,t-k} = \text{the number of chemical substances to treat medical condition } c \text{ that had been launched in Switzerland by the end of year } t-k \ (k=0, 1, 2, \ldots, 12\}
\]

\[= 1 \text{ if chemical substance } m \text{ is used to treat (indicated for) medical}
\]

\[3 \text{ Grossman and Helpman (1991) argued that "innovative goods are better than older products simply because they provide more product services in relation to their cost of production." Bresnahan and Gordon (1996) stated simply that "new goods are at the heart of economic progress," and Bils (2004) said that "much of economic growth occurs through growth in quality as new models of consumer goods replace older, sometimes inferior, models." As noted by Jovanovic and Yatsenko (2012), in "the Spence–Dixit–Stiglitz tradition...new goods [are] of higher quality than old goods."}

4 The impact on disease burden may depend on the interaction (quantity \( \times \) quality) of the two variables. The impact will increase with respect to drug age (time since launch) if the rate of increase of quantity with respect to age is greater than the rate of decline of quality with respect to age; otherwise the impact will decline.

5 The Swiss process of marketing authorization and reimbursement takes place in two steps. Step one: Drug is reviewed for safety, effectiveness and approval by Swissmedic. If approved, the drug receives market authorization. Step two: The producer negotiates a price for the drug with the Federal Office of Public Health. Once the price is determined, the drug is put on the Specialty List for reimbursement. Virtually all drugs that receive marketing authorization are put on the Specialty List. This process takes longer for some drugs than it does for others. An intermediary/broker (the Federal Drug Commission (EAK)) is responsible for recommending a price for a newly approved drug. According to Paris and Docteur (2007), "the Swiss tend to be early adopters of new pharmaceutical products."
includes multiple lag lengths.

Both measures control for changes in the distribution of YPLL or hospital utilization, by cause.

LAUNCHED \(_{m,t-k}\)

1 if chemical substance \(m\) had been registered in Switzerland by the end of year \(t-k\)

\(= 0\) if chemical substance \(m\) had not been registered in Switzerland by the end of year \(t-k\)

\(\alpha_c\)
a fixed effect for medical condition \(c\)

\(\delta_t\)
a fixed effect for year \(t\)

This formulation of the “health production function” (Koç, 2004) is consistent with Romer’s (1990) model of endogenous technological change, in which “growth in income per person is tied to growth in the total stock of ideas” (Jones (2019, p. 861), emphasis added).

Equation (3) will be estimated by weighted least-squares. For the first four dependent variables, the weight will be \(\sum_c Y_{ct}\). For the last dependent variable, the weight will be \(N_{DISCHARGES}_{ct} = \) the number of inpatient hospital discharges due to cause \(c\) in year \(t\). Disturbances will be clustered by cause.

The year fixed effects (\(\delta_t\)’s) in Eq. (3) control for the effects of changes in macroeconomic variables (e.g. population size, GDP, educational attainment), to the extent that these variables have similar effects on mortality and hospitalization caused by different diseases. The year fixed effects capture the change in the dependent variable, holding lagged CUM_DRUG constant, i.e., in the absence of previous pharmaceutical innovation. The (“counterfactual”) estimated aggregate value of the dependent variable in year \(t\) in the absence of previous pharmaceutical innovation is \((\sum_c Y_{c,1996}) \times \exp(\delta_t - \delta_{1996})\). We can estimate the (“actual”) aggregate value of the dependent variable in year \(t\) in the presence of previous pharmaceutical innovation as \((\sum_c Y_{c,1996}) \times \exp (\delta_t' - \delta_{1996}')\), where \(\delta_t'\) is the year fixed effect of the following equation:

\[
\ln (Y_{ct}) = \alpha_c^t + \delta_t' + \epsilon_{ct}
\]

For each dependent variable, we will estimate 13 versions of Eq. (3): one for each value of the lag length \(k\) \((k=0, 1, 2, ..., 12)\). We will also estimate a version that includes multiple lag lengths.

Equation (3) includes a measure of pharmaceutical innovation \((CUM\_DRUG\_{t-k,k})\), but it does not include measures of other types of biomedical innovation (e.g. innovation in diagnostic imaging, surgical procedures, and medical devices). Dorsey (2010) showed that 88% of private U.S. funding for biomedical research came from pharmaceutical and biotechnology firms. Also, some previous research indicated that non-pharmaceutical medical innovation is not positively correlated across diseases with pharmaceutical innovation. Some studies have found no mortality benefit from more intensive screening. For example, data from the Prostate, Lung, Colorectal and Ovarian randomized screening trial showed that, after 13 years of follow up, men who underwent annual prostate cancer screening with prostate-specific antigen testing and digital rectal examination had a 12 percent higher incidence of prostate cancer than men in the control group but the same rate of death from the disease. No evidence of a mortality benefit was seen in subgroups defined by age, the presence of other illnesses, or pre-trial PSA testing (National Cancer Institute, 2012). Also, a large U.S. government study found that drug therapy alone may save the lives of heart disease patients with blocked coronary arteries as effectively as bypass or stenting procedures (Kolata, 2019). Nevertheless, controlling for non-pharmaceutical medical innovation would be desirable, but measuring non-pharmaceutical medical innovation is far more difficult than measuring pharmaceutical innovation.

3 Data sources and descriptive statistics

Data on the Swiss approval dates (1933-present) of molecules (WHO ATC5 chemical substances) were obtained from Swissmedic (2021). Data on approved ICD-10 indications of WHO ATC5 chemical substances were obtained from Thériaque, a database produced by France’s Centre National Hospitalier d’Information sur le Médicament (2021). Data on Swiss drug expenditure, by molecule and year (2010–2020), were obtained from the IQVIA MIDAS database. Data on the number of years of potential life lost before ages 85, 75, and 65, by cause and year (1996–2018), were constructed from data contained in the Eurostat hith_cd_aro and hith_cd_anr files (European Commission, 2021). Data on population, by age group and year, were obtained from the Eurostat demo_pjangroup file. Data on the number of days of hospital care, by cause and year (2002–2019), were obtained from the Eurostat hith_co_hosday file. Data on inpatient average length

---

6 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.

7 Both measures control for changes in the distribution of YPLL or hospital utilization, by cause.

8 Much of the rest came from the federal government (i.e. the NIH), and new drugs often build on upstream government research (Sampat and Lichtenberg 2011). The National Cancer Institute (2021) says that it “has played a vital role in cancer drug discovery and development, and, today, that role continues”.

---
of stay (in days), by cause and year (2002–2019), were obtained from the Eurostat hlth_co_dischls file.

Annual data on mortality from all causes during 1996–2018 are shown in Table 1. Between 1996 and 2018, YPLL85 declined by 20%, and the population below age 85 increased by 19%, so the premature (before age 85) mortality rate declined by 33%, from 9789 to 6573 per 100,000 population. The pre-age-75 and pre-age-65 mortality rates declined even more, by 38% and 44%, respectively. Data on mortality by cause in 2018 are shown in Table 5 in Appendix.

Data on hospitalization for all causes during 2002–2019 are shown in Table 2. Between 2002 and 2019, the number of hospital days was essentially constant, and the population increased by 18%, so the number of hospital days per 1000 population declined by 15%, despite the aging of the population. The average length of hospital stays declined even more, by 29%. Data on the number of hospital days and average length of stay, by cause, in 2019 are shown in Table 6 in Appendix.

Data on the number of chemical substances ever registered in Switzerland, by medical condition (hospital classification), 1989–2019, are shown in Table 7 in Appendix.

4 Empirical results

4.1 Premature mortality model estimates

Estimates of $\beta_k$ from 2-way fixed-effects premature mortality models [Eq. (3)] are presented in Table 3 and plotted in Fig. 3. Each estimate is from a separate model.

Panel A of the table and figure show estimates when the dependent variable is ln(YPLL85<sub>ct</sub>). The estimates of $\beta_k$ are not statistically significant when $k \leq 5$, but they are negative and significant when $6 \leq k \leq 9$: premature (before age 85) mortality is significantly inversely related to the number of chemical substances ever registered 6–9 years earlier. It is most strongly inversely related to the number of chemical substances ever registered 6–9 years earlier.
8 years earlier. This is consistent with the evidence discussed above that utilization of a chemical substance reaches a peak 9–12 years after it was first launched, and that drugs launched more recently are likely to be of higher quality than earlier-vintage drugs.

Panel B of Table 3 and Fig. 3 shows estimates when the dependent variable is \( \ln(YPLL_{75ct}) \). In this case, the estimates are negative and significant when \( 3 \leq k \leq 9 \): the number of years of potential life lost before age 75 is significantly inversely related to the number of chemical substances ever registered 3–9 years earlier. It is most strongly inversely related to the number of chemical substances ever registered 7 years earlier.

Panel C of Table 3 and Fig. 3 shows estimates when the dependent variable is \( \ln(YPLL_{65ct}) \). In this case, the estimates are negative and significant when \( 0 \leq k \leq 9 \): the number of years of potential life lost before age 65 is significantly inversely related to the number of chemical substances ever registered 0–9 years earlier. Once again, it is most strongly inversely related to the number of chemical substances ever registered 7 years earlier. But the finding that YPLL65 is significantly inversely related to the number of chemical substances ever registered just a few years earlier may indicate that access to new drugs for diseases that kill patients at lower ages may occur earlier than access to new drugs for diseases that kill patients at higher ages.

As discussed above, by estimating both Eqs. (3) and (4), we can compute both the (“counterfactual”) aggregate value of the dependent variable in year \( t \) in the absence of previous pharmaceutical innovation, and the (“actual”) aggregate value of the dependent variable in year \( t \) in the presence of previous pharmaceutical innovation. The results of these calculations for the three premature mortality measures are shown in Fig. 4. For each measure, we use the estimate of Eq. (3) in which \( \ln(CUM_{DRUG_{c,t−k}}) \) is most strongly related to \( \ln(Y_{ct}) \).

Panels A and B of Fig. 4 compare the evolution of aggregate YPLL85 (=\( \sum_{c}YPLL_{85ct} \)) controlling for \( CUM_{DRUG_{c,t−7}} \) (i.e., if \( CUM_{DRUG_{c,t−7}} \) had remained constant) to the actual evolution of aggregate YPLL85. Between 1996 and 2018, YPLL85 declined by 20%, from 679 to 544 thousand. The estimate of \( \beta_7 \) implies that, if \( CUM_{DRUG_{c,t−7}} \) had not increased, YPLL85 would have increased by 18%, to 801 thousand. As shown in Table 1, during that period, the population below age 85 increased by 19%, which implies that, if \( CUM_{DRUG_{c,t−7}} \) had not increased, there would

### Table 2: Hospital utilization for all causes except V–Z, 2002–2019

| Year   | No. of hospital days | Population | Hospital days per 1000 population | Average length of stay |
|--------|----------------------|------------|-----------------------------------|------------------------|
| 2002   | 11,479,682           | 7,255,653  | 1582                              | 11.4                   |
| 2003   | 11,424,156           | 7,313,853  | 1562                              | 11.3                   |
| 2004   | 10,995,761           | 7,364,148  | 1493                              | 10.8                   |
| 2005   | 10,929,566           | 7,415,102  | 1474                              | 10.6                   |
| 2006   | 10,677,099           | 7,459,128  | 1431                              | 10.2                   |
| 2007   | 10,417,517           | 7,508,739  | 1387                              | 9.7                    |
| 2008   | 10,408,136           | 7,593,494  | 1371                              | 9.5                    |
| 2009   | 10,444,939           | 7,701,856  | 1356                              | 9.2                    |
| 2010   | 11,248,330           | 7,785,806  | 1445                              | 9.0                    |
| 2011   | 11,380,995           | 7,870,134  | 1446                              | 8.8                    |
| 2012   | 1,1150,469           | 7,954,662  | 1402                              | 8.7                    |
| 2013   | 11,292,607           | 8,039,060  | 1405                              | 8.6                    |
| 2014   | 11,388,407           | 8,139,631  | 1399                              | 8.5                    |
| 2015   | 11,535,738           | 8,237,666  | 1400                              | 8.4                    |
| 2016   | 11,738,624           | 8,327,126  | 1410                              | 8.3                    |
| 2017   | 11,612,636           | 8,419,550  | 1379                              | 8.2                    |
| 2018   | 11,500,553           | 8,484,130  | 1356                              | 8.2                    |
| 2019   | 11,512,426           | 8,544,527  | 1347                              | 8.2                    |
| 2019/2002 | 1.00               | 1.18       | 0.85                              | 0.71                   |
| Lag (k) | Estimate | Standard error | 95% Lower confidence | 95% Upper confidence | Z | Pr>|Z| |
|---------|----------|----------------|----------------------|---------------------|---|-------|
|         | A. Dependent variable \(\ln(YPLL85_{ct})\) | | | | | |
| 0       | -0.440   | 0.409          | -1.242               | 0.362               | -1.07 | 0.2827 |
| 1       | -0.450   | 0.376          | -1.187               | 0.287               | -1.20 | 0.2317 |
| 2       | -0.467   | 0.346          | -1.145               | 0.210               | -1.35 | 0.1766 |
| 3       | -0.482   | 0.314          | -1.098               | 0.135               | -1.53 | 0.1257 |
| 4       | -0.486   | 0.289          | -1.052               | 0.080               | -1.68 | 0.0926 |
| 5       | -0.498   | 0.265          | -1.017               | 0.022               | -1.88 | 0.0605 |
| 6       | -0.508   | 0.247          | -0.992               | -0.024              | -2.06 | 0.0395 |
| 7       | -0.514   | 0.233          | -0.971               | -0.056              | -2.20 | 0.0277 |
| 8       | -0.501   | 0.226          | -0.944               | -0.058              | -2.22 | 0.0266 |
| 9       | -0.462   | 0.222          | -0.896               | -0.027              | -2.08 | 0.0374 |
| 10      | -0.331   | 0.200          | -0.724               | 0.062               | -1.65 | 0.0986 |
| 11      | -0.252   | 0.183          | -0.610               | 0.106               | -1.38 | 0.1684 |
| 12      | -0.198   | 0.171          | -0.532               | 0.136               | -1.16 | 0.2457 |
|         | B. Dependent variable \(\ln(YPLL75_{ct})\) | | | | | |
| 0       | -0.727   | 0.477          | -1.663               | 0.208               | -1.52 | 0.1275 |
| 1       | -0.725   | 0.433          | -1.575               | 0.124               | -1.67 | 0.0943 |
| 2       | -0.735   | 0.385          | -1.490               | 0.021               | -1.91 | 0.0566 |
| 3       | -0.717   | 0.351          | -1.405               | -0.028              | -2.04 | 0.0413 |
| 4       | -0.694   | 0.316          | -1.312               | -0.076              | -2.20 | 0.0279 |
| 5       | -0.677   | 0.290          | -1.245               | -0.108              | -2.33 | 0.0197 |
| 6       | -0.669   | 0.271          | -1.200               | -0.138              | -2.47 | 0.0135 |
| 7       | -0.657   | 0.259          | -1.165               | -0.149              | -2.54 | 0.0112 |
| 8       | -0.630   | 0.258          | -1.135               | -0.124              | -2.44 | 0.0147 |
| 9       | -0.565   | 0.266          | -1.086               | -0.044              | -2.13 | 0.0335 |
| 10      | -0.398   | 0.258          | -0.904               | 0.108               | -1.54 | 0.1235 |
| 11      | -0.287   | 0.247          | -0.770               | 0.197               | -1.16 | 0.2452 |
| 12      | -0.204   | 0.236          | -0.666               | 0.257               | -0.87 | 0.3858 |
|         | C. Dependent variable \(\ln(YPLL65_{ct})\) | | | | | |
| 0       | -1.067   | 0.490          | -2.026               | -0.107              | -2.18 | 0.0294 |
| 1       | -1.042   | 0.432          | -1.890               | -0.195              | -2.41 | 0.0159 |
| 2       | -1.025   | 0.371          | -1.752               | -0.297              | -2.76 | 0.0058 |
| 3       | -0.975   | 0.337          | -1.636               | -0.314              | -2.89 | 0.0038 |
| 4       | -0.920   | 0.296          | -1.500               | -0.341              | -3.11 | 0.0019 |
| 5       | -0.878   | 0.271          | -1.410               | -0.347              | -3.24 | 0.0012 |
| 6       | -0.856   | 0.253          | -1.352               | -0.361              | -3.39 | 0.0007 |
| 7       | -0.834   | 0.242          | -1.309               | -0.359              | -3.44 | 0.0006 |
| 8       | -0.799   | 0.247          | -1.283               | -0.316              | -3.24 | 0.0012 |
| 9       | -0.722   | 0.266          | -1.243               | -0.201              | -2.71 | 0.0066 |
| 10      | -0.538   | 0.283          | -1.093               | 0.018               | -1.90 | 0.0579 |
| 11      | -0.408   | 0.292          | -0.981               | 0.166               | -1.39 | 0.1634 |
| 12      | -0.301   | 0.297          | -0.884               | 0.281               | -1.01 | 0.3105 |

Estimates in bold are statistically significant (p value <.05)
Estimates of $\beta_k$ from 2-way fixed-effects premature mortality models (eq. (3))
Solid squares denote significant (p-value < .05) estimates; hollow squares denote insignificant estimates.

A. Number of years of potential life lost before age 85

B. Number of years of potential life lost before age 75

C. Number of years of potential life lost before age 65

Fig. 3 Estimates of $\beta_k$ from 2-way fixed-effects premature mortality models [Eq. (3)] Solid squares denote significant (p-value < .05) estimates; hollow squares denote insignificant estimates
have been almost no change in the premature (before age 85) mortality rate. The new chemical substances that were registered during the period 1990–2011 are associated with a reduction in the number of years of potential life lost before age 85 in 2018 of 257 thousand (= 801 thousand – 544 thousand).

---

10 Between 1997 and 2017, some non-medical determinants of health improved, but others declined. The fraction of the population aged 15+ who were daily smokers declined from 28.9 to 19.1%, but the fraction of the population who were obese (self-reported) increased from 6.8 to 11.3% (Organisation for Economic Co-operation and Development, 2021).
Panels C and D of Fig. 4 show similar calculations for YPLL75. Between 1996 and 2018, YPLL75 declined by 26%, from 366 to 271 thousand. The estimate of \( \beta_7 \) implies that, if CUM\_DRUG\_ct–7 had not increased, YPLL75 would have increased by 18%, to 431 thousand. As shown in Table 1, during that period, the population below age 75 increased by 18%, which implies that, if CUM\_DRUG\_ct–7 had not increased, there would have been almost no change in the premature (before age 75) mortality rate. The new chemical substances that were registered during the period 1990–2011 are associated with a reduction in the number of years of potential life lost before age 75 in 2018 of 163 thousand (= 430 thousand–267 thousand).

Panels E and F of Fig. 4 show similar calculations for YPLL65. Between 1996 and 2018, YPLL65 declined by 35%, from 200 to 129 thousand. The estimate of \( \beta_7 \) implies that, if CUM\_DRUG\_ct–7 had not increased, YPLL65 would have increased by 16%, to 231 thousand. As shown in Table 1, during that period, the population below age 65 increased by 15%, which implies that, if CUM\_DRUG\_ct–7 had not increased, there would have been almost no change in the premature (before age 65) mortality rate. The new chemical substances that were registered during the period 1990–2011 are associated with a reduction in the number of years of potential life lost before age 65 in 2018 of 102 thousand (= 430 thousand–267 thousand).

As stated earlier, we also estimated a version of Eq. (3) that includes multiple lag lengths: CUM\_DRUG\_ct, CUM\_DRUG\_ct–8, and CUM\_DRUG\_ct–12. These estimates are shown in Table 8 in Appendix. In model 1 in that table, the dependent variable is ln(YPLL85\_ct). The coefficient on CUM\_DRUG\_ct–8 is negative and significant (\( p \) value < 0.0025); the coefficients on CUM\_DRUG\_ct and CUM\_DRUG\_ct–12 are insignificant. The magnitudes of the coefficient on CUM\_DRUG\_ct–8 is slightly (8%) larger than the coefficient shown in Table 3 (produced in model 2 of Table 8 in Appendix). In models 3 and 4 of Table 8 in Appendix, the dependent variable is ln(YPLL75\_ct); in models 5 and 6, the dependent variable is ln(YPLL65\_ct). In those models as well, the coefficient on CUM\_DRUG\_ct–8 is negative and significant, and the coefficients on CUM\_DRUG\_ct and CUM\_DRUG\_ct–12 are insignificant.

### 4.2 Hospital utilization model estimates

Estimates of \( \beta_k \) from 2-way fixed-effects hospital utilization models [Eq. (3)] are presented in Table 4 and plotted in Fig. 5.

Panel A of the table and figure shows estimates when the dependent variable is ln(ALOS\_ct). The estimates of \( \beta_k \) are negative and significant when 8 \( \leq k \leq 10 \): the number of hospital days is significantly inversely related to the number of chemical substances ever registered 8–10 years earlier. (The estimates of \( \beta_7 \) and \( \beta_{11} \) are marginally significant (\( p \) value < 0.07).) It is most strongly inversely related to the number of chemical substances ever registered 9 years earlier.

Panel B of the table and figure shows estimates when the dependent variable is ln(HOSP\_DAYS\_ct). The estimates of \( \beta_k \) are negative and significant when 2 \( \leq k \leq 10 \): average length of stay is significantly inversely related to the number of chemical substances ever registered 2–10 years earlier. It is most strongly inversely related to the number of chemical substances ever registered 4 years earlier. This relatively short lag might be due to more rapid diffusion of new drugs in the hospital sector than in the retail sector, which is the case in the U.S.

Panels A and B of Fig. 6 compare the actual evolution of aggregate hospital utilization to the estimated evolution, in the absence of previous pharmaceutical innovation. Between 2002 and 2019, controlling for the changing mix of causes of hospitalization, HOSP\_DAYS increased by 4%, from 11.5 million to 12.0 million. The estimate of \( \beta_8 \) implies that, if CUM\_DRUG\_ct–8 had not increased, HOSP\_DAYS would have increased by 22%, to 14.0 million. As shown in Table 2, during that period, the population increased by 18%, which implies that, if CUM\_DRUG\_ct–8 had not increased, there would have been a small (3%) increase in the number of hospital days per 1000 population. The new chemical substances that were registered during the period 1994–2010 are associated with a reduction in the number of hospital days in 2019 by 2.07 million (= 14.02 million–11.95 million).

Panels C and D of Fig. 6 compare the actual evolution of the average length of inpatient hospital stays to the estimated evolution, in the absence of previous pharmaceutical innovation. Between 2002 and 2019, controlling for the changing mix of causes of hospitalization, ALOS declined by 3.3 days, from 11.4 to 8.1 days. The estimate of \( \beta_8 \) implies that, if CUM\_DRUG\_ct–8 had not increased, ALOS would have declined by 2.9 days, to 8.5 days. The new chemical substances that were registered during the period 1999–2015 are associated with a reduction in ALOS in 2019 of 0.4 (= 8.5–8.1) days.

Estimates of hospital utilization models that include multiple lag lengths (CUM\_DRUG\_ct, CUM\_DRUG\_ct–8, and CUM\_DRUG\_ct–12) are shown as models 7 and 9 in
Table 4: Estimates of $\hat{\beta}_k$ from 2-way fixed-effects hospital utilization models [Eq. (3)]

| Lag (k) | Estimate | Standard error | 95% Lower confidence | 95% Upper confidence | Z | Pr>|Z|
|---------|----------|----------------|----------------------|----------------------|---|---------|
| A. Dependent variable $= \ln(\text{HOSP\_DAYS}_{ct})$ | | | | | | |
| 0 | 0.076 | 0.267 | -0.448 | 0.600 | 0.28 | 0.776 |
| 1 | 0.002 | 0.263 | -0.513 | 0.518 | 0.01 | 0.9929 |
| 2 | -0.071 | 0.269 | -0.598 | 0.456 | -0.27 | 0.7907 |
| 3 | -0.155 | 0.281 | -0.706 | 0.396 | -0.55 | 0.5816 |
| 4 | -0.219 | 0.279 | -0.766 | 0.329 | -0.78 | 0.434 |
| 5 | -0.251 | 0.267 | -0.774 | 0.272 | -0.94 | 0.3467 |
| 6 | -0.326 | 0.224 | -0.766 | 0.114 | -1.45 | 0.1462 |
| 7 | -0.356 | 0.195 | -0.738 | 0.026 | -1.83 | 0.0675 |
| 8 | -0.369 | 0.179 | -0.719 | -0.019 | -2.07 | 0.0388 |
| 9 | -0.370 | 0.172 | -0.707 | -0.033 | -2.15 | 0.0315 |
| 10 | -0.326 | 0.160 | -0.641 | -0.012 | -2.03 | 0.042 |
| 11 | -0.288 | 0.150 | -0.580 | 0.006 | -1.92 | 0.0544 |
| 12 | -0.233 | 0.141 | -0.508 | 0.043 | -1.66 | 0.0977 |
| B. Dependent variable $= \ln(\text{ALOS}_{ct})$ | | | | | | |
| 0 | -0.070 | 0.052 | -0.171 | 0.032 | -1.35 | 0.1779 |
| 1 | -0.097 | 0.054 | -0.203 | 0.009 | -1.79 | 0.0734 |
| 2 | -0.123 | 0.057 | -0.235 | -0.010 | -2.14 | 0.0324 |
| 3 | -0.151 | 0.060 | -0.269 | -0.032 | -2.49 | 0.0127 |
| 4 | -0.164 | 0.061 | -0.283 | -0.045 | -2.70 | 0.0069 |
| 5 | -0.160 | 0.061 | -0.279 | -0.041 | -2.63 | 0.0086 |
| 6 | -0.154 | 0.060 | -0.272 | -0.036 | -2.55 | 0.0108 |
| 7 | -0.156 | 0.060 | -0.275 | -0.038 | -2.59 | 0.0096 |
| 8 | -0.153 | 0.062 | -0.275 | -0.031 | -2.46 | 0.0137 |
| 9 | -0.141 | 0.063 | -0.263 | -0.018 | -2.24 | 0.0251 |
| 10 | -0.122 | 0.062 | -0.243 | -0.001 | -1.97 | 0.0491 |
| 11 | -0.116 | 0.062 | -0.238 | 0.007 | -1.85 | 0.0638 |
| 12 | -0.114 | 0.063 | -0.238 | 0.010 | -1.81 | 0.0708 |

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

Table 8 in Appendix. In model 7, the dependent variable is $\ln(\text{HOSP\_DAYS}_{ct})$. The coefficient on CUM\_DRUG$_{c,t}$ is positive and significant. Perhaps this is due to reverse causality: an exogenous increase in hospital utilization for a medical condition could stimulate an acceleration or increase in new drug approvals for that condition. The coefficient on CUM\_DRUG$_{c,t-8}$ remains negative and significant; its magnitude is 25% larger than the coefficient shown in Table 4 (reproduced in model 8 of Table 8 in Appendix). The coefficient on CUM\_DRUG$_{c,t-12}$ is insignificant. In model 9, the dependent variable is $\ln(\text{ALOS}_{ct})$. The coefficient on CUM\_DRUG$_{c,t-8}$ is negative and significant; the coefficients on CUM\_DRUG$_{c,t}$ and CUM\_DRUG$_{c,t-12}$ are insignificant.

5 Discussion

As shown in Panels A and B of Fig. 4, the new chemical substances that were registered during the period 1990–2011 are associated with a reduction in the number of years of potential life lost before age 85 in 2018 of 257 thousand. Now we will obtain rough estimates of the incremental cost-effectiveness (cost per life-year before age 85 gained) of those chemical substances in 2018. First, we will estimate cost-effectiveness if we ignore the reduction in hospital utilization attributable to previous pharmaceutical innovation. Then, we will estimate cost-effectiveness if we account for this reduction in hospital utilization.

As noted above, according to Eurostat, expenditure on prescribed medicines in Switzerland in 2018 was € 6288 million. Data from the IQVIA MIDAS database indicate
that 58.5% of 2018 expenditure on prescribed medicines was on new chemical substances that were registered during the period 1990–2011. These figures imply that, in 2018, €3678 million (≈58.5% × €6288 million) was spent on new chemical substances that were registered during the period 1990–2011. Therefore, if we ignore the reduction in hospital utilization attributable to previous pharmaceutical innovation, a rough estimate of the cost per life-year before age 85 gained in 2018 is €14,310 (≈€3678 million/257,000 life-years).11

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.” Switzerland’s per capita GDP in 2018 was €73,436, so the new chemical substances that were registered during the period 1990–2011 appear to have been very cost–effective overall, even if we ignore the reduction in hospital utilization attributable to previous pharmaceutical innovation.

---

11 Part of the €3678 million expenditure was on patients above age 85, so the true cost per life-year before age 85 gained was lower.
As shown in Panels A and B of Fig. 6, the new chemical substances that were registered during the period 1994–2010 are associated with a reduction in the number of hospital days in 2019 of 2.07 million (\(=14.02\) million–11.95 million). In other words, if no new chemical substances had been registered during the period 1994–2010, the number of hospital days might have been 17.3% \((=\frac{14.02\text{ million}}{11.95\text{ million}})−1)\) higher in 2019. It is plausible that expenditure on inpatient curative and rehabilitative care would also have been 17.3% higher. According to Eurostat, expenditure on inpatient curative and rehabilitative care in 2018 was €17,965 million. Therefore, we estimate that, if no new chemical substances had been registered during the period 1994–2010, expenditure on inpatient curative and rehabilitative care in 2018 might have been €3112 million \((=17.3\% \times €17,965\text{ million})\) higher. About 85% \((=€3112\text{ million}/€3678\text{ million})\) of the 2018 expenditure on drugs registered during the period 1990–2011 may have been offset by the reduction in expenditure on inpatient curative and rehabilitative care. The net cost per life-year before age 85 gained in 2018 may have been €2201 \((=1−85\% \times €14,309)\).12

6 Summary and conclusions

In this study, we analyzed the association that pharmaceutical innovation had with premature mortality from all diseases in Switzerland during the period 1996–2018, and its association with hospital utilization for all diseases in Switzerland during the period 2002–2019. Most private biomedical research funding comes from pharmaceutical and biotechnology firms.

12 To our knowledge, no studies have provided estimates of the average cost-effectiveness of other broad categories of medical innovations, such as surgical or diagnostic imaging innovations. As stated earlier, measuring non-pharmaceutical medical innovation is far more difficult than measuring pharmaceutical innovation.
The analysis was performed by investigating whether the diseases that experienced more pharmaceutical innovation had larger declines in premature mortality and hospitalization. Pharmaceutical innovation was measured by the growth in the number of drugs used to treat a disease ever registered in Switzerland. We allowed the association of innovation to be subject to a substantial lag because utilization of recently-launched drugs tends to be lower than utilization of drugs launched many years earlier. Utilization of a chemical substance reaches a peak 9–12 years after it was first launched, and then declines.

Our estimates indicated that the number of years of potential life lost before ages 85, 75, and 65 is significantly inversely related to the number of chemical substances ever registered 6–9, 3–9, and 0–9 years earlier, respectively. The new chemical substances that were registered during the period 1990–2011 are associated with reductions in the number of years of potential life lost before ages 85, 75, and 65 in 2018 of 257 thousand, 163 thousand, and 102 thousand, respectively.

The number of hospital days is significantly inversely related to the number of chemical substances ever registered 8–10 years earlier. The new chemical substances that were registered during the period 1994–2010 are associated with a reduction in the number of hospital days in 2019 of 2.07 million. Average length of inpatient hospital stays is significantly inversely related to the number of chemical substances ever registered 2–10 years earlier. The new chemical substances that were registered during the period 1999–2015 are associated with a reduction in ALOS in 2019 of 0.4 days.

If we ignore the reduction in hospital utilization attributable to previous pharmaceutical innovation, a rough estimate of the cost per life-year before age 85 gained in 2018 is €14,310.

Moreover, about 85% of the 2018 expenditure on drugs registered during the period 1990–2011 may have been offset by the reduction in expenditure on inpatient curative and rehabilitative care. The net cost per life-year before age 85 gained in 2018 may therefore have been €2201.

Our estimates are predicated on the assumption that pharmaceutical innovation is exogenous with respect to premature mortality and hospitalization, and that it is uncorrelated with other potential determinants of health outcomes. For several reasons, this assumption could be violated.13

One reason is that Switzerland implemented a mandatory health insurance system in 1996, with several reforms since then that affected the quality of health services and the drug admission process. The potential endogeneity of pharmaceutical innovation in Switzerland due to changes in the Swiss health insurance system might be addressed by using an instrument for the number of new drugs approved for a disease in Switzerland. One potential instrument is the number of new drugs approved in the U.S.14 (There is a very strong positive correlation across 58 diseases between the 1996–2018 growth in number of drugs ever approved in the USA and Switzerland: \( R^2 = 0.59; \) \( p \) value < 0.0001.) We estimated Eq. (3) using instrumental variables (IV); the instrument for the number of new drugs ever approved for a disease in Switzerland was the number of new drugs ever approved for a disease in the United States three years earlier. While the IV and OLS estimates had different magnitudes and lag structures, both sets of estimates revealed highly significant inverse associations across diseases between both premature mortality and hospital days and the lagged number of drugs ever registered.

A second potential reason for violation of the assumption is implementation of non-pharmaceutical medical innovations (e.g. medical devices) and new disease-specific treatment guidelines. A previous study (Lichtenberg, 2014) indicated that controlling for non-pharmaceutical medical innovation did not affect estimates of the effect of pharmaceutical innovation on U.S. cancer mortality. We are not aware of evidence for the hypothesis that, in general, changes in guidelines have reduced mortality or hospitalization, or that they are correlated across diseases with new drug approvals. Future studies of Swiss mortality and hospitalization should attempt to control for non-pharmaceutical medical innovation and for changes in guidelines.

Appendix
Tables 5, 6, 7 and 8.

---

13 Some violations of the exogeneity assumption would render our estimates conservative. For example, an exogenous increase in the prevalence of a disease would be likely to increase both mortality from the disease and the number of registrations of new drugs that treat the disease.

14 In 2017, US drug expenditure was 41 times as large as Swiss drug expenditure (316 billion versus 8 billion USD). It is highly implausible that reforms to Switzerland’s mandatory health insurance system had any effect on U.S. drug approvals.
Table 5  Mortality by cause in 2018

| icd10 | No. of deaths | YPLL85 | YPLL75 | YPLL65 |
|-------|---------------|--------|--------|--------|
| A–R—Y—V All causes of death (A00–Y89) excluding S00–T98 | 67,621 | 543,417 | 268,424 | 130,084 |
| A15–A19_B90 Tuberculosis | 25 | 340 | 213 | 120 |
| ACC Accidents (V01–X59, Y89, Y86) | 2912 | 38,666 | 25,848 | 17,076 |
| ACC OTH Other accidents (W20–W64, W75–X39, X50–X59, Y86) | 478 | 8924 | 5929 | 3801 |
| A_B Certain infectious and parasitic diseases (A00–B99) | 823 | 6280 | 3275 | 1693 |
| A_B OTH Other infectious and parasitic diseases (remainder of A00–B99) | 723 | 4258 | 1975 | 1015 |
| B15–B19_B942 Viral hepatitis and sequelae of viral hepatitis | 13 | 223 | 140 | 75 |
| B180–B182 Chronic viral hepatitis B and C | 9 | 203 | 133 | 75 |
| B20–B24 Human immunodeficiency virus [HIV] disease | 22 | 598 | 390 | 208 |
| C Malignant neoplasms (C00–C97) | 17,650 | 203,475 | 93,248 | 34,870 |
| C00–C14 Malignant neoplasm of lip, oral cavity, pharynx | 453 | 6533 | 3025 | 950 |
| C00–D48 Neoplasms | 18,216 | 206,715 | 94,502 | 35,337 |
| C15 Malignant neoplasm of oesophagus | 449 | 5818 | 2598 | 758 |
| C16 Malignant neoplasm of stomach | 568 | 7850 | 3980 | 1648 |
| C18–C21 Malignant neoplasm of colon, rectosigmoid junction, rectum, anus and anal canal | 1733 | 18,665 | 8523 | 3110 |
| C22 Malignant neoplasm of liver and intrahepatic bile ducts | 748 | 9140 | 3998 | 1330 |
| C25 Malignant neoplasm of pancreas | 1451 | 17,010 | 7373 | 2398 |
| C32 Malignant neoplasm of larynx | 77 | 1008 | 435 | 133 |
| C33_C34 Malignant neoplasm of trachea, bronchus and lung | 3375 | 44,498 | 19,408 | 5583 |
| C43 Malignant melanoma of skin | 289 | 3880 | 2040 | 938 |
| C50 Malignant neoplasm of breast | 1447 | 18,548 | 9620 | 4260 |
| C53 Malignant neoplasm of cervix uteri | 77 | 1603 | 1005 | 523 |
| C54_C55 Malignant neoplasm of other parts of uterus | 212 | 2243 | 970 | 303 |
| C56 Malignant neoplasm of ovary | 403 | 5165 | 2405 | 885 |
| C61 Malignant neoplasm of prostate | 1410 | 7245 | 1953 | 325 |
| C64 Malignant neoplasm of kidney, except renal pelvis | 321 | 3762 | 1777 | 737 |
| C67 Malignant neoplasm of bladder | 577 | 4175 | 1505 | 438 |
| C70–C72 Malignant neoplasm of brain and central nervous system | 568 | 11,640 | 6800 | 3565 |
| C73 Malignant neoplasm of thyroid gland | 65 | 598 | 245 | 85 |
| C81–C86 Hodgkin disease and lymphomas | 550 | 4933 | 2045 | 873 |
| C88_C90_C96 Other malignant neoplasm of lymphoid, haematopoietic and related tissue | 380 | 2903 | 1035 | 315 |
| C91–C95 Leukaemia | 622 | 6751 | 3281 | 1621 |
| C_OTH Other malignant neoplasms (remainder of C00–C97) | 1875 | 19,513 | 9231 | 4098 |
| D00–D48 Non-malignant neoplasms (benign and uncertain) | 566 | 3240 | 1255 | 467 |
| D05–D89 Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | 213 | 1336 | 743 | 486 |
| E Endocrine, nutritional and metabolic diseases (E00–E90) | 1721 | 12,362 | 5952 | 2920 |
| E10–E14 Diabetes mellitus | 1163 | 6630 | 2570 | 895 |
| E_OTH Other endocrine, nutritional and metabolic diseases (remainder of E00–E90) | 558 | 5732 | 3382 | 2025 |
| F Mental and behavioural disorders (F00–F99) | 5686 | 18,205 | 7468 | 3528 |
| F01_F03 Dementia | 4860 | 6800 | 833 | 85 |
| F10 Mental and behavioural disorders due to use of alcohol | 181 | 3345 | 1753 | 670 |
| F_OTH Other mental and behavioural disorders (remainder of F00–F99) | 556 | 4898 | 2605 | 1338 |
| G20 Parkinson disease | 757 | 2985 | 523 | 60 |
| G30 Alzheimer disease | 1518 | 3648 | 643 | 110 |
| G_H Diseases of the nervous system and the sense organs (G00–H95) | 3655 | 25,873 | 11,581 | 5538 |
| G_H OTH Other diseases of the nervous system and the sense organs (remainder of G00–H95) | 1380 | 19,241 | 10,416 | 5368 |
| I Diseases of the circulatory system (I00–I99) | 20,910 | 93,417 | 36,667 | 13,692 |
| I20–I25 Ischaemic heart diseases | 6962 | 37,240 | 14,930 | 5195 |
| I20_I25 Other ischaemic heart diseases | 4712 | 19,380 | 6888 | 2193 |
| icd10 | No. of deaths | YPLL85 | YPLL75 | YPLL65 |
|-------|--------------|--------|--------|--------|
| I21_I22 Acute myocardial infarction including subsequent myocardial infarction | 2250 | 17,860 | 8043 | 3003 |
| I30–I51 Other heart diseases | 5860 | 22,278 | 8873 | 3683 |
| I60–I69 Cerebrovascular diseases | 3539 | 16,065 | 5942 | 2172 |
| I_OTH Other diseases of the circulatory system (remainder of I00–I99) | 4549 | 17,384 | 6922 | 2642 |
| J09–J11 Influenza (including swine flu) | 4671 | 25,812 | 9072 | 2784 |
| J12–J18 Pneumonia | 1409 | 5035 | 1847 | 727 |
| J40–J44, J47 Other lower respiratory diseases | 2029 | 13,535 | 4340 | 938 |
| J40–J47 Chronic lower respiratory diseases | 2133 | 14,610 | 4985 | 1293 |
| J45_J46 Asthma and status asthmaticus | 104 | 1075 | 645 | 355 |
| J_OTH Other diseases of the respiratory system (remainder of J00–J99) | 806 | 4218 | 1395 | 405 |
| K00–K93 Diseases of the digestive system | 2497 | 20,829 | 9589 | 3739 |
| K25–K28 Ulcer of stomach, duodenum and jejunum | 120 | 553 | 163 | 58 |
| K70_K73_K74 Chronic liver disease | 607 | 10,958 | 5818 | 2285 |
| K72–K75 Chronic liver disease (excluding alcoholic and toxic liver disease) | 188 | 2420 | 1157 | 457 |
| K_OTH Other diseases of the digestive system (remainder of K00–K93) | 1770 | 9319 | 3609 | 1396 |
| L00–L99 Diseases of the skin and subcutaneous tissue | 119 | 505 | 150 | 45 |
| M00–M99 Diseases of the musculoskeletal system and connective tissue | 722 | 3867 | 1507 | 635 |
| M_OTH Other diseases of the musculoskeletal system and connective tissue (remainder of M00–M99) | 507 | 3132 | 1295 | 575 |
| N00–N99 Diseases of the genitourinary system | 1293 | 3928 | 1078 | 278 |
| N00–N29 Diseases of kidney and ureter | 807 | 2533 | 705 | 188 |
| N_OTH Other diseases of the genitourinary system (remainder of N00–N99) | 486 | 1395 | 373 | 90 |
| O00–O99 Pregnancy, childbirth and the puerperium | 6 | 305 | 245 | 185 |
| P00–P96 Certain conditions originating in the perinatal period | 160 | 13,520 | 11,920 | 10,320 |
| Q00–Q99 Congenital malformations, deformations and chromosomal abnormalities | 250 | 12,122 | 9802 | 7709 |
| R00–R99 Signs and abnormal clinical and laboratory findings, not elsewhere classified | 2575 | 23,253 | 12,986 | 6848 |
| R95 Sudden infant death syndrome | 6 | 507 | 447 | 387 |
| R96–R99 Ill-defined and unknown causes of mortality | 1893 | 21,736 | 12,176 | 6304 |
| RHEUM_ARTHRO Rheumatoid arthritis and arthrosis (M05–M06, M15–M19) | 215 | 735 | 213 | 60 |
| R_OTH Other symptoms, signs and abnormal clinical and laboratory findings (remainder of R00–R99) | 676 | 1010 | 363 | 158 |
| TOXICO Drug dependence, toxicomania (F11–F16, F18–F19) | 89 | 3163 | 2278 | 1435 |
| V01–Y89 External causes of morbidity and mortality | 4104 | 75,091 | 51,891 | 34,351 |
| V01–Y89_OTH Other external causes of morbidity and mortality (remainder of V01–Y89) | 19 | 315 | 180 | 85 |
| V_YP5 Transport accidents (V01–V99, Y85) | 337 | 10,605 | 7730 | 5410 |
| W00–W19 Falls | 1870 | 10,617 | 5782 | 3395 |
| W65–W74 Accidental drowning and submersion | 64 | 2066 | 1529 | 1094 |
| X40–X49 Accidental poisoning by and exposure to noxious substances | 163 | 6455 | 4880 | 3377 |
| X60–X84, Y870 Intentional self-harm | 1047 | 32,040 | 22,888 | 15,175 |
| X85–Y09, Y871 Assault | 43 | 1686 | 1286 | 929 |
| Y10–Y34, Y872 Event of undetermined intent | 77 | 2245 | 1607 | 1052 |
### Table 6
Hospital days and average length of stay, by cause, in 2019

| Cause | hosday | los |
|-------|--------|-----|
| A–T_Z All causes of diseases (A00–Z99) excluding V00–Y98 | 11,816,124 | 8.2 |
| A–T_Z_XNB All causes of diseases (A00–Z99) excluding V00–Y98 and Z38 | 11,631,919 | 8.4 |
| A00–A08 Intestinal infectious diseases except diarrhoea | 34,235 | 4.5 |
| A09 Diarrhoea and gastroenteritis of presumed infectious origin | 19,502 | 3.7 |
| A15–A19_B90 Tuberculosis | 6898 | 16.2 |
| A40_A41 Septicaemia | 148,320 | 11.6 |
| ABORT_OTH Other pregnancy with abortive outcome (O00–O03, O05–O08) | 4204 | 1.7 |
| ARTHROPAT_OTH Other arthropathies (M00–M15, M18–M22,M24–M25) | 167,601 | 4.8 |
| A_B Certain infectious and parasitic diseases (A00–B99) | 313,242 | 7.8 |
| A_B_OTH Other infectious and parasitic diseases (remainder of A00–B99) | 102,717 | 7.4 |
| B20–B24 Human immunodeficiency virus [HIV] disease | 1570 | 15.5 |
| C00–D48 Neoplasms | 1,039,818 | 8.0 |
| C18–C21 Malignant neoplasm of colon, rectosigmoid junction, rectum, anus and anal canal | 109,394 | 11.6 |
| C33_C34 Malignant neoplasm of trachea, bronchus and lung | 101,286 | 10.5 |
| C43_C44 Malignant neoplasms of skin | 17,985 | 5.4 |
| C50 Malignant neoplasm of breast | 60,829 | 5.6 |
| C53–C55 Malignant neoplasm of uterus | 17,304 | 7.7 |
| C56 Malignant neoplasm of ovary | 19,003 | 10.2 |
| C61 Malignant neoplasm of prostate | 53,122 | 6.5 |
| C67 Malignant neoplasm of bladder | 46,711 | 5.7 |
| C_OTH Other malignant neoplasms (remainder of C00–C97) | 499,662 | 9.9 |
| D00–D09 In situ neoplasms | 10,029 | 3.8 |
| D00–D48_OTH Other in situ neoplasms, benign neoplasms and neoplasms of uncertain or unknown behaviour (remainder of D00–D48) | 78,572 | 5.2 |
| D12 Benign neoplasm of colon, rectum, anus and anal canal | 7876 | 4.0 |
| D25 Leiomyoma of uterus | 18,045 | 3.1 |
| D50–D64 Anaemias | 25,328 | 6.7 |
| D50–D89 Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | 46,391 | 7.1 |
| D65–D89 Other diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | 21,063 | 7.6 |
| E Endocrine, nutritional and metabolic diseases (E00–E90) | 169,286 | 7.1 |
| E10–E14 Diabetes mellitus | 73,749 | 9.8 |
| E_OTH Other endocrine, nutritional and metabolic diseases (remainder of E00–E90) | 95,537 | 5.9 |
| F Mental and behavioural disorders (F00–F99) | 2,800,678 | 26.7 |
| F00–F03 Dementia | 51,487 | 20.0 |
| F10 Mental and behavioural disorders due to use of alcohol | 298,672 | 17.9 |
| F11–F19 Mental and behavioural disorders due to psychoactive substance use | 146,157 | 23.1 |
| F20–F29 Schizophrenia, schizotypal and delusional disorders | 555,997 | 36.8 |
| F30–F39 Mood [affective] disorders | 965,750 | 31.7 |
| F_OTH Other mental and behavioural disorders (remainder of F00–F99) | 782,615 | 23.2 |
| G Diseases of the nervous system (G00–G99) | 496,052 | 12.8 |
| G30 Alzheimer disease | 54,081 | 26.9 |
| G35 Multiple sclerosis | 35,210 | 17.9 |
| G40_G41 Epilepsy, status epilepticus | 85,158 | 10.4 |
| G45 Transient cerebral ischaemic attacks and related syndromes | 17,872 | 3.8 |
| G_OTH Other diseases of the nervous system (remainder of G00–G99) | 303,731 | 13.9 |
| H00–H59 Diseases of the eye and adnexa | 27,595 | 2.3 |
| H00–H59_OTH Other diseases of the eye and adnexa (remainder of H00–H59) | 24,594 | 2.5 |
| H25_H26_H28 Cataract | 3001 | 1.6 |
| H60–H95 Diseases of the ear and mastoid process | 26,236 | 3.4 |
| I Diseases of the circulatory system (I00–I99) | 1,347,121 | 8.5 |
### Table 6 (continued)

| Cause | hosday | los  |
|-------|--------|------|
| I10–I15 Hypertensive diseases | 22,811 | 4.7 |
| I20 Angina pectoris | 19,975 | 3.4 |
| I21_I22 Acute myocardial infarction including subsequent myocardial infarction | 121,883 | 6.3 |
| I23–I25 Other ischaemic heart disease | 84,861 | 5.6 |
| I26–I28 Pulmonary heart disease and diseases of pulmonary circulation | 40,421 | 7.1 |
| I44–I49 Conduction disorders and cardiac arrhythmias | 75,728 | 4.0 |
| I50 Heart failure | 244,219 | 10.7 |
| I60–I69 Cerebrovascular diseases | 408,650 | 14.7 |
| I70 Atherosclerosis | 73,163 | 8.1 |
| I83 Varicose veins of lower extremities | 10,440 | 2.9 |
| INJ_HEAD_OTH Other injuries to the head (S00–S05, S07–S09) | 26,524 | 3.1 |
| INJ_OTH Other injuries (S10–S51, S53–S81, S83–T14, T79) | 461,383 | 6.3 |
| INTESTINE_OTH Other diseases of intestine (K55, K58–K59, K63) | 36,428 | 7.3 |
| I_OTH Other diseases of the circulatory system (remainder of I00–I99) | 244,970 | 9.3 |
| J Diseases of the respiratory system (J00–J99) | 591,185 | 6.5 |
| J00–J11 Acute upper respiratory infections and influenza | 53,769 | 4.7 |
| J12–J18 Pneumonia | 192,878 | 8.4 |
| J20–J22 Other acute lower respiratory infections | 38,266 | 4.0 |
| J35 Chronic diseases of tonsils and adenoids | 14,053 | 2.2 |
| J40–J44, J47 Other lower respiratory diseases | 135,744 | 10.4 |
| J45_J46 Asthma and status asthmaticus | 18,626 | 6.7 |
| J60–J99 Other diseases of the respiratory system | 106,344 | 10.3 |
| K Diseases of the digestive system (K00–K93) | 648,439 | 5.5 |
| K00–K08 Disorders of teeth and supporting structures | 3628 | 3.0 |
| K09–K14 Other diseases of oral cavity, salivary glands and jaws | 9146 | 4.3 |
| K20–K23 Diseases of oesophagus | 18,497 | 5.5 |
| K25–K28 Ulcer of stomach, duodenum and jejenum | 24,992 | 8.5 |
| K29–K31 Dyspepsia and other diseases of stomach and duodenum | 18,970 | 5.4 |
| K35–K38 Diseases of appendix | 40,489 | 3.3 |
| K40 Inguinal hernia | 28,214 | 2.2 |
| K41–K46 Other abdominal hernia | 52,298 | 4.8 |
| K50_K51 Crohn disease and ulcerative colitis | 16,826 | 8.7 |
| K52 Other noninfective gastroenteritis and colitis | 12,690 | 6.4 |
| K56 Paralytic ileus and intestinal obstruction without hernia | 56,539 | 7.9 |
| K57 Diverticular disease of intestine | 76,212 | 7.1 |
| K60–K62 Diseases of anus and rectum | 18,540 | 3.1 |
| K70 Alcoholic liver disease | 26,864 | 12.8 |
| K71–K77 Other diseases of liver | 26,296 | 10.7 |
| K80 Cholelithiasis | 73,062 | 4.3 |
| K81–K83 Other diseases of gallbladder and biliary tract | 19,630 | 6.8 |
| K85–K87 Diseases of pancreas | 37,935 | 8.2 |
| K_OTH Other diseases of the digestive system (remainder of K00–K93) | 51,183 | 6.6 |
| L Diseases of the skin and subcutaneous tissue (L00–L99) | 108,916 | 6.7 |
| L00–L08 Infections of the skin and subcutaneous tissue | 47,653 | 4.9 |
| L20–L45 Dermatitis, eczema and papulosquamous disorders | 13,912 | 7.8 |
| L_OTH Other diseases of the skin and subcutaneous tissue (remainder of L00–L99) | 47,351 | 10.2 |
| M Diseases of the musculoskeletal system and connective tissue (M00–M99) | 1,260,110 | 7.1 |
| M16 Coxarthrosis [arthrosis of hip] | 190,749 | 8.1 |
| M17 Gonarthrosis [arthrosis of knee] | 240,339 | 9.0 |
### Table 6 (continued)

| Cause                                                                 | hosday | los  |
|----------------------------------------------------------------------|--------|------|
| M23 Internal derangement of knee                                      | 15,824 | 2.2  |
| M30–M36 Systemic connective tissue disorders                          | 18,495 | 9.3  |
| M40–M49 Deforming dorsopathies and spondylopathies                    | 192,585| 9.8  |
| M50_M51 Cervical disc disorders, other intervertebral disc disorders  | 96,232 | 6.7  |
| M53_M80–M99 Other disorders of the musculoskeletal system and connective tissue | 150,166| 9.1  |
| M54 Dorsalgia                                                         | 78,871 | 10.1 |
| M60–M79 Soft tissue disorders                                         | 109,048| 4.5  |
| N Diseases of the genitourinary system (N00–N99)                      | 337,409| 4.1  |
| N00–N16 Glomerular and renal tubulo-interstitial diseases             | 71,916 | 4.5  |
| N17–N19 Renal failure                                                | 41,461 | 8.6  |
| N20–N23 Urolithiasis                                                 | 25,446 | 2.3  |
| N25–N39 Other diseases of the urinary system                         | 83,579 | 5.4  |
| N40 Hyperplasia of prostate                                          | 33,504 | 4.1  |
| N41–N51 Other diseases of male genital organs                        | 21,038 | 3.6  |
| N60–N64 Disorders of breast                                          | 4029   | 2.4  |
| N70–N77 Inflammatory diseases of female pelvic organs                | 5618   | 3.4  |
| N91–N95 Menstrual, menopausal and other female genital conditions    | 4852   | 2.4  |
| N_OTH Other diseases of the genitourinary system (remainder of N00–N99)| 45,966 | 3.0  |
| O Pregnancy, childbirth and the puerperium (O00–O99)                 | 401,713| 4.0  |
| O04 Medical abortion                                                 | 1428   | 1.6  |
| O10–O48 Complications of pregnancy predominantly in the antenatal period | 158,301| 4.5  |
| O60–O75 Complications of labour and delivery                         | 203,351| 3.9  |
| O80 Single spontaneous delivery                                      | 13,772 | 3.0  |
| O81–O84 Other delivery                                               | 4402   | 4.2  |
| O85–O92 Complications predominantly related to the puerperium        | 5390   | 3.6  |
| O95–O99 Other obstetric conditions                                   | 10,865 | 3.8  |
| P Certain conditions originating in the perinatal period (P00–P96)   | 186,457| 6.1  |
| P07 Disorders related to short gestation and low birth weight, not elsewhere classified | 22,400 | 7.6  |
| P_OTH Other conditions originating in the perinatal period (remainder of P00–P96) | 164,057| 5.9  |
| Q Congenital malformations, deformations and chromosomal abnormalities (Q00–Q99) | 61,355 | 6.1  |
| R Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00–R99) | 327,700| 7.4  |
| R07 Pain in throat and chest                                         | 6135   | 2.2  |
| R10 Abdominal and pelvic pain                                        | 12,820 | 2.9  |
| R69 Unknown and unspecified causes of morbidity                      | 49,220 | 80.0 |
| R_OTH Other symptoms, signs and abnormal clinical and laboratory findings (remainder of R00–R99) | 259,525| 7.1  |
| S06 Intracranial injury                                              | 109,959| 5.2  |
| S52 Fracture of forearm                                              | 47,750 | 3.6  |
| S72 Fracture of femur                                                | 280,120| 14.0 |
| S82 Fracture of lower leg, including ankle                           | 121,737| 8.6  |
| S_T Injury, poisoning and certain other consequences of external causes (S00–T98) | 1,321,657| 7.0 |
| S_T_OTH Other and unspecified effects of external causes (remainder of S00–T98) | 8533 | 2.7  |
| T20–T32 Burns and corrosions                                         | 8658   | 8.2  |
| T36–T65 Poisonings by drugs, medicaments and biological substances and toxic effects | 4706 | 1.7  |
| T80–T88 Complications of surgical and medical care, not elsewhere classified | 251,591| 7.8  |
| T90–T98 Sequelae of injuries, of poisoning and of other consequences of external causes | 496 | 24.8 |
| UPRESPIR_OTH Other diseases of upper respiratory tract (J30–J34, J36–J39) | 31,505 | 2.3  |
Table 7  No. of chemical substances ever registered in Switzerland, by medical condition (hospital classification), 1989–2019

| Medical Condition                                                                 | 1989 | 1994 | 1999 | 2004 | 2009 | 2014 | 2019 |
|-----------------------------------------------------------------------------------|------|------|------|------|------|------|------|
| All medical conditions                                                           | 590  | 729  | 917  | 1068 | 1229 | 1401 | 1588 |
| A00–A08 Intestinal infectious diseases except diarrhoea                          | 11   | 13   | 13   | 16   | 17   | 17   |      |
| A09 Diarrhoea and gastroenteritis of presumed infectious origin                    | 4    | 4    | 4    | 4    | 4    | 4    |      |
| A15–A19_B90 Tuberculosis                                                          | 9    | 10   | 10   | 11   | 12   | 12   |      |
| A40_A41 Septicaemia                                                               | 16   | 17   | 18   | 20   | 22   | 23   |      |
| ABORT_OTH Other pregnancy with abortive outcome (O00–O03, O05–O08)              | 4    | 4    | 5    | 5    | 5    | 5    | 6    |
| ARTHROPAT_OTH Other arthropathies (M00–M15, M18–M22,M24–M25)                    | 45   | 47   | 54   | 56   | 62   | 66   | 69   |
| A_B_OTH Other infectious and parasitic diseases (remainder of A00–B99)           | 80   | 96   | 115  | 129  | 146  | 152  | 157  |
| B20–B24 Human immunodeficiency virus [HIV] disease                               | 2    | 3    | 8    | 16   | 26   | 31   | 35   |
| C18–C21 Malignant neoplasm of colon, rectosigmoid junction, rectum, anus and anal canal | 8    | 8    | 12   | 16   | 19   | 24   | 26   |
| C33_C34 Malignant neoplasm of trachea, bronchus and lung                         | 16   | 18   | 22   | 26   | 30   | 33   | 37   |
| C43_C44 Malignant neoplasms of skin                                              | 7    | 7    | 10   | 15   | 15   | 20   | 25   |
| C50 Malignant neoplasm of breast                                                  | 19   | 23   | 32   | 37   | 43   | 49   | 50   |
| C53–C55 Malignant neoplasm of uterus                                              | 12   | 12   | 14   | 17   | 18   | 20   | 20   |
| C56 Malignant neoplasm of ovary                                                   | 16   | 18   | 21   | 24   | 26   | 28   | 29   |
| C61 Malignant neoplasm of prostate                                                | 11   | 13   | 17   | 19   | 19   | 27   | 27   |
| C67 Malignant neoplasm of bladder                                                 | 12   | 14   | 16   | 18   | 19   | 22   | 22   |
| C_OTH Other malignant neoplasms (remainder of C00–C97)                           | 33   | 38   | 53   | 64   | 87   | 109  | 127  |
| D00–D09 In situ neoplasms                                                        | 6    | 8    | 11   | 14   | 20   | 25   | 26   |
| D00–D48_OTH Other in situ neoplasms, benign neoplasms and neoplasms of uncertain or unknown behaviour (remainder of D00–D48) | 11   | 13   | 21   | 26   | 34   | 40   | 42   |
| D12 Benign neoplasm of colon, rectum, anus and anal canal                         | 2    | 2    | 3    | 4    | 4    | 4    | 4    |
| D25 Leiomyoma of uterus                                                           | 2    | 2    | 3    | 4    | 4    | 4    | 4    |
| D50–D64 Anaemias                                                                  | 15   | 16   | 18   | 20   | 23   | 25   | 25   |
| D65–D89 Other diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism | 22   | 29   | 33   | 39   | 46   | 51   | 52   |
| E10–E14 Diabetes mellitus                                                         | 7    | 10   | 20   | 25   | 36   | 39   | 40   |
| E_OTH Other endocrine, nutritional and metabolic diseases (remainder of E00–E90) | 87   | 99   | 116  | 131  | 150  | 154  | 163  |
| F00–F03 Dementia                                                                  | 6    | 6    | 8    | 9    | 9    | 9    | 9    |
| F10 Mental and behavioural disorders due to use of alcohol                        | 18   | 18   | 19   | 20   | 21   | 22   | 22   |
| F11–F19 Mental and behavioural disorders due to psychoactive substance use        | 9    | 9    | 11   | 14   | 17   | 17   | 17   |
| F20–F29 Schizophrenia, schizotypal and delusional disorders                       | 11   | 12   | 15   | 16   | 18   | 18   | 19   |
| F30–F39 Mood [affective] disorders                                                | 16   | 24   | 28   | 31   | 32   | 34   | 37   |
| F_OTH Other mental and behavioural disorders (remainder of F00–F99)              | 46   | 55   | 61   | 69   | 79   | 81   | 85   |
| G30 Alzheimer disease                                                             | 0    | 1    | 3    | 4    | 5    | 5    | 5    |
| G35 Multiple sclerosis                                                            | 8    | 11   | 14   | 15   | 17   | 20   | 22   |
| G40_G41 Epilepsy, status epilepticus                                              | 17   | 20   | 23   | 24   | 29   | 30   | 30   |
| G45 Transient cerebral ischaemic attacks and related syndromes                    | 3    | 5    | 7    | 7    | 8    | 11   | 11   |
| G_OTH Other diseases of the nervous system (remainder of G00–G99)                | 55   | 58   | 72   | 82   | 93   | 97   | 99   |
| H00–H59_OTH Other diseases of the eye and adnexa (remainder of H00–H59)          | 34   | 41   | 53   | 61   | 66   | 68   | 71   |
| H25_H26_H28 Cataract                                                              | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| H60–H95 Diseases of the ear and mastoid process                                   | 21   | 22   | 23   | 24   | 24   | 25   | 25   |
| I10–I15 Hypertensive diseases                                                     | 22   | 35   | 50   | 55   | 67   | 72   | 74   |
| I20 Angina pectoris                                                               | 15   | 20   | 22   | 23   | 25   | 27   | 27   |
| I21_L22 Acute myocardial infarction including subsequent myocardial infarction   | 14   | 16   | 20   | 24   | 28   | 30   | 30   |
| I23–I25 Other ischaemic heart disease                                             | 15   | 16   | 19   | 23   | 24   | 24   | 24   |
| I26–I28 Pulmonary heart disease and diseases of pulmonary circulation            | 6    | 8    | 9    | 14   | 16   | 20   | 21   |
| I44–I49 Conduct disorders and cardiac arrhythmias                                 | 13   | 16   | 18   | 19   | 23   | 26   | 26   |
| I50 Heart failure                                                                 | 13   | 17   | 22   | 24   | 27   | 28   | 30   |
| I60–I69 Cerebrovascular diseases                                                  | 7    | 10   | 14   | 15   | 18   | 18   | 18   |
| Table 7 (continued) | 1989 | 1994 | 1999 | 2004 | 2009 | 2014 | 2019 |
|---------------------|------|------|------|------|------|------|------|
| I70 Atherosclerosis | 0    | 1    | 2    | 3    | 5    | 5    |
| I83 Varicose veins of lower extremities | 4 | 6 | 6 | 6 | 6 | 6 |
| JN_OTH Other injuries (S10–S51, S53–S71, S73–S81, S83–T14, T79) | 14 | 15 | 15 | 16 | 16 | 17 | 17 |
| INTESTINE_OTH Other diseases of intestine (K55, K58–K59, K63) | 33 | 37 | 41 | 41 | 43 | 46 | 49 |
| L_OTH Other diseases of the circulatory system (remainder of I00–I99) | 53 | 60 | 65 | 67 | 72 | 75 | 77 |
| J00–J11 Acute upper respiratory infections and influenza | 43 | 48 | 55 | 56 | 58 | 59 | 59 |
| J12–J18 Pneumonia | 23 | 28 | 31 | 35 | 37 | 40 | 42 |
| J20–J22 Other acute lower respiratory infections | 19 | 23 | 25 | 27 | 30 | 31 | 32 |
| J40–J44_J47 Other lower respiratory diseases | 28 | 32 | 40 | 43 | 46 | 52 | 55 |
| J45_J46 Asthma and status asthmaticus | 15 | 17 | 23 | 26 | 29 | 32 | 33 |
| J60–J99 Other diseases of the respiratory system | 19 | 20 | 20 | 21 | 21 | 25 |
| K00–K08 Disorders of teeth and supporting structures | 19 | 19 | 19 | 20 | 20 | 20 | 20 |
| K09–K14 Other diseases of oral cavity, salivary glands and jaws | 15 | 15 | 16 | 17 | 17 | 17 | 17 |
| K20–K23 Diseases of esophagus | 5 | 7 | 10 | 11 | 11 | 12 | 12 |
| K25–K28 Ulcer of stomach, duodenum and jejunum | 5 | 7 | 11 | 13 | 13 | 14 | 15 |
| K29–K31 Dyspepsia and other diseases of stomach and duodenum | 10 | 10 | 10 | 11 | 12 | 12 |
| K50_K51 Crohn disease and ulcerative colitis | 8 | 9 | 10 | 11 | 13 | 14 |
| K52 Other noninfective gastroenteritis and colitis | 0 | 1 | 2 | 2 | 2 | 2 |
| K56 Paralytic ileus and intestinal obstruction without hernia | 2 | 2 | 2 | 2 | 2 | 2 |
| K60–K62 Diseases of anus and rectum | 1 | 1 | 1 | 1 | 2 | 2 |
| K70 Alcoholic liver disease | 5 | 6 | 7 | 9 | 10 | 10 |
| K71–K77 Other diseases of liver | 12 | 15 | 16 | 18 | 20 | 20 | 22 |
| K80 Cholelithiasis | 1 | 1 | 1 | 1 | 2 | 2 |
| K81–K83 Other diseases of gallbladder and biliary tract | 5 | 5 | 5 | 6 | 6 | 6 |
| K85–K87 Diseases of pancreas | 3 | 3 | 3 | 3 | 3 | 3 |
| K_OTH Other diseases of the digestive system (remainder of K00–K93) | 22 | 26 | 26 | 29 | 29 | 30 |
| L00–L08 Infections of the skin and subcutaneous tissue | 19 | 23 | 27 | 30 | 32 | 33 |
| L20–L45 Dermatitis, eczema and papulosquamous disorders | 38 | 41 | 46 | 50 | 54 | 57 | 61 |
| L_OTH Other diseases of the skin and subcutaneous tissue (remainder of L00–L99) | 52 | 61 | 67 | 74 | 80 | 85 | 86 |
| M16 Coxarthrosis [arthrosis of hip] | 21 | 21 | 23 | 23 | 24 | 24 | 24 |
| M17 Gonarthrosis [arthrosis of knee] | 21 | 21 | 23 | 23 | 24 | 24 | 24 |
| M23 Internal derangement of knee | 11 | 11 | 12 | 12 | 12 | 12 | 12 |
| M30–M36 Systemic connective tissue disorders | 13 | 13 | 16 | 19 | 20 | 22 | 23 |
| M40–M49 Deforming dorsopathies and spondylopathies | 12 | 13 | 16 | 18 | 18 | 20 | 21 |
| M50_M51 Cervical disc disorders, other intervertebral disc disorders | 6 | 6 | 7 | 8 | 8 | 8 | 8 |
| M53_M80–M99 Other disorders of the musculoskeletal system and connective tissue | 31 | 33 | 37 | 43 | 46 | 47 | 47 |
| M54 Dorsalgia | 22 | 23 | 25 | 26 | 26 | 26 | 26 |
| M60–M79 Soft tissue disorders | 28 | 29 | 30 | 31 | 32 | 32 |
| N00–N16 Glomerular and renal tubulo-interstitial diseases | 21 | 23 | 27 | 28 | 29 | 32 | 32 |
| N17–N19 Renal failure | 11 | 13 | 16 | 20 | 23 | 23 | 25 |
| N20–N23 Urolithiasis | 3 | 3 | 3 | 4 | 5 | 5 |
| N25–N39 other diseases of the urinary system | 31 | 39 | 44 | 48 | 53 | 55 | 57 |
| N40 Hyperplasia of prostate | 2 | 5 | 7 | 9 | 10 | 11 | 12 |
| N41–NS1 other diseases of male genital organs | 14 | 15 | 19 | 20 | 21 | 21 | 21 |
| N60–N64 disorders of breast | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| N70–N77 Inflammatory diseases of female pelvic organs | 18 | 20 | 21 | 21 | 22 | 22 | 22 |
| N91–N95 Menstrual, menopausal and other female genital conditions | 22 | 23 | 29 | 33 | 35 | 36 | 36 |
| N_LOTH Other diseases of the genitourinary system (remainder of N00–N99) | 8 | 10 | 14 | 16 | 17 | 19 | 19 |
| O04 Medical abortion | 3 | 3 | 4 | 4 | 4 | 5 | 5 |
Table 7 (continued)

| Code | Description                                                                 | 1989 | 1994 | 1999 | 2004 | 2009 | 2014 | 2019 |
|------|-----------------------------------------------------------------------------|------|------|------|------|------|------|------|
| O10–O48 | Complications of pregnancy predominantly in the antenatal period               | 13   | 13   | 15   | 17   | 17   | 17   | 17   |
| O60–O75 | Complications of labour and delivery                                          | 6    | 7    | 8    | 10   | 10   | 10   |      |
| O80   | Single spontaneous delivery                                                  | 0    | 0    | 0    | 2    | 2    | 2    |      |
| O81–O84 | Other delivery                                                              | 2    | 2    | 3    | 4    | 4    | 4    |      |
| O85–O92 | Complications predominantly related to the puerperium                        | 8    | 9    | 9    | 9    | 10   | 9    |      |
| P07   | Disorders related to short gestation and low birth weight, not elsewhere classified | 4    | 5    | 5    | 5    | 5    | 5    |      |
| P_OTH | Other conditions originating in the perinatal period (remainder of P00–P96)   | 14   | 15   | 15   | 17   | 17   | 18   |      |
| Q     | Congenital malformations, deformations and chromosomal abnormalities (Q00–Q99) | 7    | 12   | 13   | 14   | 16   | 16   | 19   |
| R07   | Pain in throat and chest                                                     | 11   | 11   | 11   | 12   | 12   | 12   |      |
| R10   | Abdominal and pelvic pain                                                    | 9    | 10   | 10   | 10   | 11   | 11   |      |
| R_OTH | Other symptoms, signs and abnormal clinical and laboratory findings (remainder of R00–R99) | 112  | 127  | 150  | 168  | 172  | 180  |      |
| S06   | Intracranial injury                                                          | 4    | 4    | 4    | 4    | 4    | 4    |      |
| S72   | Fracture of femur                                                            | 0    | 0    | 0    | 3    | 4    | 4    |      |
| S82   | Fracture of lower leg, including ankle                                       | 0    | 0    | 0    | 1    | 1    | 1    |      |
| S_T_OTH | Other and unspecified effects of external causes (remainder of S00–T98)       | 13   | 17   | 17   | 18   | 19   | 19   |      |
| T20–T32 | Burns and corrosions                                                        | 13   | 14   | 15   | 16   | 16   | 17   |      |
| T36–T65 | Poisonings by drugs, medicaments and biological substances and toxic effects | 11   | 12   | 12   | 14   | 18   | 20   | 21   |
| T80–T88 | Complications of surgical and medical care, not elsewhere classified         | 20   | 23   | 29   | 33   | 37   | 38   |      |
| UPRESPIR_OTH | Other diseases of upper respiratory tract (J30–J34, J36–J39) | 34   | 41   | 50   | 54   | 57   | 59   | 59   |

Table 8  Estimates of models that include multiple lag lengths (CUM_DRUG,<sub>c</sub>,<sub>t</sub>, CUM_DRUG,<sub>c</sub>,<sub>t</sub>−8, and CUM_DRUG,<sub>c</sub>,<sub>t</sub>−12)

| Model | Dependent variable | Lag (k) | Estimate | Std. err | 95% Lower confidence | 95% Upper confidence | Z   | Pr>|Z| |
|-------|--------------------|---------|----------|----------|----------------------|----------------------|-----|-------|
| 1     | ln(YPLL85,<sub>c</sub>,<sub>t</sub>) | 0       | 0.249    | 0.224    | -0.191               | 0.688                | 1.11| 0.2676|
|       |                    | 8       | -0.544   | 0.180    | -0.896               | -0.191               | -3.02| 0.0025|
|       |                    | 12      | 0.014    | 0.166    | -0.312               | 0.339                | 0.08| 0.9344|
| 2     | ln(YPLL85,<sub>c</sub>,<sub>t</sub>) | 8       | -0.501   | 0.226    | -0.944               | -0.058               | -2.22| 0.0266|
| 3     | ln(YPLL75,<sub>c</sub>,<sub>t</sub>) | 0       | 0.115    | 0.264    | -0.402               | 0.632                | 0.44| 0.6617|
|       |                    | 8       | -0.691   | 0.213    | -1.109               | -0.273               | -3.24| 0.0012|
|       |                    | 12      | 0.148    | 0.222    | -0.288               | 0.584                | 0.67| 0.5048|
| 4     | ln(YPLL75,<sub>c</sub>,<sub>t</sub>) | 8       | -0.630   | 0.258    | -1.135               | -0.124               | -2.44| 0.0147|
| 5     | ln(YPLL65,<sub>c</sub>,<sub>t</sub>) | 0       | -0.022   | 0.385    | -0.776               | 0.733                | -0.06| 0.9553|
|       |                    | 8       | -0.893   | 0.236    | -1.355               | -0.431               | -3.79| 0.0001|
|       |                    | 12      | 0.264    | 0.325    | -0.373               | 0.902                | 0.61| 0.4164|
| 6     | ln(YPLL65,<sub>c</sub>,<sub>t</sub>) | 8       | -0.799   | 0.247    | -1.285               | -0.316               | -3.24| 0.0012|
| 7     | ln(HOSP_DAYS,<sub>c</sub>,<sub>t</sub>) | 0       | 0.749    | 0.271    | 0.218                | 1.281                | 2.76| 0.0058|
|       |                    | 8       | -0.460   | 0.218    | -0.888               | -0.033               | -2.11| 0.0348|
|       |                    | 12      | -0.199   | 0.134    | -0.462               | 0.065                | -1.48| 0.1389|
| 8     | ln(HOSP_DAYS,<sub>c</sub>,<sub>t</sub>) | 8       | -0.369   | 0.179    | -0.719               | -0.019               | -2.07| 0.0388|
| 9     | ln(ALOS,<sub>c</sub>,<sub>t</sub>) | 0       | 0.031    | 0.067    | -0.100               | 0.163                | 0.47| 0.6415|
|       |                    | 8       | -0.120   | 0.047    | -0.212               | -0.027               | -2.54| 0.0112|
|       |                    | 12      | -0.061   | 0.058    | -0.175               | 0.052                | -1.06| 0.2891|
| 10    | ln(ALOS,<sub>c</sub>,<sub>t</sub>) | 8       | -0.153   | 0.062    | -0.275               | -0.031               | -2.46| 0.0137|
Acknowledgements
Not applicable.

Authors’ contributions
All contributions to the manuscript were made by the sole author.

Funding
Financial support for this research was provided by Novartis. The funding body had no role in the design of the study, in the collection, analysis, and interpretation of data, or in writing the manuscript.

Availability of data and materials
All data, except IQVIA MIDAS data, are publicly available. The IQVIA MIDAS data are not publicly available but are available from the corresponding author on reasonable request.

Declarations

Competing interests
The authors declare that they have no competing interests.

Author details
1 Columbia University, New York, USA. 2 National Bureau of Economic Research, Cambridge, USA. 3 CESifo, Munich, Germany.

Received: 3 January 2022 Accepted: 15 February 2022 Published online: 14 March 2022

References
Association of Public Health Epidemiologists in Ontario. (2006). Calculating potential years of life lost.
Bertram, M. Y., Lauer, J. A., De Joncheere, K., Edeljer, T., Hurbubessy, R., Kierny, M. P., & Hill, S. R. (2016). Cost-effectiveness thresholds: Pros and cons. Bulletin of the World Health Organization, 94(12), 925–930.
Bils, M. (2004). Measuring the growth from better and better goods. NBER Working Paper No. 10606.
Bresnahan, T. F., & Gordon, R. J. (1996). The economics of new goods. University of Chicago Press.
Centers for Disease Control and Prevention. (2021). WISQARS years of potential life lost (YPLL) report.
Centre National Hospitalier d’Information sur le Médicament. (2021). Thériaque database.
Dorsey, E. R. (2010). Financial Anatomy of Biomedical Research, 2003–2008. Journal of the American Medical Association, 303(2), 137–143.
European Commission. (2021). Eurostat database.
Grossman, G. M., & Helpman, E. (1991). Innovation and growth in the global economy. MIT Press.
Jones, C. I., & Romer, P. (2019). Ideas, nonrivalry, and endogenous growth. The Scandinavian Journal of Economics, 121(3), 859–883. https://doi.org/10.1111/joe.12370
Jovanovic, B., & Yatsenko, Y. (2012). Investment in vintage capital. Journal of Economic Theory, 147(2), 551–569.
Koc, C. (2004). The productivity of health care and health production functions. Health Economics, 13(8), 739–747. https://doi.org/10.1002/hec.855
Kolata G (2019). Surgery for Blocked Arteries Is Often Unwarranted, Researchers Find. New York Times, November 16.
Lichtenberg, F. R. (2014). Has medical innovation reduced cancer mortality? CESifo Economic Studies, 60(1), 135–177.
Lichtenberg, F. R. (2016). The impact of pharmaceutical innovation on premature cancer mortality in Switzerland, 1995–2012. The European Journal of Health Economics, 17, 833–854.
National Cancer Institute. (2012). Long-term trial results show no mortality benefit from annual prostate cancer screening.
National Cancer Institute. (2021). Enhancing drug discovery and development. Organisation for Economic Co-operation and Development. (2021). OECD Health Statistics 2021.
Paris, V., & Docteur, E. (2007). Pharmaceutical pricing and reimbursement policies in Switzerland. OECD Health Working Papers.
Romer, P. M. (1990). Endogenous technological change. Journal of Political Economy, 98(5), S71–S102.
Sampat, B., & Lichtenberg, F. R. (2011). What are the Respective Roles of the Public and Private Sectors in Pharmaceutical Innovation? Health Affairs, 30(2), 332–9.
Swissmedic. (2021). Extended list of medicines.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.