The Effects of Pharmaceutical Innovation on Longevity, Hospitalization and Medical Expenditure in Turkey, 1999-2010

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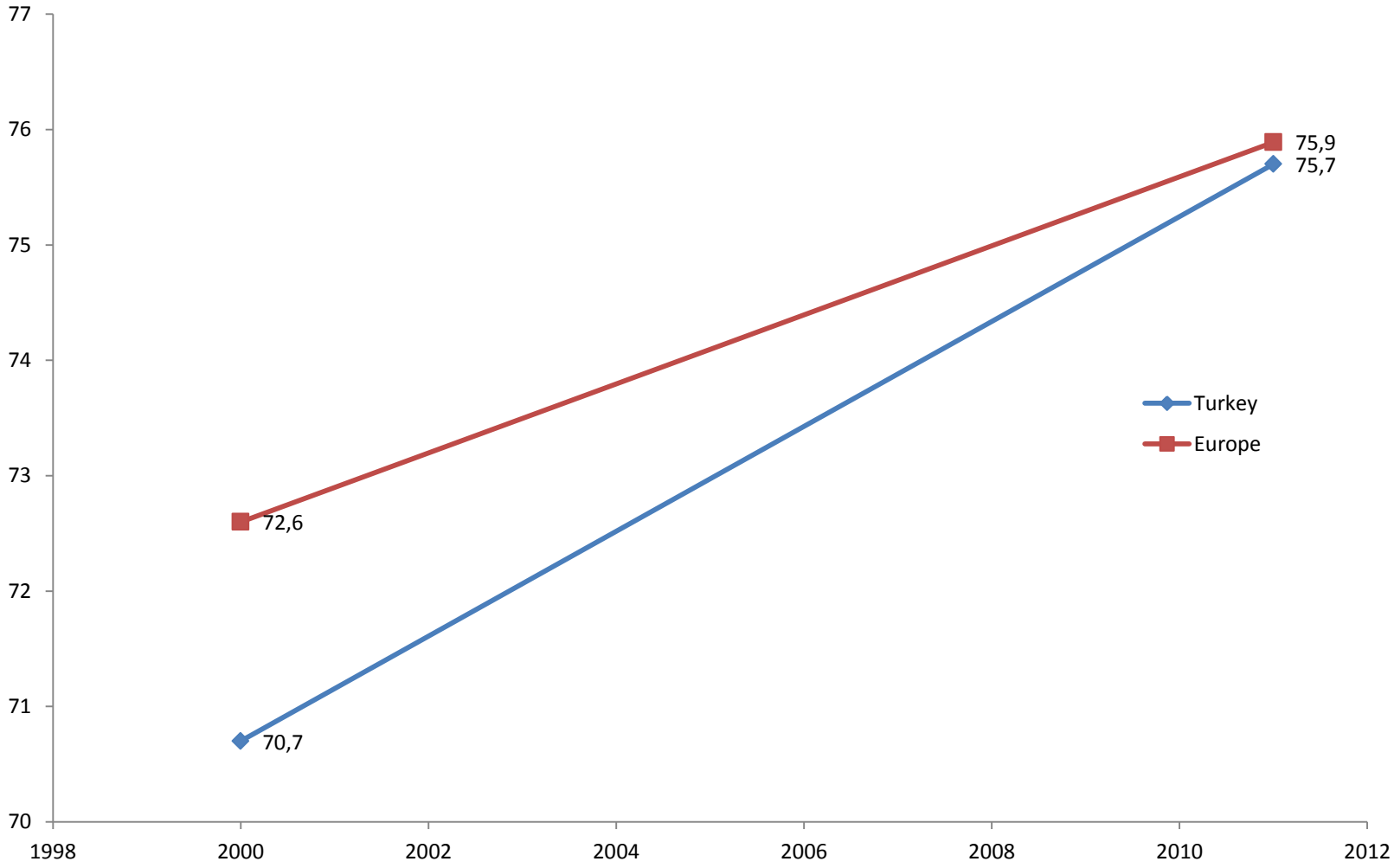
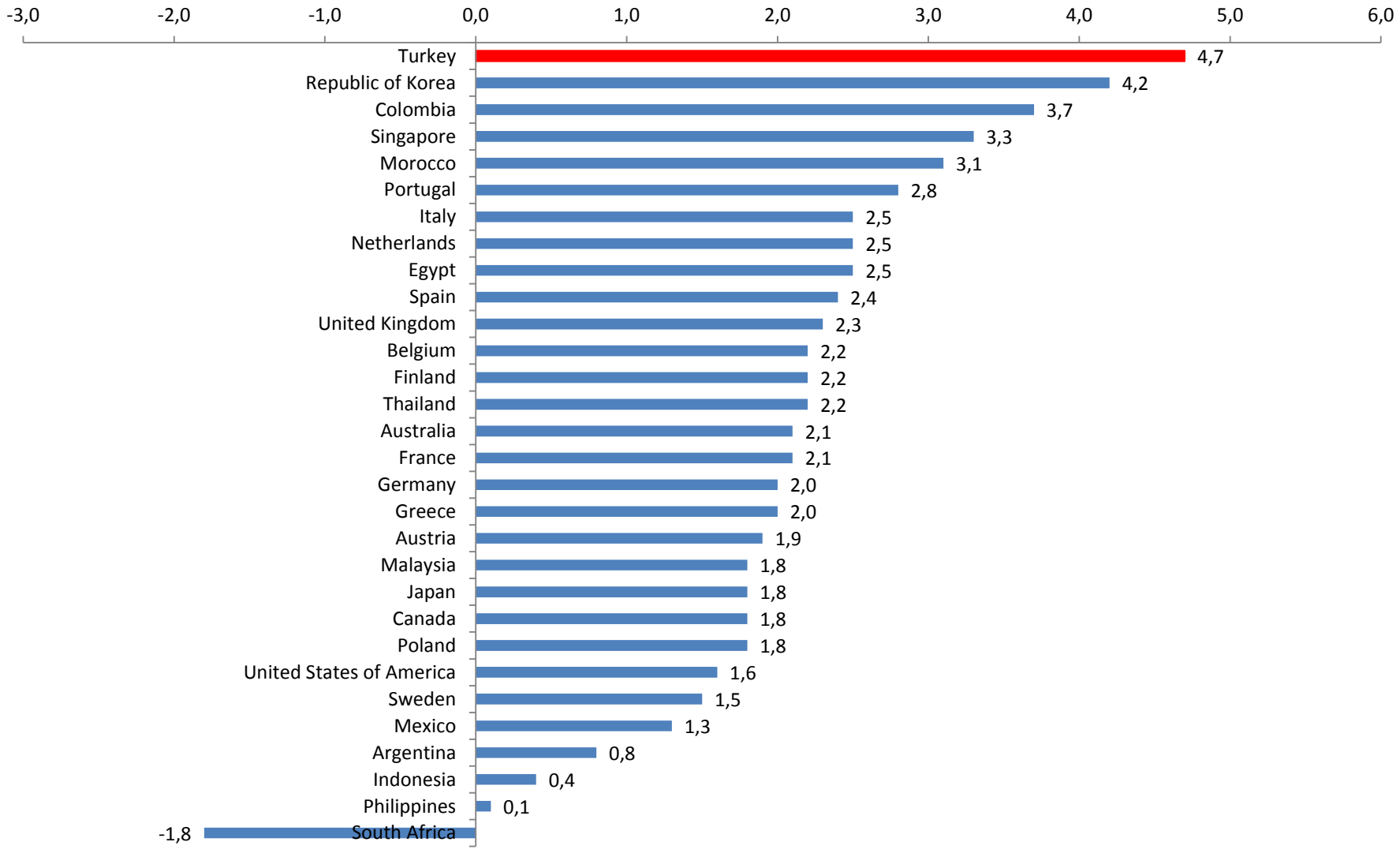
Life expectancy at birth, Turkey vs. Europe, 2000 and 2011



Source: WHO Global Health Observatory Data Repository
Turkey: Life tables Turkey, http://apps.who.int/gho/data/node.main.692?lang=en
Europe: Life expectancy by WHO region, http://apps.who.int/gho/data/node.main.688?lang=en

Increase in life expectancy at birth, 30 countries, 2000-2009



Source: Lichtenberg FR, "Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-income Countries, 2000-2009," *Health Policy and Technology* (2014) 3: 36–58

Potential explanations for Turkey's large longevity increase

- The data and analysis in Lichtenberg (2014) cast considerable doubt on two potential explanations for Turkey's large longevity increase, and provide substantial support for a third potential explanation.

- First, the data don't support the ("catch up" or "regression to the mean") hypothesis that Turkey had a large longevity increase after 2000 merely because it had below-average longevity in 2000: there was no correlation across the 30 countries between the level of longevity in 2000 and the 2000-2009 change in longevity.

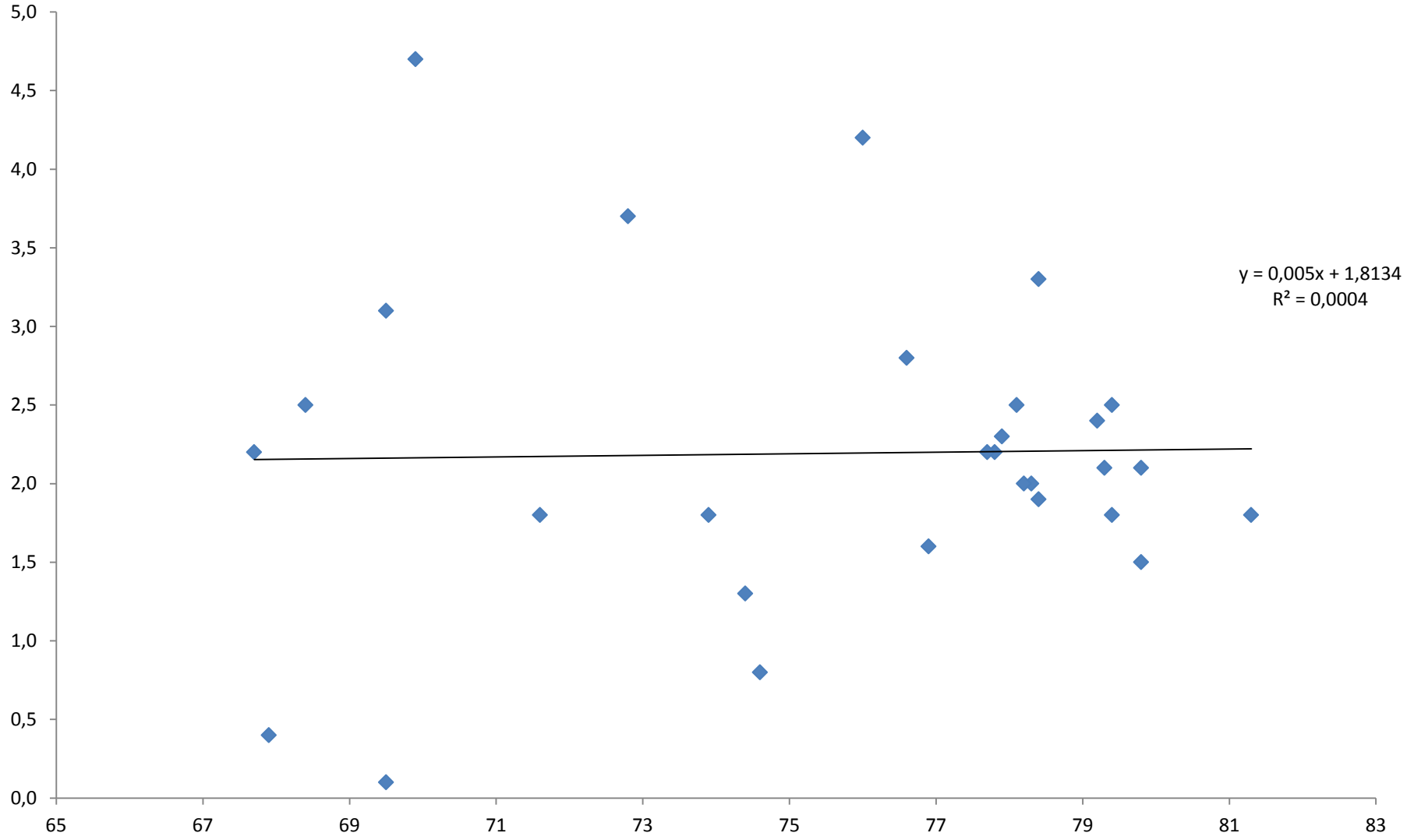
- Second, the findings in Lichtenberg (2014) don't support the hypothesis that Turkey had a large longevity increase after 2000 because it had above-average growth in socioeconomic factors such as income, education, and health expenditure; these variables were also uncorrelated across countries with longevity growth.

Potential explanations for Turkey's large longevity increase

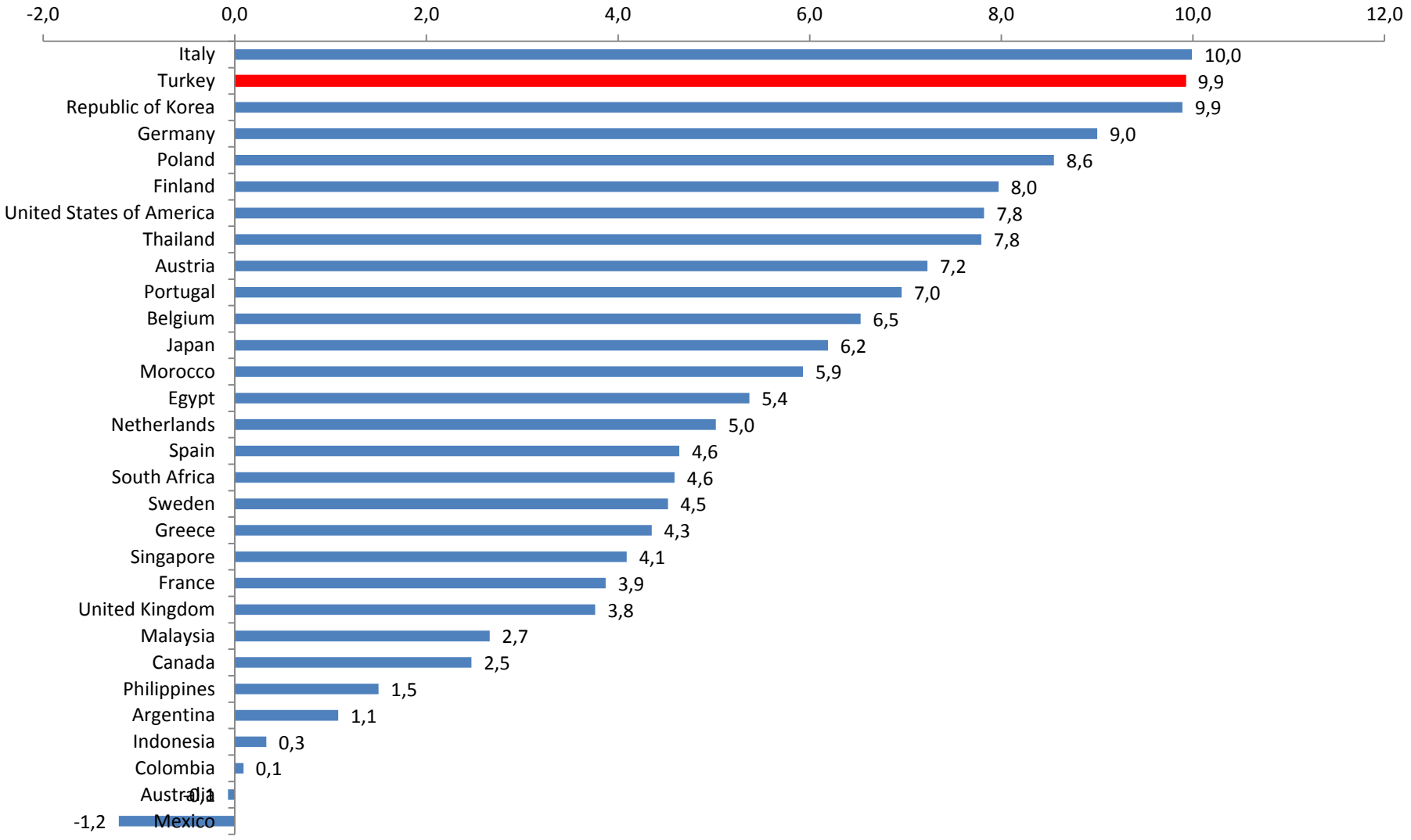
- The one variable that was strongly and consistently positively related to longevity growth, and that accounted for almost three-fourths of longevity growth, was the increase in the vintage (mean world launch year) of prescription drugs consumed—a measure of the rate of pharmaceutical innovation.

- Turkey had the second-highest increase in the vintage of prescription drugs consumed, and was barely behind the leader (Italy).

Relationship across countries between life expectancy in 2000 and increase in life expectancy, 2000-2009



Increase in mean vintage of prescription drugs, 30 countries, 2000-2009



Source: Lichtenberg FR, "Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-income Countries, 2000-2009," *Health Policy and Technology* (2014) 3: 36–58

Estimate the effects of pharmaceutical innovation on mortality and hospitalization in Turkey during 1999-2010

- Mortality, 1999-2008
  - Dependent variables:
    - Mean age at death
    - Fraction of deaths in which the decedent's age was $\geq$ 75
  - Pharmaceutical innovation measure: mean vintage of drugs consumed
- Hospitalization, 2007-2010
  - Dependent variables:
    - Number of inpatient hospital discharges
    - Number of inpatient hospital days
  - Pharmaceutical innovation measure: number of molecules previously launched

Difference-in-differences methodology

- Investigate whether diseases subject to more pharmaceutical innovation had larger increases in mean age at death and smaller increases in hospitalization

- Estimated effects of pharmaceutical innovation do *not* depend on average rates of increase of mean age at death and hospitalization

Data sources

Number of deaths, by cause of death, age, and year	WHO Mortality Database
Number of inpatient hospital discharges and days, by ICD10 and year	Eurostat hlth_co_disch1 and hlth_co_hosday tables
Quantity (no. of standard units), value (in USD), E*ph*MRA anatomical classification, and active ingredients of all pharmaceutical products; world launch years of active ingredients	IMS Health MIDAS database The number of standard units sold is determined by taking the number of counting units sold divided by the standard unit factor which is the smallest common dose of a product form as defined by IMS HEALTH. For example, for oral solid forms the standard unit factor is one tablet or capsule whereas for syrup forms the standard unit factor is one teaspoon (5 ml) and injectable forms it is one ampoule or vial. Other measures of quantity, such as the number of patients using the drug, prescriptions for the drug, or defined daily doses of the drug, are not available.
Drug indications (IND)	Thériaque (http://www.theriaque.org/), a database of official, regulatory, and bibliographic information on all drugs available in France, intended for health professionals. Funding is provided by the Centre National Hospitalier d'Information sur le Médicament.

1. Mean age at death model

$$AGE\_DEATH_{it} = \beta\, RX\_VINTAGE_{it} + \alpha_i + \delta_t + \varepsilon_{it}$$

AGE_DEATH_{it}	= mean age at death from disease i in year t (t = 1999-2002, 2004-2008); 10 diseases (ICD8 chapters)
$RX\_VINTAGE_{it}$	= $(\sum_p Q_{pit}\, WORLD\_YEAR_p) / (\sum_p Q_{pit})$ the mean vintage of drugs used to treat disease i in year t
Q_{pit}	= the quantity (number of "standard units") of product p used to treat disease i in year t
$WORLD\_YEAR_p$	= the mean world launch year of the active ingredients contained in product p
α_i	= a fixed effect for disease i
δ_t	= a fixed effect for year t

- Estimate model by weighted least squares, weighting by N_DEATHS_{it}: the number of deaths from disease i in year t
- Disturbances are clustered within diseases

Disease (ICD8 chapter) classification used in age at death analysis

ICD8 Chapter Code	ICD Chapter	EphMRA/PBIRG ANATOMICAL CLASSIFICATION
000-136	Infective and parasitic diseases	J GENERAL ANTI-INFECTIVES SYSTEMIC ; P PARISITOLOGY
140-239	Neoplasms	L ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS
240-279, 520-577	Endocrine, nutritional, and metabolic diseases + diseases of the digestive system	H SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS; A ALIMENTARY TRACT AND METABOLISM
280-289	Diseases of the blood and blood-forming organs	B BLOOD AND BLOOD FORMING ORGANS
290-315, 320-389	Mental disorders + diseases of the nervous system and sense organs	N CENTRAL NERVOUS SYSTEM; S SENSORY ORGANS
390-458	Diseases of the circulatory system	C CARDIOVASCULAR SYSTEM
460-519	Diseases of the respiratory system	R RESPIRATORY SYSTEM
580-629	Diseases of the genitourinary system	G GENITO URINARY SYSTEM AND SEX HORMONES
680-709	Diseases of the skin and subcutaneous tissue	D DERMATOLOGICALS
710-738	Diseases of the musculoskeletal system and connective tissue	M MUSCULO-SKELETAL SYSTEM

Missing data on world launch year

- World launch year data are missing for some active ingredients
- Ingredients whose world launch years are missing are generally quite old; the fraction of standard units with missing world launch years declined from 32% in 1999 to 20% in 2010
- We constructed three alternative measures of RX_VINTAGE, corresponding to three ways of dealing with missing world launch years:
  - RX_VINTAGE1: exclude products with missing world launch years
  - RX_VINTAGE2: set world launch year = 1900 for products with missing world launch years
  - RX_VINTAGE3: set world launch year = 1920 for products with missing world launch years

Summary statistics

Column	1	2	3	4	5	6
Year	number of deaths	mean age at death	fraction of deaths at age greater than 75	mean launch year--no imputation of missing launch years	mean launch year--missing launch years set equal to 1900	mean launch year--missing launch years set equal to 1920
1999	140,602	63.0	28%	1963.8	1958.8	1961.2
2000	138,136	63.1	28%	1965.1	1960.4	1962.6
2001	140,160	64.0	30%	1967.3	1962.8	1964.7
2002	143,567	65.1	32%	1967.5	1962.6	1964.7
2004	148,288	65.1	35%	1968.9	1963.6	1965.8
2005	161,823	65.2	36%	1970.5	1965.3	1967.4
2006	170,837	66.1	38%	1971.4	1966.5	1968.5
2007	173,353	66.7	40%	1972.4	1967.3	1969.3
2008	178,174	67.1	42%	1973.5	1968.6	1970.4
change, 1999 to 2008		4.1	14%	9.7	9.8	9.2

Notes:

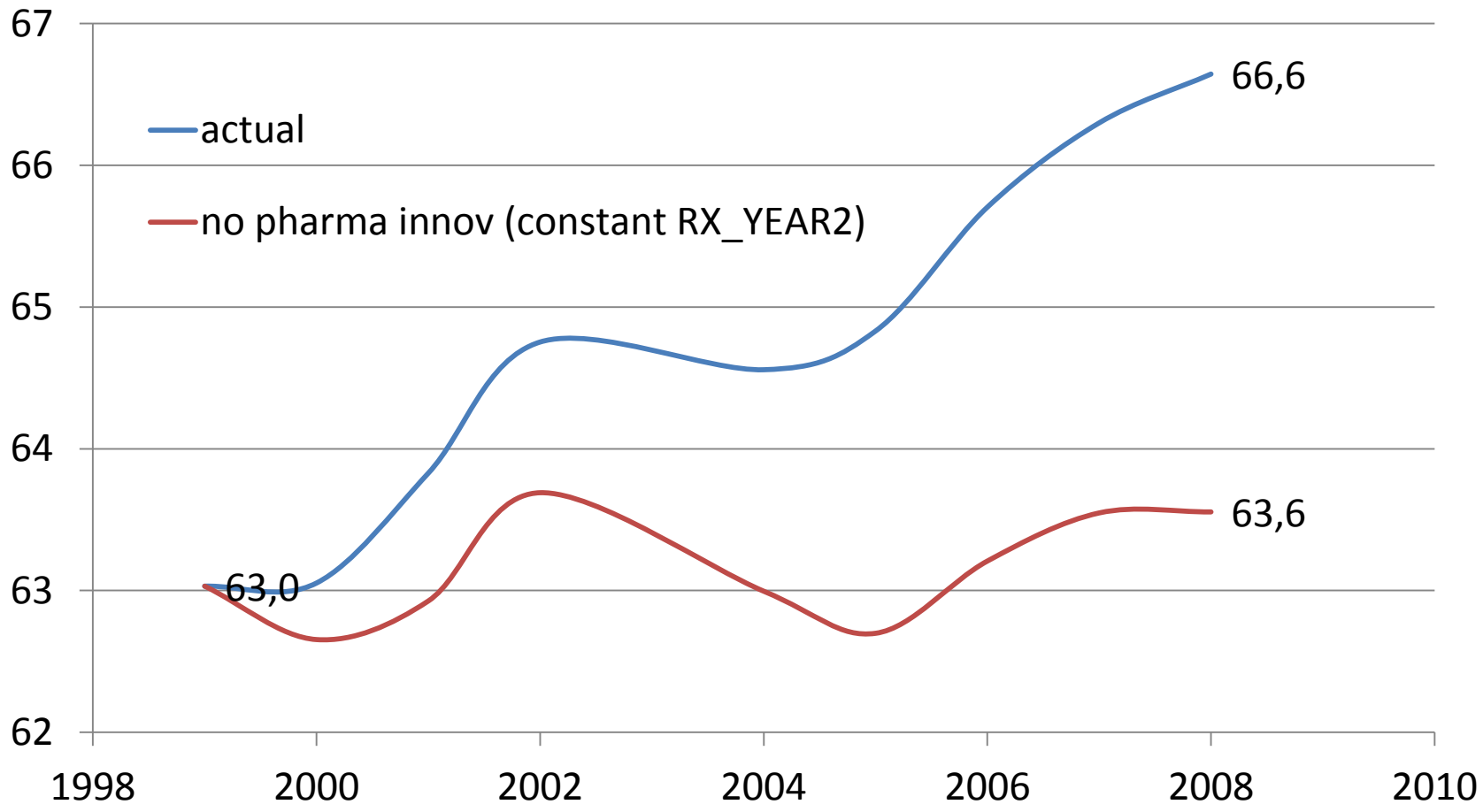
- Figures in columns 2-6 are weighted means of disease-level data, weighted by number of deaths
- 2003 is missing because the age classification of deaths used in the WHO Mortality Database in 2003 differed from the age classification used in 1999-2002 and 2004-2008

Mean age at death model estimates

Model	Independent variable	Estimate (β)	Empirical Standard Error Estimates	Z	Pr > |Z|		ΔY	ΔX	β ΔX	(β ΔX)/ ΔY
1	RX_VINTAGE1: exclude products with missing world launch years	0.2711	0.2754	0.98	0.325		4.07	9.74	2.64	65%
2	RX_VINTAGE2: set world launch year = 1900 for products with missing world launch years	0.3006	0.1054	2.85	0.0043		4.07	9.84	2.96	73%
3	RX_VINTAGE3: set world launch year = 1920 for products with missing world launch years	0.4096	0.1582	2.59	0.0096		4.07	9.23	3.78	93%

- The coefficient of RX_VINTAGE1 is not significant in model 1.
- But the coefficients of RX_VINTAGE2 and RX_VINTAGE3 are positive and highly significant in models 2 and 3.
- Those estimates suggest that most (73%-93%) of the 4.1-year increase in mean age at death was due to pharmaceutical innovation (increased drug vintage).

Mean age at death, 1999-2008



2. % of deaths at age ≥ 75 model

$$\%AGE\_GE\_75_{it} = \beta\, RX\_VINTAGE_{it} + \alpha_i + \delta_t + \varepsilon_{it}$$

$\%AGE\_GE\_75_{it}$	= the fraction of deaths from disease i in year t in which the decedent's age was ≥ 75 (t = 1999-2002, 2004-2008); 10 diseases (ICD8 chapters)

- AGE_DEATH (mean age at death) is subject to error, because mortality data are reported in age groups. I assume that deaths in age group 65-75 all occur at age 70, for example.
- %AGE_GE_75 (% of deaths at age greater than or equal to 75) is not subject to error (in principle). However, estimates of AGE_DEATH model are easier to interpret than estimates of %AGE_GE_75 model.
- Estimate model by weighted least squares, weighting by N_DEATHS_{it}: the number of deaths from disease i in year t
- Disturbances are clustered within diseases

% of deaths at age ≥ 75 model estimates

Model	Independent variable	Estimate (β)	Empirical Standard Error Estimates	Z	Pr > |Z|		ΔY	ΔX	β ΔX	(β ΔX)/ ΔY
4	RX_VINTAGE1: exclude products with missing world launch years	0.0062	0.0026	2.37	0.0177		0.14	9.74	0.06	42%
5	RX_VINTAGE2: set world launch year = 1900 for products with missing world launch years	0.0038	0.0014	2.71	0.0068		0.14	9.84	0.04	26%
6	RX_VINTAGE3: set world launch year = 1920 for products with missing world launch years	0.0055	0.0024	2.35	0.019		0.14	9.23	0.05	36%

- The vintage coefficients are positive and significant in all three models.
- These estimates suggest that 26%-42% of the 0.14 increase in the % of deaths at age greater than 75 was due to pharmaceutical innovation.

3. Number of hospital discharges model

$$\ln(HOSP\_DISCHARGES_{it}) = \beta_k \ln(CUM\_MOL_{i,t-k}) + \alpha_i + \delta_t + \varepsilon_{it}$$

$HOSP\_DISCHARGES_{it}$	= number of hospital discharges for disease i in year t (t = 2007,…,2010); 112 diseases
$CUM\_MOL_{i,t-k}$	= $\sum_m IND_{mi} APP_{m,t-k}$ = the number of molecules (drugs) to treat disease i commercialized by the end of year t-k
IND_{mi}	= 1 if molecule m is used to treat (indicated for) disease i = 0 if molecule m is not used to treat (indicated for) disease i
$APP_{m,t-k}$	= 1 if molecule m was commercialized in Turkey by the end of year t-k = 0 if molecule m was not commercialized in Turkey by the end of year t-k
α_i	= a fixed effect for disease i
δ_t	= a fixed effect for year t

Weighted least-squares estimates of β_k from the model

$$\ln(HOSP\_DISCHARGES_{it}) = \beta_k \ln(CUM\_MOL_{i,t-k}) + \alpha_i + \delta_t + \varepsilon_{it}$$

each estimate is from a separate model

weight = Σ_t $HOSP\_DISCHARGES_{it}$

disturbances are clustered within diseases

Parameter	Estimate	Empirical Standard Error Estimates	95% Lower Confidence Limit	95% Upper Confidence Limit	Z	Pr > |Z|
lcum_mol0	-0.219	0.381	-0.966	0.528	-0.58	0.5653
lcum_mol1	-0.267	0.347	-0.948	0.413	-0.77	0.4416
lcum_mol2	-0.333	0.234	-0.791	0.125	-1.43	0.1537
lcum_mol3	**-0.374**	**0.187**	**-0.741**	**-0.006**	**-1.99**	**0.0462**
lcum_mol4	**-0.325**	**0.159**	**-0.637**	**-0.013**	**-2.04**	**0.0415**
lcum_mol5	-0.201	0.154	-0.504	0.101	-1.30	0.1926
lcum_mol6	-0.018	0.158	-0.326	0.291	-0.11	0.9113

Diseases with larger increases in the cumulative number of molecules had smaller increases in the number of hospital discharges

4. Number of hospital days model

$$\ln(HOSP\_DAYS_{it}) = \beta_k \ln(CUM\_MOL_{i,t-k}) + \alpha_i + \delta_t + \varepsilon_{it}$$

$HOSP\_DAYS_{it}$	= number of hospital days for disease i in year t (t = 2007,…,2010); 112 diseases
$CUM\_MOL_{i,t-k}$	= $\sum_m IND_{mi} APP_{m,t-k}$ = the number of molecules (drugs) to treat disease i commercialized by the end of year t-k
IND_{mi}	= 1 if molecule m is used to treat (indicated for) disease i = 0 if molecule m is not used to treat (indicated for) disease i
$APP_{m,t-k}$	= 1 if molecule m was commercialized in Turkey by the end of year t-k = 0 if molecule m was not commercialized in Turkey by the end of year t-k
α_i	= a fixed effect for disease i
δ_t	= a fixed effect for year t

Weighted least-squares estimates of β_k from the model

$$\ln(HOSP\_DAYS_{it}) = \beta_k \ln(CUM\_MOL_{i,t-k}) + \alpha_i + \delta_t + \varepsilon_{it}$$

each estimate is from a separate model

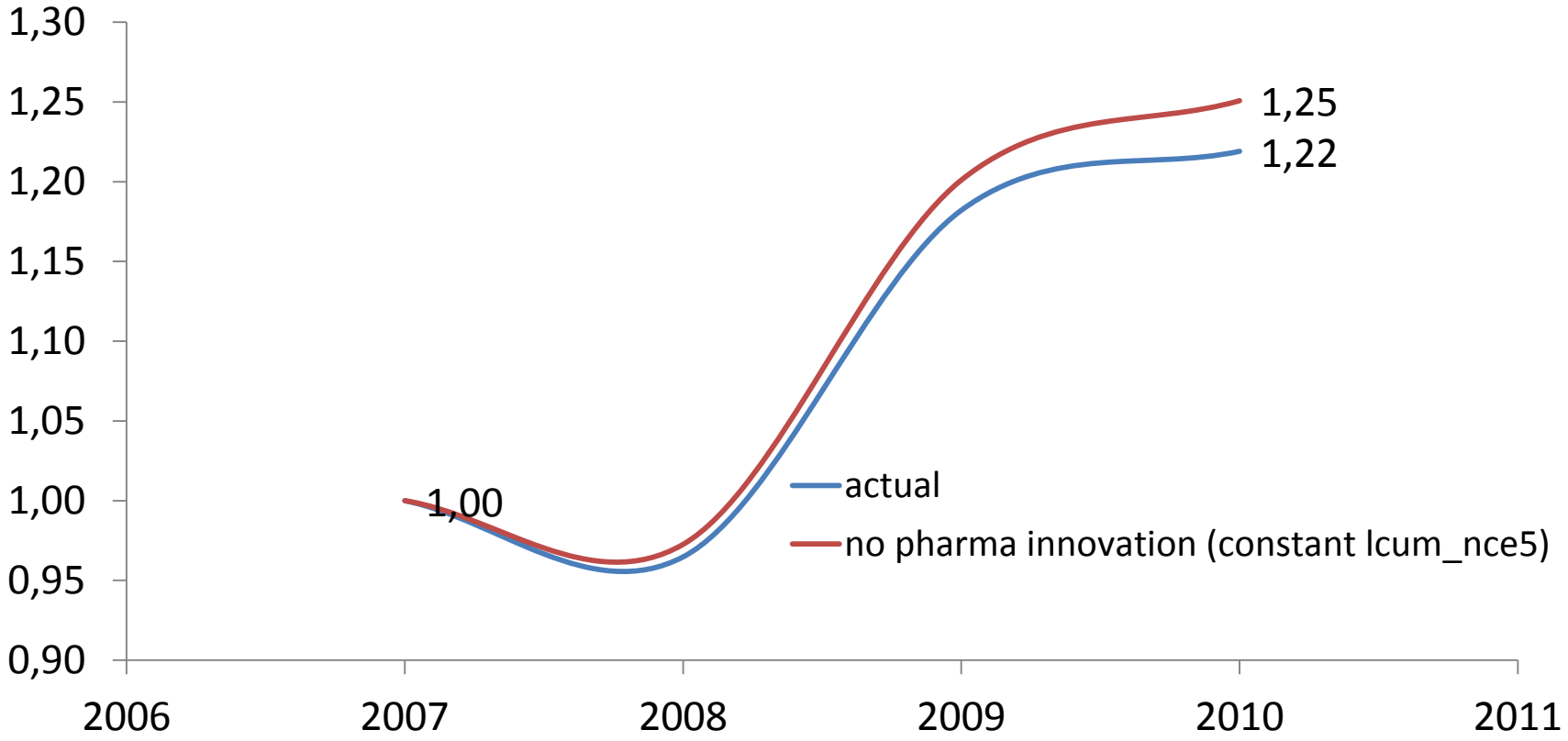
weight = Σ_t $HOSP\_DAYS_{it}$

disturbances are clustered within diseases

Parameter	Estimate	Empirical Standard Error Estimates	95% Lower Confidence Limit	95% Upper Confidence Limit	Z	Pr > |Z|
lcum_mol0	-0.166	0.312	-0.777	0.445	-0.53	0.5946
lcum_mol1	-0.481	0.283	-1.037	0.074	-1.70	0.0893
lcum_mol2	-0.270	0.205	-0.672	0.131	-1.32	0.1872
lcum_mol3	-0.147	0.222	-0.582	0.288	-0.66	0.5069
lcum_mol4	**-0.409**	**0.185**	**-0.771**	**-0.047**	**-2.21**	**0.0268**
lcum_mol5	**-0.398**	**0.137**	**-0.666**	**-0.129**	**-2.91**	**0.0037**
lcum_mol6	-0.156	0.130	-0.410	0.098	-1.20	0.2291

Diseases with larger increases in the cumulative number of molecules had smaller increases in the number of hospital days

Number of hospital days



- The number of hospital days increased 22% during the period 2007-2010
- The estimates indicate that, in the absence of pharmaceutical innovation, the number of hospital days would have increased by 25%
- Hence 3 years of pharmaceutical innovation reduced the number of hospital days in 2010 by about 3%
- Pharmaceutical innovation reduced the number of hospital days by about 1% per year

Incremental cost effectiveness of pharmaceutical innovation in Turkey, 1999-2008

Incremental cost effectiveness ratio (ICER)

$$\frac{MED\_SPEND\_LIFE_{actual} - MED\_SPEND\_LIFE_{no\_innov}}{LIFE\_EXPECT_{actual} - LIFE\_EXPECT_{no\_innov}}$$

where:

$MED\_SPEND\_LIFE_{actual}$ = actual lifetime medical expenditure (projected based on 2008 data)

$MED\_SPEND\_LIFE_{no\_innov}$ = estimated lifetime medical expenditure in absence of 9 previous years of pharmaceutical innovation

$LIFE\_EXPECT_{actual}$ = actual life expectancy (mean age at death) in 2008

$LIFE\_EXPECT_{no\_innov}$ = estimated life expectancy (mean age at death) in absence of 9 previous years of pharmaceutical innovation

Lifetime medical expenditure

$$MED\_SPEND\_LIFE_{actual} =$$

$$MED\_SPEND\_YEAR_{actual} * LIFE\_EXPECT_{actual}$$

$$MED\_SPEND\_LIFE_{no\_innov} =$$

$$MED\_SPEND\_YEAR_{no\_innov} * LIFE\_EXPECT_{no\_innov}$$

where

$MED\_SPEND\_YEAR_{actual}$ = actual (annual) per capita medical expenditure in 2008

$MED\_SPEND\_YEAR_{no\_innov}$ = estimated per capita annual medical expenditure in 2008 in absence of 9 previous years of pharmaceutical innovation = $MED\_SPEND\_YEAR_{actual} - \Delta MED\_SPEND\_YEAR$

ΔMED_SPEND_YEAR = annual per capita medical expenditure in 2008 attributable to 9 previous years of pharmaceutical innovation

Effect of pharmaceutical innovation during 1999-2008 on per capita health care spending in 2008

- $MED\_SPEND\_YEAR_{actual}$ = actual (annual) per capita medical expenditure in 2008 = 906 USD (PPP) (Source: OECD.stat)

- Between 1999 and 2008, real per capita drug expenditure increased by 104 USD (see next slide)

- Suppose that *all* of that increase was due to pharmaceutical innovation during 1999-2008
  - This assumption is probably conservative; some of the 104 USD increase in real per capita drug expenditure was probably due to other factors, e.g. aging of the population

- The hospitalization results indicate that pharmaceutical innovation during 1999-2008 reduced hospital expenditure in 2008 by about 9%

Effect of pharmaceutical innovation during 1999-2008 on per capita health care spending in 2008

- Hospital expenditure accounted for about 20% of total medical expenditure in 2000 (the most recent year for which data are available; Source: OECD.stat)

- Hence pharmaceutical innovation during 1999-2008 may have reduced per capita hospital expenditure in 2008 by about 16 USD (= 9% * 20% * 906 USD); at least 16% of the increase in drug expenditure was offset by a reduction in hospital expenditure

- We estimate that, in the absence of 9 previous years of pharmaceutical innovation, per capita medical expenditure in 2008 would have been no less than 818 USD (= 906 – 104 + 16)

Drug expenditure, Turkey, 1999-2010

year	Drug expend (USD 000s)	Population (000s)	Per capita drug expend (USD)	US CPI (2008=1.00)	Real per capita drug expend (2008 USD)
1999	$2,083,859	63,364	$33	0.77	$43
2000	$2,430,955	64,252	$38	0.80	$48
2001	$2,119,627	65,133	$33	0.82	$40
2002	$2,665,392	66,008	$40	0.84	$48
2003	$3,707,246	66,873	$55	0.85	$64
2004	$4,500,758	67,723	$66	0.88	$75
2005	$6,939,366	68,566	$101	0.91	$111
2006	$7,289,817	69,395	$105	0.94	$112
2007	$9,412,930	70,215	$134	0.96	$139
2008	$10,553,097	71,625	$147	1.00	$147
2009	$10,172,217	72,484	$140	1.00	$140
2010	$10,520,367	73,328	$143	1.01	$141

Source: IMS MIDAS database; BLS

Estimation of ICER

Column	(1)	(2)	(3) = (1) * (2)
	Life expectancy (mean age at death)	Annual per capita health expend (USD)	Lifetime per capita health expend (USD)
Actual value in 2008	67.1	$906	$60,798
Estimated value in 2008 in absence of 9 previous years of pharmaceutical innovation	64.1[a]	$818[b]	$52,471
Difference	3.0	$88	$8,327

- a: estimated from model 2
- b: assuming that entire 1999-2008 increase in real per capita pharmaceutical expenditure is due to use of newer drugs
- **ICER = $8327 / 3.0 = $2776: the cost per life-year gained is $2776**
- **If the difference in life expectancy is half as large as estimated from model 2—1.5 years instead of 3 years—the cost per life-year gained is $4808**
- This is a very small fraction of leading economists' estimates of the value of (or consumers' willingness to pay for) a one-year increase in life expectancy. Aldy and Viscusi (2008) estimate that the average value of (willingness to pay for) an American life- year is $300,000.

Aldy, J.E., Viscusi, W.K., 2008. Adjusting the value of a statistical life for age and cohort effects. Review of Economics and Statistics 90 (3) 573– 581.

Summary

- Diseases subject to more pharmaceutical innovation had larger increases in mean age at death and smaller increases in hospitalization
- The estimates indicate that most (73%-93%) of the 4.1-year increase in mean age at death was due to pharmaceutical innovation
- At least 16% of the increase in drug expenditure was offset by a reduction in hospital expenditure
- Our baseline estimate of the cost per life-year gained from pharmaceutical innovation is $2776
- If the difference in life expectancy is half as large as our estimates indicate, the cost per life-year gained is $4808
- Even the latter figure is a very small fraction of leading economists' estimates of the value of (or consumers' willingness to pay for) a one-year increase in life expectancy