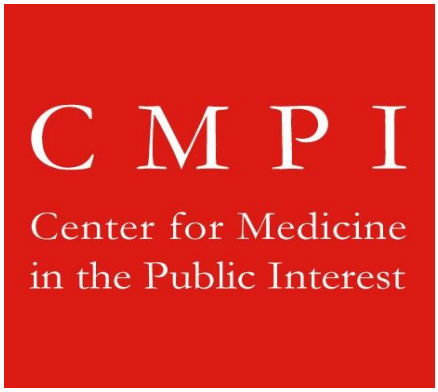

Shorter Lives, Less Prosperity: The Impact of Comparative Effectiveness Research on Health and Wealth

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Executive Summary

1. Advocates of comparative effectiveness research ("CER") claim it can be used to reduce healthcare spending because a large portion pays for medical technologies that add little health or social benefit. This assumption runs counter to evidence that medical innovation is associated with lower and greater longevity

2. To the extent that CER is used to reduce the development and use of new drugs, devices, and diagnostics, it is important to estimate what impact the reduced rate of innovation would have on quality of life and life expectancy.

3. Using empirical models that establish a direct relationship between pharmaceutical returns on investment and clinical development costs, we developed an estimate of the cost of CER and it's impact on rates of research and development ("R&D").

4. We found that CER could conservatively increase R&D costs by an amount equally to 50 percent of the most complex and time consuming part of drug development. The added cost would reduce R&D spending by $32 billion over ten years.

5. Based on research that quantified the relationship between increased R&D and greater life expectancy and well-being, we conclude that CER would cost Americans 81 million life years and $4 trillion dollars.

6. CER advocates ignore the impact of such requirements at the possible expense of longer life and economic growth.

Introduction

Many observers maintain that the increase in healthcare spending is the result of the development and overuse of new medicines, devices, and diagnostics. In making this case, proponents of this view make three assumptions. First, that most of the 'overuse' does not improve health or extend life. Second, that CER information about the costs, risks, and benefits of different treatment options, combined with new incentives reflecting the information, could eventually alter the way in which medicine is practiced and yield lower healthcare spending without having adverse effects on health. Over the long-term, the potential reduction in spending below projected levels could be substantial. Third, CER can be used so "that Medicare spending—and perhaps all health spending in the country—could be cut by about 30 percent if the more conservative practice styles used in the lowest spending one-fifth of the country could be adopted nationwide."[1]

Based on these assumptions, the Patient Protection and Affordable Care Act both requires the development of CER and its use in defining healthcare quality and in making coverage decisions. Some of the strongest proponents and contributors to the body of

[1] CBO Research on the Comparative Effectiveness of Medical Treatments: Issues and Options for an Expanded Federal Role, December 2007.

CER "as Congress moves toward substantial reductions in Medicare spending, the program will be under increasing pressure to ensure that dollars are directed to services providing known benefits." Donald Berwick, who is administrator of the Center for Medicare and Medicaid Services, put the case for CER more bluntly: "We can make a sensible social decision and say, 'Well, at this point, to have access to a particular additional benefit [new drug or medical intervention] is so expensive that our taxpayers have better use for those funds.'" [2] Indeed, the Institute of Medicine, charged with developing methods for determining what technologies and innovations should be part of and added to the package of benefits covered under the new health care law. CER will be the major tool for making such determinations.[3]

If these assumptions were true, medical innovation over time should have led to the worst of both worlds – a large increase in cost and little or no increase in well being and life expectancy with improved quality of life. Previous studies have cast doubt on such assertions. Indeed, a rich body of empirical research demonstrates that medical innovation increases in life expectancy while reducing the cost of treating disease. Frank Lichtenberg has shown that the pace and intensity of medical innovation is associated with lower growth in *per capita* medical expenditures, longer life and economic growth. [4]

Yale University Economist, William Nordhaus, has estimated the value of innovations in medicine during the second half of the twentieth century to be roughly equal to the gains in the economy's real output, as measured by the Gross Domestic Product ("GDP") over the same fifty-year period. The value of improvements in health (*e.g.*, life expectancy) unlike the economy's real productive output of goods and services, is not reflected in national accounting statistics (which when aggregated, measure economic growth and national income, *i.e.*, GDP).

Nordhaus posits a simple, and indeed, quite clever question to demonstrate the intuitive reasonableness of his conclusion, which is based on highly technical research methods:

> You must forgo either the health improvements over the last half-century or the non-health improvements. That is, you must choose either (a) 1950 health conditions and 2000 non-health living standards or (b) 2000 health conditions and 1950 non-health living standards. Which would you choose?[5]

In another study, one that was prospective rather than retrospective, University of Chicago Economists, Kevin Murphy and Robert Topel, estimated the social-economic value of a 10 percent reduction in the mortality associated with cardiovascular disease

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[2] Donald Berwick, June 2009 interview in *Biotechnology Healthcare.*

[3] http://iom.edu/Activities/HealthServices/EssentialHealthBenefits/2011-JAN-12/Agenda.aspx

[4] Frank Lichtenberg, "Why Has Longevity Increased in Some States and Not Others? The Role of Medical Innovation and Other Factors." Manhattan Institute, July 2007.

[5] William Nordhaus. "Irving Fisher and the Contribution of Improved Longevity to Living Standards" *The American Journal of Economics and Sociology* 64(1): 367-92. 2005.

and cancer around $10 trillion (roughly $4 trillion from reductions in cardiovascular mortality and $6 trillion from reductions in cancer mortality). To place this number in perspective, note that the size of the U.S. economy, as measured by the GDP, surpassed the $10 trillion level a few years ago in the early 2000's.

The productivity of investment in pharmaceutical R&D is remarkably high—perhaps one of the most productive uses of capital in the economy. Hence, our research looked at whether incentives to either maintain or increase investment in R&D would be affected by the need to conduct CER prior to and a condition for coverage of a new medicine.

En route to engaging in this research, we looked at the impact of the introduction of cholesterol lowering drugs called statins on the death rate from heart disease. Advocates of CER argue that requiring its development and use can produce better health at a lower cost. Or, to use the language of the Nordhaus Paradox, CER can lead to better health and (because it would save money) improved non-health living standards.

As Table 1 shows, the development of statins is associated with a significant decline in 10-year death rates among men and women regardless of whether or not they have a history of heart disease. CER proponents would argue that CER could produce similar gains at a lower per patient cost.

Table 1 Statin-induced Percentage Reduction in Mortality from Cardiovascular Disease

Risk Factors/ Population	Total Cholesterol	Systolic BP	Age	10-Yr Mortality Pre-statins	10-Yr Mortality Post-statins	% Reduction in CVD Mortality
Men-CHD	200 mg/dL	140mm/Hg	50	2.46%	1.70%	**30.9%**
Women-CHD	200 mg/dL	140mm/Hg	50	0.63%	0.47%	**25.4%**
Men-No CHD	200 mg/dL	140mm/Hg	50	1.28%	0.91%	**28.9%**
Women-No CHD	200 mg/dL	140mm/Hg	50	0.40%	0.31%	**22.5%**

The Impact of CER on Medical Innovation

Yet, CER is not generated overnight or at little cost to companies whose products are to be compared. Rather, as with any requirement for additional evidence, there are both direct and indirect costs associated with its production. (This is a point that CER advocates often make when justifying the establishment of a government agency that would set the CER agenda as well as subsidize CER projects.)

In previous research, we have demonstrated how CER regulations have the potential to result in increasing clinical trial sizes (and costs) and perhaps clinical development times;

the latter would increase the cost and risk of drug development from an investment, decision-making perspective.[6]

The mathematics of clinical research are the same whether an innovator needs to provide more clinical data before or as a condition of receiving Food and Drug Administration ("FDA") approval or CER data before or as a condition to being coverage by health plans or government. Either way, requirement for more information will require companies to increase the size of clinical trial samples. CER can increase the complexity of clinical trials, the number of people enrolled in a clinical trial, and the number of studies conducted after a product receives approval. In Europe, "about one-fourth to one-third of the regulatory costs are estimated to go for reimbursement issues.

Further, CER can delay time to market and reduce the rate and extent of technology diffusion. A recent study looking at the impact of CER on market access in Europe and the United States, found the process delayed use by over two years. Moreover, the same study found that CER use, as part of reimbursement decisions in cancer was associated with 60 percent fewer medications being made available than when such reviews were not used. [7]

CER also adds to the risk of investing because it increases the uncertainty about whether a product will enter the market. The uncertainty ranges "from the impossibility of demonstrating the full scope of a product's value at the time of authorization, through to the impossibility of knowing precisely what will be on the market (and how good it is compared to your product) by the time you get to seeking authorization. As research departments and company finance offers have frequently lamented, there is a profound discouragement to innovation when every new product runs the risk of flat rejection by regulators at the last minute, because of some unforeseeable arrival of another, arguably superior, therapy just before you seek authorization."[8]

Unless CER costs nothing, it will make more developmental R&D projects less attractive. That is, with higher expected drug or device development costs, slower access to market and increased uncertainty, there will be fewer R&D projects with generating positive returns (particularly cash flows). Figure 1 shows that as the cost of conducting CER increase the number of R&D projects decline in order to maintain the same rate of return on innovation.

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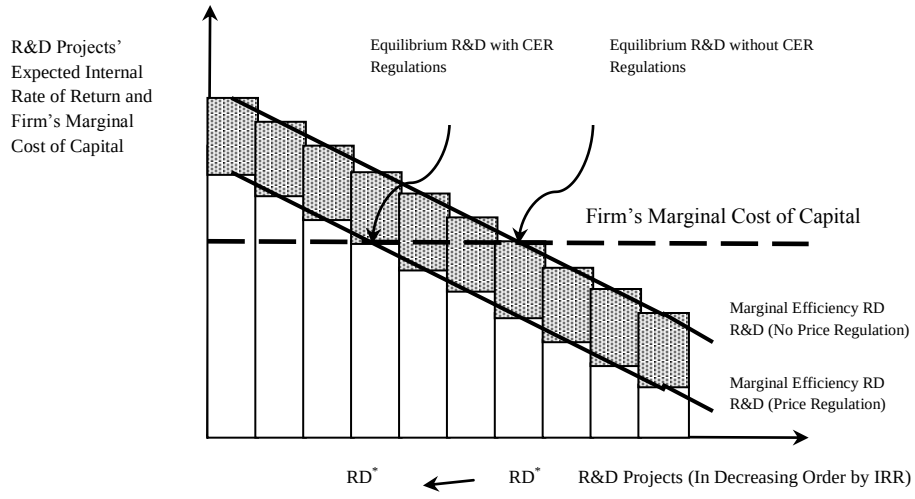
[6] Vernon JA, Goldberg R, Golec J. Economic evaluation and cost effectiveness thresholds: signals to firms and implications for R&D investment and innovation. Pharmacoeconomics 2009; 27 (10): 797-806.

[7] Anne Mason, *et al*., "Comparison of Anti-cancer Drug Coverage Decisions in the United States and United Kingdom: Does the Evidence Support the Rhetoric?" Journal of Clinical Oncology, http://jco.ascopubs.org/content/28/20/3234.abstract.

[8] Peter O'Donnell, "One Step Closer to the Fourth Hurdle: Drug Evaluation Criteria Could Soon Include an Intrusive Health Technology Assessment." Applied Clinical Trials, March 1 2010.

Figure 1: Potential Impact of Comparative Effectiveness Regulations on Equilibrium R&D Investment



Next, we estimated how much the R&D investment would decline or be "lost" due to an increase in CER costs. We assume that CER would be 50 percent of Phase III clinical development costs. This estimate is based on empirical data of development costs and the recognition that the complexity of clinical trials and number of patients required to do comparative research would increase throughout the FDA evaluation stage.

As Table 2 shows, over a 10-year period, R&D investment would decline by $31.6 billion. Over the long term, R&D would increase but at slower rate due to CER.

Table 2 Negative Impact of CER Requirements on R&D

Model	PVRD No CER Reqs	PVRD with CER Reqs	PVRD "Lost"
Short-term Model (10 Years)	$315.4 Billion	$283.8 Billion	$31.6 Billion
Long-term Model (Perpetuity)	$750 Billion	$675 Billion	$75 Billion

CER Impact on Life Expectancy and Dollars

As we discussed earlier, the investment in and consumption of new medicines continually increases life expectancy, quality of life, and productivity. To estimate the social impact of CER, we estimate how much lost R&D will cost Americans in terms of lower life expectancy and dollars. To translate life years into dollars, we use the conservative assumption that a life year is equal to $50,000. While much higher estimates exist, we are opting to be conservative in all of our assumptions so that our estimates may plausibly be viewed as lower-bound approximations. Table 2 shows that the R&D lost due to CER will cost the United States 81 million life years and $4 trillion over 20 years.

Table 3 Present Value in U.S. Life Years and Dollars Lost Due To CER

Model	PV "Lost" R&D	"Lost" Life Years	PV Cost to Economy
Short-term Model (10 Years)	$31.6 Billion	34.06 Million	$1.70 Trillion
Long-term Model (Perpetuity)	$75.0 Billion	80.99 Million	$4.05 Trillion

Conclusion

Proponents of CER have responded to general criticism of using findings to make coverage decisions by claiming that absent such research, the United States will be unable to control rising health costs because of the unfettered adoption of medical innovations. Some have gone so far as to suggest that "the antagonism toward cost-per-quality adjusted life year comparisons also suggests a bit of magical thinking — the notion that the country can avoid the difficult trade-offs that cost-utility analysis helps to illuminate…It represents another example of our country's avoidance of unpleasant truths about our resource constraints."[9]

Our research shows that there is hard evidence behind our concern about using CER to "illuminate" difficult tradeoffs. On the contrary, our analysis suggests that because CER will lead to a loss of innovation, Americans will live shorter lives, and in poorer health than would otherwise be the case. Simply put, we will produce less health. People will be less productive and less able to enjoy life. Living longer will be worthless. (Since people who are in poor health cost more to care for than healthy people even if they live longer, CER will also add to healthcare spending.) That is the 'unpleasant truth' CER advocates consistently avoid.

About the Authors

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Dr. Vernon is a professor in the Department of Health Policy and Administration at the University of North Carolina at Chapel Hill, where he holds appointments in the Kenan-Flagler School of Business and the UNC School of Pharmacy. He is a Faculty Research Fellow with the National Bureau of Economic Research and a Senior Economic Policy Advisor to the Office of the Commissioner at the US FDA.

He has twice testified before the US Senate on pharmaceutical policy issues and advises both government and industry on a wide range of policy issues. He was previously a professor in the finance department at the University of Connecticut and a visiting professor at the Wharton School of Business at the University of Pennsylvania. He also guest edited a special issue of *Managerial and Decision Economics* on the political economy of the pharmaceutical industry.

[9] Jonathan Skinner, NEJM.

Dr. Vernon has published articles in numerous publications, including the *Journal of Law and Economics*, *Health Economics*, *Healthcare Management*, the *Journal of Healthcare Management*, the *National Law Journal*, the *American Journal of Law and Medicine*, and the journal *PharmacoEconomics*, where he sits on the editorial board.

Dr. Vernon holds doctoral degrees from the University of Pennsylvania's Wharton School in management science (health policy and management) and the University of London in economics.

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Robert Goldberg is co-founder and vice president of the Center for Medicine in the Public Interest. (CMPI) Along with Peter Pitts, Dr. Goldberg hosts the popular and controversial blog on the pharmaceutical industry and healthcare, www.drugwonks.com.

Prior to founding CMPI, Goldberg was Director of the Manhattan Institute's Center for Medical Progress and Chairman of its 21st Century FDA Task Force that examined the impact of the FDA's Critical Path Initiative on drug development and personalized medicine.

He has written for The Wall Street Journal, The Washington Post, the Los Angeles Times, National Review Online, The Chicago Tribune, The Philadelphia Inquirer, The New York Sun and writes regularly for The American Spectator where he broke the story about Obama Medicare director Donald Berwick's admiration for Britain's National Health Service; the New York Post and The Weekly Standard. He is an expert on Medicare reform, comparative effectiveness and FDA's Critical Path Initiative and the author of many papers including, "Insta-Americans: The Empowered (and Imperiled) Health Care Consumer in the Age of Internet Medicine," and with John Vernon, "Alzheimer's Disease and Cost-effectiveness Analyses: Ensuring Good Value for Money?" and "Economic Evaluation and Comparative-Effectiveness Thresholds: Signals to Firms and Implications for R&D Investment and Innovation." He is also author of "Tabloid Medicine: How the Internet is Being Used To Hijack Medical Science For Fear and Profit." (Kaplan, December 2010).

About CMPI

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