Montreal Economic Institute

Ideas for a More Prosperous Nation

Debate between Frank Lichtenberg, Courtney C. Brown Professor at Columbia University Graduate School of Business, and Joel Lexchin, Associate Professor in the Department of Family and Community Medicine at the University of Toronto.

Living better, longer…
Frank R. Lichtenberg

Many economists believe new goods are at the heart of economic progress and that innovative goods are better than older products because they provide more "product services" in relation to their cost of production. The pharmaceutical industry has among the highest propensities to generate new goods; it is one of the most R&D-intensive industries in the economy.

In part because of extensive Food and Drug Administration regulation, there is unusually good data about the launch and diffusion of new pharmaceutical goods. I have used these data to perform a number of econometric studies at the individual, disease and country level, in order to assess the health and economic impacts of the development and use of new drugs. These studies are based on data covering all medical conditions and all drugs and provide evidence about the health and economic impacts of new drugs in general, not about specific drugs or their impacts on particular diseases.

In a forthcoming study in *International Journal of Health Care Finance and Economics*, I found evidence that new drug launches have added greatly to longevity in the last two decades in 52 nations, both developed and developing. Over the past half century, life expectancy around the world has increased sizeably, from an average of 46.5 years for a child born in 1950-55 to an average of 65 years for a child born in 1995-2000. The gap in life expectancy between rich and poor countries has been halved, from 25 to 12 years. Sorting out the causes for longevity improvements, however, has proved difficult. Many health researchers have primarily credited more education, higher income, better lifestyle and a safer environment for increased longevity.

By combining data from the IMS Health Drug Launches database and the World Health Organization Mortality database, I was able to link the number of new drugs with changes in the probability of surviving to certain ages for each major disease category, country, and year. When the stock of drugs is measured with a lag of three to six years, the effect on longevity is more than twice as large as in the first three years. This suggests it may take several years for a new drug to be diffused to more consumers and have its full impact on survival rates.

New drug launches account for a substantial fraction of medical innovations. Of the two years added to the average lifespan between 1986 and 2000, I calculated that about 40% can be traced to the introduction of new drugs. On average, the introduction of new drugs lengthened the life of people in these 52 countries by just short of three weeks each year.

Another forthcoming study in *Journal of Occupational and Environmental Medicine* examined the impact of the introduction of new drugs during a 15-year period on changes in the ability of non-elderly adult Americans to work. Several previous case studies have examined the impact of specific new drugs on ability to work. For example, one study found that terbutaline, an asthma drug approved by the FDA in 1974, reduced the number of work or school days missed due to asthma by 57%.

These case studies were based on relatively small samples of individuals with the same condition at the same time, and it is difficult to estimate from them the average or aggregate effect of new drugs on ability to work. I used a different approach. My analysis was based on data on about

200,000 Americans with 47 major chronic conditions observed throughout the period 1982-96. I investigated whether people with conditions for which many new drugs were introduced exhibited greater increases in ability to work than people with conditions for which few new drugs were introduced, controlling for other factors.

The study found that if the probability of being unable to work had not been reduced by new drug introductions during 1982-96, this probability would have been 29% higher in 1996 than it actually was — 5.2% instead of 4%. In 1996, the per capita annual value of the estimated reduction in the probability of being unable to work at all was about $395, while the average expenditure on new drugs per working-age person was $51. The estimated benefit of the new drugs, in terms of the value of the increase in workforce participation, is thus much greater than the estimated cost of the new drugs.

This confirms that people may obtain several kinds of benefits from using newer, as opposed to older, pharmaceutical products. These include longer life, reduced limitations on activities (including work), and reduced expenditure on hospitals and long-term care.

Frank Lichtenberg is the Courtney C. Brown Professor at Columbia University Graduate School of Business. Before joining Columbia, Prof. Lichtenberg taught at Harvard University and at the University of Pennsylvania. He is also a Research Associate of the National Bureau of Economic Research, and has served as a consultant to the Institute of Medicine. Prof. Lichtenberg has won several awards, including the 2003 Milken Institute Award for Distinguished Economic Research for his paper, "Pharmaceutical Knowledge-Capital Accumulation and Longevity."

Dr. Lichtenberg's work is both up to date and well-known when it comes to showing the value and positive economic impact of new drugs. He is one of the most eloquent defenders of pharmaceutical research companies.

… but new isn't better
Joel Lexchin

There is no denying that new drugs can be very important in the health care system. Drugs to treat HIV/AIDS have significantly improved the lives of people. But the drug companies are not primarily interested in producing drugs that meet major therapeutic needs, they are interested in making drugs that have large markets and the two are not necessarily synonymous.

While some new drugs are very valuable, that same conclusion cannot be extended to the vast majority of medications that appear on the market. Information both from the Canadian Patented Medicine Prices Review Board and the French drug bulletin *La revue Prescrire* shows that only 10% to 12% offer any substantial benefits over existing therapies.

One major example of the superiority of older medications is in the treatment of hypertension where it has been demonstrated that diuretics (water pills) are superior to the newer and much more expensive classes of calcium channel blockers and ACE inhibitors.

Even this assessment of the value of new drugs may be overly generous because most of the initial data on the value of new drugs comes from clinical trials conducted by the drug companies. Five recent studies show that if funding for trials on these medications comes from pharmaceutical companies, they are much more likely to generate results in favour of the drug being tested than if the funding comes from sources such as government, charities or hospitals.

In addition to biased outcomes, there is also the question of biases in publication. This issue was brought to the fore with GlaxoSmithKline and the use of paroxetine (Paxil) in children and adolescents with depression. Instead of publishing studies that found that Paxil was ineffective, Glaxo kept them hidden because, according to a memo "it would be commercially unacceptable to include a statement that efficacy had not been demonstrated."

The published version of the CLASS study comparing Celebrex to naproxen only included data from the first six months of the trial instead of the full 12 months of data in order to make Celebrex

appear superior. When clinical trials appear in medical journals, they often use a weak form of statistical analysis that gives a more favourable picture and positive studies are often published more than once. Companies spend hundreds of millions of dollars promoting new drugs to doctors. This heavy promotion is behind the early widespread use of many new drugs.

However, early use is not necessarily compatible with safe use. Initial doses may be too high, leading to safety problems. At least 10% of new products pose significant enough safety risks that they either acquire black box warnings (the strongest safety warning that the FDA can order) or they have to be removed from the market. Half of these serious safety problems turn up in the first two years after the drug was approved.

Heavy advertising also means that new drugs are going to be used on a much wider range of people than they were initially tested on, and we simply don't know how the drug is going to affect these people. Vioxx is one such example. Merck spent US$150-million a year on direct-to-consumer advertising of Vioxx, and this advertising helped to contribute to the widespread use of Vioxx and an estimated 88,000 to 140,000 excess cases of serious coronary heart disease in the United States.

Companies in the United States spend upwards of US$25-billion on promotion to doctors. Over the past 30 years, there have been at least a dozen studies that looked at the quality of prescribing as a function of where doctors get their information about medications. Every one of these studies has come to the same conclusion: the more that doctors rely on promotional sources, the poorer they are as prescribers. The drugs that are being promoted the most heavily and that are being inappropriately prescribed are the newer ones.

Some new drugs do show clear advantages, but they are a small minority. Most new drugs are no better than existing therapy and some older drugs are clearly superior.

Even this assessment of the value of new drugs may be skewed because of biases in the outcome of clinical trials financed by pharmaceutical companies and biases in the published literature. New drugs are heavily promoted both to consumers and to doctors. The result of this heavy promotion is exposing patients to drugs before their safety profile is known, sometimes with results like the ones we saw with Vioxx. Moreover, promotion leads to inappropriate prescribing. Any blanket statement that newer means better must be rejected.

Joel Lexchin is an Associate Professor in the School of Health Policy and Management at York University and an Associate Professor in the Department of Family and Community Medicine at the University of Toronto. He wrote numerous articles concerning pharmaceutical issues. He is the author of *The Real Pushers: A Critical Analysis of the Canadian Drug Industry* (1984) and coauthor of *Drugs of Choice: A Formulary for General Practice* (1998).

Dr. Lexchin is a particularly articulate and knowledgeable critic of "Big Pharma." He is notably highly critical of the promotional efforts of pharmaceutical companies.