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Abstract

There are two types of prescription drug cost offsets. The first type of cost offset—from prescription drug *use*—is primarily about the effect of changes in drug *quantity* (e.g. due to changes in out-of-pocket drug costs) on other medical costs. The second type of cost offset—the cost offset from prescription drug *innovation*—is primarily about the effect of prescription drug *quality* on other medical costs. Two previous studies found that pharmaceutical innovation reduced hospitalization, and that the reduction in hospital cost from the use of newer drugs was considerably greater than the innovation-induced increase in pharmaceutical expenditure. In this study, we reexamine the impact that pharmaceutical innovation has had on hospitalization, employing a different type of 2-way fixed effects research design. We estimate the impact that new drug launches that occurred during the period 1982-2015 had on hospitalization in 2015 for 67 diseases in 15 OECD countries. Our models include both country fixed effects and disease fixed effects, which control for the average propensity of people to be hospitalized in each country and from each disease. The number of hospital discharges and days of care in 2015 is significantly inversely related to the number of drugs launched during 1982-2005, but not significantly related to the number of drugs launched after 2005. (Utilization of drugs during the first few years after they are launched is relatively low, and drugs for chronic conditions may have to be consumed for several years to achieve full effectiveness.) The estimates imply that, if no new drugs had been launched after 1981, total days of care in 2015 would have been 163% higher than it actually was. The estimated reduction in 2015 hospital expenditure that may be attributable to post-1981 drug launches was 5.3 times as large as 2015 expenditure on those drugs.

JEL-Codes: I100, L650, O330.

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I. Introduction

To assess whether the benefits of a medical treatment exceed its costs, it is necessary to account for the "cost offsets" that may result from the treatment, as well as the cost of the treatment itself. For example, the true net cost of a drug may depend on potential reductions in the cost of outpatient visits and inpatient care that may result from treatment by the drug.

Previous studies have analyzed two types of prescription drug cost offsets. The first type is the cost offset from prescription drug *use*. Changes or differences in prescription drug use may be due to changes or differences in out-of-pocket drug costs. In a 2012 report, the Congressional Budget Office (CBO) said that "after reviewing recent research…CBO estimates that a 1 percent increase in the number of prescriptions filled by beneficiaries would cause Medicare's spending on medical services[1] to fall by roughly one-fifth of 1 percent" (Congressional Budget Office (2012), p. 1).[2] Given the relative magnitudes of Medicare expenditure on drugs and medical services, this suggests that the cost offsets from prescription drug use may slightly exceed the cost of the drugs themselves.[3]

The first type of cost offset—from prescription drug use—is primarily about the effect of prescription drug *quantity* on other medical costs. The second type of cost offset—the cost offset from prescription drug *innovation*—is primarily about the effect of prescription drug *quality* on other medical costs.[4] As noted by Jovanovic and Yatsenko (2012), in "the Spence–Dixit–Stiglitz tradition…new goods [are] of higher quality than old goods." Even if the average quality of new

[1] "Medical services" referred to medical and surgical services other than self-administered prescription drugs. The CBO report also said that "overall…the results from these studies suggest that people who received more generous prescription drug coverage through the implementation of Part D had fewer hospitalizations and used fewer medical services as a result" (p. 4).

[2] The "recent research" referred to by the CBO included studies by Hsu et al (2006), Gaynor, Li, and Vogt (2007), Goldman, Joyce, and Zheng (2007), Stuart, Doshi, and Terza (2009), Afendulis et al (2011), Briesacher et al (2011), and McWilliams, Zaslavsky, and Huskamp (2011).

[3] In 2015, total Medicare spending was $646 billion, and Medicare spending on prescription drugs was $94 billion (Centers for Medicare & Medicaid Services (2017)), so Medicare spending on medical and surgical services other than self-administered prescription drugs was $552 billion (= $646 billion - $94 billion). A 1% increase in the number of prescriptions filled by beneficiaries might increase Medicare spending on prescription drugs by $940 million (= 1% * $94 billion), and reduce Medicare spending on medical and surgical services other than self-administered prescription drugs by $1104 million (= 0.2% * $552 billion).

[4] In other words, the first type of offset is based on a "more vs. fewer prescriptions" contrast. The second type of offset is based on a "new drug vs. old drug" contrast. Prescription drug innovation is likely to increase the quantity as well as the quality of drugs consumed. Lichtenberg (2014a) showed that, in the US, although an increase in "new" (post-1990) drug prescriptions was associated with a reduction in old drug prescriptions, the old-drug reduction was about 74% as large as the new-drug increase.

drugs is not higher than the average quality of older drugs, drug innovation could yield cost offsets by increasing drug *variety*, enabling better matching of drugs to patients.

Studies have shown that new drugs for Crohn's disease, transthyretin amyloid cardiomyopathy, and some types of cystic fibrosis have reduced hospitalization:

- Data from the Phase 3 IM-UNITI study showed that treatment with ustekinumab lowered the risk of Crohn's disease (CD)-related hospitalization, surgery, and the need for alternative biologic therapy in patients with moderate-to-severe CD when compared with placebo. At 2 years, patients in the ustekinumab q12w group were 52% less likely to be hospitalized or require surgery vs patients in the placebo group (hazard ratio [HR] 0.477; 95% CI, 0.238, 0.957; P =.033). Patients in the ustekinumab q8w group were 40% less likely to be hospitalized or require surgery (HR 0.601; 95% CI, 0.411, 0.879; P =.006).[5]
- A phase three clinical trial has shown that tafamidis significantly reduces deaths and hospitalizations in patients with transthyretin amyloid cardiomyopathy, a progressive form of heart failure. Compared to a placebo, the drug reduced deaths by 30 percent and reduced cardiovascular-related hospitalizations by 32 percent.[6]
- Ivacaftor is a small molecule drug originally developed to treat the G551D CFTR gene variant that causes about 3-4% of Cystic fibrosis (CF) cases. Inpatient admissions decreased by 55% from 0.57 inpatient admissions per person-year pre-ivacaftor to 0.26 admissions post-ivacaftor, with similar decreases for children and adults.[7]

Other studies have provided more general evidence about cost offsets from prescription drug innovation. Lichtenberg (2009a) analyzed the impact of pharmaceutical innovation on hospitalization for a single (albeit important) disease—cardiovascular disease—in 20 OECD countries during the period 1995-2003. Lichtenberg (2014a) analyzed the impact of pharmaceutical innovation on hospitalization for 131 medical conditions in a single country—the United States—during the period 1996-2010. The measure of pharmaceutical innovation used in both studies was the mean *vintage* of prescription drugs, i.e. the utilization-weighted mean world launch year (or FDA approval year) of drugs consumed. Both studies found that pharmaceutical innovation reduced hospitalization, and that the reduction in hospital cost from the use of newer drugs was considerably greater than the innovation-induced increase in pharmaceutical expenditure.

In this study, we will reexamine the impact that pharmaceutical innovation has had on hospitalization, employing a different type of 2-way fixed effects research design. In lieu of

[5] https://www.empr.com/news/stelara-ustekinumab-crohns-disease-hospitalization-surgery-reduction-im-uniti/article/770888/
[6] https://www.nyp.org/news/Drug-Reduce-Deaths-Hospitalizations-Underdiagnosed-Heart-Failure
[7] https://blogs.cdc.gov/genomics/2018/05/08/evaluating-the-impact/

analyzing different countries over time for a single disease, or different diseases over time for a single country, we will analyze 67 diseases in 15 OECD countries in a single year (2015): we will estimate the impact that the new drug launches that occurred during the period 1982-2015 had on hospitalization in 2015 for those medical conditions in those countries .[8] The models we will estimate will include both country fixed effects and disease fixed effects, which control for the average propensity of people to be hospitalized in each country and from each disease. Lichtenberg (2018) used a similar approach to analyze the impact of new drug launches on life-years lost in 2015 from 19 types of cancer in 36 countries. The measure of pharmaceutical innovation we will use to explain hospitalization for medical condition (disease) d in country c in 2015 is the number of drugs used to treat (indicated for) disease d that were launched in country c during 1982-2015.[9] We hypothesize the existence of a lag from drug launches to hospitalization because new drugs diffuse gradually. We will provide evidence about the rate of diffusion of new drugs, and investigate whether the drug-age profiles of the hospitalization effect and of drug utilization are consistent.

The two-way fixed effects methodology is feasible because the *relative* number of drugs launched to treat different diseases varies across countries. This variation is illustrated by Figure 1, which shows the number of drugs launched In Italy and Mexico for 8 types of cancer during the period 1997-2010. The mean number of drugs launched for these 8 diseases was identical (4.9) in both countries. But Mexico had more drug launches for prostate, breast, and lung cancer, and Italy had more drug launches for skin, ovarian, and bladder cancer. I hypothesize that the ratio of hospitalization in 2015 for the first 3 cancers to hospitalization in 2015 for the latter 3 cancers should have been smaller in Mexico than it was in Italy. Instead of performing the analysis using just these 16 observations (8 diseases * 2 countries), I will perform the analysis on about 1005 observations (67 diseases * 15 countries).

In the next section, we describe the econometric model of hospitalization. Data sources are discussed in Section III. Empirical results are presented in Section IV. Implications of the results are discussed on Section V. Section VI concludes.

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[8] The 15 countries for which the necessary data were available are: Austria, Canada, Denmark, Finland, France, Germany, Ireland, Israel, Italy, Mexico, Portugal, Spain, Sweden, Switzerland, and the United Kingdom.

[9] Due to data limitations, it is not possible to measure drug vintage by disease, country, and year. Lichtenberg (2014a) provided evidence that, in the U.S., the correlation across diseases between the increase in the number of drugs ever approved and the increase in drug vintage is positive and significant.

II. Econometric model of hospitalization

Our analysis of the impact that new drug launches had on hospitalization will be based on the following two-way fixed effects model:

$$\ln(Y_{dc}) = \beta_{0\text{-}4}\, LAUNCHES\_2011\_2015_{dc} + \beta_{5\text{-}9}\, LAUNCHES\_2006\_2010_{dc} + \beta_{10\text{-}14}\, LAUNCHES\_2001\_2005_{dc} + \beta_{15\text{-}33}\, LAUNCHES\_1982\_2000_{dc} + \alpha_d + \delta_c + \varepsilon_{dc} \quad (1)$$

where Y_{dc} is one of the following variables:

$DISCHARGES_{dc}$ = the number of hospital discharges[10] for disease (diagnosis) d in country c in 2015

$ALOS_{dc}$ = average length of stay (in days) for disease d in country c in 2015

$DAYS_{dc}$ = $DISCHARGES_{dc}$ * $ALOS_{dc}$ = the total number of hospital days for disease d in country c in 2015

and

$LAUNCHES\_2011\_2015_{dc}$ = the number of post-1981[11] new chemical entities used to treat disease d launched in country c during 2011-2015

$LAUNCHES\_2006\_2010_{dc}$ = the number of post-1981 new chemical entities used to treat disease d launched in country c during 2006-2010

$LAUNCHES\_2001\_2005_{dc}$ = the number of post-1981 new chemical entities used to treat disease d launched in country c during 2001-2005

$LAUNCHES\_1982\_2000_{sc}$ = the number of post-1981 new chemical entities used to treat disease d launched in country c during 1982-2000

α_d = a fixed effect for disease d

δ_c = a fixed effect for country c

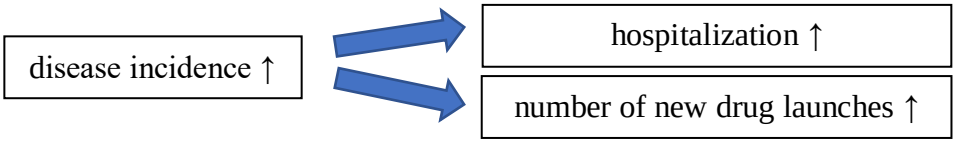
Due to data limitations, the number of drugs launched in four different periods are the only disease-and country-specific explanatory variables included in eq. (1). The disease and

[10] A hospital discharge is the formal release of a patient from a hospital. Discharges from all hospitals, including general hospitals (HP.1.1), mental health hospitals, (HP.1.2), and other specialised hospitals (HP.1.3) are included. Discharges include deaths in hospital, transfers to another hospital, and discharges of healthy newborns. Transfers to other care units within the same hospital are excluded (OECD (2017a)).

[11] My data on drug launches are left-censored: I only have data on drugs launched after 1981. A post-1981 new chemical entity is one that was first launched anywhere in the world after 1981.

country fixed effects in the equation control for some unobserved potential determinants of hospitalization, e.g. the country fixed effects (δ_c's) control for a country's attributes (e.g. the size and age structure of its population, and its average income, educational attainment, and health care expenditure) to the extent that they have similar effects on hospitalization from different diseases.[12]

If the data were available, we would like to include other regressors in eq. (1), including (1) disease incidence, and (2) the number of non-pharmaceutical medical innovations (e.g. medical device innovations) for disease d that had been launched in country c. However, there is good reason to believe that failure to control for those variables is unlikely to result in overestimation of the magnitudes of the drug launch coefficients; exclusion of those variables may even result in *underestimation* of the magnitudes of those parameters. Higher disease incidence is likely to result in more hospitalization and a larger number of drug launches:



Previous studies have shown that both innovation (the number of drugs developed) and diffusion (the number of drugs launched in a country) depend on *market size*. Acemoglu and Linn found "economically significant and relatively robust effects of market size on innovation." Danzon et al found that "countries with lower expected prices or *smaller expected market size experience longer delays in new drug access*, controlling for per capita income and other country and firm characteristics" (emphasis added).

Although incidence data are not available for most diseases, data on the incidence (number of new cases diagnosed) in 2012 in 13 countries of six major types of cancer[13] are available.[14] We used those data to analyze the relationships across countries between relative incidence and (1) relative hospitalization, and (2) the relative number of drug launches, by estimating the following equations:

$$\ln(DAYS\_2015_{sc}) = \pi_1 \ln(CASES\_2012_{sc}) + \alpha_s + \delta_c + \varepsilon_{sc} \qquad (2)$$

[12] For example, suppose that $\ln(Y_{dc})$ depends on EDU_c (where EDU_c = average educational attainment in country c), and that δ_c—the marginal effect of EDU_c on $\ln(Y_{dc})$—does not vary across diseases ($\delta_c = \delta$, all c). Then $\delta_c EDU_c = \delta EDU_c$, which can be written as δ_c.

[13] The six types of cancer are: colon, rectum and anus; trachea, bronchus and lung; skin; breast; ovary; prostate; and bladder.

[14] All types of cancer combined account for about 13% of hospital days.

$$LAUNCHES\_1982\_2015_{sc} = \pi_2 \ln(CASES\_2012_{sc}) + \alpha_s + \delta_c + \varepsilon_{sc} \quad (3)$$

where $DAYS\_2015_{sc}$ = the number of hospital days for cancer at site s in country c in 2015; $CASES\_2012_{sc}$ = the number of new cases of cancer at site s diagnosed in country c in 2012; and $LAUNCHES\_1982\_2015_{sc}$ = the number of drugs used to treat cancer at site s launched in country c during 1982-2015. Estimates of both π_1 and π_2 were positive and highly significant:

Parameter	Estimate	Std. Err.	Z	Pr > |Z|
π_1	0.7027	0.1436	4.89	<.0001
π_2	0.9639	0.2316	4.16	<.0001

This suggests that failure to control for incidence in eq. (1) is extremely unlikely to result in overestimation of the magnitudes of the drug launch parameters.

Failure to control for non-pharmaceutical medical innovation (e.g. innovation in diagnostic imaging, surgical procedures, and medical devices) is also unlikely to bias estimates of the effect of pharmaceutical innovation on hospitalization, for two reasons. First, 88% of privately-funded U.S. funding for biomedical research came from pharmaceutical and biotechnology firms (Dorsey (2010)).[15] Second, previous research based on U.S. data (Lichtenberg (2014b, 2014c)) indicated that non-pharmaceutical medical innovation is not positively correlated across diseases with pharmaceutical innovation.

According to eq. (1), hospitalization depends on the number of *drugs* that had previously been launched to treat a disease. In principle, hospitalization might depend on the number of *drug classes* instead of,[16] or in addition to, the number of drugs. However, several previous studies (e.g. Lichtenberg (2017)) have shown that premature mortality depends only on the number of drugs previously launched, not on the number of drug classes. One possible interpretation of the non-significance of the number of drug classes is that mortality depends on the number of drug classes, but some drug classes may be more important or valuable than other drug classes. Moreover, drug classes that are more important or valuable are likely to have

[15] 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 (2018) says that it "has played a vital role in cancer drug discovery and development, and, today, that role continues."

[16] If drugs within the same class were "therapeutically equivalent," hospitalization might *only* depend on the number of drug classes previously launched.

larger numbers of drugs.[17] In other words, mortality is inversely related to the number of drug classes, weighted by their relative importance, and the number of drugs in a class may be a good indicator of the relative importance of the class. This could explain why mortality is related to the number of drugs rather than the number of drug classes.

Our data on drug launches are left-censored: we only have data on drugs launched after 1981. We therefore define $LAUNCHES\_1982\_2000_{dc}$ (for example) as the number of *post-1981* new chemical entities (i.e. NCEs first launched anywhere in the world after 1981) used to treat disease d that were launched in country c during 1982-2000. Consequently, this measure is subject to error, because $LAUNCHES\_1982\_2000_{dc}$ will not (but should) include pre-1982 NCEs that were first launched in country c during 1982-2000. If this measurement error is random, it is likely to bias estimates of $\beta_{15\text{-}33}$ towards zero.[18]

In eq. (1), drugs launched in 4 different periods (0-4 years, 5-9 years, 10-14 years, and 15-33 years before 2015) are permitted to have different effects on hospitalization in 2015. The model is specified in this way because the effect of a drug's launch on hospitalization is hypothesized to depend on both the *quantity* and the *quality* (or effectiveness) of the drug. Indeed, it is likely to depend on the *interaction* between quantity and quality: a quality improvement will have a greater impact on mortality if drug utilization (quantity) is high. Drugs launched in the 4 different periods are likely to vary (in opposite ways) with respect to both quantity (in 2015) and quality. Newer drugs are likely to be of higher quality than older drugs.[19] On the other hand, utilization of new drugs tends to be much lower than utilization of old drugs.

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[17] The impact on population health of the first drug launched in a therapeutic class may be considerably smaller than the impact of subsequent launches within the class. Atorvastatin (brand name Lipitor), launched in 1997, was the fifth drug in its ATC chemical/therapeutic/pharmacological subgroup (C10AA: HMG CoA reductase inhibitors)—the first drug, lovastatin, was launched ten years earlier—but atorvastatin may have had a much larger impact on population health: it became the largest-selling drug of all time.

[18] Here is the first paragraph of Hausman's (2001, p. 57) article on mismeasured variables in econometric analysis: "The effect of mismeasured variables in statistical and econometric analysis is one of the oldest known problems, dating from the 1870s in Adcock (1878). In the most straightforward regression analysis with a single regressor variable, the least squares estimate is downward biased in magnitude toward zero. While a mismeasured right-hand side variable creates this problem, a mismeasured left-hand side variable under classical assumptions does not lead to bias. The only result is less precision in the estimated coefficient and a lower t-statistic."

[19] Grossman and Helpman (1993) argued that "innovative goods are better than older products simply because they provide more 'product services' in relation to their cost of production." Bresnahan and Gordon (1996) stated simply that "new goods are at the heart of economic progress," and Bils (2004) said that "much of economic growth occurs through growth in quality as new models of consumer goods replace older, sometimes inferior, models."

To provide evidence about the process of diffusion of new medicines, I estimated the following model, using annual data for the period 1999-2010 on utilization of 744 drugs (molecules) in 11 countries:[20]

$$\ln(N\_SU_{mcn}) = \rho_{mc} + \pi_n + \varepsilon_{mcn} \quad (4)$$

where

N_SU_{mcn} = the number of standard units[21] of molecule m sold in country c n years after it was launched in country c (n = 0, 1,…, 15)

ρ_{mc} = a fixed effect for molecule m in country c

π_n = a fixed effect for age n

Data on the launch year of molecule m in country c were obtained from the IMS Health *New Product Focus* database. Data on the number of standard units of molecule m sold in country c in year t were obtained from the IMS Health MIDAS database. The expression $\exp(\pi_n - \pi_{10})$ is a "relative utilization index": it is the mean ratio of the quantity of a cancer drug sold n years after it was launched in country c to the quantity of the same drug sold 10 years after it was launched in country c.

Estimates of the "relative utilization index" are shown in Figure 2. These estimates indicate that it takes 8-10 years for a drug to attain its peak level of utilization. The number of standard units sold 10 years after launch is 73% larger than the number of standard units sold 2 years after launch.

The MIDAS data for many countries distinguish between drugs sold to hospitals and drugs sold to other distribution channels (i.e. retail pharmacies). As shown in Figure 3, those data indicate that the adoption of new drugs occurs earlier in hospitals than it does in other settings: the fraction of a drug's sales that were to hospitals is 43% higher 0-4 years after it was launched than it was 15 or more years after it was launched.[22]

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[20] The 11 countries are Austria, Canada, France, Germany, Italy, Mexico, Portugal, Spain, Sweden, Switzerland, and the United Kingdom.

[21] The number of standard 'dose' units sold is the ratio of the number of counting units sold to the standard unit factor, which is the smallest common dose of a product form, as defined by IMS HEALTH. For example, for oral solid forms the standard unit factor is one tablet or capsule, whereas for syrup forms the standard unit factor is one teaspoon (5ml), and for injectable forms it is one ampule or vial. Other measures of quantity, such as the number of patients using the drug, prescriptions for the drug, or defined daily doses of the drug, are not available.

[22] The figures in Figure 4 were obtained by estimating the equation $HOSP\%_{mcn} = \rho_{mc} + \pi_n + \varepsilon_{mcn}$ by weighted least squares, weighting by N_SU_{mcn}, where $HOSP\%_{mcn}$ = the fraction of standard units that were sold to hospitals of molecule m sold in country c n years after it was launched in country c.

III. Data sources

Hospitalization data. Data on the number of hospital discharges and average length of stay, by diagnosis and country in 2015 were obtained from the *OECD Health Statistics database* (OECD (2017b)). The disease classification scheme is provided in OECD (2017c). Data on the number of hospital discharges, by disease and country, are shown in Appendix Table 1.

Drug launch data. Data on drug launches, by country and year (1982-2015), were obtained from the IMS Health *New Product Focus database* (now known as QuintilesIMS Ark New Product Intelligence).

Drug indications data. Data on drug indications were obtained from Theriaque, a database produced by the French Centre National Hospitalier d'Information sur le Médicament (2017). Data on the number of drugs launched during 1982-2015, by disease and country, are shown in Appendix Table 2.

Drug utilization data. Annual data on the number of standard units of drugs sold, by molecule, country, and year (1999-2010) were obtained from the IMS Health MIDAS database.

Cancer incidence data. Data on the incidence (number of new cases diagnosed) in 2012 in 13 countries of six major types of cancer were obtained from International Agency for Research on Cancer (2018).

IV. Empirical results

Estimates of the drug launch coefficients from eq. (1) are presented in Table 1. All models include disease fixed effects and country fixed effects. Each model was estimated in two different ways: with disturbances clustered by country, and with disturbances clustered by disease. The clustering choice does not affect the point estimates of the drug launch coefficients (shown in column 1). Columns 2-4 show the standard errors, Z statistics, and p-values when the disturbances are clustered by disease; columns 5-7 show them when the disturbances are

clustered by country. To account for heteroskedasticity, all models were estimated by weighted least squares, weighting by $DISCHARGES_{dc}$.[23]

The first four rows of Table 1 show estimates of the coefficients of the drug launch regressors when the dependent variable is $\ln(DISCHARGES_{dc})$. These estimates are also plotted in Panel A of Figure 4. The estimates indicate that the number of discharges in 2015 is not significantly related to the number of drugs launched during 2006-2010 and 2011-2015, but is significantly inversely related to the number of drugs launched during 1982-2000 and especially to the number of drugs launched during 2001-2005. The insignificance of $\beta_{0\text{-}4}$ and $\beta_{5\text{-}9}$ is not surprising, since the utilization of drugs during the first few years after they are launched is relatively low (Figure 2), and drugs for chronic conditions may have to be consumed for several years to achieve full effectiveness. The estimate of $\beta_{10\text{-}14}$ indicates that one additional drug for a disease launched during 2001-2005 was associated with a 10% reduction in the number of hospital discharges due to that disease in 2015. The estimate of $\beta_{15\text{-}33}$ is about half as large (and only marginally significant (p-value = .067) when disturbances are clustered by country), but the difference between the estimates of $\beta_{10\text{-}14}$ and $\beta_{15\text{-}33}$ is not statistically significant (p-value = 0.254).

Rows 5-8 of Table 1 show estimates of the coefficients of the drug launch regressors when the dependent variable is $\ln(ALOS_{dc})$; these estimates are also plotted in Panel B of Figure 4. In contrast to the estimates of the DISCHARGES model, these estimates indicate that the average length of hospital stays in 2015 is significantly inversely related to the number of drugs launched during 2006-2010 and 2011-2015, but is not significantly related to the number of drugs launched during 1982-2000 and 2001-2005. The finding that average length of stay is inversely related to relatively recent drug launches, despite the fact that overall utilization of new drugs is quite limited, seems consistent with the fact that new drugs diffuse more rapidly in the hospital sector than they do in the retail pharmacy sector (Figure 3). The sickest patients, who are more likely to be hospitalized, may obtain access to new drugs earlier than less severely ill patients.

[23] As indicated in Appendix Figure 1, the variance of residuals of observations with small values of $DISCHARGES_{dc}$ from the unweighted regression $\ln(DISCHARGES_{dc}) = \alpha_d + \delta_c + \varepsilon_{dc}$ is much larger than the variance of residuals with large values of $DISCHARGES_{dc}$.

Rows 9-12 of Table 1 show estimates of the coefficients of the drug launch regressors when the dependent variable is $\ln(DAYS_{dc})$; these estimates are also plotted in Panel C of Figure 4. The estimates of the $\ln(DAYS_{dc})$ model are qualitatively similar to the estimates of the $\ln(DISCHARGES_{dc})$ model in rows 1-4. The number of days of hospital care in 2015 is unrelated to the number of drugs launched during 2006-2010 and 2011-2015, but strongly inversely related to the number of drugs launched during 1982-2000 and 2001-2005. One additional drug launched for a disease during the two earlier periods is associated with an 8-10% reduction in the number of hospital days due to that disease in 2015.

In addition to estimating models in which drug launches were divided into four periods, we estimated models in which drug launches were divided into just two periods: 1982-2005 and 2006-2015. These estimates, which are shown in rows 13-18 of Table 1, are quite consistent with the estimates discussed previously. Average length of stay in 2015 is significantly inversely related to the number of drugs launched during 2006-2015, and the number of hospital discharges and days of care in 2015 is significantly inversely related to the number of drugs launched during 1982-2005.

V. Discussion

Now we will use the estimates of eq. (1) reported in Table 1 to obtain rough estimates of the reduction in hospital utilization and expenditure attributable to previous drug launches, and compare them to the increases in pharmaceutical expenditure resulting from those launches. These calculations are shown in Table 2.

Calculation of the number of 2015 hospital discharges which may have been prevented by drugs launched during 1982-2015 is shown in rows 1-5. The mean reduction (which we denote by Φ) in ln(DISCHARGES) in 2015 attributable to drugs launched after 1981 is $\Phi = \beta_{0\text{-}4} * \text{mean}(LAUNCHES\_2011\_2015_{dc}) + \beta_{5\text{-}9} * \text{mean}(LAUNCHES\_2006\_2010_{dc}) + \beta_{10\text{-}14} * \text{mean}(LAUNCHES\_2001\_2005_{dc}) + \beta_{15\text{-}33} * \text{mean}(LAUNCHES\_1982\_2000_{dc})$. The estimated ratio of the number of discharges in 2015 in the absence of new drugs to the actual number of discharges $= 1 / \exp(\Phi)$. The estimates imply that, if no new drugs had been launched after 1981, the number of discharges in 2015 would have been 91% (= (1 / exp(-0.645)) – 1) higher than it actually was. Similarly, as shown in rows 6-10 and 11-15, the estimates imply that, if no new

drugs had been launched after 1981, average length of stay in 2015 would have been 38% (= (1 / exp(-0.321)) – 1) higher than it actually was, and total days of care would have been 163% (= (1 / exp(-0.966)) – 1) higher than it actually was.

If hospital expenditure is proportional to total days of care, then our estimates imply that, if no new drugs had been launched after 1981, 2015 hospital expenditure would also have been 163% higher than it actually was. Data on both hospital (inpatient curative care) expenditure and prescribed medicine expenditure in 2015 are available for 9 of the 15 countries in our sample. As shown in Table 3, total hospital expenditure and prescribed medicine expenditure in those 9 countries was $275 billion and $159 billion, respectively. We estimate that, in the absence of any drug launches during 1982-2015, hospital expenditure would have been $448 billion (= 163% * $275 billion) higher than it actually was. IQVIA data indicate that drugs launched during 1982-2015 accounted for just over half (53%) of the prescribed medicine expenditure in those countries in 2015. Therefore, we estimate that, in the absence of any drug launches during 1982-2015, pharmaceutical expenditure would have been $85 billion (= 53% * $159 billion) lower than it actually was. The estimated reduction in 2015 hospital expenditure attributable to post-1981 drug launches was 5.3 (= $448 billion / $85 billion) times as large as 2015 expenditure on those drugs.

This implies that pharmaceutical innovation reduced overall medical expenditure. The magnitude of the hospital cost offset is about twice as large as those estimated in the two studies cited earlier. One of those studies examined only cardiovascular diseases, which account for about 12% of hospital discharges. The hospital cost offset from new cardiovascular drugs may be smaller than the offset from other drugs. The other study was about a single country (the US), which was excluded from our sample due to the absence of 2015 US hospitalization data in the OECD Health Statistics database. The ratio of drug expenditure to hospital expenditure in the US is about 24% higher than it is in 10 countries included in our sample for which comparable data are available; the higher US ratio may be due in part to higher drug prices in the US than in other countries. Lower prices of drugs in other countries could be a reason for the hospital cost offset in those countries to be larger than it is in the US.[24]

[24] However, prices of hospital services and procedures also tend to be higher in the US: the US nightly hospital price is slightly higher than in Switzerland and much higher than in Australia; the US prices of caesarean sections, knee replacements, and hip replacements are higher than in comparable countries with available data; and the US MRI price is significantly higher than in comparable countries (Kamal and Cox (2018)).

We have examined the impact of new drug launches on utilization of hospital care, by analyzing data on hospital utilization, by disease and country. Data on utilization of other medical care (e.g. outpatient care, home health care, and nursing home care), by disease and country, are not available. But two previous studies (Lichtenberg (2009b, 2014a)) based on U.S. data have provided evidence that the introduction and use of new drugs has also reduced utilization of nursing home care, office-based visits, outpatient care, and home health care.

VI. Summary and conclusions

There are two types of prescription drug cost offsets. The first type of cost offset—from prescription drug *use*—is primarily about the effect of changes in drug *quantity* (e.g. due to changes in out-of-pocket drug costs) on other medical costs. Previous studies indicate that the cost offsets from prescription drug use may slightly exceed the cost of the drugs themselves.

The second type of cost offset—the cost offset from prescription drug *innovation*—is primarily about the effect of prescription drug *quality* on other medical costs. Two previous studies (of a single disease or a single country) found that pharmaceutical innovation reduced hospitalization, and that the reduction in hospital cost from the use of newer drugs was considerably greater than the innovation-induced increase in pharmaceutical expenditure.

In this study, I reexamined the impact that pharmaceutical innovation has had on hospitalization, using a different kind of two-way fixed effects research design: I estimated the impact that new drug launches during the period 1982-2015 had on hospitalization for 67 medical conditions in 15 OECD countries in 2015. This design enabled me to control for the average propensity of people to be hospitalized in each country and from each disease. The relative number of new drugs launched for different diseases varied across countries.

The number of hospital discharges and days of care in 2015 is significantly inversely related to the number of drugs launched during 1982-2005, but not significantly related to the number of drugs launched after 2005. This is not surprising, since the utilization of drugs during the first few years after they are launched is relatively low, and drugs for chronic conditions may have to be consumed for several years to achieve full effectiveness. The estimates indicated that one additional drug for a disease launched during 1982-2005 was associated with an 8-10% reduction in the number of hospital days due to that disease in 2015.

The average length of hospital stays in 2015 is significantly inversely related to the number of drugs launched after 2005, but not to earlier drug launches. More rapid diffusion of new drugs in the hospital sector than in the retail pharmacy sector may partly explain this finding.

The estimates implied that, if no new drugs had been launched after 1981, the number of discharges in 2015 would have been 91% higher; average length of stay in 2015 would have been 38% higher; and total days of care would have been 163% higher than it actually was. The estimated reduction in 2015 hospital expenditure that may be attributable to post-1981 drug launches was 5.3 times as large as 2015 expenditure on those drugs. The hospital cost offset rate is about twice as large as those estimated in previous studies of a single disease and a single country. The hospital cost offset rate from cardiovascular drugs may be lower than the offset from other drugs, and the hospital cost offset rate outside the US may be larger than it is in the US, perhaps due to lower prices of drugs in other countries.

Utilization of hospital care has declined. In the US, the age-adjusted fraction of people who had one or more hospital stays in the past year declined by 18%, from 7.8% to 6.4%, between 1997 and 2016.[25] Our estimates are consistent with the hypothesis that the introduction and use of new drugs has made a significant contribution to the decline in hospitalization.

This study is subject to several limitations. Due to left-censoring of our data on drug launches, our measures of the number of drug launches are subject to error, particularly during the 1980s and early 1990s. Also, our measures of the number of drug launches are based on labeled indications only; off-label drug use is not accounted for. Our drug indications data were obtained from a French database, and some drugs launched in other countries have not been launched in France. Our estimates provide evidence about the impact of the launch of drugs for a disease on hospitalization for that disease, but they do not capture possible spillover effects of the drugs on hospitalization for *other* diseases. Also, our estimates control for the effects on hospitalization of a country's overall health system and macroeconomic conditions, to the extent that those effects don't vary across diseases, but those effects might vary across diseases.

[25] Source: National Health Interview Survey, family core and sample adult questionnaires, https://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/Health_US/hus17tables/table081.xlsx

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Figure 1
Number of drugs launched In Italy and Mexico for 8 types of cancer, 1997-2010

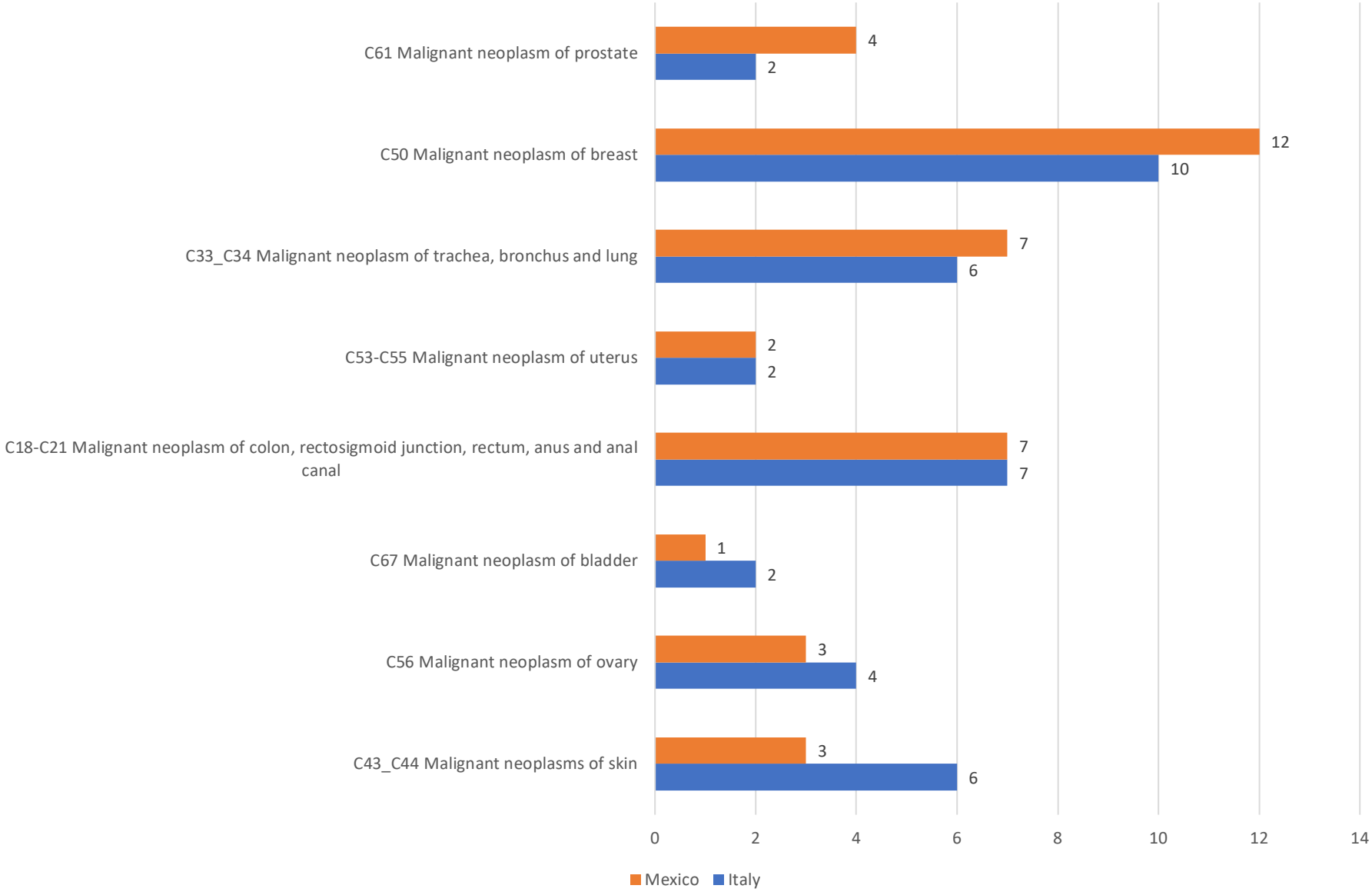


Figure 2
Relative drug utilization index

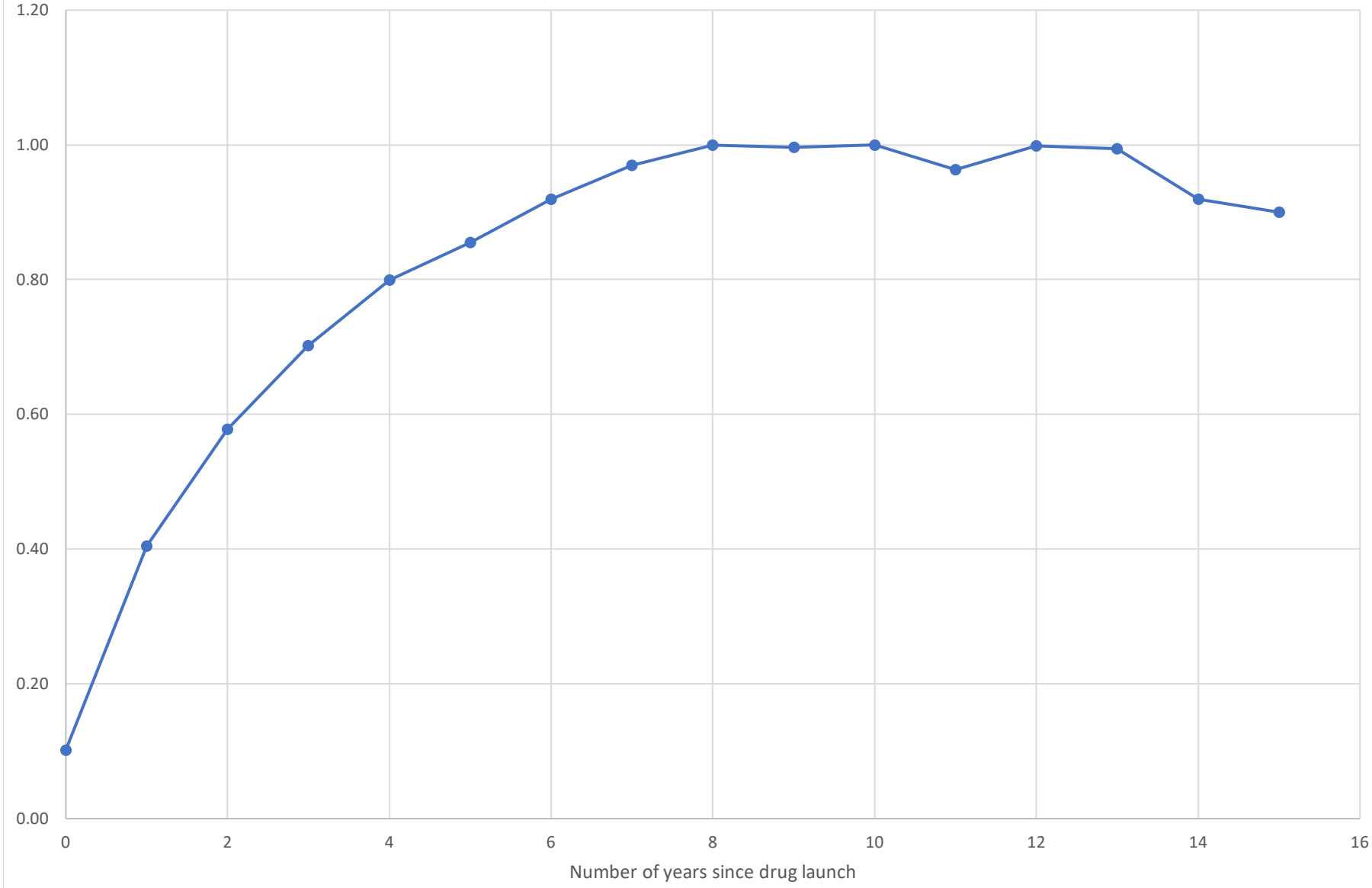


Figure 3

Fraction of standard units of drug sold to hospitals, by number of years after drug launch

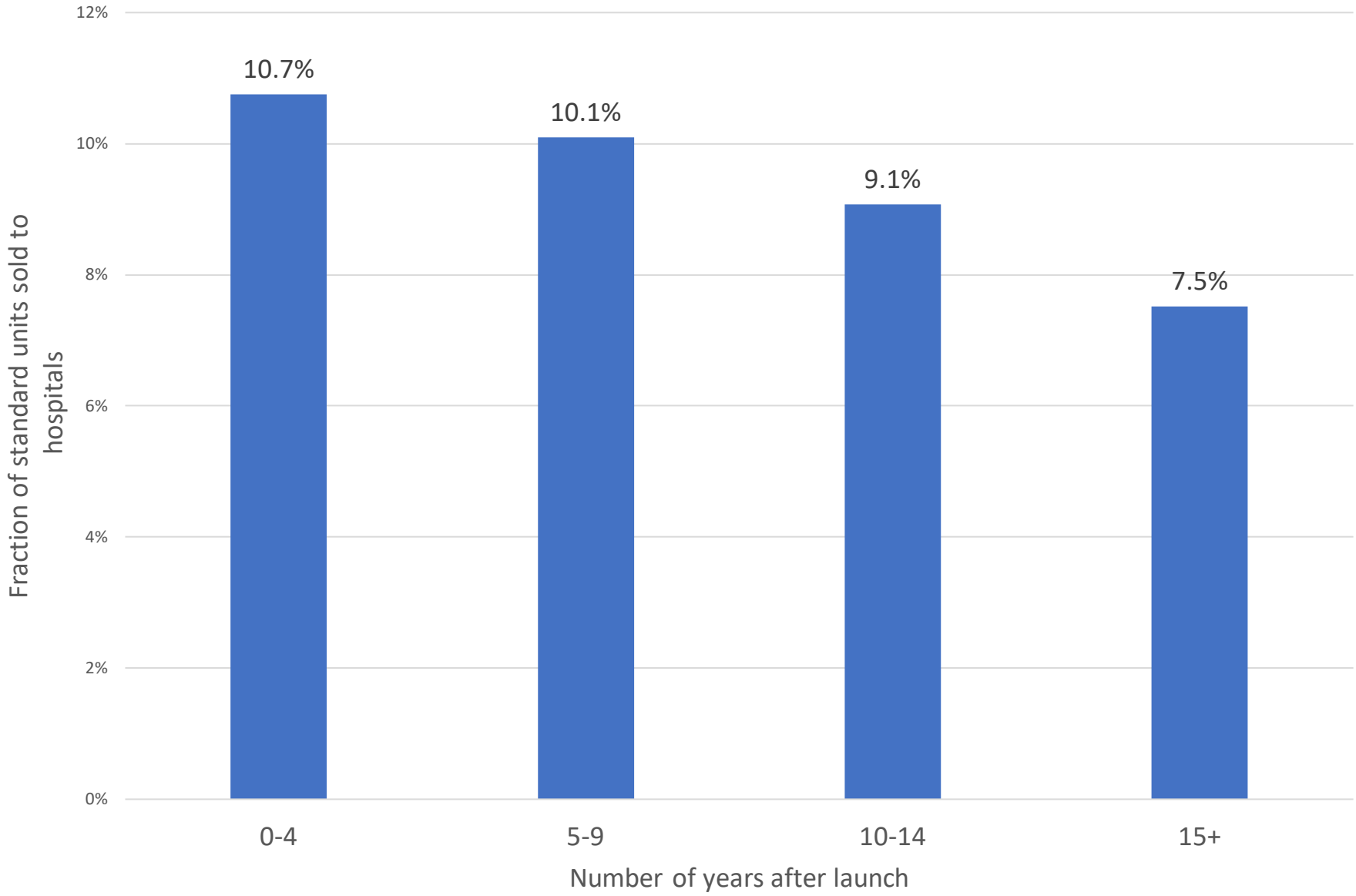
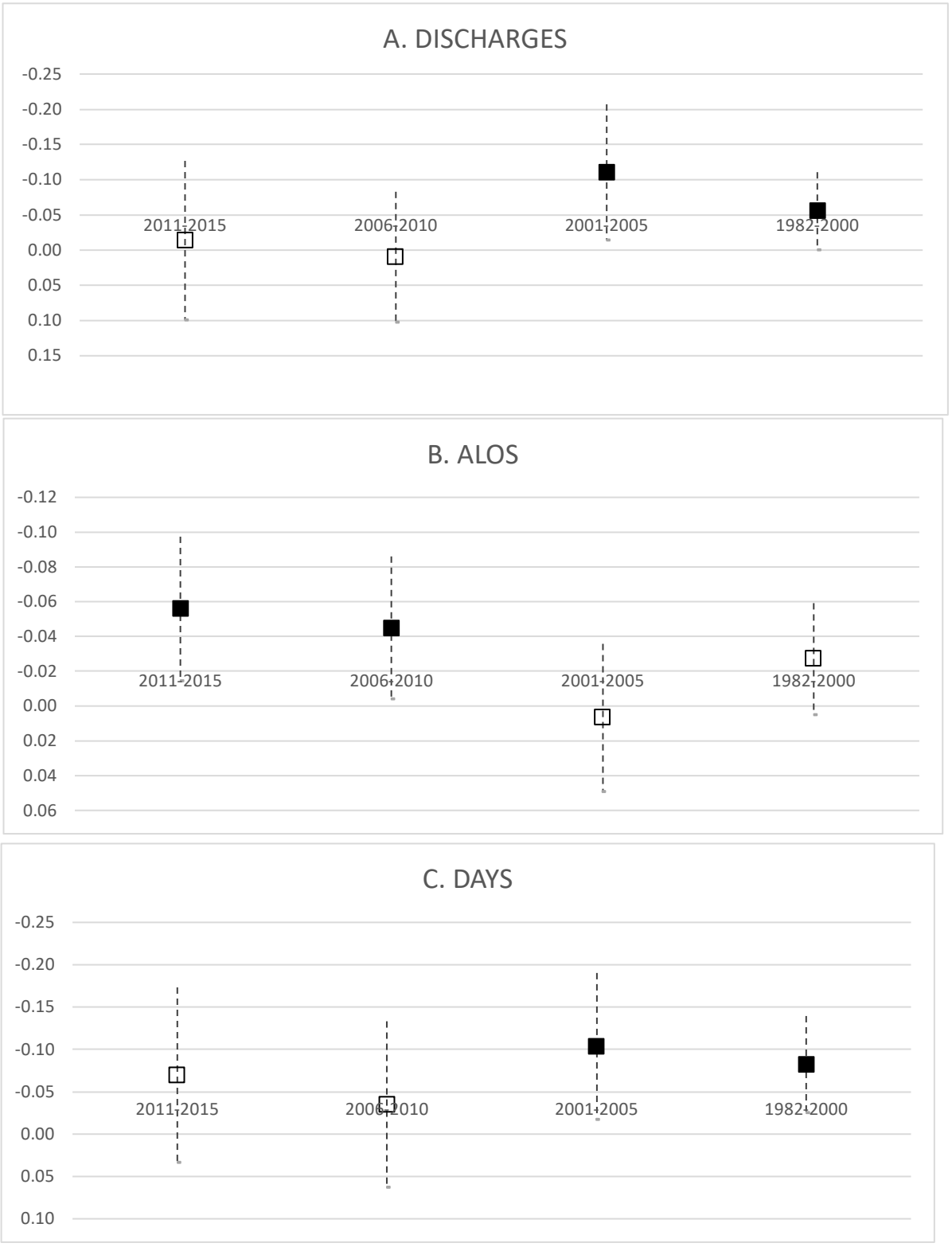


Figure 4
Estimated effects of drugs launched during 1982-2015 on hospital discharges, average length of stay, and days of care in 2015



Solid markers denote significant ($p < .05$) estimates
Hollow markers denote insignificant estimates
Vertical lines represent 95% confidence interval

Table 1

Estimates of coefficients of drug launch regressors in eq. (1)

					cluster by disease				cluster by country		
Row	**Model**	**Regressor**	**Estimate**		**Std. Err.**	**Z**	**Pr > |Z|**		**Std. Err.**	**Z**	**Pr > |Z|**
			DISCHARGES								
1	1	LAUNCHES_2011_2015	-0.014		0.058	-0.24	0.811		0.053	-0.26	0.796
2	1	LAUNCHES_2006_2010	0.010		0.047	0.21	0.836		0.059	0.16	0.869
3	1	LAUNCHES_2001_2005	-0.111		0.049	**-2.26**	**0.024**		0.044	**-2.53**	**0.011**
4	1	LAUNCHES_1982_2000	-0.056		0.028	**-1.97**	**0.049**		0.030	-1.83	0.067
			ALOS								
5	2	LAUNCHES_2011_2015	-0.056		0.021	**-2.64**	**0.008**		0.018	**-3.18**	**0.002**
6	2	LAUNCHES_2006_2010	-0.045		0.021	**-2.14**	**0.032**		0.026	-1.75	0.080
7	2	LAUNCHES_2001_2005	0.007		0.022	0.31	0.758		0.021	0.32	0.747
8	2	LAUNCHES_1982_2000	-0.027		0.016	-1.66	0.096		0.015	-1.80	0.072
			DAYS								
9	3	LAUNCHES_2011_2015	-0.070		0.053	-1.32	0.187		0.053	-1.32	0.186
10	3	LAUNCHES_2006_2010	-0.035		0.050	-0.71	0.480		0.059	-0.59	0.552
11	3	LAUNCHES_2001_2005	-0.104		0.044	**-2.36**	**0.018**		0.033	**-3.12**	**0.002**
12	3	LAUNCHES_1982_2000	-0.083		0.029	**-2.84**	**0.005**		0.032	**-2.62**	**0.009**
			DISCHARGES								
13	4	LAUNCHES_2006_2015	0.000		0.038	0.01	0.991		0.053	0.01	0.993
14	4	LAUNCHES_1982_2005	-0.062		0.028	**-2.21**	**0.027**		0.027	**-2.29**	**0.022**
			ALOS								
15	5	LAUNCHES_2006_2015	-0.051		0.018	**-2.82**	**0.005**		0.022	**-2.29**	**0.022**
16	5	LAUNCHES_1982_2005	-0.023		0.016	-1.50	0.135		0.016	-1.50	0.135
			DAYS								
17	6	LAUNCHES_2006_2015	-0.051		0.037	-1.38	0.168		0.051	-0.99	0.321
18	6	LAUNCHES_1982_2005	-0.085		0.028	**-3.04**	**0.002**		0.028	**-3.00**	**0.003**

Table 2

Estimated effect of drugs launched during 1982-2015 on hospital discharges, average length of stay, and days of care in 2015

Row	Regressor	Estimated Coefficient	Mean(Regressor)		Estimated Coefficient * Mean(Regressor)
		DISCHARGES			
1	LAUNCHES_2011_2015	-0.014	0.909		-0.013
2	LAUNCHES_2006_2010	0.010	1.460		0.014
3	LAUNCHES_2001_2005	-0.111	1.828		-0.202
4	LAUNCHES_1982_2000	-0.056	7.993		-0.444
5				sum (Φ):	-0.645
		ALOS			
6	LAUNCHES_2011_2015	-0.056	0.909		-0.051
7	LAUNCHES_2006_2010	-0.045	1.460		-0.066
8	LAUNCHES_2001_2005	0.007	1.828		0.012
9	LAUNCHES_1982_2000	-0.027	7.993		-0.217
10				sum (Φ):	-0.321
		DAYS			
11	LAUNCHES_2011_2015	-0.070	0.909		-0.063
12	LAUNCHES_2006_2010	-0.035	1.460		-0.051
13	LAUNCHES_2001_2005	-0.104	1.828		-0.190
14	LAUNCHES_1982_2000	-0.083	7.993		-0.661
15				sum (Φ):	-0.966

Note: means are weighted by $DISCHARGES_{dc}$

Table 3

Expenditure in 2015 on inpatient curative care and prescribed medicines, 9 OECD countries

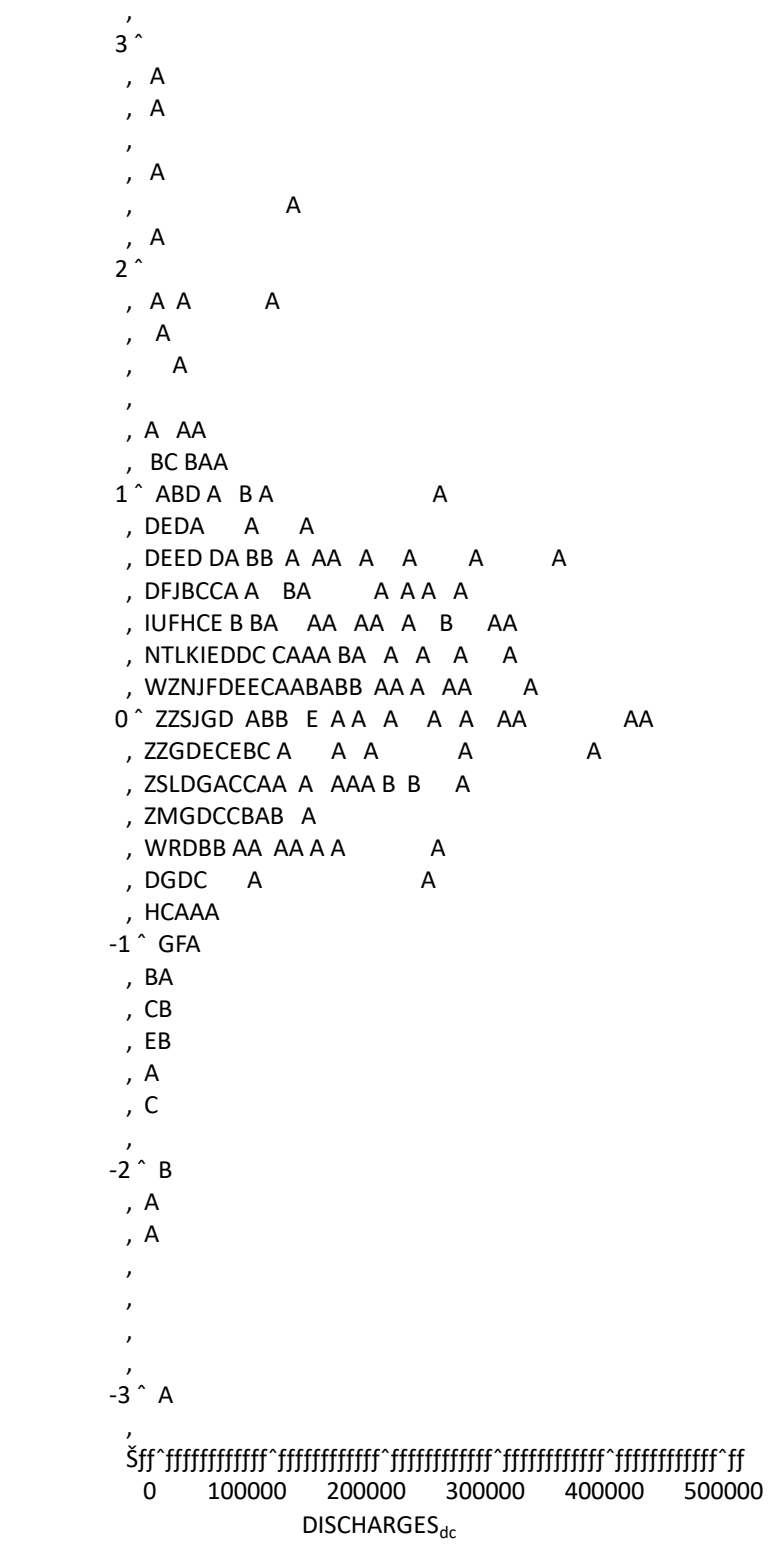
Country	Inpatient curative care	Prescribed medicines
Austria	$10,897	$3,667
Canada	$24,470	$23,464
Denmark	$6,878	$1,186
Finland	$4,483	$2,044
France	$58,082	$32,902
Germany	$95,702	$49,478
Mexico	$30,063	$25,510
Spain	$32,566	$15,472
Switzerland	$11,886	$5,351
TOTAL	**$275,027**	**$159,074**

Source: OECD Health Statistics database

Note: expenditure in millions of 2010 USD, constant prices, constant PPPs

Appendix Figure 1

Plot of the residuals from the unweighted regression $\ln(DISCHARGES_{dc}) = \alpha_d + \delta_c + \varepsilon_{dc}$ against $DISCHARGES_{dc}$



Appendix Table 1

Thousands of 2015 hospital discharges, by country and disease

cause	Austria	Canada	Denmark	Finland	France	Germany	Ireland	Israel	Italy	Mexico	Portugal	Spain	Switzerland	Sweden	UK
0101 Intestinal infectious diseases except diarrhoea	8.8	17.9	1.9	3.3	47.2	107.7	5.6	3.0	16.5	8.0	5.7	16.7	7.1	5.9	37.9
0102 Diarrhoea and gastroenteritis of presumed infectious origin	13.0		3.5	5.6	56.0	151.0		3.4	14.3	40.9	2.7	8.7	6.2	5.9	
0103 Tuberculosis	1.1	1.0	0.3	0.4	5.7	8.3	0.2	0.3	4.8		4.1		0.5	0.7	2.8
0104 Septicaemia	5.6	25.8	12.8	7.0	28.6	124.3	2.4	4.0	41.9	17.0	9.6	43.8		9.4	72.4
0105 Human immunodeficiency virus [HIV] disease	0.7	1.0	0.3	0.1	1.6	1.4	0.0	0.2	5.0	8.0	4.2	3.0	0.1	0.1	2.1
0201 Malignant neoplasm of colon, rectum and anus	22.4	22.9	6.9	7.4	54.2	168.3	2.8	3.7	53.1	13.9	9.2	46.7		9.2	45.2
0202 Malignant neoplasms of trachea, bronchus and lung	21.7	19.1	4.1	5.2	44.4	201.7	2.5	2.1	41.9	4.8	4.9	35.0		6.9	38.1
0203 Malignant neoplasms of skin	13.7	1.9	2.1	2.7	21.9	102.5	1.1	1.6	14.4	9.4	1.9	8.3		2.0	9.9
0204 Malignant neoplasm of breast	24.6	10.3	4.0	8.3	58.1	175.7	2.3	4.8	55.5	35.1	7.4	34.2		6.2	35.4
0205 Malignant neoplasm of uterus	5.9	7.2	1.9	1.9	13.4	39.5	1.0	1.3	12.4	18.6	1.8	9.3		3.1	13.7
0206 Malignant neoplasm of ovary	6.8	3.3	1.0	1.6	7.6	29.4	0.6	0.6	6.9	7.3	0.7	5.0		1.6	9.3
0207 Malignant neoplasm of prostate	10.4	10.4	3.1	4.4	34.2	94.1	0.9	1.4	23.9	6.6		17.1		7.5	23.7
0208 Malignant neoplasm of bladder	9.5	8.5	1.9	3.3	48.1	104.6	1.1	4.2	63.0	3.8	4.7	42.3		5.4	30.8
0210 Carcinoma in situ	2.8	3.8	0.5	0.7	13.5	32.2	0.5	1.1	7.7	4.1	1.0	7.4	3.0	0.8	6.8
0211 Benign neoplasm of colon, rectum and anus	3.1	3.1	1.9	1.3	31.6	33.5	0.5	0.7	9.1	0.4	1.0	5.5	1.8	0.7	6.2
0301 Anaemias	10.6	15.0	6.2	6.7	126.6	88.1	4.4	10.9	44.1	21.5	5.0	25.6	3.8	9.9	55.7
0401 Diabetes mellitus	23.2	36.6	5.9	7.3	99.3	221.8		5.5	33.1	136.3	7.9	26.5	6.6	10.0	50.3
0501 Dementia	9.7		1.2	10.7		20.7	0.5	0.6	9.9	1.1			3.1	3.4	17.7
0502 Mental and behavioural disorders due to alcohol	17.8		10.5	13.9		292.4	2.2		10.1	6.5			15.6	21.9	43.5
0503 Mental and behavioural disorders due to use of other psychoactive subst.	5.9		1.9	2.8		105.4	0.3	1.8	6.3	6.2			6.3	17.7	8.6
0504 Schizophrenia, schizotypal and delusional disorders	13.6		13.7	13.9		133.8	0.3	14.2	45.1	9.6		33.6	14.7	13.3	28.7
0505 Mood [affective] disorders	35.3		8.8	13.4		376.7	0.5	3.6	52.5	11.0		26.5	27.8	18.9	25.7
0601 Alzheimer's disease	1.3		0.1	6.6	3.0	18.9	0.2	0.1	4.9	0.3	0.2		2.1	0.2	7.3
0602 Multiple sclerosis	5.9	1.5	0.7	0.9	6.9	60.7	0.6	0.5	5.6	1.3		2.3	1.8	1.0	5.1
0603 Epilepsy	13.5	12.6	4.6	6.6	62.1	153.5	3.8	3.5	27.7	17.8	3.7	17.9	7.6	7.8	38.6
0604 Transient cerebral ischaemic attacks and related syndromes	7.8	9.4	4.2	7.2	38.0	109.8	3.3	3.8	30.6	1.7	2.9	14.9	4.4	10.3	22.7
0901 Hypertensive diseases	22.6	6.8	2.9	5.7	31.3	278.3	2.3	3.6	33.9	44.0	7.4	31.6	4.7	3.9	
0902 Angina pectoris	10.6		6.1	6.1		234.8		2.9	71.2	14.4	2.2		6.7	13.4	38.2
0903 Acute myocardial infarction	16.7	69.0	10.4	13.8		234.2	6.5	10.3	121.4	16.5	12.3	54.1	18.5	26.8	104.3
0904 Other ischaemic heart disease	44.1		4.6	10.4	123.7	253.3	5.4	13.9	76.9	21.6	8.9	41.1	13.9	4.8	73.7
0905 Pulmonary heart disease & diseases of pulmonary circulation	8.3	12.0	3.7	3.6	46.0	69.2	1.7	1.9	24.9	3.4	3.5	20.2	5.2	7.7	34.4
0906 Conduction disorders and cardiac arrhythmias	34.6	53.6	23.0	25.1	192.2	441.6	9.4	18.5	135.1	16.5	14.7	79.0	16.3	36.2	129.1
0907 Heart failure	26.3	64.2	8.0	21.8	225.6	443.3	6.2	13.8	200.7	22.3	19.2	127.4		30.8	92.5

Appendix Table 1

Thousands of 2015 hospital discharges, by country and disease

cause	Austria	Canada	Denmark	Finland	France	Germany	Ireland	Israel	Italy	Mexico	Portugal	Spain	Switzerland	Sweden	UK
0908 Cerebrovascular diseases	44.5	51.8	13.0	27.2	156.2	449.9		15.9	235.5	46.3	24.0	104.4		34.8	139.5
0909 Atherosclerosis	11.6	6.9	2.2	11.7	57.7	199.5	1.7	2.3	41.3	0.5	4.6	21.1	9.3	6.8	11.9
1001 Acute upper respiratory infections and influenza	14.5	19.5	4.3	7.8	45.4	101.4	8.8	11.8	22.5	20.5	2.4		8.2	12.4	98.4
1002 Pneumonia	38.3	67.0	32.4	39.9	180.5	310.0		27.9	146.3	84.4	7.4	129.0	22.3	42.3	298.6
1003 Other acute lower respiratory infections	11.9	14.3	3.4	8.2	84.5	152.2		8.2	33.9	33.3	14.7		8.9	6.2	144.9
1005 Other diseases of upper respiratory tract	19.0	8.0	3.4	2.6	60.1	186.2	2.8	11.6	61.3	24.4	3.5	41.6	13.6	3.0	33.8
1006 Chronic obstructive pulmonary disease and bronchiectasis	29.1	86.3	13.3	8.5	91.8	287.7		11.8	50.1	30.4	9.6	90.2	11.7	18.2	163.2
1007 Asthma	4.1	11.1	3.7	3.6	49.7	52.9	4.1	4.1	8.3	21.5	2.4	23.1	3.1	3.6	61.6
1103 Diseases of oesophagus	10.2	7.9	2.6	2.0	32.6	78.5	2.6	1.5	11.3	10.3	1.8	11.0	3.3	3.2	36.0
1104 Peptic ulcer	4.0	9.5	2.6	1.6	17.7	64.8	0.9	1.1	15.5	4.9	2.8	10.8	2.8	5.2	15.4
1105 Dyspepsia and other diseases of stomach and duodenum	14.5	7.6	1.6	0.8	28.9	153.7	3.5	1.6	19.9	15.1	2.3	14.0	3.4	2.5	31.1
1109 Crohn's disease and ulcerative colitis	6.3	10.5	3.2	2.7	16.6	48.4	2.1	2.4	15.9	1.7	1.7	11.1	1.8	4.3	27.1
1110 Other noninfective gastroenteritis and colitis	8.9		1.7	0.8	21.0	63.2	0.9		10.5	3.7	2.8	33.1	2.1	2.1	
1114 Other diseases of intestine	19.1	14.3	6.3	4.8	64.0	186.7	3.6	2.6	18.3	12.6	3.0	19.2	5.0	8.3	65.6
1116 Other diseases of liver	6.5	9.9	2.4	1.7	23.1	49.9	0.9	1.9	38.0	35.4	3.5	20.1	2.3	2.6	15.8
1119 Diseases of pancreas	6.9	24.0	4.0	5.4	43.0	74.6	1.9	3.5	26.9	21.6	6.3	31.7	4.0	6.7	41.3
1201 Infections of the skin and subcutaneous tissue	11.1	26.0	5.7	3.1	68.9	140.2	8.3	15.7	22.7	35.8	5.1	30.2	9.7	6.1	115.2
1202 Dermatitis, eczema and papulosquamous disorders	4.0	1.7	0.7	1.8	12.5	77.2	0.9	1.9	5.5	2.0	0.6	2.1	1.9	1.0	8.8
1301 Coxarthrosis [arthrosis of hip]	30.7	34.4	8.7	10.3	103.6	274.4	3.8	1.7	63.8	5.1				14.7	80.1
1302 Gonarthrosis [arthrosis of knee]	37.5	60.1	8.2	12.7	105.4	292.0	2.7	4.8	73.3	18.8				13.4	101.6
1304 Other arthropathies	32.2		5.3	10.7	170.9	301.4	5.7	6.4	51.6	17.5	15.5		34.7	13.1	104.7
1305 Systemic connective tissue disorders	4.2	3.5	1.6	1.5	14.6	47.0	0.7	1.0	11.1	4.9	1.0	6.3	1.9	3.5	6.5
1306 Deforming dorsopathies and spondylopathies	19.3	14.7	6.7	8.9	66.2	268.5		3.2	24.0	4.3	2.8		17.6	11.8	30.3
1307 Intervertebral disc disorders	28.7		5.3	5.1	47.5	235.8	1.6					32.3	15.1	4.0	34.6
1308 Dorsalgia	37.5	7.9	3.4	6.4	54.9	303.1	2.4	3.6	7.0	13.8	0.4		8.6	6.7	36.5
1309 Soft tissue disorders	31.1	12.3	3.6	4.7	113.8	268.7		7.5	75.7	30.9	5.2	51.8	25.7	8.5	61.5
1401 Glomerular and renal tubulo-interstitial diseases	12.9	23.9	6.2	16.8	118.3	175.1		5.7	34.9	30.7	9.5	31.7	11.9	15.4	61.2
1402 Renal failure	20.5	22.9	5.3	4.0	45.2	117.8	3.1	7.6	89.9	189.7	4.0	29.3	4.7	9.5	78.7
1404 Other diseases of the urinary system	26.4	41.6	13.4	12.0	83.7	236.8	13.0	22.7	64.6	53.7	19.9	88.2	16.4	20.2	226.2
1405 Hyperplasia of prostate	6.2	13.3	1.4	3.5	38.3	58.3	0.7	3.8	44.1	20.6	3.3	26.4	7.3	3.9	21.3
1406 Other diseases of male genital organs	8.4	4.2	1.5	1.8	50.6	63.4	2.1	3.2	23.6	30.0	2.4	22.2	5.5	2.4	26.1
1407 Disorders of breast					26.2				7.8	14.6	2.4				
1408 Inflammatory diseases of female pelvic organs	3.3	3.6	1.0	0.7	19.7	30.2	0.8	2.7	10.3	14.2	1.3	8.1	2.0	1.3	14.5
1409 Menstrual, menopausal and other female genital conditions	8.2		1.6	1.3	11.0	33.1	2.0	1.8	16.9	34.2	0.9	3.7	2.9	2.0	21.4

Appendix Table 2

Number of post-1981 New Chemical Entities launched during 1982-2015, by country and disease

cause	Austria	Canada	Denmark	Finland	France	Germany	Ireland	Israel	Italy	Mexico	Portugal	Spain	Switzerland	Sweden	UK
Mean	**10.5**	**8.6**	**9.7**	**10.0**	**10.3**	**10.4**	**9.3**	**6.3**	**10.0**	**9.2**	**7.4**	**9.8**	**9.7**	**9.4**	**10.0**
0101 Intestinal infectious diseases except diarrhoea	4	1	4	4	4	4	4	1	4	2	2	4	3	4	3
0102 Diarrhoea and gastroenteritis of presumed infectious origin	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1
0103 Tuberculosis	3	1	2	2	1	3	2	1	2	0	1	1	1	2	3
0104 Septicaemia	7	3	5	5	6	5	4	3	6	7	5	5	5	5	4
0105 Human immunodeficiency virus [HIV] disease	28	28	31	31	28	31	29	14	29	24	9	23	30	29	31
0201 Malignant neoplasm of colon, rectum and anus	10	9	9	9	9	8	9	4	8	8	5	7	9	9	9
0202 Malignant neoplasms of trachea, bronchus and lung	16	13	16	17	17	16	15	9	11	12	9	13	14	15	17
0203 Malignant neoplasms of skin	12	7	10	11	10	10	8	4	8	6	8	7	9	10	8
0204 Malignant neoplasm of breast	24	19	22	23	25	24	22	14	24	20	13	23	23	22	23
0205 Malignant neoplasm of uterus	2	2	2	2	2	2	2	2	2	2	1	2	2	2	2
0206 Malignant neoplasm of ovary	8	8	8	8	8	8	7	5	8	8	5	8	8	8	8
0207 Malignant neoplasm of prostate	13	12	13	14	13	13	11	6	9	11	8	12	13	12	12
0208 Malignant neoplasm of bladder	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2
0210 Carcinoma in situ	11	9	12	13	10	13	11	4	11	8	4	11	10	10	11
0211 Benign neoplasm of colon, rectum and anus	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
0301 Anaemias	7	4	6	7	5	7	6	4	7	7	3	6	6	6	7
0401 Diabetes mellitus	31	28	30	30	31	31	30	22	28	31	22	30	31	30	31
0501 Dementia	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
0502 Mental and behavioural disorders due to alcohol	1	0	1	1	0	1	1	0	1	1	0	1	1	1	1
0503 Mental and behavioural disorders due to use of other psychoactive subst.	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
0504 Schizophrenia, schizotypal and delusional disorders	7	6	7	5	5	7	7	4	7	7	6	7	6	5	6
0505 Mood [affective] disorders	20	17	18	19	19	18	17	15	17	18	19	18	17	17	17
0601 Alzheimer's disease	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
0602 Multiple sclerosis	14	12	14	13	14	15	15	9	13	10	4	14	12	13	15
0603 Epilepsy	16	11	14	15	14	15	15	7	15	9	11	15	14	14	15
0604 Transient cerebral ischaemic attacks and related syndromes	6	5	6	6	6	6	6	1	5	4	4	6	5	6	6
0901 Hypertensive diseases	31	24	29	28	37	37	29	19	34	31	32	32	31	27	30
0902 Angina pectoris	15	12	13	14	14	14	15	8	13	11	9	13	15	11	15
0903 Acute myocardial infarction	18	17	16	18	15	18	16	9	17	15	10	15	17	15	17
0904 Other ischaemic heart disease	11	11	10	12	9	12	10	6	12	9	6	9	11	9	11
0905 Pulmonary heart disease & diseases of pulmonary circulation	13	12	12	12	12	13	12	6	11	6	6	12	11	12	12
0906 Conduction disorders and cardiac arrhythmias	9	8	8	9	8	8	7	2	8	7	4	7	9	8	7
0907 Heart failure	18	16	17	17	17	19	18	13	19	19	16	18	18	19	19
0908 Cerebrovascular diseases	9	8	9	9	9	9	9	4	8	7	7	9	8	9	9
0909 Atherosclerosis	3	3	3	3	3	3	3	1	2	3	2	3	3	2	3
1001 Acute upper respiratory infections and influenza	20	14	15	17	20	18	15	15	18	20	16	18	16	17	16

Appendix Table 2

Number of post-1981 New Chemical Entities launched during 1982-2015, by country and disease

cause	Austria	Canada	Denmark	Finland	France	Germany	Ireland	Israel	Italy	Mexico	Portugal	Spain	Switzerland	Sweden	UK
Mean	**10.5**	**8.6**	**9.7**	**10.0**	**10.3**	**10.4**	**9.3**	**6.3**	**10.0**	**9.2**	**7.4**	**9.8**	**9.7**	**9.4**	**10.0**
1002 Pneumonia	22	16	19	21	23	22	19	12	20	19	14	19	20	20	19
1003 Other acute lower respiratory infections	19	13	14	16	18	17	13	13	17	18	14	16	15	16	15
1005 Other diseases of upper respiratory tract	22	15	20	22	23	23	20	14	23	21	22	23	20	20	21
1006 Chronic obstructive pulmonary disease and bronchiectasis	21	16	18	18	20	20	17	12	19	18	17	20	19	19	18
1007 Asthma	9	8	9	7	9	9	7	5	9	8	5	8	9	7	9
1103 Diseases of oesophagus	7	7	7	7	7	7	7	6	7	7	7	7	7	7	7
1104 Peptic ulcer	8	8	8	8	8	8	8	7	8	8	8	8	8	8	8
1105 Dyspepsia and other diseases of stomach and duodenum	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1109 Crohn's disease and ulcerative colitis	6	6	6	6	5	5	6	2	5	4	1	5	6	5	6
1110 Other noninfective gastroenteritis and colitis	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1
1114 Other diseases of intestine	4	2	4	5	4	5	3	1	3	2	3	4	3	5	4
1116 Other diseases of liver	10	7	9	10	9	10	8	6	10	6	4	9	9	10	10
1119 Diseases of pancreas	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1201 Infections of the skin and subcutaneous tissue	21	14	17	18	19	19	17	10	19	18	12	17	19	17	18
1202 Dermatitis, eczema and papulosquamous disorders	15	13	13	14	12	14	12	10	12	12	7	13	14	13	15
1301 Coxarthrosis [arthrosis of hip]	2	2	2	2	3	1	1	3	3	3	3	2	1	1	2
1302 Gonarthrosis [arthrosis of knee]	2	2	2	2	3	1	1	3	3	3	3	2	1	1	2
1304 Other arthropathies	24	21	23	24	20	22	21	11	22	22	15	22	22	22	24
1305 Systemic connective tissue disorders	7	7	7	6	4	7	7	4	7	4	4	7	6	6	7
1306 Deforming dorsopathies and spondylopathies	12	8	12	12	10	10	10	4	10	10	7	10	10	10	12
1307 Intervertebral disc disorders	1	0	1	1	1	1	1	0	0	0	0	1	1	1	1
1308 Dorsalgia	2	2	2	2	3	1	1	1	2	2	2	2	2	1	2
1309 Soft tissue disorders	3	4	4	4	4	3	3	2	4	3	4	4	3	3	4
1401 Glomerular and renal tubulo-interstitial diseases	16	13	15	14	15	16	13	14	16	16	14	15	15	14	15
1402 Renal failure	10	11	11	10	10	11	10	9	11	10	9	10	10	11	10
1404 Other diseases of the urinary system	28	21	26	27	29	29	25	20	28	26	24	28	26	25	27
1405 Hyperplasia of prostate	7	8	7	5	8	8	8	7	8	7	7	8	7	6	7
1406 Other diseases of male genital organs	14	11	12	13	15	16	10	11	16	15	15	16	13	12	13
1407 Disorders of breast	0	0	0	0	2	0	0	0	1	1	1	0	0	0	0
1408 Inflammatory diseases of female pelvic organs	8	8	6	7	13	12	7	6	12	12	12	12	8	6	8
1409 Menstrual, menopausal and other female genital conditions	2	0	1	2	5	1	2	2	3	3	3	3	1	1	1