The impact of pharmaceutical innovation on mortality, disability, and hospitalization:
evidence from 4 studies

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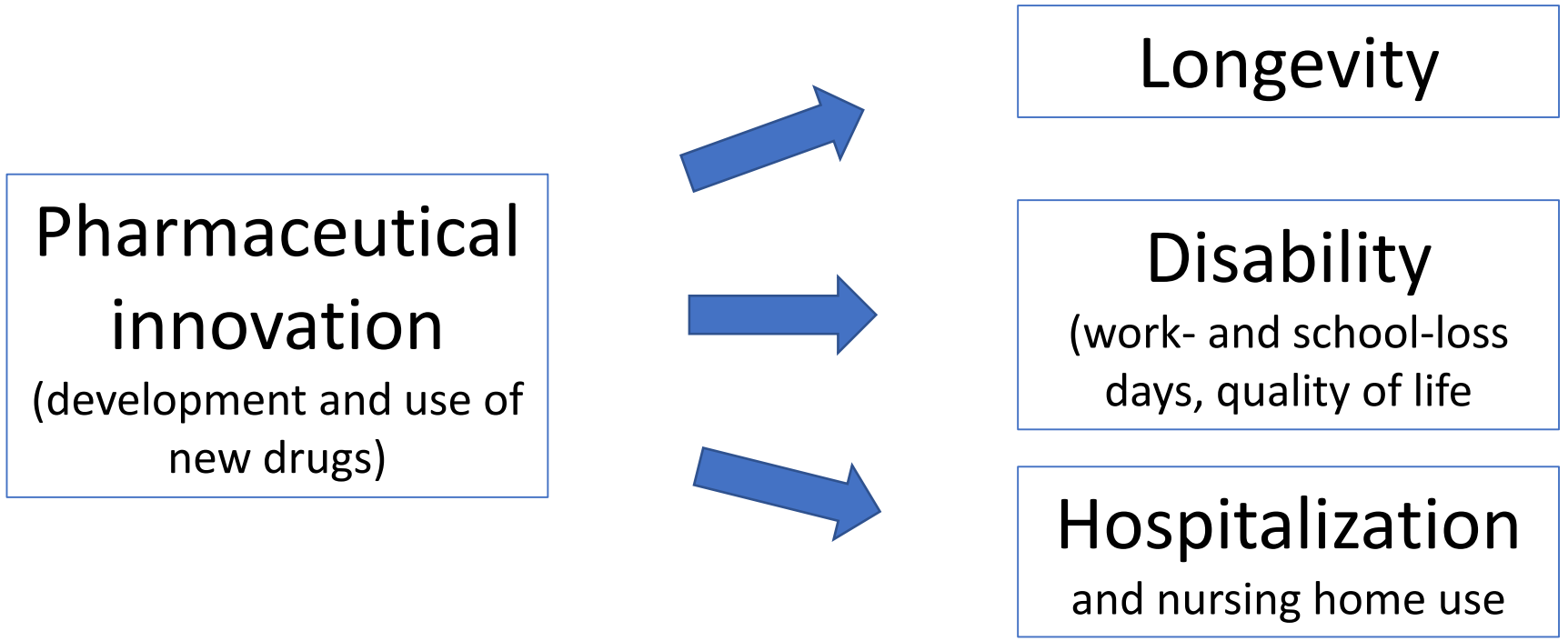
Three types of health outcomes



4 studies of impact of prescription drugs on health

study	health outcome	drug measure	region(s)	data
1	mortality	number of drugs	36 countries	19 cancer sites, 36 countries
2	disability	number of drugs	11 European countries	31 diseases, 11 countries
3	hospitalization	vintage of drugs	USA	X diseases, 15 years
4	mortality	vintage of drugs	Puerto Rico	500,000 patients

3 alternative research designs

- Studies 1 and 2: is *relative* mortality and disability from a disease in a country lower when the *relative* number of drugs available to treat that disease in that country is higher?
- Study 3: has hospitalization in the USA declined more for diseases that have experienced more pharmaceutical innovation?
- Study 4: do Puerto Rican Medicaid patients using new drugs live longer than patients using older drugs?

Two alternative measures of (access to) pharmaceutical innovation

- *Number* of drugs for a disease that have been launched
- Mean vintage (e.g. FDA approval year) of drugs used to treat a patient or a medical condition

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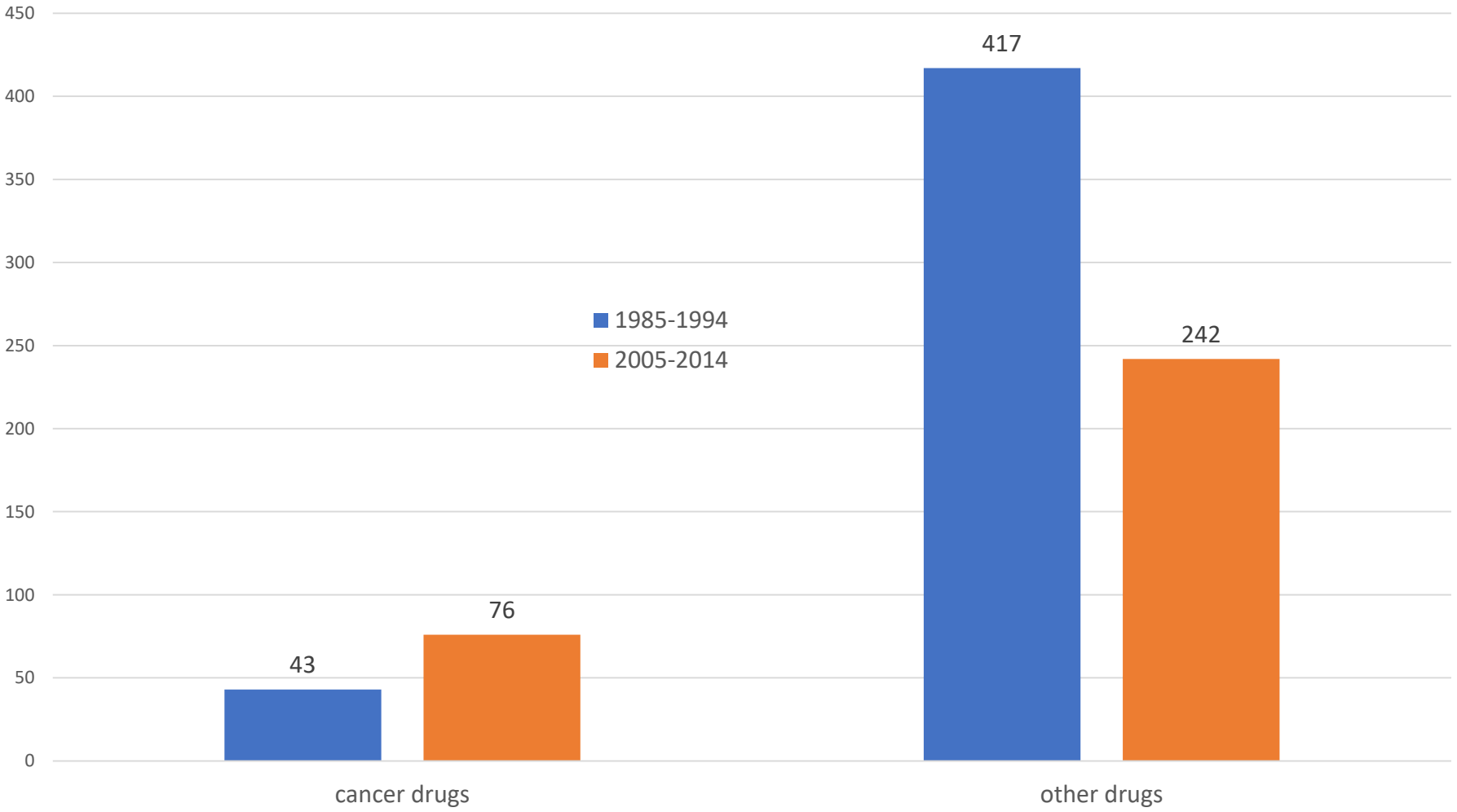
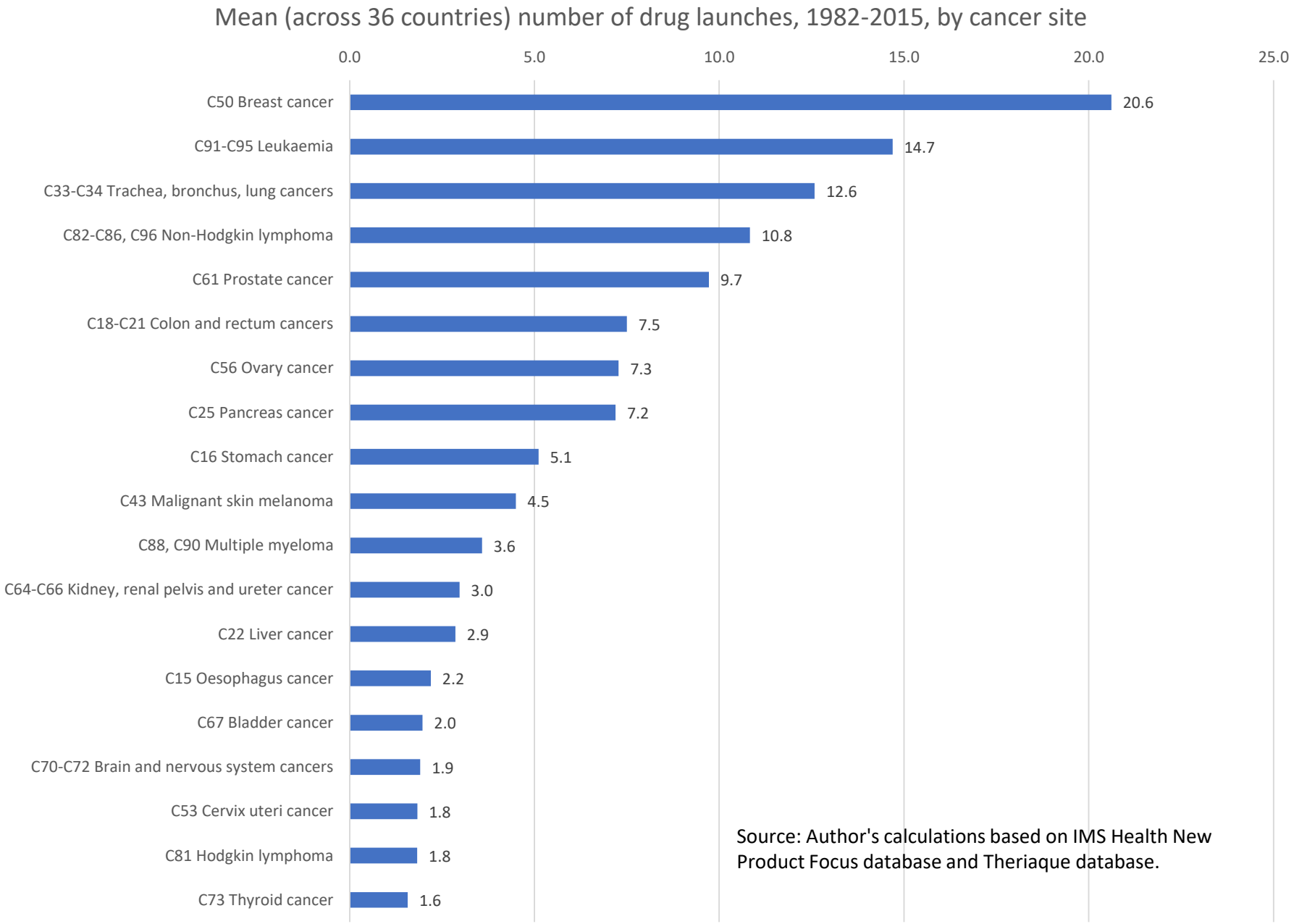
Number of new cancer drugs and other new drugs launched worldwide, 1985-1994 and 2005-2014



Source: author's calculations based on IMS Health New Product Focus database
"Cancer NMEs" are NMEs in EphMRA/PBIRG Anatomical Classification L (ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS)

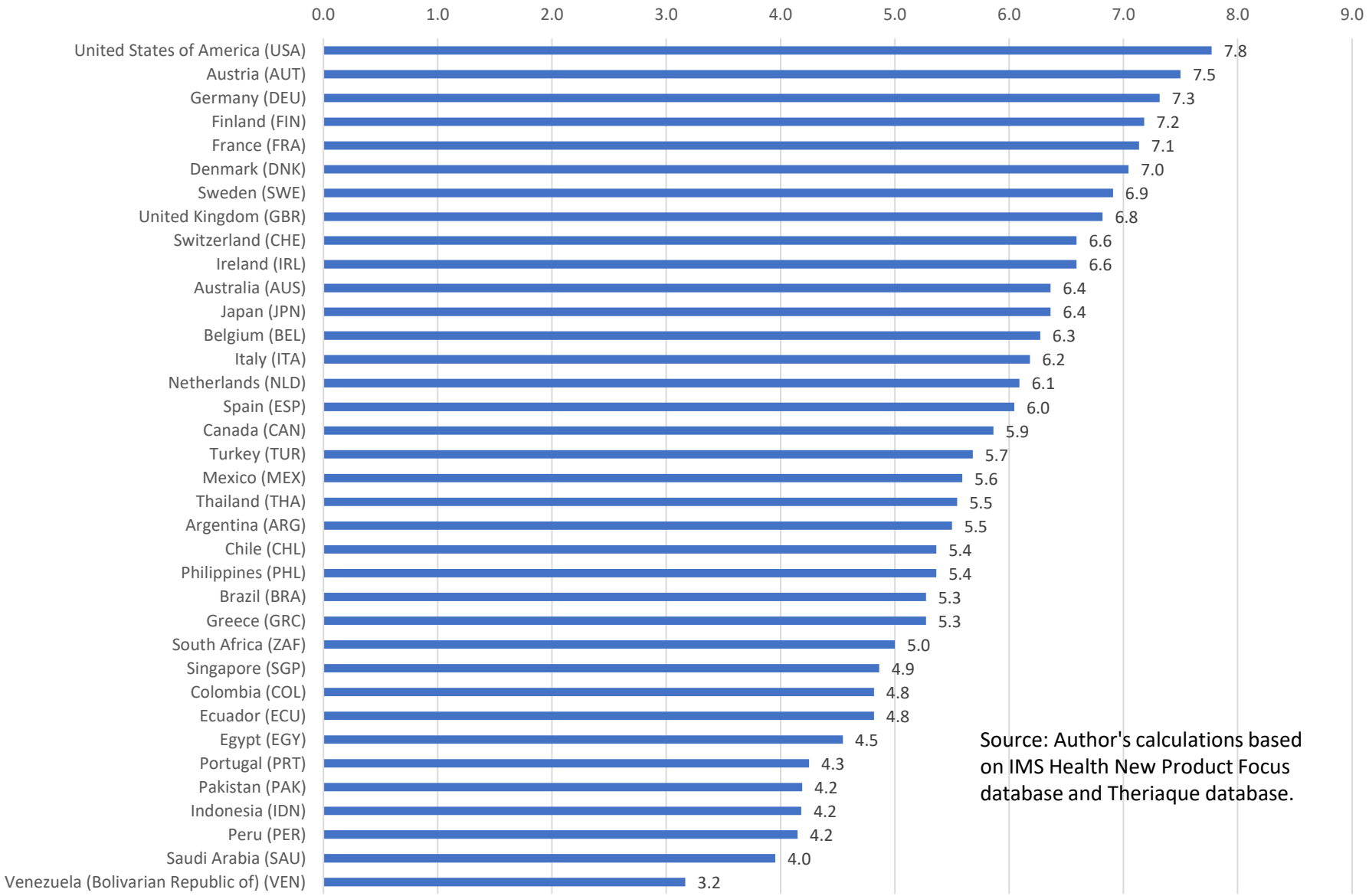
Launch of a drug in a country is a necessary condition for access, not a sufficient condition



Source: Author's calculations based on IMS Health New Product Focus database and Theriaque database.

Figure 3

Mean (across 19 cancer sites) number of drug launches, 1982-2015, by country



Source: Author's calculations based on IMS Health New Product Focus database and Theriaque database.

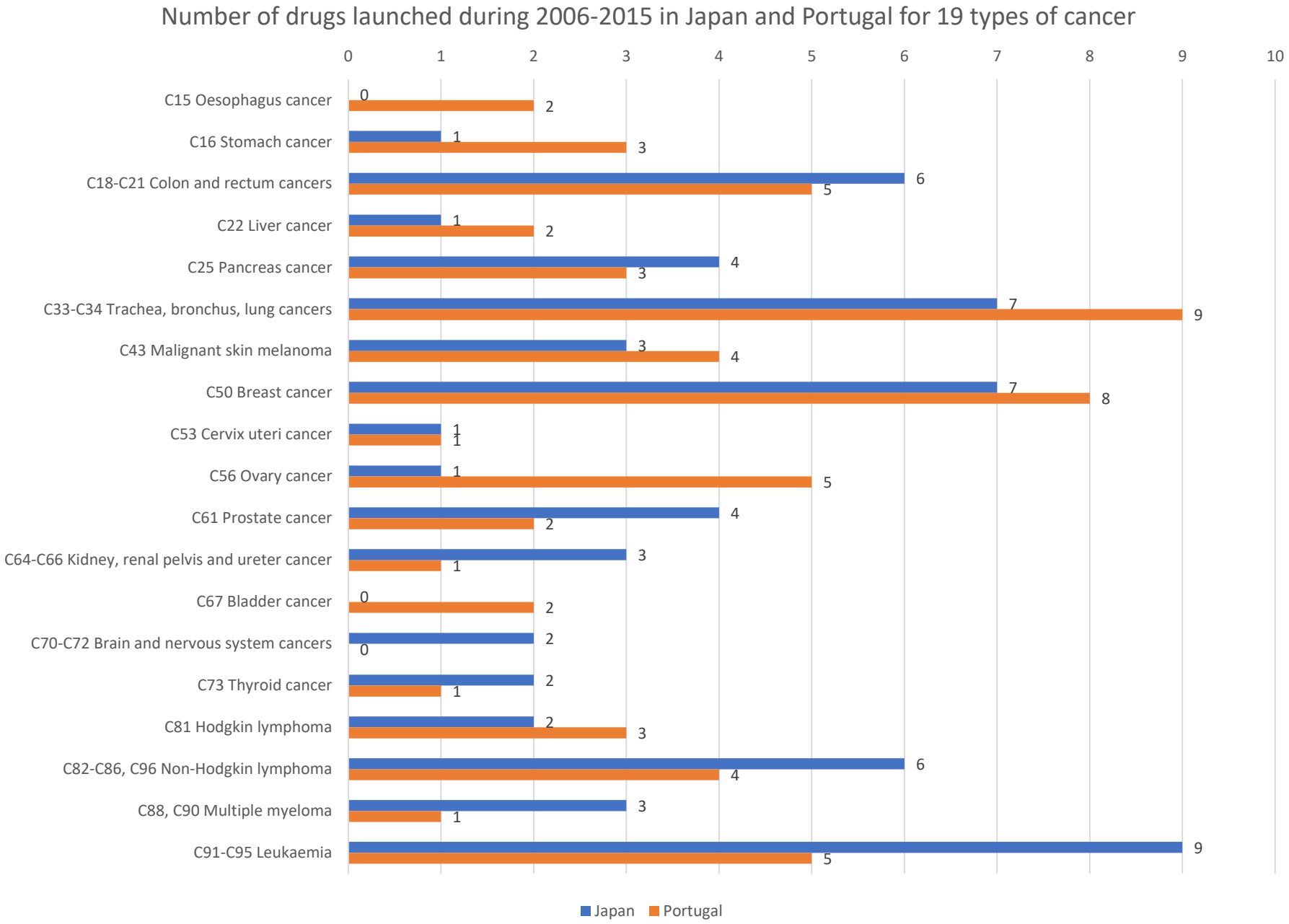
Objective

- This study seeks to determine the extent to which the number of years of life lost (YLL) due to cancer in 36 countries in 2015 was reduced by previous launches of new cancer drugs, and to measure the average cost-effectiveness of (cost per life-year gained from) those drugs.

- If 100 people die from lung cancer at age 60, they have collectively lost 500 (= 100 * (65 – 60)) years of life before age 65, and 1500 (= 100 * (75 – 60)) years of life before age 75. Hence YLL depends on the number of deaths, age at death, and the age cutoff that is used.

Research design

- I will analyze the correlation across countries between *relative* mortality from each type of cancer in 2015 and the *relative* number of drugs previously launched in that country to treat that type of cancer, controlling for relative incidence.
- The mortality models I will estimate will include both **country fixed effects**, which control for potential determinants of mortality (e.g. national per capita income, education, and average health expenditure) that are invariant across cancer sites within a country, and **cancer-site fixed effects**, which control for potential determinants of mortality that are invariant across countries within a cancer site.
- This approach is feasible because the *relative* number of drugs launched for different types of cancer has varied considerably across countries.


Number of drugs launched during 2006-2015 in Japan and Portugal for 19 types of cancer
0
1
2
3
4
5
6
7
8
9
10
C15 Oesophagus cancer
C16 Stomach cancer
C18-C21 Colon and rectum cancers
C22 Liver cancer
C25 Pancreas cancer
C33-C34 Trachea, bronchus, lung cancers
C43 Malignant skin melanoma
C50 Breast cancer
C53 Cervix uteri cancer
C56 Ovary cancer
C61 Prostate cancer
C64-C66 Kidney, renal pelvis and ureter cancer
C67 Bladder cancer
C70-C72 Brain and nervous system cancers
C73 Thyroid cancer
C81 Hodgkin lymphoma
C82-C86, C96 Non-Hodgkin lymphoma
C88, C90 Multiple myeloma
C91-C95 Leukaemia
0 2
1 3
6 5
1 2
4 3
7 9
3 4
7 8
1 1
1 5
4 2
3 1
0 2
2 0
2 1
2 3
6 4
3 1
9 5
Japan
Portugal

Econometric model of life-years lost from cancer

$$\ln(DALYS\_2015_{sc}) = \beta_{0\text{-}4}\, LAUNCHES\_2011\_2015_{sc} + \beta_{5\text{-}9}\, LAUNCHES\_2006\_2010_{sc} + \beta_{10\text{-}14}\, LAUNCHES\_2001\_2005_{sc} + \beta_{15\text{-}33}\, LAUNCHES\_1982\_2000_{sc} + \gamma \ln(CASES\_2012_{sc}) + \alpha_s + \pi_c + \varepsilon_{sc} \quad (1)$$

$DALYS\_2015_{sc}$	= the number of disability-adjusted life years (DALYs) lost due to cancer at site s in country c in 2015
$LAUNCHES\_2011\_2015_{sc}$	= the number of post-1981new chemical entities used to treat cancer at site s launched in country c during 2011-2015
$CASES\_2012_{sc}$	= the number of people diagnosed with cancer at site s in country c in 2012
α_s	= a fixed effect for cancer at site s
π_c	= a fixed effect for country c

Eq. (1) will be estimated by weighted least squares, weighting by Y_{sc}. The disturbances of eq. (1) will be clustered within countries or within cancer sites. When eq. (1) is estimated without weighting, the residuals clearly exhibit heteroskedasticity: the variance of the residuals is strongly inversely related to $Y_{sc,2015}$.

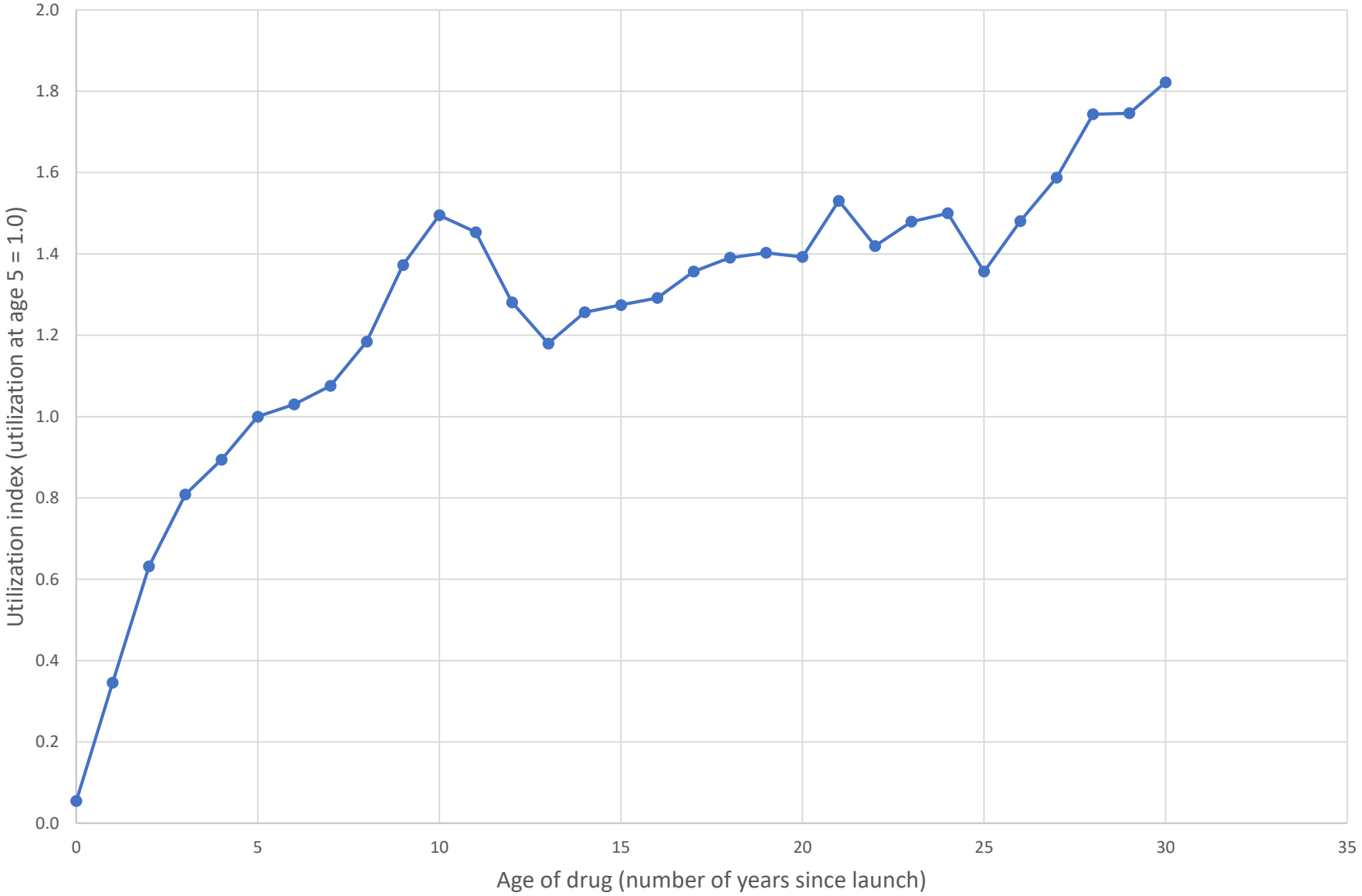
Other indicators of disease burden

$DALYS\_2015_{sc}$	= the number of disability-adjusted life years (DALYs) lost due to cancer at site s in country c in 2015
YLL_2015_{sc}	= the number of years of life lost (as measured in the WHO Global Burden of Disease Estimates) due to cancer at site s in country c in 2015
YLD_2015_{sc}	= the number of years lost to disability due to cancer at site s in country c in 2015
$YLL75\_2015_{sc}$	= the number of years of life lost before age 75 due to cancer at site s in country c in 2015
$YLL65\_2015_{sc}$	= the number of years of life lost before age 65 due to cancer at site s in country c in 2015

Impact on drug launch on YLL depends on both drug quality and drug quantity

- The effect of a drug's launch on mortality is hypothesized to depend on both the *quantity* and the *quality* (or effectiveness) of the drug.
- Indeed, it is likely to depend on the *interaction* between quantity and quality: a quality improvement will have a greater impact on mortality if drug utilization (quantity) is high.
- Drugs launched in the 4 different periods are likely to vary (in opposite ways) with respect to both quantity (in 2015) and quality:
  - Newer drugs are likely to be of higher quality than older drugs.
  - On the other hand, utilization of new drugs tends to be much lower than utilization of old drugs.

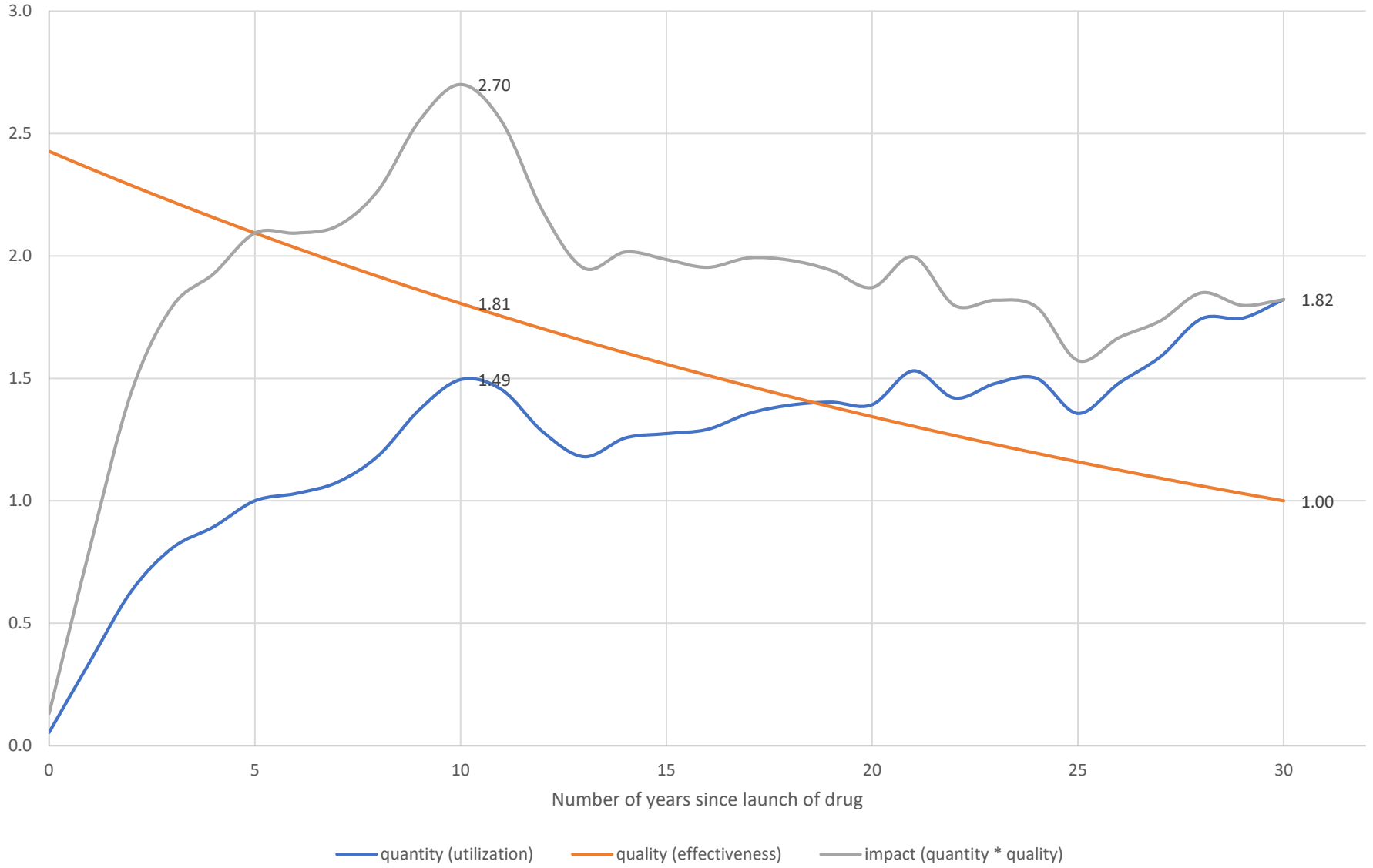
Figure 5
Cancer drug age-utilization profile



Mean utilization of a drug is about twice as high 5-9 years after launch as it was 0-4 years after launch

years since launch	mean utilization (relative to utilization 5 years after launch)
0-4	0.55
5-9	1.13
10-14	1.33
15-31	1.49

Figure 6
Hypothetical quantity, quality, and impact (= quantity * quality) of a drug when quality increases at a 3% annual rate with respect to launch year



Data sources

- *Mortality*: *WHO Global Health Estimates 2015: Disease burden by Cause* and *Deaths by Cause* databases
- *Cancer incidence*: GLOBOCAN 2002 and 2012
- *Drug indications*: *Thériaque* database (Centre National Hospitalier d'Information sur le Médicament (2017))
- *Drug launch years*: IMS Health *New Product Focus* database
- *Drug utilization*: IMS Health *MIDAS* database

Table 1			
Summary statistics, 19 major cancer sites in 36 countries			
	2005	2015	% change
disability-adjusted life years (DALYs)	68,179,003	76,596,299	12%
years of life lost, as measured in the WHO Global Burden of Disease Estimates (YLL)	65,246,858	72,439,899	11%
years lost due to disability (YLD)	2,932,144	4,156,401	42%
years of life lost before age 75 (YLL75)	23,398,525	25,137,974	7%
years of life lost before age 65 (YLL65)	11,163,603	11,545,184	3%
number diagnosed 3 years earlier (CASES)	4,474,445	5,716,879	28%
Source: Author's calculations based on WHO Global Health Estimates 2015: Disease burden by Cause database (World Health Organization (2016a)); WHO Global Health Estimates 2015: Deaths by Cause database (World Health Organization (2016b)); GLOBOCAN 2002 (Ferlay et al (2004)); and GLOBOCAN 2012 (International Agency for Research on Cancer (2017b)).			

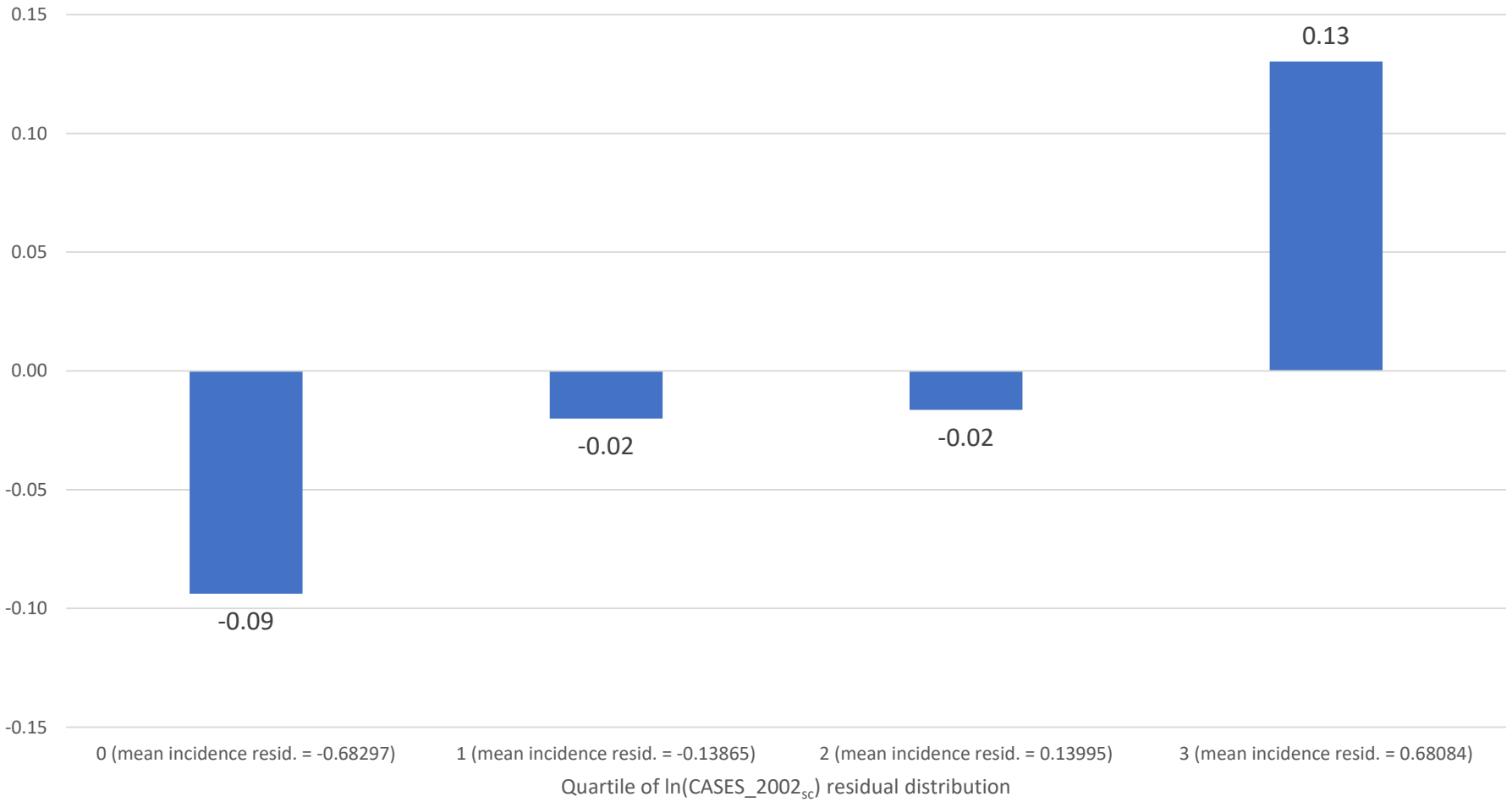
The effect of incidence on the number of new drug launches

- 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*.
- $N\_LAUNCHES\_2003\_2012_{sc} = \sigma \ln(CASES\_2002_{sc}) + \alpha_s + \delta_c + \varepsilon_{sc}$ (3)

$N\_LAUNCHES\_2003\_2012_{sc}$	= the number of drugs to treat cancer at site s launched in country c during 2003-2012
$CASES\_2002_{sc}$	= the number of patients diagnosed with cancer at site s in country c in 2002

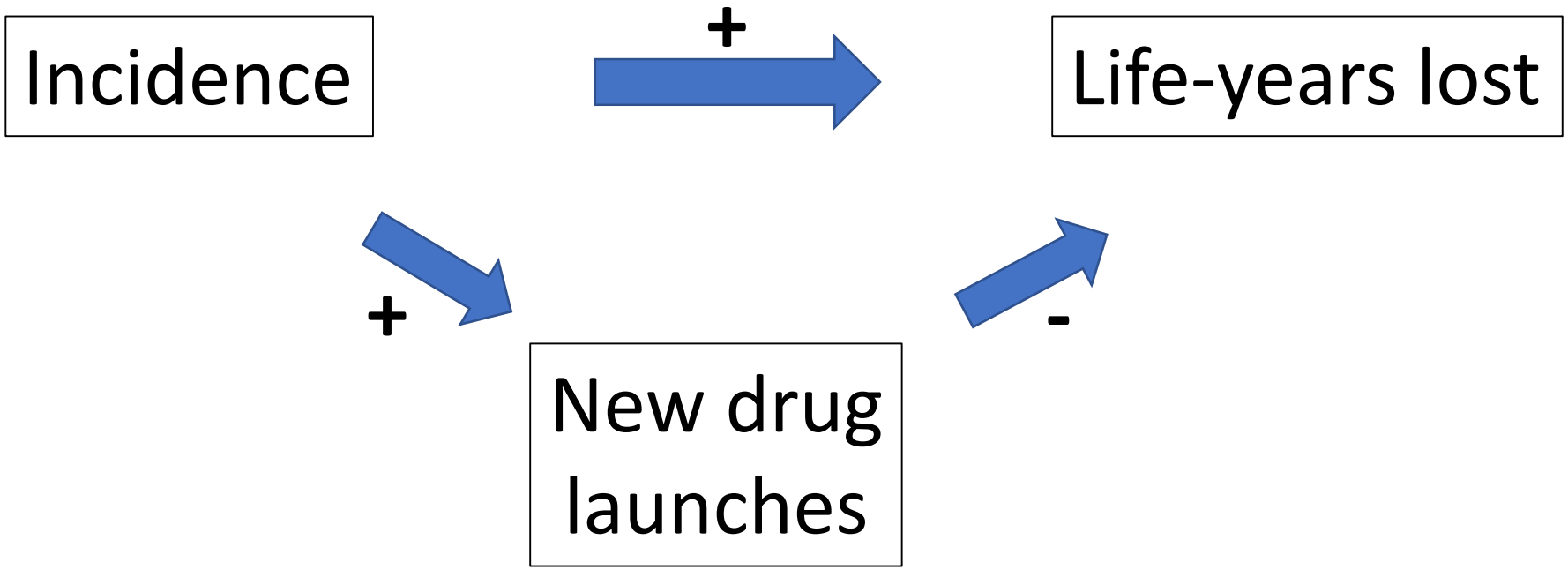
The estimate of σ is positive and significant: estimate = 0.1872; standard error = .0662; Z = 2.83; p-value = .0047. This signifies that larger relative market size (number of patients diagnosed) increases the relative number of drugs launched.

Figure 7
Mean N_LAUNCHES_2003_2012$_{sc}$ residual,
by quartile of ln(CASES_2002$_{sc}$) residual distribution



The N_LAUNCHES_2003_2012$_{sc}$ residual is the residual from the regression N_LAUNCHES_2003_2012$_{sc}$ = $\alpha_s + \pi_c + \varepsilon_{sc}$
The ln(CASES_2002$_{sc}$) residual is the residual from the regression ln(CASES_2002$_{sc}$) = $\alpha_s + \pi_c + \varepsilon_{sc}$

Direct and indirect effects of incidence on life-years lost

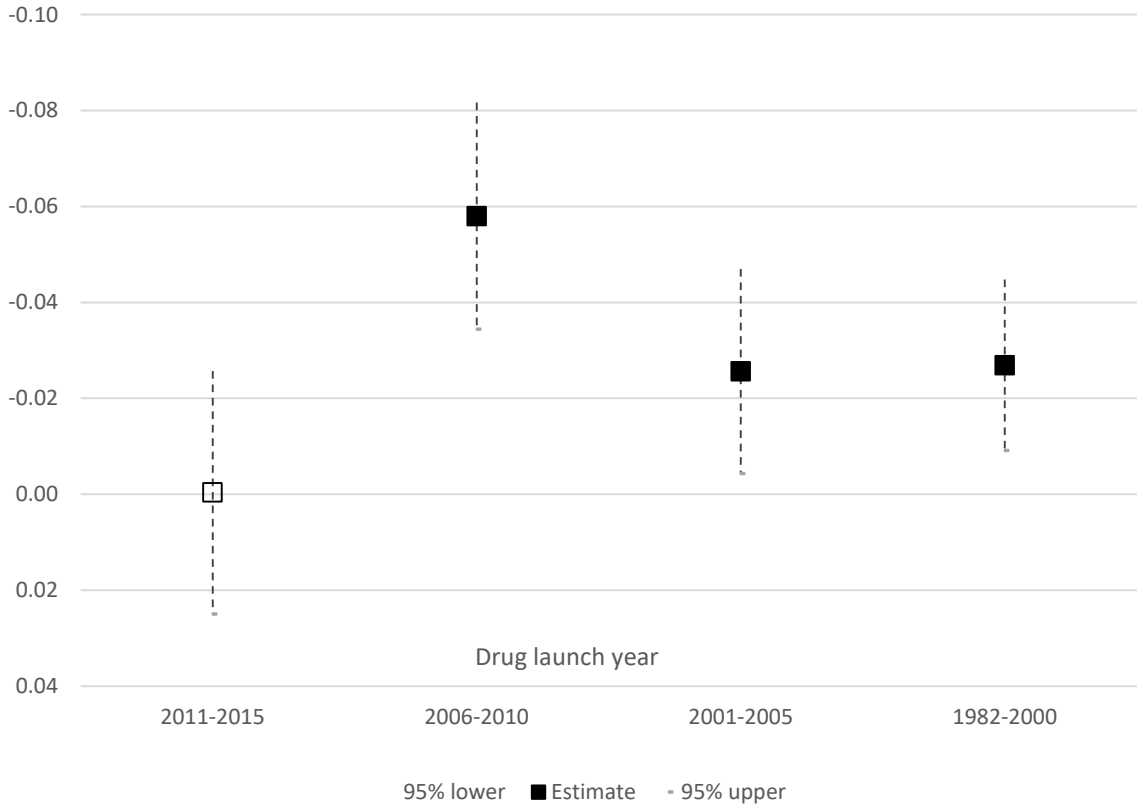


Estimates of difference-in-differences model of life-years lost (eq. (1))

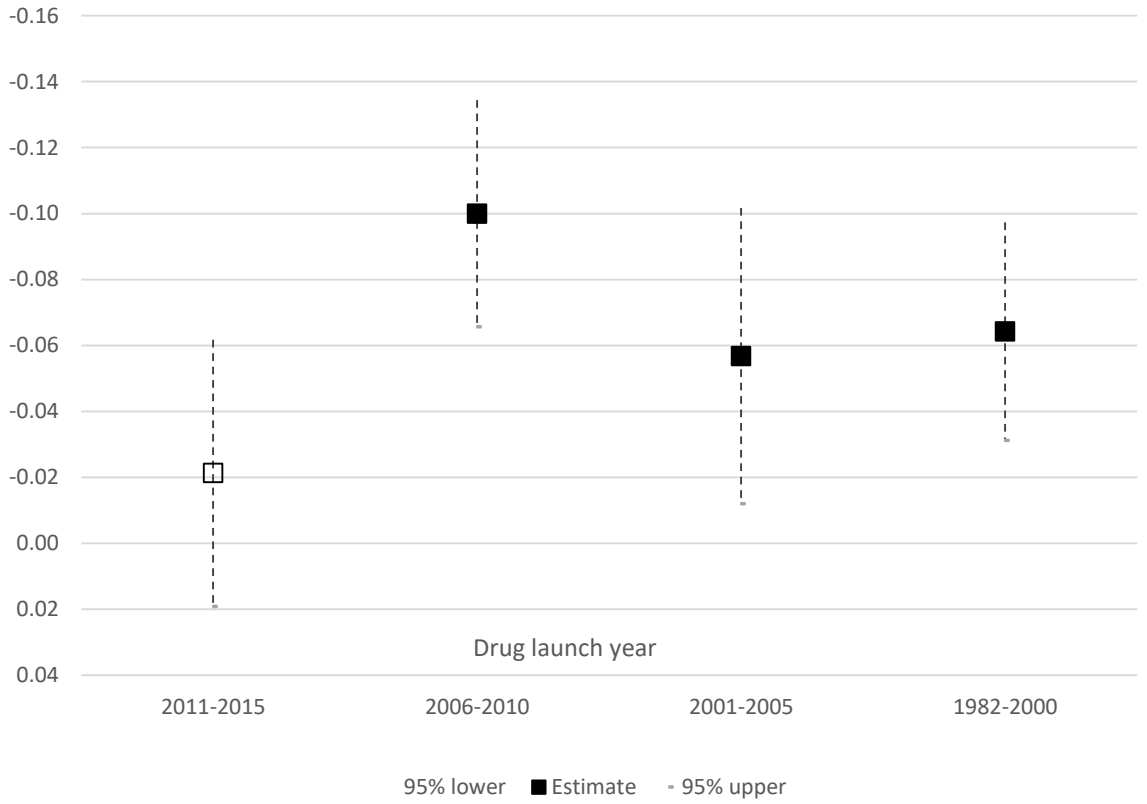
Parameter	Regressor	Estimate	Std. Err.	Z	Pr > |Z|
Dependent variable = DALYS_2015					
$\beta_{0\text{-}4}$	LAUNCHES_2011_2015	0.000	0.013	-0.03	0.977
$\beta_{5\text{-}9}$	LAUNCHES_2006_2010	**-0.058**	**0.012**	**-4.81**	**<.0001**
$\beta_{10\text{-}14}$	LAUNCHES_2001_2005	**-0.026**	**0.011**	**-2.35**	**0.019**
$\beta_{15\text{-}33}$	LAUNCHES_1982_2000	**-0.027**	**0.009**	**-2.96**	**0.003**
γ	ln(CASES_2012)	**0.849**	**0.032**	**26.27**	**<.0001**
Dependent variable = YLL65_2015					
$\beta_{0\text{-}4}$	LAUNCHES_2011_2015	-0.021	0.021	-1.03	0.303
$\beta_{5\text{-}9}$	LAUNCHES_2006_2010	**-0.100**	**0.018**	**-5.69**	**<.0001**
$\beta_{10\text{-}14}$	LAUNCHES_2001_2005	**-0.057**	**0.023**	**-2.48**	**0.013**
$\beta_{15\text{-}33}$	LAUNCHES_1982_2000	**-0.064**	**0.017**	**-3.81**	**1E-04**
γ	ln(CASES_2012)	**0.833**	**0.063**	**13.16**	**<.0001**

Estimated effects of new drug launches on DALYs and YLL65 in 2015

A. Effect of new drug launches, by period, on number of **disability-adjusted life-years** in 2015

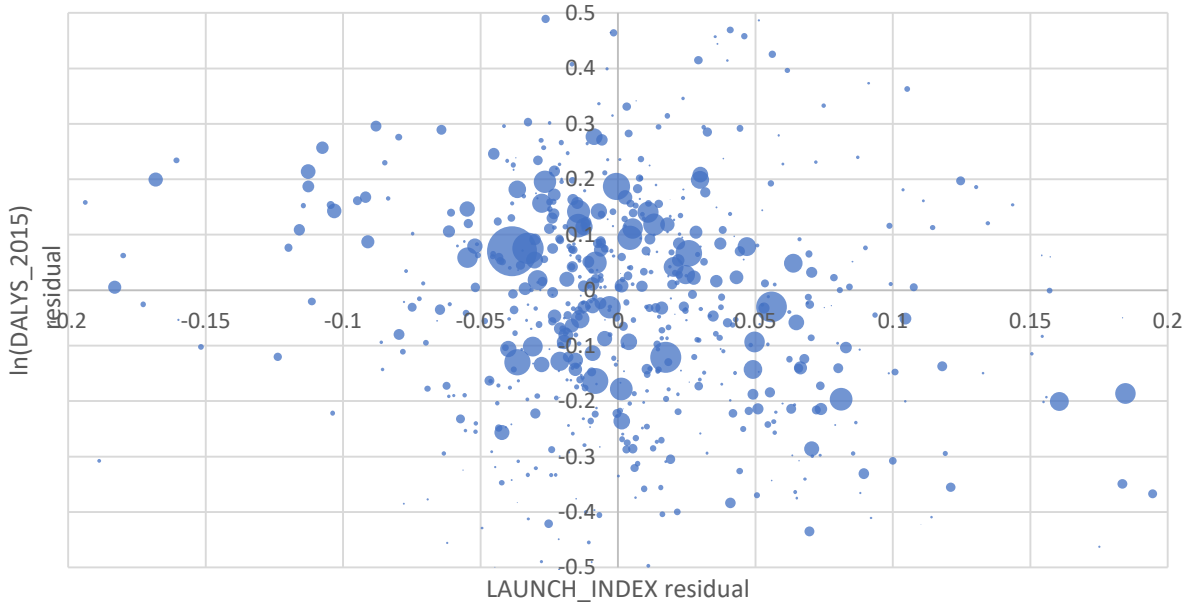


B. Effect of new drug launches, by period, on number of **years of life lost before age 65** in 2015



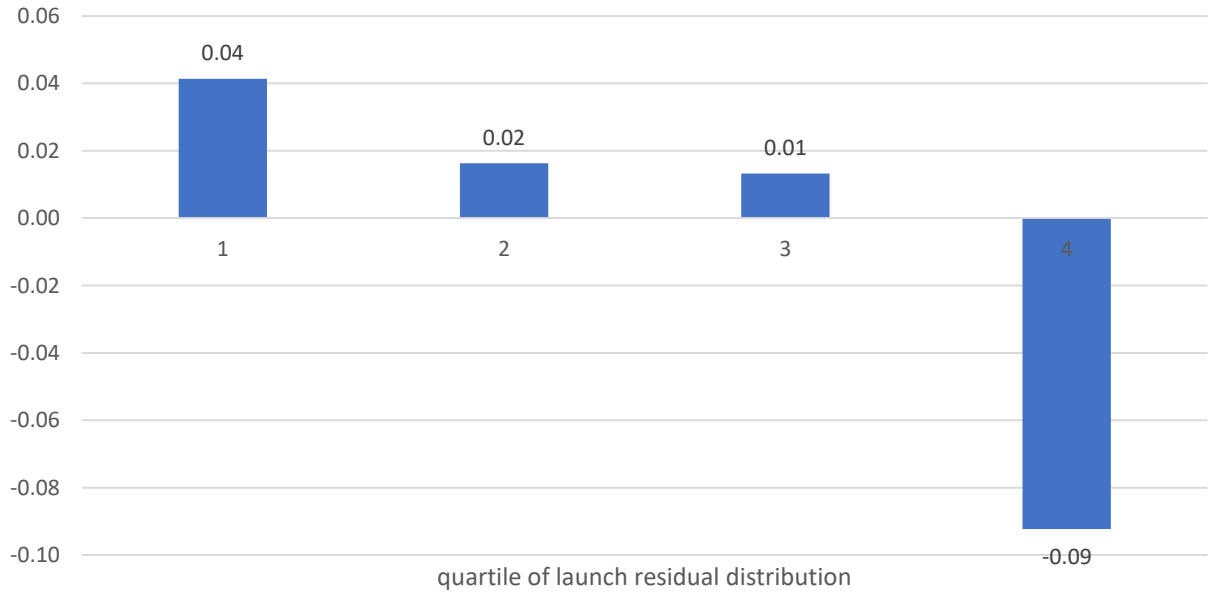
Relationship between LAUNCH_INDEX residual and ln(DALYS_2015) residual

A. Bubble plot of LAUNCH_INDEX residuals against ln(DALYS_2015) residuals



Bubble size is proportional to $DALYs\_2015_{sc}$

B. Mean ln(DALYS_2015) residual, by quartile of LAUNCH_INDEX residual distribution



Effect on mortality of one drug launch

- DALYs and life-years lost are unrelated to drug launches 0-4 years earlier.
- However, mortality is significantly inversely related to the number of drug launches at least 5 years earlier, especially to drug launches 5-9 years earlier.
  - One additional drug for a cancer site launched during 2006-2010 is estimated to have reduced the number of 2015 DALYs due to cancer at that site by 5.8%
  - One additional drug launched during 1982-2005 is estimated to have reduced the number of 2015 DALYs by about 2.6%.

Life-years gained calculation

Column		1	2	3	4	
		Disease burden measure				
Row		DALY	YLL	YLL75	YLL65	Basis
	Life-years gained calculation					
1	$b_{5\text{-}9}$	-0.058	-0.064	-0.091	-0.100	Table 2
2	weighted mean(LAUNCHES_2006_2010)	1.505	1.487	1.532	1.607	Author's calculations based on IMS New Product Focus and Theriaque databases
3	log-change in 2015 life-years lost due to LAUNCHES_2006_2010	-0.087	-0.095	-0.139	-0.161	(1) * (2)
4	life-years lost due to all types of cancer in 36 countries in 2015	88,108,225	83,467,085	30,255,229	14,451,091	World Health Organization (2016a, 2016b).
5	reduction in 2015 life-years lost due to LAUNCHES_2006_2010	8,035,792	8,280,097	4,509,546	2,520,071	(exp(-(3))-1) * (4)

Reduction in YLL

- The estimates implied that drugs launched during 2006-2010 reduced the number of cancer DALYs in 2015 by about 8.7%
- In the absence of new drug launches during 2006-2010, there would have been 8.04 million additional DALYs due to cancer in the 36 countries.
- The estimates also implied that, in the absence of new drug launches during 2006-2010, there would have been 4.51 million additional years of life lost before age 75, and 2.52 million additional years of life lost before age 65.

Reduction in DALYs

- We also estimated that drugs launched during the entire 1982-2010 period reduced the number of cancer DALYs in 2015 by about 23.0%
- In the absence of new drug launches during 1982-2010, there would have been 26.3 million additional DALYs in 2015.
- The 9 countries with the largest number of drug launches during 1982-2010 are estimated to have had 14% fewer cancer DALYs (controlling for incidence) in 2015 than the 9 countries with the smallest number of drug launches during 1982-2010.

Column		1	2	3	4	
		Disease burden measure				
Row		DALY	YLL	YLL75	YLL65	Basis
	Pharmaceutical expenditure calculation					
6	global cost (in millions) of oncology therapeutics and supportive care drugs in 2015, measured at invoice price levels	$107,000				IMS Institute for Healthcare Informatics (2016, p. 20)
7	36-country share of total pharmaceutical expenditure in 2014	78%				International Federation of Pharmaceutical Manufacturers & Associations (2017, Annex 2)
8	36-country cost (in millions) of oncology therapeutics and supportive care drugs in 2015	$83,076				(6) * (7)
9	fraction of 2010 pharma expend. on drugs launched in country during 2001-2005, 31 countries	16%				Author's calculations based on IMS MIDAS data
10	estimated 36-country expenditure (in millions) in 2015 on cancer drugs launched during 2006-2010	$13,539				(8) * (9)
	age group	All ages	All ages	Below 75	Below 65	
11	estimated age group share of cancer drug expenditure	100%	100%	76%	52%	International Agency for Research on Cancer (2017b)
12	estimated 2015 36-country expenditure (in millions) by age group on cancer drugs launched during 2006-2010	$13,539	$13,539	$10,264	$7,106	(10) * (11)
	Pharmaceutical expenditure per life-year gained calculation					
13	pharmaceutical expenditure per life-year gained	$1,685	$1,635	$2,276	$2,820	(12) / (5)

Estimated cost per life-year gained

- Estimates of the cost per life-year gained in 2015 from drugs launched during 2006-2010 ranged between $1635 (life-years gained at all ages) and $2820 (life-years gained before age 65).
- These estimates are similar to those obtained in previous country-specific studies of Belgium, Canada, and Mexico, and are well below the estimate obtained in one study of Switzerland.

Forecast

- Mortality in 2015 is strongly inversely related to the number of drug launches in 2006-2010.
- If the relationship between mortality in 2020 and the number of drug launches in 2011-2015 is similar, drug launches 5-9 years earlier will reduce mortality even more (by 9.9%) between 2015 and 2020 than they did (by 8.4%) between 2010 and 2015.

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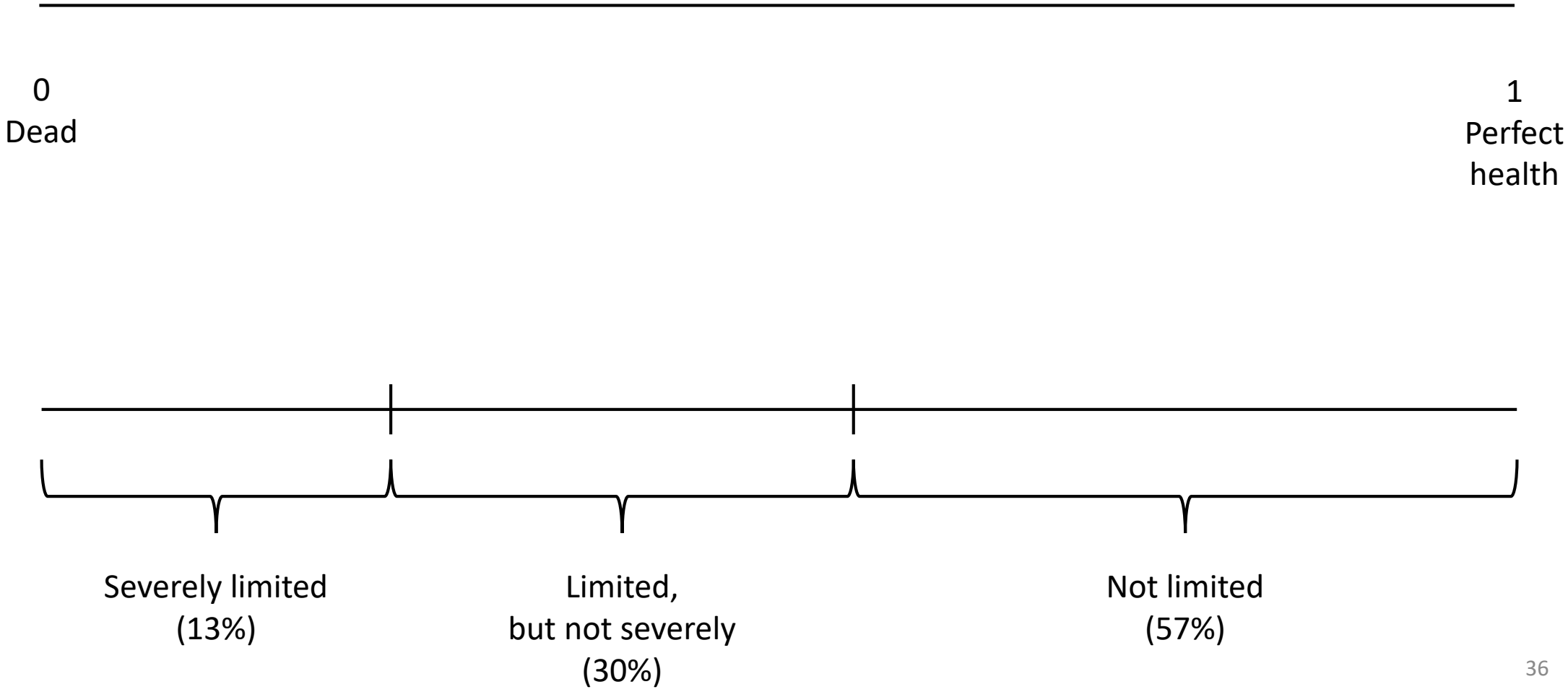
4	mortality	vintage of drugs	Puerto Rico	500,000 patients

Quality of life

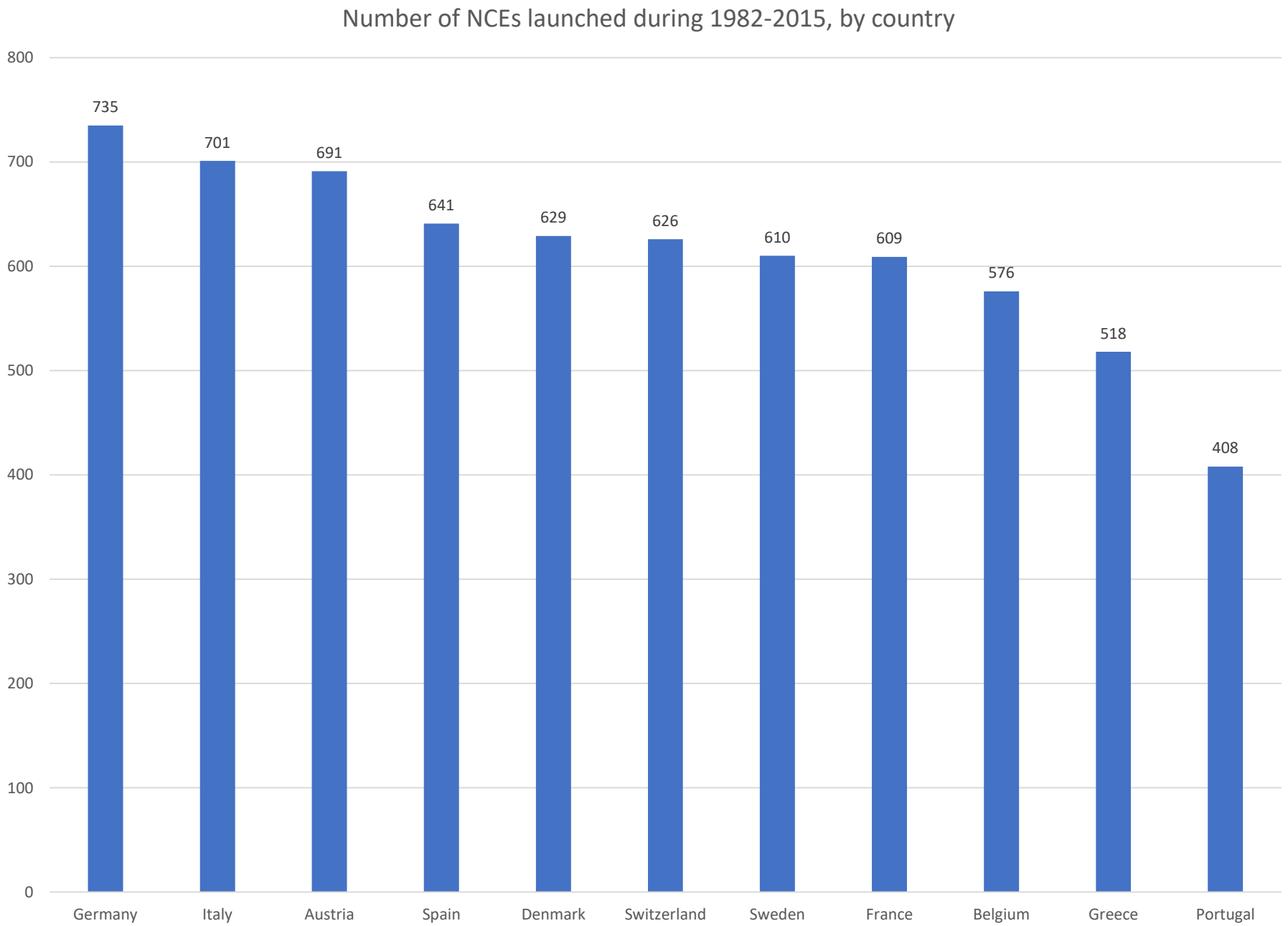


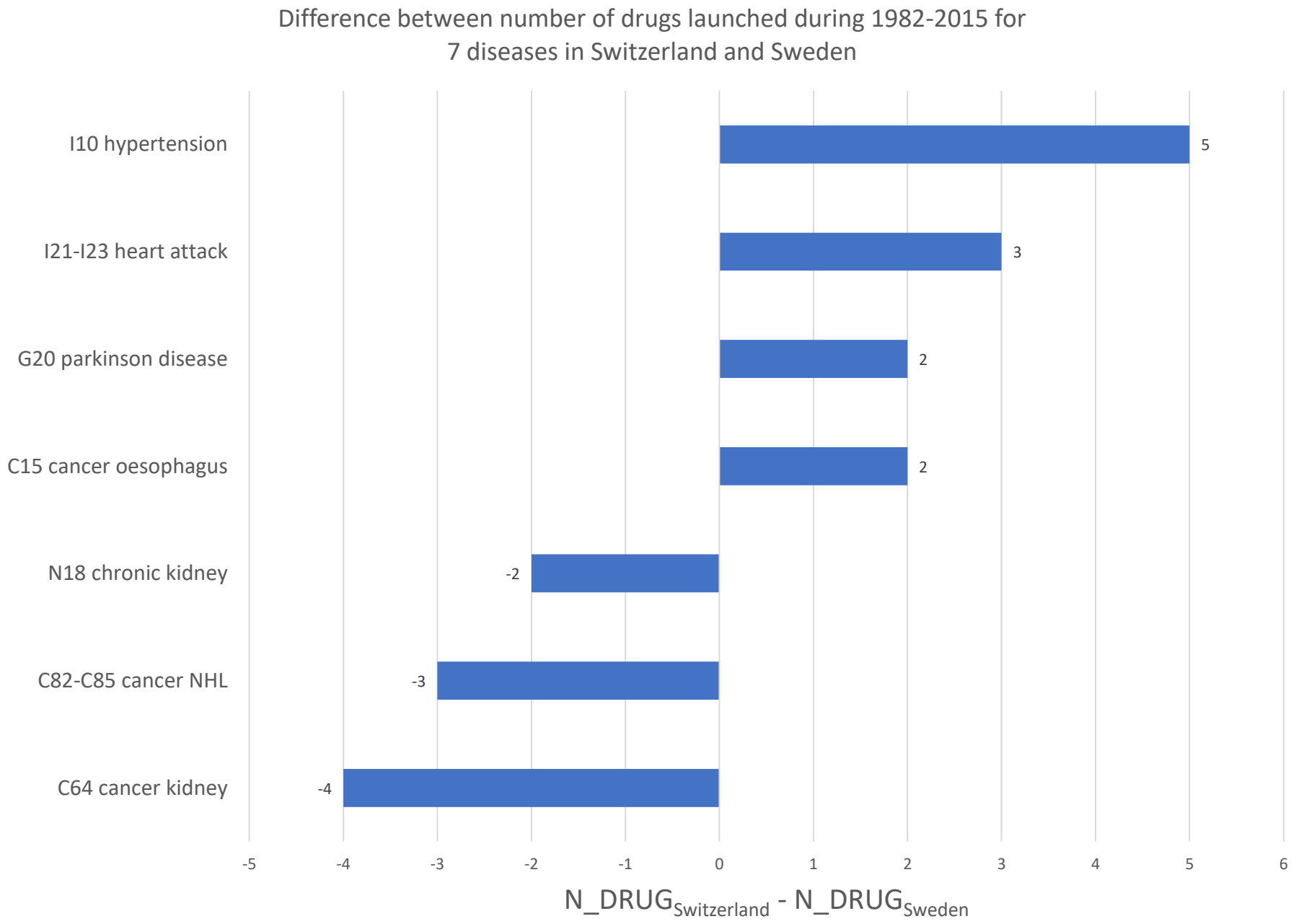
Clinical studies have shown that the use of certain drugs can reduce disability

- Post-menopausal women treated for osteoporosis with alendronate sodium for three years reported 63 per cent fewer days of disability requiring bed-rest for back pain related to those fractures.
- Etanercept, adalimumab, and infliximab reduced disability in rheumatoid arthritis patients, even those with a longstanding history and highly-active form of the disease.
- 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

- The average number of new chemical entities (NCEs) launched during 1982-2015 in Germany, Italy, and Austria (709) was 42% greater than the average number of NCEs launched in Belgium, Greece, and Portugal (501).
- 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.


Number of NCEs launched during 1982-2015, by country
800
700
600
500
400
300
200
100
0
735
701
691
641
629
626
610
609
576
518
408
Germany
Italy
Austria
Spain
Denmark
Switzerland
Sweden
France
Belgium
Greece
Portugal

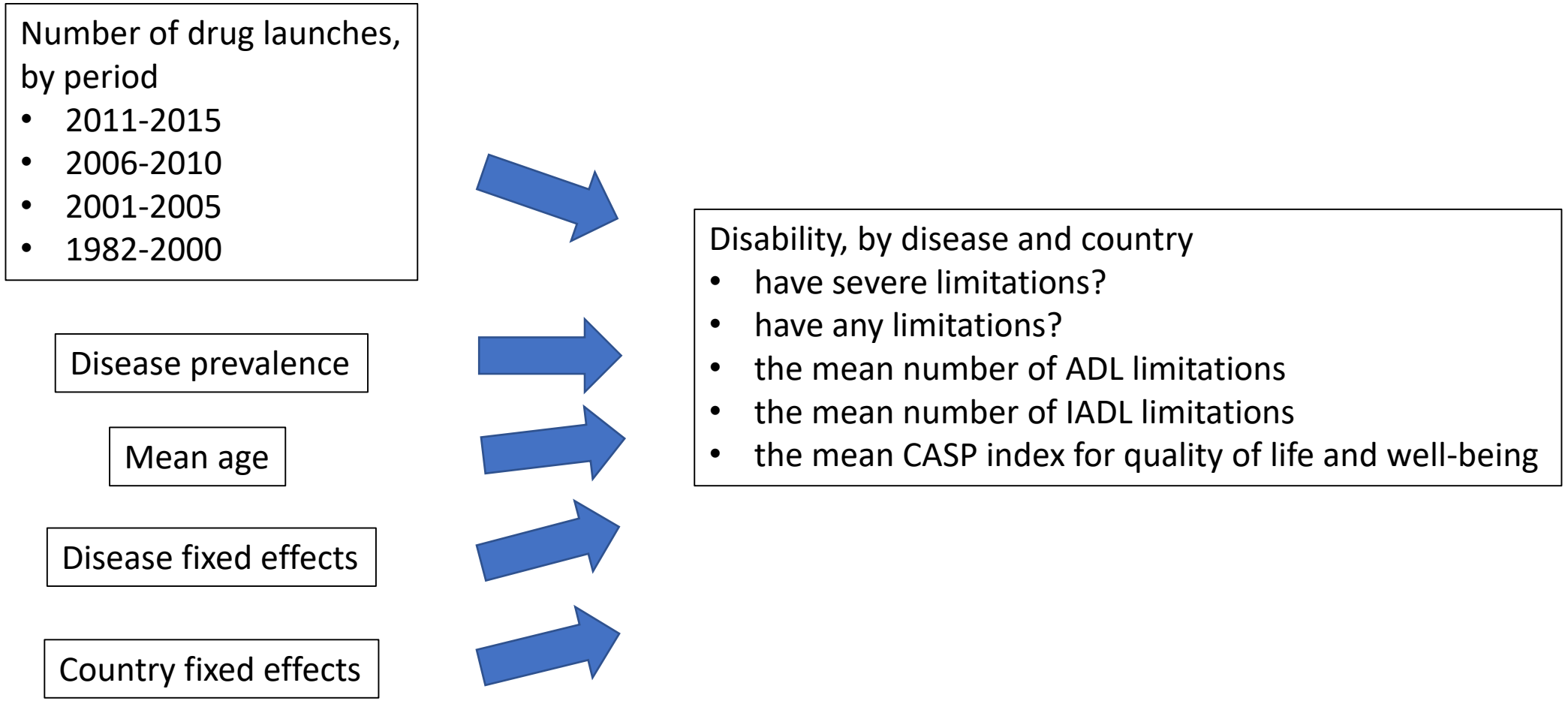

Difference between number of drugs launched during 1982-2015 for 7 diseases in Switzerland and Sweden
I10 hypertension
I21-I23 heart attack
G20 parkinson disease
C15 cancer oesophagus
N18 chronic kidney
C82-C85 cancer NHL
C64 cancer kidney
5
3
2
2
-2
-3
-4
-5
-4
-3
-2
-1
0
1
2
3
4
5
6
N_DRUG Switzerland - N_DRUG Sweden

Main hypothesis

- I will test the hypothesis that **the larger the relative number of drugs for a disease that have been launched in a country, the lower the relative disability from that disease in that country**, controlling for the average level of disability (and the average number of drug launches) in each country and for each disease, and for the number of patients with the disease and their mean age.
- The hypothesis will be tested using data about 31 diseases collected from over 45,000 people aged 50 and over in eleven European countries, partially derived from the Survey of Health, Ageing and Retirement in Europe.

Impact of a drug launch on disability in 2015 is likely to depend on launch year

- Impact is likely to depend on the interaction between drug quantity (utilization) and drug quality (effectiveness)
- Drugs launched more recently tend to be used less than drugs launched many years before: utilization increases with time since launch
- But drugs launched more recently tend to be more effective than drugs launched many years before: quality decreases with time since launch
- Impact (which depends on quantity * quality) will increase with time since launch if rate of quantity increase is greater than rate of quality decrease; otherwise, impact will decrease with time since launch


Number of drug launches, by period
• 2011-2015
• 2006-2010
• 2001-2005
• 1982-2000
Disease prevalence
Mean age
Disease fixed effects
Country fixed effects
Disability, by disease and country
• have severe limitations?
• have any limitations?
• the mean number of ADL limitations
• the mean number of IADL limitations
• the mean CASP index for quality of life and well-being

Diff-in-diff model of the effect of the number of 1982-2015 drug launches on disability in 2015 (eq. (2))

$$Y_{dc} = \beta_{0\text{-}4}\, LAUNCHES\_2011\_2015_{dc} + \beta_{5\text{-}9}\, LAUNCHES\_2006\_2010_{dc} + \beta_{10\text{-}14}\, LAUNCHES\_2001\_2005_{dc} + \beta_{15\text{-}33}\, LAUNCHES\_1982\_2000_{dc} + \gamma \ln(PREV_{dc}) + \rho\, AGE\_MEAN_{dc} + \alpha_d + \pi_c + \varepsilon_{dc}$$

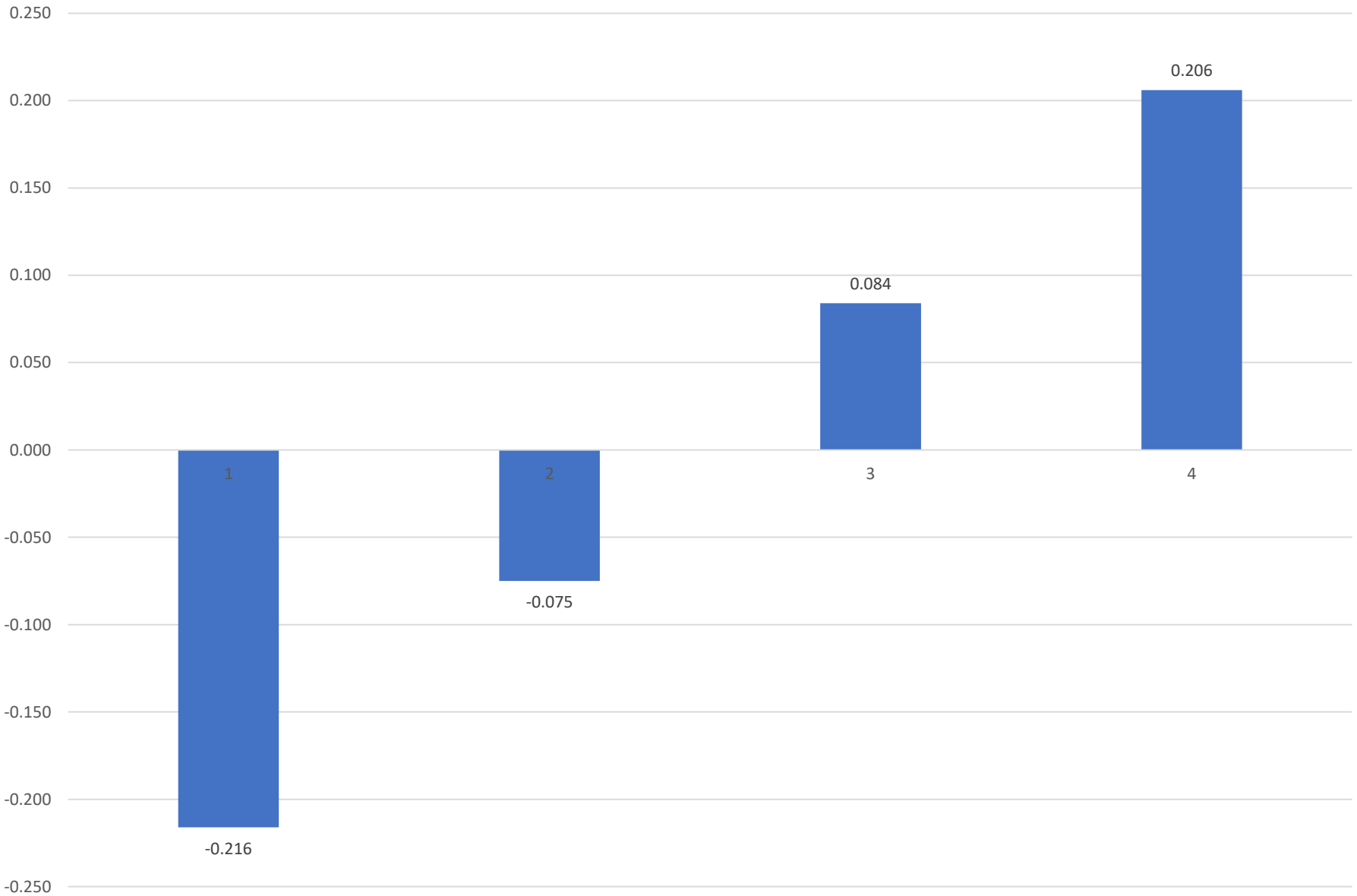
where Y_{dc} is one of the following variables:

- the log-odds that individuals with disease d in country c have **severe limitations**
- the log-odds that individuals with disease d in country c have **any limitations**
- the **mean number of limitations with activities of daily living** of individuals with disease d in country c
- the **mean number of limitations with instrumental activities of daily living** of individuals with disease d in country c
- the **mean CASP index for quality of life and well-being** of individuals with disease d in country c

$LAUNCHES\_2011\_2015_{dc}$	= the number of post-1981 new chemical entities used to treat disease d launched in country c during 2011-2015
$LAUNCHES\_2006\_2010_{dc}$	= the number of post-1981 new chemical entities used to treat disease d launched in country c during 2006-2010
$LAUNCHES\_2001\_2005_{dc}$	= the number of post-1981 new chemical entities used to treat disease d launched in country c during 2001-2005
$LAUNCHES\_1982\_2000_{dc}$	= the number of post-1981 new chemical entities used to treat disease d launched in country c during 1982-2000
$PREV_{dc}$	= the number of people in country c who said that a doctor ever told them that they had disease d
AGE_{dc}	= the mean age of people in country c who said that a doctor ever told them that they had disease d
α_d	= a fixed effect for disease d
π_c	= a fixed effect for country c

Figure 5

mean LAUNCHES_2006_2015$_{dc}$ residual, by quartile of ln(PREV_2005$_{dc}$) residual



Data sources

- 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.
- 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 (Centre National Hospitalier d'Information sur le Médicament (2017)).

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	45,592	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

Summary statistics, by medical condition

(10 most prevalent conditions)

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
I10 hypertension	17,438	69.2	10%	41%	0.21	0.44	37.3
E78 high cholesterol	11,080	68.0	10%	39%	0.18	0.39	37.1
M15-M19 osteoarthritis	8,858	68.9	17%	63%	0.30	0.58	36.8
E10-E14 diabetes	5,717	70.2	16%	53%	0.34	0.68	36.2
I21-I23 heart attack	4,581	73.0	24%	68%	0.42	0.92	35.8
M05-M06 rheumatoid arthritis	3,603	70.4	20%	68%	0.41	0.83	35.1
J40–J47 chronic lung	2,883	68.9	25%	70%	0.39	0.82	35.7
K25-K27 ulcer	1,626	66.6	17%	54%	0.35	0.62	34.6
I63-I64 stroke	1,571	73.1	43%	78%	1.24	2.34	34.6
G30 alzheimer	1,057	81.3	60%	89%	2.30	5.23	32.1

Number of drugs launched during 1982-2015, by country and medical condition

(10 conditions with highest mean number of launches)

medical condition	Austria	Belgium	Denmark	France	Germany	Greece	Italy	Portugal	Spain	Sweden	Switzerland	Mean
I10 hypertension	31	27	29	37	37	32	33	31	32	26	31	31.5
E10-E14 diabetes	33	29	32	33	33	32	30	24	32	32	32	31.1
C50 cancer breast	24	22	22	25	24	21	24	13	23	22	23	22.1
C91-C95 cancer leukaemia	22	17	21	21	25	14	20	7	17	20	19	18.5
M05-M06 rheumatoid arthritis	19	18	19	18	18	18	19	12	20	18	18	17.9
I21-I23 heart attack	17	15	16	15	18	16	17	11	15	14	17	15.5
C34 cancer lung	16	13	16	17	16	11	11	9	13	15	14	13.7
C82-C85 cancer NHL	15	12	14	12	15	9	0	5	11	14	11	10.7
C61 cancer prostate	11	11	12	12	11	10	9	8	11	11	11	10.6
N18 chronic kidney	10	10	11	10	11	11	11	8	10	11	9	10.2

Estimates of model of the effect of the number of drug launches 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_2011_2015	Estimate	-0.025	-0.015	-0.005	0.000	0.008
	Std. err.	0.026	0.018	0.006	0.009	0.045
	Pr > |Z|	0.340	0.405	0.355	0.987	0.866
LAUNCHES_2006_2010	Estimate	-0.013	-0.006	**-0.017**	-0.006	0.036
	Std. err.	0.024	0.026	**0.007**	0.013	0.045
	Pr > |Z|	0.595	0.809	**0.020**	0.638	0.423
LAUNCHES_2001_2005	Estimate	**-0.022**	**-0.023**	-0.011	-0.013	0.006
	Std. err.	**0.006**	**0.010**	0.006	0.010	0.033
	Pr > |Z|	**0.001**	**0.023**	0.055	0.198	0.864
LAUNCHES_1982_2000	Estimate	**-0.015**	**-0.017**	-0.005	0.000	0.031
	Std. err.	**0.005**	**0.006**	0.004	0.006	0.016
	Pr > |Z|	**0.004**	**0.007**	0.203	0.958	0.052
IMPACT	Estimate	**-0.282**	**-0.297**	**-0.119**	-0.039	**0.478**
	Std. err.	**0.103**	**0.108**	**0.052**	0.084	**0.230**
	Pr > |Z|	**0.006**	**0.006**	**0.022**	0.642	**0.037**
ln(PREV)	Estimate	**-0.232**	**-0.213**	**-0.045**	**-0.100**	0.119
	Std. err.	**0.060**	**0.061**	**0.018**	**0.030**	0.082
	Pr > |Z|	**0.000**	**0.000**	**0.014**	**0.001**	0.146
AGE_MEAN	Estimate	**0.038**	0.010	**0.028**	**0.078**	**-0.173**
	Std. err.	**0.013**	0.013	**0.004**	**0.009**	**0.052**
	Pr > |Z|	**0.003**	0.441	**<.0001**	**<.0001**	**0.001**

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%	21.2%	-4.3%
probability of any limitation	53.4%	60.7%	-7.3%
mean number of ADL limitations	0.34	0.46	-0.12
mean CASP index	36.58	36.10	0.48

Cost-effectiveness

- I estimate that mean pharmaceutical expenditure in 2014 by people 45 and over in the eleven European countries was $1184 (= 1.77 * $667).
- Expenditure of $1184 reduced the probability of being severely limited by 4.3 percentage points.
- If people would have been willing to pay at least $27,318 (= $1184 / 4.3%) 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 my previous research has demonstrated that new drug launches have also provided those benefits.

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

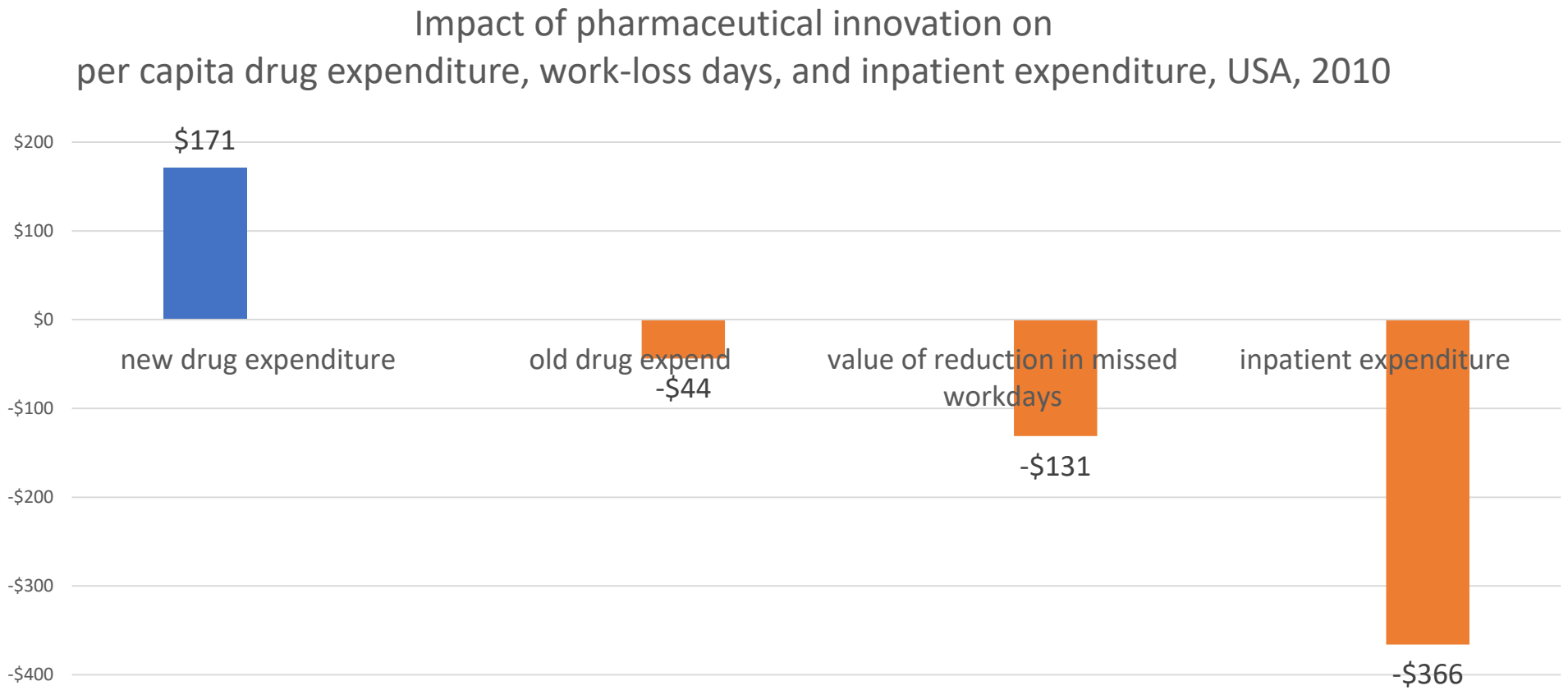
- Access to prescription drugs varies across countries: the average number of new chemical entities (NCEs) launched during 1982-2015 in Germany, Italy, and Austria (709) was 42% greater than the average number of NCEs launched in Belgium, Greece, and Portugal (501).
- Even when the total number of drugs launched in two countries is similar, the specific drugs that were launched, and the diseases those drugs are used to treat, may differ.
- I test the hypothesis that the larger the relative number of drugs for a disease that have been launched in a country, the lower the relative disability from that disease in that country, controlling for the average level of disability (and the average number of drug launches) in each country and for each disease, and for the number of patients with the disease and their mean age.
- The hypothesis is tested (and confirmed) using data about 31 diseases collected from over 45,000 people aged 50 and over in eleven European countries, partially derived from the Survey of Health, Ageing and Retirement in Europe.
- The estimates imply that drug launches during 1982-2011:
  - reduced the probability of severe limitation in 2015 by 4.3 percentage points, from 21.2% to 16.9%
  - reduced the probability of any limitation by 7.3 percentage points, from 60.7% to 53.4%
  - reduced the mean number of Activities of Daily Living limitations by about 26%
- Drug launches also yielded a small but significant increase in an index of quality of life and well-being.
- The population age 50 and over of these 11 countries in 2015 was 128 million, so we estimate that drug launches during 1982-2011 reduced the number of severely limited people in these countries by 5.5 million (= 4.3% * 128 million).
- Disability could have been reduced even more if there had been greater access to prescription drugs.

4 studies of impact of prescription drugs on health

study	health outcome	drug measure	region(s)	data
1	mortality	number of drugs	36 countries	19 cancer sites, 36 countries
2	disability	number of drugs	11 European countries	31 diseases, 11 countries
3	**hospitalization**	**vintage of drugs**	**USA**	**X diseases, 15 years**
4	mortality	vintage of drugs	Puerto Rico	500,000 patients

Pharmaceutical innovation is often *cost-saving*, not just cost-effective

- In a recent study (Lichtenberg (2014)), I investigated 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 a U.S. government household 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 reductions in work loss days and hospital admissions attributable to pharmaceutical innovation was estimated to be three times as large as the cost of new drugs consumed.
- Lichtenberg FR (2014), "The impact of pharmaceutical innovation on disability days and the use of medical services in the United States, 1997-2010," *Journal of Human Capital* 8(4): 432-480.



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4 studies of impact of prescription drugs on health

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The Effect of Drug Vintage on Survival: Micro Evidence From Puerto Rico's Medicaid Program

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THE EFFECT OF DRUG VINTAGE ON SURVIVAL: MICRO EVIDENCE FROM PUERTO RICO'S MEDICAID PROGRAM

Frank R. Lichtenberg

ABSTRACT

Using micro data on virtually all of the drugs and diseases of over 500,000 people enrolled in Puerto Rico's Medicaid program, the impact of the vintage (original FDA approval year) of drugs used to treat a patient on the patient's three-year probability of survival, controlling for demographic characteristics (age, sex, and region), utilization of medical services, and the nature and complexity of illness are examined. It is found that people using newer drugs during January–June, 2000, were less likely to die by the end of 2002, conditional on the covariates. The estimated mortality rates are strictly declining with respect to drug vintage. For pre-1970 drugs, the estimated mortality rate is 4.4%. The mortality rates for 1970s, 1980s, and 1990s drugs are 3.6%, 3.0%, and 2.5%, respectively. The actual mortality rate is about 16% (3.7% vs. 4.4%) lower than it would have been if all of the drugs utilized in 2000 had been pre-1970 drugs. Estimates for subgroups of people with specific diseases display the same general pattern.

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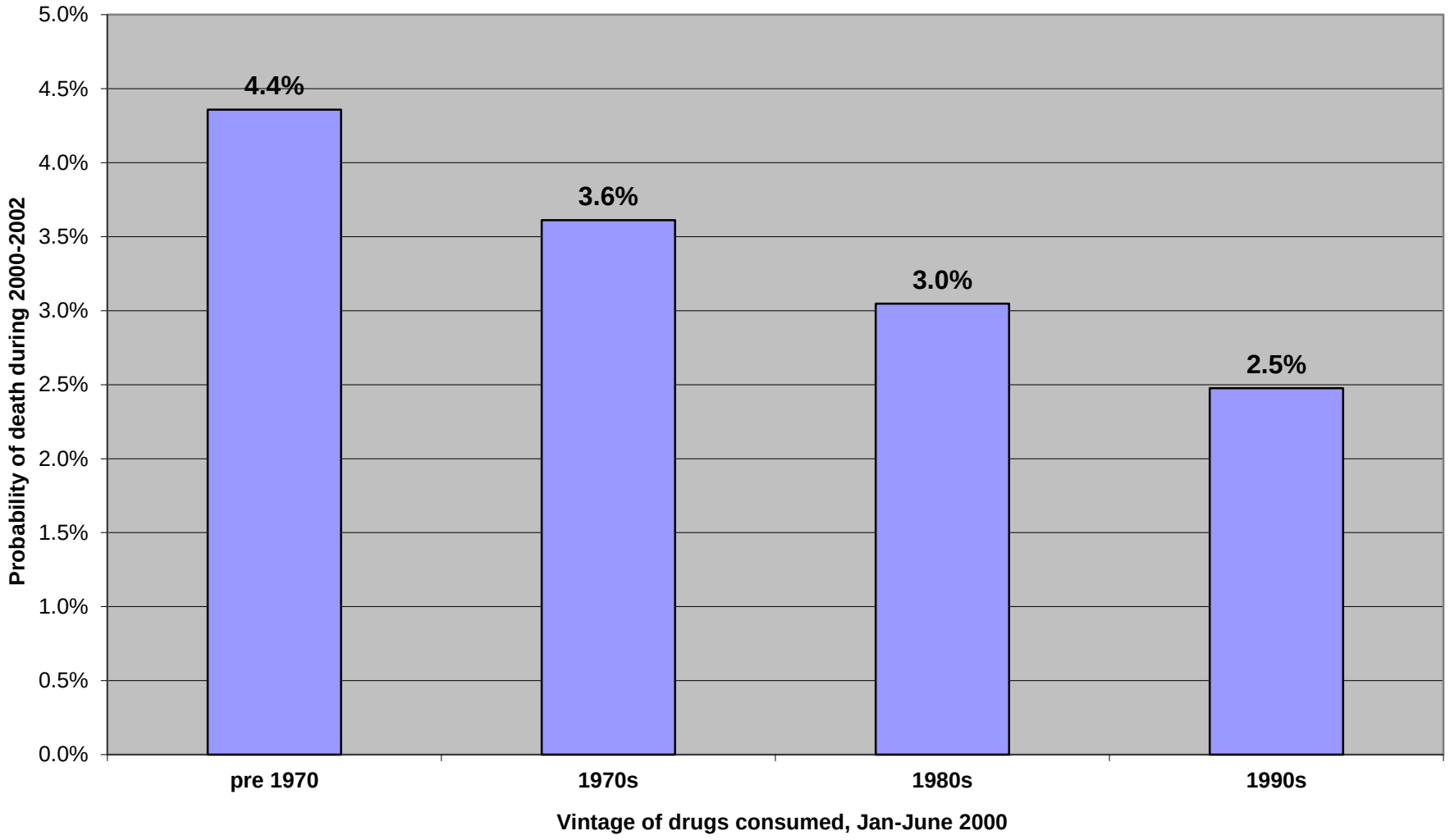
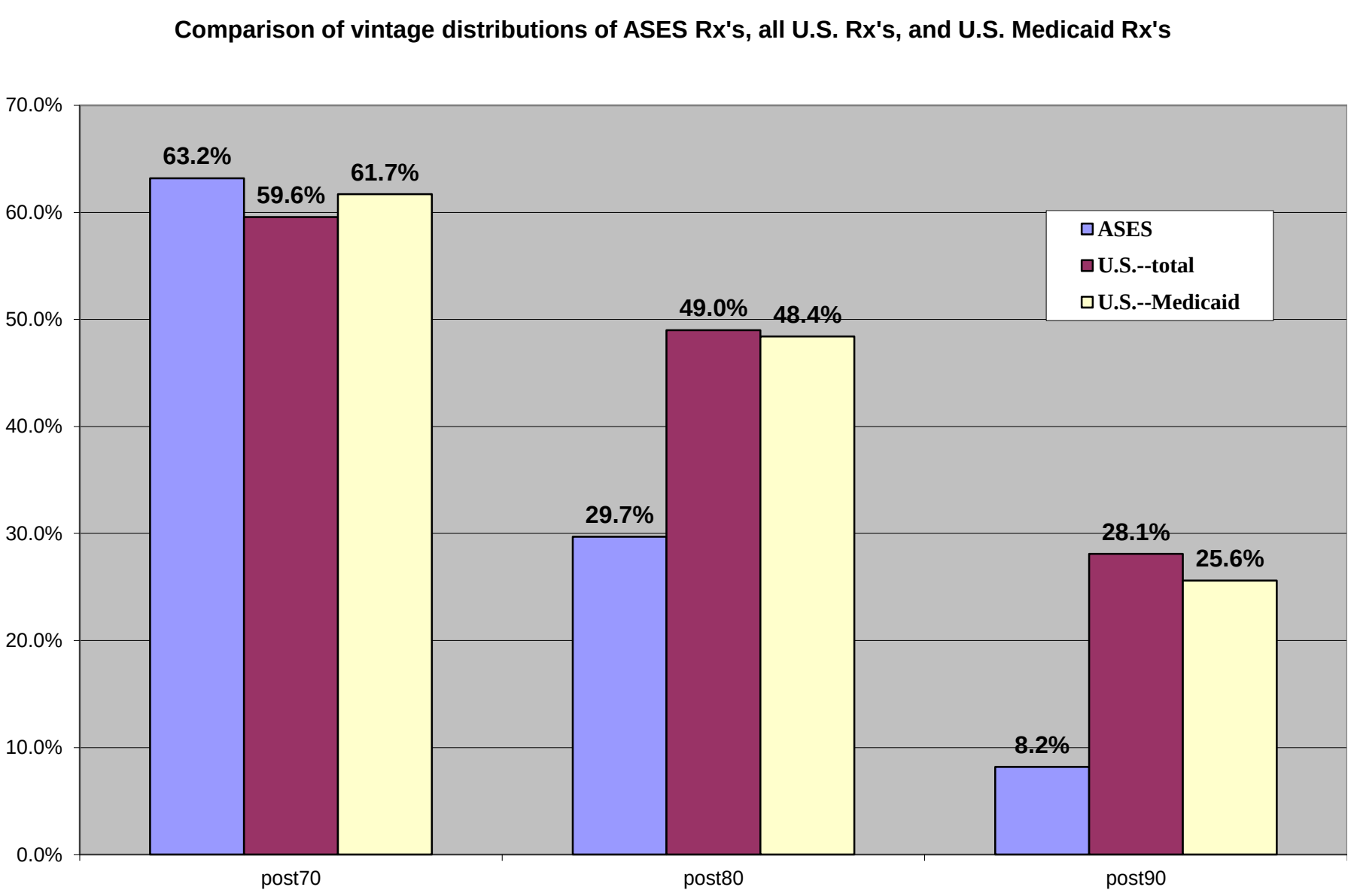
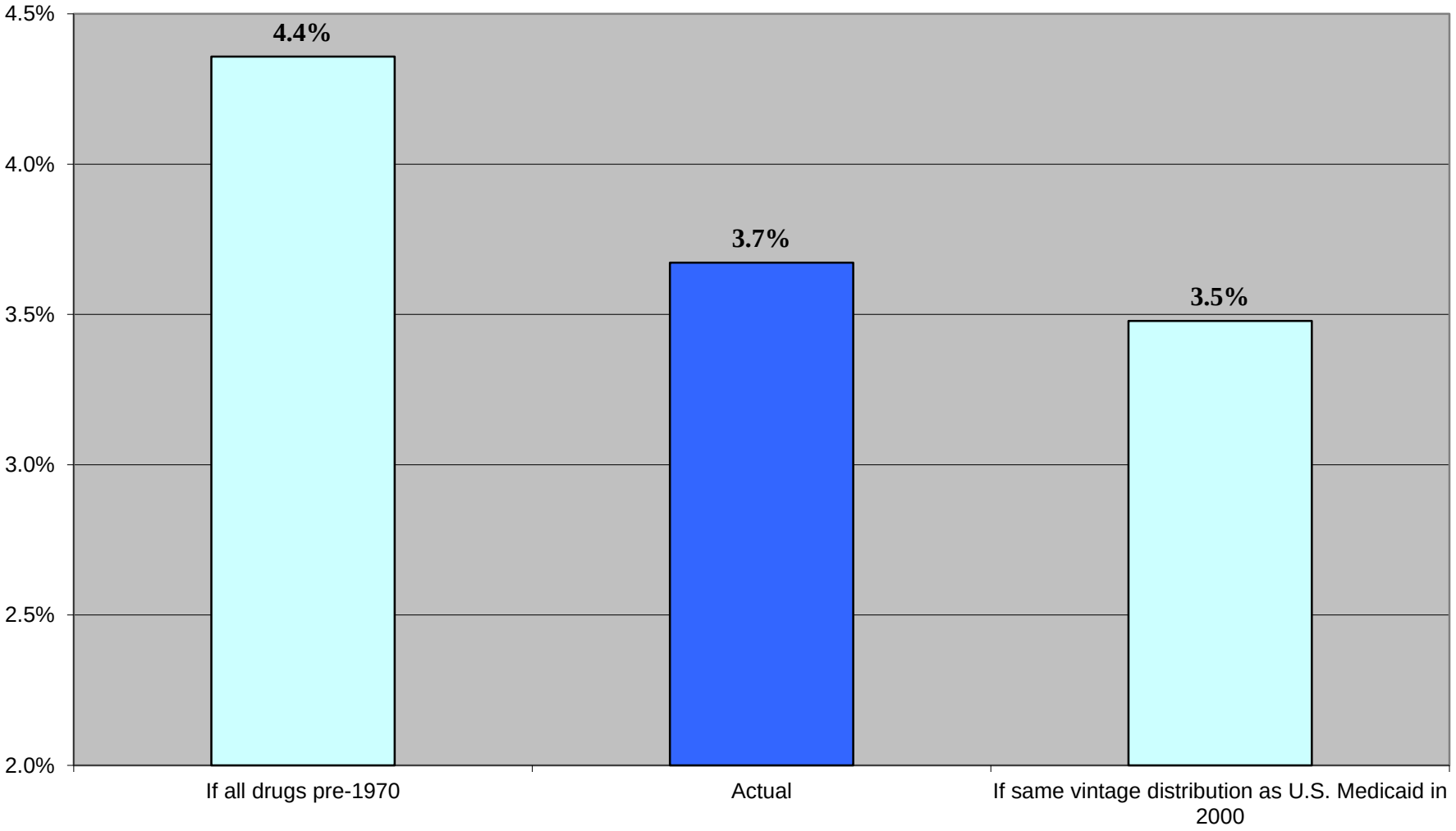
  - demographic characteristics (age, sex, and region)
  - utilization of medical services
  - the nature and complexity of illness
- I found that **people using newer drugs during January–June 2000, were less likely to die by the end of 2002, conditional on the covariates.**
- The actual mortality rate was about 16% (3.7% vs. 4.4%) lower than it would have been if all of the drugs utilized in 2000 had been pre-1970 drugs.
- Estimates for subgroups of people with specific diseases displayed the same general pattern.

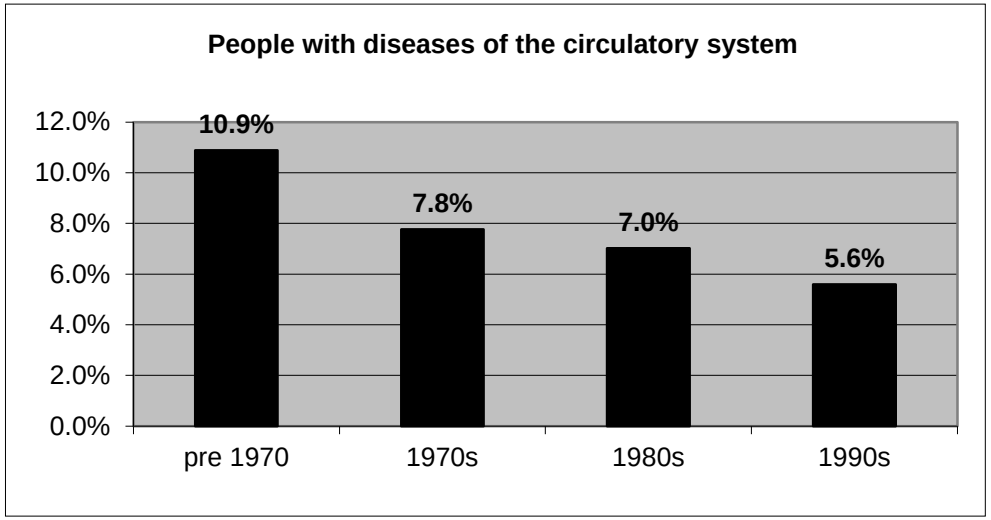
Estimated vintage-specific mortality rates, entire ASES population

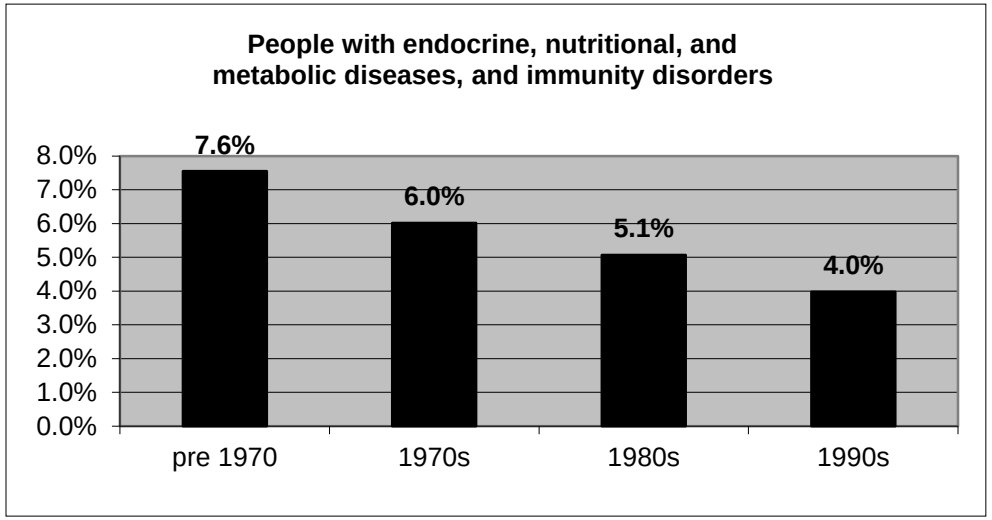


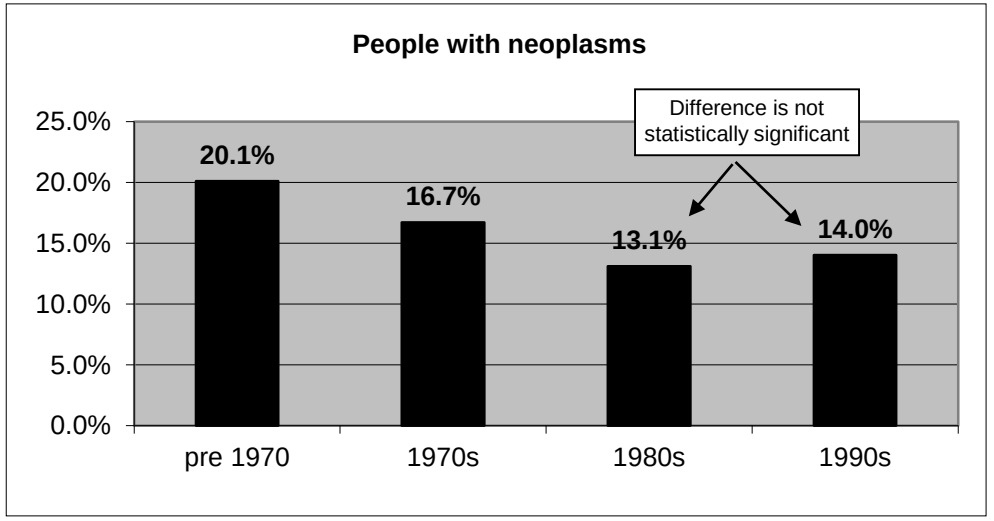

Comparison of vintage distributions of ASES Rx's, all U.S. Rx's, and U.S. Medicaid Rx's
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
63.2%
59.6%
61.7%
29.7%
49.0%
48.4%
8.2%
28.1%
25.6%
ASES
U.S.--total
U.S.--Medicaid
post70
post80
post90

Actual vs. hypothetical ASES mortality rates




People with diseases of the circulatory system
12.0%
10.0%
8.0%
6.0%
4.0%
2.0%
0.0%
10.9%
7.8%
7.0%
5.6%
pre 1970
1970s
1980s
1990s


People with endocrine, nutritional, and metabolic diseases, and immunity disorders
8.0%
7.0%
6.0%
5.0%
4.0%
3.0%
2.0%
1.0%
0.0%
7.6%
6.0%
5.1%
4.0%
pre 1970
1970s
1980s
1990s


People with neoplasms
Difference is not statistically significant
25.0%
20.0%
15.0%
10.0%
5.0%
0.0%
20.1%
16.7%
13.1%
14.0%
pre 1970
1970s
1980s
1990s

Pharmaceutical innovation has increased longevity and reduced disability and hospitalization