CELEBRATION OF SCIENCE

Washington, DC • September 7-9, 2012

The Impact of Biomedical Innovation on Longevity and Health

Frank R. Lichtenberg

Columbia University and National Bureau of Economic Research

August 31, 2012



MILKEN INSTITUTE

The Impact of Biomedical Innovation on Longevity and Health

Frank R. Lichtenberg

Columbia University and National Bureau of Economic Research

31 August 2012

During the 20th century, U.S. life expectancy at birth increased by almost 30 years (63%), from 47.3 years in 1900 to 77.0 years in 2000. Nordhaus (2002) estimated that, "to a first approximation, the economic value of increases in longevity over the twentieth century is about as large as the value of measured growth in non-health goods and services" (p. 17). Murphy and Topel (2005) observed that "the historical gains from increased longevity have been enormous. Over the 20th century, cumulative gains in life expectancy were worth over \$1.2 million per person for both men and women. Between 1970 and 2000 increased longevity added about \$3.2 trillion per year to national wealth, an uncounted value equal to about half of average annual GDP over the period." There has also been a significant decline over time in the functional limitations of older people in the United States, and probably worldwide.

A number of authors have expressed the view that a substantial portion of recent gains in the longevity and health of Americans is due to biomedical research and innovation. Cutler, Deaton and Lleras-Muney (2006) "tentatively identif[ied] the application of scientific advance and technical progress (some of which is induced by income and facilitated by education) as the ultimate determinant of health." Kramarow et al (2007) suggested that "medical advances have had an important role in the better health of older Americans." Fuchs (2010) stated that "since World War II ... biomedical innovations (new drugs, devices, and procedures) have been the primary source of increases in longevity." And the National Institutes of Health (2012) says that "thanks in large part to NIH research, Americans are living nearly 30 years longer than they did in 1900."

I have conducted a number of studies that have sought to measure the impact of biomedical innovation on the longevity and health of Americans and other populations during recent decades. I have examined the effects of several different types of medical innovation. Most of my studies have examined the impact of pharmaceutical innovation, which is easier to measure than other types of medical innovation (e.g., surgical procedure innovation). Moreover, pharmaceuticals are more "research intensive" than other types of medical care: In 2007,

prescription drugs accounted for just 10% of national health expenditure,¹ but Dorsey et al. (2010) estimated that more than half of U.S. funding for biomedical research came from pharmaceutical and biotechnology firms. Moreover, Sampat and Lichtenberg (2011) demonstrated that new drugs often build on upstream government research. I have also examined the impact of diagnostic imaging innovation (CT scans and MRIs) in several studies and the impact of inpatient hospital procedure innovation in one study (Lichtenberg (2011d)).

There are several ways to measure medical innovation. I believe that the best measure is the (mean) *vintage* of the medical goods and services used by an individual or population. One definition of vintage is "a period of origin or manufacture (e.g., a piano of 1845 vintage)" (http://www.merriam-webster.com/dictionary/vintage). Solow (1960) introduced the concept of vintage into economic analysis; this was one of the contributions to the theory of economic growth that the Royal Swedish Academy of Sciences (1987) cited when it awarded Solow the 1987 Alfred Nobel Memorial Prize in Economic Sciences. Solow's basic idea was that technical progress is "built into" machines and other goods and that this must be taken into account when making empirical measurements of their roles in production. I have often used a drug's initial FDA approval date as a measure of its vintage. Sometimes it is not feasible to measure the vintage of medical goods and services. In these cases, other measures of innovation, such as the *number* of distinct products (e.g., drugs) available for treating a condition, can be used.

I have attempted to assess the impact of medical innovation on a variety of health outcomes. The outcome that I have studied the most is longevity -- the "quantity of life." Longevity is the best-measured health outcome; it may also be the most important one. I have also studied the impact of medical (i.e., pharmaceutical) innovation on functional status, or "quality of life" -the ability of people to engage in important activities. In the nonelderly adult population, the activity of greatest interest is working. In the elderly population, the activities of greatest interest are "activities of daily living" such as dressing, eating, and bathing. In addition, I have analyzed the impact of medical innovation on the probability of being admitted to a hospital or nursing home, events that are indicative of poor health.

¹ http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/tables.pdf, Table 2.

I have used several approaches (research designs) to measure the impact of biomedical innovation on longevity and functional status. Each approach has advantages and disadvantages. Some of my studies have been based on cross-sectional patient-level data. Others have been based on longitudinal, region-level data; they have investigated whether *regions* (e.g., states) undergoing more rapid medical innovation have exhibited larger improvements in health. And some of my studies have been based on longitudinal, *disease*-level data; they have investigated whether the *medical conditions* undergoing more rapid innovation have exhibited larger gains in health outcomes.

In this article, I will briefly summarize five of my econometric studies of the impact of medical innovation on longevity and health. The first study examined the effect of pharmaceutical innovation, diagnostic imaging innovation, and other factors on longevity and medical expenditure growth using longitudinal state-level data during the period 1991-2004. The second study investigated the impact of the introduction of new orphan drugs on premature mortality from rare diseases using longitudinal, disease-level data from two countries: the U.S. (during the period 1999-2006) and France (during the period 2000-2007). The third study examined the effect of pharmaceutical innovation on the fraction of the working-age population receiving Social Security Disability Insurance benefits, again using longitudinal state-level data. The fourth study examined the effect of pharmaceutical innovation on the functional status of nursing home residents using cross-sectional, patient-level data from the 2004 National Nursing Home Survey. The fifth study examined the effect of cardiovascular system drug innovation on hospitalization and mortality due to cardiovascular disease using longitudinal country-level data on 20 OECD countries during the period 1995-2003.

The Quality of Medical Care, Behavioral Risk Factors, and Longevity Growth

The rate of longevity increase has varied considerably across U.S. states since 1991. In the eight states with the smallest increase, life expectancy at birth increased by only 0.31-1.16 years between 1991 and 2004. In the eight states with the largest increase, life expectancy increased by 2.5-4.3 years. Lichtenberg (2011a) examined the effect of the quality of medical care,

behavioral risk factors, and other variables on life expectancy and medical expenditure using longitudinal state-level data. That study examined the effects of three measures of the quality of medical care. The first is the average quality of diagnostic imaging procedures, defined as the fraction of procedures that are advanced procedures. The second is the average quality of practicing physicians, defined as the fraction of physicians that were trained at top-ranked medical schools. The third is the mean vintage (FDA approval year) of outpatient and inpatient prescription drugs.

I also examined the effects on longevity of three important behavioral risk factors —obesity, smoking, and AIDS incidence — and other variables — education, income, and health insurance coverage — that might be expected to influence longevity growth. My econometric approach controlled for the effects of unobserved factors that vary across states but are relatively stable over time (e.g., climate and environmental quality) and unobserved factors that change over time but are invariant across states (e.g., changes in federal government policies).

My indicators of the quality of diagnostic imaging procedures, drugs, and physicians almost always had positive and statistically significant effects on life expectancy. Life expectancy increased more rapidly in states where (1) the fraction of Medicare diagnostic imaging procedures that were advanced procedures increased more rapidly; (2) the vintage of self- and provider-administered drugs increased more rapidly; and (3) the quality of medical schools previously attended by physicians increased more rapidly.

Between 1991 and 2004, life expectancy at birth increased 2.37 years. The estimates implied that, during this period, the increased use of advanced imaging technology increased life expectancy by 0.62-0.71 years, use of newer outpatient prescription drugs increased life expectancy by 0.96-1.26 years, and use of newer provider-administered drugs increased life expectancy by 0.48-0.54 years. The decline in the average quality of medical schools previously attended by physicians reduced life expectancy by 0.28-0.47 years.

The rise from 44% to 59% in the fraction of the population that was overweight or obese reduced the increase in life expectancy by .58-.68 years. The decline in the incidence of AIDS is

estimated to have increased life expectancy by .18-.20 years. The small decline in smoking prevalence may have increased life expectancy by about 0.10 years.

Growth in life expectancy was uncorrelated across states with health insurance coverage and education, and inversely correlated with per-capita income growth. The 19% increase in real per-capita income is estimated to have reduced life expectancy by .34-.43 years. The sum of the contributions of all of the factors to the increase in life expectancy is in the 0.85-1.32 year range. Consequently, between 1.05 and 1.52 years of the 2.37-year increase in life expectancy is unexplained.

I performed several tests of the robustness of the life expectancy model. Controlling for percapita health expenditure (the "quantity" of healthcare) and eliminating the influence of infant mortality had virtually no effect on the healthcare quality coefficients. Controlling for the adoption of an important nonmedical innovation also had little influence on the estimated effects of medical innovation adoption on life expectancy.

Although states with larger increases in the quality of diagnostic procedures, drugs, and physicians had larger increases in life expectancy, they did not have larger increases in percapita medical expenditure. This may be the case because, while newer diagnostic procedures and drugs are more expensive than their older counterparts, they may reduce the need for costly additional medical treatment. The absence of a correlation across states between medical innovation and expenditure growth is inconsistent with the view that advances in medical technology have contributed to rising overall U.S. healthcare spending. Increased health insurance coverage is associated with lower growth in per-capita medical expenditure.

The Impact of New (Orphan) Drug Approvals on Premature Mortality from Rare Diseases in the U.S. and France, 1999-2007

Lichtenberg (2011b) investigated the impact of the introduction of new orphan drugs on premature mortality from rare diseases using longitudinal, disease-level data obtained from a number of major databases. The analysis was performed using data from two countries: the U.S. (during the period 1999-2006) and France (during the period 2000-2007). For both countries, I estimated models using two alternative definitions of premature mortality, several alternative criteria for inclusion in the set of rare diseases, and several values of the potential lag between new drug approvals and premature mortality reduction.

Both the U.S. and French estimates indicated that, overall, premature mortality from rare diseases is unrelated to the cumulative number of drugs approved 0-2 years earlier, but is significantly inversely related to the cumulative number of drugs approved 3-4 years earlier. This delay is not surprising, since most patients probably don't have access to a drug until several years after it has been launched. Earlier access to orphan drugs could result in earlier reductions in premature mortality from rare diseases.

Although the estimates for the two countries were qualitatively similar, the estimated magnitudes of the U.S. coefficients are about four times as large as the magnitudes of the French coefficients. This may be partly due to greater errors in measuring dates of drug introduction in France. It is also possible that access to new drugs is more restricted in France than it is in the U.S. Lichtenberg (2009) found that the fraction of cardiovascular drug therapy days in 2004 that were for "new" drugs — drugs launched after 1995 — was 13% in the U.S. and 8% in France. My estimates indicate that, in the U.S., potential years of life lost to rare diseases before age 65 declined at an average annual rate of 3.3%, and that, in the absence of lagged new drug approvals, potential years of life lost before age 65 (PYLL65) would have *increased* at a rate of 0.9%. Since the U.S. population age 0-64 was increasing at the rate of 1.0% per year, this means that PYLL65 per person would have remained approximately constant. The reduction in the U.S. growth rate of PYLL65 attributable to lagged new drug approvals was 4.2%.

In France, PYLL65 declined at an average annual rate of 1.8%. The estimates imply that, in the absence of lagged new drug approvals, it would have declined at a rate of 0.6%. The reduction in the French growth rate of PYLL65 attributable to lagged new drug approvals was 1.1%.

Has Pharmaceutical Innovation Reduced Social Security Disability Growth?

A number of scholars have argued that medical innovation has played a major role in the longterm decline in disability. Two studies, Lichtenberg (2005) and Lichtenberg and Virabhak (2007), investigated whether, in general, the introduction and use of newer prescription drugs reduces disability. One was based on longitudinal data on a set of diseases, the other was based on cross-sectional data on individuals. In both cases, disability status was self-reported.

Lichtenberg (2011c) reexamined the question using longitudinal state-level data during the period 1995-2004. The disability measure I analyzed is the ratio of the number of workers receiving Social Security Disability Insurance (DI) benefits to the working-age population (the "DI recipiency rate"). A previous study investigated the behavior of the DI recipiency rate using longitudinal state-level data during the period 1978-1998, but that study did not include measures of pharmaceutical use or other potential determinants of health.

I performed an econometric analysis of the effect of pharmaceutical innovation on the DI recipiency rate, controlling for other potential determinants of health (age, education, and behavioral risk factors) and other factors (DI program generosity and labor market conditions) that previous investigators have identified as important influences on DI participation. The principal contribution of this paper was the incorporation of drug vintage measures in models of DI recipiency. All of my measures of drug vintage were based on complete data on utilization of outpatient drugs paid for by state Medicaid agencies, combined with data on the initial FDA approval dates of the active ingredients of these drugs. Medicaid pays for one in seven U.S prescriptions.

I estimated models of the DI recipiency rate using alternative measures of drug vintage. The implications of all of the models were virtually identical. In every case, i.e., regardless of the precise definition of drug vintage, there was a significant inverse relationship between disability recipiency and drug vintage. Disability recipiency was also consistently inversely related to the average wage rate and the fraction of state residents with at least a college education, and directly related to mean age.

The existence of a significant inverse relationship between disability recipiency and drug vintage implies that, if mean drug vintage had not increased — i.e., if people used the same drugs in 2004 as they had used in 1995 — the DI recipiency rate would have increased more than it actually did. As shown in Figure 1, from 1995 to 2004, the actual disability rate increased 30%, from 2.62% to 3.42%. The estimates imply that in the absence of any post-1995 increase in drug vintage, the increase in the disability rate would have been 30% larger: The disability rate would have increased 39%, from 2.62% to 3.65%. This means that in the absence of any post-1995 increase in drug vintage, about 418,000 more working-age Americans would have been DI recipients, and that Social Security benefits paid to disabled workers in 2004 would have been about \$4.5 billion higher.

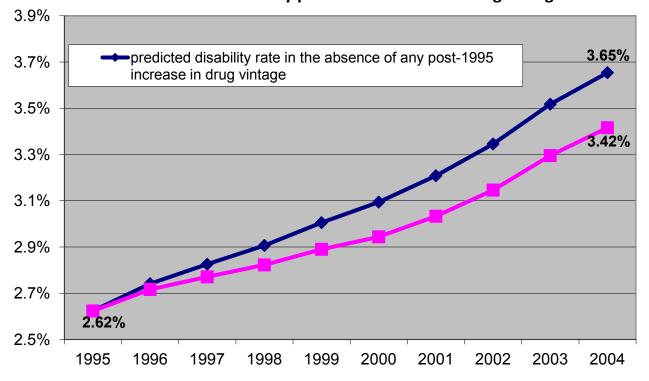


Figure 1. Predicted disability rate in year t (t = 1996,...,2004), in the absence of any post-1995 increase in drug vintage

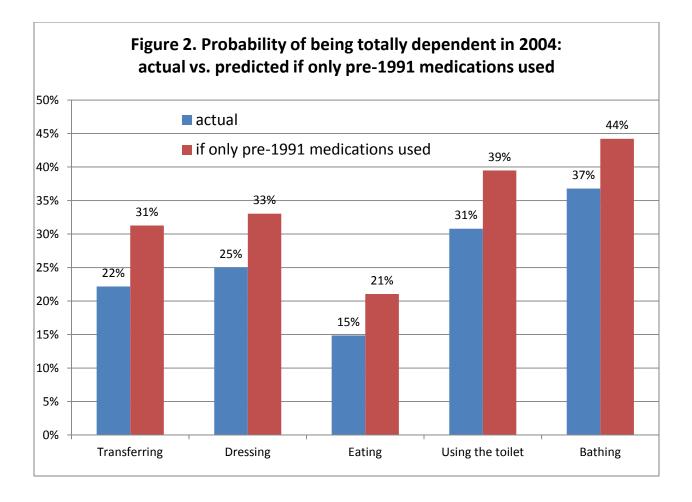
I also explored the reasons for interstate variation in the growth in Medicaid drug vintage. Some estimates indicated that less financially constrained state governments — those with higher growth in per-capita tax revenue — may have made newer drugs more available to Medicaid patients. But the variable that had the greatest influence on Medicaid drug vintage was the AIDS incidence rate. States whose AIDS incidence rates fell more slowly than average had smaller increases in Medicaid drug vintage. This may be because the Medicaid budgets of states with slowly declining numbers of AIDS cases were under greater stress than the Medicaid budgets of states with rapidly-declining numbers of AIDS cases. High AIDS incidence may have increased disability rates among patients with other conditions by causing their access to newer treatments to be restricted.

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

Previous investigators have hypothesized that medical innovation in general, and pharmaceutical innovation in particular, has made important contributions to the decline in the functional limitations of older people. Lichtenberg (2012) examined the effect of pharmaceutical innovation on the functional status of nursing home residents using crosssectional, patient-level data from the 2004 National Nursing Home Survey. This was the first public-use survey of nursing homes that contains detailed information about medication use, and it contains better data on functional status than previous surveys.

I found that residents using newer medications and a higher proportion of priority-review medications were more able to perform all five activities of daily living (ADLs), controlling for age, sex, race, marital status, veteran status, where the resident lived prior to admission, primary diagnosis at the time of admission, up to 16 diagnoses at the time of the interview, sources of payment, and facility fixed effects.

The ability of nursing home residents to perform activities of daily living is positively related to the number of "new" (post-1990) medications they consume, but unrelated to the number of old medications they consume. As shown in Figure 2, I estimated how much higher the functional limitations of 2004 nursing home residents would have been had they used old medications instead of new medications.



I estimated that the fraction of nursing home residents with all five ADL dependencies (number of activities for which the resident is not independent) would have been 58% instead of 50%. During the period 1990-2004, pharmaceutical innovation is estimated to have reduced the functional limitations of nursing home residents by between 1.2% and 2.1% per year.

Unfortunately, the NNHS does not provide information about some potential determinants of functional status, such as the resident's income, wealth, or educational attainment. However, these other potential determinants are likely to be controlled for, to an important extent, by factors included in the model, such as race, diagnoses, and sources of payment. The facility fixed effects are also likely to control for a substantial amount of variation in socioeconomic status (SES), since SES is likely to play an important role in the "assignment" of residents to

facilities. Also, analysis of data by race suggested that there is little or no correlation between medication attributes and SES.

Have Newer Cardiovascular Drugs Reduced Hospitalization? Evidence from Longitudinal Country-Level Data on 20 OECD Countries, 1995-2003

Lichtenberg (2009) examined the effect of changes in the vintage distribution of cardiovascular system drugs on hospitalization and mortality due to cardiovascular disease using longitudinal country-level data on 20 OECD countries during the period 1995-2003.

I found that countries with larger increases in the mean vintage of cardiovascular drug had smaller increases in the cardiovascular disease hospital discharge rate, controlling for the *quantity* of cardiovascular medications consumed per person, the use of other medical innovations (CT scanners and MRI units), consumption of calories, tobacco, and alcohol, and demographic variables (population size and age structure, income, and educational attainment). The estimates also indicated that use of newer cardiovascular drugs has reduced average length of stay and the age-adjusted cardiovascular mortality rate, but not the number of potential years of life lost due to cardiovascular disease before age 70 per 100,000 population.

The estimates indicate that if drug vintage had not increased during 1995-2004, hospitalization and mortality would have been higher in 2004. I estimated that per-capita expenditure on cardiovascular hospital stays would have been 70% (\$89) higher in 2004 had drug vintage not increased during 1995-2004. Per-capita expenditure on cardiovascular drugs would have been lower in 2004 had drug vintage not increased during 1995-2004. But our estimate of the increase in expenditure on cardiovascular hospital stays is about 3.7 times as large as our estimate of the reduction in per-capita expenditure for cardiovascular drugs that would have occurred (\$24).

Although our data on hospital use and especially on drug utilization were quite complete and reliable, data on cardiovascular risk factors were less complete. We can think of little reason to

expect these risk factors to be correlated with drug vintage, conditional on income, education, and average rate of drug utilization (which we control for). Nevertheless, obtaining better information on these risk factors would certainly be desirable.

References

Cutler D, Deaton A, Lleras-Muney A (2006). "The Determinants of Mortality," *Journal of Economic Perspectives* 20(3, Summer), 97-120.

Dorsey ER (2010), et al, "Financial Anatomy of Biomedical Research, 2003 – 2008," JAMA, January 13; 303(2): 137–143, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3118092/

Fuchs, VR (2010), "New Priorities for Future Biomedical Innovations," *N Engl J Med* 363:704-706 August 19, http://www.nejm.org/doi/full/10.1056/NEJMp0906597

Kramarow E, Lubitz J, Lentzner H, Gorina Y (2007), "Trends in the Health of Older Americans, 1970–2005," *Health Affairs 16 (5)*, September, 1417-1425.

Lichtenberg FR (2005), "Availability of new drugs and Americans' ability to work," *Journal of Occupational and Environmental Medicine* 47 (4), April, 373-380.

Lichtenberg FR (2009), "Have newer cardiovascular drugs reduced hospitalization? Evidence from longitudinal country-level data on 20 OECD countries, 1995-2003," *Health Economics* 18 (5), 519-534.

Lichtenberg FR (2011a), "The quality of medical care, behavioral risk factors, and longevity growth," International Journal of Health Care Finance and Economics 11(1), March 2011, 1-34.

Lichtenberg FR (2011b), "The impact of new (orphan) drug approvals on premature mortality from rare diseases in the U.S. and France, 1999-2007," *European Journal of Health Economics*, 2011 Sep 28. [Epub ahead of print] http://www.ncbi.nlm.nih.gov/pubmed/21953319.

Lichtenberg FR (2011c), "Has pharmaceutical innovation reduced Social Security Disability growth?," *International Journal of the Economics of Business* 18 (2).

Lichtenberg FR (2011d), "The Impact of Therapeutic Procedure Innovation on Hospital Patient Longevity: Evidence From Western Australia, 2000-2007," NBER Working Paper No. 17414, http://www.nber.org/papers/w17414

Lichtenberg FR (2012), "The effect of pharmaceutical innovation on the functional limitations of elderly Americans: evidence from the 2004 National Nursing Home Survey," NBER Working Paper No. 17750, http://www.nber.org/papers/w17750; Advances in Health Economics and Health Services Research 23, 71-99, forthcoming,

Lichtenberg FR, Virabhak S (2007), "Pharmaceutical-embodied technical progress, longevity, and quality of life: drugs as 'equipment for your health," *Managerial and Decision Economics* 28: 371–392.

Murphy KM, Topel RH (2006), "The Value of Health and Longevity," *Journal of Political Economy* 114 (4), August, 871-904.

National Institutes of Health (2012), *Impact of NIH Research on Our Health*, http://www.nih.gov/about/impact/health.htm

Nordhaus WD (2003), "The Health of Nations: The Contribution of Improved Health to Living Standards," in *Measuring the Gains From Medical Research: An Economic Approach*, ed. K. M. Murphy and R. H. Topel (Chicago: University of Chicago Press), 9-40.

Royal Swedish Academy of Sciences (1987), Press release, http://www.nobelprize.org/nobel_prizes/economics/laureates/1987/press.html

Sampat BN, Lichtenberg FR (2011), "What Are the Respective Roles of the Public and Private Sectors in Pharmaceutical Innovation?" *Health Affairs* 30(2):332-9, Feb.

Solow RM (1960), "Investment and Technical Progress," in K. Arrow, S. Karlin, P. Suppes (Eds.), *Mathematical Methods in the Social Sciences, 1959* (University of Chicago Press, Chicago).



1250 Fourth Street Santa Monica, CA 90401 Phone: 310-570-4600 E-mail: info@milkeninstitute.org www.milkeninstitute.org



1101 New York Ave. NW, Suite 620 Washington, DC 20005 Phone: 202.336.8900 www.fastercures.org