The impact of pharmaceutical innovation on disability days and the use of medical services in the United States, 1997-2010

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2 September 2014

Abstract

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I investigate whether diseases subject to more rapid pharmaceutical innovation experienced greater declines in Americans' disability days and use of medical services during the period 1997-2010, controlling for several other factors, using data from the Medical Expenditure Panel Survey. The mean number of work-loss days, school-loss days, and hospital admissions declined more rapidly among medical conditions with larger increases in the mean number of new (post-1990) prescription drugs consumed. The value of the reductions in work-loss days and hospital admissions attributable to pharmaceutical innovation is estimated to be three times as large as the cost of new drugs consumed.

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1. Introduction

About half a century ago, Mushkin (1962), Becker (1964), and Fuchs (1966) pointed out that health capital is one component of the stock of human capital.[1] Grossman (2000) defines health broadly to include longevity and illness-free days in a given year. Two major U.S. government surveys have collected data on restricted-activity days (also referred to as disability days)—the number of days when a person cut down on his or her usual activities because of illness or injury—for many years. Restricted-activity days include work-loss, school-loss, and bed-disability days. (U.S. Bureau of the Census (1972, table 117)). One of these surveys is the National Health Interview Survey (NHIS), which is the principal source of information on the health of the civilian non-institutionalized population of the United States, and is one of the major data collection programs of the National Center for Health Statistics. While the NHIS has been conducted continuously since 1957, the content of the survey has been updated about every 10-15 years, and a substantially revised questionnaire was implemented in 1997. Data on restricted-activity days are published annually in issues of *Vital and Health Statistics Series 10: Data from the National Health Interview Survey*.

The second survey is the Household Component of the Medical Expenditure Panel Survey (MEPS), which fields questionnaires to individual household members to collect nationally representative data on demographic characteristics, health conditions, health status, use of medical care services, charges and payments, access to care, satisfaction with care, health insurance coverage, income, and employment. The sampling frame for MEPS, which was first administered in 1996, is drawn from respondents to the NHIS.[2] The MEPS data may be more reliable, because MEPS respondents are interviewed five times during a 2.5 year period, whereas NHIS respondents are interviewed only once.[3]

Both of these surveys indicate that the average number of work-loss and school-loss days has declined since the mid-1990s; the MEPS estimates have declined more rapidly than the NHIS estimates. Figure 1 shows data from both surveys on the mean number of work-loss days per year among employed persons 18 years of age and older. The two surveys provide almost

[1] As discussed by Ehrlich and Yin (2013), the other component of human capital is "knowledge capital."
[2] In 1996, MEPS collected very limited data on restricted-activity days.
[3] MEPS-HC Panel Design and Data Collection Process, http://meps.ahrq.gov/mepsweb/survey_comp/hc_data_collection.jsp

identical estimates of the mean number of work-loss days during 1997-2000: 4.7 (NHIS) and 4.9 (MEPS). The NHIS indicates that the mean number of work-loss days declined at an average annual rate of 1.8% during the period 1997-2011; the MEPS indicates that the mean number of work-loss days declined at an average annual rate of 4.5% during the period 1997-2010. MEPS also collects information on additional days, other than work days, in which the person spent at least half a day in bed, because of a physical illness, injury or a mental or emotional problem ("additional bed-days"). The mean number of additional bed-days among employed persons 18 years of age and older declined at an average annual rate of 3.5% during the period 1997-2010. All of these declines are highly statistically significantly different from zero.[4]

Figure 2 shows data from both surveys on the mean number of school days missed per year because of illness or injury for children aged 5–17. The NHIS indicates that the mean number of missed school days declined at an average annual rate of 0.9% during the period 1997-2011; the MEPS indicates that the mean number of missed school days (and missed school days plus additional bed-days) declined at an average annual rate of about 4.6% during the period 1997-2010.[5]

In principle, the long-run declines in the mean number of work-loss, school-loss, and additional bed-disability days—which, to my knowledge, have not previously been recognized, let alone explained—could be due to a number of factors. One such potential factor is education. More educated workers tend to have fewer work-loss days: in 2011, mean work-loss days of workers with at least a bachelor's degree was 36% lower than that of less-educated workers (2.9 days vs. 4.5 days).[6] The fraction of workers with at least a bachelor's degree increased from 28% in 1997 to 36% in 2011. But a simple calculation reveals that rising educational attainment would have reduced mean work-loss days by only 3.5% between 1997 and 2011; the NHIS estimates shown in Figure 1 indicate that mean work-loss days declined by 20% during that period.

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[4] Estimates of rates of decline are estimates of the coefficient β from regressions of the form $\ln Y_t = \alpha + \beta t + \varepsilon_t$, where Y_t = mean restricted-activity days in year t. Serial correlation of residuals is accounted for.

[5] Work-loss and school-loss days also declined during the period 1960-1997. NHIS estimates of the mean number of work-loss days in 1960, 1965, and 1970 were 5.6, 5.7, and 5.4, respectively; this implies that the mean number of work-loss days declined at an average annual rate of 0.8% during the period 1960-2011. NHIS estimates of the mean number of school-loss days in 1960, 1965, and 1970 were 5.3, 5.2, and 4.9, respectively; this implies that the mean number of school-loss days declined at an average annual rate of 0.9% during the period 1960-2011.

[6] http://www.cdc.gov/nchs/data/series/sr_10/sr10_256.pdf, Table 17.

In this paper, I will test the hypothesis that medical innovation—especially pharmaceutical innovation[7]—played an important role in reducing disability days of American adults and children during the period 1997-2010. I will analyze the impact of medical innovation on three aspects of human capital: its formation (school-loss days), utilization (work-loss days), and maintenance (use of medical services).

The analysis will be based on aggregate data—longitudinal data on about 130 diseases—rather than patient-level data. In essence, I will investigate whether diseases subject to more rapid medical innovation experienced greater declines in disability days, controlling for several other factors. Stukel et al (2007) argue that comparisons of outcomes between patients treated and untreated in observational studies may be biased due to differences in patient prognosis between groups, often because of unobserved treatment selection biases. I believe that difference-in-differences estimates based on aggregate panel data are much less likely to be subject to unobserved treatment selection biases than estimates based on cross-sectional patient-level data.[8]

The rate of pharmaceutical innovation may not be strictly exogenous with respect to the rate of decline of disability, controlling for other factors such as changes in patients' socioeconomic status. Fortunately, Acemoglu and Linn (2004) developed a useful instrument for pharmaceutical innovation: the potential size of the market for drugs for a medical condition. To estimate potential market size, they constructed age profiles of users for each drug category, and then computed the implied market size from aggregate demographic and income changes given those (time-invariant) age profiles. I will obtain both OLS and instrumental-variables (IV) estimates of models of the effect of pharmaceutical innovation on disability days and the use of medical services. The instrument I will use to obtain IV estimates is the potential size of the market for drugs, by medical condition and year, which I will calculate using a methodology similar to Acemoglu and Linn's.

Almost all of the data I will analyze were obtained from MEPS. Unlike other health surveys (including the NHIS), MEPS provides *disease-specific* information about use of

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[7] Pharmaceutical innovation is defined, in this context, as the introduction and *use* of new drugs to treat medical conditions. The indices of pharmaceutical innovation I will construct give the most weight to drugs that are frequently used, less weight to drugs that are infrequently used, and no weight to drugs that were never used (e.g. because they were not approved by the FDA).

[8] Jalan and Ravallion (2001) argued that "aggregation to village level may well reduce measurement error or household-specific selection bias" (p. 10).

prescription drugs and other medical services and about disability days. MEPS Prescribed Medicines Files indicate the (household-reported) medical conditions associated with each prescribed medicine event.[9] MEPS Medical Condition Files contain three variables indicating whether a person's condition is associated with a missed work day, a missed school day, or a day spent in bed.[10] These files also contain information about the number of inpatient hospital stays, office-based visits, and other medical care utilization due to each medical condition of each person. Therefore, in addition to investigating the effect of medical innovation on disability days, I will examine its effect on the utilization of medical services. Estimates of disability day and medical service use models will be used to obtain estimates of the benefits of the new drugs, and compare them to their costs. As shown in Table 1, most prescription drug expenditure (and other medical expenditure) is paid by third parties, so it is not a foregone conclusion that the social benefits of new drugs exceed their social costs.[11]

My basic hypothesis is that the mean number of disability days attributable to a medical condition is inversely related to the *quality* of medical goods and services used to treat that condition. The quality of medical goods and services is not directly observable. However, I also hypothesize that, in general, the average quality of newer (later vintage) goods and services is higher than that of older (earlier vintage) goods and services. The hypotheses that vintage has a positive effect on quality, and that quality has a negative effect on disability days, imply that vintage has a negative effect on disability days.

Robert Solow (1960) introduced the concept of vintage into economic analysis. This was one of the contributions to the theory of economic growth that the Royal Swedish Academy of Sciences cited when it awarded Solow the 1987 Alfred Nobel Memorial Prize in Economic Sciences:

> Solow's basic idea was that technical progress is "built into" [or embodied in] machines and other capital goods and that this must be taken into account when making empirical

[9] Most prescription drug databases lack information about medical conditions (diagnosis codes).
[10] However, due to the MEPS instrument design, the specific number of disability days associated with a particular medical condition cannot be determined.
http://meps.ahrq.gov/mepsweb/data_stats/download_data/pufs/h137/h137doc.shtml#2527Disability
[11] As noted by the Australian Productivity Commission (2005), "because the direct purchase of healthcare is mostly undertaken by third parties — governments and private health insurers — normal market tests for ensuring value for money generally do not apply" (p. XXIX).

> measurements of the role played by capital.[12] This idea then gave birth to the "vintage approach"…Solow's empirical results naturally gave the formation of capital a markedly higher status in explaining the increase in production per employee. The most important aspect of Solow's article was not so much the empirical outcome, but the method of analyzing "vintage capital". Nowadays, the vintage capital concept has many other applications and is no longer solely employed in analyses of the factors underlying economic growth…The vintage approach has proved invaluable, both from the theoretical point of view and in applications..." (Nobelprize.org (2013)).

Subsequently, Grossman and Helpman (1991) argued that "almost every product exists on a *quality ladder*, with variants below that may already have become obsolete and others above that have yet to be discovered," and that "each new product enjoys a limited run at the technological frontier, only to fade when still better products come along." Harper (2007, p. 103) argued that "new improved models of high-tech equipment that embody improvements are frequently introduced and marketed alongside older models."

I will define the vintage of a prescription drug as the year in which the FDA first approved the drug's active ingredient. To approve a drug, the FDA merely requires that the drug be safe and effective; it does *not* require that the drug be superior to (safer or more effective than) previously approved drugs (Food and Drug Administration (2013a)). In fact, when the FDA begins its review of a new drug application, it designates some drugs as drugs "that appear…to represent an advance over available therapy" (priority-review drugs), and other drugs as drugs "that appear…to have therapeutic qualities similar to those of an already marketed drug" (standard-review drugs) (Food and Drug Administration (2013b)).[13] I will estimate some models that distinguish between priority-review and standard-review drugs.[14]

Disability days are likely to depend on the vintage (hence quality) of non-pharmaceutical as well as pharmaceutical goods and services, so it would be ideal to include measures of the

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[12] Solow assumed that technical progress is embodied in machines because machine manufacturers perform R&D. Since the medical substances and devices industry is much more research-intensive than the machinery industry (National Science Foundation, 2013), new medical treatments may embody even more technical progress than new machines.

[13] 56% of the new molecular entity drugs and new biologics approved during 1993-2008 were standard-review drugs or biologics, i.e. they appeared to the FDA to have therapeutic qualities similar to those of already marketed drugs or biologics (Food and Drug Administration (2013c)). Since the FDA's classification of a drug (priority vs. standard review) occurs at the beginning of the review process, it may be subject to considerable uncertainty; the fact that some drugs are withdrawn after marketing indicates that even the safety of a drug may not be well understood at the time of approval.

[14] First-in-class drugs are much more likely to receive priority-review status than follow-on drugs, so distinguishing between priority-review and standard-review drugs is similar to distinguishing between first-in-class and follow-on drugs.

vintage of medical devices and procedures as well as measures of drug vintage in models of disability days. But measuring the vintage of medical devices and procedures is much more difficult than measuring drug vintage. I will control for one indicator of non-pharmaceutical innovation that can be measured from MEPS: the fraction of patient visits in which an advanced imaging procedure (CT or MRI) was performed.[15] Although pharmaceutical innovation is certainly not the only type of medical innovation, there are good reasons to think that it has the greatest impact on health outcomes.[16] First, the number of people exposed to pharmaceutical innovation tends to be much larger than the number of people exposed to other types of medical innovation: for example, in 2007, 62% of Americans consumed prescription drugs, while only 8% of Americans were admitted to hospitals.[17] Second, pharmaceuticals are more research-intensive than other types of medical care: in 2007, prescription drugs accounted for 10% of U.S. health expenditure (Center for Medicare and Medicaid Services (2013: Table 2)), but more than half of U.S. funding for biomedical research came from pharmaceutical and biotechnology firms (Dorsey et al, 2010). 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).

In section 2, I will briefly review several previous studies that have examined the impact of pharmaceutical innovation on disability. In section 3, I will present the econometric model I will estimate to assess the impact of pharmaceutical innovation on disability days and the use of medical services. Data sources and descriptive statistics will be discussed in Section 4. Estimates of models will be presented in Section 5. The costs and benefits of pharmaceutical innovation implied by the estimates will be discussed in Section 6. The final section provides a summary and conclusions.

2. Previous research on the impact of pharmaceutical innovation on disability

Previous studies of the impact of pharmaceutical innovation on disability fall into two categories: case studies of specific new drugs, and studies of the impact of new drugs in general.

[15] This fraction increased from 1.0% in 1996 to 2.3% in 2010. Lichtenberg (2011a) found that life expectancy grew more rapidly during the period 1991-2004 in U.S. states that adopted advanced imaging procedures more rapidly, controlling for other factors.

[16] Evidence presented in Lichtenberg (2014) suggests that the rate of pharmaceutical innovation is uncorrelated across diseases with rates of innovation in imaging and other procedures.

[17] Source: Medical Expenditure Panel Survey, 2007 Full Year Consolidated Data File.

I will briefly summarize just two studies of specific new arthritis drugs.[18] Kavanaugh et al (2006) examined the effect of infliximab on employment status, time lost from work, and productivity in a double-blind, placebo-controlled study of patients with active psoriatic arthritis (PsA). Two hundred adult patients with PsA were randomized to intravenous infusions of either infliximab 5 mg/kg or placebo at Weeks 0, 2, 6, 14, and 22, with early escape at Week 16. Employment status, workdays missed, and productivity were assessed at baseline and at Week 14. The effect of PsA on daily productivity was assessed using a visual analog scale. At baseline, similar percentages of patients in both treatment groups were employed and similar percentages missed workdays; the mean productivity score at baseline was similar between groups (roughly 3 on a scale of 0 to 10). At Week 14, median productivity increased significantly in the infliximab group compared with the placebo group (67.5% vs 9.2%; $p < 0.0001$). Compared with the placebo group, higher proportions of patients in the infliximab group improved employment status from unemployed at baseline to employed at Week 14 (11.5% vs 0%; $p = 0.084$) and from part-time to full-time employment (30.0% vs 10.0%; $p = 0.582$). Among patients employed at baseline and Week 14, a lower proportion of patients in the infliximab group than in the placebo group had missed workdays in the 4 weeks prior to Week 14 ($p = 0.138$).

van Vollenhoven et al (2010) evaluated household and workplace outcomes for patients with rheumatoid arthritis who were homemakers or employed workers, respectively, and who were treated with adalimumab plus methotrexate versus methotrexate monotherapy. Over 2 years, patients who received combination therapy missed approximately half as many days as patients who received methotrexate (17.4 versus 36.9 days for employed workers; 7.9 versus 18.6 days for homemakers). Presenteeism was lower (reflecting better productivity) for combination therapy than methotrexate monotherapy. The likelihood of gaining/retaining employment over 2 years was greater for combination therapy than methotrexate monotherapy (odds ratio 1.530, 95% confidence interval 1.038-2.255; $P = 0.0318$).

Two previous studies used panel data to assess the impact of new drugs in general on indicators of disability. Lichtenberg (2011b) analyzed longitudinal state-level data during the period 1995– 2004 to investigate whether use of newer prescription drugs reduced the ratio of the number of workers receiving Social Security Disability Insurance benefits to the working-age population (the "DI recipiency rate"). All of the estimates indicated that there is a significant

[18] Lichtenberg (2005) summarized studies of specific new drugs for migraines, diabetes, and asthma.

inverse relationship between disability recipiency and a good indicator of pharmaceutical innovation use: the mean vintage (FDA approval year) of Medicaid prescriptions. From 1995 to 2004, the actual disability rate increased 30%, from 2.62% to 3.42%. The estimates implied that in the absence of any post-1995 increase in drug vintage, the increase in the disability rate would have been 30% larger: the disability rate would have increased 39%, from 2.62% to 3.65%. This means that in the absence of any post-1995 increase in drug vintage, about 418,000 more working-age Americans would have been DI recipients.

Lichtenberg (2005) used longitudinal data on 47 medical conditions (partly derived from the NHIS) to investigate the effect of the introduction of new drugs on the probability of being unable to work or limited in work, and on the number of work-loss and restricted activity days. The estimates implied that pharmaceutical innovation reduced the probability of being unable to work by 1.8% per year during the period 1982–1996, and that, in the absence of 15 years of pharmaceutical innovation, the probability of being unable to work would have been 29% higher in 1996 than it actually was—5.2% instead of 4.0%.

The econometric approach I will use in the present study is similar to that used in Lichtenberg (2005), but the present study will analyze a much more recent period (1996-2010), and can take advantage of several important data improvements. First, I will analyze disability days among children (school-loss days) and non-working adults (e.g. the elderly) as well as among working adults. Second, I will examine the effect of pharmaceutical innovation on the utilization of and expenditure on a variety of medical services, as well as on disability days. Third, I will use an improved measure of pharmaceutical innovation: the mean vintage of prescription drugs, as opposed to the number of drugs approved to treat a condition. Fourth, I will control for one type of non-pharmaceutical innovation: utilization of advanced imaging. And fifth, the analysis will be based on a much larger sample (1.4 million vs. 200,000 medical condition records), and on data on *all* medical conditions (both acute and chronic), rather than just a subset of chronic conditions.

3. Econometric model to assess the impact of pharmaceutical innovation on disability days and the use of medical services

To assess the impact of pharmaceutical innovation on disability days and the use and cost of medical services, I will estimate models of the following form using longitudinal disease-level data:

$$\ln(Y_{ct}) = \pi \, RX_VINTAGE_{ct} + \gamma \, Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct} \qquad (1)$$

where

Y_{ct} = a measure of disability days or the use or cost of medical services associated with medical condition c in period t

$RX_VINTAGE_{ct}$ = a measure of the mean vintage of prescription drugs used to treat medical condition c in period t

Z_{ct} = a measure of other attributes of medical condition c in period t

α_c = a fixed effect for medical condition c

δ_t = a fixed effect for period t

Eq. (1) may be viewed as a health production function, in which ln(Y) may be viewed as an (inverse) indicator of health output, and RX_VINTAGE may be viewed as an indicator of the level of technology.[19] These models will be estimated by weighted least-squares; the weights used will be discussed below. Standard errors will be clustered within medical conditions. I will now discuss: (1) the dependent variables I will analyze (Y_{ct}); (2) the measurement of prescription drug vintage ($RX_VINTAGE_{ct}$); and (3) other time-varying attributes of medical conditions (Z_{ct}).

Dependent variables. I will analyze two types of dependent variables. The first type is disability day measures. These measures, and the estimation weights that will be used for each, are:

Variable name	Variable description	Estimation weight[20]
$MISS_WORK\%_{ct}$	The fraction of people aged 16 and over with medical condition c in period t who missed any work days due to medical condition c	$\Sigma_t \, N_COND_{ct} \, MISS_WORK\%_{ct}$ (total number of people aged 16 and over who missed any work days due to medical condition c during 1996-2010)
$MISS_SCHOOL\%_{ct}$	The fraction of children aged 5-17 with medical condition c in period t who missed	$\Sigma_t \, N_COND_{ct} \, MISS_SCHOOL\%_{ct}$ (total number of children aged 5-17 who missed

[19] Health production functions that include measures of medical technology have been estimated by Baltagi et al (2012) and other authors.

[20] N_COND_{ct} = the number of people with medical condition c in period t.

	any school days due to medical condition c	any school days due to medical condition c during 1996-2010)
$OTHER_BED\%_{ct}$	The fraction of people with medical condition c in period t who spent additional days, other than school or work days, in bed due to medical condition c	$\Sigma_t N_COND_{ct} OTHER_BED\%_{ct}$ (total number of people who spent additional days, other than school or work days, in bed due to medical condition c during 1996-2010)

The second type of dependent variable is utilization of medical services measures. These measures, and the estimation weights that will be used for each, are:

Variable name	Variable description	Estimation weight
$INPAT_EVENTS_{ct}$	The mean number of inpatient hospital events associated with medical condition c per person with medical condition c in period t	$\Sigma_t N_COND_{ct} INPAT_EVENTS_{ct}$ (total number of inpatient hospital events associated with medical condition c during 1996-2010)
$OFFICE_EVENTS_{ct}$	The mean number of office-based events associated with medical condition c per person with medical condition c in period t	$\Sigma_t N_COND_{ct} OFFICE_EVENTS_{ct}$ (total number of office-based events associated with medical condition c during 1996-2010)
$OUTPAT_EVENTS_{ct}$	The mean number of outpatient events associated with medical condition c per person with medical condition c in period t	$\Sigma_t N_COND_{ct} OUTPAT_EVENTS_{ct}$ (total number of outpatient events associated with medical condition c during 1996-2010)
ER_EVENTS_{ct}	The mean number of emergency room events associated with medical condition c per person with medical condition c in period t	$\Sigma_t N_COND_{ct} ER_EVENTS_{ct}$ (total number of emergency room events associated with medical condition c during 1996-2010)
$HOME_EVENTS_{ct}$	The mean number of home health events associated with medical condition c per person with medical condition c in period t	$\Sigma_t N_COND_{ct} HOME_EVENTS_{ct}$ (total number of home health events associated with medical condition c during 1996-2010)

Although previous studies (e.g. Lichtenberg (2014) Lichtenberg and Pettersson (2014)) have found that pharmaceutical innovation has reduced utilization of inpatient care, one would not necessarily expect pharmaceutical innovation to reduce utilization of outpatient care, e.g. office events. The initial effect of a new drug may be to induce visits to get a prescription for the drug (a plus for outpatient activity). New and improved drugs may eventually reduce follow-up visits (a minus for outpatient activity). The overall effect cannot be signed a priori.

Measurement of prescription drug vintage. I will use the following general definition of the mean vintage of prescription drugs used to treat medical condition c in period t:[21]

$$RX_VINTAGE_{ct} = \frac{\Sigma_p N_RX_{pct} f(FDA_YEAR_p)}{\Sigma_p N_RX_{pct}} \quad (2)$$

where

N_RX_{pct} = the aggregate number of prescriptions for drug product p used to treat medical condition c during period t

FDA_YEAR_p = the year in which the FDA first approved the active ingredient contained in drug product p

To calculate mean drug vintage using eq. (2), we must choose a functional form for $f(FDA_YEAR_p)$. One possible functional form is simply $f_1(FDA_YEAR_p) = FDA_YEAR_p$. In this case, $RX_VINTAGE_{ct}$ is simply the weighted mean FDA approval year of drugs used to treat medical condition c during period t, weighted by the number of prescriptions. A drawback of this functional form is that the vintage (initial FDA approval year) of some drugs (especially very old drugs) is unknown or not reliably measured. An alternative functional form that is less subject to this kind of measurement error is:

$POST1990_p = f_2(FDA_YEAR_p)$ = 1 if $FDA_YEAR_p > 1990$

= 0 if $FDA_YEAR_p \leq 1990$ or if FDA_YEAR_p is missing

Substituting $POST1990_p$ for $f(FDA_YEAR_p)$ in eq. (2) yields the following measure of prescription drug vintage:

$$POST1990\%_{ct} = \frac{\Sigma_p N_RX_{pct} POST1990_p}{\Sigma_p N_RX_{pct}} \quad (3)$$

$POST1990\%_{ct}$ is the fraction of prescriptions used to treat medical condition c in period t that contained active ingredients approved by the FDA after 1990.

As stated in the introduction, I hypothesize that vintage has a negative effect on disability days because (1) vintage has a positive effect on treatment quality, and (2) quality has a negative effect on disability days. Now I will propose another hypothesis: the effect of drug *quality* (hence vintage) on disability days depends on (is positively related to) the average *quantity* of

[21] RX_VINTAGE is a utilization-weighted index: drugs that are used more frequently to treat a condition receive more weight. Therefore, if estimates of π in eq. (1) are negative and significant, that may be partly due to the fact that new drugs that yield greater benefits are used more.

drugs consumed. An increase in drug quality will improve health more if the average quantity of drugs consumed is high. Suppose that the effect of vintage in eq. (1) is *proportional* to the average quantity of drugs consumed:

$$\pi = \beta \, RX_EVENTS_{ct} \quad (4)$$

where RX_EVENTS_{ct} = the mean number of prescription drug events associated with medical condition c per person with medical condition c in period t. If we substitute eq. (4) into eq. (1), and also substitute $POST1990\%_{ct}$ (as defined in eq. (3)) for $RX_VINTAGE_{ct}$ in eq. (1), we obtain:

$$\ln(Y_{ct}) = \beta \, (RX_EVENTS_{ct} * POST1990\%_{ct}) + \gamma \, Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct}$$
$$= \beta \quad N_RX_POST1990_{ct} \quad + \gamma \, Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct} \quad (5)$$

where $N_RX_POST1990_{ct} = RX_EVENTS_{ct} * POST1990\%_{ct}$ = the mean *number* of prescriptions for post-1990 drugs associated with medical condition c per person with medical condition c in period t.

I will also estimate equations similar to eq. (5), but using different FDA approval year thresholds (1980, 1995, and 2000). For example, I will estimate:

$$\ln(Y_{ct}) = \beta \, (RX_EVENTS_{ct} * POST1980\%_{ct}) + \gamma \, Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct}$$
$$= \beta \quad N_RX_POST1980_{ct} + \gamma \, Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct} \quad (6)$$

where $N_RX_POST1980_{ct} = RX_EVENTS_{ct} * POST1980\%_{ct}$ = the mean number of prescriptions for post-2000 drugs associated with medical condition c per person with medical condition c in period t. Estimates based on more recent (e.g. 2000) thresholds might be of greater interest than estimates based on earlier thresholds, because the newest drugs are most likely to be patented-protected and therefore the most expensive.[22] However, the standard errors of estimates based on more recent thresholds are likely to be much higher than the standard errors of estimates based on earlier thresholds, because the fraction of prescriptions for very new

[22] Although patent expiration has a large, sudden effect on the price of a drug, there is little reason to expect that it has much effect on the drug's impact on disability days or utilization of medical services. Duflos and Lichtenberg (2012) showed that although the price of a drug generally declines 50–60% in the years immediately following generic entry, marketing expenditure also generally declines 50–60%, and the two effects of increased competition on utilization – positive (via price), and negative (via marketing) – almost exactly offset one another; the net effect of patent expiration on drug utilization is zero.

drugs is quite low.[23] For example, 36% of the prescriptions consumed during 2006-2010 were of post-1990 drugs, but only 6% were of post-2000 drugs.

As discussed in the introduction, I will obtain both OLS and instrumental-variables (IV) estimates of models of the effect of pharmaceutical innovation on disability days and the use of medical services (e.g. eqs. (5) and (6)). Following Acemoglu and Linn (2004), the instrument I will use to obtain IV estimates—the potential size of the market for drugs—will be calculated as follows:

$$MARKET_SIZE_{ct} = \Sigma_a \, RX_PER_{ac,1996\text{-}1998} * POP_{at}$$

where

$MARKET_SIZE_{ct}$ = the potential size of the pharmaceutical market (or potential number of prescriptions) for medical condition c in year t

$RX_PER_{ac,1996\text{-}1998}$ = the mean annual number of prescriptions for medical condition c per person in age group a with medical condition c during 1996-1998 (a = <1, 1-4, 5-9, 10-14,…, 80-84, 85+)

POP_{at} = the population in age group a in year t

As mentioned earlier, when the FDA begins its review of a new drug application, it designates some drugs as drugs "that appear…to represent an advance over available therapy" (priority-review drugs), and other drugs as drugs "that appear…to have therapeutic qualities similar to those of an already marketed drug" (standard-review drugs). The priority-review vs. standard-review distinction suggests that there might also be a distinction between the *actual* vintage of a drug and its *effective* vintage. Suppose a (standard-review) drug approved in 2013 is "therapeutically equivalent" to a drug approved in 2003. Then the "effective vintage" of the drug is 2003, whereas its actual vintage is 2013. (The effective vintage of a priority-review drug is the same as its actual vintage.) More generally,

$$V^*_d = V_d - STD_d \, \Delta_d$$

where

[23] If we could conduct a randomized trial to assess the relative efficacy of new and old drugs, to achieve maximum statistical efficiency, half of the subjects would receive new drugs, and half would receive old drugs.

V^*_d = the effective vintage of drug d

V_d = the actual vintage of drug d

STD_d = 1 if drug d is a standard-review drug

= 0 if drug d is a priority-review drug

Δ_d = the difference between the FDA approval year of standard-review drug d and the FDA approval year of the earliest drug with similar therapeutic qualities

If Δ_d were known, we could base all of our vintage measures on effective vintage rather than actual vintage. Unfortunately, the FDA does not identify the previously-marketed drugs to which standard-review drugs are considered similar, so data on Δ_d are not available. However suppose, for simplicity, that Δ_d were the same for all standard-review drugs: $\Delta_d = \Delta$, for all d. Then

$$V^*_d = V_d - STD_d \, \Delta$$

The (unweighted or utilization-weighted) average effective vintage of all drugs is then

$$V^* = V - STANDARD\% \, \Delta$$

where STANDARD% = the fraction of drugs that are standard-review drugs. Then, if the "true model" of health is

$$HEALTH = \beta \, V^* + \text{other variables}$$

we should estimate models of the form

$$HEALTH = \beta \, V - (\beta \, \Delta) \, STANDARD\% + \text{other variables}$$

$$= \beta \, V + \rho \, STANDARD\% + \text{other variables}$$

where $\rho = -(\beta \, \Delta)$. In other words, controlling for mean actual vintage and other variables, health should be inversely related to the fraction of drugs that are standard-review drugs. We will therefore also estimate the following model:

$$\ln(Y_{ct}) = \beta \, (N_RX_POST1990_{ct}) + \lambda \, (N_RX_STANDARD_{ct}) + \gamma \, Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct} \qquad (7)$$

where $\lambda = (\pi\ \rho)$ and $N_RX_STANDARD_{ct} = (RX_EVENTS_{ct} * STD\%_{ct})$ = the mean number of prescriptions for condition c in year t that were for standard-review drugs.

Other time-varying attributes of medical conditions. I will control for the following time-varying attributes of medical conditions:

AGE_{ct} = the mean age of people with medical condition c in period t

EDU_{ct} = the mean educational attainment (years of schooling) of people with medical condition c in period t

CT_MRI_{ct} = the fraction of patient visits associated with medical condition c in period t in which an advanced imaging procedure (CT or MRI) was performed

$\ln(INCOME_{ct})$ = the log of the mean income of people with medical condition c in period t

$BLACK\%_{ct}$ = the fraction of people with medical condition c in period t who were black

$\ln(N_COND_{ct})$ = the log of the number of people with medical condition c in period t

I control for age because older working-age people tend to have more work-loss days (and medical care use) than younger working-age people.[24] The reasons for controlling for education and advanced imaging use were discussed earlier. Utilization of new drugs may be correlated with the socioeconomic status of people who have a particular disease. Therefore, I will control for two additional indicators of socioeconomic status: mean income and race (the fraction of people with the medical condition who were black).[25]

It might also be appropriate to control for $\ln(N_COND_{ct})$ in the disability day and medical service utilization models, which are models of the *average* degree of disability and service utilization among people with medical condition c in period t. The number of people reported as having a medical condition in a given period is likely to depend on "awareness" of the condition, as well as on its underlying prevalence. Suppose that, when awareness of a condition is low, only people with severe conditions are recognized as having the condition. As awareness increases, people with less severe conditions are more likely to be recognized as

[24] In 2011, mean work-loss days of workers aged 45-64 was 57% higher than that of workers aged 18-44: 4.7 days vs. 3.0 days). http://www.cdc.gov/nchs/data/series/sr_10/sr10_256.pdf, Table 17.

[25] Controlling for (holding constant) mean income could bias estimates of π towards zero, since income is likely to depend on disability: more disabled people are likely to earn less.

having the condition. Medical conditions with greater increases in awareness would tend to have (1) larger increases in reported prevalence (N_COND) and (2) larger declines in mean disability and medical service utilization (due to larger declines in average severity). Moreover, it is plausible that the introduction of new drugs tends to increase disease awareness, since most pharmaceutical industry marketing expenditure is focused on new drugs.[26] Controlling for reported prevalence reduces the risk that estimated effects of drug vintage on disability days and the use of medical services are biased due to heterogeneous changes in awareness of medical conditions.[27]

I hypothesize that the principal driver of increases in utilization of new (e.g. post-1990) drugs for a medical condition is the introduction of new drugs for treating the condition, as opposed to changes in the socioeconomic status of people with the condition. To test this hypothesis, I will examine the relationship across medical conditions between growth in the mean number of prescriptions for new (post-1990) drugs and growth in the (lagged) cumulative number of drugs approved (and other variables, such as $\ln(INCOME_{ct})$), by estimating models of the form:

$$N_RX_\ POST1990_{ct} = \phi \ln(CUM_N_DRUGS_{c,t-k}) + \kappa Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct} \qquad (8)$$

where

$CUM_N_DRUGS_{c,t-k}$ $= \sum_d IND_{dc} APP_{d,t-k}$ = the number of chemical substances (drugs) to treat medical condition c approved by the FDA by the end of year t-k

IND_{dc} = 1 if drug d is used to treat (indicated for) medical condition c

= 0 if drug d is not used to treat (indicated for) medical condition c

$APP_{d,t-k}$ = 1 if drug d was approved by the FDA by the end of year t-k

= 0 if drug d was not approved by the FDA by the end of year t-k

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[26] Duflos and Lichtenberg (2012) showed that expenditure on the marketing of a drug typically declines by about 50–60% in the years immediately following generic entry, i.e. 12–16 years after the drug is first introduced. As Hall et al (2011) observes, at present, only the United States and New Zealand allow direct-to-consumer advertising (DTCA) of prescription medicine. In other countries where DTCA is not allowed, including Australia and the United Kingdom, pharmaceutical companies undertake disease awareness advertising (DAA). In DAA, advertisements do not name a drug directly, but provide general information about diseases and treatments, and encourage consumers to talk to their doctor.

[27] When $\ln(N_COND_{ct})$ is included in the model (i.e., held constant), the effect of drug innovation on *total* use of medical services for a condition (e.g. $\ln(N_COND_{ct} * INPAT_EVENTS_{ct})$) is identical to the effect of drug innovation on the *average* use of medical services (e.g. $\ln(INPAT_EVENTS_{ct})$).

I will also estimate models similar to eq. (1), in which $RX_VINTAGE_{ct}$ is *replaced* by $\ln(CUM_N_DRUGS_{c,t-k})$:

$$\ln(Y_{ct}) = \pi \ln(CUM_N_DRUGS_{c,t-k}) + \gamma Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct} \quad (9)$$

Although $CUM_N_DRUGS_{c,t-k}$ may be "more exogenous" with respect to $\ln(Y_{ct})$ than $RX_VINTAGE_{ct}$, $CUM_N_DRUGS_{c,t-k}$ may be a weak instrument for $RX_VINTAGE_{ct}$. Disability and use of medical services should depend much more strongly on the drugs *actually* used by patients than on the drugs previously approved and therefore *potentially* available to them.

4. Data sources and descriptive statistics

Data on disability day measures and utilization of medical services measures (including RX_EVENTS_{ct}) were obtained from 1996-2010 MEPS Household Component Full-Year Medical Conditions files. Data on AGE_{ct} and EDU_{ct} were obtained by merging Medical Conditions files with 1996-2010 MEPS Full-Year Consolidated Data files. Data on CT_MRI_{ct} were obtained from Emergency Room Visits files, Outpatient Visits files, and Office-Based Medical Provider Visits files.

Measurement of mean drug vintage requires data on N_RX_{pct} and $FDA_YEAR_{p.}$ Data on N_RX_{pct} were obtained from MEPS Prescribed Medicines files.[28] In those files, drug products are classified by National Drug Code (NDC). To measure FDA_YEAR_p for each drug product, I used two databases. The first database, the FDA's National Drug Code Directory, provides a link between NDCs and New Drug Application (NDA) numbers, which are assigned by FDA staff to each application for approval to market a new drug in the United States.[29] The second database, the Drugs@FDA database, provides a link between NDA numbers and active

[28] MEPS Prescribed Medicines files include data on (self-administered) outpatient prescriptions only; they do not include information about drugs administered by providers (e.g. chemotherapy).

[29] The National Drug Code Directory also includes Abbreviated New Drug Application (ANDA) numbers, which are assigned by FDA staff to each application for approval to market a generic drug in the United States, and Biologic License Application (BLA) numbers, which are assigned by FDA staff to each application for approval to market biological products under the provisions of the Public Health Service (PHS) Act.

ingredients, and allows me to determine the date when each active ingredient was first approved by the FDA.

MEPS data on medical conditions and medical events (including prescription drug events) are coded (classified) according to the Clinical Classification Software (CCS) system, which aggregates conditions into mutually exclusive categories, most of which are clinically homogeneous. There are about 285 CCS diagnosis categories. I have 15 years of annual data, so I could have as many as 4275 (= 285 * 15) disease-year observations.[30] However, data at this level of detail are likely to be rather noisy, and model estimation can be difficult and slow (due to clustering), so I aggregated the data both across diseases and over time. I aggregated the 285 CCS diagnosis categories to 131 CCS Level 2 Categories using the Multi-Level CCS program file. I also aggregated the data into three 5-year periods: 1996-2000, 2001-2005, and 2006-2010.[31] Thus, the dataset used for estimation contains about 393 (= 131 * 3) observations.

The data needed to calculate the potential size of the pharmaceutical market (or potential number of prescriptions) for medical condition c in year t ($MARKET_SIZE_{ct}$) were obtained from 1996-1998 MEPS Prescribed Medicines and Full-Year Consolidated Data Files and from CDC Wonder Bridged-Race Population Estimates 1990-2012 (http://wonder.cdc.gov/Bridged-Race-v2012.HTML).

The data needed to calculate the number of chemical substances (drugs) to treat medical condition c approved by the FDA by the end of year t-k ($CUM_N_DRUGS_{c,t-k} = \sum_d IND_{dc} APP_{d,t-k}$) were derived from several reliable sources. Data on IND_{dc} were obtained from Thériaque (http://www.theriaque.org/) a database of official, regulatory and bibliographic information on all drugs available in France, intended for health professionals, and funded by the *Centre National Hospitalier d'Information sur le Médicament*. Data on $APP_{d,t-k}$ were obtained from the RegActionDate file of the Drugs@FDA database.[32]

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[30] My analysis excludes data on mental disorders (conditions) during 1997-2003, because the CCS classification of mental conditions changed beginning in 2004: 15 categories numbered 650-663 and 670 replaced 11 original CCS single-level categories 65-75. Categories 65-75 accounted for about 6% of conditions in 2003. See 2013 CCS (ICD-9-CM) Software and User's Guide, Archival Single-Level CCS for Diagnoses, Single Level CCS.

[31] Aggregation into 5-year time periods may also partly address the issue of lags: disability and medical care use in year t may depend on the prescription drugs used in year t-1 and prior years.

[32] In the Thériaque database, drugs are coded using the WHO ATC classification. The FDA does not use WHO ATC codes, but a link between FDA New Drug Application numbers (used in the Drugs@FDA database) and WHO ATC codes was obtained from the Institut de Pharmacologie Moléculaire et Cellulaire (IPMC)'s chemoinfo database http://chemoinfo.ipmc.cnrs.fr/MOLDB/index.html I am grateful to Dominique Douguet of IPMC for providing me with those data.

Summary statistics, by period, are shown in Table 2. The full sample contains observations on over 1.3 million medical conditions. Almost half of these were borne by employed persons age 16-64. Over 200 thousand conditions were borne by children age 5-22. The sample contains data on over 3.2 million prescriptions.[33] Section B1 of Table 2 shows mean disability measures. The fraction of conditions borne by employed persons age 16-64 causing work loss days declined by 11% between 1997-2000 and 2006-2010, from 25.1% to 22.4%. This decline is smaller than the data depicted in Figure 1 (based on person-level MEPS data) would lead one to expect; according to those data, mean MEPS work loss days per person declined at a 4.5% annual rate during the period 1997-2010. Moreover, the fraction of employed people with any work loss days declined about 18% between 1997-2000 and 2006-2010, whereas the fraction of employed people with any conditions causing work loss days declined by only 2% between 1997-2000 and 2006-2010. Thus, there is a discrepancy between the person-level and condition-level estimates of the average rate of decline of the incidence of any work-loss days.[34] Since the equations I will estimate (e.g., eq. (5)) include year fixed effects, my estimates of the effect of pharmaceutical innovation on work-loss days do not depend on the *average* rate of decline of work-loss days; they depend only on *variation* across conditions in the rate of decline of work-loss days. Moreover, as shown in Figure 3, the cross-sectional relationship (across individuals) in 2010 between the number of conditions causing work loss days and the mean number of work loss days per person looks very reasonable. People who reported that they had more conditions causing work loss days had more work loss days, on average. Indeed, the relationship is close to proportional: people reporting that they had no conditions causing work loss days had no work loss days, and about 5 work loss days were caused by each condition causing work loss days.

The situation is similar with regard to school loss and bed days. Figure 2 shows that mean school loss days declined at an average annual rate of 4.6% during the period 1997-2010, but Table 2 shows that the fraction of conditions borne by persons age 5-22 that caused school loss days remained almost constant. But once again, the cross-sectional relationship (across individuals) in 2010 between the number of conditions causing school loss days and the mean number of school loss days per person looks very reasonable: people reporting that they had no

[33] Some prescriptions are not linked to conditions.
[34] MEPS staff informed me that MEPS does not attempt to reconcile this discrepancy. (Email correspondence with Anita Soni, PhD, MBA, Survey Analyst/Statistician, Agency for Healthcare Research and Quality, May 3, 2013.)

conditions causing school loss days had no school loss days, and about 2.6 school loss days were caused by each condition causing school loss days.

Section B2 of Table 2 shows the average number of medical services per condition, by type of service and period. Between 1997-2000 and 2006-2010, the mean number of inpatient hospital events declined by about 14%, and the mean number of prescription drug events increased by about 14%. Section B3 of Table 2 shows mean drug vintage measures. The fraction of prescriptions that were for post-1990 drugs increased from 9.4% in 1997-2000 to 36.2% in 2006-2010. The mean number of prescriptions for post-1990 drugs increased from 0.088 (8.8 prescriptions per hundred conditions) in 1997-2000 to .418 in 2006-2010. The mean number of prescriptions for post-1980 drugs increased from 0.175 to 0.585. The fraction of prescriptions that were for standard-review drugs (STANDARD%) increased from 46.0% to 52.0%. Section B4 of Table 2 shows mean values of other explanatory variables. Mean age and educational attainment and the fraction of patient visits in which an advanced imaging procedure (CT or MRI) was performed all increased.

Appendix Table 1 shows the top 10 medical conditions during 1997-2010, ranked by four alternative criteria: number of conditions, number of conditions causing work loss days, number of conditions causing school loss days, and total number of inpatient hospital admissions. (As discussed above, the latter three are used as weights in the MISS_WORK%, MISS_SCHOOL%, and INPAT_EVENTS equations, respectively. There is a certain amount of overlap among these rankings. For example, the two most frequent causes of missed work day—respiratory and intestinal infections—were also the most frequent causes of missed school days. However the leading cause of hospital admissions—heart disease—was not among the top 10 causes of either work loss or school loss days. Appendix Table 2 shows correlations across medical conditions between sums of variables (e.g. number of conditions causing missed work days or number of inpatient hospital admissions) during 1997-2010. All of the correlations are positive, and most are statistically significant, but some correlations are much larger than others. The smallest correlation (0.02) is between MISS_SCHOOL and HOME_EVENTS, which is not surprising, since most home health care is used by the elderly. The correlation between MISS_WORK and INPAT_EVENTS is only 0.35. Thus, the conditions receiving the most weight in the MISS_WORK% and INPAT_EVENTS equations are fairly different.

Appendix Table 3A shows the number of sample rx's in 1997-2000 and 2006-2010 for the top 19 drugs (ranked by number of rx's in 2006-2010) for respiratory infections. Appendix Table 3B shows the number of sample rx's in 1997-2000 and 2006-2010 for the top 20 drugs (ranked by number of rx's in 2006-2010) for diseases of the heart. Appendix Table 4 shows work-loss and pharmaceutical innovation measures in 1997-2000 and 2006-2010 of the top 30 conditions (ranked by number of employed persons who missed work because of the condition during 1997-2000). Appendix Figure 1 shows the correlation across conditions between pharmaceutical innovation and change in probability of work-loss for these top 30 conditions.

5. Empirical results

First, I will present evidence about the relationship across medical conditions between growth in mean utilization of new drugs and growth in the (lagged) cumulative number of drugs approved. Next, I will present evidence about the relationship across medical conditions between growth in mean utilization of new drugs and growth in potential market size. Then, I will present OLS and IV estimates of the three disability-days and five medical service use models.

A. The relationship across medical conditions between growth in mean utilization of new drugs and growth in the (lagged) cumulative number of drugs approved

First I will present estimates of several versions of eq. (8): the relationship across medical conditions between growth in the mean number of prescriptions for new (post-1990) drugs and growth in the (lagged) cumulative number of drugs approved (and other variables, such as $\ln(INCOME_{ct})$), Then I will present estimates of the three disability-days and five medical service use models.

Estimates of eq. (8) are shown in Table 3. The models were estimated by weighted least squares, weighting by N_COND_{ct}. Model 1 includes just one explanatory variable: $\ln(CUM_N_DRUGS_{c,t})$: the log of the number of drugs approved by the end of year t, where t is the first year of the 5-year period (1996-2000, 2001-2005, or 2006-2010). The coefficient on this variable is not statistically significant. Model 2 includes $\ln(CUM_N_DRUGS_{c,t-5})$: the log of the number of drugs approved by the end of year t-5. The coefficient on this variable is positive and

highly significant (p-value = .017). Model 3 includes ln(CUM_N_DRUGS$_{c,t-10}$): the log of the number of drugs approved by the end of year t-10. The coefficient on this variable is also positive, but it is smaller and less significant than the coefficient in model 2. This suggests that the average utilization of new drugs is most strongly related to the number of new drugs approved up until about 5 years earlier.[35]

The remaining models in Table 3 include measures of SES, either excluding or including ln(CUM_N_DRUGS$_{c,t-5}$). Model 4 includes just ln(INCOME$_{ct}$). The coefficient on this variable is positive but not statistically significant (p-value =.195). Model 5 includes ln(CUM_N_DRUGS$_{c,t-5}$) and ln(INCOME$_{ct}$). Once again, the coefficient on ln(INCOME$_{ct}$) is insignificant, and the coefficient on ln(CUM_N_DRUGS$_{c,t-5}$) is almost identical to the coefficient in model 2. In models 6-7, ln(INCOME$_{ct}$) is replaced by EDU$_{ct}$, and in models 8-9, ln(INCOME$_{ct}$) is replaced by BLACK%$_{ct}$. The coefficients on EDU$_{ct}$ and BLACK%$_{ct}$ are not significant in any of these regressions, and the coefficients on ln(CUM_N_DRUGS$_{c,t-5}$) in models 7 and 9 are almost identical to the coefficient in model 2. Models 10 and 11 include all three measures of SES, excluding and including ln(CUM_N_DRUGS$_{c,t-5}$), respectively. None of the SES coefficients are significant, and the coefficient on ln(CUM_N_DRUGS$_{c,t-5}$) in model 11 is almost identical to the coefficient in model 2.

These estimates indicate that growth in the mean number of prescriptions for new (post-1990) drugs consumed for a medical condition is strongly related to growth in the (lagged) cumulative number of drugs approved for the condition, and not related to changes in the SES (income, education, or race) of people with the condition.

B. The relationship across medical conditions between growth in mean utilization of new drugs and growth in potential market size

Table 4 presents estimates of the coefficients on ln(MARKET_SIZE$_{ct}$) from the following three regressions:

[35] This is quite consistent with results obtained in Lichtenberg (2014) from an analysis of longitudinal data on *drug classes* (as opposed to medical conditions) for France during the period 2005-2010. He found that the mean vintage of drugs used within a pharmacological class in year t was most strongly related to the cumulative number of drugs commercialized within the class up until year t-3.

$$N_RX_\ POST1990_{ct} = \phi_1 \ln(MARKET_SIZE_{ct}) + \alpha_c + \delta_t + \varepsilon_{ct}$$

$$N_RX_\ POST1980_{ct} = \phi_2 \ln(MARKET_SIZE_{ct}) + \alpha_c + \delta_t + \varepsilon_{ct}$$

$$\ln(N_COND_{ct}) = \phi_3 \ln(MARKET_SIZE_{ct}) + \alpha_c + \delta_t + \varepsilon_{ct}$$

The first two regressions may be considered alternative "first-stage" regressions in the two-stage IV estimation procedure. In column 1 of Table 4, the dependent variable is $N_RX_\ POST1990_{ct}$ (the mean number of prescriptions for post-1990 drugs). The estimate of ϕ_1 is positive and highly significant (p-value=.0024): the mean number of prescriptions for post-1990 drugs increased more rapidly for medical conditions whose market sizes increased the most due to aggregate demographic changes. In column 2 of Table 4, the dependent variable is $N_RX_\ POST1980_{ct}$ (the mean number of prescriptions for post-1980 drugs). The estimate of ϕ_2 is also positive and highly significant (p-value=.0039). The finding that per capita utilization of new products increased more in faster-growing markets is very consistent with Acemoglu and Linn's results. In column 3 of Table 4, the dependent variable is an alternative measure of market size: $\ln(N_COND_{ct})$ (the log of the number of people with medical condition c in year t). There is a significant positive correlation between the two measures of market size.

C. OLS and IV estimates of the three disability-days and five medical service use models

Now I will present estimates of the three disability-days and five medical service use models. First, I will report estimates of models in which the FDA approval year threshold is either 1990 or 1980, and in which I don't distinguish between priority-review and standard-review drugs. Then, I will report estimates of models based on more recent FDA approval year thresholds (1995 and 2000), or in which I distinguish between priority-review and standard-review drugs. Estimates of the coefficients on the drug innovation measures in eqs. (1), (5), and (6)—POST1990%, N_RX_POST1990, and N_RX_POST1980, respectively—are reported in Table 4. Estimates of all parameters of eq. (5) are reported in Appendix Table 5.

I will present OLS estimates, whose validity is predicated on the assumption that pharmaceutical innovation is exogenous with respect to disability and utilization of medical services, conditional on other included variables. I will also present IV estimates, where a measure of potential market size developed by Acemoglu and Linn ($MARKET_SIZE_{ct}$) is used

as an instrument for a measure of pharmaceutical innovation ($N_RX_\ POST1990_{ct}$, the mean number of prescriptions for post-1990 drugs). OLS estimates of π in eq. (1) (where RX_VINTAGE is defined as POST1990%) are shown in columns 1 and 6 of Table 5. All of the coefficients are negative, but only two are statistically significant (p-value < .05).

OLS estimates of β (the coefficient on the mean number of post-1990 drugs) in eq. (5) are shown in columns 2 and 7 of Table 5. Seven out of the eight coefficients are negative and significant (p-value < .03). This indicates that medical conditions that had larger increases in the number of post-1990 drugs per person tended to have larger declines in (per capita and total) disability days and use of almost all non-drug medical services. The fact that the coefficients in columns 2 and 6 are more significant than those in columns 1 and 5 is consistent with the view that an increase in drug quality improves health more when the average quantity of drugs consumed is high.[36]

OLS estimates of β (the coefficient on the mean number of post-1980 drugs) in eq. (6) are shown in columns 3 and 8 of Table 5. In this case, six out of the eight coefficients are negative and significant (p-value < .03). This indicates that estimates of the effect of the number of new drugs are not very sensitive to whether the FDA approval-year threshold used to distinguish new from old drugs is 1990 or 1980. As shown in Appendix Table 5, the coefficients on ln(N_COND), AGE, EDU, and CT_MRI are not significant in any of the disability day models. The coefficient on ln(N_COND) is negative and significant in four of the five medical service use models, indicating that mean service use increased less among conditions whose prevalence increased more. The coefficient on AGE is negative and significant in the ER_EVENTS model and positive and significant in the HOME_EVENTS model.

Estimates of the coefficient on $\ln(CUM_N_DRUGS_{c,t-5})$ in eq. (9) are shown in columns 4 and 9 of Table 5. The coefficient on $\ln(CUM_N_DRUGS_{c,t-5})$ is negative and significant (p-value < .03) in the three disability days models: medical conditions with larger growth in the cumulative number of drugs approved had larger subsequent declines in the mean number of work-loss, school-loss, and other bed days, *ceteris paribus*.[37]

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[36] As shown in Appendix Table 6, estimates of coefficients on N_RX_POST1990 in eq. (5) are quite insensitive to whether or not SES variables (education, race, and income) are included in the model.

[37] The effect of $\ln(CUM_N_DRUGS_{c,t-5})$ is less significant (lower p-value) than the effect of N_RX_POST1990 in the MISS_WORK% and OTHER_BED% models, and is less significant than the effect of N_RX_POST1980 in the MISS_SCHOOL% model,

The coefficient on ln(CUM_N_DRUGS$_{c,t-5}$) is insignificant in the five medical service use models. As noted above, ln(CUM_N_DRUGS$_{c,t-5}$) may be a weak instrument for RX_VINTAGE$_{ct}$. The insignificance of these coefficients may also be partly attributable to substantial sampling error in the medical service use variables, e.g. the mean number of inpatient events. Previous studies (Lichtenberg (2014) and Lichtenberg and Pettersson (2014)) based on census data (not subject to sampling error) rather than survey data have found that medical conditions with larger growth in the cumulative number of drugs approved had larger subsequent declines in the number of hospital admissions and days of care.

Columns 5 and 10 of Table 5 show the IV estimates of β (the coefficient on the mean number of post-1990 drugs) in eq. (5); the instrument for N_RX_ POST1990$_{ct}$ is ln(MARKET_SIZE$_{ct}$), the log of the potential size of the pharmaceutical market (or potential number of prescriptions) for medical condition c in year t. The IV estimates of β in the "other bed-days" model and five of the six medical service use models are insignificant. However the IV estimates of β in the work-loss days, school-loss days, and inpatient events models are negative and statistically significant (p-value < .03). Moreover, the IV estimates in these three models are about twice as large as the corresponding OLS estimates. Also, the increase between period 1 (1996-2000) and period 3 (2006-2010) in the "predicted" value of N_RX_ POST1990$_{ct}$ (based on the increase in ln(MARKET_SIZE$_{ct}$)) was 24% larger than the increase in the actual value of N_RX_ POST1990$_{ct}$.[38]

Table 6 provides a comparison of OLS estimates of coefficients of drug innovation measures based on three alternative FDA approval-year thresholds (1990, 1995, and 2000). As expected, the standard errors of the coefficients on N_RX_POST2000 are much larger than the standard errors of the coefficients on N_RX_POST1990. In the medical service use models, only two of the N_RX_POST1995 coefficients, and none of the N_RX_POST2000 coefficients, are statistically significant (p-value < .05). However all of the N_RX_POST1995 and N_RX_POST2000 coefficients are negative and significant in the disability-days models. Moreover, the three alternative FDA approval-year thresholds yield similar estimates of the log change in disability days that was attributable to pharmaceutical innovation.

[38] The "predicted" value of N_RX_ POST1990$_{ct}$ (based on the increase in ln(MARKET_SIZE$_{ct}$)) increased by 0.41 (from .026 to .430), while the actual value of N_RX_ POST1990$_{ct}$ increased by 0.33 (from .092 to 0.418).

Table 7 reveals the effect of controlling for the fraction of prescriptions that were for standard-review drugs, by comparing estimates of eq. (5), which excludes N_RX_STANDARD (the mean number of prescriptions that were for standard-review drugs) to estimates of eq. (7), which includes N_RX_STANDARD. The coefficient on N_RX_STANDARD is insignificant in four models, but it is positive and significant in the models of other bed days, inpatient events, office events, and emergency room events. These estimates therefore provide some support for the hypothesis that the effective vintage of standard-review drugs is earlier than their actual vintage. But the last two columns of Table 7 indicate that estimates of the log change in the dependent variable due to pharmaceutical innovation are generally insensitive to whether or not we control for N_RX_STANDARD. In light of this, and because the standard errors of the N_RX_POST1995 and N_RX_POST2000 coefficients in Table 6 are much larger than the standard errors of the N_RX_POST1990 coefficients, the analysis in the remainder of this paper will be based on the estimates of eq. (5).

6. Costs vs. benefits of pharmaceutical innovation

As shown in Table 2, the mean number of post-1990 drugs increased from .088 (8.8 prescriptions per 100 conditions) in 1997-2000 to .418 in 2006-2010. Data in the 2010 MEPS Prescribed Medicines File (linked to the FDA data described above) indicate that the mean amount paid in 2010 for a post-1990 drug was $128.[39] Hence the mean cost per condition of the increase in the use of post-1990 drugs was $128 * (.418 - .088) = $42.

The OLS estimates in Table 5 indicate that the increase in use of new drugs between 1997-2000 and 2006-2010 reduced the fraction of conditions causing work loss by 6.3%, or about 0.6% per year. As shown in Figure 3, a person's number of work loss days is approximately proportional to the number of conditions he or she has causing any work loss days. Therefore, the increase in use of new drugs probably also reduced mean number of work loss days per person by about 0.6% per year.[40] This is about one third of the average annual rate

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[39] The mean amount paid in 2010 for single-source drugs was 58% higher: $202. 18% of 2010 prescriptions were for single-source drugs.

[40] WORKLOSSDAYS $\approx$ 4.84 * N_COND_WORKLOSS = 4.84 * N_COND * Prob(WORKLOSS), where WORKLOSSDAYS = work loss days, N_COND_WORKLOSS = number of conditions causing work loss days,

of decline of NHIS work loss days shown in Figure 1. According to the NHIS, about 588 million days of work were lost due to illness or injury in 2010. Hence the increase in use of new drugs between 1997-2000 and 2006-2010 reduced the number of work loss days in 2010 by 36.9 million (= 6.3% * 588 million), or about 0.24 days per worker. The average daily earnings of Americans in 2010 was about $154, so the value per worker of the reduction in the number of work loss days in 2010 was about $37 (=$154 * 0.24). The average worker had 2.7 medical conditions in 2010, so the value of the reduction in the number of work loss days per medical condition in 2010 was about $14 (=$37/2.7).

This estimate of the productivity gains resulting from pharmaceutical innovation is likely to be conservative, because we are implicitly assuming that pharmaceutical innovation has no effect on output per hour worked. It is quite plausible that, in the long run, pharmaceutical innovation increases output per hour worked (and wage rates) as well as the number of hours worked, in part because it increases human capital formation (by reducing school-loss days).

The increase in use of new drugs between 1997-2000 and 2006-2010 also reduced the number of additional bed days by 8.3%. Among employed persons, the number of additional bed days is about half as large as the number of work loss days, so new drugs may have reduced the number of bed days in 2010 by 0.16 days per worker (= (8.3%/6.3%)*(0.24/2)). If the value of a day not spent in bed is also $154, the value of the reduction in the number of bed days of employed persons per medical condition in 2010 was about $10. The sum of the values of work loss and bed day reductions of employed persons was about $24 (=$14 + $10) per medical condition—about 57% as large as the $42 increase in expenditure on new drugs.

The OLS estimates shown in Table 5 also indicate that new drugs reduced the number of school loss days by 5.3%, or about 0.5% per year. This is more than half of the estimated rate of decline of mean school days missed based on NHIS data. According to the NHIS, about 198 million days of school were lost due to illness or injury in 2010; in the absence of a decade of pharmaceutical innovation, 10.5 million more school days would have been lost in 2010.

The OLS estimates in Table 5 indicate that the increase in the use of post-1990 drugs reduced *utilization* of other medical services. Now I will calculate the magnitude of the *expenditure* reductions (in 2010 prices) corresponding to these reductions in utilization of other

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N_COND = number of conditions, and Prob(WORKLOSS) = probability that a condition causes work loss days. Holding N_COND constant, WORKLOSSDAYS is proportional to Prob(WORKLOSS).

medical services. These calculations are summarized in Table 8. The first row shows the calculation for inpatient hospital events. Column 1 shows the OLS point estimate of β from Table 5. As shown in column 2, the 0.330 increase between 1997-2000 and 2006-2010 in the number of post-1990 drugs is estimated to have caused a 8.0% reduction in the mean number of inpatient hospital events per condition ($\Delta \ln Y = \beta * \Delta N_POST_1990$). The mean number of inpatient hospital events per condition during 1997-2010 was 0.036 (calculated from Table 2, shown in column 3 of Table 8), so the absolute reduction in the mean number of inpatient hospital events per condition ($\Delta Y = Y * \Delta \ln Y$) was -.0029 (2.9 fewer events per 1000 conditions). AHRQ estimates that mean expenditure per inpatient hospital event in 2010 was $13,131 (column 5), so the increase in the number of post-1990 drugs is estimated to have caused a $38 reduction in mean inpatient hospital expense per condition.

Similar calculations imply that the increase in the number of post-1990 drugs is estimated to have caused an $11 reduction in mean office-based expense and a $7 reduction in mean emergency room expense per condition. Since the estimate of β in the outpatient events equation was not statistically significant (p-value = .0855), I will assume that there was no reduction in mean outpatient expense. AHRQ does not provide an estimate of mean expenditure per home health event, but the reduction in mean home health expense was probably about 70% as great as the reduction in mean emergency room expense per condition.[41] In addition to reducing the utilization of non-drug medical services, increased use of new drugs may have reduced use of old drugs. I investigated this by estimating an equation similar to eq. (5), in which the dependent variable was ($RX_EVENTS_{ct} * (1 - POST1990\%_{ct})$), i.e. the mean number of "old" (pre-1991) drugs for medical condition c in period t.[42] The estimated coefficient was -0.7412 (Z = -6.11, p-value <.0001): each additional new drug was associated with 0.74 fewer old drugs. The mean amount paid in 2010 for a pre-1991 drug was $43: old drugs are about one-third as expensive as new drugs. Hence, as indicated in line 6 of Table 8, about ¼ of the $42 increase in new drug cost was offset by a reduction in old drug cost (0.7412 * (.418 - .088) * $43 = $10.56). Line 7 shows that the sum of the reductions in expenditure per condition on inpatient hospital, office-

[41] As shown in column 2 of Table 8, the increase in the number of post-1990 drugs is estimated to have reduced the number of home health events by 8.6% and the number of emergency room events by 10.0%. In 2010, aggregate expenditure on home health events was $39.9 billion, and aggregate expenditure on emergency room events was $48.3 billion, so the ratio of the home health expenditure reduction to the emergency room expenditure reduction may have been (8.6% * $39.9)/(10.0% * $48.3) = 0.71.

[42] The weight used to estimate this equation was N_COND_{ct}.

based, emergency room, home health, and pre-1991 drug events was about $71—about 70% larger than the mean increase in expenditure on post-1990 drugs. The benefit of pharmaceutical innovation—the sum of the values of non-new drug expenditure, work loss and bed day reductions of employed persons—was about $95 (=$71 + $14 + $10) per medical condition: more than twice as large as the $42 increase in expenditure on new drugs. As noted above, the mean amount paid in 2010 for single-source drugs was 58% higher than the mean amount paid in 2010 for all post-1990 drugs, but even if I raise my estimate of the cost of pharmaceutical innovation by 58% (from $42 to $66), the estimated cost is well below the $95 estimated benefit. The distributions of prescription drug and other health services expenses by source of payment shown in Table 1 indicate that the benefits, as well as the costs, of pharmaceutical innovation are shared by patients, employers, private insurers, and the government.

As shown in Table 5, the IV estimates of the percentage reduction in work-loss days, school-loss days, and inpatient events attributable to pharmaceutical innovation (14.8%, 11.0%, and 19.2%, respectively) are about 2.4 times as large as the corresponding OLS estimates. Because the IV estimates of the reduction in work-loss days and inpatient events attributable to pharmaceutical innovation are considerably larger than the corresponding OLS estimates, the value of the benefits of pharmaceutical innovation per medical condition implied by the IV estimates is about 30% larger than the value implied by the OLS estimates—$125 vs $95—despite the fact that the IV estimates of β in the "other bed-days" model and five of the six medical service use models are insignificant.[43]

7. Summary

The average number of work-loss and school-loss days declined significantly during the period 1997-2011. In this paper, I tested the hypothesis that pharmaceutical innovation played an important role in reducing disability days of American adults and children since 1997. In

[43] Value of the benefits of pharmaceutical innovation per medical condition implied by OLS and IV estimates:

	reduction in missed work days	reduction in inpatient events	other benefits (reduction in "other bed-days" and use of other medical services)	total
implied by OLS estimates	$14	$38	$43	$95
implied by IV estimates	$33	$92	$0	$125

essence, I investigated whether diseases subject to more rapid medical innovation experienced greater declines in disability days, controlling for several other factors. In addition to investigating the effect of pharmaceutical innovation on disability days, I examined its effect on the utilization of medical services, e.g. inpatient hospital stays and office-based visits.

My basic hypothesis was that the mean number of disability days attributable to a medical condition is inversely related to the quality of medical goods and services used to treat that condition, and that the average quality of newer (later vintage) goods and services is higher than that of older (earlier vintage) goods and services. This hypothesis implies that vintage has a negative effect on disability days. I also hypothesized that an increase in drug quality improves health more if the average quantity of drugs consumed is high. My tests of these hypotheses controlled for reported prevalence, to reduce the risk that estimated effects of drug vintage on disability days and the use of medical services were biased due to heterogeneous changes in awareness of medical conditions.

I presented two kinds of estimates—OLS estimates and IV estimates—of the effect of pharmaceutical innovation on disability days and use of medical services. The validity of the OLS estimates is predicated on the assumption that pharmaceutical innovation is exogenous with respect to disability and utilization of medical services, conditional on other included variables. This assumption may not be satisfied, however, so I also obtained IV estimates, using an instrument for pharmaceutical innovation—the potential size of the market for drugs for a medical condition—introduced by Acemoglu and Linn. (My analysis confirmed the validity and utility of their instrument: per capita utilization of new drugs increased more in faster-growing markets.)

My OLS estimates indicated that medical conditions that had larger increases in the number of post-1990 drugs per person tended to have larger declines in (per capita and total) disability days and use of almost all non-drug medical services. Presumably this is partly due to the fact that new drugs that yield greater benefits are used more. The estimates were consistent with the view that an increase in drug quality improves health more when the average quantity of drugs consumed is high. Estimates of the effect of the number of new drugs were not very sensitive to the threshold used to distinguish new from old drugs. The IV estimates of the pharmaceutical innovation coefficient in the "other bed-days" model and five of the six medical service use models were insignificant. However the IV estimates of this coefficient in the work-

loss days, school-loss days, and inpatient events models were negative and statistically significant, and the IV estimates of the percentage reduction in these variables attributable to pharmaceutical innovation were about 2.4 times as large as the corresponding OLS estimates.

The mean number of post-1990 drugs increased from .088 (8.8 prescriptions per 100 conditions) in 1997-2000 to .418 in 2006-2010. The mean amount paid in 2010 for a post-1990 drug was $128, so the mean cost per condition of the increase in the use of post-1990 drugs was $42. I used OLS and IV estimates of disability-day and medical service use models to obtain estimates of the benefits of the new drugs, and compare them to their costs.

The OLS estimates implied that the increase in use of new drugs reduced the mean number of work loss days per employed person by about 0.6% per year—about one third of the average annual rate of decline of NHIS work loss days. The increase in use of new drugs between 1997-2000 and 2006-2010 reduced the number of work loss days in 2010 by 36.9 million, or about 0.24 days per worker. The value per worker of the reduction in the number of work loss days in 2010 was about $37; the value per medical condition in 2010 was about $14. The sum of the values of work loss and bed day reductions of employed persons was about $24 per medical condition—about 57% as large as the $42 increase in expenditure on new drugs.

The OLS estimates also indicated that new drugs reduced the number of school loss days by 0.5% per year—more than half of the estimated rate of decline of mean school days missed based on NHIS data. This implies that, in the absence of a decade of pharmaceutical innovation, 10.5 million more school days would have been missed in 2010.

I also obtained OLS estimates of the reductions in expenditure on hospital admissions, office-based visits, emergency room visits, home health visits, and old drugs resulting from increased use of new drugs. Those estimates implied that the increase in the number of post-1990 drugs caused a $39 reduction in mean inpatient hospital expense per condition and a $32 reduction in other medical expense per condition. The sum of the values of non-new drug expenditure, work loss and bed day reductions of employed persons was about $95 per medical condition—more than twice as large as the $42 increase in expenditure on new drugs. The value of the benefits of pharmaceutical innovation per medical condition implied by the IV estimates was about 30% larger than the value implied by the OLS estimates: $125 vs $95.

The estimates obtained in this study are estimates of the (utilization-weighted) *average*, or aggregate, effect of pharmaceutical innovation on disability days and medical service use. Of

course, there may be considerable variation across diseases in the impact of pharmaceutical innovation, and even more variation across drugs. The methodology used in this study is not well-suited to identifying the effects of specific new drugs or of innovation for specific diseases. Those effects can be better identified by narrower, more targeted studies. On the other hand, given the enormous number[44] and methodological heterogeneity of studies of the effects of specific drugs and drug classes, performing a meta-analysis of such studies seems unlikely to be a fruitful way to identify the aggregate effect of pharmaceutical innovation.

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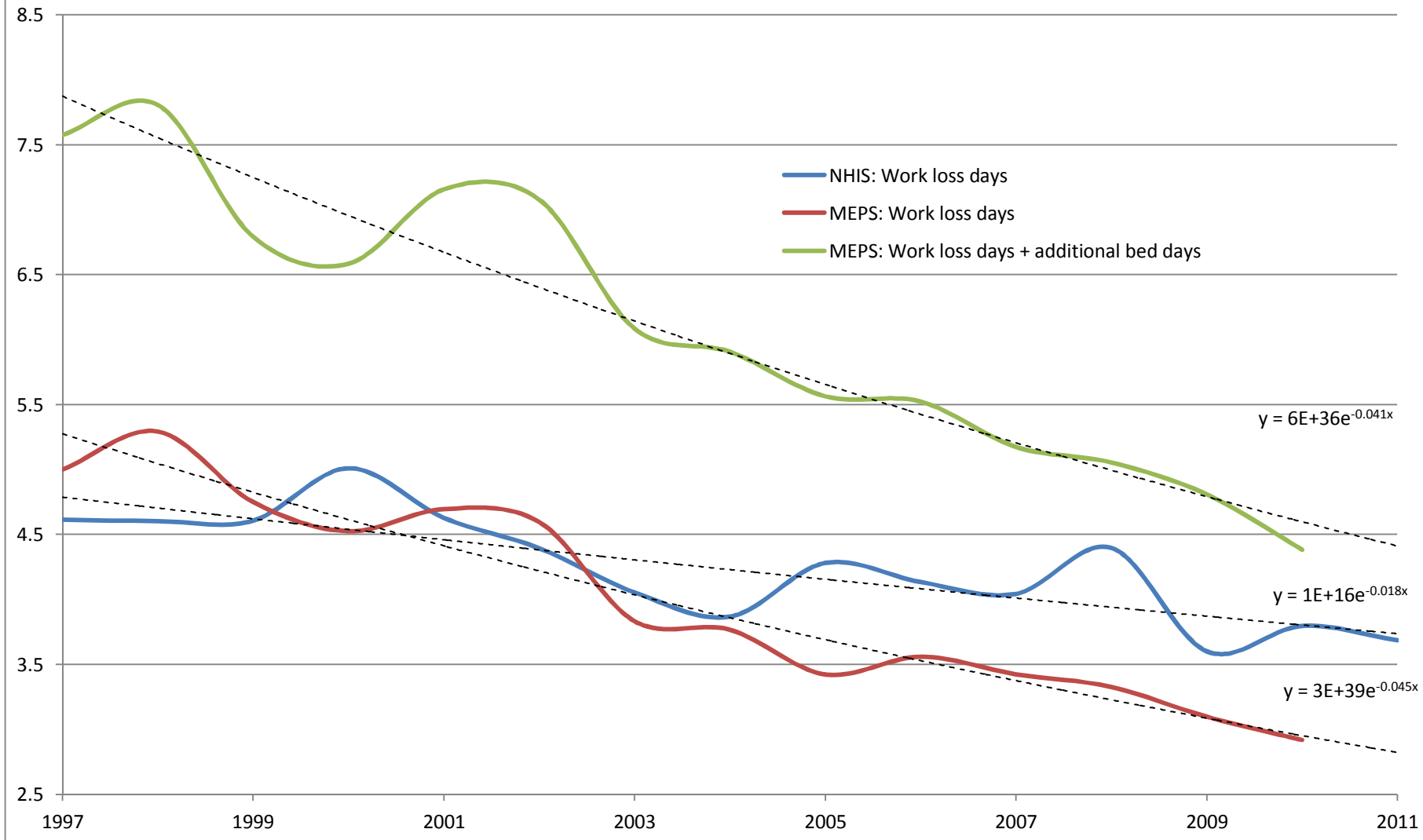
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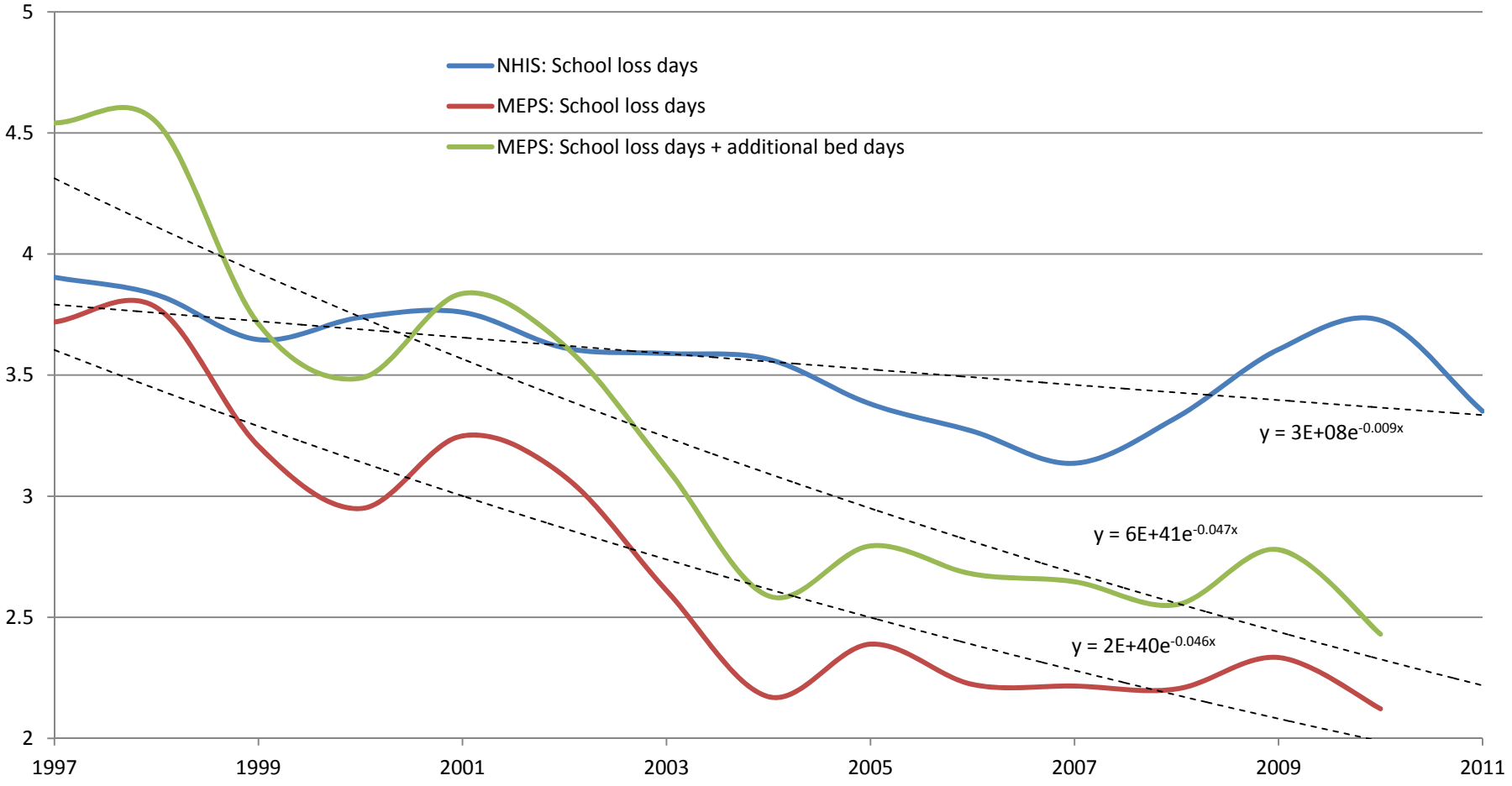
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Figure 1
Mean number of work-loss days per year,
employed persons 18 years of age and older



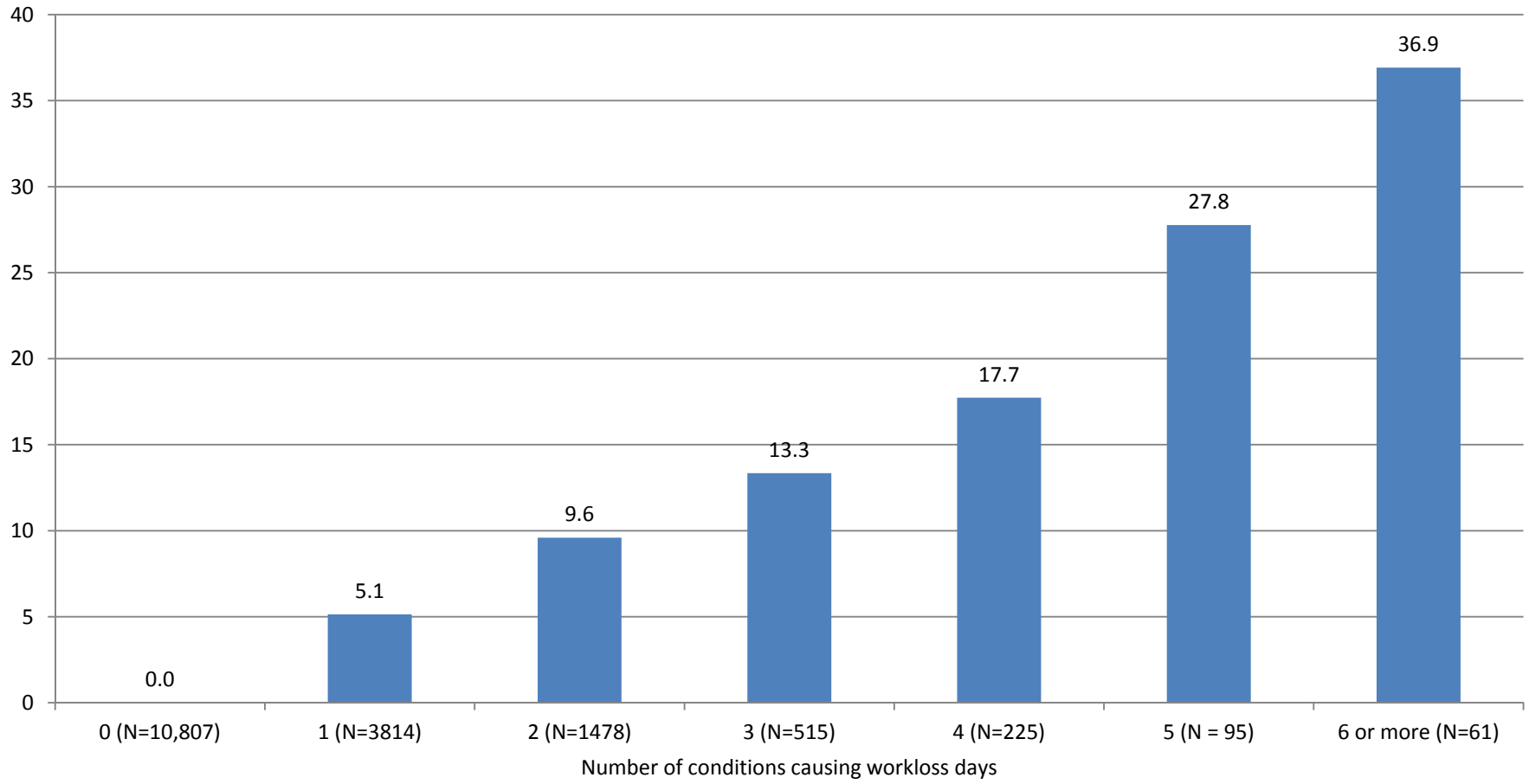
Source: author's calculations based on (1) NHIS data from Minnesota Population Center and State Health Access Data Assistance Center, Integrated Health Interview Series: Version 4.0. Minneapolis: University of Minnesota, 2011, and (2) MEPS Supplemental Public Use Files (1997-1998) and full-year consolidated data files (1996-2010)

Figure 2
Mean number of school days missed per year because of illness or injury for children aged 5–17



Source: author's calculations based on (1) NHIS data from Minnesota Population Center and State Health Access Data Assistance Center, Integrated Health Interview Series: Version 4.0. Minneapolis: University of Minnesota, 2011, and (2) MEPS Supplemental Public Use Files (1997-1998) and full-year consolidated data files (1996-2010)

Figure 3
Relationship across individuals in 2010 between number of conditions causing workloss days and mean number of workloss days per person



$WORKLOSSDAYS_i = 0.04 + 4.84\ N_COND_WORKLOSS_i$
t = 60.4, p-value < .0001
$WORKLOSSDAYS_i$ = work-loss days of person i
$N_COND_WORKLOSS_i$ = number of conditions causing work-loss days of person i

Table 1

Distribution of Health Services Expenses by Source of Payment: United States, 2010

Expenditure type	Total Expenses (in millions) in 2010	Out of pocket	Private insurance	Medicare	Medicaid	Other
Prescription Medicines	$270,877	22%	33%	25%	11%	9%
Other Health Services	$992,542	12%	42%	26%	10%	10%
Total Health Services	$1,263,419	14%	40%	26%	10%	10%

Source:
Table 1: Total Health Services-Median and Mean Expenses per Person With Expense and Distribution of Expenses by Source of Payment: United States, 2010

Table 2: Prescription Medicines-Median and Mean Expenses per Person With Expense and Distribution of Expenses by Source of Payment: United States, 2010
http://meps.ahrq.gov/mepsweb/data_stats/quick_tables.jsp

Table 2

Summary statistics, by period

Period	1997-2000	2001-2005	2006-2010
A. Sample sizes			
No. of conditions of all people	315,235	528,010	511,135
No. of conditions of employed persons age 16-64	143,892	240,246	227,759
No. of conditions of children age 5-22	54,837	85,079	74,728
No. of prescriptions	737,004	1,102,685	1,393,334
B. Sample means			
B1. Disability day measures			
MISS_WORK% (employed persons age 16-64)	25.1%	23.4%	22.4%
MISS_SCHOOL% (age 5-22)	40.5%	39.1%	40.3%
OTHER_BED%	13.2%	13.7%	12.8%
B2. Utilization of medical services measures			
INPAT_EVENTS	0.039	0.038	0.033
OFFICE_EVENTS	1.524	1.643	1.507
OUTPAT_EVENTS	0.146	0.160	0.117
ER_EVENTS	0.060	0.070	0.065
HOME_EVENTS	0.098	0.102	0.093
RX_EVENTS	1.073	1.203	1.224
B3. Drug vintage measures			
POST1980%	18.2%	38.2%	50.6%
POST1990%	9.4%	26.7%	36.2%
POST1995%	2.4%	14.2%	20.1%
POST2000%	0.0%	2.1%	5.6%
STANDARD%	46.0%	47.1%	52.0%
N_RX_ POST1980	0.175	0.417	0.585
N_RX_ POST1990	0.088	0.292	0.418
N_RX_STANDARD	0.480	0.537	0.615
B4. Other variables			
age	42.1	43.5	45.5
edu	11.1	11.2	11.5
ct_mri	1.2%	1.9%	2.3%

Table 3

Estimates of eq. (9): $N_RX_POST1990_{ct} = \phi \ln(CUM_N_DRUGS_{c,t-k}) + \kappa Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct}$

The relationship across medical conditions between growth in the mean number of prescriptions for new (post-1990) drugs and growth in the (lagged) cumulative number of drugs approved (and other variables, such as $\ln(INCOME_{ct})$)

Model	Regressor	Estimate	Standard Error	Z	Pr > |Z|
1	$\ln(CUM_N_DRUGS_{c,t})$	0.5276	0.4095	1.29	0.1976
2	$\ln(CUM_N_DRUGS_{c,t-5})$	**0.5536**	**0.2323**	**2.38**	**0.0172**
3	$\ln(CUM_N_DRUGS_{c,t-10})$	**0.4165**	**0.2015**	**2.07**	**0.0387**
4	$\ln(INCOME_{ct})$	0.294	0.2267	1.30	0.1947
5	$\ln(CUM_N_DRUGS_{c,t-5})$	**0.5349**	**0.2385**	**2.24**	**0.0249**
	$\ln(INCOME_{ct})$	0.4022	0.3191	1.26	0.2075
6	EDU_{ct}	0.089	0.0757	1.18	0.2399
7	$\ln(CUM_N_DRUGS_{c,t-5})$	**0.5432**	**0.232**	**2.34**	**0.0192**
	EDU_{ct}	0.0497	0.065	0.76	0.4445
8	$BLACK\%_{ct}$	-1.244	0.8482	-1.47	0.1425
9	$\ln(CUM_N_DRUGS_{c,t-5})$	**0.5429**	**0.2362**	**2.30**	**0.0215**
	$BLACK\%_{ct}$	-1.0052	0.9869	-1.02	0.3084
10	$\ln(INCOME_{ct})$	0.1439	0.2332	0.62	0.5373
	$BLACK\%_{ct}$	-1.0772	0.797	-1.35	0.1765
	EDU_{ct}	0.0598	0.0912	0.66	0.5118
11	$\ln(CUM_N_DRUGS_{c,t-5})$	**0.5301**	**0.2382**	**2.23**	**0.0261**
	$\ln(INCOME_{ct})$	0.4286	0.4589	0.93	0.3503
	$BLACK\%_{ct}$	-0.7341	0.8417	-0.87	0.3831
	EDU_{ct}	-0.0198	0.104	-0.19	0.849

Note: The models were estimated by weighted least squares, weighting by N_COND_{ct}. Standard errors are clustered within medical conditions.

Table 4

Estimates of coefficients from regressions of N_RX_ POST1990, N_RX_ POST1980, and ln(N_COND) on ln(MARKET_SIZE)

Column	**1**	**2**	**3**
Dependent variable	N_RX_POST1990	N_RX_POST1980	ln(N_COND)
Estimate	3.199	3.635	3.967
Std. Err.	1.052	1.260	1.443
Z	3.04	2.89	2.75
Pr > |Z|	0.0024	0.0039	0.006

Table 5

Estimates of coefficients of drug innovation measures in disability days and medical service use models (eqs. (1), (5), (6), and (9))

Column	1	2	3	4	5		6	7	8	9	10
Estimation method	OLS	OLS	OLS	OLS	IV		OLS	OLS	OLS	OLS	IV
Drug innovation measure	POST1990%	N_RX_ POST1990	N_RX_ POST1980	ln(CUM_N_ DRUGS$_{t-5}$)	N_RX_ POST1990		POST1990%	N_RX_ POST1990	N_RX_ POST1980	ln(CUM_N_ DRUGS$_{t-5}$)	N_RX_ POST1990
Dep. Var.	MISS_WORK% (AGE 16-64)						OFFICE_EVENTS				
Estimate	-0.2276	**-0.1911**	**-0.1519**	**-0.1547**	**-0.3647**		-0.1794	**-0.109**	**-0.1022**	-0.0919	0.0455
Z	-1.60	**-3.00**	**-2.83**	**-2.43**	**-4.10**		-1.43	**-2.71**	**-2.88**	-1.51	0.44
Pr > |Z|	0.109	**0.0027**	**0.0046**	**0.0149**	**<.0001**		0.1515	**0.0067**	**0.004**	0.1313	0.6573
Dep. Var.	MISS_SCHOOL% (AGE 5-22)						OUTPAT_EVENTS				
Estimate	-0.1189	**-0.1399**	**-0.1465**	**-0.2166**	**-0.2715**		-0.4172	-0.1803	-0.1363	0.043	0.0263
Z	-0.75	**-2.22**	**-3.41**	**-2.64**	**-2.19**		-1.68	-1.78	-1.53	0.28	0.09
Pr > |Z|	0.4549	**0.0265**	**0.0006**	**0.0082**	**0.0284**		0.0924	0.0746	0.1255	0.7804	0.9287
Dep. Var.	OTHER_BED%						ER_EVENTS				
Estimate	**-0.3904**	**-0.2562**	**-0.2038**	**-0.236**	-0.1617		-0.1812	**-0.3142**	-0.2175	-0.1049	-0.2421
Z	**-2.33**	**-3.51**	**-2.81**	**-2.22**	-1.14		-0.66	**-2.37**	-1.87	-0.76	-1.08
Pr > |Z|	**0.0196**	**0.0005**	**0.0049**	**0.0267**	0.2536		0.5124	**0.0179**	0.061	0.4448	0.2791
Dep. Var.	INPAT_EVENTS						HOME_EVENTS				
Estimate	**-0.4389**	**-0.2436**	**-0.1568**	-0.1228	**-0.4735**		**-0.5221**	**-0.2264**	**-0.1864**	-0.12	-0.1051
Z	**-2.31**	**-2.86**	**-2.43**	-1.29	**-3.69**		**-2.01**	**-2.49**	**-2.37**	-1.27	-0.41
Pr > |Z|	**0.0211**	**0.0043**	**0.0151**	0.1976	**0.0002**		**0.0441**	**0.0126**	**0.0179**	0.2049	0.6797

Each coefficient comes from a different model. With one exception, all models include ln(N_COND), AGE, ln(INCOME), EDU, BLACK%, CT_MRI, medical condition fixed effects, and period fixed effects. (EDU and CT_MRI were excluded from the MISS_SCHOOL% model.) Models were estimated by weighted least-squares, using weights described in the text. Standard errors are

IV estimates: The instrument for N_RX_ POST1990$_{ct}$ is ln(MARKET_SIZE$_{ct}$), the log of the potential size of the pharmaceutical market (or potential number of prescriptions) for medical condition c in year t

$MARKET_SIZE_{ct} = \Sigma_a RX_PER_{ac,1996\text{-}1998} * POP_{at}$

$MARKET_SIZE_{ct}$: the potential size of the pharmaceutical market (or potential number of

$RX_PER_{ac,1996\text{-}1998}$: the mean annual number of prescriptions for medical condition c per

POP_{at}: the population in age group a in year t

Table 6

Comparison of OLS estimates of coefficients of drug innovation measures based on three alternative FDA approval-year thresholds (1990, 1995, and 2000)

Dependent variable	Drug innovation measure	Estimate	Std. Err.	Z	Pr > |Z|	Mean change in drug innovation measure between 1997-2000 and 2006-2010	Log change in dependent variable due to mean change in drug innovation measure
MISS_WORK% (AGE 16-64)	N_RX_POST1990	-0.190	0.064	-2.99	0.003	0.328	-0.062
	N_RX_POST1995	-0.215	0.102	-2.11	0.035	0.207	-0.045
	N_RX_POST2000	-1.090	0.212	-5.14	<.0001	0.066	-0.072
MISS_SCHOOL% (AGE 5-22)	N_RX_POST1990	-0.161	0.063	-2.56	0.011	0.328	-0.053
	N_RX_POST1995	-0.211	0.104	-2.03	0.043	0.207	-0.044
	N_RX_POST2000	-0.762	0.176	-4.33	<.0001	0.066	-0.050
OTHER_BED%	N_RX_POST1990	-0.253	0.073	-3.45	0.001	0.328	-0.083
	N_RX_POST1995	-0.284	0.099	-2.87	0.004	0.207	-0.059
	N_RX_POST2000	-1.561	0.285	-5.48	<.0001	0.066	-0.103
INPAT_EVENTS	N_RX_POST1990	-0.249	0.085	-2.91	0.004	0.328	-0.081
	N_RX_POST1995	-0.202	0.130	-1.56	0.119	0.207	-0.042
	N_RX_POST2000	-0.617	0.410	-1.51	0.132	0.066	-0.041
OFFICE_EVENTS	N_RX_POST1990	-0.106	0.040	-2.67	0.008	0.328	-0.035
	N_RX_POST1995	-0.072	0.047	-1.53	0.127	0.207	-0.015
	N_RX_POST2000	-0.134	0.242	-0.55	0.580	0.066	-0.009
OUTPAT_EVENTS	N_RX_POST1990	-0.173	0.101	-1.72	0.086	0.328	-0.057
	N_RX_POST1995	-0.139	0.122	-1.14	0.256	0.207	-0.029
	N_RX_POST2000	-0.615	0.632	-0.97	0.331	0.066	-0.040
ER_EVENTS	N_RX_POST1990	-0.304	0.134	-2.27	0.023	0.328	-0.100
	N_RX_POST1995	-0.321	0.163	-1.97	0.049	0.207	-0.066
	N_RX_POST2000	-0.043	0.449	-0.10	0.923	0.066	-0.003
HOME_EVENTS	N_RX_POST1990	-0.262	0.103	-2.55	0.011	0.328	-0.086
	N_RX_POST1995	-0.298	0.123	-2.41	0.016	0.207	-0.062
	N_RX_POST2000	-0.225	0.618	-0.36	0.715	0.066	-0.015

Each coefficient comes from a different model. With one exception, all models include ln(N_COND), AGE, EDU, CT_MRI, medical condition fixed effects, and period fixed effects. (EDU and CT_MRI were excluded from the MISS_SCHOOL% model.) Models were estimated by weighted least-squares, using weights described in the text. Standard errors are clustered within medical conditions.

Table 7

The effect of controlling for the fraction of prescriptions that were for standard-review drugs

		Estimates from eq. (5): excluding N_RX_STANDARD		Estimates from eq. (7): including N_RX_STANDARD		Log change in dependent variable due to pharmaceutical innovation	
Dep. Var.		N_RX_POST1990		N_RX_POST1990	N_RX_STANDARD	eq. (5)	eq. (7)
MISS_WORK% (AGE 16-64)	Estimate	-0.1899		-0.2197	0.0845	-0.062	-0.061
	Std. Err.	0.0635		0.0613	0.0928		
	Z	-2.99		-3.59	0.91		
	Pr > |Z|	0.0028		0.0003	0.3624		
MISS_SCHOOL% (AGE 5-22)	Estimate	-0.1612		-0.1616	0.0325	-0.053	-0.049
	Std. Err.	0.063		0.06	0.0711		
	Z	-2.56		-2.69	0.46		
	Pr > |Z|	0.0105		0.0071	0.6476		
OTHER_BED%	Estimate	-0.2527		-0.3264	0.2301	-0.083	-0.076
	Std. Err.	0.0733		0.0682	0.0956		
	Z	-3.45		-4.79	2.41		
	Pr > |Z|	0.0006		<.0001	0.0161		
INPAT_EVENTS	Estimate	-0.2487		-0.3707	0.3754	-0.081	-0.071
	Std. Err.	0.0854		0.0738	0.1011		
	Z	-2.91		-5.02	3.72		
	Pr > |Z|	0.0036		<.0001	0.0002		
OFFICE_EVENTS	Estimate	-0.1063		-0.1577	0.1377	-0.035	-0.033
	Std. Err.	0.0398		0.0456	0.059		
	Z	-2.67		-3.46	2.33		
	Pr > |Z|	0.0076		0.0005	0.0196		
OUTPAT_EVENTS	Estimate	-0.1733		-0.223	0.1106	-0.057	-0.058
	Std. Err.	0.1008		0.1306	0.1809		
	Z	-1.72		-1.71	0.61		
	Pr > |Z|	0.0855		0.0877	0.5407		
ER_EVENTS	Estimate	-0.3039		-0.3738	0.3287	-0.100	-0.078
	Std. Err.	0.134		0.1087	0.0982		
	Z	-2.27		-3.44	3.35		
	Pr > |Z|	0.0234		0.0006	0.0008		
HOME_EVENTS	Estimate	-0.2617		-0.2281	-0.1109	-0.086	-0.090
	Std. Err.	0.1026		0.1087	0.137		
	Z	-2.55		-2.1	-0.81		
	Pr > |Z|	0.0108		0.0359	0.4182		

Table 8

OLS estimates of reductions in expenditure (at 2010 prices) attributable to increase in the mean number of post 1990 drugs, by type of expenditure

	Column	1	2	3	4	5	6
Line	Type of expenditure	OLS estimate of coefficient on N_RX_POST1990 in eq. (5) (β)	Percent change in mean no. of events per condition due to increase in number of post-1990 drugs ($\Delta \ln Y = \beta * \Delta N_POST_1990$)	Mean no. of events per condition (Y)	Absolute change in mean no. of events per condition due to increase in number of post-1990 drugs ($\Delta Y = Y * \Delta \ln Y$)	Expend. per event in 2010 (P)	Change in mean expend. per condition due to increase in number of post-1990 drugs ($P * \Delta Y$)
1	INPAT_EVENTS	-0.2436	-0.080	0.036	-0.0029	$13,131	-$38.14
2	OFFICE_EVENTS	-0.109	-0.036	1.564	-0.0563	$190	-$10.69
3	OUTPAT_EVENTS	insignificant		0.140		$925	$0.00
4	ER_EVENTS	-0.3142	-0.104	0.066	-0.0068	$969	-$6.63
5	HOME_EVENTS	-0.2264	-0.075	0.098	-0.0073		-$4.71
6	RX_EVENTS * (1 - POST1990%)				-0.2446	$43	-$10.56
7	TOTAL						-$70.73

Total Utilization and Mean Expenses per Event by Type of Ambulatory Health Care Service, 201C
http://meps.ahrq.gov/mepsweb/data_stats/summ_tables/hc/mean_expend/2010/table1.htm

Total Utilization and Mean Expenses for Inpatient Stays by Length of Stay, 201C
http://meps.ahrq.gov/mepsweb/data_stats/summ_tables/hc/mean_expend/2010/table2.htm

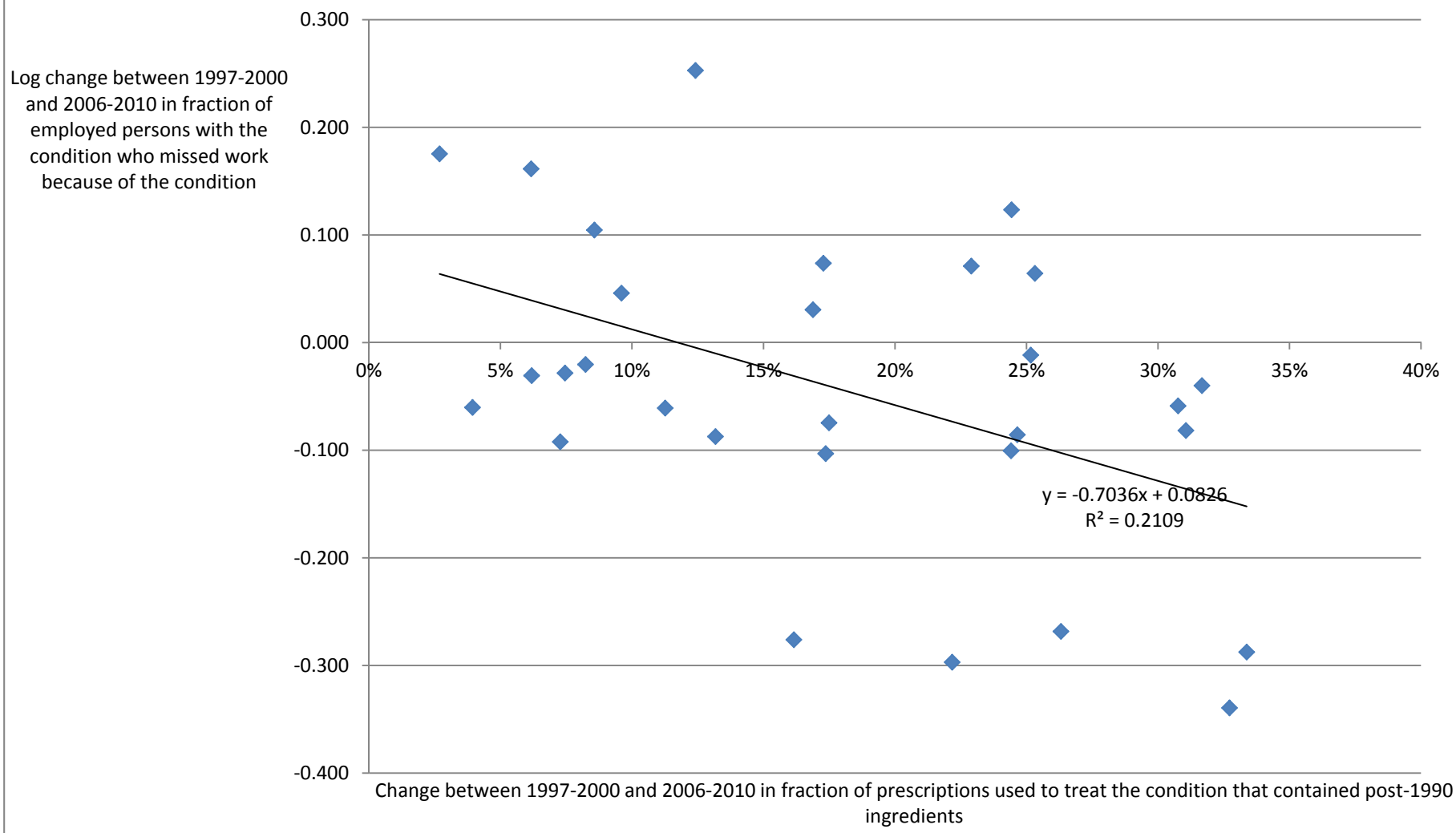
Home Health Services-Median and Mean Expenses per Person With Expense and Distribution of Expenses by Source of Payment: United States, 2010

http://meps.ahrq.gov/mepsweb/data_stats/tables_compendia_hh_interactive.jsp?_SERVICE=MEPSSocket0&_PROGRAM=MEPSPGM.TC.SAS&File=HCFY2010&Table=HCFY2010_PLEXP_H&VAR1=AGE&VAR2=SEX&VAR3=RACETH5C&VAR4=INSURCOV&VAR5=POVCAT10&VAR6=MSA&VAR7=REGION&VAR8=HEALTH&VARO1=4+17+44+64&VARO2=1&VARO3=1&VARO4=1&VARO5=1&VARO6=1&VARO7=1&VARO8=1&_Debug=

Appendix Figure 1

Correlation across conditions between pharmaceutical innovation and change in probability of work-loss,

top 30 conditions (ranked by number of employed persons who missed work because of the condition during 1997-2000)



Appendix Table 1

Top 10 medical conditions during 1997-2010, ranked by four alternative criteria

No. of conditions	
N	**Medical condition**
146,918	8.1 Respiratory infections
66,483	7.1 Hypertension
58,553	13.2 Non-traumatic joint disorders
47,918	9.1 Intestinal infection [135.]
47,877	8.9 Other upper respiratory disease [134.]
45,021	17.2 Factors influencing health care
41,835	7.2 Diseases of the heart
40,338	6.7 Eye disorders
39,237	3.6 Disorders of lipid metabolism [53.]
39,032	13.3 Spondylosis; intervertebral disc disorders; other back problems [205.]

Number of conditions causing missed school days	
N	**Medical condition**
31,834	8.1 Respiratory infections
12,768	9.1 Intestinal infection [135.]
5,173	6.8 Ear conditions
4,681	17.1 Symptoms; signs; and ill-defined conditions
4,326	8.9 Other upper respiratory disease [134.]
3,919	8.3 Asthma [128.]
3,309	9.4 Upper gastrointestinal disorders
3,305	1.3 Viral infection
2,401	6.5 Headache; including migraine [84.]
2,153	8.8 Other lower respiratory disease [133.]

Number of conditions causing missed work days	
N	**Medical condition**
30,524	8.1 Respiratory infections
15,926	9.1 Intestinal infection [135.]
6,562	13.3 Spondylosis; intervertebral disc disorders; other back problems [205.]
5,373	6.5 Headache; including migraine [84.]
4,652	16.7 Sprains and strains [232.]
4,107	8.2 Chronic obstructive pulmonary disease and bronchiectasis [127.]
3,937	8.9 Other upper respiratory disease [134.]
3,885	13.2 Non-traumatic joint disorders
3,781	16.12 Other injuries and conditions due to external causes [244.]
3,717	17.1 Symptoms; signs; and ill-defined conditions

Total number of inpatient hospital admissions	
N	**Medical condition**
6,014	7.2 Diseases of the heart
5,954	11.7 Normal pregnancy and/or delivery [196.]
2,232	8.1 Respiratory infections
1,853	10.1 Diseases of the urinary system
1,572	16.2 Fractures
1,323	7.3 Cerebrovascular disease
1,179	7.4 Diseases of arteries; arterioles; and capillaries
1,081	3.2 Diabetes mellitus without complication [49.]
982	8.8 Other lower respiratory disease [133.]
976	7.1 Hypertension

Appendix Table 2

Correlations across medical conditions between sums of variables during 1997-2010

	N_COND	MISS_WORK	MISS_SCHOOL	OTHER_BED	INPAT_EVENTS	OFFICE_EVENTS	OUTPAT_EVENTS	ER_EVENTS	HOME_EVENTS	RX_EVENTS
N_COND	1.00									
MISS_WORK	0.84	1.00								
MISS_SCHOOL	0.78	0.95	1.00							
OTHER_BED	0.89	0.96	0.88	1.00						
INPAT_EVENTS	0.41	0.35	0.23	0.47	1.00					
OFFICE_EVENTS	0.76	0.48	0.29	0.63	0.53	1.00				
OUTPAT_EVENTS	0.51	0.28	0.09	0.43	0.61	0.81	1.00			
ER_EVENTS	0.65	0.62	0.52	0.67	0.59	0.58	0.58	1.00		
HOME_EVENTS	0.48	0.17	0.02	0.39	0.50	0.71	0.68	0.40	1.00	
RX_EVENTS	0.76	0.38	0.31	0.50	0.37	0.76	0.52	0.42	0.66	1.00

Appendix Table 3A

Number of sample rx's in 1997-2000 and 2006-2010 for the top 19 drugs (ranked by number of rx's in 2006-2010) for **respiratory infections**

SUBSTANCE NAME	**Mean FDA approval year of substance(s)**	**Number of rx's in 1997-2000**	**% of rx's in 1997-2000**	**Number of rx's in 2006-2010**	**% of rx's in 2006-2010**
AMOXICILLIN	1974	1306	19.1%	3507	22.6%
AZITHROMYCIN	1991	1093	16.0%	2335	15.0%
AZITHROMYCIN MONOHYDRATE	1983	0	0.0%	1465	9.4%
FLUTICASONE PROPIONATE	1990	358	5.2%	581	3.7%
PREDNISONE	1955	18	0.3%	414	2.7%
AMOXICILLIN; CLAVULANATE POTASSIUM	1979	0	0.0%	406	2.6%
PENICILLIN V POTASSIUM	1958	73	1.1%	308	2.0%
ALBUTEROL SULFATE	1982	68	1.0%	305	2.0%
CEPHALEXIN	1971	275	4.0%	297	1.9%
MOMETASONE FUROATE MONOHYDRATE	1997	0	0.0%	292	1.9%
AZITHROMYCIN ANHYDROUS	1991	0	0.0%	280	1.8%
IBUPROFEN	1974	29	0.4%	267	1.7%
MONTELUKAST SODIUM	1998	15	0.2%	203	1.3%
CLARITHROMYCIN	1991	794	11.6%	187	1.2%
OSELTAMIVIR PHOSPHATE	1999	7	0.1%	174	1.1%
SULFAMETHOXAZOLE; TRIMETHOPRIM	1973	163	2.4%	167	1.1%
CODEINE PHOSPHATE; PROMETHAZINE HYDROCHLORIDE	1952	109	1.6%	163	1.0%
CEFDINIR	1997	0	0.0%	158	1.0%
TRIAMCINOLONE ACETONIDE	1960	57	0.8%	158	1.0%

Note: Listed drugs had at least 1% of rx's for respiratory infection in 2006-2010. 306 drugs had at least 1 rx for respiratory infection in 2006-2010.

Appendix Table 3B

Number of sample rx's in 1997-2000 and 2006-2010 for the top 20 drugs (ranked by number of rx's in 2006-2010) for **diseases of the heart**

SUBSTANCE NAME	**Mean FDA approval year of substance(s)**	**Number of rx's in 1997-2000**	**% of rx's in 1997-2000**	**Number of rx's in 2006-2010**	**% of rx's in 2006-2010**
WARFARIN SODIUM	1954	2819	10.2%	5260	9.7%
CLOPIDOGREL BISULFATE	1997	185	0.7%	5106	9.4%
DIGOXIN	1975	5646	20.4%	3353	6.2%
METOPROLOL SUCCINATE	1992	900	3.3%	3242	6.0%
CARVEDILOL	1995	218	0.8%	3220	5.9%
FUROSEMIDE	1966	2803	10.1%	3201	5.9%
METOPROLOL TARTRATE	1978	550	2.0%	3057	5.6%
ATENOLOL	1981	1296	4.7%	2230	4.1%
DILTIAZEM HYDROCHLORIDE	1982	574	2.1%	1793	3.3%
LISINOPRIL	1987	1080	3.9%	1737	3.2%
ISOSORBIDE MONONITRATE	1991	224	0.8%	1655	3.0%
AMLODIPINE BESYLATE	1992	1318	4.8%	1126	2.1%
POTASSIUM CHLORIDE	1965	152	0.5%	1118	2.1%
NITROGLYCERIN	1981	839	3.0%	864	1.6%
SIMVASTATIN	1991	380	1.4%	820	1.5%
AMIODARONE HYDROCHLORIDE	1985	388	1.4%	791	1.5%
RAMIPRIL	1991	27	0.1%	652	1.2%
SPIRONOLACTONE	1960	173	0.6%	642	1.2%
HYDROCHLOROTHIAZIDE	1959	249	0.9%	593	1.1%
VALSARTAN	1996	1	0.0%	544	1.0%

Note: Listed drugs had at least 1% of rx's for diseases of the heart in 2006-2010. 366 drugs had at least 1 rx for diseases of the heart in 2006-2010.

Appendix Table 4

Work-loss and pharmaceutical innovation measures in 1997-2000 and 2006-2010 of top 30 conditions (ranked by number of employed persons who missed work because of the condition during 1997-2000)

Condition	Number of employed persons who missed work because of the condition during 1997-2000	Fraction of employed persons with the condition who missed work because of the condition during 1997-2000	Fraction of employed persons with the condition who missed work because of the condition during 2006-2010	Log change between 1997-2000 and 2006-2010 in fraction of employed persons with the condition who missed work because of the condition	Fraction of prescriptions used to treat the condition during 1997-2000 that contained post-1990 ingredients	Fraction of prescriptions used to treat the condition during 2006-2010 that contained post-1990 ingredients	Change between 1997-2000 and 2006-2010 in fraction of prescriptions used to treat the condition that contained post-1990 ingredients
8.1 Respiratory infections	17,249	43%	46%	0.074	7%	24%	17%
9.1 Intestinal infection [135.]	8,002	63%	65%	0.031	5%	22%	17%
6.8 Ear conditions	2,848	26%	23%	-0.092	6%	13%	7%
13.3 Spondylosis; intervertebral disc disorders; other back problems [205.]	2,416	27%	26%	-0.020	6%	14%	8%
8.2 Chronic obstructive pulmonary disease and bronchiectasis [127.]	2,328	43%	41%	-0.059	6%	37%	31%
17.1 Symptoms; signs; and ill-defined conditions	2,061	29%	30%	0.046	3%	13%	10%
6.5 Headache; including migraine [84.]	2,047	40%	40%	-0.012	8%	34%	25%
8.9 Other upper respiratory disease [134.]	2,009	18%	16%	-0.086	2%	27%	25%
7.2 Diseases of the heart	1,968	22%	16%	-0.297	9%	31%	22%
16.7 Sprains and strains [232.]	1,895	36%	34%	-0.060	4%	8%	4%
16.12 Other injuries and conditions due to external causes [244.]	1,848	35%	34%	-0.028	4%	12%	7%
1.3 Viral infection	1,815	36%	33%	-0.082	19%	50%	31%
9.4 Upper gastrointestinal disorders	1,757	27%	19%	-0.339	2%	35%	33%
13.2 Non-traumatic joint disorders	1,487	14%	13%	-0.075	9%	27%	17%
16.2 Fractures	1,457	45%	43%	-0.031	2%	8%	6%

Appendix Table 4

Work-loss and pharmaceutical innovation measures in 1997-2000 and 2006-2010 of top 30 conditions (ranked by number of employed persons who missed work because of the condition during 1997-2000)

Condition	Number of employed persons who missed work because of the condition during 1997-2000	Fraction of employed persons with the condition who missed work because of the condition during 1997-2000	Fraction of employed persons with the condition who missed work because of the condition during 2006-2010	Log change between 1997-2000 and 2006-2010 in fraction of employed persons with the condition who missed work because of the condition	Fraction of prescriptions used to treat the condition during 1997-2000 that contained post-1990 ingredients	Fraction of prescriptions used to treat the condition during 2006-2010 that contained post-1990 ingredients	Change between 1997-2000 and 2006-2010 in fraction of prescriptions used to treat the condition that contained post-1990 ingredients
10.1 Diseases of the urinary system	1,396	23%	24%	0.064	8%	33%	25%
13.8 Other connective tissue disease [211.]	1,287	20%	18%	-0.103	6%	23%	17%
11.7 Normal pregnancy and/or delivery [196.]	1,186	31%	37%	0.175	1%	3%	3%
8.8 Other lower respiratory disease [133.]	1,149	27%	29%	0.071	4%	27%	23%
8.3 Asthma [128.]	1,081	21%	15%	-0.288	4%	38%	33%
10.3 Diseases of female genital organs	1,065	16%	17%	0.105	2%	10%	9%
6.7 Eye disorders	1,036	10%	12%	0.123	16%	41%	24%
9.2 Disorders of teeth and jaw [136.]	945	20%	23%	0.162	1%	7%	6%
7.1 Hypertension	909	7%	6%	-0.276	12%	29%	16%
9.12 Other gastrointestinal disorders [155.]	772	24%	22%	-0.087	2%	15%	13%
6.9 Other nervous system disorders [95.]	689	23%	21%	-0.101	7%	32%	24%
16.6 Open wounds	668	18%	23%	0.253	2%	14%	12%
3.2 Diabetes mellitus without complication [49.]	657	13%	10%	-0.268	16%	42%	26%
16.8 Superficial injury; contusion [239.]	623	27%	25%	-0.061	2%	13%	11%
9.5 Abdominal hernia [143.]	506	39%	37%	-0.040	1%	33%	32%

Appendix Table 5
Estimates of eq. (5)

	Estimate	Std. Err.	Z	Pr > |Z|		Estimate	Std. Err.	Z	Pr > |Z|
Dep. Var.	MISSWORK% (AGE 16-64)					OFFICE_EVENTS			
N_RX_ POST1990	**-0.1911**	**0.0637**	**-3.00**	**0.0027**		**-0.109**	**0.0402**	**-2.71**	**0.0067**
ln(INCOME)	0.0304	0.1629	0.19	0.852		-0.2129	0.1432	-1.49	0.1372
BLACK%	-0.5659	0.6967	-0.81	0.4166		-0.1261	0.4889	-0.26	0.7965
ln(N_COND)	-0.103	0.0559	-1.84	0.0654		-0.1518	0.0323	-4.70	<.0001
AGE	-0.0138	0.0104	-1.32	0.1853		0.0101	0.0074	1.38	0.1688
EDU	0.0016	0.0727	0.02	0.9819		-0.0099	0.0484	-0.21	0.8375
CT_MRI	-0.6306	0.9424	-0.67	0.5034		-1.2649	0.9944	-1.27	0.2033
period 1996-2000	-0.1007	0.0464	-2.17	0.03		-0.1647	0.0584	-2.82	0.0048
period 2001-2005	-0.0267	0.0369	-0.72	0.469		0.0672	0.0305	2.21	0.0274
Dep. Var.	MISS_SCHOOL% (AGE 5-22)					OUTPAT_EVENTS			
N_RX_ POST1990	**-0.1399**	**0.0631**	**-2.22**	**0.0265**		-0.1803	0.1011	-1.78	0.0746
ln(INCOME)	-0.2041	0.1539	-1.33	0.1846		-0.2131	0.3764	-0.57	0.5714
BLACK%	0.572	0.7835	0.73	0.4654		-0.3171	1.0769	-0.29	0.7684
ln(N_COND)	-0.0605	0.0319	-1.90	0.0581		**-0.2601**	**0.0904**	**-2.88**	**0.004**
AGE	-0.0316	0.0233	-1.36	0.1735		-0.0017	0.0157	-0.11	0.9147
EDU						-0.0408	0.1229	-0.33	0.74
CT_MRI						-5.1621	2.5377	-2.03	0.0419
period 1996-2000	-0.0797	0.0511	-1.56	0.1189		-0.2003	0.0941	-2.13	0.0334
period 2001-2005	-0.0462	0.0378	-1.22	0.2212		0.2493	0.0669	3.73	0.0002
Dep. Var.	OTHER_BED%					ER_EVENTS			
N_RX_ POST1990	**-0.2562**	**0.0731**	**-3.51**	**0.0005**		**-0.3142**	**0.1328**	**-2.37**	**0.0179**
ln(INCOME)	-0.0703	0.1249	-0.56	0.5735		0.1111	0.3088	0.36	0.7191
BLACK%	-0.4587	0.6463	-0.71	0.4779		-0.3241	1.0652	-0.30	0.7609
ln(N_COND)	-0.0513	0.0455	-1.13	0.2594		-0.304	0.0964	-3.15	0.0016
AGE	0.0103	0.0067	1.53	0.1255		-0.0261	0.0115	-2.27	0.0229
EDU	-0.022	0.042	-0.52	0.6009		0.0982	0.0888	1.11	0.2685
CT_MRI	-0.9555	1.0004	-0.96	0.3395		-0.5406	1.2513	-0.43	0.6657
period 1996-2000	-0.1359	0.0447	-3.04	0.0024		-0.4488	0.1087	-4.13	<.0001
period 2001-2005	0.0187	0.0296	0.63	0.5292		0.044	0.0579	0.76	0.4473
Dep. Var.	INPAT_EVENTS					HOME_EVENTS			
N_RX_ POST1990	**-0.2436**	**0.0852**	**-2.86**	**0.0043**		**-0.2264**	**0.0907**	**-2.49**	**0.0126**
ln(INCOME)	0.0854	0.1423	0.60	0.5485		-1.2726	0.3261	-3.90	<.0001
BLACK%	0.2536	0.7352	0.34	0.7302		1.1987	1.1016	1.09	0.2765
ln(N_COND)	-0.4138	0.0864	-4.79	<.0001		-0.0917	0.0874	-1.05	0.2939
AGE	0.0044	0.0069	0.64	0.5213		0.0607	0.0131	4.63	<.0001
EDU	-0.0943	0.0641	-1.47	0.141		-0.0633	0.1036	-0.61	0.5413
CT_MRI	-0.4402	1.0718	-0.41	0.6813		-3.356	1.9283	-1.74	0.0818
period 1996-2000	-0.2721	0.0734	-3.71	0.0002		-0.2203	0.1421	-1.55	0.1211
period 2001-2005	0.0953	0.0446	2.13	0.0328		0.0387	0.0664	0.58	0.5595

Appendix Table 6

Effect of controlling (or not controlling) for SES variables (income, education, and race) on estimates of β in eq. (5), $\ln(Y_{ct}) = \beta$ N_RX_ POST1990$_{ct} + \gamma Z_{ct} + \alpha_c + \delta_t + \varepsilon_{ct}$

Y	MISS_WORK% (AGE 16-64)	MISS_SCHOOL% (AGE 5-22)	OTHER_BED%	INPAT_EVENTS	OFFICE_EVENTS	OUTPAT_EVENTS	ER_EVENTS	HOME_EVENTS
	including SES variables							
Estimate	-0.1911	-0.1399	-0.2562	-0.2436	-0.109	-0.1803	-0.3142	-0.23
Std. Err.	0.0637	0.0631	0.0731	0.0852	0.0402	0.1011	0.1328	0.091
Z	-3.00	-2.22	-3.51	-2.86	-2.71	-1.78	-2.37	-2.49
Pr > |Z|	0.0027	0.0265	0.0005	0.0043	0.0067	0.0746	0.0179	0.013
	excluding SES variables							
Estimate	-0.1901	-0.1612	-0.2589	-0.2638	-0.1126	-0.1826	-0.2867	-0.25
Std. Err.	0.0629	0.063	0.0743	0.0847	0.0402	0.102	0.1335	0.107
Z	-3.02	-2.56	-3.49	-3.11	-2.80	-1.79	-2.15	-2.35
Pr > |Z|	0.0025	0.0105	0.0005	0.0018	0.0051	0.0735	0.0318	0.019