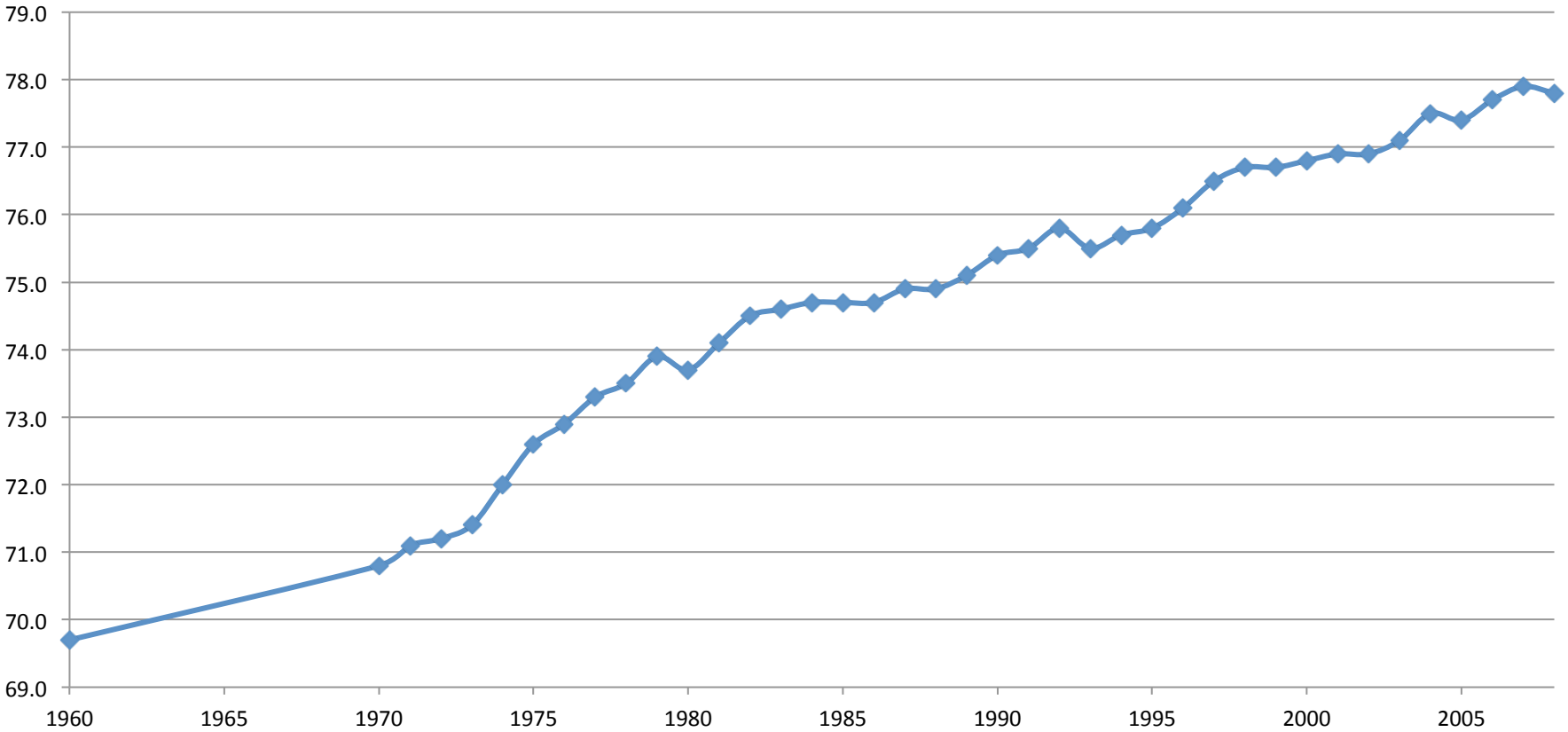
The impact of pharmaceutical innovation on longevity and other health outcomes

Frank R. Lichtenberg
Columbia University and
National Bureau of Economic Research
frank.lichtenberg@columbia.edu

U.S. life expectancy at birth, 1960-2008

Life expectancy has increased substantially during the past 50 years,
even during periods (like the last decade) when per capita GDP barely increased



Hypothesis

A substantial part of longevity growth during recent decades has been due to medical innovation.

Hypothesis

- I hypothesize that the health and longevity of a population depends on how technologically advanced the medical goods (including drugs) and services its members use are.
- Furthermore, how technologically advanced a medical good or service is depends on its *vintage*, defined as its year of invention or first use.
  - Solow (1960) introduced the concept of vintage into economic analysis. Solow's basic idea was that technical progress is "built into" machines and other goods and that this must be taken into account when making empirical measurements of their roles in production.

    Solow RM (1960), "Investment and technological progress," in K. Arrow, S. Karlin and P. Suppes (eds.), *Mathematical Methods in Social Sciences 1959* (Stanford: Stanford University Press), 89-104.
  - This was one of the contributions to the theory of economic growth that the Royal Swedish Academy of Sciences cited when it awarded Solow the 1987 Alfred Nobel Memorial Prize in Economic Sciences.

This hypothesis is consistent with the literature on economic growth

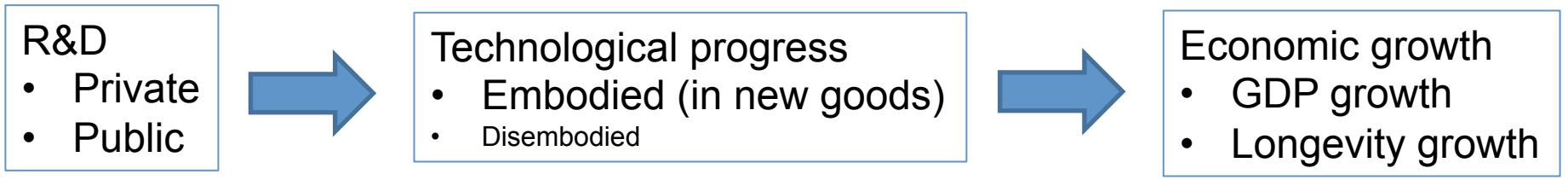
- Longevity increase is an important part of economic growth and development.
  - Nordhaus estimated that, "to a first approximation, the economic value of increases in longevity over the twentieth century is about as large as the value of measured growth in non-health goods and services".
- In the long run, the rate of economic growth is determined by the rate of technological progress, which is generated by private and public R&D investment.
- Most technological progress is *embodied* in new goods.
  - Hercowitz: "'embodiment' is the main transmission mechanism of technological progress to economic growth."
- Therefore, the welfare of consumers (and the productivity of producers) depends on the *vintage* of the goods and services (or inputs) they use, especially when those goods are R&D-intensive.
  - According to the Merriam Webster dictionary, one definition of vintage is "a period of origin or manufacture (e.g. a piano of 1845 vintage)".
  - I define the vintage of a drug as the year the drug was first approved by the FDA, e.g. the vintage of atorvastatin is 1997.
- NSF: The pharmaceutical and medical devices industries are the most R&D-intensive industries in the economy

New products and economic growth

Economists believe that the development of new products is the main reason why people are better off today than they were several generations ago.

- Grossman and Helpman (*Innovation and Growth in the Global Economy*, Cambridge: MIT Press, 1991) 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 (*The Economics of New Goods*, 1996) stated simply that "new goods are at the heart of economic progress."
- Jones (*Introduction to Economic Growth*, 1998) argues that "technological progress [is] the ultimate driving force behind sustained economic growth" (p.2), and that "technological progress is driven by research and development (R&D) in the advanced world" (p. 89).
- Bils (*Measuring the Growth from Better and Better Goods*, 2004) makes the case that "much of economic growth occurs through growth in quality as new models of consumer goods replace older, sometimes inferior, models."

R&D, technological progress, and economic growth



Dartmouth Atlas of Health Care

- "Studies that have looked carefully at the additional services provided in high-spending regions have shown that the higher volume of care does not produce better outcomes for patients. Medicare beneficiaries in high-spending regions do not receive more "effective care" (services shown by randomized trials to result in better health outcomes, such as making sure that heart attack patients get proper medication)."
- http://www.dartmouthatlas.org/downloads/reports/Spending_Brief_022709.pdf

Conventional wisdom

- There is considerable regional variation in medical expenditure
- Medical expenditure is uncorrelated across regions with health outcomes
- Therefore, “money doesn’t matter”
- Moreover, much of the growth and variation in medical expenditure is due to medical technology
- Therefore, “technology doesn’t matter”

Medical innovation → health

	Study 1	Study 2	Study 3	Study 4	Study 5
Measures of health					
• Longevity (quantity of life)	x	x	x		
• Functional status (quality of life)				x	x
Measures of innovation					
• Vintage of drugs	x	x		x	x
• Number of drugs			x		
Research design					
• Patient-level data	x			x	
• Aggregate data					
• Longitudinal region-level data		x			x
• Longitudinal disease-level data			x		
Population	Elderly Americans, 1996-2006	Entire population of 30 developing and high income countries, 2000-2009	Swedish population, 1997-2010	U.S. nursing home residents, 2004	U.S. working-age population, 1995-2004

The impact of pharmaceutical innovation on the longevity and health of the Medicare population: evidence from linked Medical Expenditure Panel Survey-National Death Index data, 1996-2006

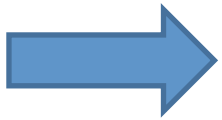
Key hypothesis

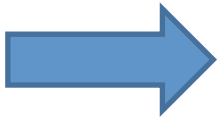
- Patients using newer drugs have longer time till death than patients using older drugs, controlling for an extensive set of patient characteristics
  - I am able to track the patient's vital status for up to 10 years after the period of prescription drug use
- Pharmaceutical innovation, which causes the mean vintage of prescription drugs consumed to increase over time, accounts for a significant amount of longevity growth

General approach

Rx vintage:
- Mean FDA approval year of Rx active ingredients
- Fraction of prescriptions that are for “new” drugs

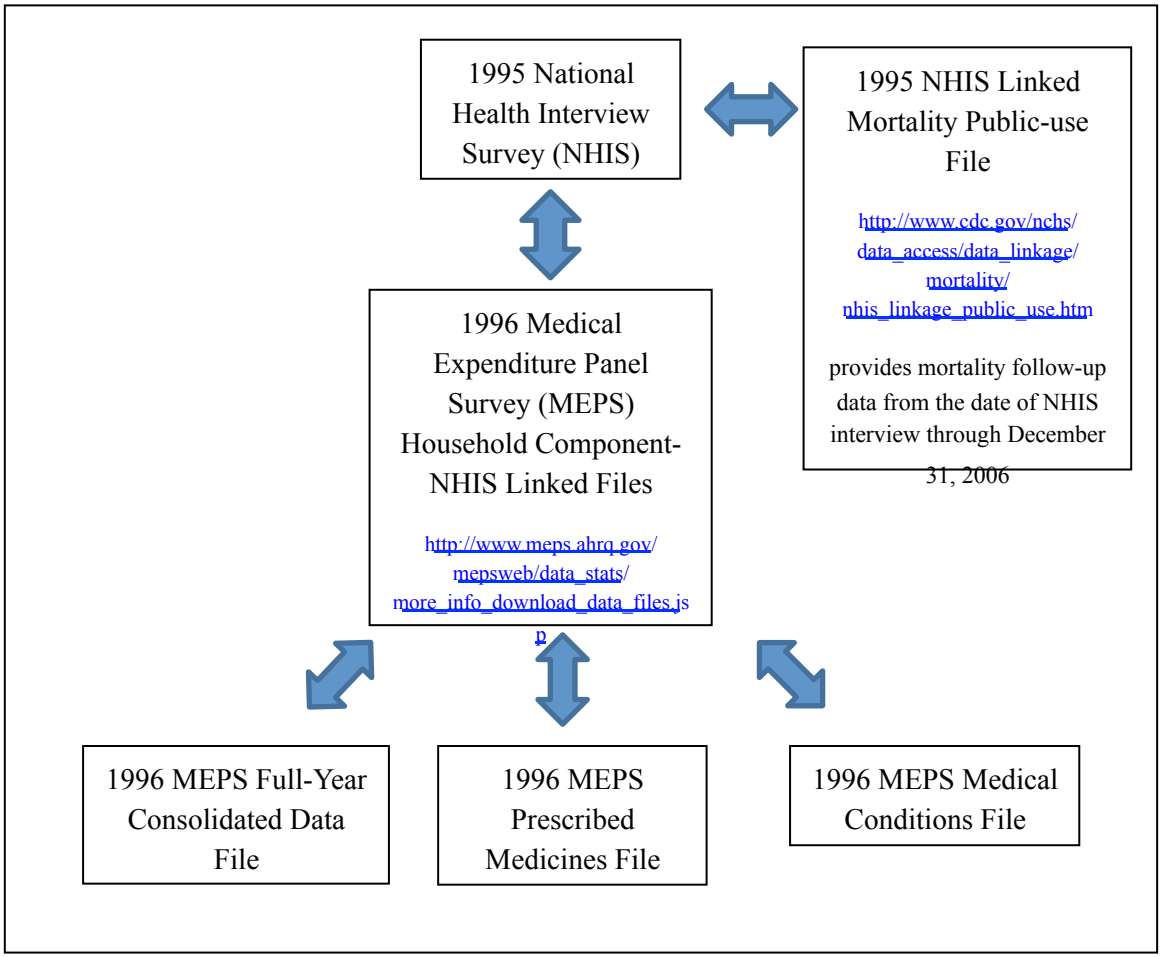
Other individual attributes
- interview year
- age
- sex
- race
- marital status
- Census region
- insurance coverage
- education
- income (poverty group category)
- BMI
- smoking participation
- presence of medical conditions—4 different sources of information
- how long person has taken the medication
- activity limitations



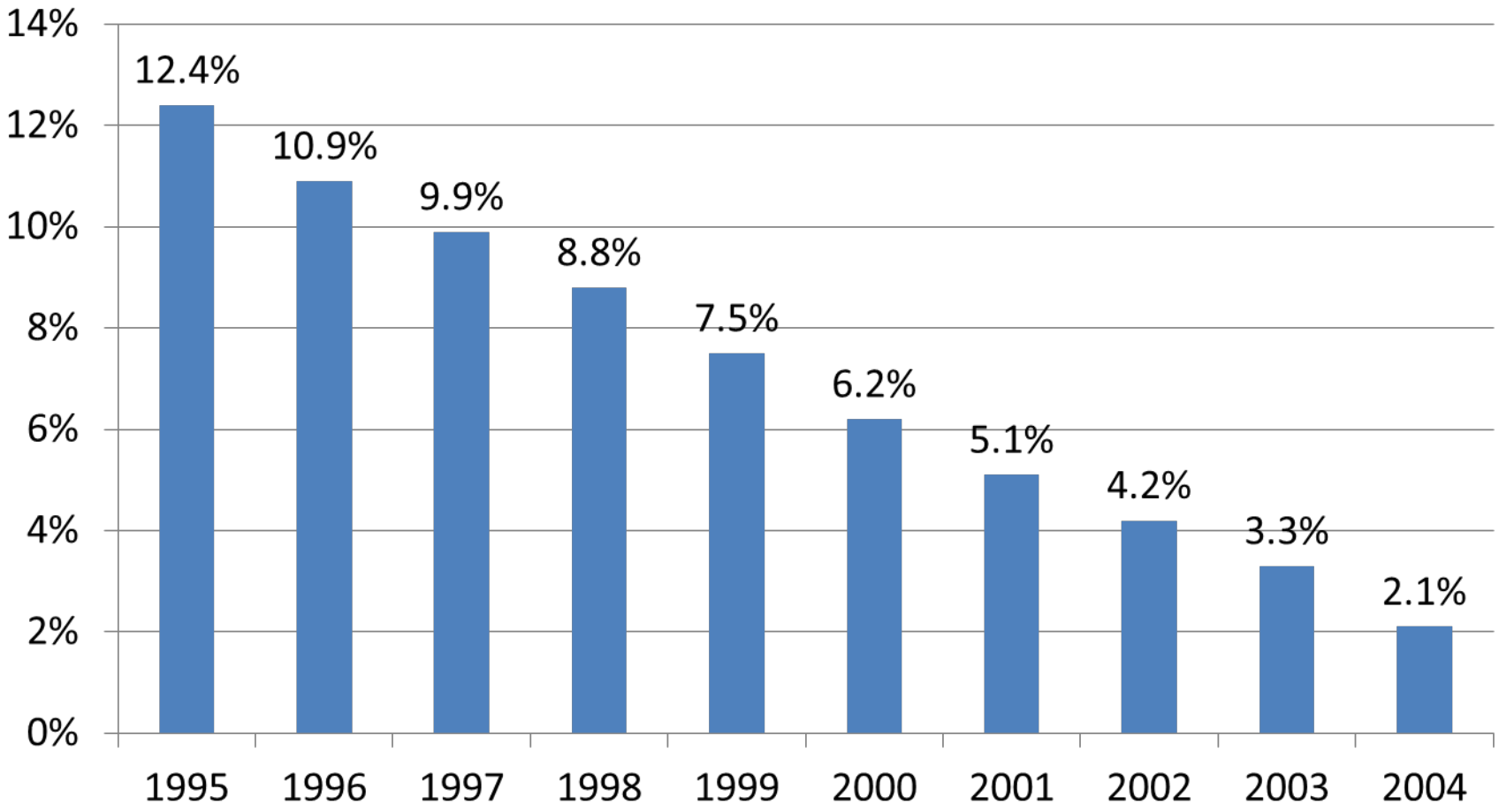


Survival: Number of years till death (right-censored)

Data


1995 National Health Interview Survey (NHIS)
1995 NHIS Linked Mortality Public-use File
http://www.cdc.gov/nchs/data_access/data_linkage/mortality/nhis_linkage_public_use.htm
provides mortality follow-up data from the date of NHIS interview through December 31, 2006
1996 Medical Expenditure Panel Survey (MEPS) Household Component-NHIS Linked Files
http://www.meps.ahrq.gov/mepsweb/data_stats/more_info_download_data_files.jsp
1996 MEPS Full-Year Consolidated Data File
1996 MEPS Prescribed Medicines File
1996 MEPS Medical Conditions File

Fraction of NHIS interviewees who had died by 12/31/2006, by year of NHIS interview



Exclusions

- Provider-administered drugs (e.g. chemotherapy)
  - These may account for about 15% of total drug expenditure
- Nursing home residents
  - 43.3 nursing home residents per 1000 population 65 and over in 1999 http://www.cdc.gov/nchs/data/hus/hus09.pdf#105

Reduced form model

$survival\_time_i = b\ rx\_vintage_i + age\_dummies + sex\_dummies + race\_dummies + medical\_condition\_dummies\ educational\_attainment\_dummies + income\_dummies + + region\_dummies + insurance\_coverage\_dummies + marital\_status\_dummies + e_i$

where

$survival\_time_i$ = the number of years patient i lived after being interviewed = $death\_date_i - interview\_date_i$

$rx\_vintage_i$ = the mean vintage of prescription drugs used by patient i

Medical conditions

MEPS Medical Conditions files contain variables describing medical conditions reported by respondents in several sections of the MEPS questionnaire, including the Condition Enumeration section, all questionnaire sections collecting information about health provider visits, prescription medications, and disability days.

Conditions can be added to the MEPS conditions roster in several ways:

- A condition can be reported in the Priority Condition Enumeration section in which persons are asked if they have ever been diagnosed with specific conditions.
- The condition can be identified as the reason reported by the household respondent for a particular medical event (hospital stay, outpatient visit, emergency room visit, home health episode, prescribed medication purchase, or medical provider visit).
- The condition may be reported as the reason for one or more episodes of disability days.
- Finally, the condition may be reported by the household level respondent as a condition "bothering" the person during the reference period.

Right censoring

- Since most NHIS respondents were still alive on 12/31/2006, most observations are right censored.
- I will account for this by using a statistical procedure (the SAS LIFEREG procedure) that fits parametric models to failure time data that can be uncensored, right censored, left censored, or interval censored.
- To reduce the degree of censoring, I will analyze people who were 65 and over when interviewed during 1996-1999. (Drawback: data on BMI and smoking are not available before 2001. However, these variables are not correlated with rx_vintage.)

Measuring vintage

I will analyze a number of alternative measures of vintage. One measure is based on the mean vintage of the ingredients contained in a patient's prescriptions:

$$rx\_vintage_i = \frac{\sum_a n\_rx_{ai}\ fda\_ingredient\_year_a}{\sum_a n\_rx_{ai}}$$

where

n_rx_{ai} = the number of prescriptions for patient i that contained active ingredient a

$fda\_ingredient\_year_a$ = the year in which the FDA first approved active ingredient a

Alternative measure of vintage

The fraction of prescriptions containing "new" (e.g. post-1990) active ingredients

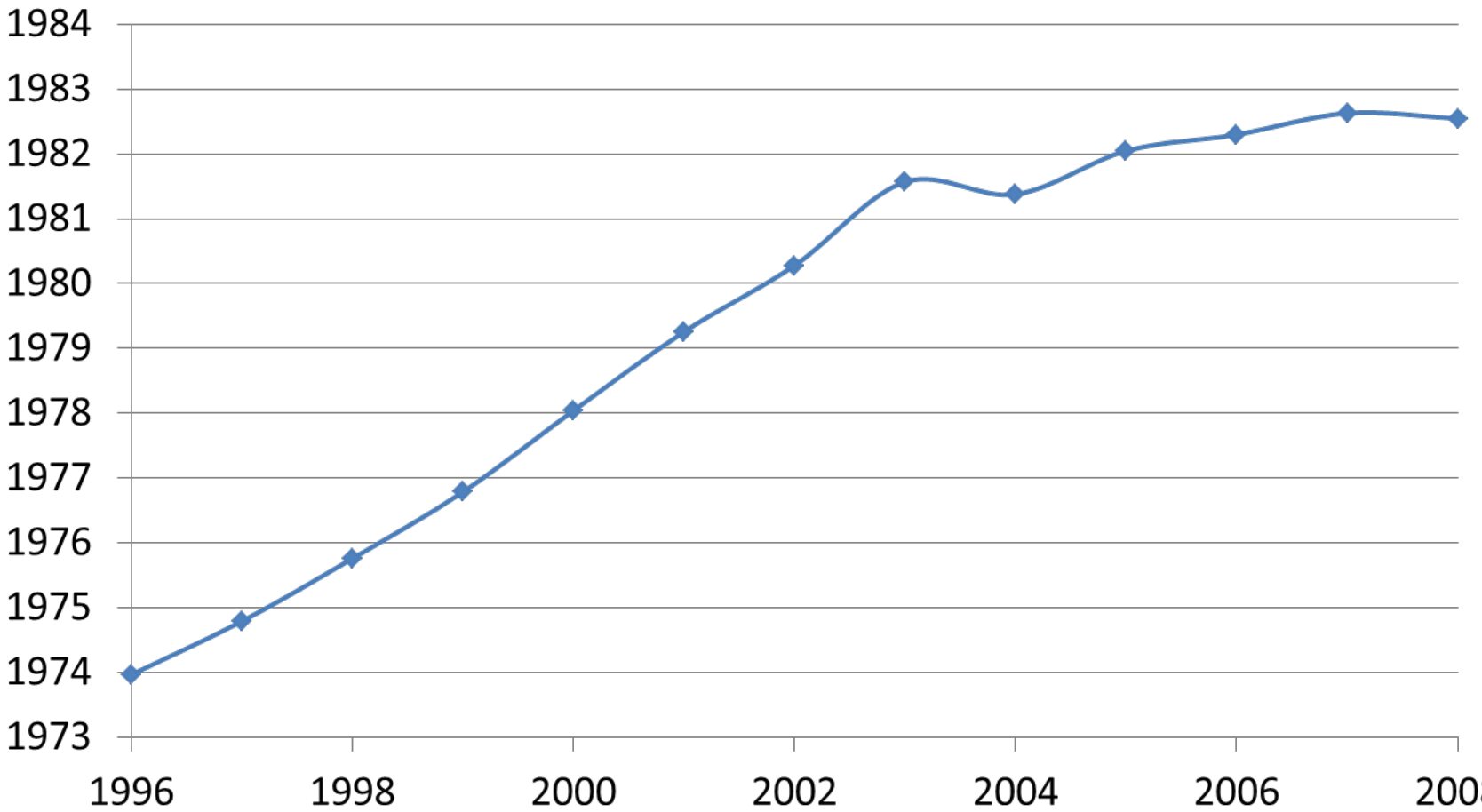
$$rx\_post1990\%_i = \frac{\sum_a n\_rx_{ai}\ post1990_a}{\sum_a n\_rx_{ai}}$$

where

$post1990_a = 1$ if $fda\_ingredient\_year_a > 1990$

$= 0$ if $fda\_ingredient\_year_a \leq 1990$

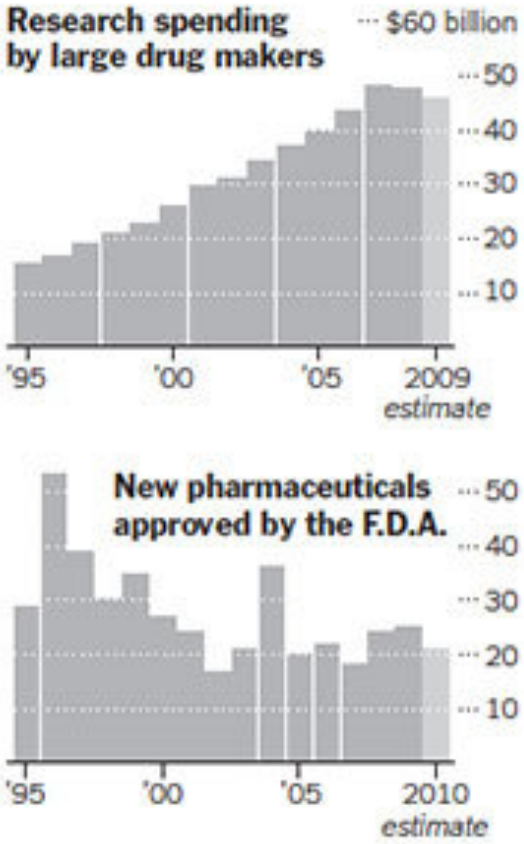
rx_vintage


1984
1983
1982
1981
1980
1979
1978
1977
1976
1975
1974
1973
1996
1998
2000
2002
2004
2006
2008

year	fda_year	post1990	n_rx
1996	1974.0	16%	122,436
1997	1974.8	20%	197,795
1998	1975.8	24%	144,039
1999	1976.8	28%	143,729
2000	1978.0	33%	146,989
2001	1979.3	37%	213,830
2002	1980.3	40%	254,411
2003	1981.6	44%	207,673
2004	1981.4	43%	241,603
2005	1982.0	44%	279,824
2006	1982.3	44%	303,009
2007	1982.6	45%	255,473
2008	1982.5	45%	253,902
1996-2003	7.6	27%	
2003-2008	1.0	2%	

Fewer New Drugs

Large drug makers have begun to reduce spending on research and development, while the industry's output of new drugs approved by the Food and Drug Administration remains in decline.



Sources: Pharmaceutical Research and Manufacturers of America; F.D.A.

THE NEW YORK TIMES

Only one tenth of individual variation in drug vintage is explained

Explanatory variables:

- Sex
- Age
- Year
- Educational attainment
- Race
- Region
- Marital status
- Poverty category
- Insurance coverage
- BMI
- Smoking
- 110 medical condition dummy variables

Estimates with no explanatory variables for population age 65+ (whose mean age is 74.3)

l	14.61
k	1.24
mean = l G(1+(1/k))	12.99

As expected, k > 1: the mortality rate increases with time.
Estimated life expectancy of this population is 12.99 years.
When I include sex and age dummy variables, coefficient on female = .26, implying that mean life expectancy of females is about 26% higher than mean life expectancy of males.
Comparison with published estimates from National Vital Statistics Reports, Vol. 58, No. 21, June 28, 2010 :

Average number of years of life remaining at age 75 in 2000, both sexes	11.1
Average number of years of life remaining at age 75 in 2000, males	9.9
Average number of years of life remaining at age 75 in 2000, females	12.0

Published estimates of life expectancy, and of female-male differential (19%), are somewhat smaller than estimates implied by my model.
Period vs. cohort life table.

Dependent Variable	Log(surv_time)
Censoring Variable	MORTSTAT
Censoring Value(s)	0
Number of Observations	5093
Noncensored Values	2054
Right Censored Values	3039
Left Censored Values	0
Interval Censored Values	0
Name of Distribution	Weibull
Log Likelihood	-4526.52068

Selected estimates from survival model

(model also includes 100+ medical condition dummy variables)

Parameter	Level1	Estimate	StdErr	ChiSq	ProbChiSq
fda_year		**0.005751**	**0.001841**	**9.757118**	**0.001786**
age	65-69	1.410315	0.095705	217.1539	3.78E-49
age	70-74	1.119716	0.091164	150.8568	1.13E-34
age	75-79	0.798467	0.087746	82.80492	9.06E-20
age	80-84	0.477265	0.086717	30.2911	3.72E-08
age	85-89	0.299828	0.092506	10.50525	0.00119
age	90+	0			
SEX	Female	0.35397	0.040451	76.5739	2.12E-18
year	1996	-0.16854	0.048472	12.08982	0.000507
year	1997	-0.12759	0.052521	5.901103	0.015131
year	1998	0.003216	0.058061	0.003067	0.955832
year	1999	0			
race2	ASIAN OR PACIFIC ISLANDER	0.352128	0.162779	4.679572	0.030523
race2	BLACK	-0.10803	0.049858	4.694412	0.030261
race2	WHITE	0			
POVCAT	1	-0.11144	0.055403	4.046054	0.044275
POVCAT	2	-0.15482	0.066244	5.461927	0.019435
POVCAT	3	-0.08299	0.05122	2.625103	0.105186
POVCAT	4	-0.00395	0.047386	0.00695	0.933559
POVCAT	5	0			
inscov	ANY PRIVATE	-0.43498	0.51335	0.717988	0.396805
inscov	PUBLIC ONLY	-0.4881	0.512997	0.905308	0.341362
educyr	00 - 08 ELEMENTARY GRADES 1 - 8	-0.16692	0.093448	3.190755	0.074056
educyr	09 - 11 HIGH SCHOOL GRADES 9 - 11	-0.27049	0.094643	8.167902	0.004264
educyr	12 GRADE 12	-0.19545	0.091087	4.60409	0.031896
educyr	13-15 1-3 YEARS COLLEGE	-0.0824	0.098066	0.7061	0.400742
educyr	16 4 YEARS COLLEGE	-0.09733	0.106128	0.841051	0.359096
educyr	17 5+ YEARS COLLEGE	0			
region	MIDWEST	0.067647	0.05099	1.760055	0.184618
region	NORTHEAST	0.042646	0.053109	0.644799	0.421978
region	SOUTH	0.034806	0.047306	0.541361	0.461869
region	WEST	0			

Calculation of incremental cost-effectiveness ratio (ICER)

	Life expectancy at age 75 (years)	Annual medical expend	Lifetime medical expend	Incremental cost effectiveness ratio
Baseline	11.10	$6,817	$75,666	
Baseline + effect of 7.6-year increase in rx vintage	11.59	$7,121	$82,498	
Effect of 7.6-year increase in rx vintage	0.49	$304	$6,832	$14,080

This ICER estimate is broadly consistent with estimates derived from clinical trials as reported in the CEA Registry.

Consistency with study based on longitudinal German state-level data

- In that study, I estimated that the increase in drug vintage increased life expectancy by 0.45 years between 2001 and 2007.
- The implied ICER is € 11,597 (= € 5,187 / 0.45 years), or $16,173 (at the current exchange rate of 1.39 $/€) per life-year.
- Lichtenberg, Frank, "The contribution of pharmaceutical innovation to longevity growth in Germany and France, 2001-2007," *PharmacoEconomics* 30(3), 2012 Mar 1; pp. 197-211.

Pharmaceutical innovation and longevity growth in 30 developing and high-income countries, 2000-2009

- We examine the impact of pharmaceutical innovation, as measured by the vintage (world launch year) of prescription drugs used, on longevity using longitudinal, country-level data on 30 developing and high-income countries during the period 2000-2009.
- The difference-in-differences estimation approach controls for unobserved determinants of longevity that varied across countries but were constant (or very stable) over time, and for unobserved determinants of longevity that changed over time but were invariant across countries.
- We also control for a number of time-varying country attributes that some previous studies have indicated may be important determinants of longevity: real per capita income, the unemployment rate, mean years of schooling, the urbanization rate, real per capita health expenditure (public and private), the DPT immunization rate among children ages 12-23 months, and some risk factors (HIV prevalence and tuberculosis incidence).

Model of longevity

$$LONGEVITY_{ct} = b\ VINTAGE_{ct} + g\ Z_{ct} + a_c + p_t + e_{ct} \qquad (1)$$

$LONGEVITY_{ct}$ = a measure of longevity in country c in year t

$VINTAGE_{ct}$ = a measure of the vintage of prescription drugs used in country c in year t

Z_{ct} = a vector of other attributes (e.g. income, education, risk factors, health expenditure) of country c in year t

a_c = a fixed effect for country c

p_t = a fixed effect for year t

e_{ct} = a disturbance

Model of longevity

$$LONGEVITY_{ct} = b\ VINTAGE_{ct} + g\ Z_{ct} + a_c + p_t + e_{ct} \qquad (1)$$

- The country fixed effects (a_c) control for unobserved determinants of longevity that vary across countries but are constant (or very stable) over time
- The year fixed effects (p_t) control for unobserved determinants of longevity that change over time but are invariant across countries.
- Eq. (1) is a difference-in-differences model: a positive and significant estimate of b would signify that countries with larger increases in vintage had larger longevity increases, controlling for changes in other included attributes.

Long differences

There are only two years (2000 and 2009) for which data on LONGEVITY and VINTAGE are both available. We can write versions of eq. (1) for each of these two years:

$LONGEVITY_{c,2000} = b\ VINTAGE_{c,2000} + g\ Z_{c,2000} + a_c + p_{2000} + e_{c,2000}$ (2)

$LONGEVITY_{c,2009} = b\ VINTAGE_{c,2009} + g\ Z_{c,2009} + a_c + p_{2009} + e_{c,2009}$ (3)

When we subtract eq. (2) from eq. (3), the country fixed effects vanish:

$DLONGEVITY_c = b\ DVINTAGE_c + g\ DZ_c + Dp + De_c$ (4)

where, for example,

$DLONGEVITY_c = LONGEVITY_{c,2009} - LONGEVITY_{c,2000}$ and

$Dp = p_{2009} - p_{2000}$.

Eq. (4) indicates that **the 2000-2009 *change* in longevity in country c depends on the *change* in drug vintage and the *changes* in other determinants of longevity in country c**. We will estimate eq. (4) by weighted least squares, weighting by 2009 country population.

Other potential determinants of longevity

We will control for a number of other country attributes that some previous studies have indicated may be important determinants of longevity:

- income (real per capita GDP in constant 2000 US$)
- unemployment rate
- education (mean years of schooling, 15+, total)
- urbanization rate
- real per capita health expenditure (public and private)
- DPT immunization rate (% of children ages 12-23 months)
- risk factors (HIV prevalence (% of population ages 15-49) and tuberculosis incidence)

Although the effects on longevity of at least some of these variables might seem obvious, the effects of some of them are theoretically ambiguous, or there is mixed evidence about their effects.

Other risk factors

- Unfortunately, data on some potentially important risk factors is missing so frequently that it is infeasible to include them in the longevity models we estimate, or to investigate their correlation with pharmaceutical innovation.
- However, more complete data on the following risk factors are available for OECD countries from the OECD Health database:
  - BMI_GT25: Overweight or obese population, self-reported, % of total population
  - BMI_GT30: Obese population, self-reported, % of total population
  - TOBACCO: Tobacco consumption, % of population aged 15+ who are daily smokers
  - ALCOHOL: Alcohol consumption, liters per capita (15+)
- **The increase in drug vintage was not correlated across OECD countries with the growth in obesity, tobacco use, or alcohol use.** It was significantly *positively* correlated with growth in the fraction of the population that was either overweight or obese (whose mean value was 54%), but Flegal et al (2005) concluded that "overweight [is] not associated with excess mortality."
- Therefore, **failure to control for these variables in the longevity growth equation (eq. (4)) is unlikely to bias estimates of the effect of pharmaceutical innovation on longevity growth.**

Non-pharmaceutical medical innovation

- Non-pharmaceutical medical innovation is much more difficult to measure than pharmaceutical innovation.
- However, data on one important type of non-pharmaceutical medical innovation—advanced imaging equipment—is available for OECD countries during the period 1999-2009 from the OECD Health database.
- Two indicators contained in that database are the number of Computed Tomography (CT) scanners and the number of Magnetic Resonance Imaging (MRI) units per million population
- **The increase in drug vintage** is positively correlated across OECD countries with growth in the number of MRI units per million population. However, it is negatively correlated with growth in the number of CT scanners per million population, and it **is not significantly correlated with growth in the overall quantity of advanced imaging equipment (CT + MRI) per million population.**
- This suggests that **failure to control for non-pharmaceutical medical innovation in the longevity growth equation (eq. (4)) is unlikely to bias estimates of the effect of pharmaceutical innovation on longevity growth.**

Measurement of longevity

- Beginning with the year 1999, the World Health Organization (WHO) began producing annual life tables for all Member States. These life tables form the basis of all WHO's estimates about mortality patterns and levels worldwide. Life tables have been developed for all Member States for the reference year 1990, 2000 and 2009 starting with a systematic review of all available evidence from surveys, censuses, sample registration systems, population laboratories and vital registration on levels and trends in under-five and adult mortality rates. WHO applies standard methods to the analysis of Member State data to ensure comparability of estimates across countries.
- We will analyze two types of measures contained in the WHO life tables:
  - **life expectancy at different ages (0, 25, 45, 65)**
  - **survival from age a_0 to age a_1 (birth to 25, 25 to 65, 65 to 75, and birth to 75).**

Pharmaceutical innovation measurement

- We construct measures of pharmaceutical innovation from the IMS Health MIDAS database, which provides annual data on the quantity (number of "standard dose units") of every prescription drug product sold in each country during the period 1999-2010.
- The database also indicates the molecules (active ingredients) contained in each product, and the world launch year of many molecules (world launch years of some (apparently very old) molecules are unknown).
- We use a two-step procedure to measure pharmaceutical innovation.

Vintage of each "international product"

$$POST1990\%_p = \frac{\sum_m INGRED\_OF_{pm}\ POST1990_m}{\sum_m INGRED\_OF_{pm}}$$

$POST1990\%_p$ = the fraction of product p's active ingredients that were launched after 1990

$INGRED\_OF_{pm}$ = 1 if product p contains molecule m
= 0 otherwise

$POST1990_m$ = 1 if $LAUNCH\_YEAR_m > 1990$
= 0 if $LAUNCH\_YEAR_m \leq 1990$ or $LAUNCH\_YEAR_m$ is unknown

$LAUNCH\_YEAR_m$ = the world launch year of molecule m

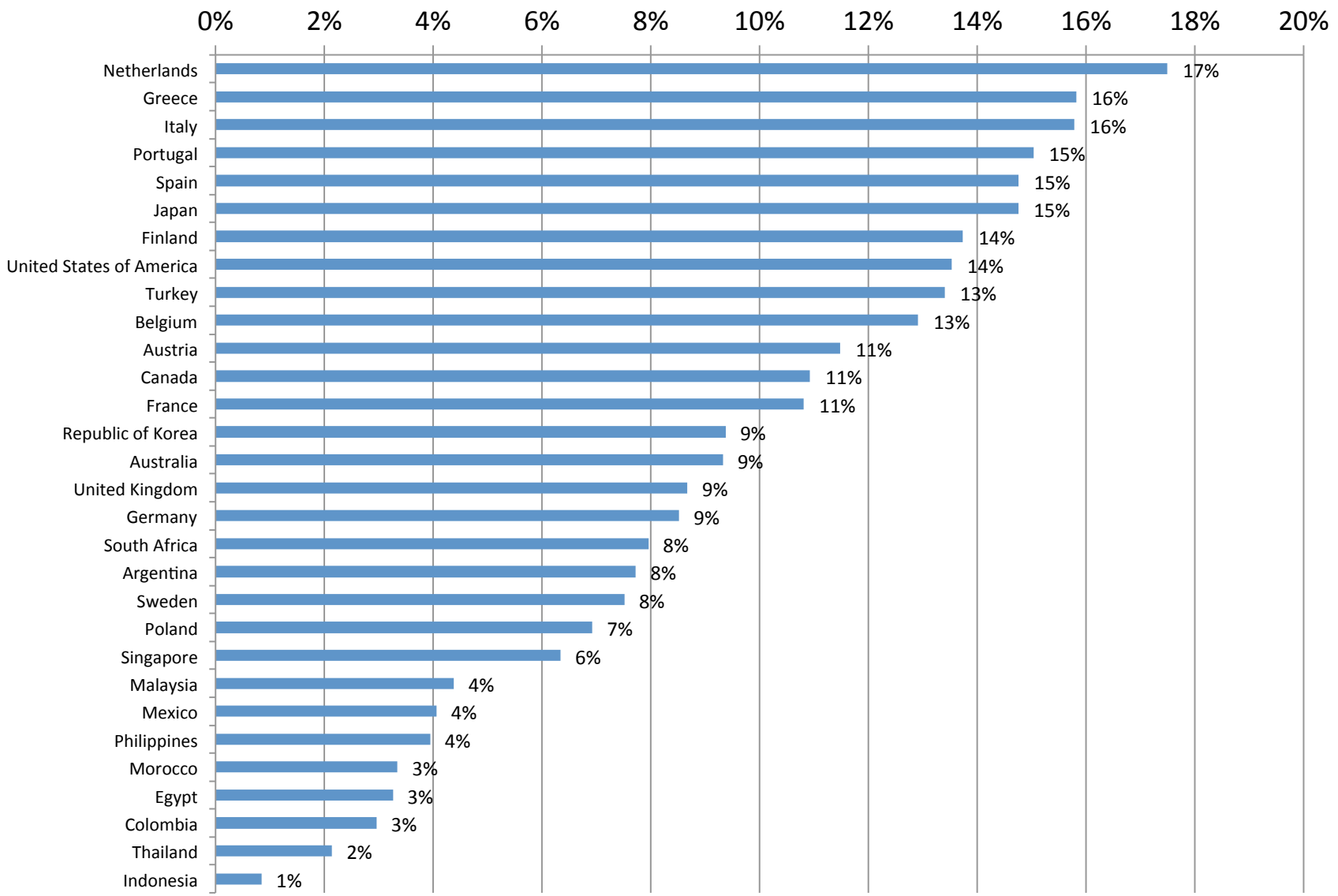
Mean vintage of pharmaceuticals consumed in a country in a given year

$$POST1990\%_{ct} = \frac{\sum_p Q_{pct} \, POST1990\%_p}{\sum_p Q_{pct}}$$

$POST1990\%_{ct}$ = the quantity-weighted fraction of products sold in country c in year t that were launched after 1990

Q_{pct} = the quantity (number of standard dose units) of product p sold in country c in year t

Quantity-weighted fraction of products sold in 2009 that were launched after 1990 (POST1990%) , by country



Descriptive statistics (population weighted) for 30 countries

Statistic	MEAN		MIN		MAX	
Year	2000	2009	2000	2009	2000	2009
Life expectancy at						
Birth	74.1	75.7	56.3	54.5	81.3	83.1
Age 25	51.5	52.5	37.8	35.4	57.0	58.7
Age 45	33.1	34.0	25.1	25.1	37.7	39.4
Age 65	16.8	17.6	12.3	13.7	20.2	21.7
Probability of survival from:						
Birth to 25	96.5%	97.2%	88.4%	88.5%	99.1%	99.3%
25 to 65	81.0%	82.0%	53.0%	46.0%	89.0%	91.0%
65 to 75	75.0%	78.0%	57.0%	62.0%	85.0%	88.0%
Birth to 75	59.8%	63.2%	26.6%	25.3%	75.4%	79.3%
Pharmaceutical variables						
LAUNCH_YEAR	1946.5	1951.2	1928.0	1928.3	1960.5	1967.5
POST1970%	20.6%	27.8%	5.6%	8.3%	39.6%	49.8%
POST1980%	10.8%	18.2%	1.2%	2.6%	22.4%	34.5%
POST1990%	3.4%	8.4%	0.3%	0.8%	7.6%	17.5%
Per capita quantity of prescription drugs	773	848	129	145	1725	1744

Correlation between changes in drug vintage and changes in other variables in the longevity growth model

- There is a significant correlation between the change in the fraction of post-1990 drugs (DPOST1990%) and just two variables: the log change in GDP per capita, and the change in urbanization rate.
- Both correlations are *negative*: countries with higher GDP growth had smaller increases in the fraction of post-1990 drugs.
- Countries with larger increases in educational attainment had smaller increases in drug vintage (weighted mean launch year).

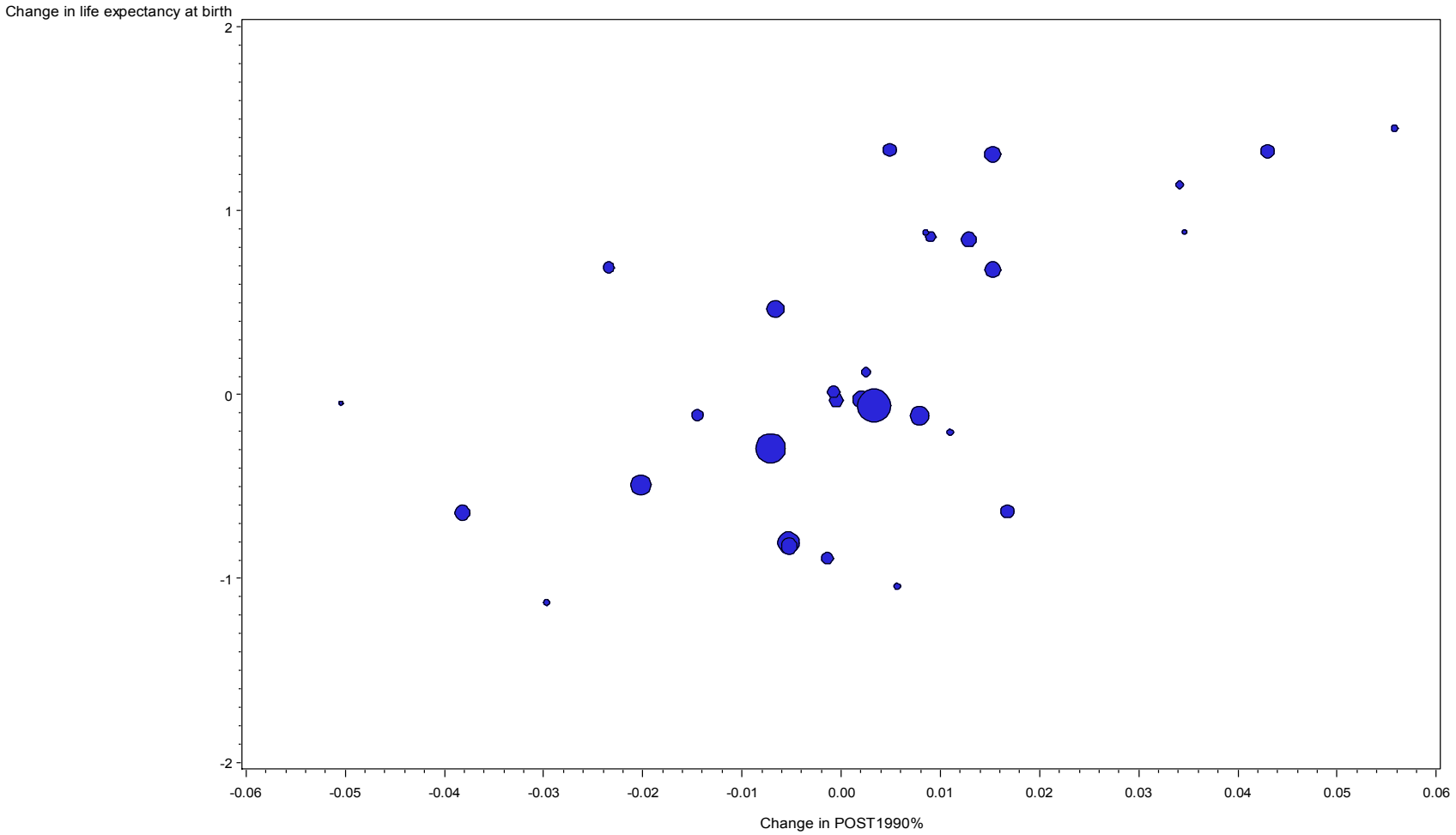
Drug vintage coefficients from estimates of the longevity change model (eq. (4))

Model		1	2	3	4	5	6	7	8
Dependent variable		change in life expectancy at							
		Birth		Age 25		Age 45		Age 65	
Regressor	statistic								
DPOST1990%	estimate	19.150	25.358	26.994	27.202	27.276	23.088	21.509	17.429
	t value	2.867	3.194	4.527	4.594	7.013	4.035	7.778	3.821
	prob > |t|	0.008	0.005	0.000	0.000	0.000	0.001	0.000	0.001
10 other variables included?		no	yes	no	yes	no	yes	no	yes
Model		9	10	11	12	13	14	15	16
Dependent variable		log change in probability of survival from							
		birth to age 25		age 25 to 65		age 65 to 75		birth to age 75	
Regressor	statistic								
DPOST1990%	estimate	-0.118	-0.019	0.422	0.502	0.656	0.519	0.960	1.002
	t value	-2.438	-0.353	1.958	2.567	5.238	2.953	3.451	2.555
	prob > |t|	0.021	0.728	0.060	0.019	0.000	0.009	0.002	0.020
10 other variables included?		no	yes	no	yes	no	yes	no	yes

Note: N = 30. Weighted least squares estimates, weighting by 2009 population.
DPOST1990% = change in quantity-weighted fraction of products sold that were launched after 1990

Correlation across countries between 2000-2009 change in life expectancy at birth and change in drug vintage (POST1990%),

controlling for changes in income, unemployment rate, education, urbanization, health expenditure, immunization rate, HIV prevalence and tuberculosis incidence



Note: size of bubble is proportional to country population.

Findings

- Life expectancy at all ages and survival rates above age 25 increased faster in countries with larger increases in drug vintage (measured in three different ways), controlling for an extensive set of other factors.
- The increase in drug vintage was the only variable that was significantly related to all of these measures of longevity growth.
  - Pharmaceutical innovation did not have a significant effect on survival from birth to age 25, controlling for the other variables, but a very small fraction of aggregate drug utilization is by young people.
- Controlling for all of the other potential determinants of longevity did not reduce the vintage coefficient by more than 20%.

Implications

We can use the estimates to assess:

- how much of the global growth in life expectancy was due to pharmaceutical innovation
- the extent to which international differences in life expectancy in 2009 were attributable to differences in drug vintage

World longevity growth

- For the 30 countries in our sample, between 2000 and 2009 population-weighted mean life expectancy at birth increased by 1.74 years.
- The estimates imply that **the increase in life expectancy at birth due to the increase in the fraction of drugs consumed that were launched after 1990 was 1.27 years--73% of the actual increase in life expectancy at birth.**
  - During this period, HIV prevalence and urbanization increased, and the estimates imply that these trends may have reduced longevity.
  - Moreover, obesity has increased (at least in OECD countries), and previous research (Flegal et al (2005)) indicates that this has also reduced longevity.
  - Although per capita income and educational attainment have also increased, there does not appear to be a consensus among scholars about the effects of these trends on longevity growth, and our estimates in and evidence from some other studies suggest that they have not made a contribution to survival gains among adults.

International longevity differences in 2009

- We compare the top 5 countries (ranked by POST1990% in 2009) with the bottom 5 countries (ranked by the same criterion).

	POST1990% in 2009	Life expectancy at birth in 2009
Top 5 countries (ranked by POST1990% in 2009): Netherlands, Greece, Italy, Portugal, Spain	16%	80.7
Bottom 5 countries: Morocco, Egypt, Colombia, Thailand, Indonesia	3%	71.6
Difference	13%	9.1

- The estimates imply that **the difference between these two groups in life expectancy at birth due to the difference in the fraction of drugs consumed that were launched after 1990 was 3.4 years--37% of the actual difference between these two groups in life expectancy at birth.**

The impact of pharmaceutical innovation on longevity and medical expenditure in Sweden, 1997-2010: evidence from longitudinal, disease-level data

Frank R. Lichtenberg, PhD
frank.lichtenberg@columbia.edu
Columbia University
and
National Bureau of Economic Research

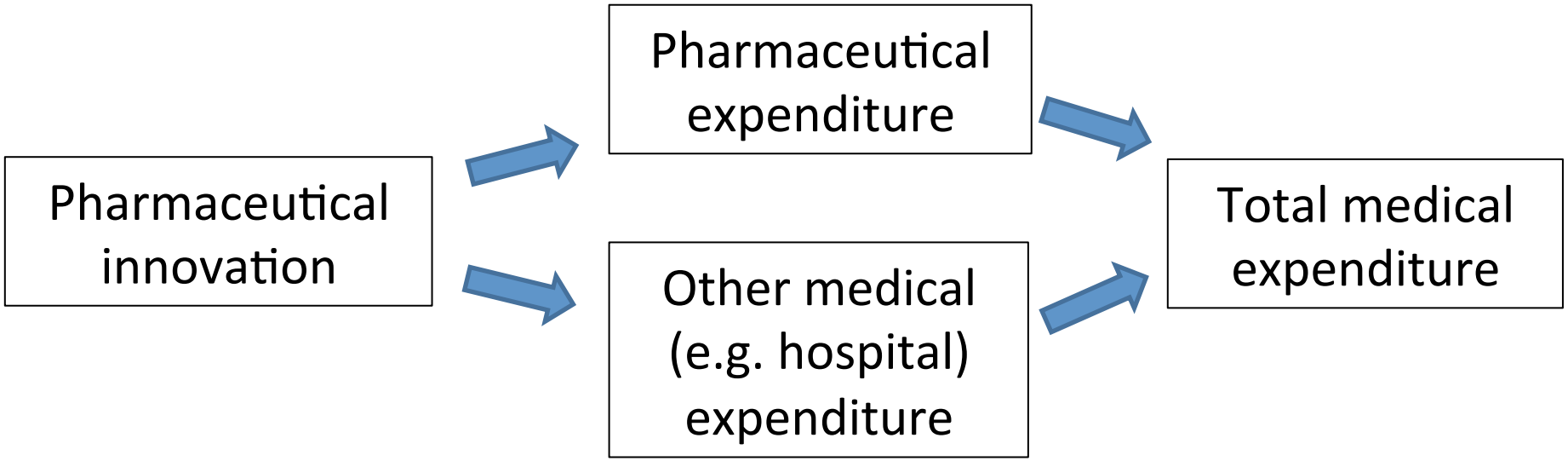
Billie Pettersson, PhD
billie_pettersson@merck.com
MSD Sweden

Preview

- We use longitudinal, disease-level data to analyze the impact of pharmaceutical innovation on longevity and medical expenditure in Sweden during the period 1997-2010.
- In essence, we will investigate whether the diseases that experienced more pharmaceutical innovation had larger increases in longevity.
- Our models will include year and disease fixed effects, so they will control for the overall increase in Swedish longevity and for stable between-disease differences in mortality.
- The measures of longevity we use are based on the age distribution of deaths caused by a disease in a given year.
- Our estimates do not capture between-disease spillover effects, but these effects appear to be quite modest in practice.
- The measure of pharmaceutical innovation we use is based on the number of drugs (chemical substances) previously introduced to treat a condition.

Impact on medical expenditure

- New drugs are generally more expensive than old drugs, so pharmaceutical innovation is likely to have increased pharmaceutical expenditure.
- We will investigate whether there were larger increases in expenditure on classes of drugs that experienced more pharmaceutical innovation.
- Previous research has shown that pharmaceutical innovation may also have an impact on other types of medical expenditure, especially expenditure on hospitals and nursing homes.
- We will investigate whether the diseases that experienced more pharmaceutical innovation had larger declines in hospital utilization.
- By combining our estimates of the effect of pharmaceutical innovation on longevity, pharmaceutical expenditure, and hospital utilization, we can obtain an estimate of the incremental cost-effectiveness (cost per life-year gained) of pharmaceutical innovation in Sweden during the period 2000-2009.


Pharmaceutical innovation
Pharmaceutical expenditure
Other medical (e.g. hospital) expenditure
Total medical expenditure

Data sources

- Market authorization dates of drugs: Läkemedelsverket (Medical Products Agency)
- Indications of drugs: Thériaque
- Mortality data: WHO Mortality Database
- Hospital utilization: Eurostat
- Pharmaceutical expenditure: IMS Health

Model of the impact of pharmaceutical innovation on longevity

$$LONGEVITY_{it} = b\ Rx\_MEASURE_{it} + a_i + d_t + e_{it}$$

$$(i = 1,\ldots, I;\ t = 1997,\ldots,2010)$$

$LONGEVITY_{it}$ = a measure of longevity associated with disease i in year t

$Rx\_MEASURE_{it}$ = a measure related to pharmaceutical innovation associated with disease i in year t

a_i = a fixed effect for disease i

d_t = a fixed effect for year t

e_{it} = a disturbance

A positive and significant estimate of b would signify that diseases for which there was more pharmaceutical innovation had larger increases in longevity.

Measurement of longevity

- Life expectancy at birth is probably the most commonly cited measure of longevity. However, this is not the measure of life expectancy we will use.
- The main reason is that life expectancy at birth (or at higher ages) cannot be measured for specific diseases.
- A more minor "disadvantage" of this indicator is that it is "hypothetical," rather than "actual": it is based on the period life table, which describes what *would* happen to a hypothetical (or synthetic) cohort if it experienced throughout its entire life the mortality conditions of a particular time period

Age distribution of deaths

- The measures of longevity we will use will be based on the age distribution of deaths caused by a disease in a given year.
- These measures can easily be calculated from data contained in the WHO Mortality Database, which provides data on the number of deaths, by cause, age group, country, and year.
- The most informative measure is mean age at death.
- A second measure is the fraction of deaths that occur above a given age, e.g. age 75.

Longevity trends

Year	Number of deaths	Mean age at death	% of deaths at age > 75
1997	78,547	78.40	69.0%
1998	78,649	78.57	69.8%
1999	78,978	78.74	70.4%
2000	77,507	78.87	70.7%
2001	77,620	79.19	71.3%
2002	79,067	79.43	72.0%
2003	78,344	79.40	71.7%
2004	75,858	79.38	71.5%
2005	75,970	79.53	71.7%
2006	76,041	79.74	72.1%
2007	75,940	79.92	72.5%
2008	75,583	80.00	72.2%
2009	74,296	79.97	71.8%
2010	74,146	80.28	72.4%

Two potential problems

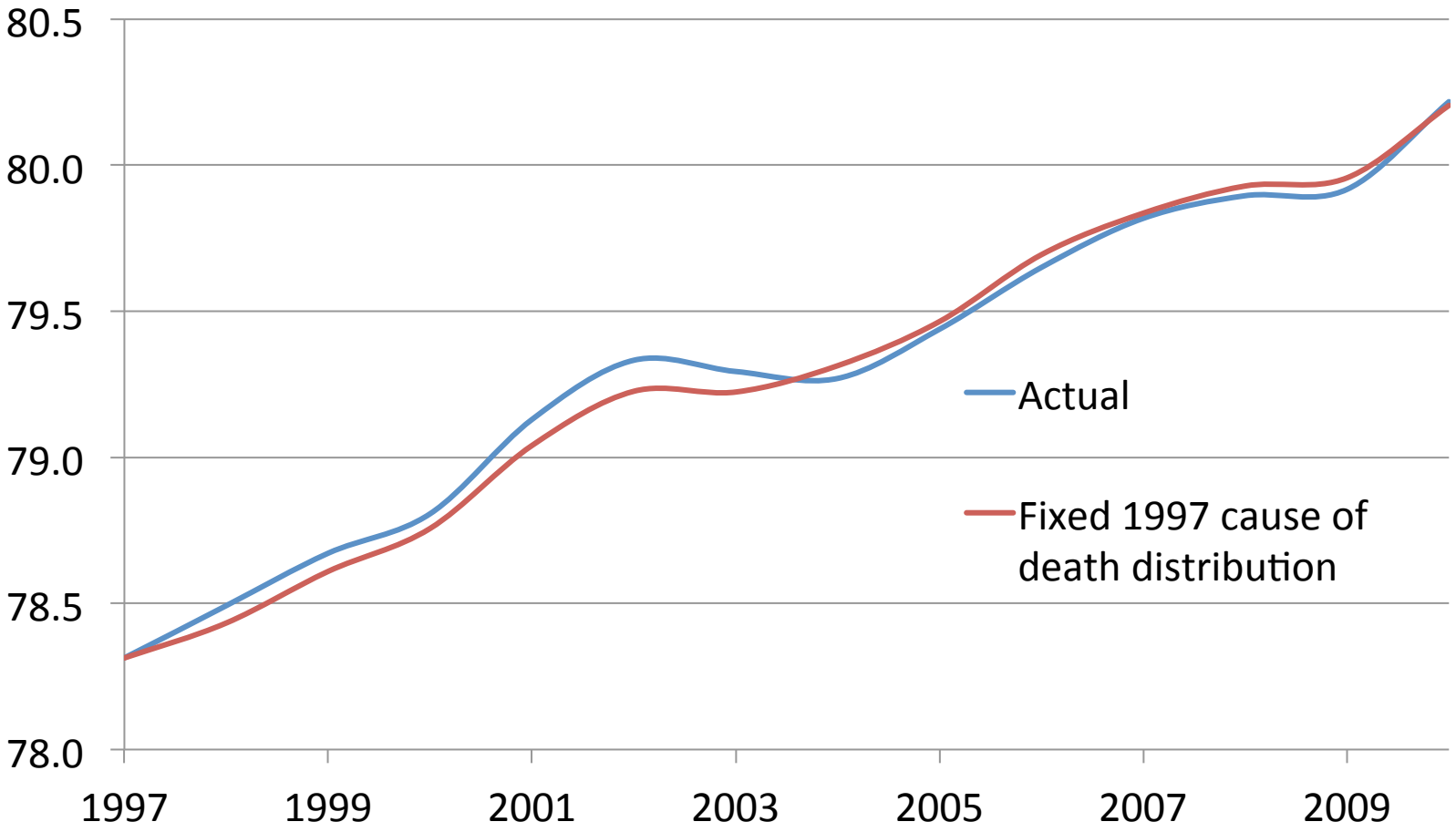
- Between-disease spillover effects
- Other medical innovation

Between-disease spillover effects?

- There is a potential pitfall in analyzing the relationship between pharmaceutical innovation related to a disease and the age distribution of deaths from the disease.
- Suppose that the introduction of a new drug for a disease reduces the number of people who die from the disease; people who would have died from the disease, absent the new drug, die from other diseases instead.
- Our estimates will not capture between-disease spillover effects.
- In principle, such between-disease spillover effects could be substantial. However, they appear to be quite modest in practice.

Mean age at death:

variable vs. fixed cause of death distribution



Other medical innovation

- Pharmaceutical innovation is not the only type of medical innovation that is likely to contribute to longevity growth.
- Other medical innovation, such as innovation in diagnostic imaging, surgical procedures, and medical devices, is also likely to affect longevity growth.
- Therefore, measures of these other types of medical innovation should be included in the longevity model.
- Unfortunately, longitudinal disease-level measures of non-pharmaceutical medical innovation are not available for Sweden.
- However, longitudinal disease-level measures of non-pharmaceutical and pharmaceutical medical innovation are available for the U.S. during the period 1997-2007.
- Estimates based on U.S. data suggest that failure to control for other medical innovation is very unlikely to result in overestimation of the effect of pharmaceutical innovation on longevity growth, and may even result in underestimation of this effect.

Measure of pharmaceutical innovation

The measure of pharmaceutical innovation we will use will be based on the *number* of drugs (chemical substances) previously introduced to treat a condition. We will refer to this as the *stock* of drugs for a condition. The stock of drugs will be computed as follows:

$$N\_CHEM\_SUBSTANCES_{it} = \sum_d IND_{di} APP_{dt}$$

IND_{di} = 1 if drug d is used to treat (indicated for) disease i

= 0 if drug d is not used to treat (indicated for) disease i

APP_{dt} = 1 if drug d has been commercialized by the beginning of year t

= 0 if drug d has not been commercialized by the beginning of year t

Chemical **substances** for C43-C44 Melanoma and other malignant neoplasms of skin

H02AB02 Dexamethasone	1959
H02AB04 Methylprednisolone	1959
H02AB01 Betamethasone	1963
L01AD02 Lomustine	1978
L01AX04 Dacarbazine	1979
V03AF03 Calcium folinate	1984
B01AB04 Dalteparin	1988
B03XA01 Erythropoietin	1989
J02AC01 Fluconazole	1989
V03AF04 Calcium levofolinate	1995
D06BB10 Imiquimod	1998
L03AB04 Interferon alfa-2a	1999
L03AB05 Interferon alfa-2b	2000
B03XA02 Darbepoetin alfa	2001
L01XD03 Methyl aminolevulinate	2001
L01XE01 Imatinib	2001
M05BA08 Zoledronic acid	2001
V09DB06 Technetium Tc-99M rheniumsulfide colloid	2002
L01XC11 Ipilimumab	2011

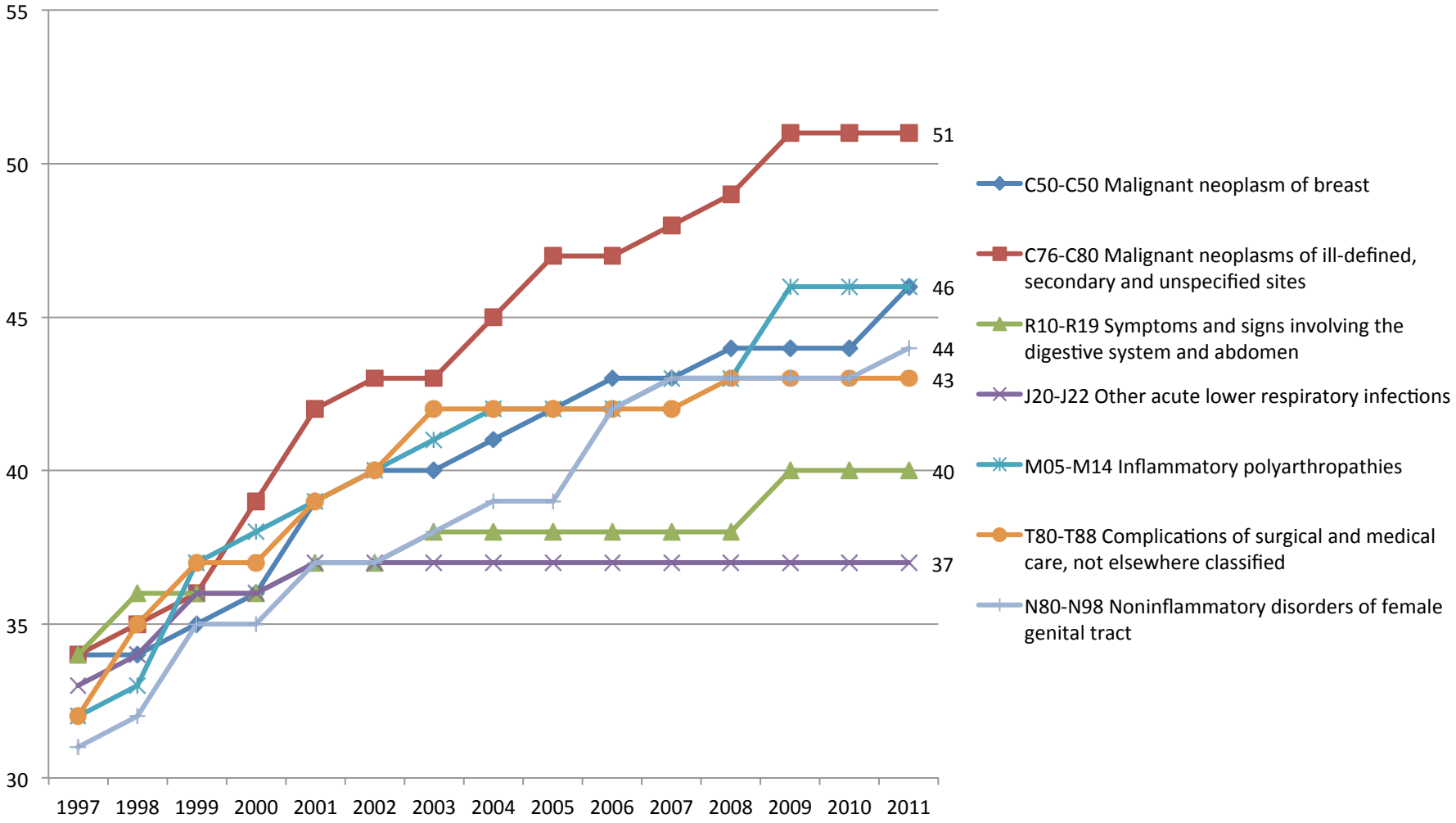
Sources: Thériaque and Läkemedelsverket

Illustrative data: top 9 diseases

ranked by number of deaths in 1997

	Number of deaths		Mean age at death		% of deaths at age > 75		Number of drugs	
ICD-10 block	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**	**1997**	**2010**
I20-I25 Ischaemic heart diseases	21,974	15,012	79.6	82.1	72%	78%	36	50
I60-I69 Cerebrovascular diseases	10,402	7,602	81.7	83.8	81%	85%	11	17
I30-I52 Other forms of heart disease	6,766	8,684	83.8	85.7	88%	89%	68	79
C15-C26 Malignant neoplasms of digestive organs	6,694	6,634	74.6	74.8	55%	53%	17	31
I70-I79 Diseases of arteries, arterioles and capillaries	3,859	2,169	82.2	82.0	80%	77%	23	29
C30-C39 Malignant neoplasms of respiratory and intrathoracic organs	3,110	3,681	70.8	72.5	38%	42%	28	35
C60-C63 Malignant neoplasms of male genital organs	2,482	2,433	78.5	80.6	70%	76%	25	29
J40-J47 Chronic lower respiratory diseases	2,373	2,727	78.1	80.1	67%	73%	46	57
C81-C96 Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue	2,021	1,862	72.5	75.6	52%	60%	39	61

Number of chemical substances for 7 diseases, 1997-2011



Sources: Thériaque and Läkemedelsverket

Longevity equations

The longevity equations we will estimate are:

$$AGE\_DEATH_{it} = b\ N\_CHEM\_SUBSTANCES_{i,t-k} + a_i + d_t + e_{it}$$

$$AGE\_GT75_{it} = b\ N\_CHEM\_SUBSTANCES_{i,t-k} + a_i + d_t + e_{it}$$

$(i = 1,\ldots, I;\ t = 1997,\ldots,2010)$

AGE_DEATH_{it} = mean age at death from disease i in year t

AGE_GT75_{it} = the fraction of deaths from disease i in year t that occurred after age 75

Endogenous technological change

- In his model of endogenous technological change, Romer (1990) hypothesized an aggregate production function such that an economy's output depends on the "stock of ideas" that have previously been developed, as well as on the economy's endowments of labor and capital.
- These equations may be considered health production functions, in which age at death is an indicator of health output or outcomes, and the cumulative number of drugs approved is analogous to the stock of ideas.

Complete classification of metformin

A	Alimentary tract and metabolism (1st level, anatomical main group)
A10	Drugs used in diabetes (2nd level, therapeutic subgroup)
A10B	Blood glucose lowering drugs, excl. insulins (3rd level, pharmacological subgroup)
A10BA	Biguanides (4th level, chemical subgroup)
A10BA02	Metformin (5th level, chemical substance)

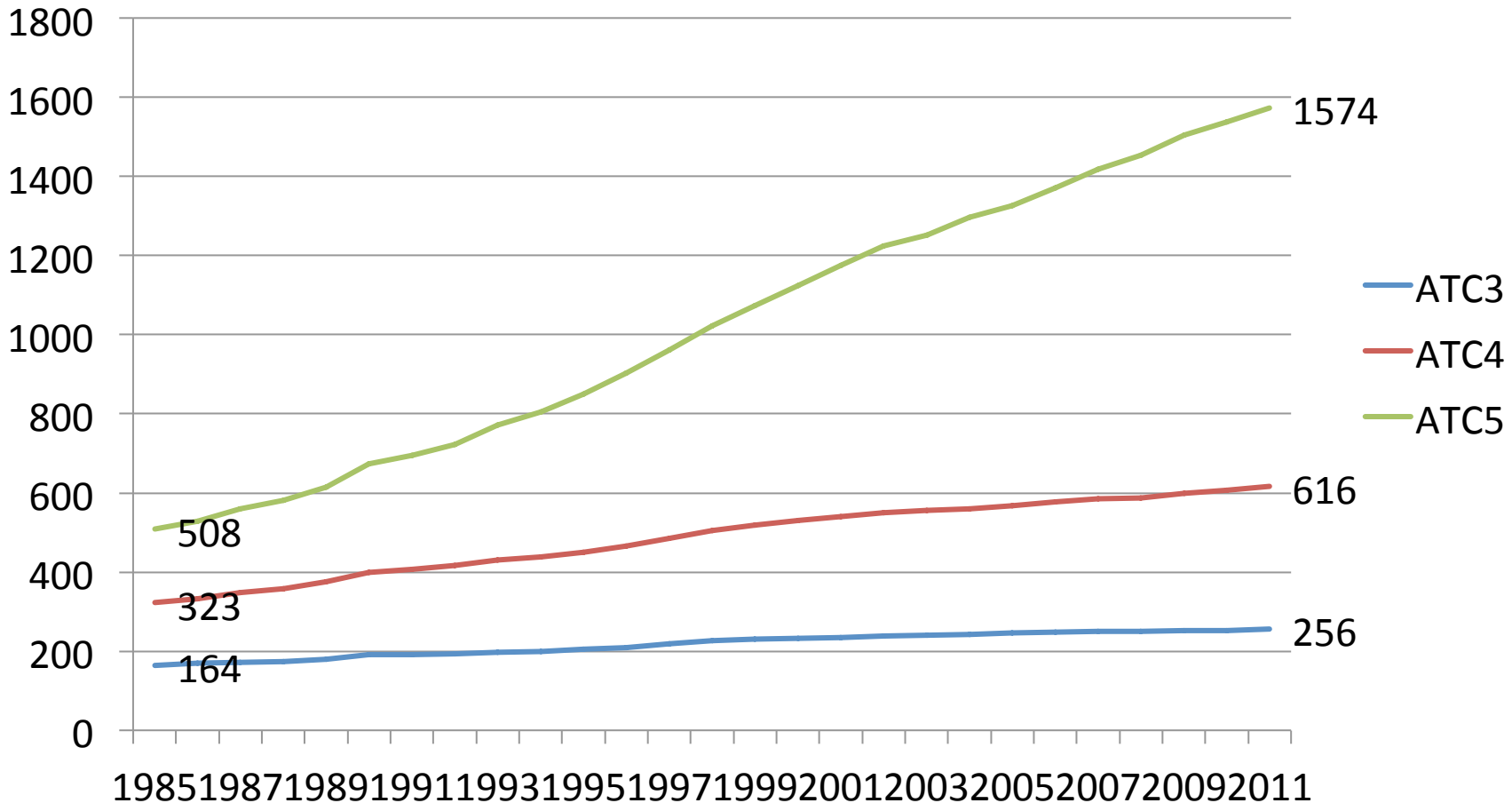
http://www.whocc.no/atc/structure_and_principles/

Chemical **subgroups** for C43-C44 Melanoma and other malignant neoplasms of skin

H02AB Glucocorticoids	1958
L01AD Nitrosoureas	1978
L01AX Other alkylating agents	1979
B01AB Heparin group	1981
V03AF Detoxifying agents for antineoplastic treatment	1984
D06BB Antivirals	1985
M05BA Bisphosphonates	1985
B03XA Other antianemic preparations	1989
J02AC Triazole derivatives	1989
V09DB Technetium Tc-99M, particles and colloids	1990
L03AB Interferons	1993
L01XC Monoclonal antibodies	1998
L01XD Sensitizers used in photodynamic/radiation therapy	2000
L01XE Protein kinase inhibitors	2001

Sources: Thériaque and Läkemedelsverket

Cumulative number of 3rd-level pharmacological subgroups, 4th-level chemical subgroups, and 5th-level chemical substances, Sweden, 1985-2011



Sources: Thériaque and Läkemedelsverket

Drugs vs. drug classes

Age at death from a disease may depend on the number of chemical (or pharmacological) *subgroups* that have previously been developed to treat the disease rather than, or in addition to, the number of chemical *substances* (drugs) that have previously been developed to treat the disease. We will investigate this by estimating models like the following:

$$AGE\_DEATH_{it} = b\ N\_CHEM\_SUBGROUP_{i,t-k} + a_i + d_t + e_{it}$$

$N\_CHEM\_SUBGROUP_{it}$ $= \sum_g IND_{gi}\ APP_{gt}$

IND_{gi} = 1 if any drugs in chemical subgroup g are used to treat (indicated for) disease i

= 0 if no drugs in chemical subgroup g are used to treat (indicated for) disease i

APP_{gt} = 1 if any drugs in chemical subgroup g had been commercialized by the beginning of year t

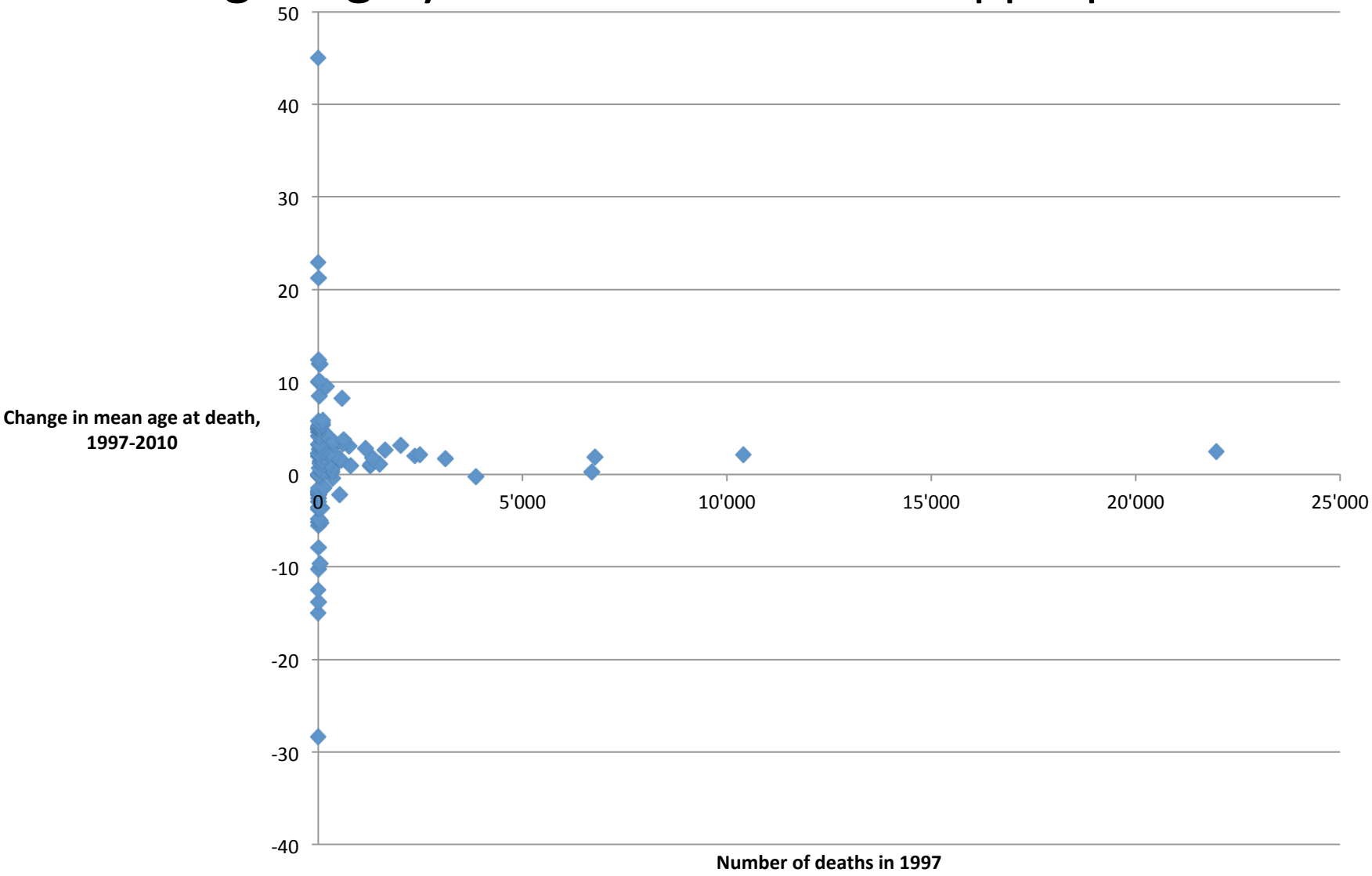
= 0 if no drugs in chemical subgroup g had been commercialized by the beginning of year t

Disease classification

- Data on IND_{di} were obtained from Theriaque.
- In that database, drug indications are coded using the International Classification of Diseases, Tenth Revision (ICD-10; http://www.who.int/classifications/icd/en/).
- Sweden began using the ICD-10 system to classify its mortality data in 1997. The most recent year for which mortality data are available for Sweden in the WHO Mortality Database is 2010. Our analysis will therefore cover the period 1997-2010.
- The ICD-10 contains 12,131 distinct disease codes. These are grouped into 263 "blocks," such as "A00-A09 Intestinal infectious diseases," and "C30-C39 Malignant neoplasms of respiratory and intrathoracic organs." We will perform the analysis using data at the ICD-10 block level.

Weighted least squares

weighting by number of deaths is appropriate



AGE_DEATH equation estimates

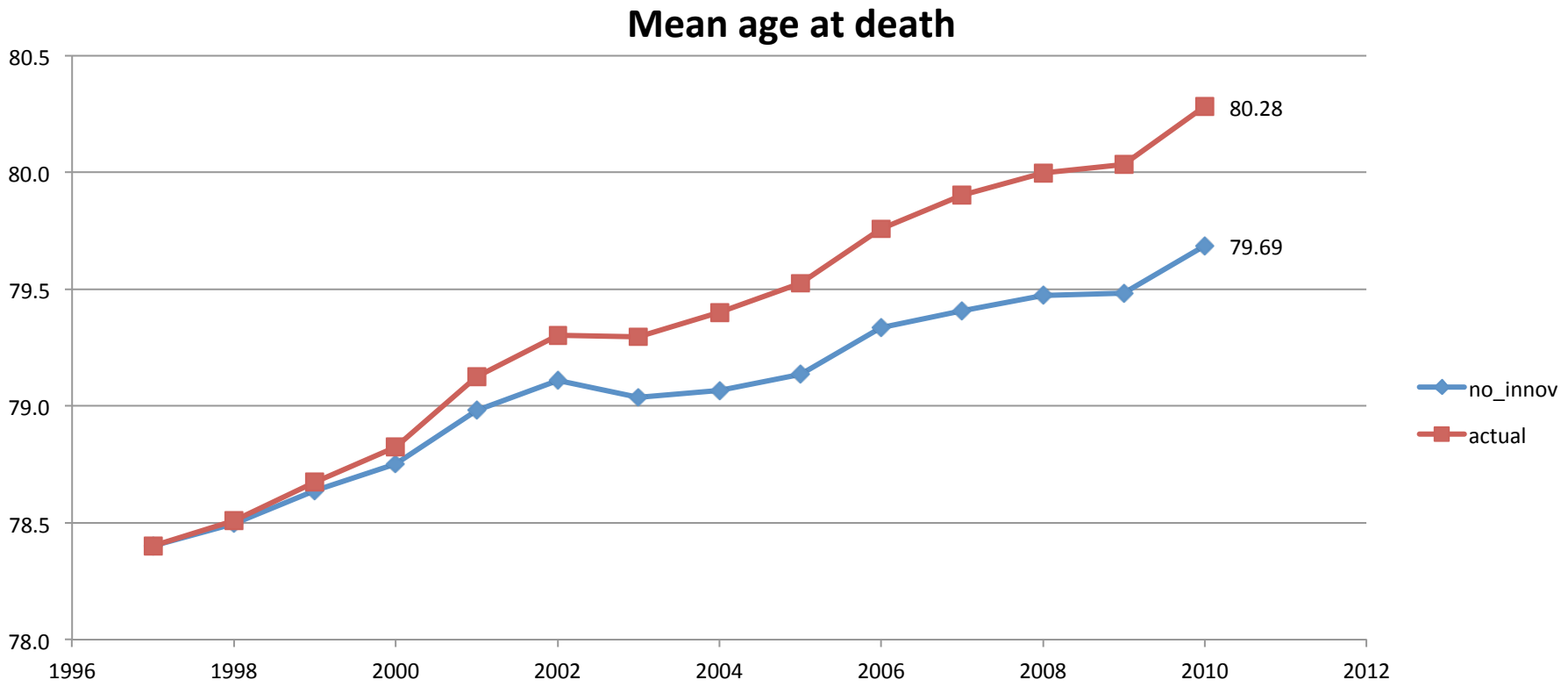
Model	Parameter	Estimate	Empirical Standard Error Estimates	Z	Pr > |Z|
1	$N\_CHEM\_SUBSTANCES_{i,t}$	0.0466	0.0310	1.50	0.1324
2	$N\_CHEM\_SUBSTANCES_{i,t-1}$	0.0458	0.0289	1.58	0.1130
3	$N\_CHEM\_SUBSTANCES_{i,t-2}$	0.0447	0.0252	1.77	0.0768
4	$N\_CHEM\_SUBSTANCES_{i,t-3}$	0.0494	0.0235	2.10	0.0354
5	$N\_CHEM\_SUBSTANCES_{i,t-4}$	0.0489	0.0207	2.36	0.0182
6	$N\_CHEM\_SUBSTANCES_{i,t-5}$	0.0498	0.0175	2.85	0.0044
7	**$N\_CHEM\_SUBSTANCES_{i,t-6}$**	**0.0478**	**0.0167**	**2.87**	**0.0041**
8	$N\_CHEM\_SUBSTANCES_{i,t-7}$	0.0441	0.0171	2.57	0.0101
9	$N\_CHEM\_SUBSTANCES_{i,t-8}$	0.0414	0.0162	2.56	0.0105
10	$N\_CHEM\_SUBSTANCES_{i,t-9}$	0.0432	0.0165	2.61	0.0090
11	$N\_CHEM\_SUBSTANCES_{i,t-10}$	0.0443	0.0182	2.43	0.0151
12	$N\_CHEM\_SUBGROUPS_{i,t}$	0.0495	0.0405	1.22	0.2217
13	$N\_CHEM\_SUBGROUPS_{i,t-1}$	0.0447	0.0397	1.13	0.2597
14	$N\_CHEM\_SUBGROUPS_{i,t-2}$	0.0262	0.0402	0.65	0.5152
15	$N\_CHEM\_SUBGROUPS_{i,t-3}$	0.0166	0.0440	0.38	0.7069
16	$N\_CHEM\_SUBGROUPS_{i,t-4}$	0.0134	0.0400	0.34	0.7372
17	$N\_CHEM\_SUBGROUPS_{i,t-5}$	0.0102	0.0417	0.24	0.8074
18	$N\_CHEM\_SUBGROUPS_{i,t-6}$	-0.0005	0.0461	-0.01	0.9922

- Mean age at death is most strongly related to the number of chemical substances with market authorization for the disease 6 years earlier.
- It is not related to the contemporaneous number of chemical substances or to the number of chemical subgroups.

AGE_GT75 equation estimates

Model	Parameter	Estimate	Empirical Standard Error Estimates	Z	Pr > |Z|
1	$N\_CHEM\_SUBSTANCES_{i,t}$	0.0019	0.0009	2.25	0.0241
2	$N\_CHEM\_SUBSTANCES_{i,t-1}$	0.0018	0.0008	2.22	0.0263
3	$N\_CHEM\_SUBSTANCES_{i,t-2}$	0.0016	0.0007	2.23	0.0259
4	$N\_CHEM\_SUBSTANCES_{i,t-3}$	0.0018	0.0007	2.54	0.0110
5	$N\_CHEM\_SUBSTANCES_{i,t-4}$	0.0017	0.0006	2.76	0.0058
6	**$N\_CHEM\_SUBSTANCES_{i,t-5}$**	**0.0018**	**0.0005**	**3.45**	**0.0006**
7	$N\_CHEM\_SUBSTANCES_{i,t-6}$	0.0017	0.0005	3.32	0.0009
8	$N\_CHEM\_SUBSTANCES_{i,t-7}$	0.0014	0.0006	2.57	0.0102
9	$N\_CHEM\_SUBSTANCES_{i,t-8}$	0.0013	0.0005	2.43	0.0151
10	$N\_CHEM\_SUBSTANCES_{i,t-9}$	0.0014	0.0005	2.73	0.0062
11	$N\_CHEM\_SUBSTANCES_{i,t-10}$	0.0014	0.0005	2.67	0.0077
12	$N\_CHEM\_SUBGROUPS_{i,t}$	0.0021	0.0015	1.38	0.1687
13	$N\_CHEM\_SUBGROUPS_{i,t-1}$	0.0016	0.0014	1.12	0.2618
14	$N\_CHEM\_SUBGROUPS_{i,t-2}$	0.0005	0.0012	0.46	0.6471
15	$N\_CHEM\_SUBGROUPS_{i,t-3}$	0.0001	0.0012	0.11	0.9161
16	$N\_CHEM\_SUBGROUPS_{i,t-4}$	0.0002	0.0012	0.13	0.8956
17	$N\_CHEM\_SUBGROUPS_{i,t-5}$	0.0000	0.0012	-0.01	0.9946
18	$N\_CHEM\_SUBGROUPS_{i,t-6}$	-0.0004	0.0014	-0.26	0.7972

Increase in mean age at death:
actual vs. without pharma. innovation



Pharmaceutical innovation accounts for almost 1/3 (31.6%) of the 1.88-year increase in mean age at death during the period 1997-2010

Hospital utilization

year	discharges	days	Average length of stay
2000	1,155,668	8,174,953	7.07
2001	1,144,199	8,047,420	7.03
2002	1,127,627	7,830,114	6.94
2003	1,126,880	7,740,285	6.87
2004	1,118,033	7,555,441	6.76
2005	1,129,524	7,567,728	6.70
2006	1,208,424	8,155,973	6.75
2007	1,240,672	8,250,456	6.65
2008	1,250,509	8,417,075	6.73
2009	1,265,570	8,321,934	6.58

Source: Eurostat

Hospital utilization model

We estimated relationships between hospital utilization and pharmaceutical innovation, such as the following:

$\ln(DAYS_{it}) = b \ln(N\_CHEM\_SUBSTANCES_{i,t-k}) + a_i + d_t + e_{it}$

$\ln(DAYS_{it}) = b \ln(N\_CHEM\_SUBGROUPS_{i,t-k}) + a_i + d_t + e_{it}$

where

$DAYS_{it}$ = the number of hospital days for disease i in year t (t = 2000,…,2009)

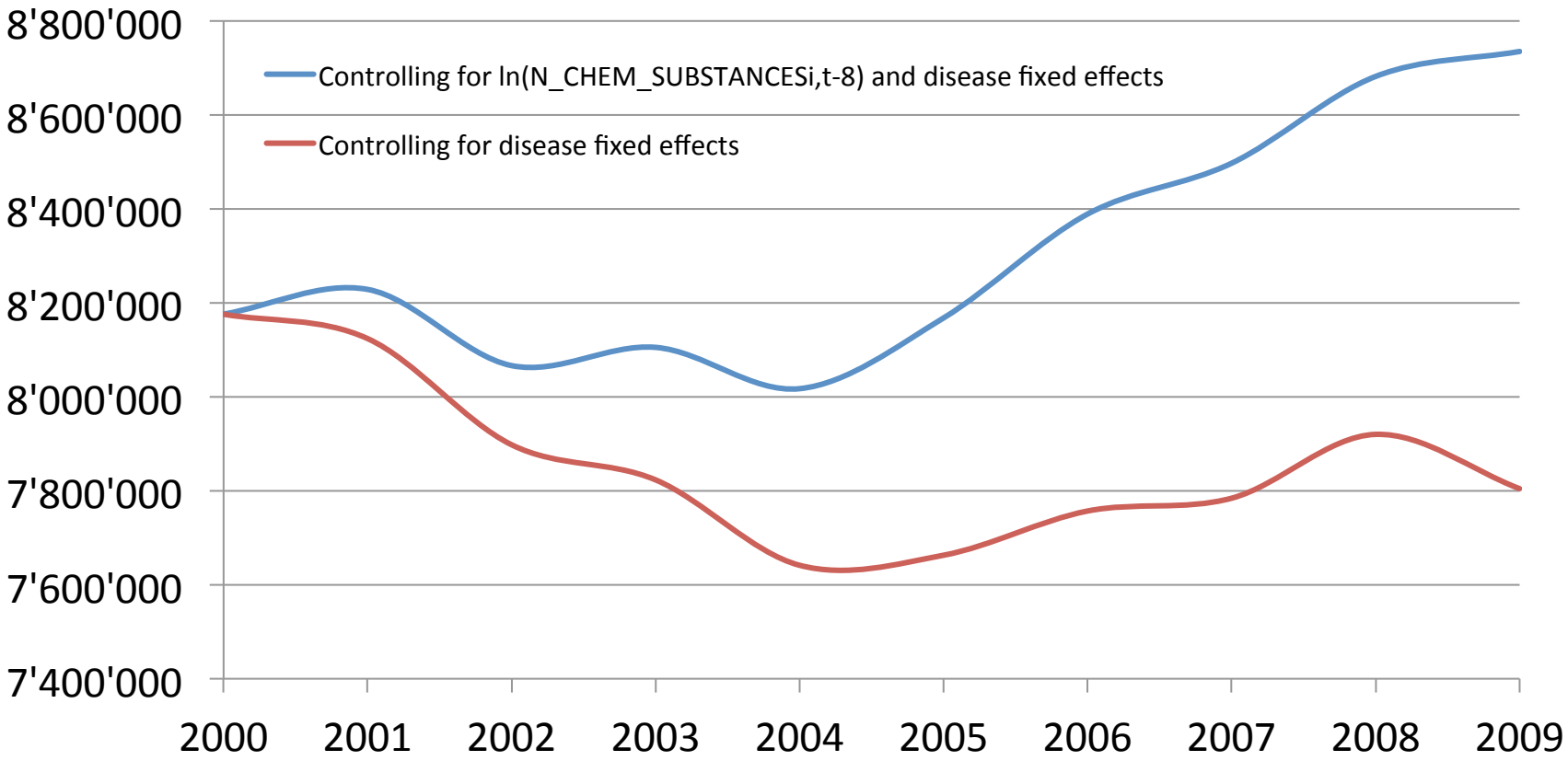
These equations were estimated by weighted least squares, weighting by the total number of hospital days for disease i during the entire period ($DAYS_{i.} = (1/10) \sum_t DAYS_{it}$).

ln(DAYS) equation estimates

Model	Parameter	Estimate	Empirical Standard Error Estimates	Z	Pr > |Z|
1	ln N_CHEM_SUBSTANCES$_{i,t}$	0.0124	0.2620	0.05	0.9622
2	ln N_CHEM_SUBSTANCES$_{i,t-1}$	0.0056	0.2084	0.03	0.9785
3	ln N_CHEM_SUBSTANCES$_{i,t-2}$	-0.0711	0.1624	-0.44	0.6615
4	ln N_CHEM_SUBSTANCES$_{i,t-3}$	-0.2357	0.1447	-1.63	0.1033
5	ln N_CHEM_SUBSTANCES$_{i,t-4}$	-0.2877	0.1214	-2.37	0.0178
6	ln N_CHEM_SUBSTANCES$_{i,t-5}$	-0.2991	0.1063	-2.81	0.0049
7	ln N_CHEM_SUBSTANCES$_{i,t-6}$	-0.2534	0.0825	-3.07	0.0021
8	ln N_CHEM_SUBSTANCES$_{i,t-7}$	-0.2635	0.0827	-3.19	0.0014
9	**ln N_CHEM_SUBSTANCES$_{i,t-8}$**	**-0.3021**	**0.0871**	**-3.47**	**0.0005**
10	ln N_CHEM_SUBSTANCES$_{i,t-9}$	-0.3248	0.0995	-3.27	0.0011
11	ln N_CHEM_SUBSTANCES$_{i,t-10}$	-0.2789	0.1071	-2.60	0.0092
12	ln N_CHEM_SUBGROUPS$_{i,t}$	-0.4775	0.4176	-1.14	0.2528
13	ln N_CHEM_SUBGROUPS$_{i,t-1}$	-0.4343	0.3315	-1.31	0.1901
14	ln N_CHEM_SUBGROUPS$_{i,t-2}$	-0.3747	0.2773	-1.35	0.1767
15	ln N_CHEM_SUBGROUPS$_{i,t-3}$	-0.3084	0.2924	-1.05	0.2915
16	ln N_CHEM_SUBGROUPS$_{i,t-4}$	-0.3968	0.2521	-1.57	0.1156
17	ln N_CHEM_SUBGROUPS$_{i,t-5}$	-0.2871	0.1865	-1.54	0.1237

Hospital days, 2000-2009

actual vs. without pharma. innovation



New drugs introduced during the period 1992-2001 are estimated to have reduced the number of hospital days in 2009 by about 15%.

Effect of pharmaceutical innovation on prescription drug expenditure

- Now we will assess the impact of pharmaceutical innovation—the expansion of the number of chemical substances—on pharmaceutical expenditure using longitudinal data on about 300 classes of drugs from IMS Health.
- We have annual data on both the ex-manufacturer value (expressed in US dollars) and quantity (number of "standard units") of all pharmaceutical products sold to pharmacies and hospitals during the period 1999-2010.
- Each product is assigned to one 3-digit EphMRA Anatomical Therapy Class (ATC3).
- We also know the active ingredient(s) ("molecules") contained in each product. The "molecules" identified in the IMS MIDAS database do not coincide exactly with "chemical substances" identified in the Theriaque database.

Pharma. expenditure model

Assess the impact of the expansion of the number of molecules on pharmaceutical expenditure by estimating the equation:

$$\ln(MANU\_VALUE_{ct}) = b \ln(N\_MOLECULE_{c,t-k}) + a_c + d_t + e_{ct}$$

(c=1,…, 303; t = 2005,…,2010; k = 0,…,5)

$MANU\_VALUE_{ct}$ = the ex-manufacturer value (expressed in US dollars) of products in ATC3 sold during year t

$N\_MOLECULE_{ct}$ = the number of molecules in ATC3 at the end of year t

$= \sum_m IN\_CLASS_{mc}\ ON\_MARKET_{mt}$

IN_CLASS_{mc} = 1 if any product in ATC class 3 sold during 1999-2010 contains molecule m

= 0 if no product in ATC class 3 sold during 1999-2010 contains molecule m

ON_MARKET_{mt} = 1 if any product containing molecule m is sold by the end of year t

= 0 if no product containing molecule m is sold by the end of year t

ln(MANU_VALUE) equation estimates

Model	Parameter	Estimate	Empirical Standard Error Estimates	Z	Pr > |Z|
1	$\ln(N\_MOLECULE_{c,t})$	0.7373	0.3022	2.44	0.0147
2	$\ln(N\_MOLECULE_{c,t-1})$	0.8198	0.2866	2.86	0.0042
3	$\ln(N\_MOLECULE_{c,t-2})$	0.8930	0.2057	4.34	<.0001
4	**$\ln(N\_MOLECULE_{c,t-3})$**	**0.8912**	**0.1772**	**5.03**	**<.0001**
5	$\ln(N\_MOLECULE_{c,t-4})$	0.6803	0.1914	3.56	0.0004
6	$\ln(N\_MOLECULE_{c,t-5})$	0.5923	0.1572	3.77	0.0002

Model 4 implies that new drugs introduced during the period 1997-2006 increased pharmaceutical expenditure in 2009 by 31.6%.

Data on the number of molecules (as defined by IMS) sold in Sweden prior to 1999 are not available. We will therefore use Läkemedelsverket data on the number of chemical substances in 1997 and 2006 instead.

Cost-effectiveness analysis

Line	Variable	Actual values, 2009 (Y_{actual})	Estimated values in 2009 in the absence of 9 prior years of pharmaceutical innovation ($Y_{no\_innovation}$)	Difference ($Y_{no\_innovation}$ - Y_{actual})	Basis for $Y_{no\_innovation}$ estimate
1	Life expectancy (Mean age at death)	79.97	79.49	-0.48	$Y_{actual} + b_{age}$ (N_CHEM_SUBSTANCE$_{1994}$ - N_CHEM_SUBSTANCE$_{2003}$)
	Per capita medical expenditure in 2009, USD PPP				
2	Prescription drug expenditure	$336	$230	-$106	$Y_{actual} * \exp[b_{rx\_expend} * \ln(N\_CHEM\_SUBSTANCE_{1997}/ N\_CHEM\_SUBSTANCE_{2006})]$
3	Hospital expenditure	$935	$1,083	$148	$Y_{actual} * \exp[b_{hosp\_days} * \ln(N\_CHEM\_SUBSTANCE_{1992}/ N\_CHEM\_SUBSTANCE_{2001})]$
4	Other medical expenditure	$2,450	$2,450	$0	Assumption that pharma. Innovation has no effect on other medical expenditure
5	Total medical expenditure	$3,722	$3,763	$41	Sum of Rx, hospital, and other medical expenditure
6	Lifetime medical expenditure (= life expectancy * total medical expenditure in 2009)	$297,620	$299,130	$1,510	
	Note:				
	Source for data on actual medical expenditure in 2009: http://stats.oecd.org/				
	b_{age} = the coefficient on $N\_CHEM\_SUBSTANCE_{i,t-6}$ in mean age at death model				
	b_{rx_expend} = the coefficient on $\ln(N\_MOLECULE_{c,t-3})$ in ln(MANU_VALUE) model				
	b_{hosp_days} = the coefficient on $\ln(N\_CHEM\_SUBSTANCE_{i,t-8})$ in ln(DAYS) model				

Cost-effectiveness analysis

- We estimate that new drugs introduced during the period 1997-2006 increased pharmaceutical expenditure in 2009 by 31.6%. According to the OECD, mean per capita drug expenditure in Sweden in 2009 was 336 USD. We estimate that, in the absence of 8 prior years of pharmaceutical innovation, mean per capita drug expenditure in 2009 would have been $106 lower: $230.
- New drugs introduced during the period 1992-2001 are estimated to have reduced the number of hospital days in 2009 by about 15%. According to the OECD, mean per capita hospital expenditure in Sweden in 2009 was $935. We estimate that, in the absence of 8 prior years of pharmaceutical innovation, mean per capita hospital expenditure in 2009 would have been $148 higher: $1083.
- New drugs have been *cost-saving*: the reduction in annual hospital expenditure induced by pharmaceutical innovation has been larger than the induced increase in annual pharmaceutical expenditure.
- New drugs have reduced *lifetime* medical expenditure, despite the fact that they increased life expectancy by 6 months during 2000-2009

Summary

- We used longitudinal, disease-level data to analyze the impact of pharmaceutical innovation on longevity and medical expenditure in Sweden during the period 1997-2010.
- Diseases that experienced more pharmaceutical innovation had larger increases in longevity.
- Pharmaceutical innovation accounts for almost 1/3 (31.6%) of the 1.88-year increase in mean age at death during the period 1997-2010
- Longevity depends on the number of drugs to treat a disease, not the number of chemical subgroups (drug classes) developed to treat the disease.
- Diseases that experienced more pharmaceutical innovation had smaller increases in hospital utilization.
- New drugs have been *cost-saving*: the reduction in annual hospital expenditure induced by pharmaceutical innovation has been larger than the induced increase in annual pharmaceutical expenditure.
- New drugs have reduced *lifetime* medical expenditure, despite the fact that they increased life expectancy by 6 months during 2000-2009.

The Effect of Pharmaceutical Innovation on the Functional Limitations of Elderly Americans: Evidence from the 2004 National Nursing Home Survey

NBER Working Paper No. 17750, January 2012
http://www.nber.org/papers/w17750
forthcoming, *Advances in Health Economics and Health Services Research*

Activity limitations

- People who use newer drugs are less likely to have (contemporaneous) activity limitations than people using older drugs, controlling for all of the variables described above.
- Controlling for activity limitations reduces the magnitude of the rx_vintage coefficient in the survival equation by a small amount (about 10-15%)
- This is also true among nursing-home residents, even when we control for facility fixed effects.

Table 1

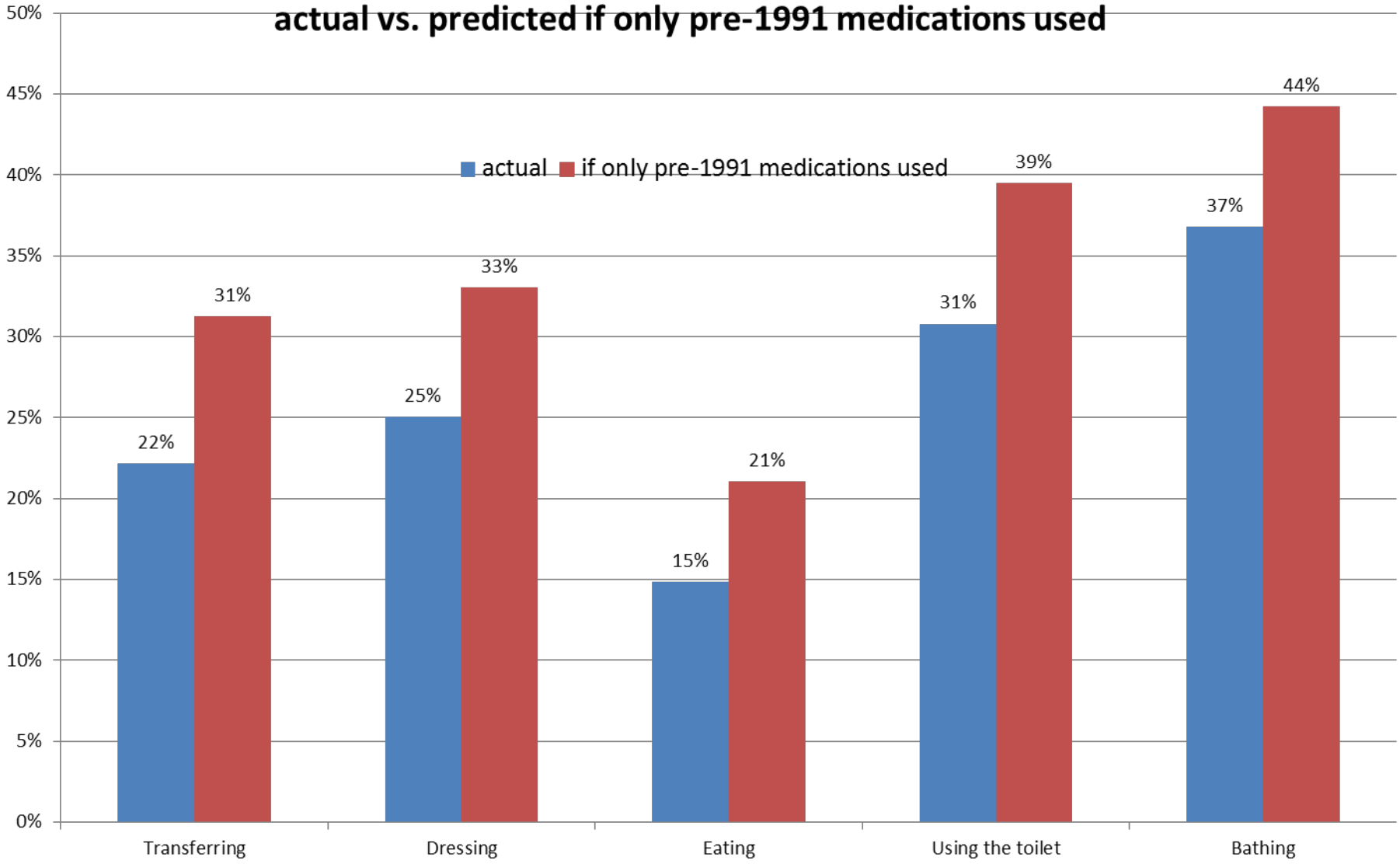
Percent distribution of nursing home residents, according to extent of assistance required with activities of daily living

	Activity				
Extent of assistance required	transfer	dress	eat	toilet	bath
Independent	22%	11%	44%	18%	2%
Supervision	7%	7%	23%	6%	6%
Limited assistance	20%	22%	10%	17%	9%
Extensive assistance	28%	35%	9%	28%	46%
Total dependence	22%	25%	15%	31%	37%
	100%	100%	100%	100%	100%

Number of ADL dependencies (number of activities for which the resident is not independent)	Percentage of nursing home residents
0	2%
1	7%
2	7%
3	6%
4	28%
5	50%
	100%

N = 12,357.

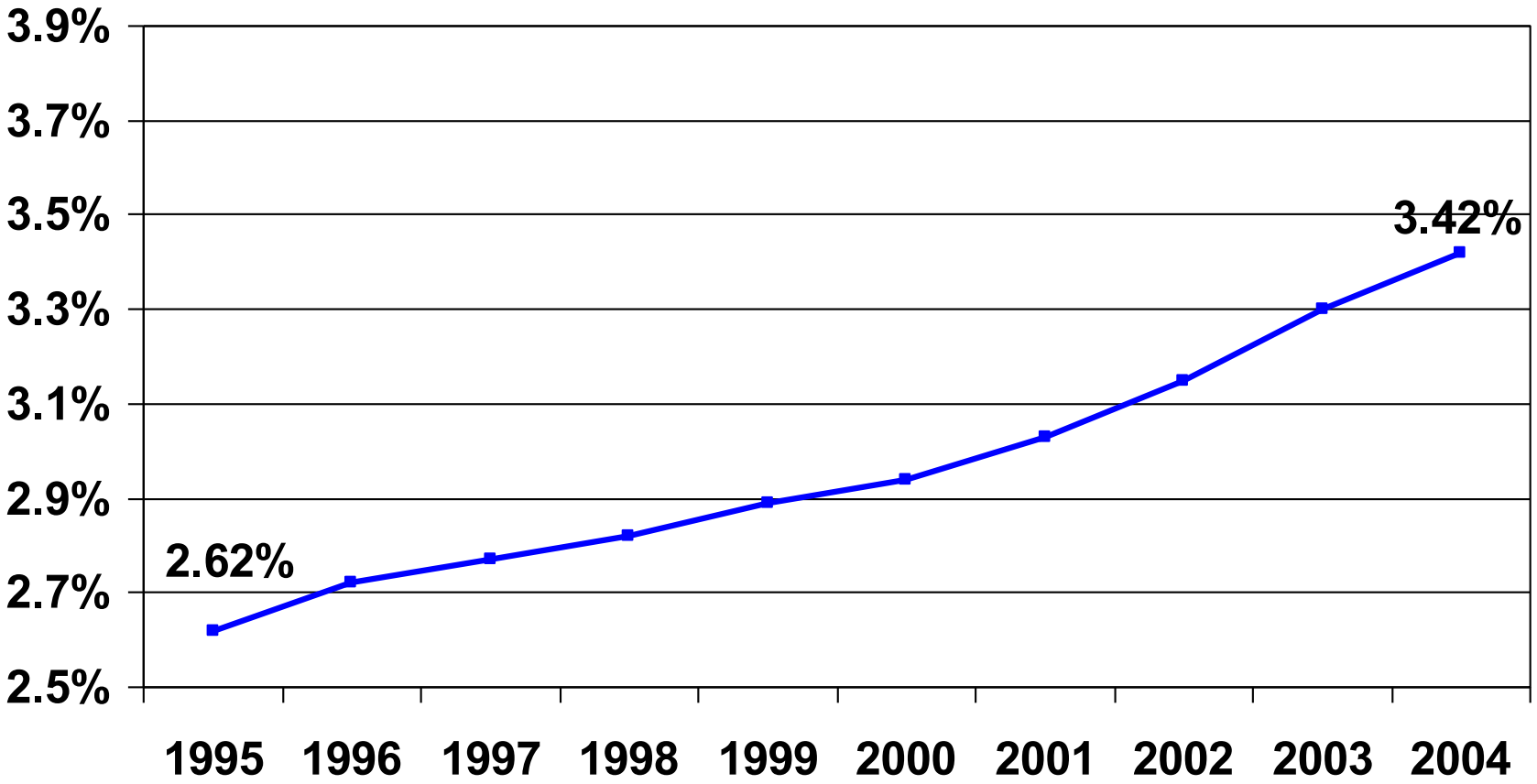
Figure 2
Probability of being totally dependent in 2004: actual vs. predicted if only pre-1991 medications used



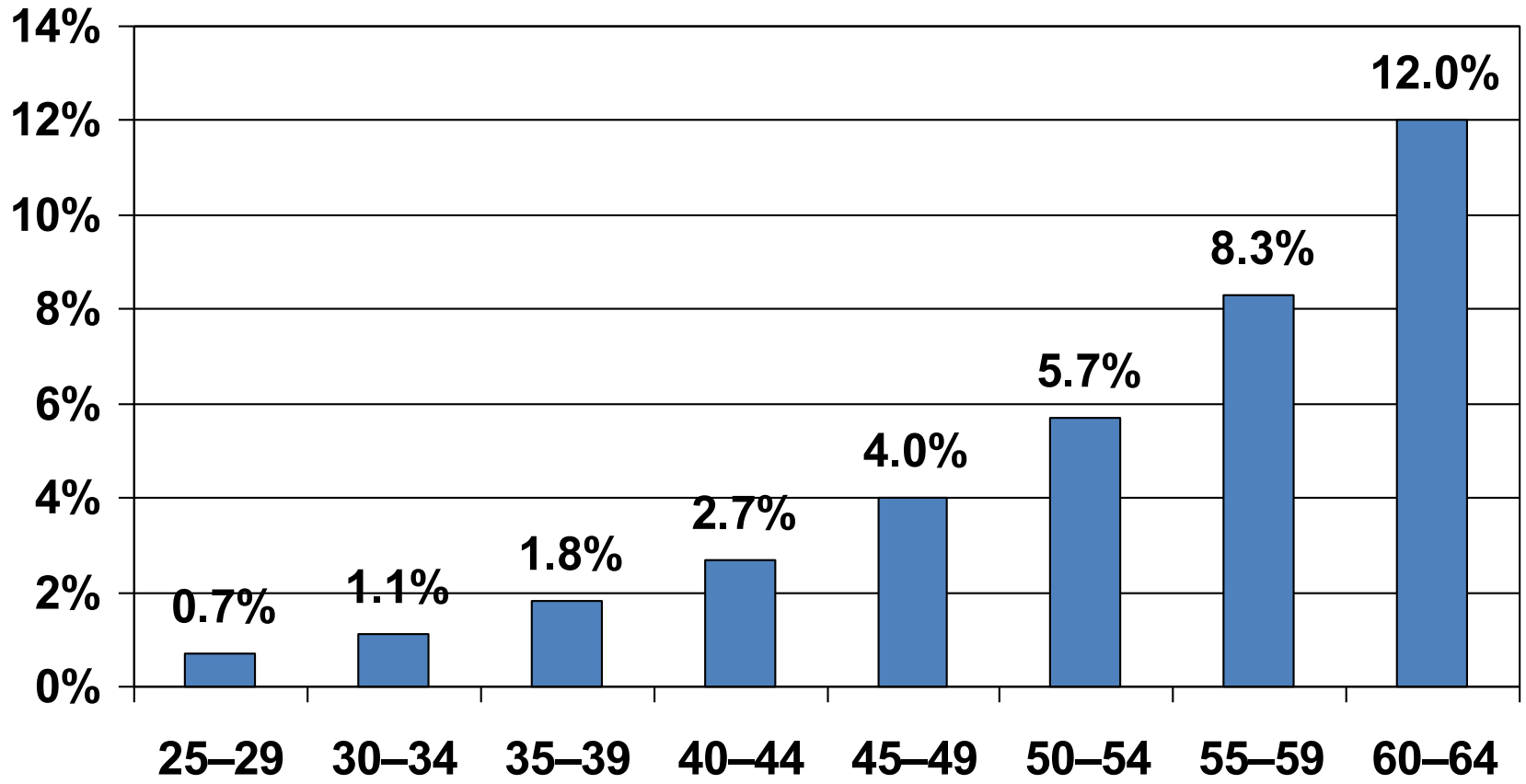
Has pharmaceutical innovation reduced Social Security Disability growth?

International Journal of the Economics of Business 18 (2), 2011.

Disability rate, 1995-2004



Disabled workers as % of population, by age, 2006



Objective

- Investigate whether, in general, the introduction and use of newer prescription drugs reduces disability

Methodology

- Use longitudinal state-level data during the period 1995-2004.
- Disability measure:

$$\frac{\text{number of workers receiving Social Security Disability Insurance benefits}}{\text{working-age population}}$$

Methodology:
Other factors controlled for

- Age
- Education
- Behavioral risk factors
  - Obesity
  - Smoking
  - HIV/AIDS incidence
- DI program generosity & labor market conditions
  - Average wage
  - Index of employment opportunity

Key findings

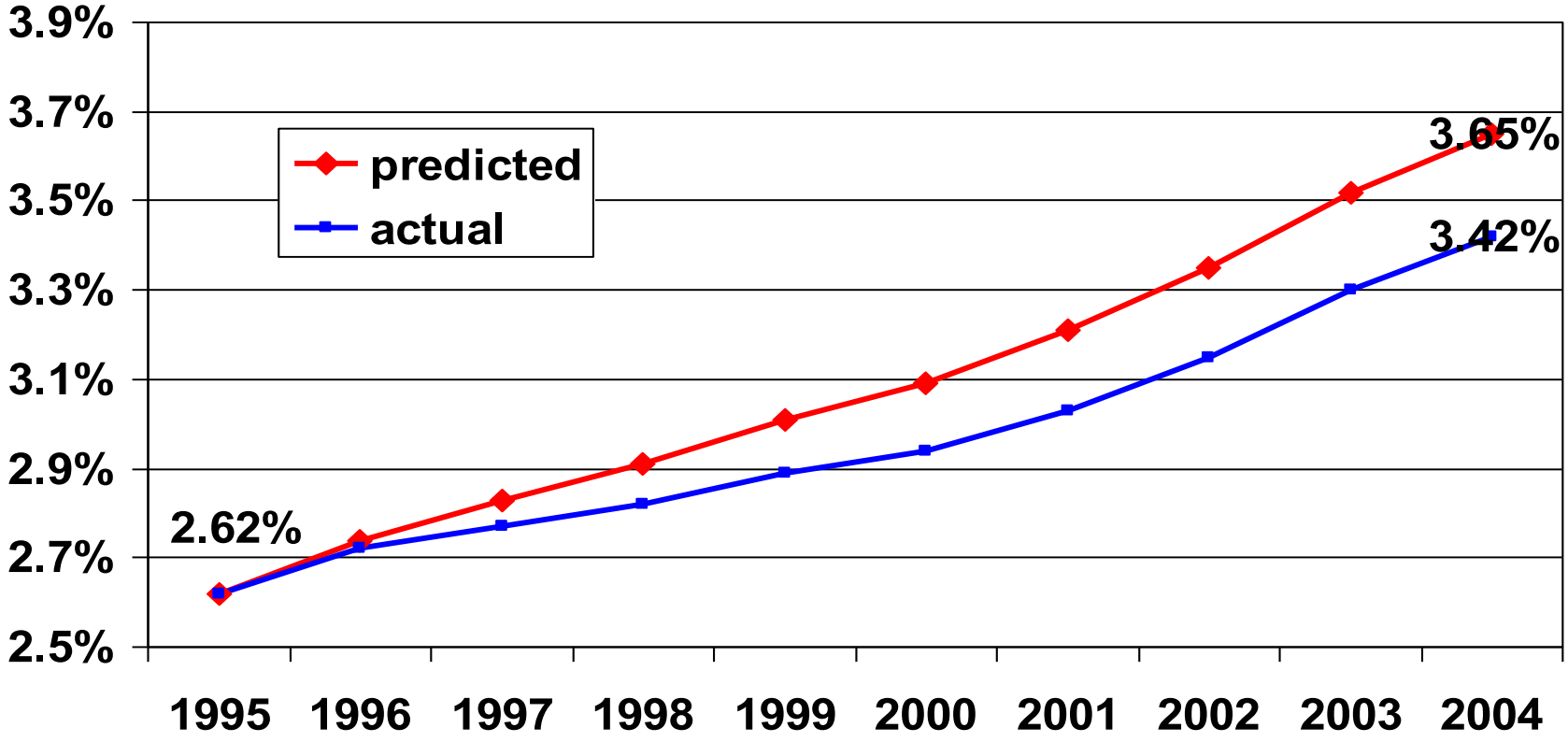
Disability recipiency inversely related to:

- drug vintage
- average wage rate
- the fraction of state residents with at least a college education

Disability recipiency directly related to:

- mean age

Predicted disability rate in year t (t = 1996,…,2004), in the absence of any post-1995 increase in drug vintage



In the absence of any post-1995 increase in drug vintage, about 418,000 more working-age Americans would have been DI recipients, and Social Security benefits paid to disabled workers in 2004 would have been about $4.5 billion higher.