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Original Article

The impact of access to prescription drugs on disability in eleven European countries

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ABSTRACT

Background: Clinical studies have shown that the use of certain drugs can reduce disability. Access to prescription drugs varies across countries. Even when the total number of drugs launched in two countries is similar, the specific drugs that were launched, and the diseases those drugs are used to treat, may differ.

Objective/Hypothesis: We test the hypothesis that the larger the relative number of drugs for a disease that were launched during 1982–2015 in a country, the lower the relative disability in 2015 of patients with that disease in that country, controlling for the average level of disability in that country and from that disease, and the number of patients with the disease and their mean age.

Methods: We estimate two-way (by country and disease) fixed-effects models of several measures of disability for 31 diseases in eleven European countries using data from the Survey of Health, Ageing and Retirement in Europe and from other sources.

Results: The estimates imply that drug launches during 1982–2015 reduced the probability of severe limitation in 2015 by 4.9 percentage points, from 21.8% to 16.9%; they reduced the probability of any limitation by 7.7 percentage points, from 61.1% to 53.4%; and they reduced the mean number of Activities of Daily Living limitations by about 29%. Drug launches also yielded a small increase in an index of quality of life and well-being.

Conclusions: In general, the larger the number of drugs for a disease that were launched during 1982–2015 in a country, the lower the average disability in 2015 of patients with that disease in that country, controlling for the average level of disability in that country and from that disease, and the number of patients with the disease and their mean age.

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Clinical studies have shown that the use of certain drugs can reduce disability. Nevitt et (2000)[1] showed that in postmenopausal women with preexisting vertebral fracture, alendronate therapy for 3 years reduced the number of days of bed disability and days of limited activity caused by back pain. Filippini et al. (2014)[2] demonstrated that etanercept, adalimumab, and infliximab reduced disability in rheumatoid arthritis patients, even those with a longstanding history and highly-active form of the disease. Andalo (2016)[3] showed that multiple sclerosis patients given alemtuzumab (first launched in 2001) were almost twice as likely to achieve an improvement in physical disabilities as those given interferon beta-1a (first launched in 1995).

Access to prescription drugs varies across countries. Fig. 1 shows the number of new chemical entities (NCEs) that were launched in eleven European countries during the period 1982–2015. The average number of NCEs launched in the top 3 countries (709) was 42% higher than the number of NCEs launched in the bottom 3 countries (501). Even when country A had more launches than country B, country A may have had fewer drugs launched for some diseases. As shown in Fig. 2, at least two more drugs were launched in Italy than in Spain for four diseases, and at least two fewer drugs were launched in Italy for three other diseases.

This study will empirically investigate two hypotheses about relative access to prescription drugs for different diseases in different countries. The first hypothesis is about the *determinants* of relative access. The hypothesis is that the greater the relative prevalence of a disease in a country, the larger the relative number of drugs for the disease that will be launched in the country. The

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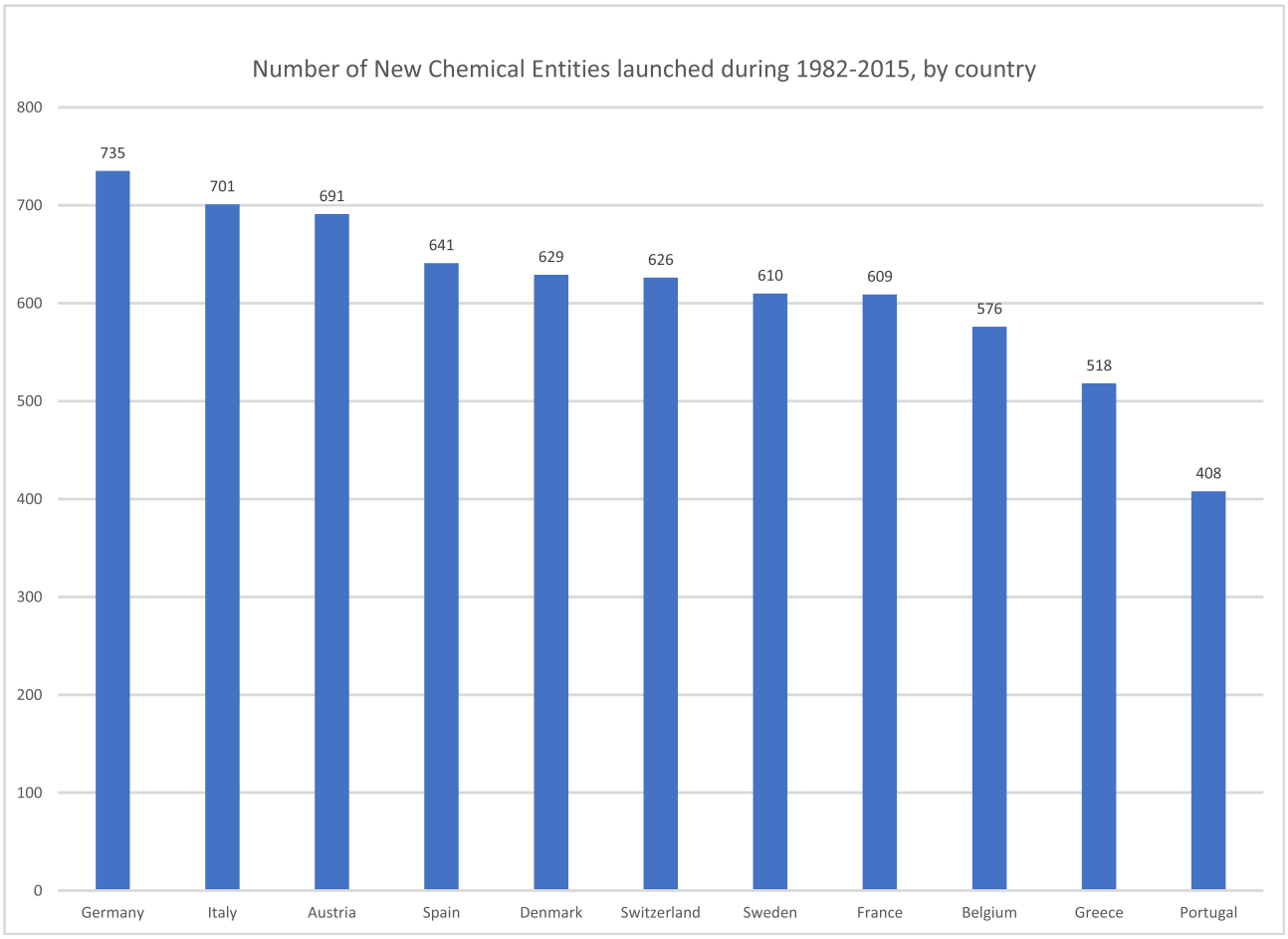


Fig. 1. Number of New Chemical Entities launched during 1982–2015, by country.

second hypothesis is about the *consequences* of relative access. The hypothesis is that the larger the relative number of drugs for a disease that have been launched in a country,[1] the lower the relative disability of patients with that disease in that country, controlling for several other factors. As shown in Fig. 3, relative disability from different diseases varies across countries: French people who had had chronic kidney disease and hip fractures were more likely to be severely limited than Germans, but French people who had had ulcers, breast cancer, and strokes were less likely to be severely limited than Germans.

Both of these hypotheses will be tested using a two-way, fixed-effects, cross-sectional research design, based on group-level data on 31 diseases in 11 countries derived from Wave 6 of the Survey of Health, Ageing and Retirement in Europe (SHARE) and other sources. The models we will estimate will include both country fixed effects and disease fixed effects, which control for the average level of disability (and the average number of drug launches) in each country and for each disease.[2] Several alternative (self-reported) measures of disability (and quality of life) will be analyzed, including the fraction of people with severe limitations or any limitations, and the number of activities of daily living limitations.

In the next section, we describe econometric models of the determinants and consequences of relative prescription drug access, and data sources and descriptive statistics. Empirical results are presented in Section III. Implications of the estimates are discussed in Section IV. Section V provides a summary and conclusions.

Methods

Model of the effect of disease prevalence on the number of drug launches

Previous studies have shown that both innovation (the number of drugs developed) and diffusion (the number of drugs launched in a country) depend on *market size*. Acemoglu and Linn (2004)[7] found "economically significant and relatively robust effects of

[1] International differences in drug *expenditure* are not meaningful indicators of international differences in access to drugs due to substantial variation in drug prices. For example, in 2017 the price of the hepatitis C drug Harvoni was over 200 times as high in the U.S. as it was in Egypt. See Civio (2017)[4] and Lichtenberg (2010).[5]

[2] Lichtenberg (2018)[6] employed a similar methodology (two-way fixed effects model of different diseases in different countries). That study differs from this study in several major ways, including the following:

	Present study	Lichtenberg (2018)[4]
outcome measures	disability	mortality
diseases	primarily non-cancer diseases	cancer only
data source (outcomes data)	Survey of Health, Ageing and Retirement in Europe (SHARE)	WHO Global Health Estimates 2015

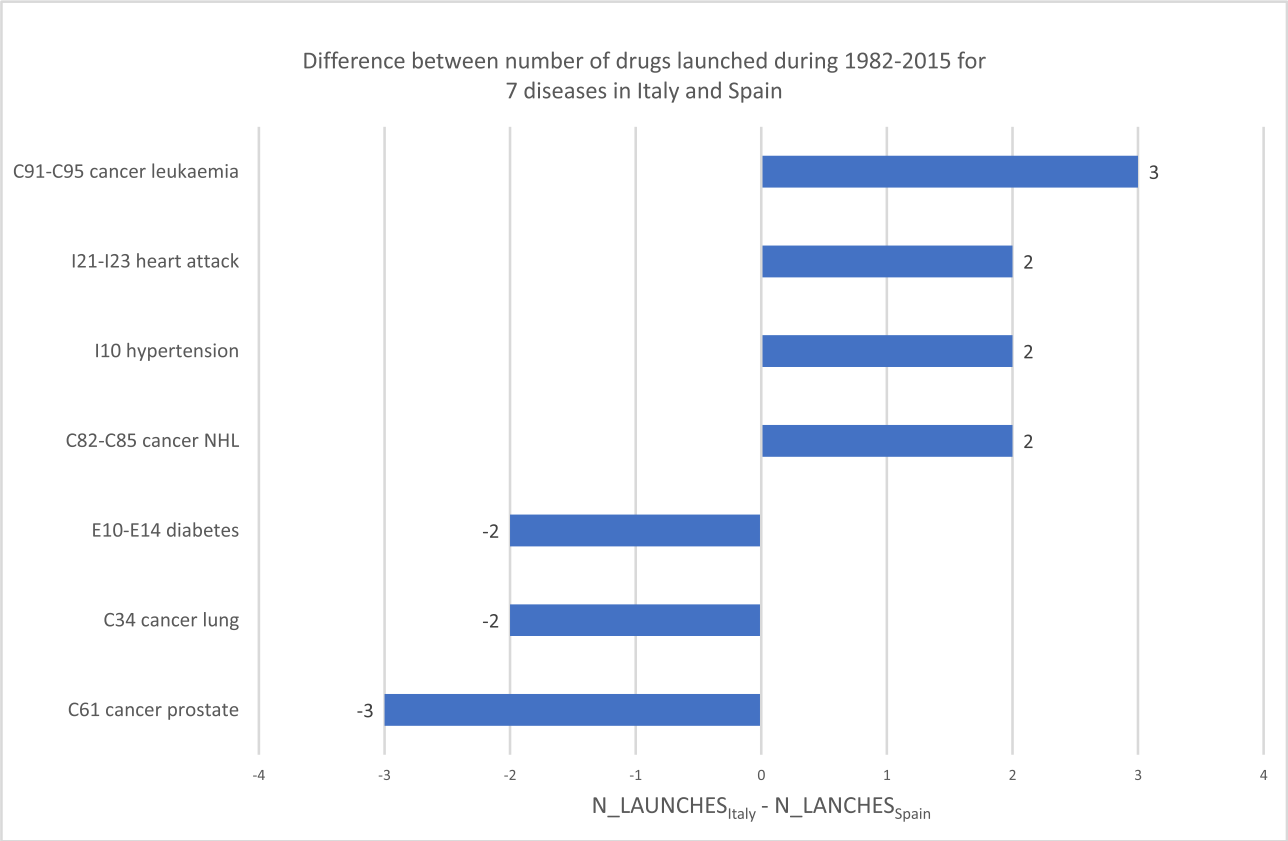


Fig. 2. Difference between number of drugs launched during 1982–2015 for 7 diseases in Italy and Spain.

market size on innovation." Danzon et al. (2005)[8] found that "countries with lower expected prices or *smaller expected market size experience longer delays in new drug access*, controlling for per capita income and other country and firm characteristics" (emphasis added).

The hypothesis that the number of drug launches is influenced by market size can be investigated in a two-way fixed-effects framework by estimating the following equation:

$$LAUNCHES_2006_2015_{dc} = \sigma \ln(PREV_2005_{dc}) + \alpha_d + \delta_c + \varepsilon_{dc} \quad (1)$$

where

$LAUNCHES_2006_2015_{dc}$ = the number of drugs to treat disease d launched in country c during 2006–2015
$PREV_2005_{dc}$ = the number of patients in country c in 2005 who had ever been told by a doctor that they had disease d
α_d = a fixed effect for disease d
π_c = a fixed effect for country c

Model of the effect of the number of drug launches on disability

The basic model we will estimate to investigate the effect of prescription drug access on disability is:

$$Y_{dc} = \beta_{0\text{-}33}\, LAUNCHES_1982_2015_{dc} + \gamma \ln(PREV_{dc}) + \rho\, AGE_MEAN_{dc} + \Lambda_1\, OVERWEIGHT\%_{dc} + \Lambda_2\, OBESE\%_{dc} + \alpha_d + \pi_c + \varepsilon_{dc} \quad (2)$$

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

$\ln(limit_severe\%_{dc}/(1 - limit_severe\%_{dc}))$ = the log-odds that individuals with disease d in country c in 2015 have severe limitations
$\ln(limit_any\%_{dc}/(1 - limit_any\%_{dc}))$ = the log-odds that individuals with disease d in country c in 2015 have any limitations
N_ADL_{dc} = the mean number of limitations with activities of daily living of individuals with disease d in country c in 2015
N_IADL_{dc} = the mean number of limitations with instrumental activities of daily living of individuals with disease d in country c in 2015
$CASP_{dc}$ = the mean CASP index[3] for quality of life and well-being of individuals with disease d in country c in 2015

and

$LAUNCHES_1982_2015_{dc}$ = the number of post-1981[4] new chemical entities used to treat disease d launched in country c during 1982–2015

[3] The CASP index was designed to cover the active and beneficial experiences of later life rather than simply focus on the medical and social care issues that had traditionally been seen to typify ageing research. The scale is composed of 4 subscales, the initials of which make up the acronym: Control, Autonomy, Self-Realization and Pleasure. https://casp19.com/background/See also Hyde et al. (2003)[9] and Howel (2012).[10]

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

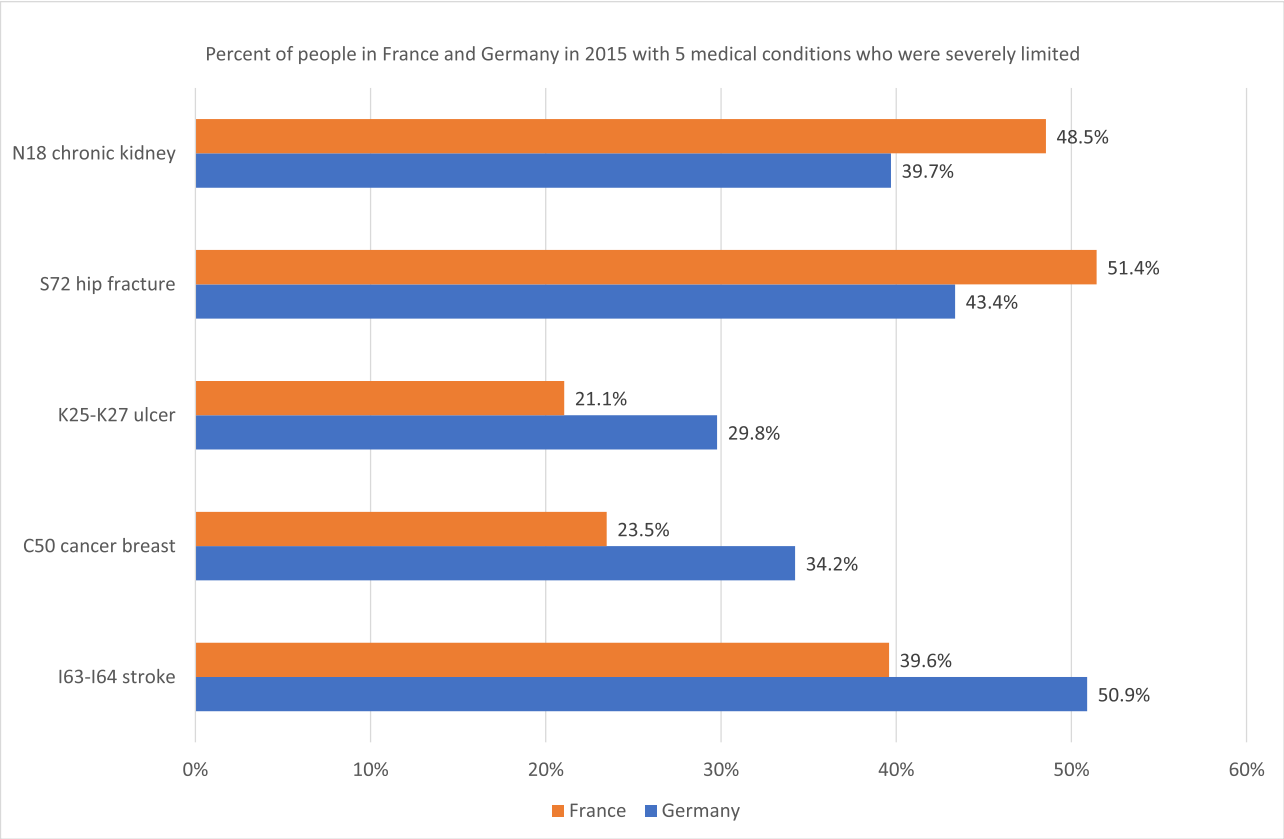


Fig. 3. Percent of people in France and Germany in 2015 with 5 medical conditions who were severely limited.

$PREV_{dc}$ = the number of people in country c in 2015 who said that a doctor ever told them that they had disease d
AGE_{dc} = the mean age of people in country c in 2015 who said that a doctor ever told them that they had disease d
$OVERWEIGHT\%_{dc}$ = the fraction of people with disease d in country c in 2015 who were overweight
$OBESE\%_{dc}$ = the fraction of people with disease d in country c in 2015 who were obese[5]

A person is considered to have a disease if he or she said that a doctor had ever told them that they had the disease. Sixty percent of individuals in the sample who had at least one disease had more than one disease. From the survey, we know whether someone was disabled, but we don't know which medical conditions caused the disability.[6] We will account for this in the following way: an individual with N diseases will contribute N observations (one for each disease), but each observation will be given a weight of (1/N).[7] Eq. (2) will be estimated by weighted least squares; the disturbances will be clustered within countries or within diseases. The following weights will be used:

Dependent variable	Weight[8]
$\ln(limit_severe\%_{dc}/(1 - limit_severe\%_{dc}))$	$PREV_ADJ_{dc} * limit_severe\%_{dc} * (1 - limit_severe\%_{dc})$
$\ln(limit_any\%_{dc}/(1 - limit_any\%_{dc}))$	$PREV_ADJ_{dc} * limit_any\%_{dc} * (1 - limit_any\%_{dc})$
N_ADL_{dc}	$PREV_ADJ_{dc}$
N_IADL_{dc}	$PREV_ADJ_{dc}$
$CASP_{dc}$	$PREV_ADJ_{dc}$

$PREV_ADJ_{dc}$ is the "adjusted prevalence" of disease d in country c. Let $HAS_DISEASE_{idc} = 1$ if person i in country c has disease d, and = 0 if person i in country c does not have disease d. The number of diseases patient i has is $N_DISEASES_{i.c} = \sum_d HAS_DISEASE_{idc}$.

The prevalence of disease d in country c is $PREV_{dc} = \sum_i HAS_DISEASE_{idc}$. The adjusted prevalence of disease d in country c is $PREV_ADJ_{dc} = \sum_i (HAS_DISEASE_{idc}/N_DISEASES_{i.c})$, where $N_DISEASES_{i.c} \geq 1$.

The indicator in eq. (2) of prescription drug access in 2015 of patients with disease d in country c is the number of post-1981 new chemical entities used to treat disease d launched in country c during 1982–2015.[9] The launch of a drug in a country indicates that

[5] Armour et al. (2012)[11] documented "high prevalence of disability among those who are obese."

[6] In contrast, the U.S. Medical Expenditure Panel Survey provides some information about the specific causes of activity limitations.

[7] Weighting the observations in this way does not have a significant impact on the estimates of eq. (2).

[8] The first two weights are based on the fact that the variance of the binomial distribution with parameters n and p (where n is the number of trials and p is the "success" probability) is n * p * (1 - p).

[9] More than a dozen studies published in high-quality peer-reviewed journals (e.g. Refs.[6,12–14]) have examined the impact of drug launches on mortality. Also, a study based on U.S. data[15] showed 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 launched for the condition and not related to changes in the socioeconomic status (income, education, or race) of people with the condition.

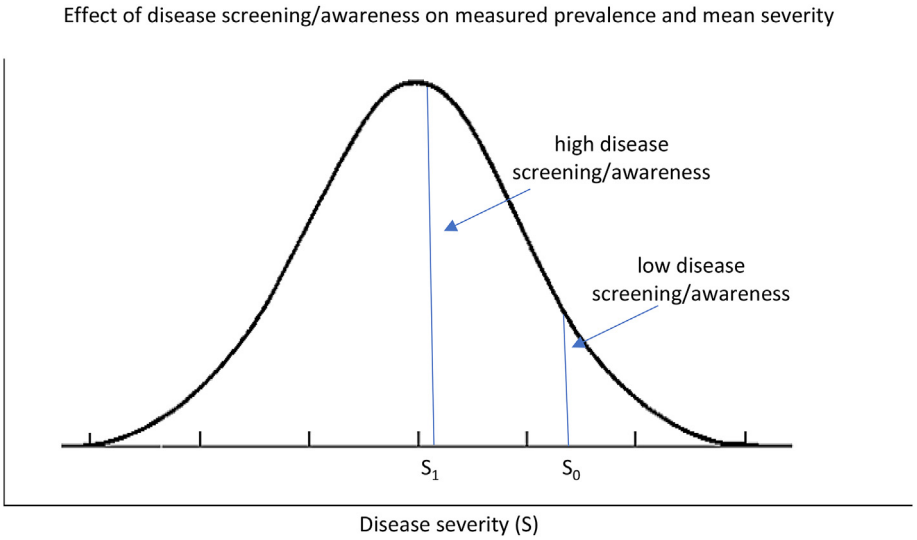


Fig. 4. Effect of disease screening/awareness on measured prevalence and mean severity.

patients *could* have been treated with that drug, not necessarily that patients *were* treated with that drug. We would prefer to estimate models in which the explanatory variables measured the drugs *actually used* to treat patients, by disease and country. We have 2015 data on the utilization of each drug in each country. However, many drugs have multiple indications—48% of drugs have 2 or more indications (causes of disability), and 8% of drugs have 6 or more indications—and our data do not enable us to determine how often each drug was used for each of its indications.

In eq. (2), the number of drugs launched at different times during 1982–2015 (e.g. before and after 2000) are constrained to have equal effects on disability in 2015. It is possible, however, that the effect of more recently-launched drugs could differ from the effect of drugs launched longer ago. The effect of a drug's launch on disability is likely to depend on both the *quantity* and the *quality* (or effectiveness) of the drug. Indeed, it is likely to depend on the *interaction* between quantity and quality: a quality improvement will have a greater impact on disability if drug utilization (quantity) is high. Drugs launched in different periods are likely to vary (in opposite ways) with respect to both quantity (in 2015) and quality. Newer drugs are likely to be of higher quality than older drugs.[10] On the other hand, utilization of new drugs tends to be much lower than utilization of old drugs.[11] To allow for the possibility that drugs launched at different times during 1982–2015 had different effects on disability in 2015, we will also estimate two more general versions of eq. (2).[12] In the first version, we differentiate between the number of launches in 3 periods, by replacing ($\beta_{0\text{-}33}$ LAUNCHES_1982_2015$_{dc}$) in eq. (2) with ($\beta_{0\text{-}9}$ LAUNCHES_2006_2015$_{dc}$ + $\beta_{10\text{-}19}$ LAUNCHES_1996_2005$_{dc}$ + $\beta_{20\text{-}33}$ LAUNCHES_1982_1995$_{dc}$). In the second version, we differentiate between the number of launches in 4 periods, by replacing ($\beta_{0\text{-}33}$ LAUNCHES_1982_2015$_{dc}$) in eq. (2) with ($\beta_{0\text{-}4}$ LAUNCHES_2011_2015$_{dc}$ + $\beta_{5\text{-}9}$ LAUNCHES_2006_2010$_{dc}$ + $\beta_{10\text{-}14}$ LAUNCHES_2001_2005$_{dc}$ + $\beta_{15\text{-}33}$ LAUNCHES_1982_2000$_{dc}$). We will compare the overall effect of drug launches in the three different versions of the model. In eq. (2), the impact is $\beta_{0\text{-}33}$ * mean(-LAUNCHES_1982_2015$_{dc}$); in the model that differentiates between the number of launches in 4 periods, the impact is ($\beta_{0\text{-}4}$ * mean(LAUNCHES_2011_2015$_{dc}$) + $\beta_{5\text{-}9}$ * mean(-LAUNCHES_2006_2010$_{dc}$)+ $\beta_{10\text{-}14}$ * mean(LAUNCHES_2001_2005$_{dc}$) + $\beta_{15\text{-}33}$ * mean(LAUNCHES_1982_2000$_{dc}$)).

The disease prevalence variable (ln(PREV$_{dc}$)) is included as a regressor in eq. (2) to control for potential variation in disease screening intensity or awareness. Suppose that the severity of a disease is normally distributed, as depicted in Fig. 4. If disease screening/awareness is low, only the most severe cases (those with severity $S > S_0$) will be detected and reported, and mean disability from the disease will be high. If disease screening/awareness is high, less severe cases (those with severity $S > S_1$) will be detected and reported, and mean disability from the disease will be lower. Hence one would expect that the higher the relative reported prevalence of a disease, the lower the relative mean disability from the disease. As discussed above, higher (true or measured) disease prevalence is also likely to cause more drug launches. Therefore, as shown in Fig. 5, failure to control for prevalence could bias estimates of the drug launch coefficients away from zero. On the other hand, controlling for prevalence may make our estimates of the drug launch coefficients to be conservative. Targeted efforts and programs to reduce disease burden are likely to depend on disease prevalence, so controlling for prevalence will also control at least to some extent for the effects of those efforts and programs on disability.

The fixed effects in eq. (2) control for many unobserved potential determinants of disability. The disease fixed effects (α_d's) control for the fact that (for example) average disability from chronic kidney disease is higher than average disability from ulcers. The country fixed effects (π_c's) control for a country's attributes

[10] Grossman and Helpman (1993)[16] argued that "innovative goods are better than older products simply because they provide more 'product services' in relation to their cost of production." Bresnahan and Gordon (1996)[17] stated simply that "new goods are at the heart of economic progress," and Bils (2004)[18] said that "much of economic growth occurs through growth in quality as new models of consumer goods replace older, sometimes inferior, models." As noted by Jovanovic and Yatsenko (2012),[19] in "the Spence–Dixit–Stiglitz tradition … new goods [are] of higher quality than old goods."

[11] For example, a previous study [6] showed that mean utilization of a cancer drug is about twice as high 5–9 years after launch as it was 0–4 years after launch.

[12] However, our ability to distinguish between the effects of launches in different periods will be limited by (negative) serial correlation in drug launches, which results in multicollinearity between the number of launches in different periods. This serial correlation is evident from estimates of the following model: LAUNCHES_2001_2015$_{dc}$ = ω LAUNCHES_1982_2000$_{dc}$ + α_d + π_c + ε_{dc}. The estimate of ω is negative and highly significant: estimate = −0.29; Z = 4.77; p-value < .0001. The larger the relative number of drugs launched during 1982–2000, the smaller the relative number of drugs launched during 2001–2015.

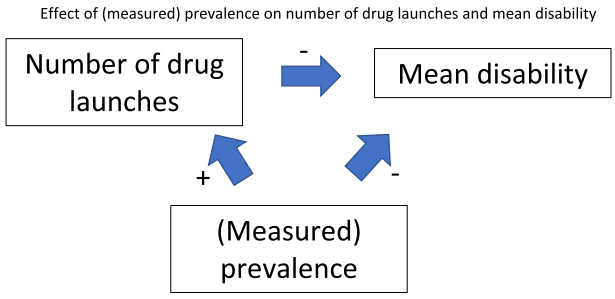


Fig. 5. Effect of (measured) prevalence on number of drug launches and mean disability.

(e.g. its average income, educational attainment, and health care expenditure) to the extent that they have similar effects on disability from different diseases.[13]

Data sources and descriptive statistics

Data on disability were obtained from Wave 6 of the Survey of Health, Ageing and Retirement in Europe (SHARE), a multidisciplinary and cross-national panel database of micro data on health, socio-economic status and social and family networks of more than 120,000 individuals aged 50 or older.[20] The fieldwork of Wave 6 was completed in November 2015. Although SHARE covers 27 European countries and Israel, data on drug launches since 1982 were available for only eleven of those countries.[14]

Summary statistics, by country, are shown in Table 1. The total number of survey respondents in the eleven countries was 45,592, and their mean age was 67.8. The average number of medical conditions reported (including persons with no medical conditions) was 1.6. Thirteen percent of respondents indicated that they were severely limited, and 43% indicated that they had either a severe or mild limitation. The mean number of ADL and IADL limitations reported were 0.3 and 0.5, respectively.

Summary statistics, by medical condition, are shown in Table 2. Two cardiovascular conditions (I10 hypertension and E78 high cholesterol) were the most prevalent by far. However, disability associated with these conditions was lower than disability associated with other medical conditions. Ten percent of people with either of the two cardiovascular conditions were severely limited, whereas 17% of people with all conditions were severely limited. Therefore, although the number of people who had hypertension was almost twice as great as the number who had osteoarthritis, the weight given to hypertension in the $\ln(\text{limit_severe}\%_{dc}/(1 - \text{limit_severe}\%_{dc}))$ model is only 28% larger than the weight given to osteoarthritis.

Data on the number of SHARE Wave 6 respondents who reported that they had each medical condition, by country, are shown in Appendix Table 1.

Data on drug launch years, by molecule and country, were obtained from the IMS Health *New Product Focus database*. Data on the indications of each drug were obtained from the *Thériaque* database.[21,15] Data on the number of drugs launched during 1982–2015, by country and medical condition, are shown in Table 3.

Results

Estimate of model of the effect of disease prevalence on the number of drug launches

The estimate of σ, the $\ln(\text{PREV_2005}_{dc})$ coefficient in the model of the effect of disease prevalence on the number of drug launches (eq. (1)), is positive and significant: estimate = 0.366; standard error = 0.162; Z = 2.26; p-value = .0237. This signifies that larger relative market size (number of patients diagnosed) increases the relative number of drugs launched for a disease in a country. This finding is broadly consistent with the notion that "misery loves company" (Lichtenberg and Waldfogel (2009)[22]): the relative number of drugs launched for a disease in a country is higher when the relative prevalence of that disease is greater.

Estimates of model of the effect of the number of drug launches on disability

Estimates of the model of the effect of the number of drug launches on disability (eq. (2)) are presented in Table 4. All models

Table 1
Summary statistics, by country.

Country	number of persons in sample	mean age	mean number of medical conditions	% severely limited	% with any limitation	mean number of ADL limitations	mean number of IADL limitations	mean CASP index of quality of life and well-being
11 countries combined	45592	67.8	1.6	13%	43%	0.26	0.54	37.4
Austria	3402	69.1	1.5	17%	50%	0.27	0.64	39.8
Belgium	5823	66.4	1.7	16%	48%	0.31	0.62	38.3
Denmark	3733	65.6	1.3	9%	38%	0.17	0.37	41.4
France	3948	68.0	1.6	16%	46%	0.28	0.54	37.9
Germany	4412	66.3	1.7	18%	55%	0.23	0.40	39.2
Greece	4937	66.8	1.6	8%	30%	0.18	0.50	31.8
Italy	5313	67.2	1.4	14%	40%	0.27	0.53	34.8
Portugal	1676	67.7	2.3	23%	60%	0.52	0.83	33.3
Spain	5636	70.0	1.7	7%	40%	0.37	0.82	36.1
Sweden	3906	70.4	1.3	13%	44%	0.17	0.36	39.5
Switzerland	2806	68.6	1.1	9%	35%	0.12	0.26	40.8

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

[14] Data on medical condition prevalence in 2005 (used to estimate eq. (1)) were obtained from Wave 1 of SHARE.

[15] The *Thériaque* database provides data on labeled indications, not on unlabeled indications. To the extent that drugs are used off-label, the drug launch variables in eq. (2) are measured with error. If this measurement error is random, it is likely to bias estimates of the drug launch coefficients towards zero.

Table 2
Summary statistics, by medical condition.

medical condition	number of conditions in sample	mean age	% severely limited	% with any limitation	mean number of ADL limitations	mean number of IADL limitations	mean CASP index of quality of life and well-being
31 medical conditions combined	62,424	69.7	17%	54%	0.36	0.73	36.4
C00-C14 cancer oral cavity	27	73.7	37%	65%	0.75	1.15	35.9
C15 cancer oesophagus	15	72.0	46%	81%	1.16	2.40	34.8
C16 cancer stomach	71	69.3	39%	87%	0.68	1.27	34.1
C18-C20 cancer colon or rectum	194	70.3	32%	72%	0.28	0.56	37.1
C22 cancer liver	62	69.5	39%	83%	0.40	0.96	34.8
C25 cancer pancreas	31	71.4	54%	65%	1.19	2.15	32.5
C34 cancer lung	116	71.2	52%	90%	0.34	0.98	33.8
C43-C44 cancer skin	160	68.3	17%	48%	0.22	0.44	39.1
C50 cancer breast	495	66.2	23%	62%	0.28	0.56	36.5
C53 cancer cervix	64	67.7	40%	71%	0.53	0.90	33.9
C56 cancer ovary	58	66.7	34%	62%	0.64	1.23	36.8
C61 cancer prostate	369	73.4	22%	61%	0.34	0.64	37.2
C64 cancer kidney	65	70.3	17%	53%	0.29	0.42	37.7
C67 cancer bladder	82	70.0	31%	67%	0.37	0.64	37.2
C71 cancer brain	39	68.8	30%	97%	1.11	2.11	35.9
C73 cancer thyroid	57	65.0	16%	71%	0.18	0.44	36.0
C82-C85 cancer NHL	60	71.1	36%	68%	0.42	0.75	38.1
C91-C95 cancer leukaemia	60	69.7	22%	54%	0.54	0.76	37.1
E10-E14 diabetes	5717	70.2	16%	53%	0.34	0.68	36.2
E78 high cholesterol	11,080	68.0	10%	39%	0.18	0.39	37.1
G20 parkinson disease	405	75.2	47%	84%	1.54	2.61	33.4
G30 alzheimer	1057	81.3	60%	89%	2.30	5.23	32.1
I10 hypertension	17,438	69.2	10%	41%	0.21	0.44	37.3
I21-I23 heart attack	4581	73.0	24%	68%	0.42	0.92	35.8
I63-I64 stroke	1571	73.1	43%	78%	1.24	2.34	34.6
J40–J47 chronic lung	2883	68.9	25%	70%	0.39	0.82	35.7
K25-K27 ulcer	1626	66.6	17%	54%	0.35	0.62	34.6
M05-M06 rheumatoid arthritis	3603	70.4	20%	68%	0.41	0.83	35.1
M15-M19 osteoarthritis	8858	68.9	17%	63%	0.30	0.58	36.8
N18 chronic kidney	720	71.2	32%	74%	0.64	1.25	34.3
S72 hip fracture	860	75.0	34%	71%	0.91	1.62	34.8

include disease fixed effects and country fixed effects, but to conserve space, estimates of these parameters are not shown in Table 4. Complete estimates of one model (the model of the log-odds of severe limitation) are shown in Appendix Table 2.

In column 1 of Table 4, the dependent variable is the log-odds of severe limitation. The coefficient on LAUNCHES_1982_2015 is negative and highly significant (p-value = .004), which signifies that the larger the relative number of drugs launched during 1982–2015, the lower were the relative odds of severe limitation in 2015. The impact of drug launches on the log-odds of severe limitation ($\beta_{0\text{-}33}$ * mean(LAUNCHES_1982_2015$_{dc}$)), was −0.317. This signifies that drug launches during the entire 1982–2015 period reduced the log-odds of severe limitation in 2015 by 27% (= 1 − exp(-0.317)). The coefficient on ln(PREV) is negative and significant; this may be due to the effects of disease screening/awareness on measured prevalence and mean disability. The coefficient on AGE_MEAN is positive and significant; older people are more likely to have severe limitations. The coefficient on OVERWEIGHT% is also positive and significant, but the coefficient on OBESE% is insignificant.

In column 2 of Table 4, the dependent variable is the log-odds of any (severe or mild) limitation. The estimates of this model are very similar to the estimates in column 1. Drug launches during the entire 1982–2015 period are also estimated to have reduced the log-odds of any limitation in 2015 by 27%.

In column 3, the dependent variable is the mean number of ADL limitations. Drug launches during the 1982–2015 period are estimated to have reduced the mean number of ADL limitations in 2015 by 0.136. The mean number of ADL limitations among people with at least one medical condition was 0.341. This implies that drug launches during the entire 1982–2015 period reduced the mean number of ADL limitations in 2015 of people with at least one medical condition by 29% (= 0.136/(0.341 + .136)).

In column 4, the dependent variable is the mean number of IADL limitations. The estimates indicate that drug launches did not have a statistically significant effect on mean number of IADL limitations.

In column 5, the dependent variable is the mean CASP index of quality of life and well-being. The estimate of the drug launch coefficient is positive and marginally significant (p-value = .075). The mean CASP index among people with at least one medical condition was 36.58, so this implies that drug launches during the entire 1982–2015 period increased the mean CASP index of people with at least one medical condition by 1.6% (= 0.576/36.58).

As discussed above, to allow for the possibility that drugs launched at different times during 1982–2015 had different effects on disability in 2015, we also estimated two more general versions of eq. (2), in which we differentiated between the number of launches in 3 or 4 periods. Appendix Table 3 provides a comparison of the estimated impacts of new drug launches on disability in the three different versions of the model. The magnitudes and

Table 3
Number of drugs launched during 1982–2015, by medical condition and country.

medical condition	Austria	Belgium	Denmark	France	Germany	Greece	Italy	Portugal	Spain	Sweden	Switzerland	mean
C00-C14 cancer oral cavity	2	2	2	2	2	2	2	2	2	2	2	2.0
C15 cancer oesophagus	2	2	2	3	3	2	2	2	2	2	2	2.2
C16 cancer stomach	6	5	5	6	5	5	5	4	4	6	5	5.1
C18-C20 cancer colon or rectum	10	8	9	9	8	6	8	5	7	9	9	8.0
C22 cancer liver	3	3	3	3	3	3	3	2	3	3	3	2.9
C25 cancer pancreas	9	7	8	8	8	7	7	4	7	8	9	7.5
C32 cancer larynx	0	0	0	0	0	0	0	0	0	0	0	0.0
C34 cancer lung	16	13	16	17	16	11	11	9	13	15	14	13.7
C43-C44 cancer skin	12	7	10	10	10	5	8	8	7	10	9	8.7
C50 cancer breast	24	22	22	25	24	21	24	13	23	22	23	22.1
C53 cancer cervix	2	2	2	2	2	2	2	1	2	2	2	1.9
C54.1 cancer endometrium	0	0	0	0	0	0	0	0	0	0	0	0.0
C56 cancer ovary	8	8	8	8	8	7	8	5	8	8	8	7.6
C61 cancer prostate	13	13	13	13	13	10	9	8	12	12	13	11.7
C62 cancer testicle	0	0	0	0	0	0	0	0	0	0	0	0.0
C64 cancer kidney	4	3	4	3	4	3	2	2	3	4	3	3.2
C67 cancer bladder	2	2	2	2	2	2	2	2	2	2	2	2.0
C71 cancer brain	2	2	1	2	1	2	2	0	1	1	1	1.4
C73 cancer thyroid	3	2	3	2	3	1	1	1	1	3	3	2.1
C82-C85 cancer NHL	17	14	15	14	17	10	15	6	13	16	13	13.6
C91-C95 cancer leukaemia	22	17	22	21	24	14	20	8	17	21	20	18.7
E10-E14 diabetes	31	27	30	31	31	30	28	22	30	30	31	29.2
E78 high cholesterol	8	9	8	9	8	9	8	9	8	8	9	8.5
G20 parkinson disease	9	9	9	9	9	9	9	8	9	7	9	8.7
G30 alzheimer	4	4	4	4	4	4	4	4	4	4	4	4.0
H26.9 cataracts	0	0	0	0	0	0	0	0	0	0	0	0.0
I10 hypertension	31	28	29	37	37	32	34	32	32	27	31	31.8
I21-I23 heart attack	19	17	18	17	20	18	19	12	17	16	19	17.5
I63-I64 stroke	8	7	7	7	7	6	6	6	7	7	7	6.8
J40–J47 chronic lung	23	19	20	22	22	20	21	18	22	21	21	20.8
K25-K27 ulcer	8	8	8	8	8	8	8	8	8	8	8	8.0
M05-M06 rheumatoid arthritis	18	17	18	17	17	17	18	11	19	17	17	16.9
M15-M19 osteoarthritis	7	5	7	8	6	8	8	8	8	6	6	7.0
N18 chronic kidney	10	10	11	10	11	11	11	9	10	11	10	10.4
S72 hip fracture	3	3	3	3	3	3	3	3	3	3	3	3.0
mean	9.6	8.4	9.1	9.5	9.6	8.2	8.8	6.6	8.7	8.9	9.0	8.8

Table 4
Estimates of model of the effect of the number of drug launches and other variables on disability (eq. (2)).

Column		1	2	3	4	5
Dependent variable						
Regressor		log-odds of severe limitation	log-odds of any limitation	number of ADL limitations	number of IADL limitations	CASP index
LAUNCHES_1982_2015	Estimate	**−0.020**	**−0.018**	**−0.008**	−0.004	0.033
	Z	**−2.85**	**−2.13**	**−2.25**	−0.81	1.78
	Pr > |Z|	**0.004**	**0.033**	**0.024**	0.415	0.075
ln(PREV)	Estimate	**−0.228**	**−0.220**	−0.038	**−0.092**	0.116
	Z	**−3.29**	**−2.97**	−0.78	**−2.21**	1.05
	Pr > |Z|	**0.001**	**0.003**	0.433	**0.027**	0.296
AGE_MEAN	Estimate	**0.042**	0.004	**0.028**	**0.076**	**−0.173**
	Z	**3.10**	0.21	**3.06**	**5.45**	**−4.39**
	Pr > |Z|	**0.002**	0.834	**0.002**	**<.0001**	**<.0001**
OVERWEIGHT%	Estimate	**0.866**	0.244	−0.031	−0.061	−0.454
	Z	**3.12**	0.63	−0.18	−0.20	−0.62
	Pr > |Z|	**0.002**	0.528	0.855	0.841	0.537
OBESE%	Estimate	0.383	−0.299	0.370	0.300	**−3.145**
	Z	0.90	−0.57	1.42	0.89	**−3.12**
	Pr > |Z|	0.369	0.570	0.155	0.376	**0.002**
Number of observations		289	273	330	330	327

Estimates in bold are statistically significant (p-value < .05).
Eq. (2): $Y_{dc} = \beta_{0\text{-}33}\ \text{LAUNCHES_1982_2015}_{dc} + \gamma\ \ln(\text{PREV}_{dc}) + \rho\ \text{AGE_MEAN}_{dc} + \Lambda_1\ \text{OVERWEIGHT\%}_{dc} + \Lambda_2\ \text{OBESE\%}_{dc} + \alpha_d + \pi_c + \varepsilon_{dc}$.

Table 5
Estimated effects of 1982–2015 drug launches on mean 2015 disability of people with at least one medical condition.

Column	1	2	3
Disability measure	actual mean	counterfactual (no 1982–2015 drug launches) mean	effect of 1982–2015 drug launches
probability of severe limitation	16.9%	21.8%	−4.9%
probability of any limitation	53.4%	61.1%	−7.7%
mean number of ADL limitations	0.34	0.48	−0.14
mean CASP index	36.58	37.16	0.58

significance of the estimated effects on each of the disability measures are almost identical in the three models. This may be attributable to multicollinearity between the number of launches in different periods. A multivariate regression model with collinear predictors can indicate how well the entire bundle of predictors predicts the outcome variable, but it may not give valid results about any individual predictor, or about which predictors are redundant with respect to others.[23]

Discussion

Estimates of the effects of 1982–2015 drug launches on the mean 2015 disability of people with at least one medical condition are summarized in Table 5. The first column shows the actual mean values, which are approximately equal to the values for 31 medical conditions combined in Table 2. The second column shows the counterfactual mean value, under the (admittedly unrealistic) assumption that no drugs had been launched during 1982–2015. The third column shows the difference between the actual and counterfactual means, i.e. the estimated effect of 1982–2015 drug launches on the disability measure. The estimates imply that drug launches during 1982–2015 reduced the probability of severe limitation in 2015 by 4.9 percentage points, from 21.8% to 16.9%. They reduced the probability of any limitation in 2015 by 7.7 percentage points, from 61.1% to 53.4%.[16]

Verropoulou and Tsimbos (2017)[24] analyzed disability trends among older adults in ten European countries over 2004–2013, using various indicators and Survey of Health, Ageing and Retirement in Europe (SHARE) data, and did not detect any significant trend in severe disability. However, the reduction in disability attributable to increasing availability of prescription drugs may have been offset by adverse trends in behavioral risk factors, such as obesity. SHARE data indicate that the fraction of the population aged 50 and over that was obese (BMI $\geq$ 30) increased from 17.1% in 2004 to 22.2% in 2015.

Comparison of the benefit, in terms of 2015 disability reduction, of 1982–2015 drug launches to the cost of these drugs in 2015 may be of interest. Data published by the International Federation of Pharmaceutical Manufacturers & Associations on pharmaceutical expenditure in the eleven countries in 2014 (2015 data are not available) are shown in Appendix Table 4.[25] Population-weighted average pharmaceutical expenditure was $667. Data from IQVIA for 9 of the 11 countries[17] indicate that just over half (52%) of pharmaceutical expenditure was on drugs launched after 1981, so we estimate that population-weighted average pharmaceutical expenditure on drugs launched after 1981 was $345 (= 52% * $667). This represents average expenditure for the entire population, i.e. for all age groups. Data on pharmaceutical expenditure by age group are not available for these countries, but they are available for the U.S. According to the U.S. Medical Expenditure Panel Survey, in 2014 in the U.S., mean pharmaceutical expenditure of people 45 and over was 77% higher than mean pharmaceutical expenditure of the entire population. Hence it seems reasonable to estimate that mean pharmaceutical expenditure on drugs launched after 1981 by people 45 and over in the eleven European countries was $611 (= 1.77 * $345). Expenditure of $611 reduced the probability of being severely limited by 4.9 percentage points. If people would have been willing to pay at least $12,469 (= $611/4.9%) to avoid being severely limited, drugs launched during 1982–2015 would have been cost-effective, even if they did not provide any other benefits, e.g. increased longevity and reduced hospitalization. However previous research[11,13] has demonstrated that new drug launches have also provided those benefits.

Our analysis is subject to several limitations. Our measure of access to prescription drugs (the number of drugs previously launched in a country) is imperfect. Launch of a drug is a necessary condition for access, not a sufficient condition. Our drug launch data are left-censored—only drugs launched anywhere in the world after 1981 are captured. Our analysis did not account for off-label uses of a drug. Our drug indications data were obtained from a French database, and some drugs launched in other countries have not been launched in France. Our estimates control for the effects on disability of a country's overall health system and macroeconomic conditions, to the extent that those effects don't vary across diseases, but those effects might vary across diseases. The effects of targeted efforts and programs to reduce disease burden may be imperfectly controlled for by including disease prevalence in the disability models. Our data enabled us to measure the average disability of people *with* a medical condition, not the average disability of people *caused by* a medical condition. Future research may enable these limitations to be superseded.

Conclusion

Access to prescription drugs varies across countries. Even when the total number of drugs launched in two countries is similar, the specific drugs that were launched, and the diseases those drugs are used to treat, may differ.

We used data on 31 diseases in eleven European countries, partially derived from the Survey of Health, Ageing and Retirement in Europe, to test the hypothesis that the larger the relative number of drugs for a disease that were launched during 1982–2015 in a country, the lower the relative disability of patients aged 50 and over with that disease in that country, controlling for the average level of disability (and the average number of drug launches) in that country and from that disease, and for the number of patients with the disease and their mean age.

The estimates imply that drug launches during 1982–2015 reduced the probability of severe limitation in 2015 by 4.9 percentage points, from 21.8% to 16.9%; they reduced the probability of any limitation by 7.7 percentage points, from 61.1% to 53.4%; and they reduced the mean number of Activities of Daily Living limitations by about 29%. Drug launches also yielded a small increase in

[16] Combining these estimates implies that drug launches during 1982–2015 reduced the probability of mild limitation in 2015 by 2.9 percentage points, from 39.4% to 36.5%.

[17] Data for 2 small countries (Denmark and Greece) were not available.

an index of quality of life and well-being.

Previous research has demonstrated that new drug launches have reduced mortality: they have enabled people who would have died if the drugs had not been launched to remain alive. Presumably, those additional survivors were the most severely ill and disabled: biomedical innovation tends to offset natural selection. Therefore, the reduction in the average disability of living people due to new drug launches would probably have been greater if the drugs had not reduced mortality.

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Appendix Table 1
Number of SHARE Wave 6 respondents who reported that they had each medical condition, by country

cause	Austria	Belgium	Denmark	France	Germany	Greece	Italy	Portugal	Spain	Sweden	Switzerland	Mean
C00-C14 cancer oral cavity	0	3	2	2	4	0	6	1	5	1	3	2
C15 cancer oesophagus	1	2	3	2	1	2	0	0	3	0	1	1
C16 cancer stomach	1	8	2	1	12	5	18	6	9	7	2	6
C18-C20 cancer colon or rectum	16	40	17	21	22	12	7	10	24	20	5	18
C22 cancer liver	4	6	5	5	9	7	8	2	8	4	4	6
C25 cancer pancreas	1	2	1	2	6	1	11	1	2	3	1	3
C34 cancer lung	6	17	12	15	8	13	14	4	15	5	7	11
C43-C44 cancer skin	24	25	17	8	49	5	1	2	8	12	9	15
C50 cancer breast	33	76	23	59	55	31	71	31	49	42	25	45
C53 cancer cervix	8	16	4	8	8	4	4	5	2	3	2	6
C56 cancer ovary	4	8	7	2	3	4	14	4	5	5	2	5
C61 cancer prostate	19	45	33	35	53	25	22	15	41	58	23	34
C64 cancer kidney	2	5	4	12	11	7	9	2	9	4	0	6
C67 cancer bladder	7	11	2	9	22	6	3	7	9	5	1	7
C71 cancer brain	2	6	2	4	5	2	7	0	7	2	2	4
C73 cancer thyroid	0	6	2	9	8	11	12	4	5	0	0	5
C82-C85 cancer NHL	5	10	10	4	10	4	0	2	1	9	5	5
C91-C95 cancer leukaemia	5	9	8	7	6	1	2	3	5	12	2	5
E10-E14 diabetes	439	645	282	451	613	654	628	363	1003	412	227	520
E78 high cholesterol	716	1724	883	872	791	1518	1206	709	1622	587	452	1007
G20 parkinson disease	30	50	21	33	37	56	41	13	74	30	20	37
G30 alzheimer	130	106	37	70	74	94	108	52	286	75	25	96
I10 hypertension	1462	1944	1253	1268	1850	2046	2111	827	2351	1477	849	1585
I21-I23 heart attack	410	553	313	490	447	550	473	187	570	406	182	416
I63-I64 stroke	212	199	114	134	160	155	159	90	140	165	43	143
J40–J47 chronic lung	217	414	296	250	351	282	275	137	358	176	127	262
K25-K27 ulcer	115	327	88	119	91	347	152	135	155	65	32	148
M05-M06 rheumatoid arthritis	385	389	102	124	522	414	353	196	926	82	110	328
M15-M19 osteoarthritis	230	1866	867	1391	945	679	793	244	612	622	609	805
N18 chronic kidney	53	96	39	71	95	46	94	65	106	31	24	65
S72 hip fracture	36	121	47	81	67	132	73	40	122	106	35	78
Mean	148	282	145	179	204	229	215	102	275	143	91	

Appendix Table 2
Complete estimates of model of log-odds of severe limitation

Parameter	Estimate	Std. Err.	Z	Pr > |Z|
LAUNCHES_1982_2015	−0.020	0.007	−2.85	0.004
ln(PREV)	−0.228	0.069	−3.29	0.001
AGE_MEAN	0.042	0.013	3.10	0.002
OVERWEIGHT%	0.866	0.277	3.12	0.002
OBESE%	0.383	0.426	0.90	0.369
Austria	0.771	0.061	12.70	<.0001
Belgium	0.863	0.094	9.16	<.0001
Denmark	0.162	0.097	1.67	0.095
France	0.816	0.053	15.37	<.0001
Germany	0.996	0.095	10.50	<.0001
Greece	0.008	0.083	0.09	0.926
Italy	0.764	0.080	9.51	<.0001
Portugal	1.010	0.098	10.29	<.0001
Spain	−0.220	0.090	−2.44	0.015

Appendix Table 2 (*continued*)

Parameter	Estimate	Std. Err.	Z	Pr > |Z|
Sweden	0.428	0.057	7.53	<.0001
Switzerland	0.000	0.000	.	.
C00-C14 cancer oral cavity	−0.305	0.211	−1.45	0.147
C15 cancer oesophagus	0.868	0.219	3.96	<.0001
C16 cancer stomach	0.051	0.181	0.28	0.776
C18-C20 cancer colon or rectum	−0.156	0.156	−1.00	0.320
C22 cancer liver	−0.418	0.233	−1.80	0.072
C25 cancer pancreas	0.034	0.236	0.14	0.887
C32 cancer larynx	−0.586	0.274	−2.14	0.032
C34 cancer lung	0.649	0.209	3.10	0.002
C43-C44 cancer skin	−1.001	0.171	−5.86	<.0001
C50 cancer breast	−0.051	0.221	−0.23	0.818
C53 cancer cervix	0.068	0.196	0.35	0.727
C54.1 cancer endometrium	−0.838	0.193	−4.34	<.0001
C56 cancer ovary	0.053	0.225	0.24	0.813
C61 cancer prostate	−0.661	0.120	−5.51	<.0001
C62 cancer testicle	−1.072	0.253	−4.24	<.0001
C64 cancer kidney	−1.329	0.202	−6.58	<.0001
C67 cancer bladder	−0.452	0.165	−2.75	0.006
C71 cancer brain	−0.360	0.222	−1.62	0.105
C73 cancer thyroid	−1.140	0.215	−5.31	<.0001
C82-C85 cancer NHL	−0.092	0.231	−0.40	0.689
C91-C95 cancer leukaemia	−0.523	0.271	−1.93	0.053
E10-E14 diabetes	−0.028	0.216	−0.13	0.895
E78 high cholesterol	−0.745	0.187	−3.99	<.0001
G20 parkinson disease	0.537	0.087	6.20	<.0001
G30 alzheimer	1.067	0.091	11.75	<.0001
H26.9 cataracts	−0.720	0.104	−6.94	<.0001
I10 hypertension	−0.143	0.263	−0.55	0.585
I21-I23 heart attack	0.125	0.133	0.94	0.349
I63-I64 stroke	0.560	0.055	10.27	<.0001
K25-K27 ulcer	−0.444	0.134	−3.31	0.001
M05-M06 rheumatoid arthritis	0.071	0.143	0.50	0.618
M15-M19 osteoarthritis	−0.173	0.171	−1.02	0.310
N18 chronic kidney	0.071	0.081	0.88	0.379
S72 hip fracture	0.000	0.000	.	.
Intercept	−3.560	1.084	−3.28	0.001

Appendix Table 3
Comparison of estimated effects of drug launches on disability when drug launches are categorized into 1, 3, and 4 periods

Dependent variable	No. of launch periods	Mean Estimate	Standard Error	Chi-Square	Pr > ChiSq
log-odds of severe limitation	1	−0.317	0.111	8.12	0.004
	3	−0.301	0.122	6.11	0.013
	4	−0.327	0.126	6.75	0.009
log-odds of any limitation	1	−0.317	0.149	4.54	0.033
	3	−0.282	0.141	3.97	0.046
	4	−0.304	0.142	4.60	0.032
number of ADL limitations	1	−0.136	0.060	5.07	0.024
	3	−0.144	0.056	6.65	0.010
	4	−0.144	0.054	7.27	0.007
number of IADL limitations	1	−0.072	0.088	0.66	0.415
	3	−0.078	0.100	0.61	0.434
	4	−0.079	0.085	0.85	0.357
CASP index	1	0.576	0.324	3.16	0.075
	3	0.641	0.376	2.91	0.088
	4	0.573	0.323	3.15	0.076

no. of launch periods
1 $\beta_{0\text{-}33}$ * mean(LAUNCHES_1982_2015$_{dc}$)

3 ($\beta_{0\text{-}9}$ * mean(LAUNCHES_2006_2015$_{dc}$)) + ($\beta_{10\text{-}19}$ * mean(LAUNCHES_1996_2005$_{dc}$)) + ($\beta_{20\text{-}33}$ * mean(LAUNCHES_1982_1995$_{dc}$))

4 ($\beta_{0\text{-}4}$ * mean(LAUNCHES_2011_2015$_{dc}$)) + ($\beta_{5\text{-}9}$ * mean(LAUNCHES_2006_2010$_{dc}$)) + ($\beta_{10\text{-}14}$ * mean(LAUNCHES_2001_2005$_{dc}$)) + ($\beta_{15\text{-}33}$ * mean(LAUNCHES_1982_2000$_{dc}$))

Appendix Table 4
2014 Pharmaceutical expenditure, by country

Country	TOTAL PHARMACEUTICAL SALES (USD BILLION)	PHARMACEUTICAL SALES (USD PER CAPITA)	Population (millions)
Austria	$8.1	$951	8.5
Belgium	$7.7	$689	11.2
Denmark	$3.8	$675	5.6
France	$44.7	$697	64.1
Germany	$68.9	$667	103.2
Greece	$6.6	$598	11.0
Italy	$35.3	$591	59.8
Portugal	$4.6	$437	10.4
Spain	$32.8	$709	46.2
Sweden	$5.5	$566	9.7
Switzerland	$7.7	$939	8.2
TOTAL	$225.6	$667	338.1

Source: International Federation of Pharmaceutical Manufacturers & Associations (2017).

References

1. Nevitt MC, Thompson DE, Black DM, et al. Effect of alendronate on limited-activity days and bed-disability days caused by back pain in postmenopausal women with existing vertebral fractures. Fracture Intervention Trial Research Group. *Arch Intern Med*. 2000;160(1):77–85. Jan. 10.
2. Filippini M, Bazzani C, Atzeni F, et al. Effects of anti-TNF alpha drugs on disability in patients with rheumatoid arthritis: long-term real-life data from the lorhen registry. *BioMed Res Int*. 2014;2014:416892, 2014 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4109221/.
3. Andalo D. Alemtuzumab reduces disability in patients with MS. *Pharmaceut J*; 2016, 14 October https://www.pharmaceutical-journal.com/news-and-analysis/news/alemtuzumab-reduces-disability-in-patients-with-ms/20201832.article.
4. Civio. *4 Years after the Hepatitis C Revolution, How Much Do New Drugs Cost?*; 2017. https://civio.es/medicamentalia/2017/10/25/sovaldi-4-years-after-the-hepatitis-c-revolution-how-much-do-new-drugs-cost/.
5. Lichtenberg FR. Pharmaceutical price discrimination and social welfare. *Capitalism Soc*. 2010;5(1).
6. Lichtenberg FR. The impact of new drug launches on life-years lost in 2015 from 19 types of cancer in 36 countries. *J Demographic Economics*. 2018;84:309–354. https://doi.org/10.1017/dem.2018.11.
7. Acemoglu D, Linn J. Market size in innovation: theory and evidence from the pharmaceutical industry. *Q J Econ*. 2004;119(3):1049–1090 (August).
8. Danzon PM, Wang YR, Wang L. The impact of price regulation on the launch delay of new drugs—evidence from twenty-five major markets in the 1990s. *Health Econ*. 2005;14(3):269–292 (March).
9. Hyde M, Wiggins RD, Higgs P, Blane DB. A measure of quality of life in early old age: the theory, development and properties of a needs satisfaction model (CASP-19). *Aging Ment Health*. 2003;7(3).
10. Howel D. Interpreting and evaluating the CASP-19 quality of life measure in older people. *Age Ageing*. 2012;41(5):612–617.
11. Armour BS, Courtney-Long E, Campbell VA, Wethington HR. Estimating disability prevalence among adults by body mass index: 2003-2009 National Health Interview Survey. *Prev Chronic Dis*. 2012;9:E178.
12. Lichtenberg FR. The impact of new (orphan) drug approvals on premature mortality from rare diseases in the U.S. and France, 1999-2007. *Eur J Health Econ*. 2013;14(1):41–56.
13. Lichtenberg FR. "The impact of pharmaceutical innovation on longevity and medical expenditure in France, 2000–2009. *Econ Hum Biol*. 2014;13:107–127 (March).
14. Hostenkamp G, Lichtenberg FR. The impact of recent chemotherapy innovation on the longevity of myeloma patients: US and international evidence. *Soc Sci Med*. 2015;130:162–171.
15. Lichtenberg FR. The impact of pharmaceutical innovation on disability days and the use of medical services in the United States, 1997-2010. *J Hum Cap*. 2014;8(4):432–480 (Winter).
16. Grossman Gene M, Helpman Elhanan. *Innovation and Growth in the Global Economy*. Cambridge: MIT Press; 1993.
17. Bresnahan TF, Gordon RJ. *The Economics of New Goods*. Chicago: University of Chicago Press; 1996.
18. Bils M. *Measuring the Growth from Better and Better Goods*. July; 2004. NBER working paper no. 10606.
19. Jovanovic B, Yatsenko Y. Investment in vintage capital. *J Econ Theor*. 2012;147(2):551–569.
20. Börsch-Supan A. *Survey of Health, Ageing and Retirement in Europe (SHARE) Wave 6. Release Version: 6.0.0*. SHARE-ERIC. Data set; 2017. https://doi.org/10.6103/SHARE.w6.600.
21. Centre National Hospitalier d'Information sur le Médicament. *Thériaque Database*. 2018.
22. Lichtenberg FR, Waldfogel J. Does misery love company? Evidence from pharmaceutical markets before and after the orphan drug act. *Mich Telecommun Technol Law Rev*. 2009;335.
23. Wikipedia. *Multicollinearity*; 2018. https://en.wikipedia.org/wiki/Multicollinearity.
24. Verropoulou G, Tsimbos C. Disability trends among older adults in ten European countries over 2004–2013, using various indicators and Survey of Health, Ageing and Retirement in Europe (SHARE) data. *Ageing Soc*. 2017;37(10):2152–2182. https://www.cambridge.org/core/journals/ageing-and-society/article/disability-trends-among-older-adults-in-ten-european-countries-over-20042013-using-various-indicators-and-survey-of-health-ageing-and-retirement-in-europe-share-data/7368F81F1968E763F219C6BFFA0.
25. International Federation of Pharmaceutical Manufacturers & Associations. *The Pharmaceutical Industry and Global Health: Facts and Figures 2017*; 2017. https://www.ifpma.org/wp-content/uploads/2017/02/IFPMA-Facts-And-Figures-2017.pdf.