PharmAus19

Presented by Medicines Australia

Session Three:

Medicines Matter to the Economy

The impact medical intervention can have on the economy and the value metrics we use.

PharmAus19

Presented by Medicines Australia

Professor Frank Lichtenberg

Courtney C. Brown Professor of Business at the Columbia University Graduate School of Business

Keynote Address – Professor Lichtenberg will present key findings from:
"The Impact of pharmaceutical innovation on premature mortality and hospitalization in Australia, 1998-2018."

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The impact of pharmaceutical innovation on premature mortality and hospitalization in Australia, 1998-2018

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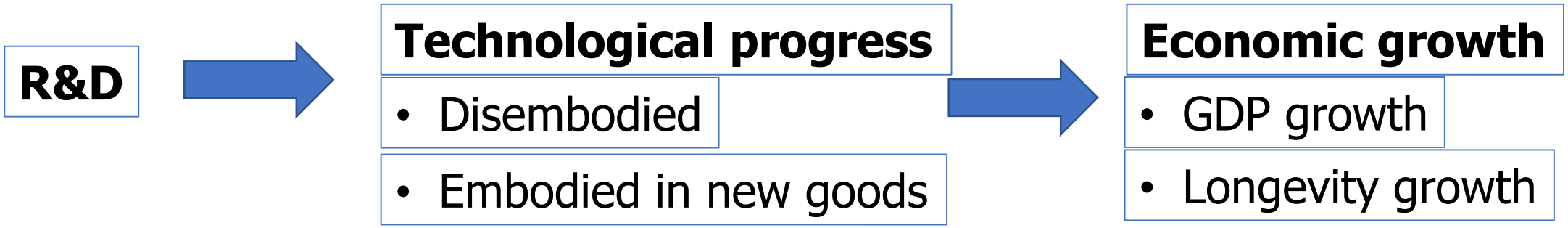
R&D, technological progress, and economic growth



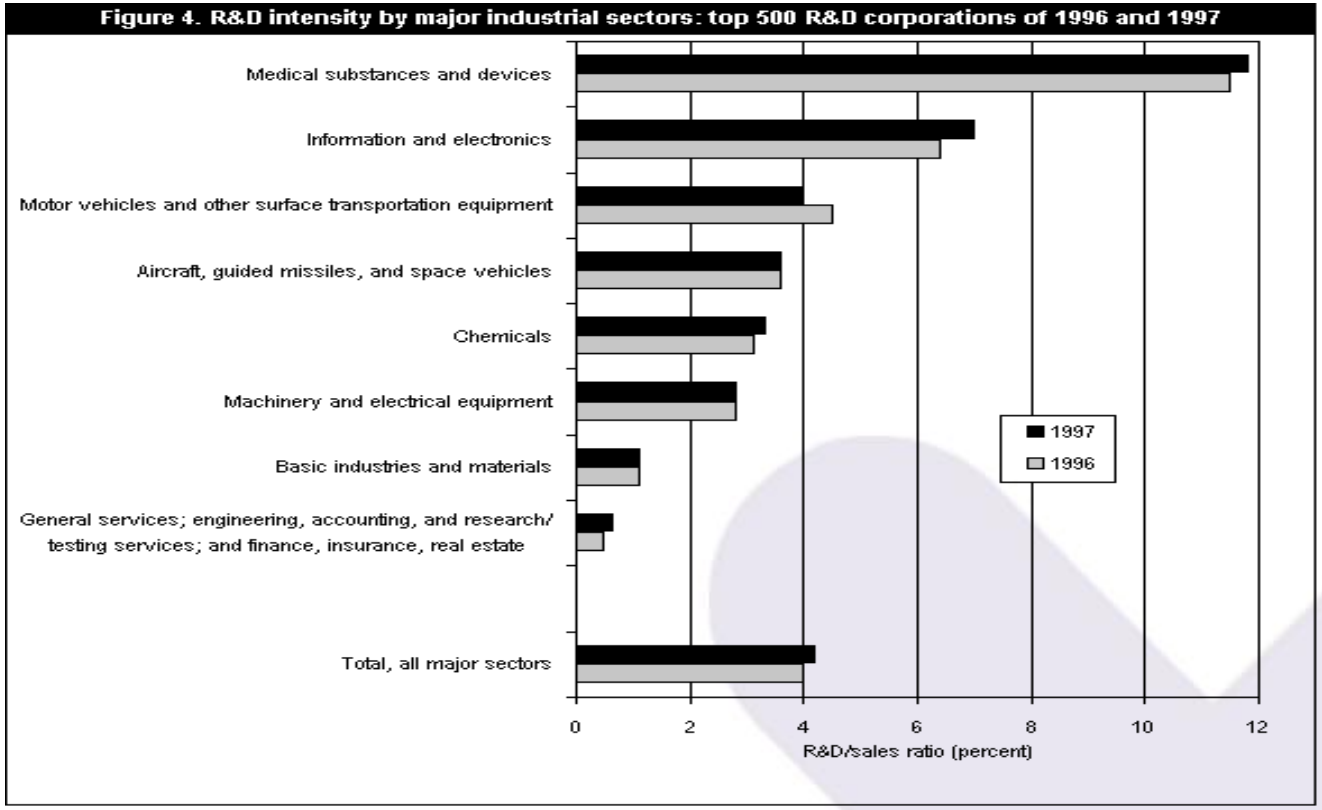
Nordhaus (2005): "To a first approximation, the economic value of increases in longevity in the last hundred years is about as large as the value of measured growth in non-health goods and services."

Romer (1990): "growth…is driven by technological change…"

Hercowitz (1998): "'embodiment' is the main transmission mechanism of technological progress to economic growth" (p. 223).

Jones (1998): "technological progress is driven by research and development (R&D) in the advanced world"; NSF: the medical substances and devices sector is the most R&D-intensive major industrial sector in the U.S.; Dorsey et al (2010): 88% of privately-funded U.S. biomedical research expenditure was funded by pharmaceutical and biotechnology firms; the remaining 11% was funded by medical device firms.

Which industry innovates the most?



SOURCE: Standard & Poor's Compustat, Englewood, CO

wayback.archive-it.org/5902/20150819114914/http:/www.nsf.gov/statistics/nsf00301/expendit.htm#intensity

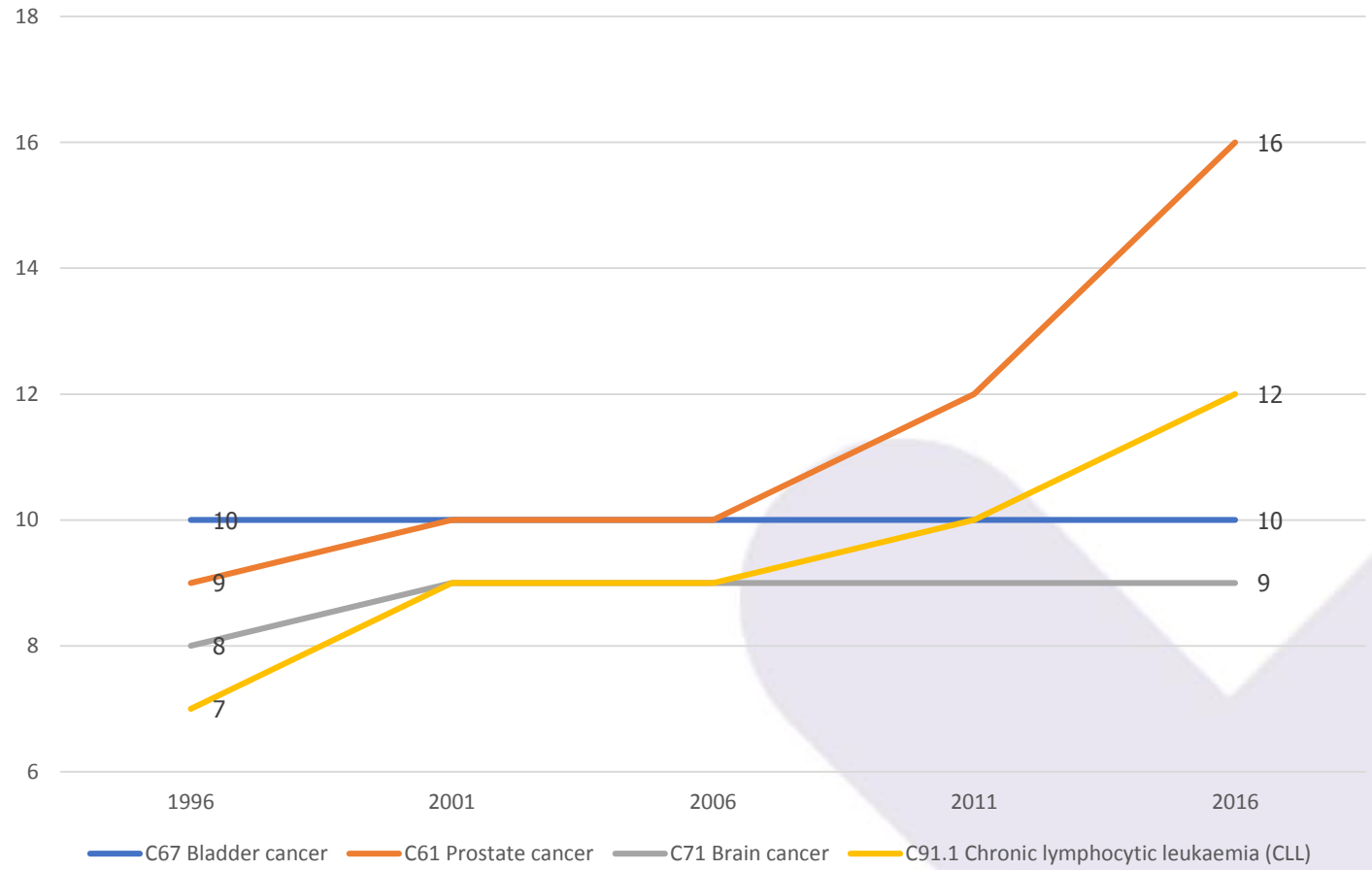
Study design and hypothesis

- I analyzed the impact that pharmaceutical innovation had on premature mortality and hospital separations in Australia up until 2015, and its impact on cancer survival rates up until 2018.

- The basic approach is estimation of difference-in-differences (2-way fixed effects) models using longitudinal data on different diseases.

- **Hypothesis: diseases for which more new drugs were launched in Australia had larger reductions in mortality and hospitalization.**

Number of drugs used to treat 4 types of cancer that had ever been launched in Australia, 1996-2016



Model of mortality from all diseases

$$\ln(MORT_{dt}) = \beta_k \, CUM\_DRUG_{d,t-k} + \alpha_d + \delta_t + \varepsilon_{dt}$$

where $MORT_{dt}$ is one of the following variables

$YLL80_{dt}$	= the number of years of life lost before age 80 due to disease (cause) d in year t (t = 1998, 2015)
$YLL85_{dt}$	= the number of years of life lost before age 85 due to disease d in year t
$YLL90_{dt}$	= the number of years of life lost before age 90 due to disease d in year t
N_DEATHS_{dt}	= the number of deaths due to disease d in year t
$CUM\_DRUG_{d,t-k}$	= $\sum_m IND_{md} \, LAUNCHED_{m,t-k}$ = the number of post-1981 chemical substances to treat disease d that had been launched in Australia by the end of year t-k (k = 0, 1, 2,…,15)
IND_{md}	= 1 if chemical substance m is used to treat (indicated for) disease d = 0 if chemical substance m is not used to treat (indicated for) disease d
$LAUNCHED_{m,t-k}$	= 1 if chemical substance m had been launched in Australia by the end of year t-k = 0 if chemical substance m had not been launched in Australia by the end of year t-k
α_d	= a fixed effect for disease d
δ_t	= a fixed effect for year t

CUM_DRUG is not an ideal measure of exposure to pharmaceutical innovation

- The launch of a drug indicates that 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 year.

- However, many drugs have multiple indications—50% of drugs have 2 or more indications (causes of disease in the WHO Global Health Estimates disease classification), and 7% of drugs have 5 or more indications—and our data do not enable us to determine how often each drug was used for each of its indications.

Imperfect measurement ➔ conservative estimates

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

Hausman J (2001). Mismeasured Variables in Econometric Analysis: Problems from the Right and Problems from the Left. *Journal of Economic Perspectives* 15(4): 57-67, Autumn.

Long-difference model

$$\Delta \ln(MORT_d) = \beta_k \, \Delta CUM\_DRUG\_k_d + \delta + \varepsilon_d'$$

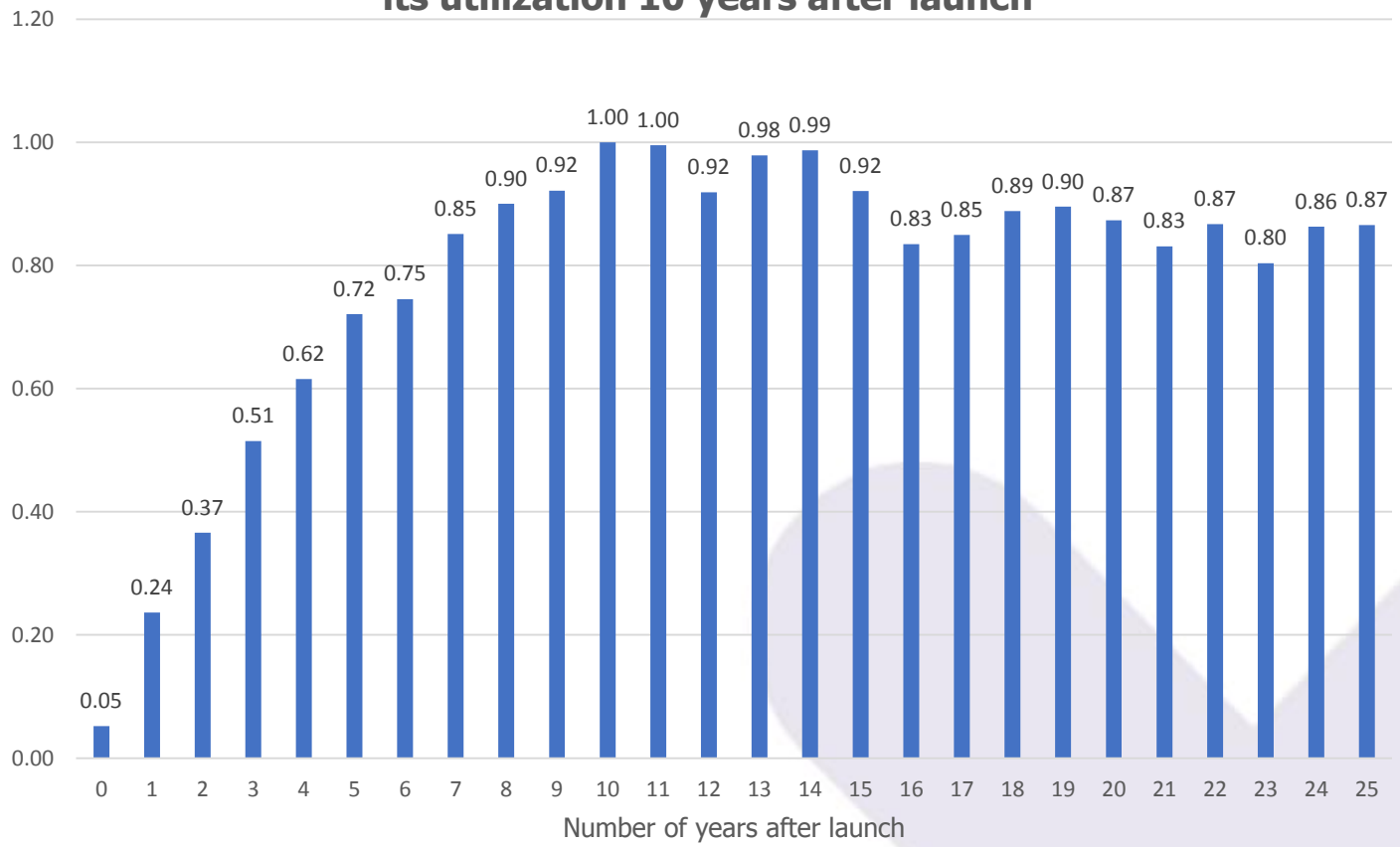
$\Delta \ln(MORT_d)$	$= \ln(MORT_{d,2015}) - \ln(MORT_{d,1998})$ = the 1998-2015 log change in mortality from disease d
$\Delta CUM\_DRUG\_k_d$	$= CUM\_DRUG_{d,2015-k} - CUM\_DRUG_{d,1998-k}$ = **the number of drugs used to treat disease d launched in Australia during the years 1999–k to 2015–k**
δ	$= \delta_{2015} - \delta_{1998}$
ε_d'	$= \varepsilon_{d,2015} - \varepsilon_{d,1998}$

- δ is an estimate of what the 1998-2015 log change in mortality would have been in the absence of pharmaceutical innovation
- This model was estimated by weighted least squares, weighting by (Σ_t $MORT_{dt}$).

Lagged effect of drug launches on mortality

- There is likely to be a substantial lag between the launch of a new drug and its maximum impact on mortality.
- Utilization of recently-launched drugs tends to be much lower than utilization of drugs launched many years earlier.
- Utilization of a drug reaches a peak about 10-14 years after it was launched. It is used about twice as much then as it was 3 years after launch.

Mean ratio of utilization of a drug n years after launch to its utilization 10 years after launch



Source: Author's calculations based on data from IQVIA New Product Focus and MIDAS databases.

Lags

- Due to gradual diffusion of new drugs, the maximum impact of a drug on disease burden is likely to occur many years after it was launched, but the peak effect could occur either more than or less than 10-14 years after launch.

- The lag might be longer because some drugs for chronic diseases (e.g. statins) may have to be consumed for several years to achieve full effectiveness.

- But the lag might be shorter because the impact of a drug on disease burden is likely to depend on its quality (or effectiveness) as well as on its quantity (utilization), and drugs launched more recently are likely to be of higher quality than earlier-vintage drugs

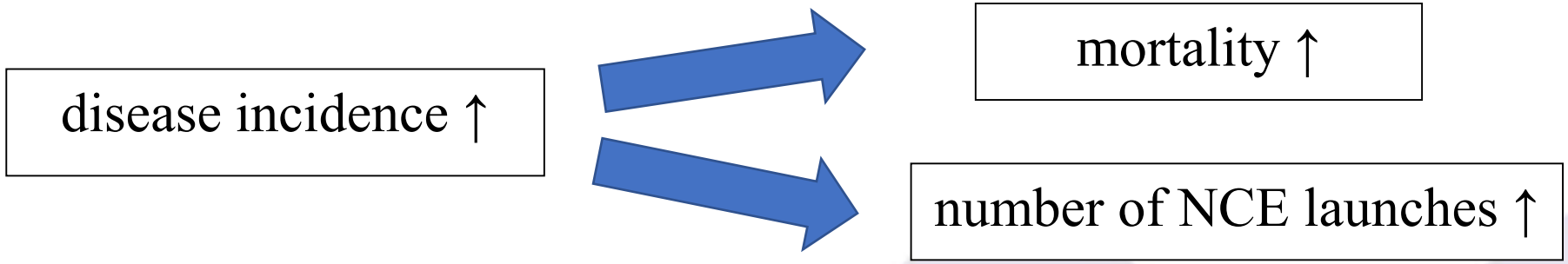
Spillovers between diseases

- Estimates based on eq. (2) will provide evidence about the impact of the launch of drugs for a disease on the burden of that disease, but they will not capture possible spillover effects of the drugs on the burden of *other* diseases.
- These spillovers may be either positive or negative:
  - For example, the launch of cardiovascular drugs could reduce mortality from cardiovascular disease, but increase mortality from the "competing risk" of cancer.
  - On the other hand, the launch of drugs for mental disorders could reduce mortality from other medical conditions. Prince et al (2007) argued that "mental disorders increase risk for communicable and non-communicable diseases, and contribute to unintentional and intentional injury. Conversely, many health conditions increase the risk for mental disorder, and comorbidity complicates help-seeking, diagnosis, and treatment, and influences prognosis."

Other potential determinants of mortality change

- If the data were available, we would like to include other regressors in eq. (2), including (1) changes in disease incidence, and (2) the number of non-pharmaceutical medical innovations (e.g. medical device innovations) launched in Australia.

- However, there is good reason to believe that failure to control for those variables is unlikely to result in overestimation of the magnitude of β_k; exclusion of those variables may even result in *underestimation* of the magnitude of β_k. Higher disease incidence is likely to result in both higher disease burden and a larger number of chemical substance launches.


disease incidence ↑
mortality ↑
number of NCE launches ↑

Other medical innovation

- 88% of privately-funded U.S. funding for biomedical research came from pharmaceutical and biotechnology firms (Dorsey (2010)).

- Also, previous research based on U.S. data (Lichtenberg (2014a, 2014b)) indicated that non-pharmaceutical medical innovation is not positively correlated across diseases with pharmaceutical innovation.

Model of cancer survival and mortality

$$MORT\_CANCER_{st} = \beta_{0\text{-}4}\, LAUNCHES\_0\_4_{st} + \beta_{5\text{-}9}\, LAUNCHES\_5\_9_{st} + \beta_{10+}\, LAUNCHES\_GE\_10_{st} + \gamma \ln(CASES_{st}) + \alpha_s + \delta_t + \varepsilon_{st}$$

where $MORT\_CANCER_{st}$ is one of the following variables:

$\ln[SURV5\%_{st}/(1 - SURV5\%_{st})]$	= the log odds of surviving at least 5 years after diagnosis of cancer at site s in year t (t = 2005, 2015)
$\ln(N\_DEATHS_{st})$	= the log of the number of deaths due to cancer at site s in year t (t = 2008, 2018)
AGE_DEATH_{st}	= mean age at death from cancer at site s in year t
$\ln(YLL65_{st})$	= the log of the number of years of life lost before age 65 due to cancer at site s in year t
$\ln(YLL75_{st})$	= the log of the number of years of life lost before age 75 due to cancer at site s in year t
$\ln(YLL85_{st})$	= the log of the number of years of life lost before age 85 due to cancer at site s in year t

$LAUNCHES\_0\_4_{st}$	= the number of new drugs to treat cancer at site s that were launched in Australia 0-4 years before year t
$LAUNCHES\_5\_9_{st}$	= the number of new drugs to treat cancer at site s that were launched in Australia 5-9 years before year t
$LAUNCHES\_GE\_10_{st}$	= the number of new drugs to treat cancer at site s that were launched in Australia more than 9 years before year t
$CASES_{st}$	= the number of patients diagnosed with cancer at site s in year t

Model of utilization of hospitals for all diseases

$$\ln(HOSP_{dt}) = \beta_k \ln(CUM\_DRUG_{d,t-k}) + \alpha_d + \delta_t + \varepsilon_{dt}$$

where $HOSP_{dt}$ is one of the following variables:

$DISCHARGES_{dt}$	= the number of inpatient hospital discharges due to disease (diagnosis) d in year t (t = 2000, 2015)
$DAYS_{dt}$	= the number of days of inpatient hospital care due to disease d in year t

Data sources

- *Drug launch data.* IQVIA's *New Product Focus* database.
- *Drug indications data.* Thériaque, a database produced by the French Centre National Hospitalier d'Information sur le Médicament (2019).
- *Drug utilization and expenditure data.* IQVIA MIDAS database.
- *Mortality from all diseases.* WHO Cause of Death Query online database (World Health Organization (2019)), a web-based system for extracting trend series detailed cause-of-death data.
- *Cancer mortality, incidence, and survival.* Cancer in Australia 2019 (Australian Institute of Health and Welfare (2019)).
- *Hospitalization data. OECD Health Statistics database.*

Number and rates of deaths and years of life lost from all causes in Australia, 1998 and 2015

		1998	2015	% change, 1998-2015
Number of deaths		127,349	159,050	24.9%
Number of years of life lost before age:	90	2,201,153	2,157,774	-2.0%
	85	1,682,490	1,609,071	-4.4%
	80	1,262,105	1,193,199	-5.5%
Total population		18,711,271	23,781,169	27.1%
Population below age:	90	18,642,544	23,611,382	26.7%
	85	18,486,307	23,309,041	26.1%
	80	18,193,473	22,857,317	25.6%
		Rate per 100,000 population		
Number of deaths		681	669	-1.7%
Number of years of life lost before age:	90	11807	9139	-22.6%
	85	9101	6903	-24.2%
	80	6937	5220	-24.7%

Cancer incidence, survival, and mortality

A. Incidence

Year	Number of people diagnosed	Crude incidence rate	Age-standardized incidence rate
1982	47,462	312.6	383.5
1987	57,129	351.3	408.1
1992	69,531	397.8	443.9
1997	81,113	440.3	463.6
2002	94,161	483.0	477.3
2007	111,166	533.7	502.2
2012	125,842	553.3	500.5
2017	137,559		485.3
2018	141,538		483.9
2019	144,713		482.7
2020	147,956		481.6
2021	151,332		480.7

B. Survival

Diagnosis Period	5-year survival rate (%)	95% lower bound	95% upper bound
1986–1990	50.0	49.8	50.2
1991–1995	54.6	54.4	54.8
1996–2000	59.3	59.2	59.5
2001–2005	62.1	61.9	62.2
2006–2010	66.1	65.9	66.2
2011–2015	68.9	68.8	69.1

C. Mortality

Year	Number of deaths	Crude mortality rate	Age-standardized mortality rate	Mean age at death	YLL85	YLL75	YLL65
1982	24,915	164.1	209.0	66.9	448,303	244,363	110,758
1987	28,778	176.9	212.0	68.1	485,783	257,190	112,960
1992	32,062	183.4	209.7	69.0	512,925	266,260	116,703
1997	35,109	190.6	203.1	70.2	524,515	265,328	115,788
2002	37,946	194.6	191.9	71.6	525,743	260,735	113,025
2007	40,537	194.6	180.8	72.2	534,910	266,165	112,293
2012	43,677	192.1	169.4	73.2	540,468	263,093	105,350
2017	47,566		161.3		575,940	276,663	110,720
2021	52,208		157.1		614,668	289,758	116,130

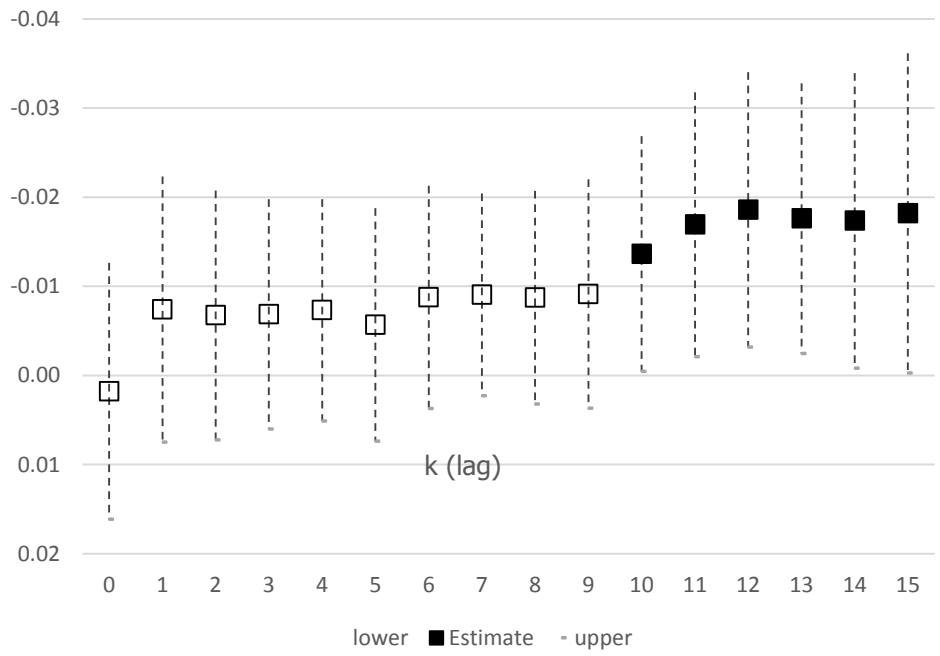
Number of hospital discharges, average length of stay, and days of care, all diagnoses, 2000-2015

Year	discharges	alos	days
2000	3,024,067	6.4	19,354,029
2001	3,043,099	6.5	19,780,144
2002	3,070,062	6.5	19,955,403
2003	3,120,960	6.3	19,662,048
2004	3,167,281	6.3	19,953,870
2005	3,264,101	6.2	20,237,426
2006	3,354,428	6.2	20,797,454
2007	3,437,977	6.2	21,315,457
2008	3,490,798	6.0	20,944,788
2009	3,599,497	5.9	21,237,032
2010	3,721,307	5.8	21,583,581
2011	3,856,812	5.8	22,369,510
2012	3,922,940	5.7	22,360,758
2013	3,985,367	5.5	21,919,519
2014	4,081,875	5.5	22,450,313
2015	4,235,825	5.5	23,297,038

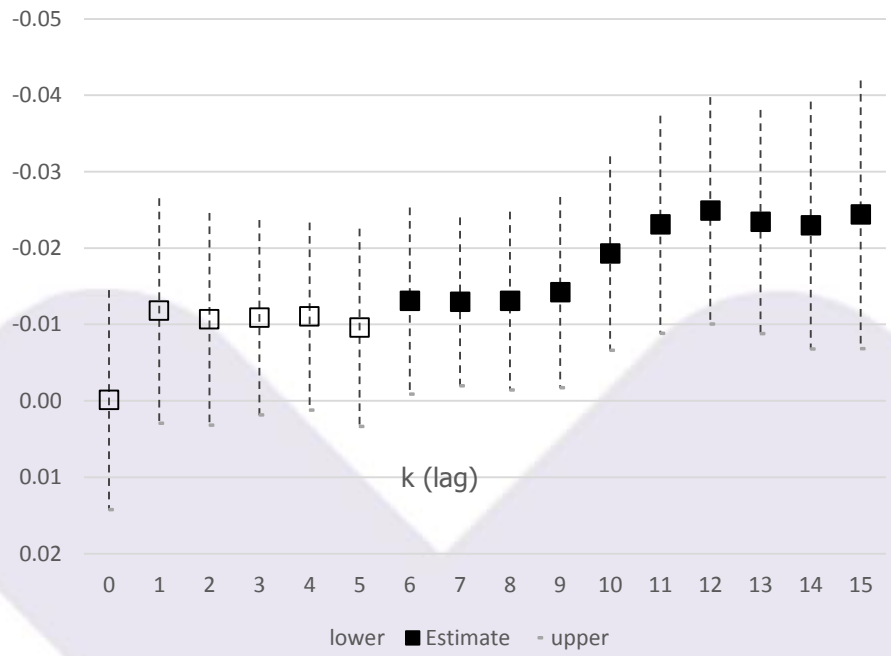
Empirical results

Estimates of β_k from model of the 1998-2015 log change in mortality from all diseases (eq. (2))

A. YLL80



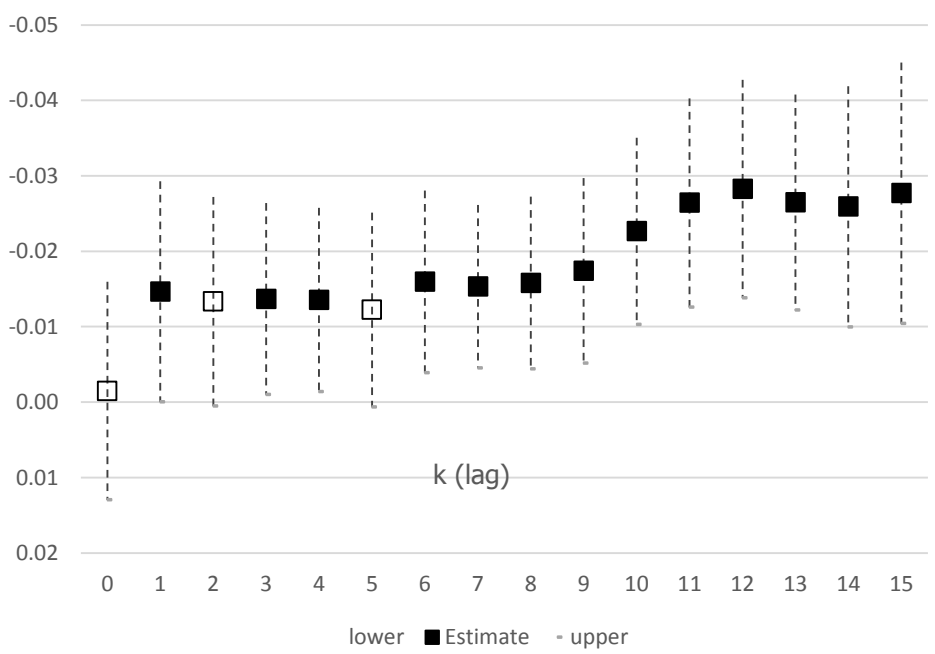
B. YLL85



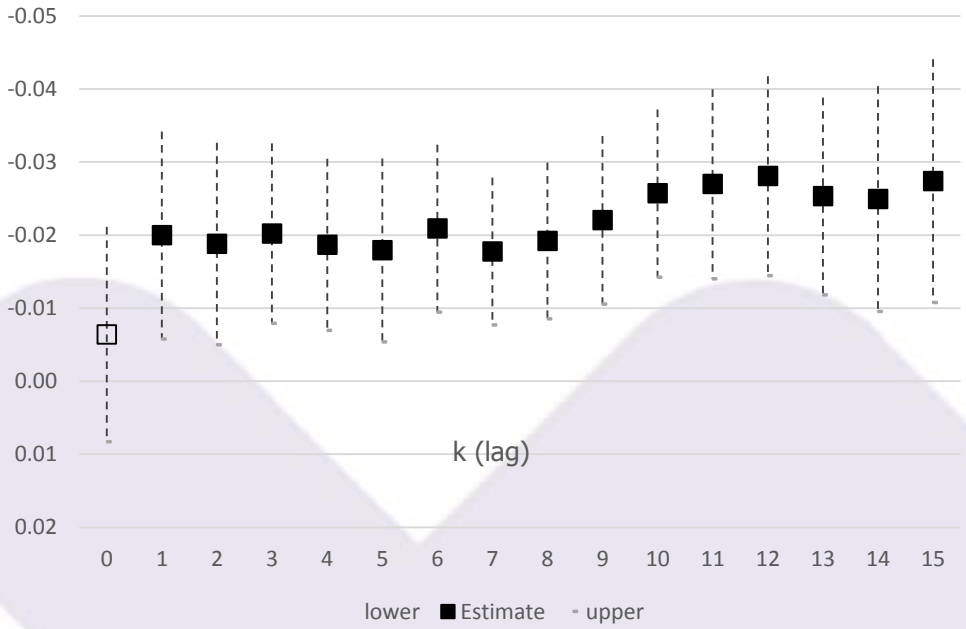
Note: vertical scale is inverted. Hollow markers denote insignificant (p-value > .05) estimates; solid markers denote significant estimates.

Estimates of β_k from model of the 1998-2015 log change in mortality from all diseases (eq. (2))

C. YLL90



D. Number of deaths



Note: vertical scale is inverted. Hollow markers denote insignificant (p-value > .05) estimates; solid markers denote significant estimates.

Premature (before age 80) mortality

- YLL80 is not significantly related to the number of drugs that had ever been launched 0-9 years earlier, but is significantly inversely related to the number of drugs that had ever been launched 10-15 years earlier.
- The substantial lag from drug launch to mortality reduction is not surprising, since utilization of a drug reaches a peak about 10-14 years after it is launched, and some drugs for chronic diseases may have to be consumed for several years to achieve full effectiveness.
- The log-change in YLL80 is most significantly related to the change in CUM_DRUG 12 years earlier.
- The estimate of β_{12} indicates that one additional drug for a disease launched at least 12 years before year t reduced YLL80 from that disease in year t by 1.9%.

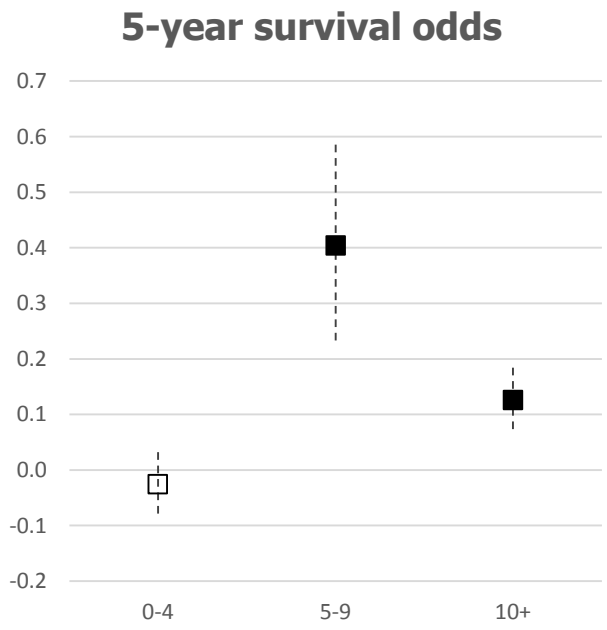
Premature (before ages 85 and 90) mortality

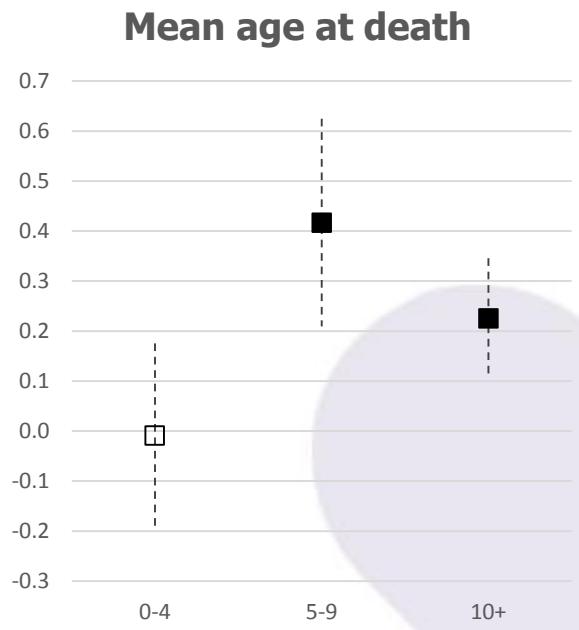
- **YLL85** is significantly inversely related to the number of drugs that had ever been launched 6-15 years earlier.
  - One additional drug for a disease launched at least 12 years before year t reduced YLL85 from that disease in year t by 2.5%.
- **YLL90** is significantly inversely related to the number of drugs that had ever been launched 1-15 years earlier.
  - One additional drug for a disease launched at least 12 years before year t reduced YLL90 from that disease in year t by 2.8%.
- The **number of deaths** is significantly inversely related to the number of drugs that had ever been launched 1-15 years earlier.
  - One additional drug for a disease launched at least 12 years before year t reduced the number of deaths from that disease in year t by 2.8%.

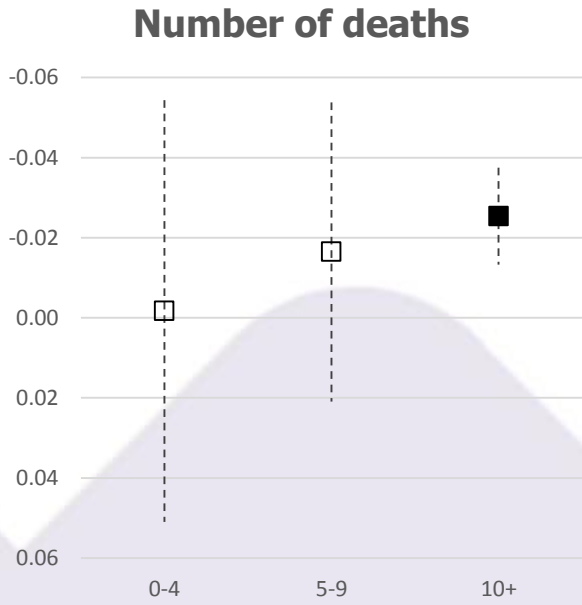
Reduction in the number of years of life lost

- If no drugs had been launched during 1987-2003, we estimate that YLL90 would have been 27.2% higher than it actually was in 2015.
- We estimate that the drugs that were launched during 1987-2003 reduced YLL90 in 2015 by 586,714 (= 27.2% * 2,157,774).
- Similar calculations indicate that the drugs that were launched during 1987-2003 reduced YLL85 and YLL80 in 2015 by 370,891 and 194,905, respectively.
- The estimates indicate that about half (53%) of the 1998-2015 decline in the pre-age-80 premature mortality rate, three-fourths (75%) of the decline in the pre-age-85 premature mortality rate, and almost all (94%) of the decline in the pre-age-90 premature mortality rate, was due to pharmaceutical innovation.

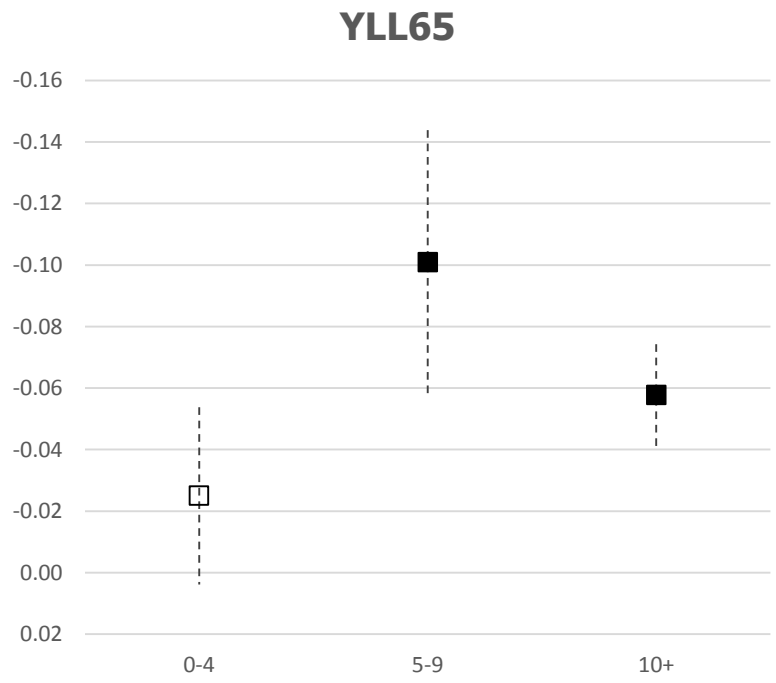
Estimates of parameters of model of cancer survival and mortality (eq. (5))

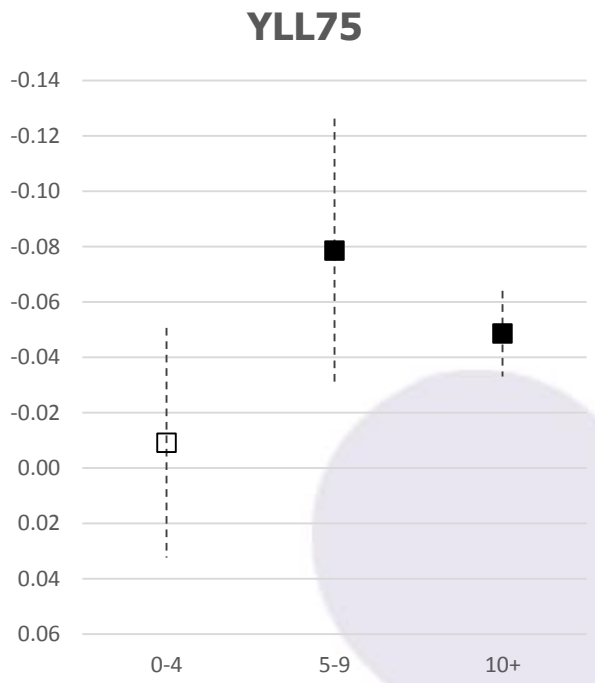


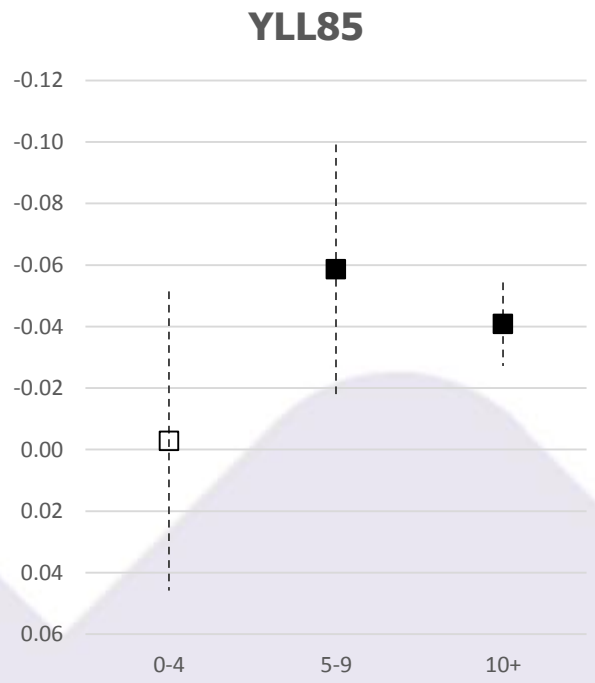




Estimates of parameters of model of cancer survival and mortality (eq. (5))







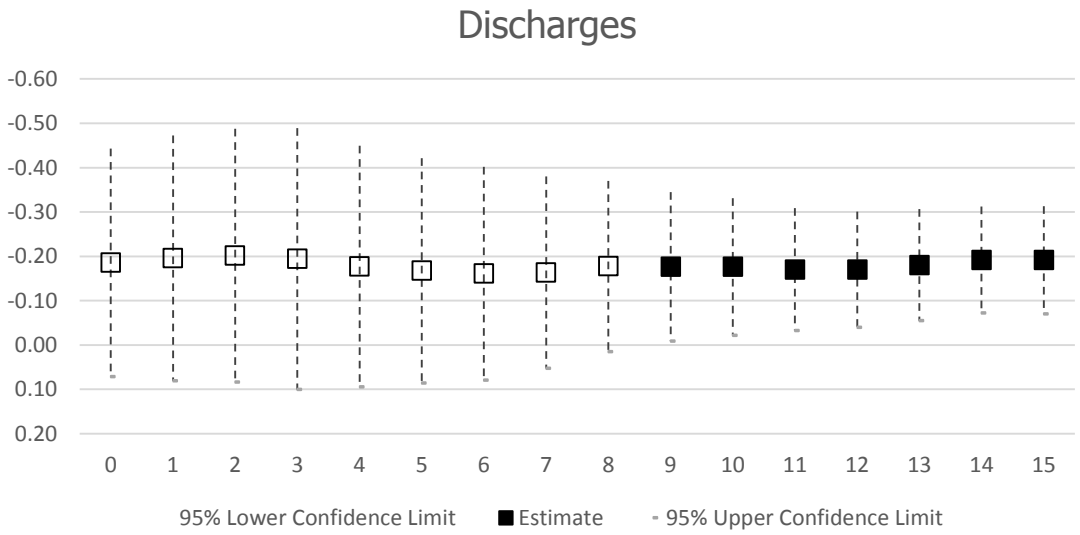
Cancer survival

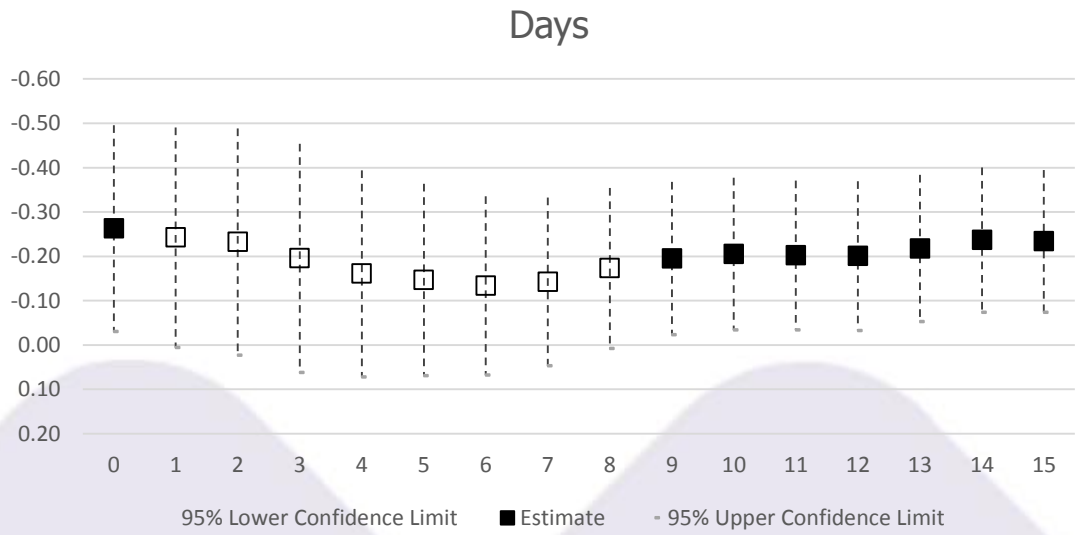
- The probability that a person diagnosed with cancer at site s during the period t-4 to t (e.g. 2011-2015) survived at least 5 years after being diagnosed was not related to the number of drugs for cancer at site s launched during the period t-4 to t. It is likely that very few of those patients were treated with newly launched drugs.
- However, the estimates indicate that **the greater the number of drugs that were launched by the end of year t-5, the higher the survival rate of patients diagnosed during the period t-4 to t.**
- The estimate of $\beta_{5\text{-}9}$ is about three times as large as the estimate of β_{10+}; this may be due to higher quality of later-vintage drugs.
- Our estimates suggest that about **44% of the increase in the 5-year survival rate** (from 62.1% in 2001-2005 to 69.9% in 2011-2015) **was due to the 2006-2016 increase in the number of cancer drugs that had been launched.**

Cancer mortality

- One additional drug for a cancer site is estimated to have reduced the **number of deaths** from cancer at that site by 2.5% after 10 years.
- The age-standardized cancer mortality rate declined by about 11% (from 180.8 to 161.3) between 2007 and 2017; the estimates indicate that cancer drugs launched during 1998-2008 reduced the number of cancer deaths in 2018 by 7.8%.
- Between 2008 and 2018, mean age at death from cancer increased by 1.06 years. Our estimates imply that almost half (48%) of this increase was due to the expansion in the number of cancer drugs.
- The estimates also imply that **cancer drugs launched during 2004-2013 reduced YLL65, YLL75, and YLL85 by 14.4%, 13.0%, and 11.4%, respectively.**

Estimates of parameters of model of utilization of hospitals for all diseases (eq. (6))





Utilization of hospitals for all diseases

- The number of hospital discharges and days of care are significantly inversely related to the number of drugs that had ever been launched 9-15 years earlier.
  - They are most closely related to the number of drugs that had ever been launched 14-15 years earlier.
- The estimates indicate that, if no new drugs had been launched during 1986-2000, the number of hospital days in 2015 would have been 7.3% higher than it actually was.
- We estimate that the new drugs launched during 1986-2000 reduced the number of hospital days in 2015 by 1.71 million (= 7.3% * 23.3 million).

Average cost-effectiveness: initial estimate

- We estimated that the drugs that were launched during 1987-2003 reduced YLL90 from all diseases in 2015 by 586,714.
- IQVIA data indicate that 2015 expenditure on drugs launched during 1987-2003 was 3.45 billion AUD.
- Hence if the drugs launched during 1987-2003 had had no effect on other medical expenditure in 2015, the cost per life-year gained before age 90 would not have exceeded 5888 AUD (= 3.45 billion AUD / 586,714 life-years).
    - The cost per life year gained before ages 85 and 80 would not have exceeded 9307 AUD and 17,709 AUD, respectively.

Average cost-effectiveness: initial estimate

- As noted by Bertram et al (2016), authors writing on behalf of the WHO's *Choosing Interventions that are Cost–Effective* project (WHO-CHOICE) suggested in 2005 that "interventions that avert one disability-adjusted life-year (DALY) for less than average per capita income for a given country or region are considered very cost–effective; interventions that cost less than three times average per capita income per DALY averted are still considered cost–effective."
- Australia's per capita GDP was 83,145 AUD in 2015, so these estimates indicate that, **even if we ignore the effect of new drugs on hospital utilization, the drugs launched during 1987-2003 were very cost–effective, overall.**

Accounting for hospital cost reduction

- **When the effect of new drugs on hospital utilization is taken into account, the evidence indicates that, in the long run, pharmaceutical innovation was cost-saving as well as life-year saving.**
- We estimated that, if no new drugs had been launched during 1986-2000, the number of hospital days in 2015 would have been 7.3% higher than it actually was.
- 2015 expenditure on inpatient curative and rehabilitative care was 47.5 billion AUD, so new drugs launched during 1986-2000 may have reduced 2015 hospital expenditure by 3.47 billion AUD (= 7.3% * 47.5 billion AUD).
- This figure is 71% higher than 2015 expenditure on drugs launched during 1986-2000 (2.03 billion AUD).

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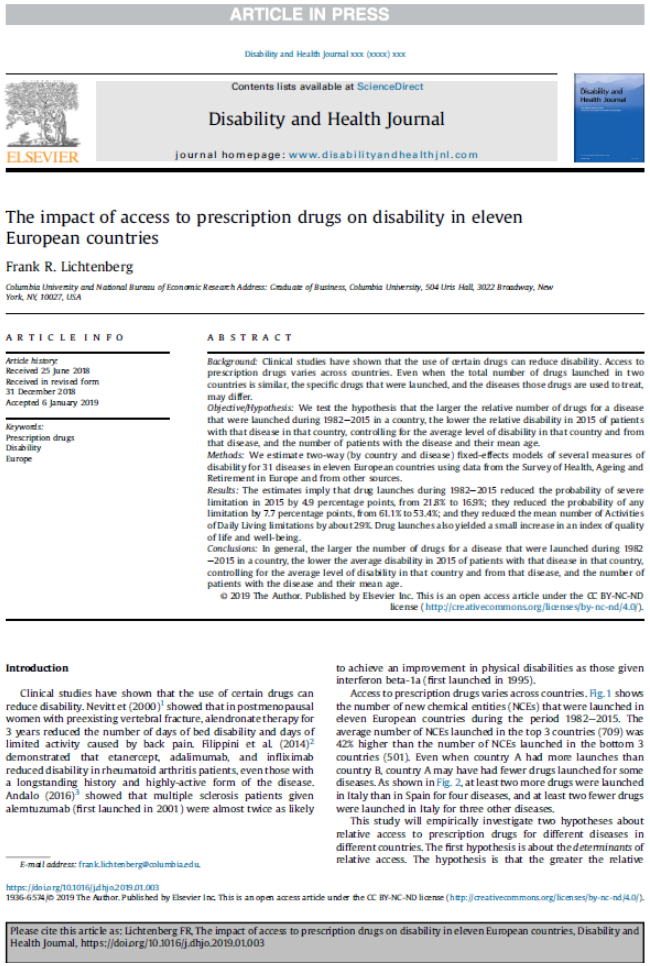

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The impact of access to prescription drugs on disability in eleven European countries

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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.

Introduction

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

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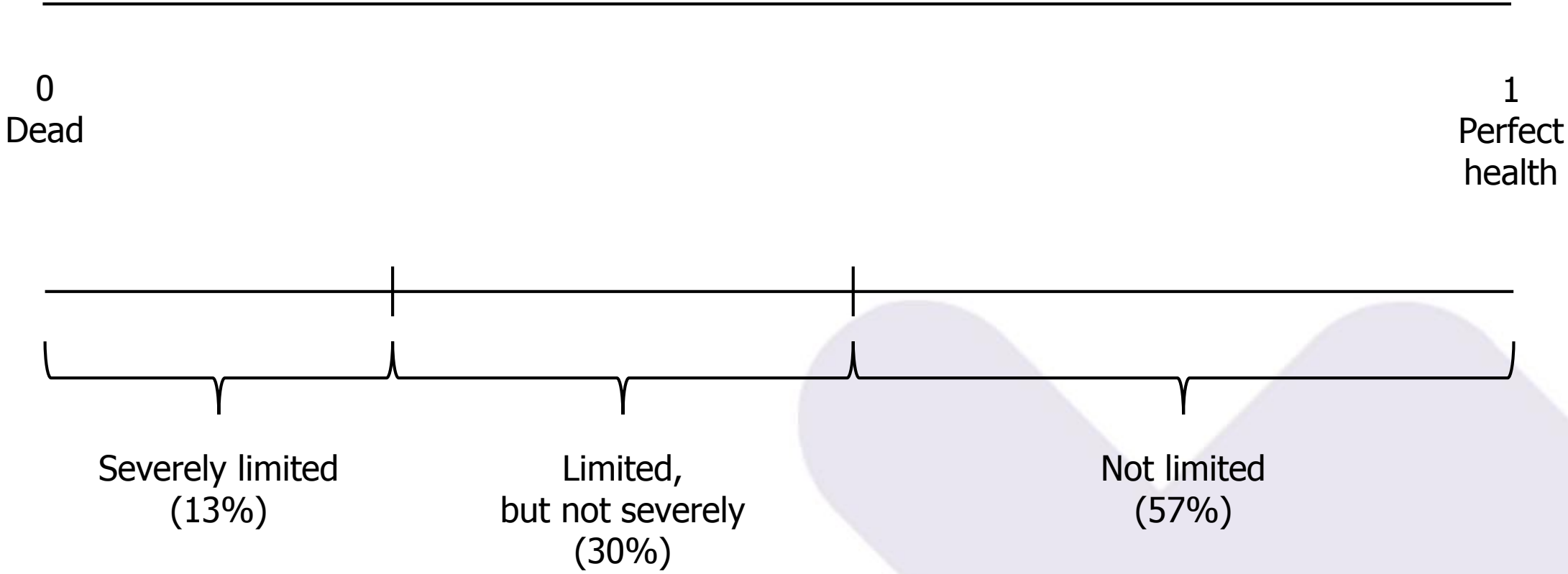
[The impact of access to prescription drugs on disability in eleven European countries]

Disability and Health Journal 2019

Quality of life



Quality of life

Disability = 1 – (quality of life)

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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).

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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.

Figure 1
Number of NCEs launched during 1982-2015, by country

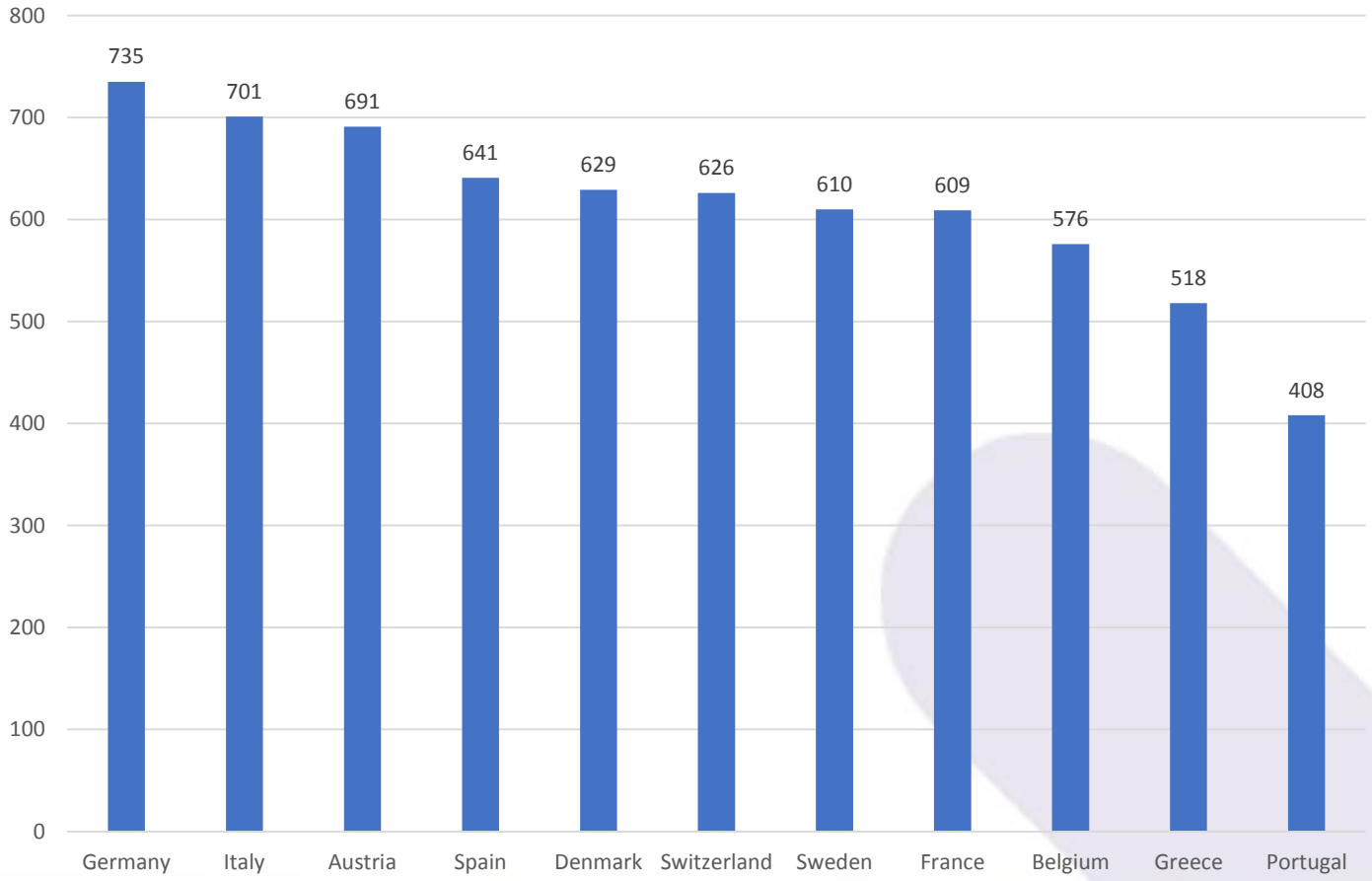
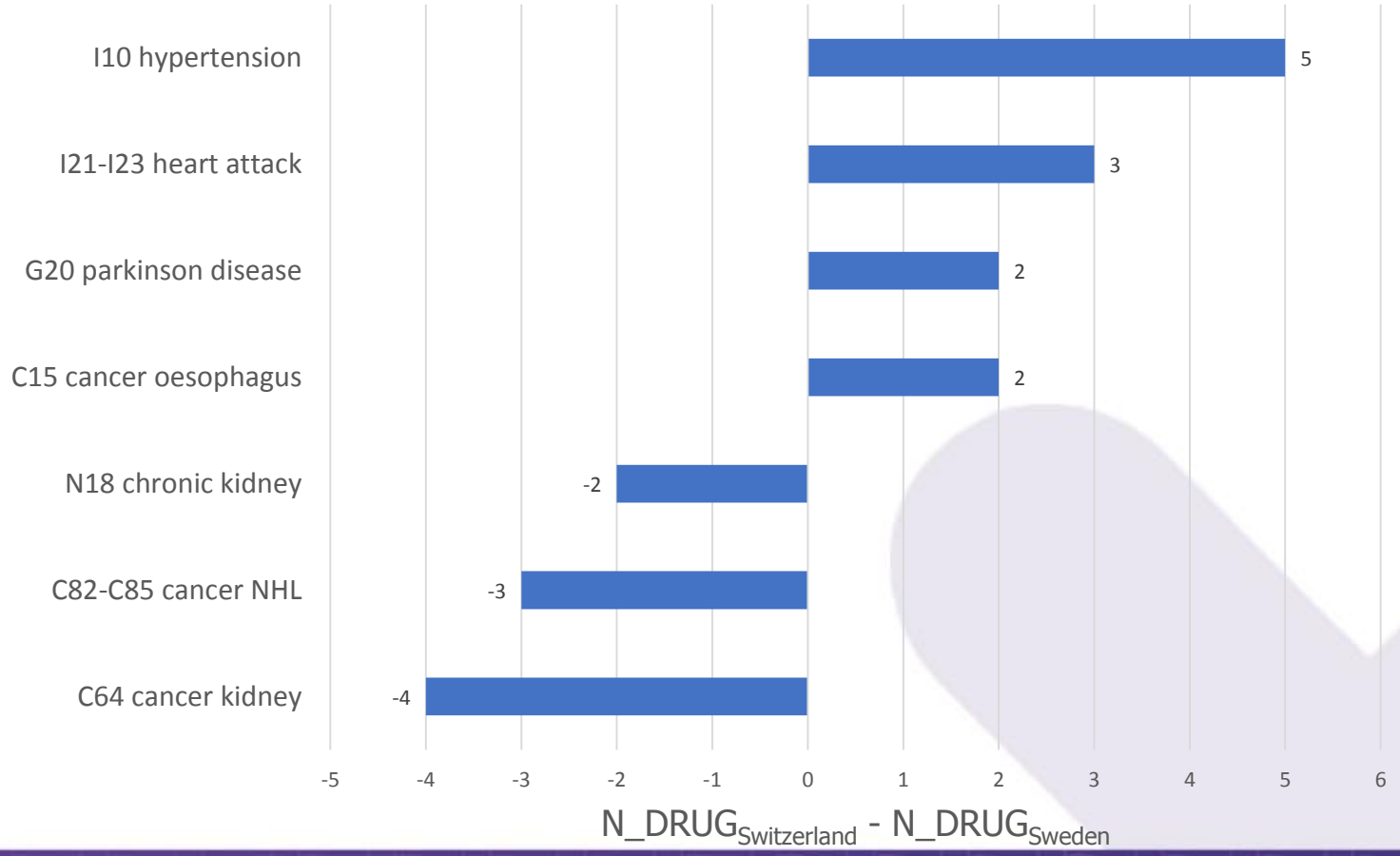
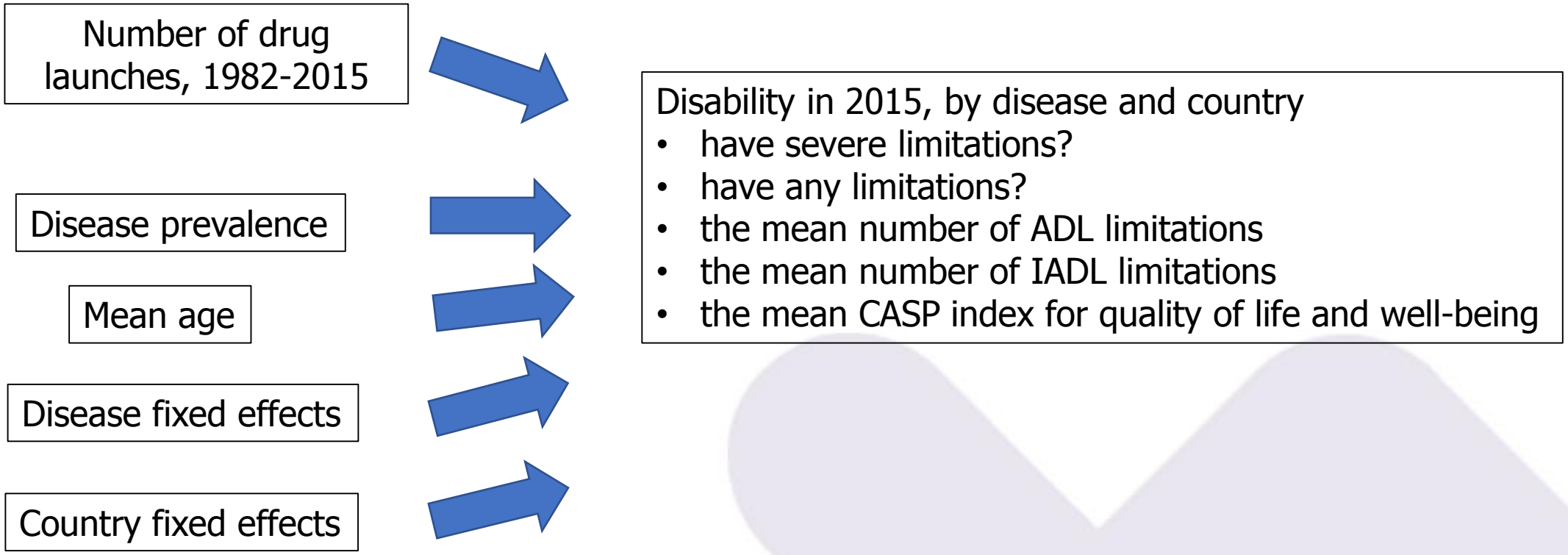


Figure 2
Difference between number of drugs launched during 1982-2015 for 7 diseases in Switzerland and Sweden



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.


Number of drug launches, 1982-2015
Disease prevalence
Mean age
Disease fixed effects
Country fixed effects
Disability in 2015, 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

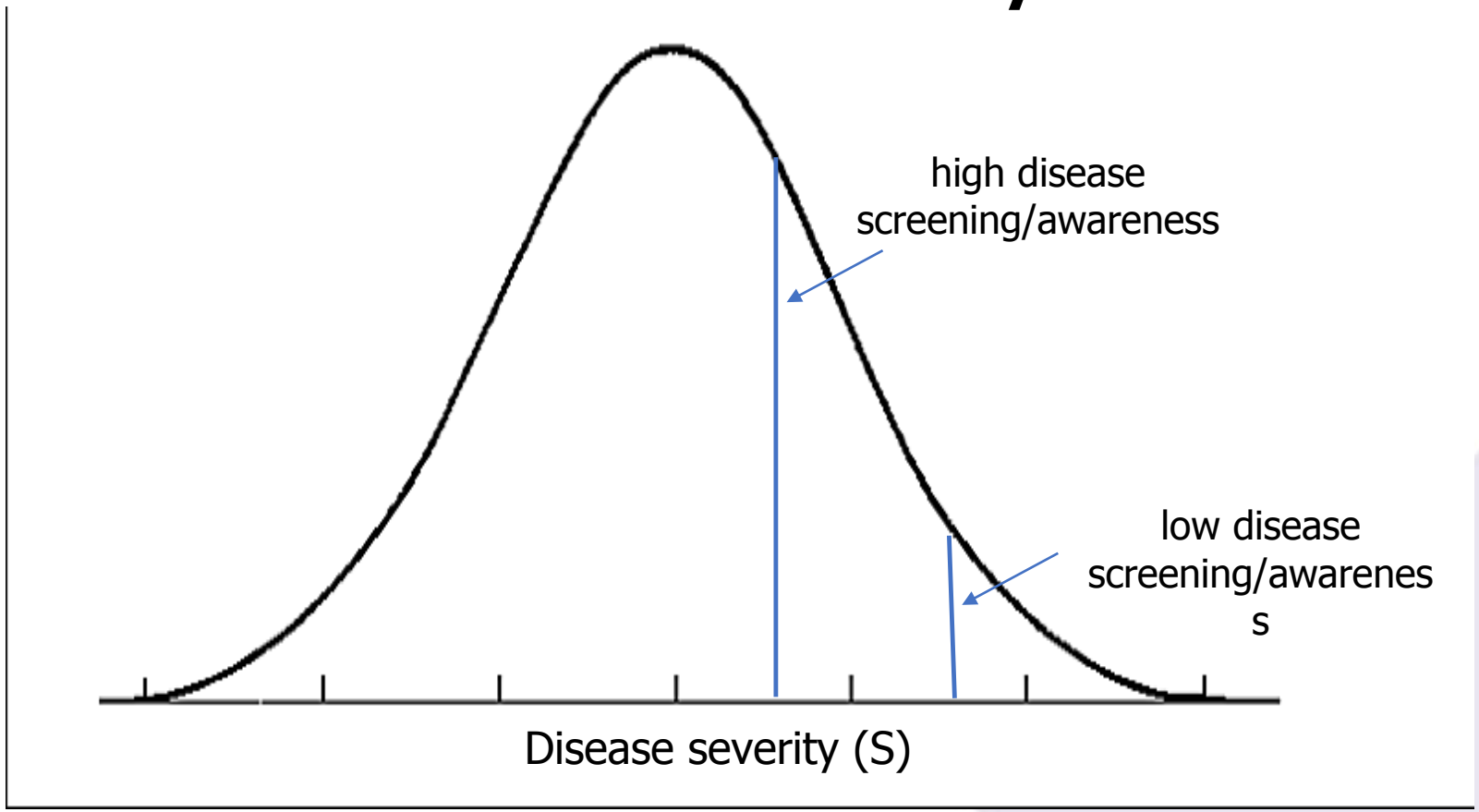
Diff-in-diff model of the effect of the number of 1982-2015 drug launches on disability in 2015 (eq. (2))

$$Y_{dc} = \beta\ LAUNCHES\_1982\_2015_{dc} + \gamma\ \ln(PREV_{dc}) + \rho\ AGE\_MEAN_{dc} + \alpha_d + \pi_c + \varepsilon_{dc}$$

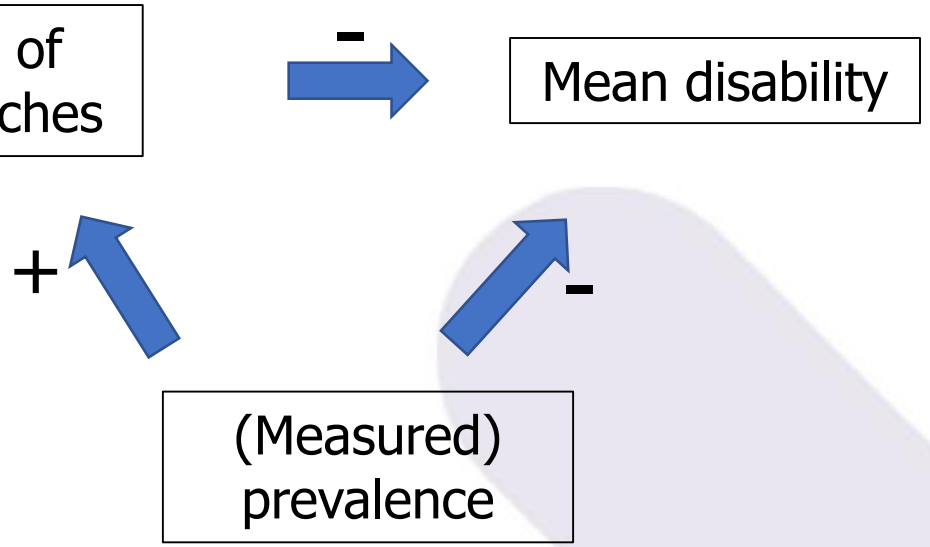
where Y_{dc} is one of the following variables:

- 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

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



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



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

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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

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 on drugs launched after 1981 by people 45 and over in the eleven European countries was $611.
- Expenditure of $611 reduced the probability of being severely limited by 4.3 percentage points.
- If people would have been willing to pay at least $12,469 (= $611 / 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.

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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.