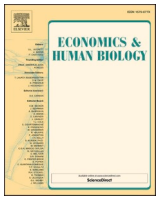
Economics and Human Biology 46 (2022) 101124

Contents lists available at ScienceDirect

Economics and Human Biology

journal homepage: www.elsevier.com/locate/ehb



The effect of pharmaceutical innovation on longevity: Evidence from the U. S. and 26 high-income countries

Frank R. Lichtenberg

Cain Brothers & Company Professor of Healthcare Management, Columbia University, Kravis Hall 522, 665 West 130th Street, New York, NY 10027, USA

ARTICLE INFO

Keywords:
Pharmaceutical
Innovation
Longevity
Life expectancy

ABSTRACT

This study examines the impact that pharmaceutical innovation, which accounts for most private biomedical research expenditure, has had on longevity. We perform two types of two-way fixed-effects analyses, which control for the effects of many potentially confounding variables. First, we analyze long-run (2006–2018) *changes* in longevity associated with different diseases in a single country: the U.S. Then, we analyze relative longevity *levels* associated with different diseases in 26 high-income countries during a single time period (2006–2016). The measure of longevity we analyze, mean age at time of death, is strongly positively correlated across countries with life expectancy at birth. The measure of pharmaceutical innovation we use is the mean vintage (year of initial world launch) of the drugs used to treat each disease in each country. Changes in the vintage distribution of drugs are due to both entry of new drugs and exit of old drugs. Our analysis of U.S. data indicates that the diseases for which there were larger increases in drug vintage tended to have larger increases in the longevity of Americans of all races and both sexes. In other words, the lower the mean age of the drugs, the higher the mean age at death. We test, and are unable to reject, the "parallel trends" hypothesis. We estimate that the 2006–2018 increase in drug vintage increased the mean age at death of Americans by about 6 months (66% of the observed increase). Controlling for sex, race, and education has only a small effect on the estimate of the vintage coefficient. The estimates indicate that drug vintage did not have a significant effect on the mean age at death of decedents with less than 9 years of education. Drug vintage had a positive and significant effect on the mean age at death of decedents with at least 9 years of education, and a larger effect on the mean age at death of decedents with at least 13 years of education. The finding that pharmaceutical innovation has a larger effect on the longevity of people with more education is consistent with previous evidence that more educated people are more likely to use newer drugs. Our analysis of data on 26 high-income countries indicates that the higher the vintage of drugs available to treat a disease in a country, the higher mean age at death was, controlling for fixed disease and country effects. The increase in drug vintage is estimated to have increased mean age at death in the 26 countries by 1.23 years between 2006 and 2016—73% of the observed increase. We obtain estimates of the cost of pharmaceutical innovation—its impact on drug expenditure—as well as estimates of an important benefit of pharmaceutical innovation—the number of life-years gained from it—and of their ratio, i.e., the incremental cost-effectiveness ratio. Estimates of the cost per life-year gained for the U.S. and the 26 countries are $35,817 and $13,904, respectively. Both figures are well below per capita GDP in the respective regions, suggesting that, overall, pharmaceutical innovation was highly cost-effective.

1. Introduction

Longevity increase is a very important part of economic growth, broadly defined. Nordhaus (2005) argued that "improvements in health status have been a major contributor to economic welfare over the twentieth century. To a first approximation, the economic value of increases in longevity in the last hundred years is about as large as the value of measured growth in non-health goods and services." Murphy and Topel (2006) estimated that cumulative gains in life expectancy after 1900 were worth over $1.2 million to the representative American in 2000, whereas post-1970 gains added about $3.2 trillion per year to national wealth, equal to about half of GDP. The United Nations' Human Development Index, which is used to rank countries into four tiers of human development, is a composite statistic of life expectancy, income per capita, and education (United Nations Development Program, 2022).

There is a consensus among macroeconomists that technological progress is the principal source of GDP growth. Romer, (1990) (p. S71) argued that "growth…is driven by technological change that arises from intentional investment decisions made by profit-maximizing agents."

https://doi.org/10.1016/j.ehb.2022.101124
Received 2 September 2021; Received in revised form 30 December 2021; Accepted 11 March 2022
Available online 19 March 2022

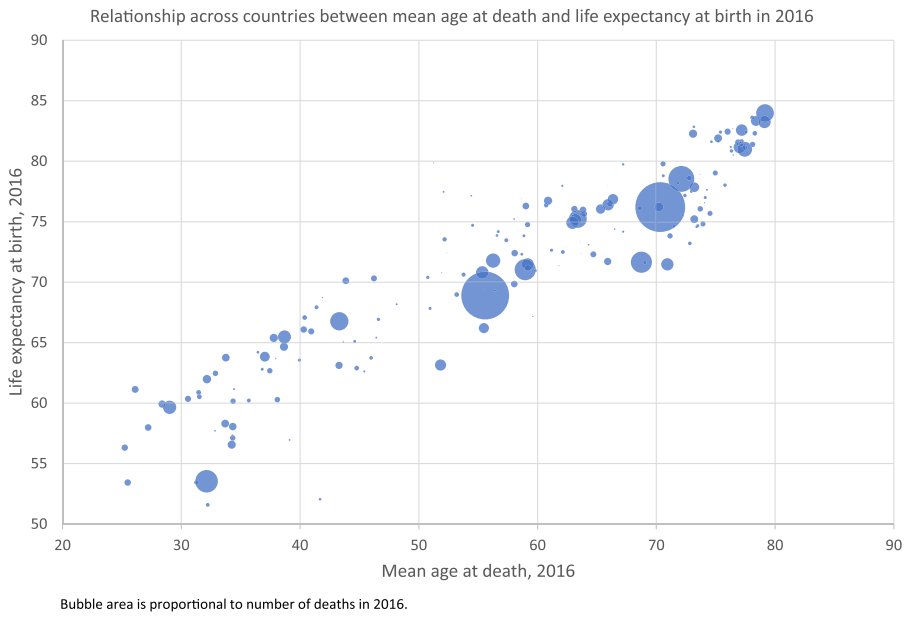


Fig. 1. Relationship across countries between mean age at death and life expectancy at birth in 2016.

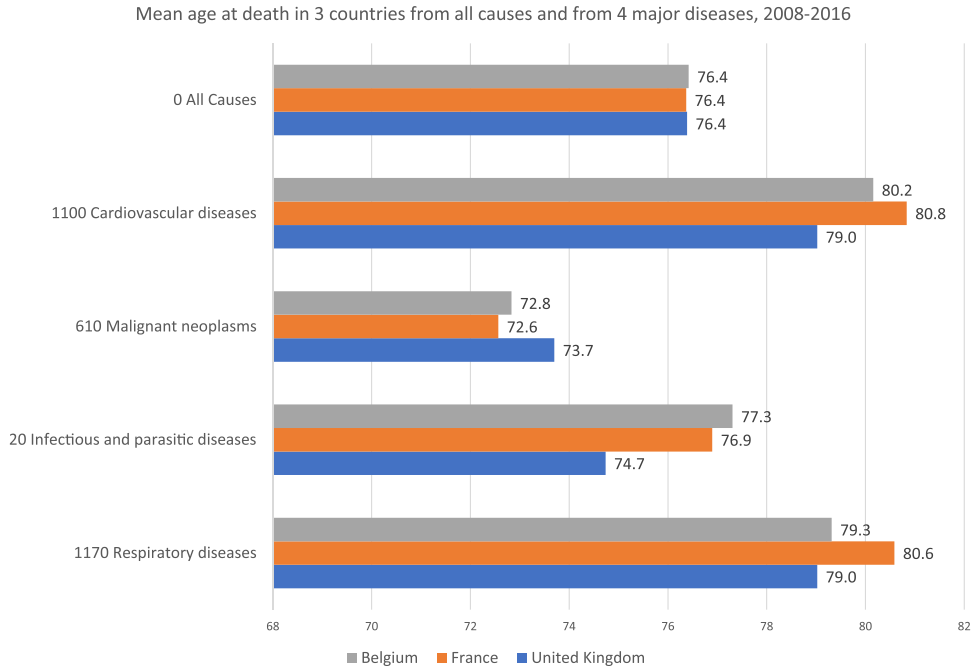


Fig. 2. Mean age at death in 3 countries from all causes and from 4 major diseases, 2008–2016.

Jones (2002) argued that "long-run growth is driven by the discovery of new ideas throughout the world." Aghion and Howitt (2005) said that "technological progress, the mainspring of long-run economic growth, comes from innovations that generate new products, processes and markets. Innovations in turn are the result of deliberate research and development activities that arise in the course of market competition." Grossman and Helpman (1991) developed "a model of repeated product improvements in a continuum of sectors. Each product follows a stochastic progression up a quality ladder." Bresnahan and Gordon (1997) said that "new goods are at the heart of economic progress." As noted by Jovanovic and Yatsenko (2012), in "the Spence–Dixit–Stiglitz tradition…new goods [are] of higher quality than old goods." And Chien (2015) said that 'it has been shown, both theoretically and empirically, that technological progress is the main driver of long-run growth.'.

This study will examine the impact that pharmaceutical innovation, which accounts for most private biomedical research expenditure, had on longevity.[1] We will perform two types of two-way fixed-effects analyses. First, we will analyze long-run (2006–2018) *changes* in longevity associated with different diseases in a single country: the U.S. (We will analyze changes in longevity by sex, race and education.) de de de Chaisemartin and D'Haultfœuille (2020) demonstrated that the validity of the standard two-way fixed-effects model relies on the assumption of "parallel trends," and on the assumption that the treatment effect is constant across units and time periods. Therefore, in addition to

[1] According to Dorsey et al. (2010), 88% of private U.S. funding for biomedical research came from pharmaceutical and biotechnology firms.

estimating the standard model using longitudinal U.S. data, we will estimate the alternative model they developed, which does not rely on the constant treatment effect assumption, and allows us to test the parallel trends assumption by generating "placebo estimators."

Second, we will analyze relative longevity *levels* associated with different diseases in 26 high-income countries during a single time period (2006–2016). Since that analysis is cross-sectional, rather than longitudinal, it is not subject to the potential problem afflicting many difference-in-differences models: violation of the "parallel trends" assumption.

Life expectancy at birth, calculated from age-specific death rates using life table methods, is undoubtedly the best-known measure of longevity. The measure of longevity we will analyze is mean age at time of death.[2] As shown in Fig. 1, these two measures are strongly positively correlated across countries. Mean age at death can be calculated for specific diseases (causes of death), but life expectancy cannot.[3] Also, mean age at death is less likely to be subject to "competing risks" than other disease-specific measures of longevity or mortality, e.g., potential years of life lost.

According to Robine (2018), "age at death provides unique information that is becoming increasingly important as we are experiencing the longevity revolution" and that "interest in the average age at death as a natural indicator of typical longevity has continued to grow. The most recent and the most innovative approaches focus on differences in the distribution of ages at death between occupational categories or causes of death."

Fig. 2 shows data on mean age at death from all causes and from four major diseases in Belgium, France, and the United Kingdom during 2008–2016. Mean age at death from all causes was virtually identical in the three countries: 76.4 years. But mean age at death from cardiovascular and respiratory diseases was at least 1.6 years higher in France than it was in the U.K., and mean age at death from malignant neoplasms was 1.1 years higher in the U.K. than it was in France. We hypothesize that international differences in relative longevity like these may be related to international differences in relative access to pharmaceutical innovations.[4]

The measure of pharmaceutical innovation we will use is the mean *vintage* (year of initial world launch) of the drugs for the treatment of disease d that have previously been launched in country c. In 1987, the Royal Swedish Academy of Sciences (1987) awarded the Alfred Nobel Memorial Prize in Economic Sciences to Robert Solow for his contributions to the theory of economic growth. The Academy cited Solow's (1960) article, *Investment and Technical Progress,* in which he presented a.

new method of studying the role played by capital formation in economic growth. His basic assumption was that technical progress is "built into" machines and other capital goods and that this must be taken into account when making empirical measurements of the role played by capital. This idea then gave birth to the "vintage approach" (a similar idea was discussed by Leif Johansen in Norway at about the same time) …The most important aspect of Solow's article was not so much the empirical outcome, but the method of analyzing "vintage capital." Nowadays, the vintage capital concept has many other applications and is no longer solely employed in analyses of the factors underlying economic growth…The vintage approach has proved invaluable, both from the theoretical point of view and in applications such as the analysis of the development of industrial structures.

Three decades later, Boucekkine et al. (2018) cited the "increasingly common view that some fundamental economic growth issues (like technology diffusion, for example) do require the vintage structure to be better appraised…much work is needed to bring the vintage models closer to the data."

In the next section, we describe our econometric models of mean age at death. Data sources and descriptive statistics are discussed in section III. Empirical results are presented in section IV, and their implications are considered in section V. The final section provides a summary and conclusions.

2. Econometric models

2.1. Model of U.S. longevity growth, 2006–2018

To assess the effect of pharmaceutical innovation on U.S. longevity growth, we will estimate the following 2-way fixed-effects model:

$$age\_death_{sredt} = \beta\ rx\_vintage_{dt} + \sigma_s + \theta_r + \phi_e + \alpha_d + \gamma_t + \varepsilon_{sredt} \quad (1)$$

where.

age_death_{sredt}	= mean age at death of decedents of sex s and race r and education e from disease d in year t (t = 2006, 2018)
$rx\_vintage_{dt}$	= the mean vintage (initial world launch year) of molecules used to treat disease d that were sold in the U.S. in year t = ($\sum_m sold_{mt}$ * $treat_{md}$ * $vintage_m$) / ($\sum_m sold_{mc}$ * $treat_{md}$)
$sold_{mt}$	= 1 if molecule m was sold in the U.S. in year t; = 0 otherwise
$treat_{md}$	= 1 if molecule m is used to treat disease d; = 0 otherwise
$vintage_m$	= the initial world launch year of molecule m
n_deaths_{sredt}	= the number of deaths of decedents of race r and education e caused by disease d in the U.S. in year t
σ_s	= a fixed effect for sex s (s = female, male)
θ_r	= a fixed effect for race r (r = White, Black, American Indian, Asian/Pacific Islander)
ϕ_e	= a fixed effect for education e (e = 00–08 years, 09–12 years, 13 + years)
α_d	= a fixed effect for disease d
γ_t	= a fixed effect for year t

Eq. (1) will be estimated by weighted least-squares, weighting by n_deaths_{sredt}. The disturbances of Eq. (1) will be clustered by disease. The fixed disease effects control for disease characteristics (e. g. severity) that are constant or that change slowly. The year fixed effects control for macroeconomic variables (e. g. per capita incomeand access to health care) that are common or similar across diseases. In addition to estimating Eq. (1), which controls for sex, race and education, we will estimate separate models for each sex, race and education group.

The mean age of drugs available to treat disease d in year t may be defined as $rx\_age_{dt} = (t - rx\_vintage_{dt})$. The hypothesis that $\beta > 0$ therefore implies that age_death is inversely related to rx_age: the lower the mean age of the drugs, the higher the mean age at death, ceteris paribus.

Due to data limitations, our measure of drug vintage gives equal weight to the vintages of all molecules that were sold in the U.S. in year t that could have been used to treat disease d. We would prefer to use the following (weighted) measure of drug vintage: ($\sum_m n\_rx_{mdt}$ * $vintage_m$) / ($\sum_m n\_rx_{mdt}$), where n_rx_{mdt} = the number of units of (or prescriptions for) molecule m sold in the U.S. in year t that were used to treat disease d. Although we have data on the total utilization of each molecule in each year ($n\_rx_{mt} = \sum_d n\_rx_{mdt}$), many molecules are used to treat

[2] CDC officials (Brown et al., 2009) published data on mean age at death from COPD in the United States during 1980–2005. State of New Jersey Department of Health (2021) publishes data on mean age at death from 10 leading causes, and says that "average age at death can be used as an easier-to-calculate proxy for life expectancy."

[3] An indicator called "potential gain in life expectancy" (PGLE), constructed using multiple-decrement life table techniques, was developed to estimate the added years of life expectancy for the population if the deaths from a specific cause were reduced or eliminated as a competing cause of death. But Lichtenberg (2020) demonstrated that estimates of PGLE may be unreliable.

[4] International differences in relative access to pharmaceutical innovations may be due, in part, to international differences in pricing and reimbursement policies.

multiple diseases,[5] and we lack data on n_rx_{mdt}. Inclusion in Eq. (1) of an unweighted rather than a weighted measure of drug vintage may result in measurement error, which would be likely to bias estimates of β towards zero.[6]

Changes in the vintage distribution of drugs are due to both entry of new drugs and exit of old drugs. 327 drugs sold in the U.S. in 2018 had not been sold in 2006. 150 drugs sold in 2006 were no longer sold in 2018.[7] 1148 drugs were sold in both years.

2.2. Model of the level of longevity in 26 high-income countries

To assess the effect of pharmaceutical innovation on the level of longevity in 26 high-income countries, we will estimate several versions of the following 2-way fixed-effects model:

$$age\_death_{sdc} = \beta\ rx\_vintage_{dc} + \sigma_s + \alpha_d + \gamma_c + \varepsilon_{sdc} \quad (2)$$

where.

age_death_{sdc}	= mean age at death of decedents of sex s from disease d in country c during 2006–2016
$rx\_vintage_{dc}$	= the mean vintage (initial world launch year) of molecules used to treat disease d that were sold in country c during 2006–2016 = ($\sum_m sold_{mc} * treat_{md} * vintage_m$) / ($\sum_m sold_{mc} * treat_{md}$)
$sold_{mc}$	= 1 if molecule m was sold in country c during 2006–2016; = 0 otherwise
n_deaths_{sdc}	= the number of deaths of decedents of sex s caused by disease d in country c during 2006–2016
σ_s	= a fixed effect for sex s (s = female, male)
α_d	= a fixed effect for disease d
γ_c	= a fixed effect for country c

Eq. (2) will be estimated by weighted least-squares, weighting by n_deaths_{sdc}. The disturbances of Eq. (2) will be clustered by disease. The fixed disease effects control for disease characteristics (e. g. severity) that are common or similar across countries. The country fixed effects control for country characteristics (e. g. per capita income, educational attainment, and access to health care) that are common or similar across diseases.

2.3. The effect of pharmaceutical innovation on drug expenditure

Estimates of Eqs. (1) and (2) will enable us to estimate an important *benefit* of pharmaceutical innovation: the number of life-years gained from it. It is also worthwhile to estimate the *cost* of pharmaceutical innovation: its impact on drug expenditure. The ratio of the estimate of the effect of vintage on drug expenditure to the estimate of its effect on the number of life-years is an estimate of the *incremental cost-effectiveness ratio (ICER)*[8]:

$$\text{ICER} = \frac{\Delta\ \text{drug\_expenditure}/\Delta\text{vintage}}{\Delta\ \text{life} - \text{years}/\Delta\text{vintage}} = \frac{\Delta\ \text{drug\_expenditure}}{\Delta\ \text{life} - \text{years}}$$

To assess the effect that pharmaceutical innovation had on drug expenditure in the U.S., we will analyze the correlation across *drug classes* between the 2006–2018 changes in drug vintage and drug expenditure, by estimating the following model:

$$\ln(drug\_expend_{pt}) = \eta\ vintage_{pt} + \alpha_p + \delta_t + \varepsilon_{pt} \quad (3)$$

where.

$drug\_expend_{pt}$= U.S. drug expenditure on drug class (WHO ATC3 pharmacological subgroup) p[9] in year t (t = 2007, 2017).

$vintage_{pt}$= weighted mean vintage of standard units of chemical substances in drug class p sold in the U.S. in year t.

α_p = a fixed effect for drug class p.

δ_t = a fixed effect for year t.

Eq. (3) will be estimated by weighted least-squares, weighting by total expenditure on drug class p during the period 2007–2017. Disturbances will be clustered by drug class.

To assess the effect that pharmaceutical innovation had on drug expenditure in 19 high-income countries, we will analyze the correlation across *countries* between the 2006–2016 changes in drug vintage and drug expenditure, by estimating the following model:

$$\ln(drug\_expend_{ct}) = \eta\ vintage_{ct} + \alpha_c + \delta_t + \varepsilon_{ct} \quad (4)$$

where.

$drug\_expend_{ct}$= drug expenditure in country c in year t (t = 2006, 2016).

$vintage_{ct}$= weighted mean vintage of standard units of chemical substances sold in country c in year t.

α_c= a fixed effect for country c.

δ_t = a fixed effect for year t.

Eq. (4) will be estimated by weighted least-squares, weighting by total drug expenditure in country c during the period 2006–2016. Disturbances will be clustered by country.

3. Data sources and descriptive statistics

3.1. Pharmaceutical data were obtained from four sources

- Annual data on the availability of molecules in each of 26 countries during 2006–2018 ($sold_{mc}$) were obtained from the IQVIA MIDAS database. The dataset contains information about 3173 molecules.
- Data on the vintage (initial world launch year ($vintage_m$)) of 1993 of those molecules were obtained from the DrugCentral (2021) Online Drug Compendium (DrugCentral, 2021).[10]
- Data on the diseases that each molecule is used to treat ($treat_{md}$) were obtained from the Thériaque database (Centre National Hospitalier d'Information sur le Médicament, 2021).
- Data on per capita expenditure (in U.S. dollars) on prescription drugs, by country and year, were obtained from the OECD Health Statistics 2021 database (OECD, 2021).

U.S. mortality data were obtained from 2006 and 2018 Vital Statistics NCHS Multiple Cause of Death Data files distributed by the National

[5] 48% of molecules have at least 2 indications (WHO Global Health Estimates causes), 23% have at least 3 indications, and 14% have at least 4 indications.

[6] Although we cannot compute utilization-weighted vintage by *disease* and year, we can compute utilization-weighted (and unweighted) vintage by *country* and year for 41 countries. Both the 2017 levels of, and long-run (2007–2017) changes in, weighted and unweighted vintage are significantly positively correlated across countries. The estimate of β in the regression $vintage\_weighted_{c,2017} = \alpha + \beta\ vintage\_unweighted_{c,2017} + \varepsilon$, where the c subscript denotes country c, is 1.01 (std. err. = 0.26; t value = 3.86; p-value = 0.0004). The estimate of β in the regression $vintage\_weighted_{ct} = \beta\ vintage\_unweighted_{ct} + \alpha_c + \delta_t + \varepsilon_{ct}$, for t = (2007, 2017), is 0.65 (std. err. = 0.22; Z value = 2.99; p-value = 0.0027).

[7] Our data cover prescription (Rx) drugs, not over-the-counter (OTC) drugs. A small number of drugs may have been converted from Rx to OTC.

[8] See U.S. Department of Veterans Affairs Health Economics Resource Center (2021).

[9] There are 179 WHO ATC3 pharmacological subgroups. See World Health Organization (2021c).

[10] The vintage of 88% of the 1676 molecules sold in the U.S. in 2018 could be determined. Those molecules accounted for 72% of standard units sold in the U. S. in 2018 and 78% of total expenditure.

Table 1
U.S. mortality and drug vintage in 2006 and 2018.

row		No. of deaths			Mean age at death			Mean vintage		
		2006	2018	% change	2006	2018	change	2006	2018	change
1	All	2,083,376	2,5,10,031	20.5%	74.3	75.1	0.8	1980.5	1983.8	3.3
	By sex									
2	Female	1,0,76,633	1,2,50,789	16.2%	77.2	77.7	0.5	1980.5	1983.8	3.3
3	Male	1,0,06,743	1,2,59,242	25.1%	71.3	72.5	1.3	1980.5	1983.9	3.4
	By race									
4	White	1,801,222	2,125,088	18.0%	75.4	76.1	0.7	1980.4	1983.8	3.3
5	Black	232,414	299,933	29.1%	66.5	68.7	2.2	1980.8	1983.8	3.0
6	American Indian	11,139	17,153	54.0%	64.4	65.7	1.3	1980.4	1983.7	3.3
7	Asian or Pacific Islander	38,601	67,857	75.8%	71.4	74.5	3.0	1980.7	1984.4	3.7
	By education									
8	00–08 years	354,114	251,178	-29.1%	75.2	74.7	-0.5	1980.0	1983.2	3.2
9	09–12 years	1,139,695	1,341,873	17.7%	74.3	75.1	0.8	1980.6	1983.7	3.2
10	13 + years	589,567	916,980	55.5%	73.7	75.1	1.4	1980.6	1984.1	3.5

These figures are based on diseases for which both mortality data and drug vintage data are available. Those diseases accounted for 88% of deaths in 2018. Mean vintage figures are weighted by the number of deaths.

Bureau of Economic Research (2021). These data files contain one record for each death. They enable calculation of the number of deaths, by race, education group,[11] cause and single year of age. We use the World Health Organization Global Health Estimates cause of death classification shown in Annex Table A of World Health Organization (2021a). Deaths from external causes are excluded.[12]

Appendix Table 1 presents data on U.S. mortality and drug vintage in 2006 and 2018, by WHO Global Health Estimates cause of death. Between 2006 and 2018, the number of deaths increased by 20.7%, from 2.21 million to 2.67 million, and mean age at death increased by 0.9 years, from 73.0 to 73.9. The number of deaths from opioid use disorders (cause 871), alcohol use disorders (cause 860), and self-harm (cause 1610) increased much more: by 117%, 67%, and 49%, respectively. Since the mean age at death from these causes (40.3, 53.3, and 46.0 in 2006, respectively) is much lower than the mean age at death from other causes, the substantial increase in the number of "deaths of despair" (Case and Deaton, 2020) reduced the overall increase in mean age at death.

Table 1 presents aggregate data on U.S. mortality and drug vintage in 2006 and 2018, based on diseases for which both mortality data and drug vintage data are available. Those diseases accounted for 88% of deaths in 2018. Mean vintage figures are weighted by the number of deaths. As shown in row 1, mean age at death increased by 0.8 years.[13] The mean vintage of drugs increased by 3.3 years, from 1980.5 to 1983.8. Rows 2–3 show data on U.S. mortality and drug vintage, by sex.

Table 2
Mortality and drug vintage data for 26 high-income countries during the entire 2006–2016 period.

	No. of deaths	Mean age at death	Mean vintage
All	94,826,064	77.3	1982.4
By sex			
Female	47,524,246	80.1	1982.3
Male	47,301,818	74.5	1982.5
By country			
Australia	1,675,184	78.6	1982.7
Austria	962,360	78.9	1982.9
Belgium	968,982	78.4	1981.7
Canada	3,065,596	76.6	1982.1
Croatia	561,656	75.8	1982.0
Czech Republic	1,348,186	76.1	1982.3
Finland	590,186	77.4	1983.5
France	4,722,040	78.5	1982.7
Germany	10,857,653	78.4	1982.3
Hungary	1,647,005	74.2	1982.3
Ireland	229,974	76.9	1982.5
Italy	6,386,406	80.1	1983.0
Japan	13,196,208	79.7	1981.4
Korea, Republic of	2,782,974	73.3	1983.1
New Zealand	292,122	77.3	1980.9
Norway	380,592	79.8	1982.0
Poland	4,175,543	74.1	1981.1
Portugal	1,060,221	78.0	1982.7
Romania	2,871,368	73.6	1982.3
Saudi Arabia	34,434	51.9	1980.1
Singapore	123,187	73.9	1982.1
Slovakia	377,465	73.5	1982.7
Spain	4,153,981	79.3	1982.9
Switzerland	649,001	80.0	1982.6
United Kingdom	5,586,951	78.2	1982.7
United States	26,126,789	75.8	1982.8

These figures are based on diseases for which both mortality data and drug vintage data are available. Mean vintage figures are weighted by the number of deaths.

[11] Different detailed education classifications were used in 2006 and 2018. Both classifications allowed us to group education into 3 broad categories: 00–08 years, 09–12 years, 13 + years.

[12] An external cause of death, as mentioned in chapter XX of the WHO's ICD-10, is a death due to accidents and violence including environmental events, circumstances and conditions as the cause of injury, poisoning, and other adverse effects. In 2017, 9% of U.S. deaths were due to external causes (U.S. Centers for Disease Control and Prevention, 2019).

[13] There has been almost no growth in median income during this period, and there have been sharp increases in obesity and "deaths of despair." Between 1999 and 2017, real median household income increased by only 1.8%, from $61,526 to $62,626 (Federal Reserve Bank of St. Louis, 2021). Between 1999 and 2000 and 2015–2016, the prevalence of obesity increased from 30.5% to 39.6% among adults, and from 13.9% to 18.5% among youths aged 2–19 years (Hales et al., 2017). Obesity-related conditions, including heart disease, stroke, type 2 diabetes and certain types of cancer, are some of the leading causes of preventable, premature death (Centers for Disease Control and Prevention, 2020). The number of opioid-related deaths in the United States increased by 345% between 2001 and 2016 (Gomes et al., 2018).

Table 3
Weighted (by number of standard units sold) mean vintage of drugs sold in the U.S. and in 26 high-income countries, by year, 2006–2018.

year	U.S.	26 countries
2006	1978.7	1978.5
2007	1978.8	1978.8
2008	1978.9	1979.1
2009	1979.2	1979.4
2010	1979.8	1979.9
2011	1980.0	1980.3
2012	1980.5	1980.6
2013	1980.8	1981.0
2014	1981.0	1981.1
2015	1981.1	1981.4
2016	1981.3	1981.7
2017	1981.7	1981.9
2018	1981.8	1982.1
change, 2006–2018	3.2	3.5

The number of male deaths increased much more than the number of female deaths: 25.1% vs. 16.2%.[14] Rows 4–7 show data on U.S. mortality and drug vintage, by race. In 2006, mean age at death of whites was 4–11 years higher than mean ages at death of other races. But during the next 12 years, the mean ages at death of other races increased much more than the mean age at death of whites. Rows 8–10 show data on U.S. mortality and drug vintage, by educational attainment of the decedent. The mean age at death in 2006 was highest for the least educated decedents and lowest for the most educated decedents. Since there is considerable evidence that education increases longevity, this finding might seem quite surprising. However, we think that there is a simple explanation for it. By definition, birth_year = 2006 – age_death_2006, where birth_year denotes year of birth and age_death_2006 denotes the age at death of a 2006 decedent. People who died at a higher age in 2006 were born in an earlier year. People born in earlier years tended to receive less education (Bauman, 2016). The negative correlation between education and mean age at death is therefore undoubtedly due to "reverse causality," from birth year to educational attainment.

Between 2006 and 2018, the mean age at death of decedents with less than a high school education (0–8 years) declined by 6 months, whereas the mean age at death of decedents with more than a high school education (13 + years) increased by 1.4 years. Due to increasing educational attainment, the number of decedents with less than a high school education declined by 29%, whereas the number of decedents with more than a high school education increased by 56%.

International mortality data were obtained from the WHO Mortality Database (World Health Organization, 2021b). Once again, we use the World Health Organization Global Health Estimates cause of death classification. In that dataset, deaths are grouped into the following age categories: 0 years, 1 year, 2 years, 3 years, 4 years, 5–9 years, 10–14 years, …, 85–89 years, 90–94 years, and 95years and over. We assumed that deaths in all but the highest category occurred at the midpoint of the category (e.g. deaths in the 75–79 years category occurred at age 77.5), and that deaths in the 95 years and over category occurred at age 97.5.

Table 2 presents data on age at death and weighted mean drug vintage, by country, during the entire 2006–2016 period. Table 3 presents data on the weighted (by number of standard units sold) mean vintage of drugs sold in the U.S. and in 26 high-income countries, by year, 2006–2018.

[14] Data from the CDC's Multiple Cause of Death website (U.S. Centers for Disease Control and Prevention, 2021) also indicate that the number of male deaths increased much more between 2006 and 2018 than the number of female deaths: 21.3% vs. 12.8%.

Table 4
Estimates of models of U.S. mean age at death, 2006–2018 (Eq. (1)).

Column	1	2	3	4
disease fixed effects included?	**no**	**yes**	**yes**	**yes**
Parameter				
year 2006	-0.796	-0.3581	0.2508	-0.3183
std. err.	0.3045	0.2168	0.3004	0.336
p-value	0.0089	0.0985	0.4039	0.3436
vintage			0.1774	0.1592
std. err.			0.0514	0.0455
p-value			0.0006	0.0005
sex				
female				4.4507
std. err.				0.6385
p-value				< .0001
race				
White				1.8292
std. err.				0.383
p-value				< .0001
Black				-4.2972
std. err.				0.4562
p-value				< .0001
American Indian				-5.8878
std. err.				0.4837
p-value				< .0001
education				
00–08 years				2.885
std. err.				0.6764
p-value				< .0001
09–12 years				0.1027
std. err.				0.1714
p-value				0.549

All models include intercepts (not shown). Year 2018 fixed effects are normalized to zero. In column 4 model, fixed effects for male sex, Asian or Pacific Islander race, and 13 + years education are also normalized to zero.

4. Empirical results

4.1. Estimates of model of U.S. longevity growth, 2006–2018

Estimates of several versions of the model of U.S. longevity growth during 2006–2018 (Eq. (1)) are shown in Table 4. These estimates are based on 4258 observations.[15] The model in column 1 contains only year fixed effects.[16] The estimate of the fixed effect for year 2006 (γ_{2006}) indicates that the mean age at death of all Americans increased by 0.796 years between 2006 and 2018, which is consistent with the figures shown in Table 1. The model in column 2 also includes 125 disease fixed effects. Controlling for disease fixed effects reduces the magnitude of γ_{2006} by 55%. This indicates that 55% of the increase in mean age at death was due to changes in the distribution of deaths, by cause ("between-disease changes"); 45% was due to within-disease increases.

The model in column 3 also includes drug vintage. As hypothesized, the coefficient of this variable is positive and highly significant (p-value = 0.0006), which indicates that diseases for which there were larger increases in drug vintage tended to have larger increases in mean age at death. The model in column 4 also includes sex, race, and education fixed effects. Controlling for these demographic variables reduces the estimate of the vintage coefficient (β), but only by 10%, and it remains

[15] There are 125 diseases, 2 years, 2 sexes, 4 races, and 3 education groups. 125 * 2 * 2 * 4 * 3 = 6000. Some cells had zero observations.

[16] The model also contains an intercept (not shown), so the fixed effect for year 2018 (γ_{2018}) is normalized to zero.

Table 5
Estimates of vintage coefficient (β) from models of U.S. mean age at death (Eq. (1)), by sex, race, and education.

row	Parameter	Estimate	Std. Err.	95% Confidence Limits		Z	Pr > |Z|	covariates
	pooled model							
1	vintage	0.177	0.051	0.077	0.278	3.45	0.0006	year, cause
2	vintage	0.159	0.046	0.070	0.248	3.49	0.0005	year, cause, sex, race, education
	disaggregate by sex							
3	vintage	0.151	0.046	0.060	0.242	3.25	0.0011	year*sex, cause*sex, race*sex, education*sex
4	vintage(female)	0.142	0.071	0.003	0.281	2.00	0.0459	year*sex, cause*sex, race*sex, education*sex
5	vintage(male)	0.159	0.056	0.050	0.269	2.84	0.0045	year*sex, cause*sex, race*sex, education*sex
	disaggregate by race							
6	vintage	0.165	0.045	0.077	0.254	3.67	0.0002	year*race, cause*race, sex*race, education*race
7	vintage(White)	0.158	0.046	0.069	0.247	3.47	0.0005	year*race, cause*race, sex*race, education*race
8	vintage(Black)	0.207	0.062	0.085	0.329	3.31	0.0009	year*race, cause*race, sex*race, education*race
9	vintage(American Indian)	0.287	0.050	0.189	0.384	5.74	< .0001	year*race, cause*race, sex*race, education*race
10	vintage(Asian or Pacific Islander)	0.221	0.048	0.128	0.315	4.64	< .0001	year*race, cause*race, sex*race, education*race
	disaggregate by education							
11	vintage	0.129	0.040	0.050	0.208	3.19	0.0014	year*education, cause*education, sex*education, race*education
12	vintage(00–08 years)	0.004	0.057	-0.107	0.116	0.08	0.9399	year*education, cause*education, sex*education, race*education
13	vintage(09–12 years)	0.119	0.048	0.025	0.212	2.47	0.0134	year*education, cause*education, sex*education, race*education
14	vintage(13 + years)	0.199	0.039	0.121	0.276	5.04	< .0001	year*education, cause*education, sex*education, race*education

highly significant (p-value = 0.0005).

As discussed above, the validity of the standard two-way fixed-effects model relies on the assumption of "parallel trends," and on the assumption that the treatment effect is constant across units and time periods. Therefore, we also estimated a version of Eq. (1) using the STATA DID_MULTIPLEGT procedure (de Chaisemartin, D'Haultfœuille, and Guyonvarch, 2021) for estimating the effect of a treatment on an outcome, in sharp difference-in-differences designs with multiple groups and periods. Estimates generated by this procedure do not rely on the constant treatment effect assumption, and allow us to test the parallel trends assumption by generating "placebo estimators." To implement this procedure, we used data for 3 years (2006, 2012, and 2018), and replaced the continuous rx_vintage ("treatment") variable by a categorical variable (rx_vintage_rank) which has 3 values: low, medium, and high vintage.

As discussed by de Chaisemartin, D'Haultfœuille, and Guyonvarch

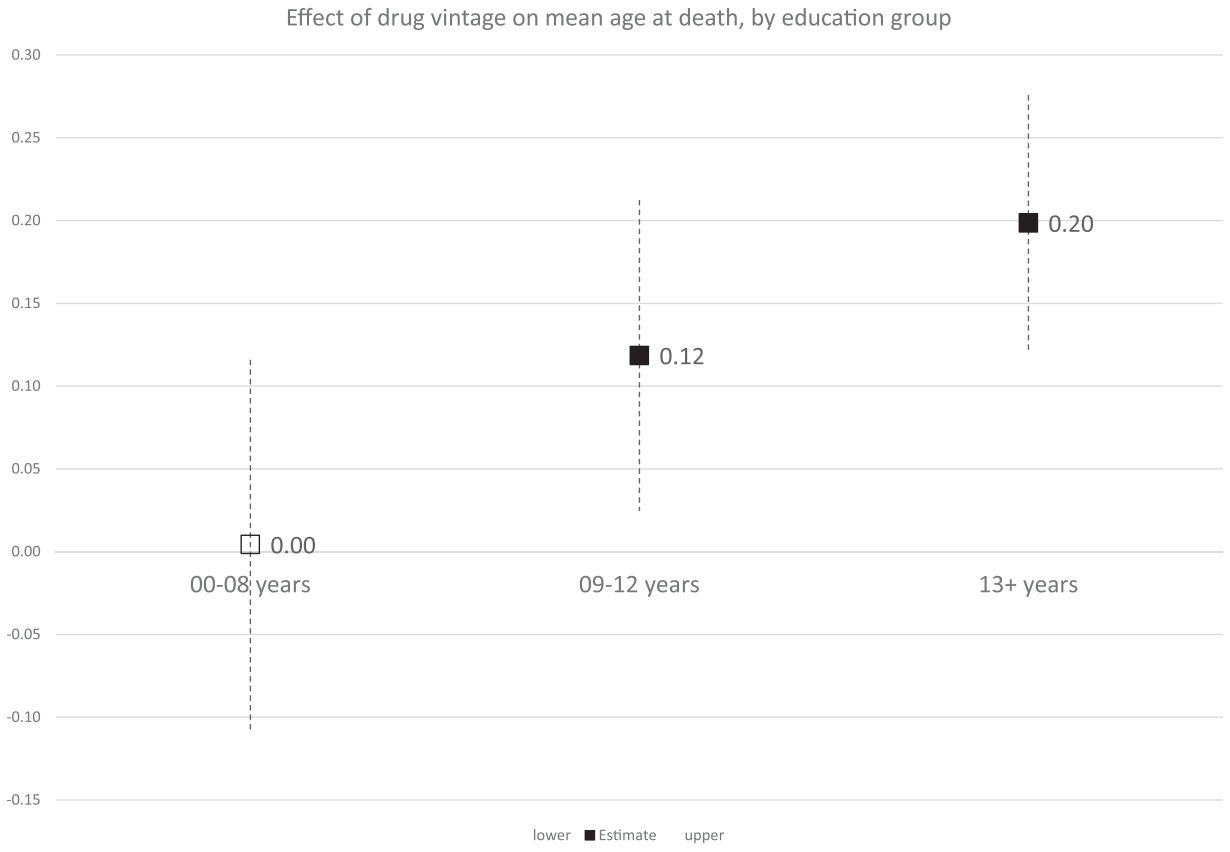


Fig. 3. Effect of drug vintage on mean age at death, by education group.

Table 6
Estimates of models of mean age at death in 26 high-income countries during 2006–2016 (Eq. (2)), by sex.

row	Parameter	Estimate	Std. Err.	95% Confidence Limits		Z	Pr > |Z|	covariates
	pooled model							
1	vintage	0.356	0.137	0.087	0.625	2.6	0.0095	country, cause
2	vintage	0.344	0.129	0.092	0.596	2.7	0.0075	country, cause, sex
	disaggregate by sex							
3	vintage	0.342	0.131	0.085	0.599	2.6	0.0091	country*sex, cause*sex
4	vintage(female)	0.295	0.124	0.051	0.538	2.4	0.0176	
5	vintage(male)	0.390	0.139	0.118	0.663	2.8	0.005	

(2021), the DID_MULTIPLEGT procedure estimator uses as controls groups whose treatment does not change between consecutive time periods. With a continuous treatment, there may not be any pair of consecutive time periods between which the treatment of at least one group remains perfectly stable. Here are descriptive statistics about rx_vintage_rank: rx_.

rx_vintage_rank	No. of observations	mean	minimum	maximum
low	370	1961.2	1898.0	1976.5
medium	368	1979.9	1976.5	1982.6
high	367	1988.7	1982.7	2002.0

The DID_MULTIPLEGT estimate of the coefficient of rx_vintage_rank was positive and highly significant: estimate = 0.813; std. err. = 0.290; Z = 2.80. The DID_MULTIPLEGT estimate of the placebo was far from significant: estimate = −0.012; std. err. = 0.642; Z = 0.02. This indicates that we are unable to reject the null hypothesis of parallel trends, and that standard two-way fixed-effects estimates are valid.

As indicated above, in addition to estimating the model in column 4 of Table 4, which controls for sex, race and education, we estimated separate models for each sex, race and education group. Estimates of the vintage coefficients from these models are shown in Table 5. The estimates in the first two rows of Table 5 replicate the estimates in columns 3 and 4 of Table 4. Estimates of β from models of mean age at death, by sex, are shown in rows 3–5 of Table 5. The estimates of β for females and males are both positive and significant (p-value <.05), and their magnitudes are quite similar. The difference between the female and male estimates is far from statistically significant (p-value = 0.84).

Estimates of β from models of mean age at death, by race, are shown in rows 6–10 of Table 5. The estimates of β for all four races are positive and highly significant (p-value <.001). The estimate of β for Whites is smaller than the other 3 estimates, but the differences between the estimates may not be statistically significant.

Estimates of β from models of mean age at death, by education, are shown in rows 11–14 of Table 5 and plotted in Fig. 3. The estimate in row 12 indicates that drug vintage did not have a significant effect on the mean age at death of decedents with less than 9 years of education. Drug vintage had a positive and significant effect on the mean age at death of decedents with at least 9 years of education, and a larger effect on the mean age at death of decedents with at least 13 years of education.[17] The finding that pharmaceutical innovation has a larger effect on the longevity of people with more education is consistent with evidence provided by Lleras-Muney and Lichtenberg (2005). Using data from the 1997 Medical Expenditure Panel Survey, they showed that more educated people are more likely to use newer drugs, controlling for other individual characteristics, such as income and insurance status.

4.2. Estimates of the model of the level of longevity in 26 high-income countries

Estimates of the vintage coefficient (β) from several versions of the 2-way fixed-effects model of the level of longevity in 26 high-income countries (Eq. (2)) are shown in Table 6. These estimates are based on 5427 observations.[18] The model in row 1 controls for fixed disease and country effects. The estimate of the vintage coefficient is positive and highly significant (p-value =.0095), indicating that the higher the relative vintage of drugs available to treat a disease in a country, the higher the relative mean age at death (relative to the mean age at death in that country and from that disease). The point estimate of β is about twice as large as the estimates from U.S. data shown in Tables 4 and 5. The effect of pharmaceutical innovation on longevity may have been twice as large in high-income countries in general as it was in the U.S. The model in row 2 of Table 6 also includes sex fixed effects. This has very little effect on the estimate of β.

We estimated separate models for each sex. Estimates of β from models of mean age at death, by sex, are shown in rows 3–5 of Table 6. The estimates of β for females and males are both positive and significant (p-value <.02). The estimate for males is 32% larger than the estimate for females; the difference between the female and male estimates is marginally significant (p-value = 0.0667). The effect of pharmaceutical innovation on longevity in 26 high-income countries may have been greater for men than it was for women.

4.3. Estimates of the effect of pharmaceutical innovation on drug expenditure

The estimate of the vintage coefficient (η) from the model of drug expenditure (Eq. (3)) based on U.S. data by drug class and year (2007 and 2017) is 0.0956 (std. err. = 0.0377; Z = 2.53; p-value = 0.0113). This indicates that drug classes that had larger increases in drug vintage tended to have larger increases in drug expenditure. The estimate implies that 53% of the 2007–2017 increase in U.S. drug expenditure was due to pharmaceutical innovation (the increase in drug vintage).[19]

The estimate of the vintage coefficient (η) from the model of drug expenditure (Eq. (4)) based on data by country and year (2006 and 2016) is 0.0804 (std. err. = 0.0165; Z = 4.87; p-value <.0001). This estimate, which is quite similar to the estimate from Eq. (3), indicates that *countries* that had larger increases in drug vintage tended to have larger increases in drug expenditure. The estimate implies that 86% of the 2006–2016 increase in drug expenditure in 26 high-income countries was due to pharmaceutical innovation (the increase in drug vintage).

[17] The difference between the 0–8 years and 9–12 years coefficients is highly significant (p-value =.0057); the difference between the 9–12 years and 13 + years coefficients is marginally significant (p-value =.0583).

[18] There are 137 diseases, 26 countries, and 2 sexes. 137 * 26 * 2 = 7124. Some cells had zero observations.

[19] Population growth, aging and inflation may also have contributed to pharmaceutical expenditure growth.

Table 7
Calculation of the incremental cost-effectiveness ratio of pharmaceutical innovation in the U.S. and in 26 high-income countries.

row	Column	1	2
	region	USA	26 high-income countries
	period	2006–2018	2006–2016
1	β	0.1592	0.344
2	Δvintage	3.3	3.59
3	β * Δvintage	0.52536	1.23496
4	Δage_death	0.796	1.683
5	(β * Δvintage)/Δage_death	66%	73%
6	no. of deaths in last year of period	2,839,205	7,585,653
7	life-years gained in last year of period	1,491,605	9,367,978
8	% of the increase in expend due to the increase in vintage	53.3%	86.3%
9	increase in per capita drug expenditure	$307	$164
10	estimated increase in per capita expend. due to increase in vintage	$164	$142
11	population in last year of period	326,687,500	920,119,000
12	estimated increase in total expend. due to increase in vintage	$53.4 billion	$130.3 billion
13	Δexpend/Δlife-years	$35,817	$13,904
14	per capita GDP in last year of period	$63,064	$48,002

5. Discussion

Now we will use our estimates to calculate (1) an important benefit of pharmaceutical innovation (the number of life-years gained from it); (2) the cost of pharmaceutical innovation (its impact on drug expenditure); and (3) the incremental cost-effectiveness ratio of pharmaceutical innovation, in the U.S. and in 26 high-income countries. These calculations are summarized in Table 7.

Calculations pertaining to the U.S. during the period 2006–2018 are shown in column 1. As shown in row 1, our estimate of the effect of drug vintage on mean age at death, controlling for disease, year, sex, race, and education, is 0.16 (Table 4, column 4). Between 2006 and 2018, weighted (by number of deaths) mean drug vintage increased by 3.3 years (row 2). This increase in drug vintage is estimated to have increased mean age at death by 0.53 years (= 0.16 * 3.3 years)—about 6 months (row 3). During that period, mean age at death increased by 0.80 years (row 4), so we estimate that 66% of the increase in mean age at death was due to pharmaceutical innovation (row 5). In 2018, there were 2.84 million deaths in the U.S. (row 6). If pharmaceutical innovation did not affect the number of deaths or their distribution, by cause, then 1.49 million (= 0.53 * 2.84 million) life-years were gained in 2018 from the 2006–2018 increase in drug vintage (row 7).

As indicated above, the estimate of Eq. (3) implies that 53% of the 2007–2017 increase in U.S. drug expenditure was due to the increase in drug vintage (row 8). Suppose that 53% of the 2006–2018 increase in U.S. drug expenditure was also due to the increase in drug vintage. During that period, OECD data indicate that per capita U.S. drug expenditure increased by $307, from $764 to $1071 (row 9). Hence, we estimate that the 2006–2018 increase in drug vintage increased per capita U.S. drug expenditure by $164 (= 53% * $307) in 2018 (row 10). The U.S. population in 2018 was 326.7 million (row 11), so we estimate that the 2006–2018 increase in drug vintage increased U.S. drug expenditure by $53.4 billion (= 326.7 million * $164) (row 12). These figures imply that, in the U.S. during the period 2006–2018, the ICER (Δdrug_expenditure/Δlife-years) was $35,817 (= $53.4 billion / 1.49 million life-years gained) (row 13).

Calculations pertaining to the 26 high-income countries during the period 2006–2016 are shown in column 2 of Table 7. As shown in row 1, our estimate of the effect of drug vintage on mean age at death, controlling for disease, year, and sex, is 0.34 (Table 6, row 2). Between 2006 and 2016, weighted (by number of deaths) mean drug vintage increased by 3.6 years (row 2). This increase in drug vintage is estimated to have increased mean age at death by 1.23 years (= 0.34 * 3.6 years) (row 3). During that period, mean age at death increased by 1.68 years (row 4), so we estimate that 73% of the increase in mean age at death was due to pharmaceutical innovation (row 5). In 2016, there were 7.59 million deaths in these countries (row 6). If pharmaceutical innovation did not affect the number of deaths or their distribution, by cause, then 9.37 million (= 1.23 * 7.59 million) life-years were gained in 2016 from the 2006–2016 increase in drug vintage (row 7).

As indicated above, the estimate of Eq. (4) implies that 86% of the 2006–2016 increase in drug expenditure in these countries was due to the increase in drug vintage (row 8). During that period, OECD data indicate that weighted (by population) per capita drug expenditure in these countries increased by $164, from $532 to $696 (row 9). Hence, we estimate that the 2006–2016 increase in drug vintage increased per capita drug expenditure by $142 (= 86% * $164) in 2016 (row 10). The population in 2016 was 920.1 million (row 11), so we estimate that the 2006–2016 increase in drug vintage increased drug expenditure in these countries by $130.3 billion (= 920.1 million * $142) (row 12). These figures imply that, in the 26 countries during the period 2006–2016, the ICER was $13,904 (= $130.3 billion / 9.37 million life-years gained) (row 13).

As noted by Bertram et al. (2016), authors writing on behalf of the WHO's *Choosing Interventions that are Cost–Effective* project (WHO-CHOICE) suggested in 2005 that "interventions that avert one disability-adjusted life-year (DALY) for less than average per capita income for a given country or region are considered very cost–effective; interventions that cost less than three times average per capita income per DALY averted are still considered cost–effective." U.S. per capita GDP in 2018 was $63,064; weighted (by population) mean per capita GDP in the 26 countries in 2016 was $48,002. In both cases, the ICER is well below per capita GDP.[20] Moreover, previous studies (e.g. Lichtenberg, 2018) have shown that pharmaceutical innovation has reduced expenditure on other medical services (especially hospitalization), so our ICER estimates are likely to be overestimates.

6. Summary and conclusions

This study has examined the impact that pharmaceutical innovation, which accounts for most private biomedical research expenditure, has had on longevity. We performed two types of two-way fixed-effects analyses, which control for the effects of many potentially confounding variables. First, we analyzed long-run (2006–2018) *changes* in longevity associated with different diseases in a single country: the U.S. Then, we analyzed relative longevity *levels* associated with different diseases in 26 high-income countries during a single time period (2006–2016). The measure of longevity we analyzed, mean age at time of death, is strongly positively correlated across countries with life expectancy at birth. The measure of pharmaceutical innovation we used is the mean vintage (year of initial world launch) of the drugs used to treat each disease in each country. Changes in the vintage distribution of drugs are due to both entry of new drugs and exit of old drugs.

Our analysis of U.S. data indicated that the diseases for which there were larger increases in drug vintage tended to have larger increases in the longevity of Americans of all races and both sexes. In other words, the lower the mean age of the drugs, the higher the mean age at death. We tested, and were unable to reject, the "parallel trends" hypothesis. We estimated that the 2006–2018 increase in drug vintage increased the mean age at death of Americans by about 6 months (66% of the observed increase). Controlling for sex, race, and education had only a small effect on the estimate of the vintage coefficient.

[20] Previous studies (e.g. Lichtenberg, 2019) have shown that pharmaceutical innovation has reduced disability, so the cost per DALY gained is not necessarily higher than the cost per life-year gained.

The estimates indicated that drug vintage did not have a significant effect on the mean age at death of decedents with less than 9 years of education. Drug vintage had a positive and significant effect on the mean age at death of decedents with at least 9 years of education, and a larger effect on the mean age at death of decedents with at least 13 years of education. The finding that pharmaceutical innovation has a larger effect on the longevity of people with more education is consistent with previous evidence that more educated people are more likely to use newer drugs. Since educational attainment has been rising, the average impact of pharmaceutical innovation on longevity may be increasing.

Our analysis of data on 26 high-income countries indicated that the higher the vintage of drugs available to treat a disease in a country, the higher mean age at death was, controlling for fixed disease and country effects. The increase in drug vintage is estimated to have increased mean age at death in the 26 countries by 1.23 years between 2006 and 2016—73% of the observed increase.

We obtained estimates of the cost of pharmaceutical innovation—its impact on drug expenditure—as well as estimates of an important benefit of pharmaceutical innovation—the number of life-years gained from it—and of their ratio, i.e., the incremental cost-effectiveness ratio. Estimates of the cost per life-year gained in the U.S. and the 26 countries were $35,817 and $13,904, respectively. Both of these figures are well below per capita GDP in the respective regions, suggesting that, overall, pharmaceutical innovation was highly cost-effective.

A limitation of this study is that we were unable to control for non-pharmaceutical biomedical innovation (e.g. innovation in diagnostic imaging, surgical procedures, and medical devices), which is far more difficult to measure than pharmaceutical innovation. Most (88%) private U.S. funding for biomedical research comes from pharmaceutical and biotechnology firms, and a previous study (Lichtenberg, 2014) indicated that controlling for non-pharmaceutical medical innovation did not affect estimates of the effect of pharmaceutical innovation on U.S. cancer mortality. Nevertheless, controlling for non-pharmaceutical medical innovation would be desirable.

Author statement

None.

Funding

Financial support for this research was provided by the National Pharmaceutical Council. The funding body had no role in the design of the study, in the collection, analysis, and interpretation of data, or in writing the manuscript.

Authors' contributions

All contributions to the manuscript were made by the sole author.

Data Availability

All data, except IQVIA MIDAS data, are publicly available. The IQVIA MIDAS data are not publicly available but are available from the corresponding author on reasonable request.

Acknowledgements

Not applicable.

Competing interests

The author declares that he has no competing interests.

Appendix

See Table A1.

Table A1
U.S. mortality and drug vintage in 2006 and 2018, by WHO Global Health Estimates cause of death.

	no. of deaths			mean age at death			mean drug vintage			no. of drugs	
WHO Global Health Estimates cause of death	2006	2018	% change	2006	2018	change	2006	2018	change	2006	2018
ALL CAUSES	**2,212,092**	**2,669,371**	**20.7%**	**73.0**	**73.9**	**0.9**					
50 Syphilis	32	36	12.5%	65.7	69.8	4.1	1960.8	1960.8	0.0	4	4
60 Chlamydia	.	.	.	.	.	.	1962.8	1962.8	0.0	4	4
70 Gonorrhoea	3	2	-33.3%	60.3	67.0	6.7	1978.6	1977.6	-1.1	8	7
80 Trichomoniasis	.	1	.	.	.	.	1963.0	1963.0	0.0	1	1
85 Genital herpes	.	.	.	.	.	.	1988.3	1988.3	0.0	4	4
90 Other STDs	93	108	16.1%	69.3	71.5	2.2	1979.3	1979.8	0.6	12	11
100 HIV/AIDS	10,950	5,173	-52.8%	46.1	53.0	7.0	1996.8	1999.0	2.2	26	29
110 Diarrhoeal diseases	6,393	7,796	22.0%	80.3	76.0	-4.4	1969.1	1969.8	0.7	14	14
130 Whooping cough	10	9	-10.0%	8.3	33.8	25.5	.	.	.	.	.
140 Diphtheria	.	1	.	.	75.0	.	.	.	.	.	.
160 Tetanus	4	1	-75.0%	69.0	73.0	4.0	1967.5	1967.5	0.0	2	2
170 Meningitis	704	638	-9.4%	46.9	54.1	7.1	1976.0	1977.9	1.9	17	16
180 Encephalitis	1,236	1,191	-3.6%	65.1	68.9	3.8	.	.	.	.	.
185 Hepatitis	6,890	4,648	-32.5%	57.2	62.0	4.8	1999.8	2001.6	1.8	8	9
220 Malaria	10	8	-20.0%	57.4	55.8	-1.7	1972.4	1972.4	0.0	5	5
230 Trypanosomiasis	.	.	.	.	.	.	1984.0	1984.0	0.0	1	1
240 Chagas disease	3	2	-33.3%	64.7	46.0	-18.7	.	.	.	.	.
250 Schistosomiasis	.	1	.	.	62.0	.	1982.0	1982.0	0.0	1	1
260 Leishmaniasis	.	.	.	.	.	.	1974.0	1974.0	0.0	2	2
270 Lymphatic filariasis	.	1	.	.	73.0	.	1996.0	1996.0	0.0	1	1
280 Onchocerciasis	.	.	.	.	.	.	1996.0	1996.0	0.0	1	1
285 Cysticercosis	12	6	-50.0%	43.8	41.2	-2.7	.	.	.	.	.
295 Echinococcosis	.	1	.	.	61.0	.	1985.0	1985.0	0.0	2	2
320 Rabies	2	3	50.0%	13.0	43.3	30.3	.	.	.	.	.
340 Ascariasis	.	.	.	.	.	.	1985.0	1985.0	0.0	2	2
350 Trichuriasis	.	.	.	.	.	.	1996.0	1996.0	0.0	1	1
360 Hookworm disease	.	.	.	.	.	.	1985.0	1985.0	0.0	2	2
362 Food-bourne trematodes	12	12	0.0%	63.8	65.4	1.6	1983.3	1988.7	5.4	4	3

(*continued on next page*)

Table A1 (*continued*)

	no. of deaths			mean age at death			mean drug vintage			no. of drugs	
WHO Global Health Estimates cause of death	2006	2018	% change	2006	2018	change	2006	2018	change	2006	2018
365 Leprosy	.	2	.	.	75.0	.	1982.7	1982.7	0.0	3	3
370 Other infectious diseases	36,293	47,249	30.2%	72.9	73.1	0.1	1976.8	1978.7	1.8	108	105
390 Lower respiratory infections	53,612	58,436	9.0%	80.1	78.0	-2.1	1980.0	1981.0	1.0	48	46
400 Upper respiratory infections	167	247	47.9%	62.4	68.2	5.8	1974.1	1973.9	-0.2	42	37
410 Otitis media	31	28	-9.7%	54.6	58.7	4.2	1974.2	1975.1	1.0	16	14
420 Maternal conditions	737	965	30.9%	31.5	32.3	0.8	1971.2	1971.4	0.2	25	25
500 Preterm birth complications	5,952	4,158	-30.1%	0.4	0.5	0.2	1966.3	1966.3	0.0	6	6
510 Birth asphyxia and birth trauma	1,722	1,336	-22.4%	0.4	1.0	0.5	.	.	.	.	.
520 Neonatal sepsis and infections	924	673	-27.2%	0.2	1.0	0.7	.	.	.	.	.
530 Other neonatal conditions	4,477	3,422	-23.6%	0.2	0.5	0.3	1965.6	1966.3	0.7	8	7
550 Protein-energy malnutrition	2,228	9,146	310.5%	80.0	83.2	3.2	1946.0	1946.0	0.0	1	1
560 Iodine deficiency	.	2	.	.	60.5	.	1978.0	1978.0	0.0	2	2
570 Vitamin A deficiency	.	.	.	.	.	.	1953.0	1953.0	0.0	1	1
580 Iron-deficiency anaemia	155	336	116.8%	83.3	82.2	-1.0	1988.7	1991.3	2.6	6	7
590 Other nutritional deficiencies	267	369	38.2%	82.2	79.3	-2.9	1975.6	1979.9	4.3	18	23
621 Lip and oral cavity	3,677	5,198	41.4%	69.1	70.5	1.4	1979.9	1983.8	3.9	12	12
622 Nasopharynx	613	701	14.4%	62.3	64.3	2.0	1979.9	1983.8	3.9	12	12
623 Other pharynx	3,041	4,088	34.4%	66.6	67.5	0.9	1979.9	1983.8	3.9	12	12
630 Oesophagus cancer	13,109	15,228	16.2%	68.8	69.7	1.0	1981.6	1984.9	3.4	14	14
640 Stomach cancer	10,843	10,894	0.5%	70.5	69.7	-0.8	1983.8	1988.1	4.3	17	18
650 Colon and rectum cancers	51,269	52,409	2.2%	72.6	71.1	-1.4	1986.2	1992.5	6.3	17	20
660 Liver cancer	15,770	27,183	72.4%	68.0	69.3	1.3	1984.3	1988.3	3.9	12	12
670 Pancreas cancer	32,201	44,559	38.4%	71.7	72.0	0.3	1985.9	1991.0	5.1	17	19
680 Trachea, bronchus, lung cancers	151,326	140,299	-7.3%	70.7	72.0	1.3	1984.4	1991.0	6.6	31	38
691 Malignant skin melanoma	8,110	8,134	0.3%	66.8	70.6	3.8	1978.9	1993.2	14.3	13	20
692 Non-melanoma skin cancer	2,515	4,095	62.8%	74.4	76.4	2.1	1982.7	1989.1	6.4	11	12
700 Breast cancer	39,482	42,605	7.9%	67.8	69.4	1.7	1983.0	1988.7	5.8	39	47
710 Cervix uteri cancerd	3,787	4,084	7.8%	58.5	59.5	1.0	1980.9	1984.1	3.1	15	15
720 Corpus uteri cancerd	3,320	6,368	91.8%	70.8	70.3	-0.5	1977.2	1981.5	4.3	11	11
730 Ovary cancer	14,305	13,651	-4.6%	69.6	69.6	0.0	1980.3	1984.0	3.7	27	29
740 Prostate cancer	27,064	31,115	15.0%	78.9	78.5	-0.4	1984.7	1993.1	8.5	18	24
742 Testicular cancer	346	396	14.5%	42.5	44.0	1.5	1976.4	1979.3	2.9	16	16
745 Kidney, renal pelvis and ureter cancer	12,256	14,414	17.6%	70.4	71.7	1.3	1977.5	1985.2	7.7	13	15
750 Bladder cancer	12,982	16,475	26.9%	76.5	77.6	1.1	1977.3	1979.7	2.5	19	19
751 Brain and nervous system cancers	12,408	16,984	36.9%	61.6	63.9	2.3	1972.8	1978.6	5.8	20	22
752 Gallbladder and biliary tract cancer	3,309	4,075	23.2%	73.2	72.7	-0.5	1980.8	1985.5	4.7	10	10
753 Larynx cancer	3,611	3,705	2.6%	68.4	69.0	0.6	1979.1	1984.3	5.2	9	9
754 Thyroid cancer	1,463	2,008	37.3%	71.7	72.7	1.0	1979.1	1986.0	6.9	11	12
755 Mesothelioma	2,379	2,414	1.5%	73.1	75.2	2.1	1982.3	1988.4	6.2	14	16
761 Hodgkin lymphoma	1,278	1,026	-19.7%	59.8	67.5	7.7	1974.6	1980.2	5.6	25	28
762 Non-Hodgkin lymphoma	19,917	20,228	1.6%	72.4	74.3	2.0	1978.0	1985.9	7.9	40	48
763 Multiple myeloma	10,682	12,701	18.9%	72.9	74.4	1.5	1980.3	1990.0	9.7	21	28
770 Leukaemia	21,121	23,198	9.8%	69.9	72.4	2.4	1982.4	1990.2	7.8	42	57
780 Other malignant neoplasms	19,396	24,614	26.9%	67.5	68.8	1.3	1982.6	1991.0	8.4	56	72
790 Other neoplasms	13,511	15,492	14.7%	74.8	76.5	1.7	1982.4	1988.4	6.1	39	46
800 Diabetes mellitus	69,293	83,541	20.6%	72.4	71.7	-0.8	1993.8	1995.4	1.6	37	38
811 Thalassaemias	21	16	-23.8%	41.6	70.2	28.6	1989.2	1994.9	5.7	5	7
812 Sickle cell disorders and trait	440	517	17.5%	38.4	42.5	4.1	1981.6	1984.8	3.2	7	8
813 Other haemoglobinopathies and haemolytic anaemias	272	302	11.0%	69.3	68.5	-0.8	1974.8	1980.8	6.0	12	13
814 Other endocrine, blood and immune disorders	30,464	47,570	56.2%	70.2	71.7	1.4	1981.6	1985.5	3.9	142	154
831 Major depressive disorder	594	507	-14.7%	82.7	79.3	-3.4	1981.0	1982.9	1.8	31	33
840 Bipolar disorder	79	131	65.8%	68.2	69.6	1.4	1980.1	1981.9	1.8	15	16
850 Schizophrenia	462	591	27.9%	72.9	67.3	-5.6	1976.8	1978.8	2.0	18	18
860 Alcohol use disorders	7,411	12,405	67.4%	53.3	55.3	2.0	1974.5	1973.8	-0.7	17	16
871 Opioid use disorders	12,925	28,028	116.9%	40.3	41.6	1.3	1975.1	1975.1	0.0	10	10
872 Cocaine use disorders	636	287	-54.9%	43.8	51.9	8.0	1978.0	1978.0	0.0	6	6
873 Amphetamine use disorders	95	473	397.9%	42.9	48.6	5.8	1978.0	1978.0	0.0	6	6
874 Cannabis use disorders	2	13	550.0%	34.5	42.6	8.1	1978.0	1978.0	0.0	6	6
875 Other drug use disorders	1,407	6,156	337.5%	43.7	46.3	2.6	1978.0	1978.0	0.0	6	6
880 Anxiety disorders	111	239	115.3%	72.6	75.3	2.7	1981.2	1982.3	1.1	27	28
890 Eating disorders	123	101	-17.9%	67.9	52.5	-15.3	1970.0	1970.7	0.7	14	13
900 Autism and Asperger syndrome	32	82	156.3%	24.5	33.1	8.7	1978.0	1978.0	0.0	6	6
911 Attention deficit/hyperactivity syndrome	3	4	33.3%	58.3	68.0	9.7	1978.1	1978.1	0.0	8	8
912 Conduct disorder	4	18	350.0%	62.0	82.8	20.8	1980.1	1980.1	0.0	7	7
920 Idiopathic intellectual disability	369	209	-43.4%	52.5	59.2	6.7	1980.1	1980.1	0.0	7	7
930 Other mental and behavioural disorders	3,167	2,419	-23.6%	77.5	76.5	-1.1	1976.2	1979.4	3.2	41	44
950 Alzheimer disease and other dementias	143,872	263,425	83.1%	86.2	86.8	0.6	1987.7	1987.2	-0.5	12	11
960 Parkinson disease	18,830	33,540	78.1%	82.0	82.0	0.0	1982.0	1989.1	7.1	18	16
970 Epilepsy	1,336	2,935	119.7%	49.0	54.7	5.7	1974.7	1983.1	8.4	25	31
980 Multiple sclerosis	3,341	4,200	25.7%	61.7	66.1	4.4	1980.3	1988.4	8.0	18	22
990 Migraine	3	6	100.0%	63.7	39.0	-24.7	1990.8	1987.4	-3.4	12	13
1000 Non-migraine headache	.	.	.	.	.	.	1969.7	1975.0	5.3	9	9
1010 Other neurological conditions	21,017	32,384	54.1%	63.0	65.9	2.9	1974.2	1978.9	4.8	40	40

(*continued on next page*)

Table A1 (*continued*)

	no. of deaths			mean age at death			mean drug vintage			no. of drugs	
WHO Global Health Estimates cause of death	2006	2018	% change	2006	2018	change	2006	2018	change	2006	2018
1030 Glaucoma	9	3	-66.7%	82.9	88.7	5.8	1983.8	1985.4	1.6	18	17
1050 Uncorrected refractive errors	7	11	57.1%	46.3	55.3	9.0	1988.7	1988.7	0.0	3	3
1060 Macular degeneration	3	8	166.7%	98.0	91.3	-6.8	1989.5	1991.9	2.4	8	9
1070 Other vision loss	10	13	30.0%	69.8	84.1	14.3	1967.6	1972.2	4.5	11	11
1080 Other hearing loss	2	1	-50.0%	92.5	80.0	-12.5	1961.0	.	.	1	.
1090 Other sense organ disorders	44	81	84.1%	70.4	73.4	3.0	1978.4	1979.3	0.9	53	50
1110 Rheumatic heart disease	3,156	3,523	11.6%	75.4	76.1	0.8	1950.6	1949.6	-0.9	12	11
1120 Hypertensive heart disease	39,964	71,418	78.7%	75.1	76.3	1.3	1980.8	1981.4	0.6	46	47
1130 Ischaemic heart disease	406,852	359,257	-11.7%	77.5	76.9	-0.6	1980.7	1981.8	1.1	47	47
1140 Strokeg	130,684	145,917	11.7%	78.9	79.6	0.7	1977.7	1984.3	6.6	12	15
1150 Cardiomyopathy, myocarditis, endocarditis	30,237	28,725	-5.0%	71.3	71.1	-0.3	1965.6	1964.5	-1.1	20	17
1160 Other circulatory diseases	163,387	223,534	36.8%	79.0	79.3	0.3	1976.0	1980.1	4.1	101	112
1180 Chronic obstructive pulmonary diseasef	114,068	152,171	33.4%	77.0	77.2	0.1	1976.7	1979.1	2.5	44	42
1190 Asthma	3,437	3,382	-1.6%	61.5	59.5	-2.0	1975.3	1977.1	1.8	28	24
1200 Other respiratory diseases	43,653	63,500	45.5%	77.3	77.3	0.1	1976.8	1979.9	3.1	57	57
1220 Peptic ulcer disease	3,117	3,242	4.0%	75.8	73.9	-1.8	1988.2	1988.2	0.0	13	13
1230 Cirrhosis of the liver	26,142	41,956	60.5%	60.1	61.2	1.1	1981.3	1986.3	5.0	12	12
1240 Appendicitis	399	357	-10.5%	67.0	69.8	2.8	.	.	.	.	.
1241 Gastritis and duodenitis	285	259	-9.1%	75.0	73.1	-1.9	.	.	.	.	.
1242 Paralytic ileus and intestinal obstruction	5,461	6,671	22.2%	79.8	79.8	0.0	1971.0	1971.0	0.0	1	1
1244 Inflammatory bowel disease	3,134	1,244	-60.3%	70.1	71.7	1.6	1973.2	1981.0	7.8	14	16
1246 Gallbladder and biliary diseases	3,951	5,207	31.8%	78.0	78.9	0.9	1963.3	1963.3	0.0	4	4
1248 Pancreatitis	3,730	3,860	3.5%	67.2	67.3	0.1	1964.7	1964.7	0.0	3	3
1250 Other digestive diseases	36,729	44,913	22.3%	73.2	73.5	0.3	1977.9	1981.3	3.4	57	58
1271 Acute glomerulonephritis	30	587	1856.7%	70.7	79.2	8.5	1981.5	1987.8	6.3	4	5
1273 Other chronic kidney disease	43,599	51,478	18.1%	77.0	76.7	-0.3	1979.7	1982.9	3.1	47	49
1280 Benign prostatic hyperplasia	488	563	15.4%	85.1	84.3	-0.8	1993.6	1995.2	1.6	8	9
1290 Urolithiasis	296	598	102.0%	74.8	76.7	1.9	1973.4	1975.0	1.6	5	4
1300 Other urinary diseases	15,125	17,677	16.9%	82.0	79.3	-2.7	1979.4	1981.1	1.7	63	63
1310 Infertility	.	.	.	.	.	.	1973.4	1976.0	2.6	9	7
1320 Gynecological diseases	301	457	51.8%	75.3	76.2	0.9	1972.6	1972.6	0.0	20	20
1330 Skin diseases	3,611	5,089	40.9%	74.9	74.0	-1.0	1975.2	1980.4	5.2	115	123
1350 Rheumatoid arthritis	2,382	2,027	-14.9%	76.1	76.5	0.3	1976.7	1980.7	4.1	38	42
1360 Osteoarthritis	779	461	-40.8%	84.6	84.2	-0.4	1972.9	1975.0	2.1	21	20
1370 Gout	84	61	-27.4%	81.3	75.6	-5.7	1956.8	1964.0	7.2	11	11
1380 Back and neck pain	573	1,036	80.8%	76.2	76.5	0.3	1981.3	1986.2	4.9	15	18
1390 Other musculoskeletal disorders	9,338	9,823	5.2%	70.7	71.5	0.7	1978.1	1980.7	2.6	71	76
1410 Neural tube defects	478	389	-18.6%	20.2	27.5	7.3	1946.0	1946.0	0.0	1	1
1420 Cleft lip and cleft palate	9	10	11.1%	10.0	26.4	16.5	.	.	.	.	.
1430 Down syndrome	742	1,226	65.2%	46.4	53.2	6.8	.	.	.	.	.
1440 Congenital heart anomaliesf	3,302	2,778	-15.9%	25.0	31.3	6.2	1986.0	1995.7	9.7	2	3
1450 Other chromosomal anomalies	1,088	869	-20.1%	3.2	7.2	4.0	1976.0	1976.0	0.0	1	1
1460 Other congenital anomalies	4,093	3,816	-6.8%	24.9	29.8	4.9	1972.9	1987.3	14.5	7	9
1480 Dental caries	2	4	100.0%	84.0	63.8	-20.3	1973.7	1973.7	0.0	3	3
1490 Periodontal disease	9	3	-66.7%	73.3	67.7	-5.7	1966.8	1966.8	0.0	4	4
1502 Other oral disorders	182	232	27.5%	77.2	76.4	-0.8	1979.5	1979.5	0.0	11	11
1530 Road injury	42,615	38,677	-9.2%	41.0	45.3	4.4	.	.	.	.	.
1540 Poisonings	986	1,509	53.0%	48.2	48.3	0.1	.	.	.	.	.
1550 Falls	19,826	37,082	87.0%	76.4	80.1	3.7	.	.	.	.	.
1560 Fire, heat and hot substances	2,969	2,978	0.3%	51.1	57.1	6.0	.	.	.	.	.
1570 Drowning	3,408	3,674	7.8%	35.7	40.6	4.9	.	.	.	.	.
1575 Exposure to mechanical forces	3,478	3,293	-5.3%	37.3	37.4	0.1	.	.	.	.	.
1580 Natural disasters	221	182	-17.7%	42.8	48.6	5.8	.	.	.	.	.
1590 Other unintentional injuries	19,429	22,221	14.4%	63.7	66.5	2.9	1966.8	1985.3	18.5	4	7
1610 Self-harm	32,126	47,955	49.3%	46.0	46.7	0.7	.	.	.	.	.
1620 Interpersonal violence	17,318	18,306	5.7%	32.2	34.7	2.5	.	.	.	.	.
1630 Collective violence and legal intervention	425	610	43.5%	34.6	38.0	3.4	.	.	.	.	.

References

Aghion, P., Howitt, P., 2005. Growth with quality-improving innovations: an integrated framework. In: Aghion, P., Steven, N. (Eds.), Handbook of Economic Growth Volume 1, Part A. Durlauf, pp. Pages 67–110.

Bauman K., 2016. College Completion by Cohort, Age and Gender, 1967 to 2015. U.S. Census Bureau Education and Social Stratification Branch, Social, Housing and Economic Statistics Division, Working Paper 2016–04.

Bertram, M.Y., Lauer, J.A., De Joncheere, K., Edejer, T., Hutubessy, R., Kieny, M.P., Hill, S.R., 2016. Cost-effectiveness thresholds: pros and cons. Bull. World Health Organ 94 (12), 925–930. Dec 1.

Boucekkine, R., de la Croix, D., Licandro, O., 2018. Vintage Capital, in The New Palgrave Dictionary of Economics, 2018th ed. Macmillan Publishers Ltd,.

The economics of new goods, V. In: Bresnahan, T.F., Gordon, R.J. (Eds.), 1997. 58 Studies in Income and Wealth. University of Chicago Press, Chicago.

Brown, D.W., Croft, J.B., Greenlund, K.J., Giles, W.H., 2009. Average age at death from COPD in the United States: 1980–85, 1990–95, 2000–05. COPD J. Chronic Obstr. Pulm. Dis. 6, 152–154.

Case, A., Deaton, A., 2020. Deaths of Despair and the Future of Capitalism. Princeton University Press, Princeton.

Centers for Disease Control and Prevention, 2020. Adult Obesity Facts.

Centre National Hospitalier d'Information sur le Médicament, 2021. Thériaque database.

de Chaisemartin, C., D'Haultfœuille, X., 2020. Two-way fixed effects estimators with heterogeneous treatment effects. Am. Econ. Rev. 110 (9), 2964–2996.

de Chaisemartin, C., D'Haultfœuille, X., Guyonvarch, Y., 2021. DID_MULTIPLEGT: stata module to estimate sharp Difference-in-Difference designs with multiple groups and periods. Statistical Software Components S458643. Boston Coll. Dep. Econ. Revis. 03 Jan 2021.

Chien Y.L., 2015. What Drives Long-Run Economic Growth?. Federal Reserve Bank of St. Louis.

Dorsey, E.R., de Roulet, J., Thompson, J.P., et al., 2010. Financial anatomy of biomedical research, 2003 – 2008. J. Am. Med. Assoc. (13).

DrugCentral (2021). DrugCentral 2020 Online drug compendium.
Federal Reserve Bank of St. Louis , 2021. Real Median Household Income in the United States.
Gomes, T., Tadrous, M., Mamdani, M.M., Paterson, J.M., Juurlink, D.N., 2018. The burden of opioid-related mortality in the united states. JAMA Netw. Open 1 (2), e180217.
Grossman, G.M., Helpman, E., 1991. Quality ladders in the theory of growth. Rev. Econ. Stud. 58 (1), 43–61.
Hales, C.M., Carroll, M.D., Fryar, C.D., Ogden, C.L., 2017. Prevalence of obesity among adults and youth: United States, 2015–2016. NCHS data brief, no 288. Hyattsville. MD Natl. Cent. Health Stat.
Jones, C.I., 2002. Sources of U.S. economic growth in a world of ideas. Am. Econ. Rev. 220–239.
Jovanovic, B., Yatsenko, Y., 2012. Investment in vintage capital. J. Econ. Theory 147 (2), 551–569.
Lichtenberg, F.R., 2014. Has medical innovation reduced cancer mortality? CESifo Econ. Stud. 60 (1), 135–177.
Lichtenberg, F.R., 2018. The impact of new drug launches on hospitalization in 2015 for 67 medical conditions in 15 OECD countries: a two-way fixed-effects analysis. Forum Health Econ. Policy 21 (2) (December.).
Lichtenberg, F.R., 2019. The impact of access to prescription drugs on disability in eleven European countries. Disabil. Health J. 12 (3), 375–386.
Lichtenberg, F.R., 2020. Are estimates of 'potential gains in life expectancy' potentially unreliable? Public Health 189, 115–116.
Lleras-Muney A., Lichtenberg F.R., 2005. The Effect of Education on Medical Technology Adoption: Are the More Educated More Likely to Use New Drugs? Annales d'Economie et Statistique 79/80: 671–696.
Murphy, K.M., Topel, R.H., 2006. The value of health and longevity. J. Political Econ. 114 (5), 871–904.
National Bureau of Economic Research, 2021. Vital Statistics NCHS Multiple Cause of Death Data files.
Nordhaus, W.D., 2005. Irving fisher and the contribution of improved longevity to living standards. Am. J. Econ. Sociol. 64 (1), 367–392.
OECD, 2021. OECD Health Statistics 2021 database.
Robine, J.-M., 2018. Age at death, the return of an old metric whose importance is growing. Aging Clin. Exp. Res. 30, 1147–1149.
Romer, P., 1990. Endogenous technological change. J. Political Econ. 98 (5), S71–S102. Part 2:
Royal Swedish Academy of Sciences, 1987. The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 198.
Solow, R., 1960. Investment and technological progress. In: Arrow, K., Karlin, S., Suppes, P. (Eds.), Mathematical methods in the social sciences, 1959. Stanford. CA: Stanford University Press.
State of New Jersey Department of Health, 2021. New Jersey State Health Assessment Data, Health Indicator Report of Average Age at Death.
U.S. Centers for Disease Control and Prevention QuickStats: Percentage of Deaths from External Causes, by Age Group — United States, 2017 MMWR Morb. Mortal. Wkly Rep. 68 2019 710.
U.S. Centers for Disease Control and Prevention, 2021. National Center for Health Statistics. Multiple Cause of Death 1999–2020 on CDC WONDER Online Database.
U.S. Department of Veterans Affairs Health Economics Resource Center, 2021. Cost-Effectiveness Analysis.
United Nations Development Programme, 2022. Human Development Index.
World Health Organization, 2021a.
World Health Organization, 2021b. WHO Mortality Database.
World Health Organization, 2021c. Anatomical Therapeutic Chemical (ATC) Classification.