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Medical Innovations and Ageing: A Health Economics Perspective

Abstract

This paper discusses the relationship between medical innovations and ageing from a health economics perspective and surveys empirical evidence on medical R&D incentives, R&D costs of pharmaceuticals, and the cost-effectiveness of health innovations. Particular focus is on the endogeneity of medical technological progress to expected market size and on the conceptualization of ageing as an accumulation of health deficits. The paper also discusses the role of medical progress for longevity and health inequality and presents a framework to assess the effect of increased longevity on the value of life.

JEL-Codes: I100, O300.

Keywords: healthcare, health deficits, health innovations, medical technological progress, longevity.

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1 Introduction

Starting with 19th-century smallpox vaccination programs in most advanced countries, medical technological progress has had a major impact on the evolution of human well-being by reducing morbidity at any age and increasing life expectancy (Cutler et al., 2006a, 2006b; Skinner and Staiger, 2015).

The extent of these effects is inevitably linked to the access of the population to health innovations. The well-known conjecture of Newhouse (1992) holds that medical innovations induce health spending to grow faster than income. Three channels are conceivable. First, diagnosing or treating any given health condition could become more expensive as medical technology advances. Examples are computed tomography (CT) and magnetic resonance imaging (MRI) which have greatly improved medical imaging compared to standard radiography (X-ray) but are also more costly. Similarly, personalized cancer medicine – based on an analysis of human gene mutations that cause cancer – is typically more expensive than standard chemotherapy (Tannock and Hickman, 2016). With respect to communicable diseases, human immunodeficiency virus (HIV) or hepatitis C virus (HCV) infections have only become treatable quite recently due to modern anti-viral pharmaceuticals. Second, broad utilization of new health goods induces demographic change towards a larger fraction of the elderly in the population. This is likely to raise costs for medical treatment despite health status improvements over time for a given age (e.g., Zweifel et al., 2005; Bech et al., 2011; Breyer et al., 2015). Third, better medical technology is likely to increase the demand for health insurance and treatments, thus raising health expenditure for given income (Weisbrod, 1991; Chandra and Skinner, 2012).

In turn, medical technological progress itself is endogenous to healthcare utilization, as expected market size faced by potential innovators affects research and development (R&D) investments (e.g., Romer, 1990; Weisbrod, 1991). Thus, limiting healthcare access may have severe long-term consequences for morbidity and longevity advancements by disincentivizing medical R&D effort (Okunade and Murthy, 2002; Böhm et al., 2021).

This paper discusses the relationship between medical innovations, demographic change, health expenditure, longevity, and health inequality in the light of empirical evidence. Specifically, it explains how the dynamic interaction between medical technological progress and healthcare spending drives biological ageing.[1] The paper also develops a framework to evaluate the effect of increased longevity on the value of life, examines policy implications, and identifies open research questions.

The remainder of the paper is structured as follows. The following section presents evidence on the evolution of healthcare expenditure, morbidity, and life expectancy. Section 3 reviews the literature on the effectiveness of medical technological progress for improving longevity while section 4 discusses evidence on medical research and development (R&D) costs and patent values. Section 5 develops a life-cycle model with stochastic survival and discusses how health outcomes affect the value of a statistical life (VSL). Section 6 presents possible conceptualizations to capture the dynamic relationship between medical technological progress and the ageing process in life-cycle models. Section 7 discusses the impact of health innovations on health inequality and section 8 suggests avenues for future research. The last section concludes.

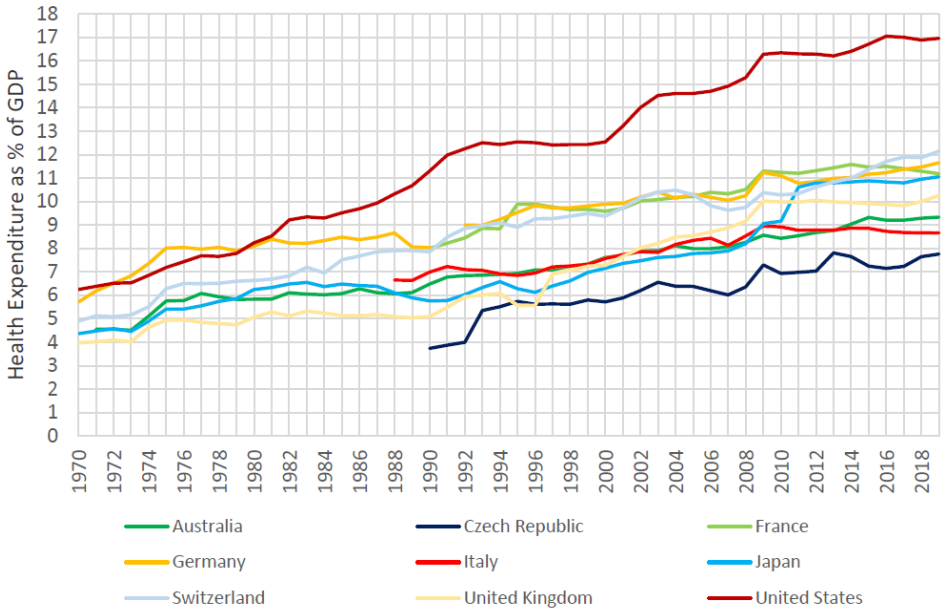
2 Trends in Health Expenditure, Morbidity, and Life Expectancy

Okunade and Murthy (2002) analyze to what extent per capita real income and technological change (proxied by total R&D and health R&D spending) have driven real healthcare expenditure per capita in the United States during the 1960–1997 period. In support of Newhouse (1992), they find a stable, statistically significant, and positive long-run relationship between income, productivity, and health spending. Underlining the importance of health innovations in determining the fraction of total income devoted

[1] The focus of this chapter is thus different to static contexts addressing, for instance, the role of co-payment rates in health insurance contracts and price-setting power of pharmaceutical companies for medical innovations (Garber et al., 2006; Lakdawalla and Sood, 2009, 2013; Grossmann, 2013).

to healthcare, Acemoglu et al. (2013) and Baltagi et al. (2017) argue that rising income over time (exogenously driven by rising total productivity) cannot explain rising health expenditure shares. In fact, they estimate an income elasticity of health expenditure below unity. Also institutional changes like healthcare reforms and other only occasionally changing variables are inconsistent with the continuous rise of health expenditure shares over time (Chernew and Newhouse, 2011).

Figure 1. Evolution of total health expenditure as percent of GDP, 1970-2018



Data source: OECD (2020)

Figure 1 shows the evolution of total health expenditure relative to the gross domestic product (GDP) of selected Organisation for Economic Co-operation and Development (OECD) countries. We see a secular increase in all countries. In the United States, the health expenditure share increased from 6.5 percent in 1970 to 17 percent in 2019, the highest level among OECD countries. Other advanced countries like Germany had similar health expenditure shares as the United States in 1970 but ended up with considerably lower ones (12 percent or less). Transition countries, represented in Figure 1 by the Czech

Republic, started out at lower levels in 1990 but show a similar upward trend. About 12–14 percent of total health spending was on nondurable medical goods like pharmaceuticals in France, Germany, Switzerland, the United Kingdom, and the United States and about 18 percent in Italy and Japan (OECD, 2020).

Table 1. Health care utilization and health care resources (selected indicators), 2018 or nearest year

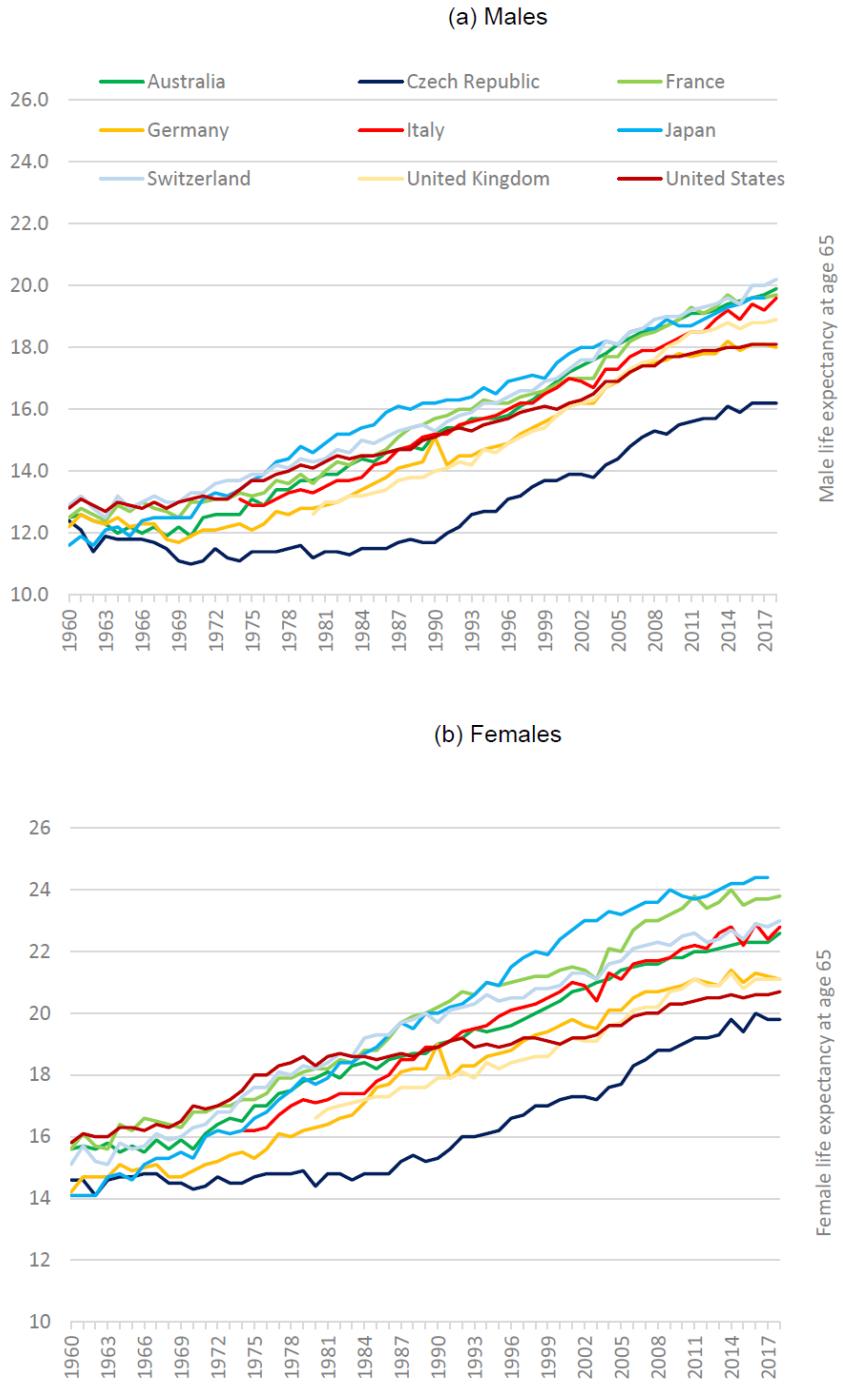
	CT exams per 1000 pop.	*MRI exams per 1000 pop.*	*Doctors consultations per capita*	*Hospital beds per 1000 pop.*	*Physicians per 1000 pop.*	*Nurses per 1000 pop.*
Australia	134.6	48.1	7.8	3.8[b]	3.8	11.9
Czech Republic	110.9	54.7	8.2	6.6	4.0	8.1
France	195.7	119.6	5.9[a]	5.9	3.2	10.8
Germany	153.2[a]	149.2[a]	9.9	8.0[a]	4.3	13.2
Italy	93.6	73.7	6.8[d]	3.1	4.0	5.7
Japan	230.8[c]	112.3[c]	12.6[a]	13.0	2.5	11.8
Switzerland	113.9[g]	77.8[g]	4.3[a]	4.6	4.3	17.6
United Kingdom	101.2[g]	66.9[g]	5.0[f]	2.5	2.8	7.8
United States	271.5	119.4	4.0[e]	2.9[a]	2.6	11.9

a. 2017, b. 2016, c. 2014, d. 2013, e. 2011, f. 2009, g. Exams in hospitals only.

Data source: OECD (2020)

Remarkably, according to Table 1, doctor visits per capita in the United States (2.5 in 2019) are considerably fewer than, say, in Germany and Japan (9.9 and 12.6 in 2019, respectively), despite considerably higher per capita health spending in the United States. Also the number of physicians and hospital beds relative to population size in the United States are at the lower end among the advanced countries while there is a more extensive use of technology-intensive examinations (particularly CT exams) than in other countries. Switzerland stands out with respect to the number of nurses relative to its population size, whereas Japan has the highest number of hospital beds.

Figure 2. Evolution of remaining period life expectancy at age 65, 1960-2018



Data source: OECD (2020)

Figure 2 documents for both males and females considerable and gradual increases of remaining life expectancy at age 65 in most countries since 1960, based on contemporaneous mortality rates (period life expectancy). The increase was particularly high in Japan, with about 8 years for males and 10 years for females. Japan also has the highest remaining life expectancy for females in 2018 (24.4 years) and is in the top group for males jointly with Switzerland, France, Italy, and Australia. Remaining life expectancy of males in the United States, Germany, and the United Kingdom are about 18 years – about 2 years less than in the leading countries. In these countries, females can expect to live about 21 more years when reaching age 65, which is about 3 years less than in Japan and France.

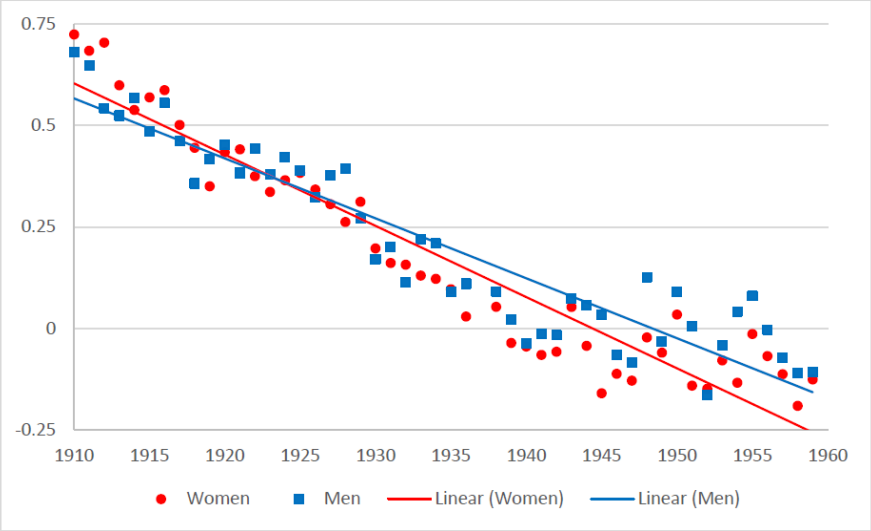
Paralleling rising life expectancy over time is a slowdown in the biological ageing process as represented by the evolution of the so-called health deficit (or frailty) index, which is defined as the fraction of bodily impairments present in a person out of a sufficiently large list of potential health deficits.[2] Empirically, health deficits correlate exponentially with age (e.g., Mitnitski et al., 2002a; Harttgen et al., 2013) and are a highly relevant determinant of the probability of death (e.g., Mitnitski et al., 2002a, 2002b, 2005, 2006, 2007). Abeliansky and Strulik (2019) compute a health deficit index for a panel of 14 European Countries and six waves of the Survey of Health, Ageing, and Retirement in Europe (SHARE). They document that later born cohorts, at the same age, are healthier than earlier born cohorts. For each year of later birth, health deficits decline by 1.4–1.5 percent on average. Differences between men and women, among countries, and over time are insignificant. The level of health deficits experienced at age 65 by individuals born in 1920 resembles that experienced at age 85 by individuals born in 1945.

In a similar vein, Abeliansky et al. (2020) focus on the 50–90 age group to study the evolution of the health deficit index of U.S. Americans born 1904–1966. Using 13 waves of the Health and Retirement Study (compiled by the RAND Center of the Study of Aging)

[2]See, e.g., Searle et al. (2008). Strulik (2022) provides an excellent introduction to the conceptualization of the frailty index as a measure of aging.

from 1992 to 2016, they find that the average elderly American develops 5 percent more health deficits per year. For each year of later birth, health deficits decline by about 1 percent on average, documenting steady improvements in the health status over time. Figure 3 visualizes the health trend by plotting the estimated coefficients of year-of-birth dummy variables for birth cohorts 1910–1959 in a regression with the log of the individual health deficit index as dependent variable. The main explanatory variable is individual age, capturing that health deficits grow exponentially over the life-cycle (e.g., Mitnitski et al., 2002a; Harttgen et al., 2013).[3] We see a slightly slower decline in health deficits over time for men than for women.

Figure 3. Year-of-birth effects in the relationship between the log of health deficits and age in the U.S., birth cohorts 1910-1959



Data source: Abeliansky, Erel and Strulik (2020).

Note: Displays coefficients of year-of-birth (*yob*) dummies in a regression of the type $\log(d_i) = \alpha + \beta \cdot age_i + \sum_t \gamma_t \cdot yob_{it} + \varepsilon_i$, where d_i denotes the health deficit index of individual *i*, *t* is the year of birth, and ε_i is the error term. See Abeliansky et al. (2020) for details. Red circles: women, blue squares: men. The lines show linear time trends of gender-specific coefficients γ_t (red for women, blue for men).

[3] Harttgen et al. (2013) document the pattern for 14 European countries and for China, Ghana, India, Mexico, the Russian Federation, and South Africa.

3 Health Effects and Cost-Effectiveness of Medical Innovations

Mounting evidence highlights the importance of medical innovations in health outcomes and the cost-effectiveness of health treatments.

For instance, antibiotics like penicillin and sulfa drugs, which were invented in the 1930s and 1940s for treating bacterial infections that cause pneumonia, tuberculosis, syphilis, dysentery, and bacterial meningitis, substantially reduced mortality rates in the United States in the mid-20th century (Cutler et al., 2006a). Incremental advances to overcome resistance to the first- and second-generation antibiotics followed.

Lichtenberg (2007) showed that pharmaceutical innovation significantly improves health outcomes for treating 92 potentially lethal diseases. Using prescription drug use data from 1996–2003 he finds that a higher percentage of prescriptions of later vintages have led to larger declines in mortality rates and hospitalization in the United States. More recently, Lichtenberg (2020) showed that increases in the approvals of new cancer drugs in the United States in the period 2000–2014 have been associated with larger declines in premature mortality and hospitalization. Zhuo et al. (2020) developed a microsimulation model for Japan to show that directly-acting antivirals (DAAs), a class of HCV infection treatment available since 2014, cost less than US$ 10,000 per quality-adjusted life year (QALY) gained by the treatment.[4] At the mean age of those infected with HCV (age 60), life expectancy rose by about 3 years. Drugs suppressing HIV may be less cost-effective. Borre et al. (2017) estimated that implementing the U.S. National HIV/AIDS Strategy would on average cost US$ 68,900 per QALY gained. However, that figure is still below the US$ 100,000–150,000 cost-effectiveness threshold suggested by more recent literature (e.g., Neumann et al., 2014).

Critics point out that not all pharmaceutical R&D effort is targeted to improving health effects of treatments. So-called "me-too" drugs are a prime example. These have

[4]Nevertheless, given the comparably high treatment costs in absolute terms, severe rationing measures to limit coverage of such drugs had been in place in many advanced countries (WHO, 2016).

similar chemical structures as an original drug and are used for the same therapeutic purposes as "first-in-class" drugs (Gagne and Choudhry, 2011; Aronson and Green, 2020). Examples are the many tricyclic antidepressants, beta-blockers, and statins. Some "me-too" drugs are the outcome of parallel development in different companies, whereas others come from R&D targeted to the purpose of obtaining a new patent with comparably little effort (Régnier, 2013). The latter is problematic when it raises costs for consumers vis-a-vis generics without extra value. However, some "me-too" drugs have fewer side effects, less drug-drug interactions, and show greater efficiacy at least for some patient groups (Lakdawalla, 2018).

Cutler et al. (2006a) argued that, despite large morbidity effects, vaccination has played a minor role in short-run mortality reduction, except for the successful eradication of poliomyelitis in many countries. That said, morbidity caused by diseases like measles, hepatitis B, yellow fever, and tetanus may significantly raise mortality risk in the longer run. In other words, vaccination against these diseases could significantly improve longevity. The same is potentially true for COVID-19 vaccines that do not only reduce the number of immediate deaths but also prevent longer-term bodily impairments after convalescence (Long Covid) that could lead to the development of further health deficits.

An example of nonpharmaceutical medical technological progress involves treating stenosis, a coronary artery disease that narrows coronary arteries in a life-threatening way. Instead of placing bare-metal stents (BMS) via balloon dilation during a percutaneous coronary intervention, it is now possible to use coronary drug-eluting stents (DES). These release antiproliferative and anti-inflammatory substances to avoid the frequent recurrence of stenosis associated with BMS (Baschet et al., 2016). Second-generation DES have been introduced to prevent thrombosis that may be triggered by placing stents. In a meta-analysis, Baschet et al. (2016) showed that DES lead to fewer complications than BMS and are generally cost-effective. Ford et al. (2007) argued that about half of the decrease in the age-adjusted death rate for coronary heart disease can be attributed to

treatments and the other half to changes in risk factors (e.g., lower cholesterol levels and lower systolic blood pressure).

4 R&D Costs and Patent Values

An extensive literature addresses the R&D costs of new drug discoveries. Such information is important to discuss whether price-setting power is stronger than needed to provide R&D incentives. The potential to lower prices of pharmaceuticals without compromising on medical progress may indirectly improve longevity by extending drug access in healthcare systems.

In a meta-study based on 13 articles published from 1980 to 2009, Morgan et al. (2011) reported estimates of the average non-capitalized cost of drug development in the wide range of US$ 92 million to US$ 883.6 million in 2009 dollars, where estimates for later periods are larger.[5] DiMasi et al. (2016) estimated the R&D costs of 106 randomly selected new drugs from 10 pharmaceutical firms that were first tested in humans between 1995 and 2007. They accounted for abandoned compounds during clinical trials by linking them to the costs of compounds that obtained market approval; that is, they corrected for R&D failure risk.[6] Their evidence suggests an average non-capitalized R&D cost per new drug prior to approval of US$ 1,395 million in 2013 dollars (and, on average, additional R&D costs of US$ 566 million after initial approval). Average capitalized costs based on an annual real interest rate of 10.5 percent amount to US$ 2,558 million. DiMasi et al. (2016) also provided a literature review suggesting that R&D costs have risen substantially in the last decades while success rates have decreased.

Estimating R&D costs from publicly available sources is preferable to self-reported

[5] Noncapitalized cost does not account for opportunity costs of the use of capital that arises from the time lag between clinical trials and market introduction.

[6] DiMasi et al. (2016) find that drugs entering clinical trials have a 12 percent probability of success (POS). Lo et al. (2020) evaluate the POS of clinical trials for 2,544 vaccine and 6,829 nonvaccine programs targeting infectious diseases. They arrive at average POS estimates of 39.6 percent for industry-sponsored vaccine programs and 16.3 percent for industry-sponsored anti-infective therapeutics.

costs.[7] Wouters et al. (2020) provided high-quality estimates for 63 (out of 355) new therapeutic drugs and biologic agents approved by the U.S. Food and Drug Administration (FDA) between 2009 and 2018. Dividing R&D expenditures by clinical phase–specific success rates to correct for failed trials, the estimated median capitalized R&D cost (based on a real interest rate of 10.5 percent) for a single drug was US $985 million in 2018 dollars (mean costs were US$ 1,335.9 million). Prasad and Mailankody (2017) estimated the R&D costs for 10 cancer drugs approved by the FDA between 2005 and 2015, reporting noncapitalized median and mean cost of development of a single drug of US $648 million and US$719.8 million in 2017 dollars, respectively. Capitalized with an interest rate of 9 percent, the median cost was US$ 793.6 million and the mean cost was US$ 969.4 million. R&D costs for novel drugs were higher than for next-in-class drugs. Prasad and Mailankody (2017) reported a mean sales revenue of US$ 6,699.1 million. This suggests that R&D costs were covered by a wide margin also when correcting for R&D failure risk. In a similar vein, Tay-Teo et al. (2019) estimated for 99 cancer drugs approved by the FDA from 1989 to 2017 that the median sales revenue was about 14.5 times higher than the median R&D costs estimated by Prasad and Mailankody (2017). They also found that the drugs continued to generate high revenues after patent expiry.

Revenue is not profit, however. Estimating profits also requires data on production and marketing costs. Songane and Grossmann (2021) estimated the ratio of R&D costs to the global present-discounted value (PDV) of annual profits until patent expiry of the leading human papillomavirus (HPV) vaccine Gardasil by Merck. They arrived at an estimate of 2.5–6.8 percent, depending on the assumed discount rate. This is considerably lower than the success rates in clinical trials for vaccines reported in the literature, suggesting stronger market power than needed to incentivize R&D.[8] Songane and Grossmann (2021) also estimated that marketing costs for Gardasil are at least as high as

[7] Cost information provided by pharmaceutical companies is often upward biased for strategic reasons (e.g., for price negotiations with healthcare providers). Light et al. (2009) discussed the issue for the case of rotavirus vaccines.

[8] Profits and mark-ups have been particularly high in the United States and China. The noncapitalized Gardasil R&D costs in clinical trials were around US$ 1.1 billion in 2018 dollars.

R&D costs. This parallels Lakdawalla (2018, p. 438) who states: "The pharmaceutical industry spends approximately the same amount of money on marketing as it does on innovation investments."

5 Life-Cycle Considerations and the Value of Life

This section presents a life-cycle model with stochastic survival. The framework enables us to discuss how health improvements affect welfare and to analyze the endogenous interaction between medical R&D investment and longevity.

5.1 Lifetime Utility, Budget Constraint, and Optimization

Consider an age-structured population in discrete time with a homogenous group of individuals of size $N_{v,t}$ from cohort v in period t. Each period a new cohort is born. Accounting for survival probabilities and discounting, expected remaining lifetime utility at age $s \geq 0$ of a representative agent from cohort v is given by[9]

$$U_v^s(i) = \sum_{t=v+s}^{v+T-1} \rho^{t-v} N_{v,t} S_{v,t} u(c_{v,t}, \ell_{v,t}; d_{v,t}), \tag{1}$$

where $S_{v,t}$ is the unconditional probability to survive to age $t-v$, $c_{v,t}$ denotes the per capita consumption level of a single final good (with price normalized to unity) in period t, $\ell_{v,t}$ the hours worked, $d_{v,t}$ the individual health deficits, $\rho \in (0,1]$ the discount rate, and $T > 0$ the maximum length of life. $u(c, \ell; d)$ is the instantaneous utility function which is quasi-concave as a function of choice variables (c, ℓ) and has derivatives $u_c > 0$, $u_\ell < 0$, $u_d < 0$. Moreover, suppose cross-derivative $u_{cd} < 0$ holds, in line with the evidence that lower health status (more health deficits) is associated with a lower marginal utility of

[9] See, e.g., Arthur (1981), Rosen (1988), Murphy and Topel (2006), and Hall and Jones (2007) for lifetime utility formulations in the context of stochastic survival.

consumption (Finkelstein et al., 2013).[10]

For $t \geq v$, financial wealth of cohort v accumulates according to

$$A_{v,t+1} = (1 + r_{v,t})A_{v,t} + N_{v,t}(y_{v,t} - c_{v,t}), \tag{2}$$

where $1 + r_{v,t}$ is the cohort-specific interest factor in a perfect annuity market between date t and $t + 1$ and $y_{v,t}$ is (net) non-wealth income. Initial asset holding $A_{v,v+s} \geq 0$ is given and terminal condition $A_{v,v+T} \geq 0$ must hold. Denote by $w_{v,t}$ the cohort-specific wage rate. Non-wealth income consists of net earnings and other life-contingent income (like pension benefits), $I_{v,t}$, that, for simplicity, is considered exogenous:

$$y_{v,t} = F_{v,t}(w_{v,t}\ell_{v,t}) + I_{v,t}, \tag{3}$$

where function $F_{v,t}$ transforms gross earnings, $w_{v,t}\ell_{v,t}$, into net earnings (after taxes, social security contributions, and health insurance contributions).[11]

The mortality rate is the probability $m_{v,t}$ of a member from cohort v dying between period t and $t + 1$, conditional on having reached age $t - v \geq 0$. By definition, survival rates, $S_{v,t}$, and mortality rates are related by $m_{v,t} = -\frac{S_{v,t+1} - S_{v,t}}{S_{v,t}}$. For simplicity, consider a small open economy with exogenous market interest rate, $\bar{r}$. In a perfect annuity market with fair insurance within a cohort,[12]

$$1 + r_{v,t} = \frac{1 + \bar{r}}{1 - m_{v,t-1}}. \tag{4}$$

Using (3), (4), $m_{v,v+s-1} = 0$, $S_{v,t} = S_{v,v+s}\prod_{u=v+s}^{t-1}(1 - m_{v,u})$, and the fact that terminal condition, $A_{v,v+T} \geq 0$, must be binding (as not holding wealth after certain death is

[10] We could also assume $u_{\ell d} < 0$ to capture that lower health status raises the disutility from effort provision (Grossmann et al., 2021).

[11] Function F may differ before and after statutory retirement age and may depend on time because of social security reforms. We abstract from out-of-pocket health expenditure. This may be restrictive when health insurance does not cover innovative treatments that significantly impact life expectancy.

[12] That is, zero-profit insurance companies pay a rate of return above the market interest rate, $\bar{r}$, and keep the wealth of the deceased.

optimal), equation of motion (2) for asset accumulation from the perspective of age s implies that

$$0 = \tilde{A}_{v,v+s} + \sum_{t=v+s}^{v+T-1} \left(N_{v,t} S_{v,t} \frac{F(w_{v,t}\ell_{v,t}) + I_{v,t} - c_{v,t}}{(1+\bar{r})^{t-v-s}} \right), \tag{5}$$

where $\tilde{A}_{v,v+s} \equiv (1+\bar{r}) A_{v,v+s} \geq 0$. The utility-maximization problem from the perspective of age s then reads as

$$\max_{\{c_{v,t},\ell_{v,t}\}} \sum_{t=v+s}^{v+T-1} \rho^{t-v} N_{v,t} S_{v,t} u(c_{v,t}, \ell_{v,t}; d_{v,t}) \text{ s.t. } (5). \tag{6}$$

The first-order conditions result in the standard Euler equation that governs the motion of consumption. When time path $\{I_{v,t}\}$ is exogenous,[13] the well-known labor supply condition that equates the marginal rate of substitution (MRS) between consumption and working hours with the derivative of net earnings (3) with respect to labor supply also holds.

5.2 Value of a Statistical Life (VSL)

The VSL is defined as the willingness to pay for an additional person at age s in terms of wealth (Hall and Jones, 2007).[14] Combining the first-order conditions of the household optimization problem (6) with (5), one can derive in analogy to Murphy and Topel (2006) the VSL for a member of cohort v at age s, VSL_v^s, as[15]

$$VSL_v^s = \sum_{t=v+s}^{v+T-1} \frac{S_{v,t}}{(1+\bar{r})^{t-v}} \frac{u(c_{v,t}, \ell_{v,t}; d_{v,t})}{u_c(c_{v,t}, \ell_{v,t}; d_{v,t})} - \frac{\tilde{A}_{v,v+s}}{N_{v,v+s}}. \tag{7}$$

[13] When $I_{v,t}$ is pension income, however, it is endogenous to labor supply – a fact that rational households consider (e.g. Grossmann et al., 2021).

[14] That is, the VSL is the MRS between $N_{v,v+s}$ and $\tilde{A}_{v,v+s}$, using the Lagrangian for the optimization problem (6). In the presented framework, the definition of the VSL is identical to the MRS between wealth and mortality risk (Murphy and Topel, 2006).

[15] Murphy and Topel (2006) derived the VSL expression in continuous time for a single agent.

It is given by the PDV of the expected stream of the life-year utility values, u/u_c, minus initial per capita wealth. Adjustment for the marginal utility of consumption transforms utils into real dollars. Interestingly, for given survival rates and a given age, the VSL is not necessarily higher for those with better health. According to (7), this would require $u(c, \ell, d)$ to decrease faster in health deficits d than $u_c(c, \ell, d)$.

Murphy and Topel (2006) gauged the impact of exogenous longevity improvements on the VSL in a calibrated life-cycle model with stochastic survival.[16] The quality of life (health status) entering instantaneous utility u is not linked to mortality and u/u_c is independent of the quality of life. Notably, these assumptions imply that the VSL is independent of the quality of life, too. According to their analysis, the representative U.S. individual gained about 1.2 million US$ over the 20th century and that the gains to society between 1970 and 2000 are worth about half of the GDP. This suggests that health innovations that improve longevity have substantial effects on the value of life – a result that is best understood from the feature that the marginal intertemporal utility from increasing survival rates is non-decreasing, according to (1) and (7). Lakdawalla et al. (2017) argued that Murphy and Topel even underestimate the benefits from improvements in the quality of life because they neglect the insurance value from lowering health risk that comes from health innovations.

Jones and Klenow (2016) measured welfare gains from increased longevity by consumption equivalents rather than by estimating the effects on the value of life. They argue that Western Europe is closer to the United States in terms of welfare than in terms of GDP per capita thanks to higher life expectancy. In contrast, welfare differences between developing countries and the United States are greater than GDP per capita differences.

[16] Calibration typically uses estimates of the risk premium for the likelihood of fatal injury in the labor market. Viscusi and Aldy (2003) provide a meta-analysis of the related literature and find a median estimated VSL at birth of US$ 7 million in the United States (in 2000 US$).

6 Morbidity, Healthcare Demand, and Medical R&D

This section links healthcare demand to incentives for health innovations under alternative conceptualizations of the relationship between health status and mortality.

6.1 Health Deficit Approach

Assuming that the quality of life enters instantaneous utility u independently of mortality, Murphy and Topel (2006) noted that: "For example, technologies that improve mental health or reduce the effects of arthritis may increase instantaneous utility without affecting longevity" (p. 876). This view starkly contrasts gerontology research on the health deficit index, as surveyed by Strulik (2022). Mitnitski et al. (2002a, 2002b, 2005, 2006, 2007) showed that the presence of (many) health deficits is conducive to the development of further health deficits and that a lower health deficit index is associated with lower mortality rates in the elderly population. Their list of potential health deficits includes, for instance, the physical difficulty to move, that may contribute to developing cardiovascular disease. This blurs the border between life-threatening diseases and bodily impairments.

Formally, the argument suggests that the (average) mortality rate within cohort v in period t can be written as $m_{v,t} = M(d_{v,t})$, $M' > 0$, where $d_{v,t}$ follows a first-order difference equation. Consequently, cohort-specific mortality rates become path dependent (i.e., technically, they are state variables). Hence, even if the quality of life as measured by health deficits did not affect u/u_c in the VSL expression in Eq. (7), it could still affect the VSL by affecting mortality.

Dalgaard and Strulik (2014) have incorporated the notion of human ageing as an (approximately exponential) health deficit accumulation process in a life-cycle model.[17]

[17] Dalgaard and Strulik (2014) focus on a single cohort in continuous-time to explain the Preston curve by deliberate health spending patterns. Their approach has been applied in numerous non-innovation contexts (e.g., Dalgaard and Strulik, 2017; Schünemann et al., 2017a, 2017b, 2020; Strulik, 2018a, 2018b; Strulik and Werner, 2021).

For our purposes, suppose health deficits of a member from cohort v evolve according to

$$d_{v,t+1} - d_{v,t} = \alpha_v \cdot d_{v,t} - g(h_{v,t}), \tag{8}$$

where $h_{v,t}$ is a measure of health inputs (preventive and curative health care) and $g(\cdot)$ is an increasing function. From the perspective of age s, $d_{v,v+s} > 0$ is given. Parameter $\alpha_v > 0$ is the growth rate of the health deficit index absent health interventions. It may be cohort-specific because of environmental and cultural factors.

To capture the higher need for health treatment of more impaired individuals, suppose the health input is an increasing function of both health deficits and the average quality of the latest vintages in a wide range of health goods (and services) available in the market. Böhm et al. (2021) motivated the form $g(h_{v,t}) = h_{v,t} = \kappa_t \cdot d_{v,t} \cdot q_t$, where κ_t may be interpreted as a policy parameter that captures the access to health treatment in the health insurance system. Combined with Eq. (8), the growth rate of (average) health deficits in cohort v is given by $\alpha_v - \kappa_t \cdot q_t$. It depends on the interaction between access and quality of health goods, which is consistent with Murray (2017). Medical progress raising the quality of health goods thus reduces the growth rate of health deficits over time, consistent with the observation of Abeliansky and Strulik (2019) and Abeliansky et al. (2020) that later born cohorts display, for a given age, fewer health deficits (Figure 3). The effect is enlarged when access to modern health goods improves.

Analogously to models of endogenous technological change in growth economics (e.g., Romer, 1990; Grossman and Helpman, 1991; Aghion and Howitt, 2005), the evolution of the average quality of health goods may be conceptualized as first-order difference equation

$$q_{t+1} - q_t = Q(L_t, q_t), \tag{9}$$

where Q is an increasing function of medical R&D (labor) input, L, and may depend on health good quality, q.[18] For instance, Böhm et al. (2021) arrived at process (9) in a

[18] That quality index q enters $Q(L, q)$ may capture externalities from R&D investment (e.g., Jones and

framework where competitive R&D firms invest in risky medical R&D. R&D incentives are determined by the expected PDV of the profit stream resulting from a successful innovation. Consequently, medical R&D investments critically depend on the size of the market for a new health good (vintage), i.e., on health deficits among the current and future age-structured population and on healthcare coverage (parameter κ_t). The latter assumption echoes Weisbrod (1991) who conjectured that the expansion of U.S. healthcare insurance has incentivized medical R&D.

The baseline calibrated model of Böhm et al. (2021) suggests substantial future increases in cohort life expectancy.[19] Cohort life expectancy at birth for those born in the 21st century is predicted to exceed 100 years, and considerably lower health deficits are expected among the elderly for later cohorts. This is caused by endogenous medical progress that raises q_t over time. The associated change in the demographic structure is predicted to increase the health expenditure share moderately, which is in line with empirical evidence (e.g., Zweifel et al., 2005; Bech et al., 2011; Breyer et al., 2015). Pervasively limiting access to healthcare in advanced economies (leading to a decrease in κ_t over time) to prevent health expenditure shares from increasing is predicted to considerably lower life expectancy for future generations compared with the baseline model. Calibrating the VSL to US$ 6 million, this would lead to a welfare loss (measured by consumption equivalents) of about one fifth for those born in the beginning of the 21st century. The welfare loss is even higher for later cohorts. The main reason for the considerable size of the detrimental effects of healthcare rationing is the associated reduction in market size that disincentivizes health innovations. This echoes Chandra and Skinner (2012) who pointed to the economic and political resistance in the United States to finance possibly rising health expenditure, with potentially adverse effects on medical technological progress.

Williams, 2000) or quality depreciation that may follow from mutations of viruses and bacteria (Böhm et al., 2021). Quality depreciation may imply that $Q(L, q)$ becomes zero in finite time, avoiding the "end of ageing" (De Grey and Rae, 2007) scenario, where $\alpha_v \leq \kappa_t \cdot q_t$.

[19] Cohort life expectancy accounts for predicted future declines in mortality rates while period life expectancy employs contemporaneously observed mortality rates.

6.2 Health Capital Approach

A key feature of the health deficit approach that makes it particularly suitable to analyze healthcare rationing effects is the path dependence of health deficits and mortality rates. The widely used health capital approach of Grossman (1972) also captures path dependence of health status. This approach treats individual health status as a latent state variable (health capital) that individuals can invest in and views ageing as depreciation of the health capital stock rather than as an accumulation of health deficits. Formally this is like capturing human capital accumulation (e.g., Lucas, 1988). It is fair to say, however, that it lacks foundation in medical science and has some undesirable implications. For instance, the health capital model assumes that an individual with good health experiences a greater decline of health than an individual with poor health (via health capital depreciation), contrary to the empirically established exponential growth of health deficits over the life cycle. It also implies that health investments decline in old age and near death (Strulik, 2015), contrary to the evidence suggesting the opposite.

The most interesting application for the purpose of this paper is the contribution by Fonseca et al. (2021), who analyzed an elaborate stochastic life-cycle model, where agents choose consumption, medical expenditure, and labor market participation (labor supply at the extensive margin). According to their analysis, medical technological progress is responsible for half of the increase in U.S. life expectancy over the period 1965–2005 but does not significantly contribute to observed healthcare spending growth. Rather, their evidence suggests that health insurance extension and general income growth have driven health expenditure growth. In line with this result, Finkelstein (2007) found that the introduction of Medicare in 1965 led to a large increase in U.S. hospital spending. Her analysis suggests that the overall spread of health insurance since 1950 could be responsible for about half of the increase in real per capita health spending.

6.3 Non-Path-Dependent Mortality

Hall and Jones (2007) and Jones (2016) made eye-opening contributions on the evolution of socially optimal investments in health in a growing economy. The models consider a representative individual of a single cohort, assuming that health spending contemporaneously affects mortality rates. In the context of an age-structured population, this means that the mortality rate of a member of cohort v at time t is given by $m_{v,t} = \tilde{m}(h_{v,t})$ with $\tilde{m}' < 0$, where $h_{v,t}$ denotes health spending. Thus, unlike in the health deficit approach where $m_{v,t} = M(d_{v,t})$, the mortality rate is a flow variable rather than a state variable.

Both papers point to a major role of the elasticity of consumption utility, $\gamma \equiv -cu_{cc}/u_c$. According to Hall and Jones (2007), if the marginal consumption utility is falling rapidly (i.e., if γ is significantly above unity), the health expenditure share in the economy should increase more than 30 percent until 2050. The result can be understood by the fact that, unlike consumption utility, increased survival linearly raises lifetime utility. As a result of rising health spending, life expectancy at birth would also increase significantly. In fact, $\gamma \gg 1$ is in line with most empirical estimates of the intertemporal elasticity of substitution (e.g., Havránek, 2015).[20]

In Hall and Jones (2007), medical technological progress is exogenous and reduces mortality rates over time for given health spending. In contrast, Jones (2016) endogenized the health technology. R&D labor can be directed to improving the effectiveness of health spending on mortality reduction or the quantity of the material consumption flow. This puts the optimal direction of technological change at the center of the analysis. Assuming $\tilde{m}(h) = h^{-\beta}$, Jones (2016) showed that in his favored case where $\gamma > 1 + \beta$ letting the fraction of scientists into medical R&D and the fraction of non-R&D labor for producing the health input both approach unity in the long run is optimal. For $\gamma < 1 + \beta$, the opposite result holds, i.e., the fraction of labor allocated to the life-saving sector approaches zero in the long run.

[20] The intertemporal elasticity of substitution measures the optimal substitution of present consumption for future consumption if the interest factor $(1 + \bar{r})$ increases. It is given by $1/\gamma$.

Frankovic and Kuhn (2018) proposed a multi-period overlapping generations model with endogenous health innovations that interact with the demand for healthcare. Mortality risk depends on health spending and the state of medical knowledge. Medical R&D investments are paid for by profits made in the healthcare sector, which features decreasing returns. The analysis shows that the expansion of health insurance was more important for U.S. health expenditure growth in the period 1960-2010 than (exogenous) income growth. The model can also explain a significant part of the observed U.S. life expectancy gains. As in Böhm et al. (2021), better access to healthcare fosters medical technological progress. Both contributions shed light on the interrelation between health expenditure and health innovations that are driven by the demand for healthcare.

6.4 Market Size Effects: Empirical Evidence

Does the empirical evidence support the transmission channel from changes in market size to changes in medical technology, as hypothesized by Weisbrod (1991)? Empirical estimates differ in both the measure of market size and the outcome measure (medical R&D investments or patents). Acemoglu and Linn (2004) and Dubois et al. (2015) were interested in the determinants of the number of prescription drug approvals. Acemoglu and Linn (2004) exploited that market demand for each therapeutic class changes over time as the age structure changes because the risk of specific illnesses varies with age. Specifically, they constructed for different drug categories potential drug market size by summing up the products of age-specific total income and age-specific drug expenditure shares over age groups, using U.S. data for the period 1970–2000. Their analysis suggests a major role of current market size for nongeneric drug approvals. Moreover, they found that both current and future market size considerably affect the approval of new molecular entities and generics. Anticipated increases in market size with a 10–20 year lead time significantly raises R&D investments. This is plausible given the considerable time span between the start of R&D investments and drug approvals. By contrast, past market size does not play a significant role.

Dubois et al. (2015) exploited data for 14 countries (10 advanced countries plus Brazil, China, Mexico and Turkey) and focused on new chemical entities. Market size for a therapeutic category is measured by the PDV of global sales revenue over 20 years (partly imputed). To address potential reverse causality problems, sales revenue for each country is instrumented by its GDP per capita, population size by gender and age (total and elderly), and mortality by disease targeted by a therapeutic category. The estimated equations include fixed effects for therapeutic categories and time. They found that a 1 percent increase in market size raises the number of innovations by 0.23 percent. Split by therapeutic categories, the market size elasticity is lowest for the cardiovascular system and blood-forming organs; it is highest for the nervous system and sensory organs.

Finkelstein (2004) and Blume-Kohout and Sood (2013) exploited policy reforms in the United States that affect market size and looked at their effect on clinical trials. Finkelstein (2004) evaluated the effect on the number of new vaccine clinical trials of (i) the adoption of the 1991 Centers for Disease Control and Prevention (CDC) recommendation that all infants be vaccinated against hepatitis B; (ii) the 1993 decision that Medicare (U.S. government health insurance for the elderly) covers all costs of influenza vaccinations for beneficiaries; and (iii) the introduction of the Vaccine Injury Compensation Fund in 1986 that liberated manufacturers from liability in case of adverse reactions to vaccination against polio, diphtheria-tetanus, measles-mumps-rubella, and pertussis. On average, these policies increased the number of clinical trials for new vaccines by a factor of 2.5.

Blume-Kohout and Sood (2013) considered the effect of introducing coverage of prescription drugs by Medicare Part D in 2006 on the number of pre-clinical and clinical trials. They found that a higher market share of prescriptions filled by Medicare beneficiaries is associated with larger increases of pharmaceutical R&D effort after implementation of Medicare Part D. Combined with the evidence that Medicare Part D has substantially increased the demand for pharmaceuticals among the elderly (e.g., Lichtenberg and Sun, 2007; Duggan et al., 2008; Schneeweiss et al., 2009), this is compelling evidence that

market size matters for R&D incentives.

Looking specifically at developing countries is also interesting. Using patent data for the period 1993–2009, Zhang and Nie (2021) showed that the implementation of a public health insurance program for rural residents in China considerably affected the number of pharmaceutical patents targeting diseases that are prevalent in rural areas. This does not necessarily mean, however, that stronger patent protection in developing countries spurs pharmaceutical innovation of foreign-based multinationals. Kyle and McGahan (2012) estimated how market size − defined as the number of deaths from a certain disease − contemporaneously affects the number of new clinical trials targeting the disease, and how it interacts with the adoption of the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement.[21] They found that TRIPS has not significantly raised R&D effort targeted to the diseases that are most prevalent in developing countries and explained the result with low drug affordability in those markets.

7 Effect of Health Innovations on Health Inequality

A pronounced socioeconomic health gradient exists. For instance, OECD (2019, Figure 3.5) indicated that the gap in life expectancy at age 30 between the tertiary educated and those with less than secondary schooling is, on average for 25 OECD countries, 6.9 years for men and 4 years for women. The gap among OECD members is highest in Eastern European countries. The literature offers various explanations for a socioeconomic health gradient related to differences in education, financial means, and the job environment. In their seminal contribution, Ehrlich and Chuma (1990) showed within the health capital framework of Grossman (1972) that optimal health expenditure and longevity that is endogenous to health spending depends on initial wealth. Becker (2007) discussed the education-health gradient in a two-period framework with endogenous investments in skill and health. Strulik (2018a, 2018b, 2019) endogenized unhealthy consumption within the

[21] TRIPS basically requires World Trade Organization (WTO) members to secure intellectual property rights of multinational firms.

health deficit framework. Strulik (2018a) showed that a higher return to education is not only linked to more education but also to a healthier lifestyle. Strulik (2019) explained unhealthy consumption by limited self-control. Strulik (2018b) and Galama and van Kippersluis (2019) presented life-cycle models with unhealthy behavior suggesting that declining marginal consumption utility is key for understanding the socioeconomic health gradient. Galama et al. (2020) surveyed the literature on causal effects of education (and education policy) vis-a-vis noncognitive skills on health (and unhealthy behavior) and reported mixed evidence. Conti et al. (2010) pointed to the important role of cognitive, noncognitive, and health endowments during childhood in health disparities among adults.

How do medical innovations affect the socioeconomic health gradient? To address this question, Glied and Lleras-Muney (2008) employed data on disease-specific mortality rates for 1980 and 1990 and cancer registry data for 1973–1993. Using state-level and cohort-level variation in compulsory schooling years, they found that a higher number of active ingredients (new molecular entities) approved by the FDA for treating a disease increasingly reduces mortality risk from that disease as compulsory schooling levels rise. Chang and Lauderdale (2009) provided further evidence, finding that for the period 1976–2004 higher-income earners had higher cholesterol levels before and lower ones after the introduction of statins. Frankovic and Kuhn (2019) developed an overlapping-generations framework, where individual income is positively associated with healthcare utilization and education affects the effectiveness of medical progress on individual mortality reduction. Goldman and Lakdawalla (2005) showed that the effects of health innovations on health inequality depends on the complexity of treatment regimens. If these are complex, as in the case of HIV medicine, better educated individuals benefit more. The opposite holds if treatments become easier to adopt. For instance, new drugs to treat hypertension have led to a decline in cardiovascular disparities.

The evidence for the United States suggests rising survival inequalities over time (e.g., Chetty et al., 2016), as reviewed by Bor et al. (2017). For Europe though, Abeliansky

and Strulik (2019) found that health deficits of individuals with low socioeconomic status decline at about the same rate as for individuals with high socioeconomic status – albeit from a higher starting point. Even though socioeconomic health disparities may not be increasing, their evidence suggests long-run persistence of health inequality. Grossmann and Strulik (2019) also pointed to the possibility that, with path dependent health status, medical technological progress benefits particularly those initially in good health, thus potentially raising health inequality.

8 Avenues for Future Research

A particularly fruitful area for future research would be to examine in more detail the mechanisms that govern the interaction between the socioeconomic health gradient and medical technological progress. Allowing for out-of-pocket health spending or private health insurance in a heterogenous agent version of the presented health deficit framework with endogenous medical R&D would be interesting. This would enable more affluent individuals to supplement publicly provided healthcare. Healthcare rationing would then potentially raise health inequality. A better quantitative assessment of the effect would be highly desirable to understand the resulting distributional conflict. Also, more evidence is needed to understand potentially differential effects of health innovations on ageing in heterogenous populations stratified by income, education, wealth, or occupation. For instance, knowing which policies provide information on the availability, safety, and effective use of state-of-the-art diagnosis, treatment, and vaccines could improve healthcare utilization of less educated individuals. We also need to know more about the role of differences in the practice patterns of medical professionals for healthcare access (e.g., Chandra and Skinner, 2004).

Regarding the effect of health improvements in the VSL, incorporating a feedback effect of higher life expectancy on investments in human capital and entrepreneurship in the analysis of stochastic life-cycle models would be interesting. Particularly in a devel-

opment context, an increase in longevity means that the returns from such investments can be spread over longer time horizons, in turn fostering economic activity and potentially raising welfare (e.g., Cervellati and Sunde, 2011; Strulik and Werner, 2016). Also importantly, longevity gains are not entirely exogenous to the individual. Future research should thus incorporate health investment choices and their interaction with public health systems and medical R&D incentives in VSL estimates. Accounting for unhealthy consumption choices would also be interesting. Relatedly, there is yet no conclusive evidence on the contribution of medical technological progress on longevity vis-a-vis other factors like behavioral changes and public health efforts.

Finally, studying policies that foster the diffusion of health innovations among healthcare providers (e.g., hospitals) would be important. In fact, empirical evidence suggests that technology diffusion is slow, producing a significant time gap between early and late adoption (e.g., Skinner and Staiger, 2015). This may imply a sizable welfare loss (Frankovic et al., 2020).

9 Conclusion

In the medical literature, explaining and predicting life expectancy trends is typically based on estimating statistical time trends (e.g., Kontis et al., 2017). However, medical technological progress is largely affected by R&D incentives that, in turn, depend on the evolution of demand for health goods and services. Market size is critically determined by healthcare access that is endogenous to public health policies.

The key insights of this paper may be summarized as follows. First, medical technological progress has potentially large effects on the evolution of life expectancy and the value of life. Second, new health treatments that improve health status are typically cost-effective, but likely to raise health expenditure as a fraction of income. Third, rising health expenditure shares over time can be socially optimal in a growing economy. Fourth, expected market size is an important determinant of medical R&D expenditure.

Demand for health innovations in advanced countries is therefore the driving force of medical technological progress. Scope may still exist to reduce the market power of pharmaceutical companies, however. Typically, revenues and profits considerably exceed R&D costs even when accounting for failure risk. Fifth, the gerontologically founded health deficit model that displays positive path dependence of both individual health status and mortality rates is particularly suited to address the future of human longevity in interaction with healthcare spending. It suggests that healthcare rationing could have severe negative consequences on the future of health and longevity not only for given medical technology but also by suppressing R&D incentives. Finally, medical technological progress that increases longevity could also raise health inequality. It may asymmetrically benefit more educated individuals, those with higher income, and those with better initial health status.

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