The effect of pharmaceutical innovation on longevity, hospitalization and medical expenditure in Turkey, 1999–2010

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A B S T R A C T

We investigate the impact of pharmaceutical innovation on longevity, hospitalization and medical expenditure in Turkey during the period 1999–2010 using longitudinal, disease-level data.

From 1999 to 2008, mean age at death increased by 3.6 years, from 63.0 to 66.6 years. We estimate that in the absence of any pharmaceutical innovation, mean age at death would have increased by only 0.6 years. Hence, pharmaceutical innovation is estimated to have increased mean age at death in Turkey by 3.0 years during the period 1999–2008. We also examine the effect of pharmaceutical innovation on hospital utilization. We estimate that pharmaceutical innovation has reduced the number of hospital days by approximately 1% per year.

We use our estimates of the effect of pharmaceutical innovation on age at death, hospital utilization and pharmaceutical expenditure to assess the incremental cost-effectiveness of pharmaceutical innovation, i.e., the cost per life-year gained from the introduction of new drugs. The baseline estimate of the cost per life-year gained from pharmaceutical innovation is $2776. 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.

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1. Introduction

There have been impressive gains in longevity in Turkey since the year 2000. As shown in Fig. 1, in the year 2000, life expectancy at birth in Turkey was 1.9 years lower than it was in Europe. In 2011, life expectancy at birth in Turkey was only 0.2 years lower than it was in Europe; almost nine-tenths of the longevity gap was closed within an eleven-year period. Longevity growth in Turkey was also greater than it was in other non-European middle-income and low-income countries. Lichtenberg [1] analyzed longevity growth during the period 2000–2009 in 30 developing and high-income countries. As shown in Fig. 2, Turkey had the largest increase in life expectancy at birth: 4.7 years, versus a (population-weighted) average increase of 1.7 years.

In principle, the substantial increase in Turkish longevity could be due to a variety of factors. The data and analysis in Lichtenberg [1] cast considerable doubt on two potential explanations for Turkey’s large longevity growth.
increase, and provide substantial support for a third potential explanation. First, the data do not 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. As shown in Fig. 3, 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 [1] do not 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. 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. As shown in Fig. 4, Turkey had the second-highest increase in the vintage of prescription drugs consumed, and was barely behind the leader (Italy).

In this paper, we reexamine the role of pharmaceutical innovation in Turkish longevity growth from a different perspective. The previous study was a between-country study based on aggregate data (i.e., data on mortality from all causes combined) for each country. Only one-thirtieth

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1 A plot based on data for the half of the sample with below-median life expectancy in 2000 suggests the same conclusion.
of the data were data about Turkey, and the longevity measure was life expectancy at birth (and other ages). Longevity was the only outcome variable examined, and drug vintage was the only measure of pharmaceutical innovation. In this paper, we will perform a within-country analysis based entirely on data about Turkey. We will analyze longitudinal disease-specific data, i.e., data on mortality by cause and pharmaceutical innovation by class of drugs. The longevity measure will be mean age at death rather than life expectancy at birth, and we will examine the impact of pharmaceutical innovation on hospitalization and total medical expenditure as well as on longevity. In addition to drug vintage, we will use another measure of pharmaceutical innovation: the number of drugs previously launched to treat a condition.

This study will investigate the effects of pharmaceutical innovation on longevity, hospitalization and medical expenditure in Turkey during the period 1999–2010 using data obtained from several rich databases. In essence, we will investigate whether diseases that experienced more pharmaceutical innovation had larger increases in longevity and smaller increases in hospitalization. The difference-in-differences research design we will use will control for the effects of macroeconomic trends and overall economic conditions.

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2 Lichtenberg [2] shows that mean age at death is highly correlated across countries with life expectancy at birth.
changes in the health care system, assuming that these trends had similar effects on different diseases. Since our models will be estimated using aggregate data rather than patient-level data, the risk of selection biases (nonrandom assignment of drugs to patients) is greatly reduced or eliminated. As illustrated in Fig. 5, by combining the estimates of the effect of pharmaceutical innovation on longevity, hospital utilization, and drug expenditure, the incremental cost-effectiveness (cost per life-year gained) of pharmaceutical innovation in Turkey during the period 1999–2010 will be estimated.

The theoretical framework for our analysis is discussed in Section 2. Econometric models of longevity and hospital utilization are described in Section 3. Data sources and descriptive statistics are briefly discussed in Section 4. Empirical results are presented in Section 5. We use the estimates to calculate the incremental cost-effectiveness of pharmaceutical innovation in Turkey in Section 6. A summary and conclusions are provided in Section 7.

2. Theoretical framework

Economists have shown that longevity increase is an important part of economic growth and development [4]. Nordhaus [5] 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.” The United Nations Development Programme [6] combines indicators of life expectancy, educational attainment and income into a composite Human Development Index.

Economists have also shown that “growth . . . is driven by technological change that arises from intentional [R&D] investment decisions made by profit-maximizing agents” [7] and by government agencies such as the National Institutes of Health. Jones [8] argued that “technological progress [is] the ultimate driving force behind sustained economic growth” and that “technological progress is driven by research and development (R&D) in the advanced world.” According to the National Science Foundation [9], the medical devices and substances industries are the most research intensive industries in the economy.

In principle, technological change could be either disembodied or embodied in new goods. Solow [10] hypothesized that most technological change is embodied: to benefit from technological progress, one must use newer, or later vintage, goods and services. Bresnahan and Gordon [11] argued that “new goods are at the heart of economic progress,” and Hercowitz [12] also reached the “conclusion . . . that ‘embodiment’ is the main transmission mechanism of technological progress to economic growth.” We 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. Pharmaceutical-embodied medical innovation can be measured in two different ways. The first, theoretically superior, way is to measure changes over time in the mean vintage of drugs used to treat a condition. We define the vintage of a product as its year of invention or first use. Solow [10] 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. A number of econometric studies Bahk and Gort [13], Hulten [14], Sakkarlis and Wilson [15] have shown that manufacturing firms using later-vintage equipment have higher productivity.

The second way to measure pharmaceutical-embodied medical innovation is to measure changes over time in the cumulative number of drugs used to treat a condition. In his model of endogenous technological change, Romer [7] hypothesized an aggregate production function in which an economy’s output depends on the “stock of

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3 Major changes were made in the organization and financing of health care services in Turkey beginning in 2003, which resulted in substantial increases in utilization of health care services. According to Ministry of Health [3] statistics, the annual average number of physician visits per person has increased to 8.2 in 2011 from 3.2 in 2002.

4 Estimates based on patient-level data can be biased if the sickest patients tend to get the newest (or oldest) treatment.

5 According to the Merriam Webster dictionary, one definition of vintage is “a period of origin or manufacture (e.g. a piano of 1845 vintage”). http://www.merriam-webster.com/dictionary/vintage.

6 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.
ideas” that have previously been developed as well as on the economy’s endowments of labour and capital. The hospitalization models we will estimate may be viewed as health production functions in which hospitalization is an inverse indicator of health output or outcomes, and the cumulative number of drugs approved is analogous to the stock of ideas.

Pharmaceutical innovation is not the only type of medical innovation that is likely to contribute to premature mortality. Other medical innovation, such as innovation in diagnostic imaging, surgical procedures, and medical devices, is also likely to affect premature mortality. Therefore, ideally measures of these other types of medical innovation should be included in models of longevity and hospitalization. Unfortunately, longitudinal disease-level measures of non-pharmaceutical medical innovation are not available for Turkey. But failure to control for non-pharmaceutical medical innovation is unlikely to bias estimates of the effect of pharmaceutical innovation on longevity and hospitalization, for several reasons.

First, the number of people exposed to pharmaceutical innovation tends to be much larger than the number of people exposed to other types of medical innovation: for example, in 2007, 62% of Americans consumed prescription drugs, while only 8% of Americans were admitted to hospitals. Second, pharmaceuticals are more research-intensive than other types of medical care: in 2007, prescription drugs accounted for 10% of U.S. health expenditure, but more than half of U.S. funding for biomedical research came from pharmaceutical and biotechnology firms [17]. Much of the rest came from the federal government (i.e., the NIH), and new drugs often build on upstream government research [18].

Third, previous research based on U.S. data indicates that non-pharmaceutical medical innovation is not positively correlated across diseases with pharmaceutical innovation. In Appendix 2 of Lichtenberg [2], it is shown that, in the U.S., during the period 1997–2007, the rate of pharmaceutical innovation was not positively correlated across diseases with the rate of medical procedure innovation and may have been negatively correlated with the rate of diagnostic imaging innovation. Also, Lichtenberg [19] found that estimates of the effect of pharmaceutical innovation on U.S. cancer mortality rates were insensitive to the inclusion or exclusion of measures of non-pharmaceutical medical innovation. This suggests that failure to control for other medical innovation is unlikely to result in overestimation of the effect of pharmaceutical innovation on longevity growth.

In principle, there are numerous factors other than new drugs, devices, and medical procedures that might have contributed to the increase in longevity, such as disease management innovations or quality assurance programmes, and effective public health interventions in the area of environmental and occupational health and product and transport safety. Unfortunately, these factors are more difficult to measure than pharmaceutical innovation. However, previous research based on longitudinal region-level (country- or state-level) data [1,28,29] has found little or no correlation between longevity growth and factors such as income, education, unemployment, and public and private health expenditure. Moreover, we can think of little reason to expect other factors (e.g., disease management innovations or quality assurance programmes) to be correlated across diseases with pharmaceutical innovation. Nevertheless, such factors should be accounted for in future research.

3. Econometric models of longevity and hospital utilization

3.1. Longevity models

To investigate the impact of pharmaceutical innovation on longevity in Turkey, we will estimate models of the following two forms:

\[ \text{AGE\_DEATH}_{it} = \beta \text{RX\_VINTAGE}_{it} + \alpha_i + \delta t + \epsilon_{it} \]  
\[ \%\text{AGE\_GE\_75}_{it} = \beta \text{RX\_VINTAGE}_{it} + \alpha_i + \delta t + \epsilon_{it} \]  

where

\[ \text{AGE\_DEATH}_{it} = \text{mean age at death from disease } i \text{ in year } t \text{ ( } t = 1999-2002, 2004-2008); 10 \text{ diseases (ICD8 chapters)} \]

\[ \%\text{AGE\_GE\_75}_{it} = \text{the fraction of deaths from disease } i \text{ in year } t \text{ in which the decedent’s age was } \geq 75 \]

\[ \text{RX\_VINTAGE}_{it} = \sum_{p} \sum_{Q_{it}} \text{WORLD\_YEAR}_{ip} (\sum_{Q_{it}}), \text{ the mean vintage of drugs used to treat disease } i \text{ in year } t \]

\[ \alpha_i = \text{a fixed effect for disease } i; \]

\[ \delta t = \text{a fixed effect for year } t. \]

In principle, the dependent variable in Eq. (1) (mean age at death) is a more meaningful measure of longevity than the dependent variable in Eq. (2) (the fraction of deaths in which the decedent’s age was \( \geq 75 \)). However, because mortality data are reported in age groups (e.g., the number of deaths at ages 65–69, 70–74, etc.), mean age at death is subject to measurement error, whereas the fraction of

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7 Source: U.S. Medical Expenditure Panel Survey, 2007 Full Year Consolidated Data File. Lichtenberg [16] found that therapeutic procedure innovation increased the life expectancy of Western Australian hospital patients (whose mean life expectancy was about 10 years) by 2–3 months between 2000 and 2007. Since the fraction of the population that is hospitalized is fairly low, the implied contribution of hospital procedure innovation to aggregate longevity growth is fairly modest—much smaller than estimates of the contribution of pharmaceutical innovation to aggregate longevity growth.

8 For example, there was a dramatic reduction of fatal traffic accidents in some European countries (e.g., Germany), which increased life expectancy substantially. However, WHO data indicate that in Turkey during the period 2004–2008, the decline in road traffic accidents accounted for just 2.1% of the decline in the age-standardized death rate.

9 To construct AGE\_DEATH, we assumed that deaths within in age interval occur at the midpoint of the interval, e.g. deaths at ages 65–69 occur at age 67.5.
deaths in which the decedent’s age was \( \geq 75 \) is not subject to measurement error.

Also, in principle, one might want to include a measure of the average quantity, as well as the quality (vintage), of pharmaceuticals consumed in Eqs. (1) and (2). The average quantity is the total consumption of medicines divided by the number of patients. Unfortunately, data on the number of patients with each disease (e.g., the number of cancer patients) are not available, so we are unable to measure the average quantity of pharmaceuticals consumed, by disease and year. However Lichtenberg [128] found that the change in log of per capita quantity of prescription drugs did not have a statistically significant effect on longevity at either the country level or the state level.

In Eqs. (1) and (2), it is postulated that mean age at death (or alternatively, the fraction of deaths with the decedent’s age over 74 years) in year \( t \) is exclusively a function of the mean vintage of drugs in this year. However, for many diseases (particularly many chronic diseases) it is much more plausible to assume that the value of the dependent variable in year \( t \) is a function not only of the mean vintage of drugs in this year, but of the mean vintage of drugs in the preceding years, as well, probably with declining weight of influence, indicating that a model specification similar to traditional distributed time lag models might be a more suitable structural specification. Unfortunately, the potential gain in model validity would come at a price—its application would require longer time series data.

Due to the presence of fixed disease effects and year effects, Eqs. (1) and (2) are difference-in-differences models. A positive and significant estimate of \( \beta \) in Eq. (1), for example, would signify that there were above-average increases in mean age at death for diseases with above-average increases in mean vintage of drugs.\(^{10}\) The fixed year effects control for the effects of macroeconomic trends and overall changes in the health care system.

To address the issue of heteroskedasticity—diseases with low numbers of deaths tend to have higher (positive and negative) fluctuations in age at death—Eqs. (1) and (2) will be estimated via weighted least-squares, weighting by the number of deaths from disease \( i \) in year \( t \) (\( N_{\text{DEATHS}_{it}} \)). The disturbances will be clustered within diseases.

For some active ingredients, there were missing data for the world launch year. However, the 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 will estimate Eqs. (1) and (2) using 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

3.2. Hospitalization models

We will estimate two types of models of the relationship between hospital utilization and pharmaceutical innovation. The first of these is a model of the number of hospital discharges, and the second is a model of the number of hospital days:

\[
\ln(\text{HOSP\_DISCHARGES}_{it}) = \beta_k \ln(\text{CUM\_MOL}_{t,k}) + \alpha_i + \delta_t + \epsilon_{it}
\]

(3)

\[
\ln(\text{HOSP\_DAYS}_{it}) = \beta_k \ln(\text{CUM\_MOL}_{t,k}) + \alpha_i + \delta_t + \epsilon_{it}
\]

(4)

where

- HOSP\_DISCHARGES\(_{it}\): the number of hospital discharges for disease \( i \) in year \( t \) (\( t = 2007, \ldots, 2010 \));
- HOSP\_DAYS\(_{it}\): the number of hospital days for disease \( i \) in year \( t \);
- CUM\_MOL\(_{t-k}\): \( \sum_m n_{\text{IND}_m} n_{\text{MP}_{im}} \) – the number of molecules (drugs) to treat disease \( i \) commercialized by the end of the year \( t - k \);
- IND\(_m\): 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\(_{m,i,k}\): 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 \( t - k \);
- \( \alpha_i \): a fixed effect for disease \( i \);
- \( \delta_t \): a fixed effect for year \( t \).

In the longevity models (Eqs. (1) and (2)), the pharmaceutical innovation measure is drug vintage, whereas in the hospital utilization models (Eqs. (3) and (4)) the pharmaceutical innovation measure is the number of molecules. Drug vintage is the theoretically superior measure, but data on drug vintage are not available at this low level of aggregation. However Lichtenberg [2] showed that there is a significant positive relationship between mean vintage and the number of molecules 1–5 years earlier, and that the number of molecules 3 years earlier has the largest effect on mean vintage.

The hospital utilization analysis is at a much lower level of aggregation (110 diseases) than the longevity analysis (10 diseases). In the hospital utilization analysis, a drug is allocated to each of the diseases that it is indicated for. For example, the drug vinblastine (ATC code L01CA01) is allocated to the following diseases: C45–C49 Malignant neoplasms of mesothelial and soft tissue; C50 Malignant neoplasm of breast; C51–C58 Malignant neoplasms of female genital organs; C60–C63 Malignant neoplasms of male genital organs; C64–C68 Malignant neoplasms of urinary tract; C81–C96 Malignant neoplasms, stated or

\(^{10}\) 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 may die from other diseases instead. Our estimates will not capture between-disease spillover effects.
presumed to be primary, of lymphoid, haematopoietic and related tissue.

To address the issue of heteroskedasticity—diseases with low average numbers of discharges tend to have higher (positive and negative) percentage fluctuations in the number of discharges—Eqs. (3) and (4) will be estimated via weighted least-squares. In Eq. (3), observations will be weighted by the total number of hospital discharges for disease $i$ during the entire period ($\sum HOSPDISHARCHES_{i,t}$); in Eq. (4), observations will be weighted by the total number of hospital days for disease $i$ during the entire period ($\sum \text{HOSP}_{i,t}$).

### 4. Data sources and descriptive statistics

The four databases used to construct longitudinal, disease-level data on the vintage of number of drugs, longevity, and hospital utilization are shown in Table 1. The disease (ICD8 chapter) classification used in age at death analysis is shown in Table 2.\footnote{\textsuperscript{13} To construct the weighted mean vintage of drugs by disease, we use the Anatomical Therapeutic Chemical (ATC) classification of drug products. Products containing the same active ingredient can be classified in more than one anatomical main group. For example, some products containing ciprofloxacin are classified in the anatomical main group “J GENERAL ANTI-INFECTIVES SYSTEMIC,” whereas others are classified in the anatomical main group “S SENSORY ORGANS.” At the high level of aggregation used in the longevity analysis, the number of drugs that are used to treat multiple diseases is likely to be small. See WHOCC–Structure and principle, \url{http://www.whocc.no/atc/structure_and_principles/}.}

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Data sources.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of deaths by cause of death, age and year</td>
<td>WHO Mortality Database [20]</td>
</tr>
<tr>
<td>Number of inpatient hospital discharges and days by ICD10 and year</td>
<td>Eurostat hith_co_disch1 and hith_co_hosday tables [21]</td>
</tr>
<tr>
<td>Quantity (no. of standard units*)</td>
<td>IMS Health MIDAS database [22]</td>
</tr>
<tr>
<td>Drug indications (IND)</td>
<td>Thérinaque (\url{<a href="http://www.theriaque.org/%7D">http://www.theriaque.org/}</a>), 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 [23]</td>
</tr>
</tbody>
</table>

\*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 for injectable forms, it is one ampoule or vial. Other measures of quantity, such as the number of units of patients using the drug, prescriptions for the drug, or defined daily doses of the drug, are not available.

### 5. Empirical results

Estimates of drug vintage coefficients ($\beta$) from longevity (mean age at death) models are presented in Table 4.\footnote{\textsuperscript{12} Estimates of all parameters of one model (the model that includes RX_VINTAGE2) are shown in Appendix Table A1.}

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Disease (ICD8 chapter) classification used in age at death analysis.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD8 chapter code</td>
<td>ICD chapter</td>
</tr>
<tr>
<td>000–136</td>
<td>Infective and parasitic diseases</td>
</tr>
<tr>
<td>140–239</td>
<td>Neoplasms</td>
</tr>
<tr>
<td>240–279, 520–577</td>
<td>Endocrine, nutritional and metabolic diseases + diseases of the digestive system</td>
</tr>
<tr>
<td>280–289</td>
<td>Diseases of the blood and blood-forming organs</td>
</tr>
<tr>
<td>290–315</td>
<td>Mental disorders + diseases of the nervous system and sense organs</td>
</tr>
<tr>
<td>390–458</td>
<td>Diseases of the circulatory system</td>
</tr>
<tr>
<td>460–519</td>
<td>Diseases of the respiratory system</td>
</tr>
<tr>
<td>580–629</td>
<td>Diseases of the genitourinary system</td>
</tr>
<tr>
<td>680–709</td>
<td>Diseases of the skin and subcutaneous tissue</td>
</tr>
<tr>
<td>710–738</td>
<td>Diseases of the musculoskeletal system and connective tissue</td>
</tr>
</tbody>
</table>

on longevity and pharmaceutical innovation in Turkey are shown in Table 3. The average annual number of deaths during 1999–2008 was approximately 155,000. Mean age at death increased by 4.1 years, from 63.0 to 67.1 years, and the fraction of deaths that occurred at an age greater than 75 increased from 28% to 42%.
Table 3
Summary statistics.

<table>
<thead>
<tr>
<th>Column Year</th>
<th>1 Number of deaths</th>
<th>2 Mean age at death</th>
<th>3 Fraction of deaths at age greater than 75</th>
<th>4 Mean launch year—no imputation of missing launch years</th>
<th>5 Mean launch year—missing launch years set equal to 1900</th>
<th>6 Mean launch year—missing launch years set equal to 1920</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>140.602</td>
<td>63.0</td>
<td>28%</td>
<td>1963.8</td>
<td>1958.8</td>
<td>1961.2</td>
</tr>
<tr>
<td>2000</td>
<td>138.136</td>
<td>63.1</td>
<td>28%</td>
<td>1965.1</td>
<td>1960.4</td>
<td>1962.6</td>
</tr>
<tr>
<td>2001</td>
<td>140.160</td>
<td>64.0</td>
<td>30%</td>
<td>1967.3</td>
<td>1962.8</td>
<td>1964.7</td>
</tr>
<tr>
<td>2002</td>
<td>143.567</td>
<td>65.1</td>
<td>32%</td>
<td>1967.5</td>
<td>1962.6</td>
<td>1964.7</td>
</tr>
<tr>
<td>2003</td>
<td>148.288</td>
<td>65.1</td>
<td>35%</td>
<td>1968.9</td>
<td>1963.6</td>
<td>1965.8</td>
</tr>
<tr>
<td>2004</td>
<td>161.823</td>
<td>65.2</td>
<td>36%</td>
<td>1970.5</td>
<td>1965.3</td>
<td>1967.4</td>
</tr>
<tr>
<td>2005</td>
<td>170.837</td>
<td>66.1</td>
<td>38%</td>
<td>1971.4</td>
<td>1966.5</td>
<td>1968.5</td>
</tr>
<tr>
<td>2006</td>
<td>173.353</td>
<td>66.7</td>
<td>40%</td>
<td>1972.4</td>
<td>1967.3</td>
<td>1969.3</td>
</tr>
<tr>
<td>2007</td>
<td>178.174</td>
<td>67.1</td>
<td>42%</td>
<td>1973.5</td>
<td>1968.6</td>
<td>1970.4</td>
</tr>
<tr>
<td>Change, 1999 to 2008</td>
<td>4.1</td>
<td>14%</td>
<td>9.7</td>
<td>9.8</td>
<td>9.2</td>
<td></td>
</tr>
</tbody>
</table>

Notes: Figures in columns 2–6 are weighted means of disease level data, weighted by number of deaths. The 2003 data are missing as 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.

Table 4
Estimates of drug vintage coefficients ($\beta$) from mean age at death model.

| Model | Independent variable | Estimate ($\beta$) | Empirical standard error | Z | Pr > |ΔY | ΔX | $\beta$ΔX | (Δ$\beta$)/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% |

Note: Each coefficient is from a separate model. All models include disease fixed effects and year fixed effects. Models were estimated via weighted least-squares, weighting by the number of deaths from disease $i$ in year $t$ ($N_i$DEATHS$_t$). Disturbances are clustered within diseases.

Fig. 6. Comparison of the actual increase in mean age at death to the increase that would have occurred in the absence of any increase in drug vintage. Weighted least-squares estimates of $\beta_k$ from the model of hospital discharges (Eq. (3)) are presented in Table 6. The estimates indicate that an increase in the number of molecules used to treat a disease reduces the number of hospital discharges due to the disease 3 and 4 years later. The estimated elasticity when $k = 4$ (when the Z value is largest) is −0.325: a 10% increase in the number of drugs for a disease reduces the number of hospital

imply that in the absence of any increase in drug vintage, mean age at death would have increased by only 0.6 years.

Table 5 presents the estimates of the model of %AGE,GE,75$\_t$ (Eq. (2)). As seen from the estimates, 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.
discharges due to the disease by 3.3% 4 years later. Diseases with larger increases in the cumulative number of molecules had smaller increases in the number of hospital discharges.

Weighted least-squares estimates of $\beta_k$ from the model of hospital days (Eq. (4)) are presented in Table 7, and implications of the estimates are illustrated in Fig. 7. Diseases with larger increases in the cumulative number of molecules had smaller increases in the number of hospital days. According to the model estimates, the number of hospital days increased 22% during the period 2007–2010. The estimates of indicate that in the absence of pharmaceutical innovation, the number of hospital days would have increased by 25% during this period. Hence, 3 years of pharmaceutical innovation reduced the number of hospital days in 2010 by approximately 3%. Pharmaceutical innovation reduced the number of hospital days by approximately 1% per year.

### 6. The incremental cost-effectiveness of pharmaceutical innovation in Turkey, 1999–2008

We have presented estimates of the effect of pharmaceutical innovation on age at death (Table 4), % of deaths at age ≥ 75 (Table 5) and hospital utilization (Tables 6 and 7). Now, we will use these estimates to calculate the incremental cost-effectiveness of pharmaceutical innovation, i.e., the cost per life-year gained from pharmaceutical innovation. We define the incremental cost-effectiveness ratio (ICER) as follows:

$$ICER = \frac{\text{MED\_SPEND\_LIFE}_{\text{actual}} - \text{MED\_SPEND\_LIFE}_{\text{no\_innov}}}{\text{LIFE\_EXPECT}_{\text{actual}} - \text{LIFE\_EXPECT}_{\text{no\_innov}}}$$

where

- $\text{MED\_SPEND\_LIFE}_{\text{actual}}$ = actual lifetime medical expenditure (projected based on 2008 data)
- $\text{MED\_SPEND\_LIFE}_{\text{no\_innov}}$ = estimated lifetime medical expenditure in the absence of 9 previous years of pharmaceutical innovation
- $\text{LIFE\_EXPECT}_{\text{actual}}$ = actual life expectancy (mean age at death) in 2008
- $\text{LIFE\_EXPECT}_{\text{no\_innov}}$ = estimated life expectancy (mean age at death) in the absence of 9 previous years of pharmaceutical innovation

$\text{MED\_SPEND\_LIFE}_{\text{actual}}$ and $\text{MED\_SPEND\_LIFE}_{\text{no\_innov}}$ are calculated as follows:

$$\text{MED\_SPEND\_LIFE}_{\text{actual}} = \text{MED\_SPEND\_YEAR}_{\text{actual}} \ast \text{LIFE\_EXPECT}_{\text{actual}}$$

$$\text{MED\_SPEND\_LIFE}_{\text{no\_innov}} = \text{MED\_SPEND\_YEAR}_{\text{no\_innov}} \ast \text{LIFE\_EXPECT}_{\text{no\_innov}}$$
Table 7
Estimates of drug coefficients ($\beta_i$) from hospital days model.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Empirical standard error estimates</th>
<th>95% Lower confidence limit</th>
<th>95% Upper confidence limit</th>
<th>Z</th>
<th>Pr &gt;</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_0$</td>
<td>-0.166</td>
<td>0.312</td>
<td>-0.777</td>
<td>0.445</td>
<td>-0.530</td>
<td>0.5946</td>
<td></td>
</tr>
<tr>
<td>$\beta_1$</td>
<td>-0.481</td>
<td>0.283</td>
<td>-1.037</td>
<td>0.074</td>
<td>-1.700</td>
<td>0.0893</td>
<td></td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>-0.270</td>
<td>0.205</td>
<td>-0.672</td>
<td>0.131</td>
<td>-1.320</td>
<td>0.1872</td>
<td></td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>-0.147</td>
<td>0.222</td>
<td>-0.582</td>
<td>0.288</td>
<td>-0.660</td>
<td>0.5069</td>
<td></td>
</tr>
<tr>
<td>$\beta_4$</td>
<td>-0.409</td>
<td>0.185</td>
<td>-0.771</td>
<td>-0.047</td>
<td>-2.210</td>
<td>0.0268</td>
<td></td>
</tr>
<tr>
<td>$\beta_5$</td>
<td>-0.398</td>
<td>0.137</td>
<td>-0.666</td>
<td>-0.129</td>
<td>-2.910</td>
<td>0.0037</td>
<td></td>
</tr>
<tr>
<td>$\beta_6$</td>
<td>-0.156</td>
<td>0.130</td>
<td>-0.410</td>
<td>0.098</td>
<td>-1.200</td>
<td>0.2291</td>
<td></td>
</tr>
</tbody>
</table>

Note: Each coefficient is from a separate model. All models include disease fixed effects and year fixed effects. Models were estimated via weighted least-squares, weighting by the total number of hospital days for disease i during the entire period ($\sum \text{HOSP\_DAYS}_i$). Disturbances are clustered within diseases. Estimates shown in bold are statistically significant (p-value ≤ 0.05).

Fig. 7. Hospital days, 2007–2010: actual vs. in the absence of pharmaceutical innovation (index 2007: 1.00).

where

\[
\text{MED\_SPEND\_YEAR}_{\text{Actual}} = \text{actual (annual) per capita medical expenditure in 2008}
\]

\[
\text{MED\_SPEND\_YEAR}_{\text{estimated}} = \text{estimated per capita annual medical expenditure in 2008 in the absence of 9 previous years of pharmaceutical innovation}
\]

\[
\Delta \text{MED\_SPEND\_YEAR} = \text{annual per capita medical expenditure in 2008 attributable to 9 previous years of pharmaceutical innovation}
\]

The 2008 actual expenditure values (expressed in USD PPP) were obtained from OECD [24]. According to the OECD data, actual (annual) per capita health expenditure in 2008 in Turkey (MED\_SPEND\_YEAR\_actual) was $906. As shown in Table 8, between 1999 and 2008, real per capita drug expenditure increased by $104. In this analysis, we assume that all of that increase was due to pharmaceutical innovation during 1999–2008. This assumption is very conservative, as some of the $104 increase in real per capita drug expenditure was probably due to other factors.

Table 9 shows a baseline calculation of the ICER. Column 1 shows the actual value of life expectancy (mean age at death) in 2009 (67.1 years) and the estimated value (64.1 years, derived from model 2 in Table 4) if no pharmaceutical innovation had occurred from 1999 to 2008. We estimate that life expectancy would have been 3.0 years lower in 2008 in the absence of pharmaceutical innovation.

The hospitalization results indicated that pharmaceutical innovation during the study period reduced hospital expenditures in 2008 by approximately 9%. Unfortunately, the share of hospital expenditure in total health expenditures data is only available for the year 2000. According to the available figures, hospital expenditures accounted for approximately 20% of total health expenditures in 2000 (source: OECD health data). This indicates that pharmaceutical innovation during 1999–2008 may have reduced per capita hospital expenditures in 2008 by approximately $16 (9% * 20% * $906); at least 16% of the increase in drug expenditure was offset by a reduction in hospital expenditure. We estimated that in the absence of 9 previous years of pharmaceutical innovation, per capita medical expenditure in 2008 would have been no less than $818 ($906 – 104 + 16).

As shown in Table 9, these calculations imply that the cost per life-year gained was $2776. If the difference in life expectancy is half as large as that estimated from model
Table 8
Prescription drug (Rx) expenditure, Turkey, 1999–2010.

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

Source: IMS MIDAS database; BLS.

Table 9

<table>
<thead>
<tr>
<th>Column</th>
<th>(1)</th>
<th>(2)</th>
<th>(3)= (1)* (2)</th>
<th>ICER ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual value in 2008</td>
<td>Life expectancy (mean age at death) 66.6</td>
<td>Annual per capita health expenditure (USD) $33</td>
<td>Lifetime per capita health expenditure (USD) $2776</td>
<td>$2.776</td>
</tr>
<tr>
<td>Estimated value in 2008 in the absence of 9 previous years of pharmaceutical innovation</td>
<td>64.1</td>
<td>$818</td>
<td>$52.471</td>
<td>$2.776</td>
</tr>
<tr>
<td>Difference</td>
<td>3.0</td>
<td>$88</td>
<td>$8.327</td>
<td>$2.776</td>
</tr>
</tbody>
</table>

* Estimated from model 2.

Assuming that the entire 1999–2008 increase in real per capita pharmaceutical expenditure was due to the use of newer drugs.

2–1.5 years instead of 3 years—the cost per life-year gained was $4808. Aldy and Viscusi [25] estimated that, in the U.S., the average value of (willingness to pay for) a life-year is $300,000.

7. Summary and conclusions

This study has investigated the impact of pharmaceutical innovation on longevity, hospitalization and medical expenditure in Turkey during the period 1999–2010 using longitudinal, disease-level data. The measures of longevity were 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 data from other countries (e.g., France and Sweden) indicate that these effects are quite modest in practice: almost all of the increase in mean age at death was due to within-disease increases rather than a shift in the distribution of causes of death.

From 1999 to 2008, mean age at death increased by 3.6 years, from 63.0 to 66.6 years. We estimated that in the absence of any pharmaceutical innovation, mean age at death would have increased by only 0.6 years. Hence, pharmaceutical innovation was estimated to have increased mean age at death in Turkey by 3.0 years during the period 1999–2008. This finding is consistent with the finding from a previous study of 30 developing and high-income countries [1] that pharmaceutical innovation accounted for almost three-fourths of longevity growth. However, as shown in Table 10, our estimates of the marginal effect of drug vintage on mean age at death in Turkey (Table 4) are larger than estimates of the marginal effect of drug vintage on mean age at death or life expectancy at birth in four previous studies. Future research should attempt to determine the reason for this differential.

We also examined the effect of pharmaceutical innovation on hospital utilization. The estimates indicated that an increase in the number of molecules used to treat a disease reduces the number of hospital days due to the disease 3–4 years later. We estimated that pharmaceutical innovation has reduced the number of hospital days by approximately 1% per year.

We used our estimates of the effect of pharmaceutical innovation on age at death, hospital utilization and pharmaceutical expenditure to assess the incremental cost-effectiveness of pharmaceutical innovation, i.e., the cost per life-year gained from the introduction of new drugs. The 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 would be $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.

This study is subject to several limitations. One limitation is that the longevity analysis is based on incomplete mortality data. Data on cause of death and age at death are available for only about 44% of the deaths that occurred in Turkey during the sample period.14 Because in Turkey,
a partially functioning vital registration system in urban areas yields fragmentary evidence on levels and causes of mortality” [30]. A second limitation is our inability to measure potential determinants of longevity and hospitalization other than pharmaceutical innovation, although other factors may not be correlated across diseases with pharmaceutical innovation, and some previous research has found little or no correlation between longevity growth and factors such as income, education, unemployment, and public and private health expenditure. A third limitation is our inability to estimate distributed time lag models due to the relatively short time series data available to us.

As shown in Fig. 8, the number of new chemical entity (NCE) launches in Turkey has declined substantially in recent years: the mean number during 2011–2012 (12.5) was less than half of the mean number during 1999–2003 (26.6). Our findings suggest that, as a result, Turkish longevity will increase much more slowly in the next decade than it has in the previous decade.

The U.S. Congressional Budget Office [26] has stated that “the largest single factor driving [healthcare] spending growth [is] the greatly expanded capabilities of medicine brought about by technological advances in medical science over the past several decades.” As noted by the Australian Productivity Commission [27], even if advances in medical technology drive increased healthcare expenditure, the critical question is whether the benefits outweigh the costs. In other markets, increased expenditure generally would indicate increased consumer benefits. But because the direct purchase of healthcare is mostly undertaken by third parties—governments and private health insurers—normal market tests for ensuring value for money generally do not apply. Although assessing the benefits of medical innovation—its impact on health outcomes—is as important as assessing the costs—its impact on health expenditure—the Commission noted that “most formal studies...have focused on the expenditure impacts of medical technology, partly because costs are more easily identified and quantified than are benefits.” Our findings suggest that when policymakers

Table 10
Estimates of the marginal effect of drug vintage on longevity (ΔLONGEVITY/ΔLAUNCH_YEAR) from four previous studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Period</th>
<th>Longevity measure</th>
<th>Methodology</th>
<th>ΔLONGEVITY/ΔLAUNCH_YEAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>[31]</td>
<td>Australia</td>
<td>1995–2003</td>
<td>Mean age at death</td>
<td>Longitudinal disease-level</td>
<td>0.182</td>
</tr>
<tr>
<td>[29]</td>
<td>USA</td>
<td>1991–2004</td>
<td>Life expectancy at birth</td>
<td>Longitudinal state-level</td>
<td>0.135</td>
</tr>
<tr>
<td>[28]</td>
<td>Germany</td>
<td>2001–2007</td>
<td>Life expectancy at birth</td>
<td>Longitudinal state-level</td>
<td>0.208</td>
</tr>
<tr>
<td>[1]</td>
<td>30 developing and high-income countries</td>
<td>2000–2009</td>
<td>Life expectancy at birth</td>
<td>Longitudinal country-level</td>
<td>0.121</td>
</tr>
</tbody>
</table>

Fig. 8. Number of NCE launches, Turkey, 1990–2012.

http://en.wikipedia.org/wiki/Demographics_of_Turkey. As shown in Table 3, our age-at-death estimates are based on data on about 170,000 deaths per year.
make reimbursement and coverage decisions, they should properly account for the benefits as well as the costs of medical innovations.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.healthpol.2014.06.002.

References


[22] IMS Health MIDAS database.


