

# Measuring Biomedical Progress: How do we align use with estimates of “value” in clinical medicine?

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## Introduction

Advances in science and medicine have inspired advances that correspond to historical inflection points of rapidly improving health. These periods of medical progress have changed the contour of history. During the first period from the mid-18th to the mid-19th centuries, discoveries about proper nutrition played a large role in improving health. From the 1890s to the early 20th century, the most significant health gains emanated from our improved understanding about the transmission of disease and the public health improvements it prompted. The third phase dating from 1930s up until today is the era of big medicine — starting with the development of modern vaccines and antibiotics, and culminating in the intensive personal interventions that characterize our current drug pipeline.<sup>1</sup>

By many objective measures, this third phase will eclipse prior periods in both its sheer impact on health as well as the magnitude of that change. The health benefits of medical innovation are becoming more numerous and profound as we develop better knowledge about the molecular basis of disease and how to intervene on biological processes. This is especially true when it comes to new medicines. For example, looking back three decades it is clear that we had very little direct understanding of how most of our medicines worked to mitigate disease targets. Today it is rare that a new drug is developed, or approved by the Food and Drug Administration (FDA) for marketing, without a firm understanding of its likely mechanism of action. In fact, understanding how a medicine works has become a pre-requisite for funding development programs and valuing new molecules. This improved understanding is one important part of the unfolding story of biopharmaceutical innovation. It is opening up perhaps a new phase in medical progress — the fourth historical inflection point where medical care is more personal, more rational, and far more effective.

But these innovations do not come cheap. For one thing, they drive growth in health spending. This was famously shown in Victor Fuchs’s 1999 analysis of Medicare spending trends. Fuchs found inflation-adjusted increases in Medicare spending per beneficiary of 4-5% per year, versus real gross domestic product (GDP) increases of 1.2% during the same period.<sup>2</sup> He attributed these increases to new medical technologies, while acknowledging the positive impact they have on life expectancy and health status for the elderly. Fuchs found an obvious and simple truth. Many new medical technologies reduce direct health costs — delaying or precluding surgeries, for example, or reducing hospital admissions. But when they reduce costs in the short run, they often increase costs over the

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<sup>1</sup> DM Cutler. Making Sense of Medical Technology. *Health Affairs*, March/April 2006; 25(2): w48-w50.

<sup>2</sup> VR Fuchs. Health Care for the Elderly: How Much? Who Will Pay for It? *Health Affairs* (January/February 1999):11

long run – for one thing, from people who survive acute illness and go on to live longer lives, only to incur still more healthcare costs down the road. The key component of these costs is not rising prices or an aging population. The key driver is simply more people getting more treatments combined with that longer life expectancy. One practical example of this phenomenon is implantable defibrillators. Tucked under the skin in the chest, these lifesaving devices sense when the heart’s rhythm has gone awry and deliver a small electric shock to bring it back to normal. The devices save lives, but studies show they increase costs, and not only from the price of the procedure. All those patients who would have died of irregular heartbeats now go on to require additional expensive hospitalizations from symptoms of progressive heart disease.<sup>3</sup>

### **Using measures of “value” as a rationing tool in policy and payment decisions**

Extending life and reducing morbidity clearly has significant value in spite of the costs. But the costs are often far more apparent to a strained healthcare system struggling to pay today’s bills than the subsequent value that these expenditures deliver. The uncomfortable fact is that innovation often increases spending even while it improves peoples’ health. Even technologies that can reduce immediate costs often raise long-term expenditures by enabling higher healthcare utilization down the road.<sup>4</sup> These immediate costs, of course, are not only more obvious but also more easily measured. So while new technology is only one factor in rising health expenses, it is the most visible and easily targeted since it surrounds single products made by a handful of manufacturers that can be easily identified. The resulting frustrations give rise to efforts to “rationalize” the use of new technologies, through cost shifting to consumers, explicit restrictions imposed on the settings where products can be used, or temptations to directly control prices.<sup>5</sup> None of these efforts take adequate measure of the benefits being delivered by a new product. They are a triumph of cost control over outcomes.

Recognizing this shortcoming, policymakers are increasingly arguing that what’s needed are better tools for measuring “value” in healthcare and better policy approaches to aligning these concepts with coverage and payment decisions.<sup>6</sup> It seems a forgone conclusion that government purchasers are going to play an increasingly prominent role in decisions about access – and perhaps price — of new medical technologies. Medicare has recently demonstrated its willingness to promulgate narrow rules around the use of some high-cost drugs as a means to “promote drug safety.”<sup>7</sup> Transitioning these safety-based efforts to similar policies pursued in the name of “value” and “benefit” is not hard to envision. So imbuing these judgments with accurate measures of the benefit being delivered seems paramount to ensuring appropriate discretion for patients and doctors to take decisions that maximize the utility of new medical products. Some noted healthcare economists have advocated attempts to recognize value by linking payment directly to results through arrangements where sponsors agree to bear some of the therapeutic risk and accept full payment only when patients have

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<sup>3</sup> S Gottlieb. Devices Prolong Life – But at a Big Expense. USA Today, Thursday, April 4, 2002. P. A12.

<sup>4</sup> JD Kleinke. The Price of Progress: Prescription Drugs in the Health Care Market. Health Affairs. Volume 20, No 5, September/October 2001. 43-60.

<sup>5</sup> RG Frank. Prescription-Drug Prices. New England Journal of Medicine 2004;351:1375-1377

<sup>6</sup> Report of the Institute of Medicine. Rewarding provider performance: aligning incentives in Medicare. Washington, DC: National Academies Press, 2007

<sup>7</sup> D Glendinning. Medicare imposes limits on anemia drugs. Physician organizations will keep trying to get CMS to reopen its decision on treating cancer patients. American Medical News, August 27, 2007

a positive outcome on a new treatment.<sup>8</sup> This kind of “payment for results” enables perhaps the most direct measure of value. But these arrangements are unsuitable for the vast majority of medicines, especially those for chronic conditions where clinical response can’t be immediately measured. So policymakers have begun to search for other quantitative measures of “value,” especially when it comes to reducing costs inside the Medicare program. These measures aren’t straightforward since so much of the value creation occurs long after products are first introduced, after new technologies are put into real world, practical use. While the value offered by treatment for acute conditions such as infections, or a treatment for prevention such as vaccines, may be easier to estimate at the time of a product’s first launch, for the vast majority of treatments it’s much harder to prospectively measure “value” at the time of initial market access.

To probe these challenges, this paper attempts to explore some of the qualities of science and medicine that challenge our ability to assign fixed parameters on the value of medical products. It then summarizes some of the recent work by economists to develop rigorous methods for assessing the value of new innovations and discusses the difficulties we face in making practical use of these measures in policy decisions impacting access and price. Finally, this paper will make some proposals about how these constructs can be best adapted to federal decisionmaking inside Medicare. When viewed over time, the contributions of individual medical advances seem obvious. But when viewed in the present, benefits of new technology may not be so apparent. Without the indulgence of hindsight, the individual contribution offered by each new technology can be hard to measure and easily overlooked by today’s increasingly cost-based decisionmaking. This clash between the present and the future is a core challenge to efforts to restrain the use of new products. This is especially true when it comes to new drugs, where the process for uncovering the full range of benefits is often dependent on discoveries made through more widespread application of these products. In the end, the best tool for unlocking value may be policy approaches that expose consumers to a reasonable portion of the cost of incremental decisions to use treatments in clinical situations where there is less evidence substantiating their benefit. Ultimately, the most effective way to create institutional incentives to maximize the value of new medical products would be through systems that fold the delivery of new drugs into the delivery of care through comprehensive contracting with health plans for full health services.

### **The nature of medical progress and how value of technologies is realized**

Aligning payment policies with measures of “value” is not easy, largely owing to the characteristics of medical innovation that make it hard to quantify the potential benefits of a brand new medical treatment. This is especially true for “a priori” measures that try to place binary, quantitative or qualitative scores on a product at the time of its initial launch.

- First, medical progress occurs in episodic waves, with an accumulation of small advances consolidating to produce periods of rapid improvements in outcomes. This makes the contribution of any single innovation hard to prospectively measure;
- Second, scientific principles are being translated into new treatments more quickly than at any time in history, meaning that more of the learning about optimizing the use of new products is likely to be done post-approval; and

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<sup>8</sup> AM Garber, MB McClellan. Satisfaction Guaranteed — “Payment by Results” for Biologic Agents. *New England Journal of Medicine* October 2007;357:1575 (Perspective)

- Finally, real value to patients is best recognized in the post market, when patients and doctors are able to make practical use of new products in real world environments.

On the first point, medical progress does not occur in a straight line. Instead, it occurs as a stepwise progression of sharp, sudden but in most cases modest improvements in outcomes. These correspond to periods when the introduction of a new technology or the realization of better ways of delivering care or detecting illness, all coalesce to affect how people confront illness. Any one new treatment might not be enough, in isolation, to significantly move the needle on our measures of outcomes. But over time, a series of advances are consolidated into new approaches to medical care that enable us to realize small but meaningful improvements in health. This can be seen when it comes to the treatment of cancer, where careful tracking of health statistics show that improvements in mortality rates have not been a smooth curve but rather a stepwise series of small gains — sometimes realized over the course of several years. These periods of advance correspond with the adoption of better screening techniques, the introduction of better drugs to prevent and treat disease, or better approaches to combining existing drugs into effective therapeutic cocktails. Each period of improvement is by itself modest, but taken over time, these accumulated inflection points leave us dramatically better off when it comes to many cancers.<sup>9</sup>

Recent experience with breast cancer provides a visible example of how this progress unfolds. Treatment of breast cancer has benefited from better and more widespread screening with tools such as mammography. It is also benefited by successive product introductions, from Taxols to aromatase inhibitors to selective estrogen receptor modulators (SERMs) to more targeted drugs like Herceptin and Avastin. Each new medicine had an individual impact on treating the disease and preventing its recurrence. Sometimes the impact was small. In other instances it was more measurable, such as the introduction of Taxols and Herceptin, each of which can dramatically reduce the chance of breast cancer recurrence. Over time and when taken together, the individual improvements offered by each of these different drugs coalesced to give women significantly better odds of surviving the disease.

Today, many say the same phenomenon is being realized when it comes to the treatment of colon cancer. Similar to breast cancer in the 1990s, colon cancer has recently benefited from improved and more routine screening, but also the recent introduction of a number of new and more effective drugs. These include the angiogenesis inhibitor Avastin which blocks the formation of blood vessels that feed tumors, the targeted medicine Erbitux that turns off a molecular switch that stimulates colon cancer cells to propagate, or the more traditional chemotherapeutic agent Eloxatin, which was originally approved as a last-line drug for the treatment of advanced colon cancer, but is now a mainstay in the treatment of earlier stage tumors. The combination of these new medicines and earlier detection is resulting in significant improvements in people's survival. Colon cancer death rates have recently been dropping by an average of 2.1% a year in the U.S., a near doubling of decreases that began in 1993.<sup>10 11</sup> Improvement in the treatment of colon cancer has followed the same basic clinical principle as improvement in the treatment of breast cancer – it's only after

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<sup>9</sup> Statistics from the National Cancer Institutes Surveillance Epidemiology and End Results (SEER) database are available at [http://seer.cancer.gov/csr/1975\\_2004/](http://seer.cancer.gov/csr/1975_2004/)

<sup>10</sup> DK Espey, XC Wu, J Swan, C Wiggins, et al. Annual report to the nation on the status of cancer, 1975-2004, featuring cancer in American Indians and Alaska Natives (p 2119-2152). Published Online: 15 Oct 2007 DOI: 10.1002/cncr.23044

<sup>11</sup> D Grady. U.S. Cancer Death Rates Are Found to Be Falling Faster. The New York Times, October 15, 2007

seemingly small or incremental improvements in drugs or other technologies accumulate and are consolidated into new approaches to care that the benefits start to become visible in our health statistics.<sup>12</sup> This incremental character of medical progress means it is especially hard to prospectively value the benefits of any single new product at the time of its initial approval. It's only through real world use, and the accumulation of new products into better approaches to care, that the public health benefit of any single innovation is made obvious.

### **The time it takes to translate scientific discoveries is becoming compressed**

The second characteristic of medical innovation that makes it hard to prospectively measure the potential benefits of a brand new medical treatment deals with the sequence by which a clinical product is developed in relation to its enabling science. Just as it's true that recent progress in terms of new drug development is translating into practical gains in life expectancy and health improvement, it's also true that the development and realization of these better treatments are occurring in greater proximity to the fundamental scientific breakthroughs that makes a particular new innovation possible. Whereas one time we would have to wait many decades for an advance in our basic understanding of biology and science to be translated into a practical new treatment, in some cases the lag between a fundamental scientific discovery and the final development of a new medicine that capitalizes on it is occurring in under a decade — and sometimes even shorter.

This phenomenon can be seen, for example, in the strengthening of our understanding of how the immune system works and the creation of drugs that enable its manipulation. We now have drugs — monoclonal antibodies — that can replicate the activity of specific aspects of our immune processes. We have other medicines like Tysabri (for the treatment of Multiple Sclerosis and Crohn's Disease) that are highly targeted and able to down-regulate specific aspects of cellular immunity. Until now, all of our tools for regulating the immune system used drugs like steroids or interferon that caused significant side effects precisely because they are so imprecise. Because we have recently developed a fundamentally better understanding of how the immune system works, many of the new drugs being developed are far more precise and effective, and are associated with fewer systemic side effects.

More recently, we are seeing this same phenomenon — of the shortening time period between firming up of enabling science and the creation of a new medical product — unfold in respect to our improved understanding of the genetic basis of disease. The science of genomics is already being rapidly translated into new treatments and approaches to medical care. If you look at the early drug pipeline — embodied by the investigational new drug applications filed with FDA, where sponsors ask the agency for permission to start testing a drug in human subjects for the first time — you see many drugs derived entirely through techniques of genomics and proteomics. The latter is the science of how genes use proteins to regulate complex biological processes. Some say this same phenomenon is again occurring when it comes to even more novel science, such as glycobiology, which is the<sup>13</sup> science that deals with the ways that proteins are “tweaked” through the attachment of sugars. These carbohydrate appendages help determine the three-dimensional structures of proteins, which in turn is directly related to their function. While the first attempts in the 1980s to use novel drugs to regulate the function of carbohydrates failed, a discovery made in the early 1990s opened

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<sup>12</sup> A Wertheimer, A., R Levy, T O'Conner. Too Many Drugs? The Clinical and Economic Value of Incremental Innovations. *Research In Human Capital and Development: Investing in Health: The Social and Economic Benefits of Health Care Innovation*, 2001; 14: pp. 77-118

<sup>13</sup> A Dove. The bittersweet promise of glycobiology. *Nature Biotechnology*, October 2001, Volume 19

up new insights. Now a number of highly promising medicines that target the functions of carbohydrates are about to enter human trials for diseases as diverse as sickle cell anemia and cancer.<sup>14 15</sup> It's been only 15 years since these basic scientific findings and the development of promising products that capitalize on them. That is a blip in the span of scientific history but a great leap in terms of the medicinal progress being manifested.

This relationship between the first scientific discovery and its payoff in the form of effective medical product development stands in opposition to popular convention that we are not “getting enough innovation” from our investment in science. We may be seeing fewer new drugs coming to market, but we are seeing novel medicines reach patients in closer proximity to the fundamental scientific advance that made a particular medicine possible. Past medical products have taken decades and even centuries to be made manifest on the heels of the scientific discoveries that enabled them. Today's FDA is already seeing dozens of drugs derived wholly from science developed less than a decade ago.<sup>16</sup> This is all good news, because it means the payoff from science is reaching patients more quickly than perhaps at any other time. But from a practical standpoint, this success has also come with its own challenges. This is especially true when it comes to measuring the value of each new innovation. The more rapid translation of basic science into medical products means that in some cases – because the underlying science is so novel — even more of the clinical learning will take place after products are first introduced into the market. There will be more cases where the most important uses of a new drug are worked out after it's first launched.

### **Greatest advances occur over time, after doctors apply new innovations**

This leads to the third characteristic of medical innovation that makes it hard to prospectively measure the potential benefits of a brand new medical treatment – the most significant advances made through introduction of new drugs often occur after approval when doctors apply treatments to novel, often unapproved indications.

There are countless examples where this clinical discovery process has uncovered the most important and significant applications of a new product. Sometimes this owes to the fact that doctors and patients have a higher tolerance for uncertainty and risk than FDA regulators. Doctors may be willing to apply a product “off label” in situations where the available evidence hasn't reached the same level of certainty that would inspire FDA reviewers to write it into a drug's label. These follow-on discoveries and real-world applications aren't taken into consideration when payers or government authorities like NICE place an economic value on the benefits of a new treatment at the time of its launch.

In contemplating the value of a new product, these follow-on uses embody substantial current and future benefits. The history of recent medical progress shows that the number of drugs that went on to prove far more significant benefits — beyond their initial indication — is a far longer list than the number of drugs that went on to prove no significant additional uses, or worse, disappointed relative

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<sup>14</sup> T Gebhard, W Kinzy, C Bruns, JT Patton, JL Magnani, and R Banteli. Synthesis and Biological Evaluation of a Potent E-Selectin Antagonist. *Journal of Medicinal Chemistry* 1999: 42, 4909-13

<sup>15</sup> J Magnani. The discovery, biology, and drug development of sialyl Lea and sialyl Lex. *Archives of Biochemical Biophysics* 2004: 426(2), p. 122-131

<sup>16</sup> S Gottlieb. FDA's Drug Approval Process, Up to the Challenge? Testimony before the Senate Committee on Health, Education, Labor, and Pensions, March 1, 2005, Washington, DC

to their initial profile. Herceptin, which was initially approved for advanced breast cancer, is perhaps even more valuable in early stage breast cancer, for which it was recently shown to reduce relapse in new breast cancers by up to 50%.<sup>17</sup> Eloxatin for colon cancer was initially approved for treatment of advanced cancer but went on to demonstrate significant benefits when used in earlier stages of the disease.<sup>18</sup> In each case, the clinical benefits offered by these drugs in new applications were clear to clinicians long before they were reflected in regulatory or reimbursement decisions.<sup>19</sup> These same phenomena apply to drugs used to treat primary care conditions. For example, a class of drugs first approved to treat osteoporosis are now approved for primary prevention of breast cancer.<sup>20</sup> <sup>21</sup> Certain classes of blood thinners initially approved to treat symptoms of poor circulation are now indicated for the treatment of patients with certain life-threatening consequences of heart disease.<sup>22</sup>

The common response from drug critics is that sponsors should be compelled to prove these additional benefits in rigorous clinical trials aimed at regulatory approval before the drugs are widely used or reimbursed in these indications. The fact is most drugs are under active investigation for a range of additional uses at the time of their initial approval, and often the FDA requires, as condition for approving a new product, that sponsors have additional studies underway for likely off-label uses. But this doesn't cover every circumstance, especially new uses that can't be fully envisioned at the time of approval. Many new uses of drugs would never be established if not for the willingness of patients and doctors to tolerate some additional uncertainty for the opportunity to use drugs in new indications. Moreover, even after substantial evidence becomes available that a drug has a benefit in a new use, it can still take the FDA up to two years to put the new indication on the drug's label. In the case of Herceptin, it took FDA almost two years to approve the drug in front line breast cancer (adjuvant treatment) from the day that the results were first published in the *New England Journal of Medicine*.<sup>23</sup> How many early stage breast cancer patients should have

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<sup>17</sup> EH Romond, EA Perez, J Bryant, VJ Suman, et al. Trastuzumab plus Adjuvant Chemotherapy for Operable HER2-Positive Breast Cancer. *New England Journal of Medicine* 2005;353:1673-84.

<sup>18</sup> JA Meyerhardt, RJ Mayer. Systemic Therapy for Colorectal Cancer, 2005;Volume 352:476-487

<sup>19</sup> The pivotal trial evaluating Herceptin in earlier stage breast cancer was first revealed in the fall of 2007 and published in the *New England Journal of Medicine*. It was a large, randomized phase III study that found that patients given paclitaxel plus Avastin show significantly prolonged progression-free survival as compared with those getting paclitaxel alone (median, 11.8 vs. 5.9 months; hazard ratio for progression, 0.60; P<0.001) — Oncologists applaud when the results are unveiled at a major medical meeting. FDA didn't grant "conditional" approval for use of the drug in this setting until February 2008 after it initially delayed approval. Eloxatin was first approved by Europeans in 1996 for the second-line treatment of metastatic colon cancer. Results of a very large study in July 2003, the MOSAIC (Multicenter International Study of Oxaliplatin/5FU-LV in the Adjuvant Treatment of Colon Cancer) trial were presented at the 39th annual meeting of the American Society of Clinical Oncology (ASCO) showing that the addition of Eloxatin to the current standard of post-operative (adjuvant) chemotherapy for colon cancer reduces the risk of recurrence by 23% in patients who have undergone surgery for their primary tumor — "Oxaliplatin is the first agent which, in combination with 5-FU and leucovorin shows a significant benefit over the current standard treatment in adjuvant colon cancer" the authors wrote. The FDA first approved the drug in January 2005 for use in combination with infusional 5-fluorouracil and leucovorin for the initial treatment of advanced colorectal cancer, and only expanded its use to more fully match the European approval in March 2006

<sup>20</sup> Elizabeth Barrett-Connor, Lori Mosca, Peter Collins, M.D., Mary Jane Geiger, et al, for the Raloxifene Use for The Heart (RUTH) Trial Investigators. Effects of Raloxifene on Cardiovascular Events and Breast Cancer in Postmenopausal Women. *New England Journal of Medicine*, Volume 355:125-137 July 13, 2006 Number 2

<sup>21</sup> Food and Drug Administration, Evista Approved for Reducing Breast Cancer Risk, Sept. 17, 2007. <http://www.fda.gov/consumer/updates/evista091707.html>

<sup>22</sup> M Mitka. Results of CURE Trial for Acute Coronary Syndrome. *Journal of the American Medical Association* 2001;285:1828-1829

<sup>23</sup> EH Romond, EA Perez, J Bryant, Ph.D., VJ Suman, et al. Trastuzumab plus Adjuvant Chemotherapy for Operable HER2-Positive Breast Cancer. *New England Journal of Medicine* 2005;353:1673-84

forgone the opportunity to reduce their chance of a cancer recurrence by about 50% and death by 33% by adding Herceptin — simply because government agencies had not yet taken final action on the new information? Yet some payers, who take a very strict approach to access, equating “value” with the contents of the drug’s FDA approved labeling, were refusing to pay for Herceptin in this use until FDA had added the indication to its label.<sup>24</sup> The consequences of these approaches are increasingly seen in the U.K., whose drug authority has the most experience at making explicit assessments of value (the National Institute for Clinical Excellence or NICE) at the time of product launch. The U.K. process routinely ignores important off-label applications of new products when it issues its assessments. Because access to new products often turns on these assessments, the penetration of new products in Britain and their application to important new uses is slower than in the U.S. This may be one factor to help explain the growing disparities in outcomes between British and American patients for a number of diseases, especially fields of rapid scientific change, such as cancer. Because of the rapid evolution of science, in cancer the ability to prescribe off-label often defines the standard of care.<sup>25 26 27 28 29 30 31</sup>

### **Finding measures of value that accommodate medical innovation’s unique attributes**

Notwithstanding these challenges to establishing early measures of value, our policy environment is increasingly demanding that we draw early conclusions about the value of new medical products in order to set more narrow rules about access. In the future, more active management of price and use of new technologies seem a forgone conclusion as a response to growing concerns about healthcare spending. So as government payers claim leverage to influence prices rather than just accept them, the lexicon increasingly turns to talk about “value” as a way for establishing rules about price and access.

So far, many different methods have been put forward for making these measurements.<sup>32 33 34</sup> Where policymakers have adopted explicit tools for measuring benefit of new medical technologies (mostly in Europe) these approaches have relied on assumptions about expected benefit that are

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<sup>24</sup> S Gottlieb. Breast Cancer Breakthroughs. *The Wall Street Journal*, A12, March 26, 2007

<sup>25</sup> J Ferlay, P Autier, M Boniol, M Heanue, M Colombet and P Boyle. Estimates of the cancer incidence and mortality in Europe in 2006-2007 *Annals of Oncology* 18: 581–592, 2007

<sup>26</sup> G Gatta et al. (1996) Substantial variation in therapy for colorectal cancer across Europe: EUROCORE analysis of cancer registry data for 1987. *European Journal of Cancer* 32A: 831–835

<sup>27</sup> MP Coleman, G Gatta, A Verdecchia, J Estève, M Sant, H Storm, C Allemani, L Ciccolallo, M Santaquilani, F Berrino and the EUROCORE Working Group EUROCORE-3 summary: cancer survival in Europe at the end of the 20th century 2003, *Annals of Oncology* 14 (Supplement 5): v128–v149

<sup>28</sup> S Gottlieb. Breast Cancer Breakthroughs. *The Wall Street Journal*, A12, March 26, 2007

<sup>29</sup> L Ciccolallo, R Capocaccia, MP Coleman, FBerrino, JWW Coebergh, RAM Damhuis, J Faivre, C Martinez-Garcia, H Møller, M Ponz de Leon, G Launoy, N Raverdy, EM Williams and G Gatta. Survival differences between European and US patients with colorectal cancer: role of stage at diagnosis and surgery. *Gut* 2005;54:268-273

<sup>30</sup> M Sant et al. (2003) EUROCORE-3: survival of cancer patients diagnosed 1990–94—results and commentary. *Annals of Oncology* 14 (Suppl 5): v61–v118

<sup>31</sup> HG Welch et al. Are increasing 5-year survival rates evidence of success against cancer? *Journal of the American Medical Association* 2000 283: 2975–2978

<sup>32</sup> PA Ubel et al., What Is the Price of Life and Why Doesn’t It Increase at the Rate of Inflation? *Archives of Internal Medicine* 163, no. 14 (2003): 1637–1641

<sup>33</sup> DM Cutler, AB Rosen, and S Vijan, Value of Medical Spending in the United States: 1960–2000. *New England Journal of Medicine* 355, no. 9 (2006): 920–927

<sup>34</sup> P Neumann, et al. Are Pharmaceuticals Cost-Effective? A Review of the Evidence, *Health Affairs*, 2000; 19(2): pp. 92-109

extrapolated from registration trials. Prominent among these measurement tools is the quality adjusted life year (QALYs) that is based on the number of years of life that would be added by the intervention. Under this approach, each year in perfect health is assigned the value of 1.0 down to a value of 0 for death. If the extra years would not be lived in full health (and associated with a comorbidity that reduces quality of their life) then the extra life-years are valued at between 0 and 1.<sup>35 36</sup> In recent years, British health authorities have used a general ceiling on how much they will pay for a QALY. This policy has supported decisions to deny reimbursement for some new and arguably effective products, including some treatments for cancer that offer clear benefit but at a high financial cost.<sup>37</sup> In other cases, wrangling over QALYs has been seen as a negotiating tool by British health authorities to convince sponsors to lower their price. Although NICE does not make decisions solely on the basis of QALYs, it has indicated that it generally accepts interventions with cost-effectiveness ratios below about £30,000 per quality-adjusted life-year for the intended population.<sup>38</sup> This cutoff is widely believed to be based on the estimated value of dialysis that was used to craft the 1972 decision by the U.S. Congress to expand Medicare coverage to those requiring long-term dialysis for end-stage renal disease.<sup>39</sup> Ironically, this valuation considerably underestimated the dialysis program's eventual costs.

Some have proposed the U.S. import concepts similar to the QALY to make payment decisions inside Medicare. This view is, in part, reflected in the current discussion in the U.S. for the creation of a new federal agency to weigh the “comparative effectiveness” of similar and sometimes clinically interchangeable drugs.<sup>40</sup> Even if comparative effectiveness would not assign an explicit measure of numerical “value” to a new medical product, presumably it could help government payers like Medicare develop a “relative” value scale by comparing new technologies to presumably cheaper alternatives. The older and presumably cheaper treatments could be established as benchmarks for making decisions about price and access.

The problem with each of these approaches is that the process of realizing the most significant value of new medical innovations is complex. It's unlikely that a prospective measure can accommodate all of the benefits embodied by many innovations. Restricting access on the basis of metrics that aren't sufficiently comprehensive can forestall later value creation and the accumulation of new evidence.<sup>41</sup> Left out of these numerical measures are also a myriad of other secondary societal benefits offered by new medical technologies, from direct benefits of improved productivity of people who are able

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<sup>35</sup> M Drummond, B O'Brien, G Stoddart, G Torrance. *Methods for the Economic Evaluation of Health Care Programmes*. Oxford: Oxford University Press, 1997; and Kobelt G. *Health Economics: An Introduction to Economic Evaluation*. London: Office of Health Economics, 1996

<sup>36</sup> JS Pliskin, D S Shepard, and MC Weinstein. 1980. Utility Functions for Life Years and Health Status. *Operations Research*, Vol. 28, 206—224

<sup>37</sup> J Ferlay, P Autier, M Boniol, M Heanue, M Colombet and P Boyle. Estimates of the cancer incidence and mortality in Europe in 2006. *Annals of Oncology* 18: 581–592, 2007. doi:10.1093/annonc/mdl498. Published online 7 February 2007

<sup>38</sup> Devlin N, Parkin D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health Economics* 2004;13:437-452.

<sup>39</sup> F. Laufer, “Thresholds in Cost-Effectiveness Analysis—More of the Story,” *Value in Health* 8, no. 1 (2005):86–87; and R.A. Hirth et al., “Willingness to Pay for a Quality-Adjusted Life Year: In Search of a Standard,” *Medical Decision Making* 20, no. 3 (2000): 332–342.

<sup>40</sup> S Gottlieb. *The War on (Expensive) Drugs*. Wall Street Journal, Editorial Page, August 30, 2007

<sup>41</sup> JE Calfee and E DuPre. The Emerging Market Dynamics of Targeted Therapeutics – How the Market for High Profile, High-Cost Drugs Differs from that of their Traditional Counterparts. *Health Affairs* September/October 2006;1302-1308; and John E Calfee. The Golden Age of Medical Innovation. *The American*, March/April 2007

to better accommodate chronic conditions to the indirect benefits through job creation.<sup>42</sup> Basic biopharmaceutical research has also given rise to new bioprocesses important in other economic sectors besides health, including chemistry, food and feed, paper and pulp, textiles, energy, and the environment. While these attributes are excluded from discussions about valuing the health benefits of new technologies, they are certainly affected by those considerations.

Can any prospective measure of “value” be truly comprehensive, taking consideration of both the obvious and eventual benefits offered by a new technology? One place to look for some direction is economic literature. Many economists have already set out to take more comprehensive measure of the health benefits of new medical innovations. This includes work by David M. Cutler of Harvard University; Frank R. Lichtenberg of Columbia University; Mark B. McClellan of Stanford University; and Thomas J. Philipson of the University of Chicago. While their methodologies may be hard to apply to the kinds of binary and a priori metrics sought for making prospective policy decisions about price and access, the approaches taken by these economists provide some useful lessons. They all rely on largely retrospective evaluations to accurately measure the contribution of new technology. This underscores the difficulty of estimating benefit when so much remains to be worked out about the best application of new products. This reality perhaps reveals the need for a shared obligation among product developers and payers to use post-approval information to allow decisions about access and price to be tailored – after initial market entry — to reflect subsequent value creation.<sup>43 44 45</sup> This kind of an approach would have the benefit of enabling access, and facilitate the kind of utilization that leads to the demonstration of follow on benefits — while providing some assurance that decision about price and access will remain aligned with agreeable – and evolving — notions of value.<sup>46</sup>

### **Weighing the methodologies for judging value**

In one recent study, Cutler and colleagues examined trends in the value of coronary heart disease (CHD) care in the U.S. over a fifteen-year period. They reported major improvements in life expectancy from investment in CHD care for the elderly and, overall, good value from spending on CHD, especially from pharmacotherapy over surgical intervention. They measured the value of CHD spending as the incremental change in lifetime spending (from 1987 to 2002) divided by the incremental change in life expectancy over that same time period. Both costs and life expectancy were adjusted to the demographic distribution of the population in 2000. This ratio could then be compared with conventional estimates of the value of a year of life. Death from CHD has greatly

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<sup>42</sup> J Rizzo, et al. Labor Productivity Effects of Prescribed Medicines for Chronically Ill Workers, *Health Economics*, 1996; 5(3): pp. 249-65.

<sup>43</sup> JD Kleinke. Access Versus Excess: Value-Based Cost Sharing For Prescription Drugs. *Health Affairs*, 23, no. 1 (2004): 34-47 doi: 10.1377/hlthaff.23.1.34

<sup>44</sup> AM Garber, Mark B. McClellan. Satisfaction Guaranteed — “Payment by Results” for Biologic Agents. *New England Journal of Medicine* October 18, 2007;357:1575

<sup>45</sup> For additional work by Garber see also: Garber AM, Jones CI, Romer PM. Insurance and incentives for medical innovation. *Forum for Health Economics and Health Policy* (published online April 2006; [http://www.bepress.com/fhep/biomedical\\_research/](http://www.bepress.com/fhep/biomedical_research/)); Garber AM. To use technology better. *Health Affairs*, w51-w53 (published online 7 February 2006;10.1377/hlthaff.25.w51)]; Garber AM. Cost-effectiveness and evidence evaluation as criteria for coverage decisions and benefit design. *Health Affairs*, Web Exclusive <http://content.healthaffairs.org/cgi/content/full/hlthaff.w4.284v1/DC1, 2004>

<sup>46</sup> Re-pricing a drug in the post market is a tall order, and certainly many of the drugs that have gone on to demonstrate significantly more value than first anticipated haven’t seen their prices rise to keep pace, if at all. Likewise, drugs that have disappointed from initial expectations haven’t always been accompanied by price breaks from manufacturers

declined in the U.S. during the past thirty years. Yet CHD remains a major cause of death and disability and is the leading source of medical spending. The authors write that “to understand the value of our sizable economic investment in CHD care, it is important to understand trends in disease incidence, mortality, and costs as they relate to trends in both risk factors and the uptake of medical technologies overtime.” Methodologically, Cutler’s results showed the importance of forming disease-based measures of medical spending and productivity.<sup>47</sup> Other work that Cutler did in collaboration with McClellan that focused on acute treatment of heart attacks found that the interventions themselves do not tell the entire cost equation. Perhaps more importantly, they considered the long-term costs and benefits of different types of care, differentiating between preventive care and acute treatment.<sup>48 49</sup>

Other work underscores the fact that the value of new medical products is often measured not only in the context of the disease in which they are used, but also through their impact on other factors such as worker productivity. In a recent National Bureau of Economic Research Working Paper Frank Lichtenberg used evidence drawn from longitudinal, disease-level data to examine the effect of the introduction of new laboratory procedures and other medical goods and services on the health of Americans during the period 1990-2003. They measured innovation in five types of medical procedures or products: pathology & laboratory procedures, outpatient prescription drugs, inpatient prescription drugs, surgical procedures, and diagnostic radiology procedures; examining two kinds of (inverse) indicators of health: mortality and disability. The mortality indicator they analyzed is the mean age at death of people whose underlying cause of death is medical condition. The disability measures they analyzed was the fraction of people with medical condition who either (1) missed work, or (2) spent one or more days in bed, due to that condition. Their estimates indicate that conditions with higher rates of lab and outpatient drug innovation had larger increases in mean age at death, controlling for other medical innovation rates and initial mean age at death. The 1990-1998 increase in mean age at death attributable to use of new lab procedures is estimated to be about six months.<sup>50</sup> In the analysis of disability, when they did not control for the initial level of disability, they found that conditions with higher rates of lab and outpatient innovation had greater declines in the chance of missed workdays. This suggests that use of new procedures reduced missed workdays in 2003 by 42 million.<sup>51</sup>

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<sup>47</sup> AB Rosen, DM Cutler, DM Norton, HM Hu, and S Vijan. The Value of Coronary Heart Disease Care For The Elderly: 1987–2002, Data from a variety of sources indicate that major progress has been made but much remains to be done to ensure value. *Health Affairs* 2007;26, Number 1: 111–123

<sup>48</sup> DM Cutler and MB McClellan. Is Technological Change in Medicine Worth It? *Health Affairs* 2001; Volume 20, Number 5; 11–29 and PA Heidenreich and MB McClellan. Trends in Treatment and Outcomes for Acute Myocardial Infarction: 1975–1995. *American Journal of Medicine* 2001,110, Number 3: 165–174

<sup>49</sup> See also: DM Cutler, G Long, ER Berndt, J Royer, AA Fournier, A Sasser and P Cremieux. The Value of Antihypertensive Drugs: A Perspective on Medical Innovation. *Health Affairs* 2007; 26(1), 97-100; and DM Cutler, AB Rosen and S Vijan. Value of Medical Innovation in the United States: 1960-2000. *New England Journal of Medicine*, 2006; 355:920-927. Also see DM Cutler, AB Rosen, DC Cutler, DM North, HM Hu, S Vijan. The value of coronary heart disease care in the elderly: 1987 to 2002. *Health Affairs*

<sup>50</sup> This is 42% of the total increase in mean age at death (1.18 years) in their sample of diseases. New laboratory procedures introduced during 1990-1998 were estimated to have saved 1.13 million life-years in 1998. Expenditure per life-year gained from new lab procedures was estimated to be \$6,093

<sup>51</sup> FR Lichtenberg. The Impact of New Laboratory Procedures and Other Medical Innovations on the Health of Americans, 1990-2003: Evidence from Longitudinal, Disease-Level Data. National Bureau of Economic Research Working Paper No. 12120, Issued in March 2006

A more recent analysis by Lichtenberg that looked at the trends in use of new technology across states found a correlation between higher spending on newer drugs and improved outcomes and productivity.<sup>52</sup> <sup>53</sup> In another study, Lichtenberg found in a recent study that pharmaceutical-embodied technical progress increases per capita output via its effect on labor supply (the employment rate and hours worked per employed person). Conditions for which there were above-average increases in utilization of prescriptions during 1996-1998 tended to have above-average reductions in the probability of missed workdays. He estimated value to employers of the reduction in missed workdays appears to exceed the employer's increase in drug cost.<sup>54</sup> A similar study by another author looked at the effects of prescription medicines on hourly wages and days lost from work are examined for four major chronic illnesses: hypertension, heart disease, non-insulin dependent (type II) diabetes and depression. It found that the net benefits to employers from having workers take prescription medicines for their chronic illnesses are substantial. Assuming average compliance rates are achieved, net benefits to employers in 1987 amounted to \$286 per hypertensive employee, \$633 per employee with heart disease; \$822 per depressed employee, and \$1,475 per type II diabetic employee under medication from a physician. These estimated benefits accrue because prescription medications substantially lower absenteeism among chronically ill workers.<sup>55</sup>

Recently, Philipson and his colleagues used a different analysis to try and capture the economic benefits of innovation, seeking to measure the value of a new technology by dividing between consumers (whose willingness to pay may exceed the price paid) and producers or innovators (whose costs may be lower than the price charged). As they write, “consumer surplus is central to static efficiency after an innovation has been discovered, while producer surplus, which forms the incentive for firms to engage in costly R&D to bring an innovation to market, is central to dynamic efficiency. Therefore, understanding the degree to which innovation benefits consumers versus producers is important for policies aimed at trading off the two forms of efficiency, such as intellectual property and R&D policies.” In one analysis they did to try and develop empirical evidence on the division of social surplus arising from new health care they investigated a major breakthrough in medicine—the new drugs to treat HIV and AIDS that came on the market after the late 1980’s. Their major finding is that innovators captured only 5% of the social surplus arising from these new technologies. More precisely, consumer and producer surplus from these drugs amounted to roughly \$1.33 trillion and \$63 billion, respectively.<sup>56</sup>

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<sup>52</sup> FR Lichtenberg. Why Has Longevity Increased More in Some States than in Others? The Role of Medical Innovation and Other Factors. Medical Progress Report No 4, July 2007, The Manhattan Institute.

<sup>53</sup> For similar work by Lichtenberg see: Lichtenberg, F. Are the Benefits of Newer Drugs Worth Their Cost? Evidence From the 1996 MEPS. *Health Affairs*, 2001; 20(5): pp. 241-51; FR Lichtenberg. Pharmaceutical-Embodied Technical Progress, Longevity, and the Quality of Life: Drugs as Equipment for Your Health; Lichtenberg, F. Pharmaceutical Innovation, Mortality Reduction, and Economic Growth, presented at the Conference on The Economic Value of Medical Research, December 1999; FR Lichtenberg. Sources of U.S. Longevity Increase: 1960-1997. Working Paper No. 405. December 2000. Center for Economic Studies and Ifo Institute for Economic Research. Munich, Germany

<sup>54</sup> Frank R. Lichtenberg. National Bureau of Economic Research Working Paper No. 9139 Issued in September 2002

<sup>55</sup> J Rizzo, et al. “Labor Productivity Effects of Prescribed Medicines for Chronically Ill Workers,” *Health Economics*, 1996; 5(3): pp. 249-65.

<sup>56</sup> TJ Philipson and AB Jena. Who Benefits from New Medical Technologies? Estimates of Consumer and Producer Surpluses for HIV/AIDS Drugs. National Bureau of Economic Research Working Paper No. 11810, December 2005. JEL No. I1

## **Conclusion: Considerations for policymakers**

The clear implication of analyses like those of Lichtenberg, Cutler, Philipson and others is that measuring the full value of medical innovation is complex. It does not lend itself easily to credible metrics that can be seamlessly incorporated into binary policy choices. Comprehensive assessments like those done by these economists tend to show that new technologies are on average worth their cost. But this is little solace to policymakers forced to control spending in the short run and asked to come up with defensible measures for doing so. This challenge is exacerbated by the fact that spending often increases, even when technologies produce value in the long run.

But measuring a new product's "value" at its introduction is antithetical to how benefits get demonstrated in medicine<sup>57</sup> and builds off an overly simplistic view of how the scientific process unfolds. This is one reason for the attractiveness of "comparative effectiveness" – it doesn't require policymakers to come up with sophisticated tools for "measuring value." Comparing the clinical usefulness of similar products enables policymakers to develop a scale of relative benefit and cost. Once again, however, comparisons between old and new products are likely to underestimate the subsequent value creation as doctors and patients work out new uses. Decisions to limit access at the time of initial product entry can undermine these real world applications.

To mitigate these challenges and shortcomings, a few minimum standards should apply to efforts for aligning centrally planned measures of "value" with determinants of access, whether it's done through more explicit regimes such as NICE's QALY system or an implicit approach such as the establishment of a comparative effectiveness mandate:

First, value should be measured from the perspective of how doctors and patients optimize new products and not how those products are directed for use from registration trials. The highly structured clinical trials done for regulatory approval often fail to approximate real world use of products, especially in complicated medical conditions and unmet needs. There's a mistaken belief that off label use of medical products is uniformly inappropriate use. But in many cases off label prescriptions represent attempts by doctors and patients to optimize the use of products to match individual circumstances. While it's beneficial to formally study the full complement of off-label possibilities, many of these are not only hard to envision prior to approval but prohibitively difficult to evaluate in any reasonably sized pre-approval package. Schemes that try to apply quantitative measures of value should not be extrapolated off the data from registration trials but subsequent real-world, practical use that takes into consideration these follow-on uses of new products.

Second, measures of value should be dynamic — evolving as new benefits are demonstrated. In this regard, higher value and pricing can come not only from new uses that expand the market for a drug, but discoveries about a drug that narrow its market but more effectively target it to patients that are most likely to recognize its benefits or suffer fewer of its side effects. Right now the marketplace doesn't reward efforts to better target new medicines after the time of approval, so development programs are often aimed at studies that can help sponsors expand the use of existing products into new indications rather than narrow their use based on science that more effectively targets them to the right patients. A system that pays for value should reward efforts to better apply

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<sup>57</sup> JE Calfee and E DuPre. The Emerging Market Dynamics of Targeted Therapeutics – How the Market for High Profile, High-Cost Drugs Differs from that of their Traditional Counterparts. *Health Affairs* September/October 2006;1302-1308; and JE Calfee. The Golden Age of Medical Innovation. *The American*, March/April 2007

therapies, especially when that means that new products can be given to a smaller number of patients selected for their propensity to benefit. “Value” based reimbursement needs to reward this kind of benefit creation.

Third, schemes for developing quantitative measures of “value” should take into consideration the strength of evidence that substantiates the various uses of a product. Just because patients or doctors choose to make use of a product in a circumstance that has been judged to be “lower-value” or for an indication where the evidence is less convincing, reimbursement should not be uniformly rejected or access denied. In this regard, the prevailing approach to co-pays may be inappropriate since it creates wide bands of “suitability” based more on price than value — and sometimes shifts equal costs to patients regardless of whether their intended use is based on substantial evidence of benefit or encompasses an off label use where there is less evidence.<sup>58</sup> If access and reimbursement is based on measuring the value of a proposed use, the same continuum of evidence that often exists for estimating clinical value should exist for setting rules about access and payment. Drugs are rarely totally devoid of clinical evidence to support their use, nor is the evidence so overwhelming as to guarantee a positive outcome for every patient. Clinical evidence supporting the use and potential benefit offered by medical technologies exists on a gradual continuum of credibility and completeness. Systems for measuring “value” – and approaches to cost sharing — should titrate to reflect this same gradual continuum.

Fourth and finally, measures of value should rely on post-market data collection and not solely on the information gleaned from registration trials. Highly structured clinical studies done for FDA approval are not always representative of real world use and benefit. To these ends, sponsors need to embrace efforts to engage in post-market data collection as a condition of broader reimbursement where the value of a product in certain indications is not readily apparent from the limited data available at the time of approval. This is better accomplished in direct discussions with the private market. This kind of approach, dubbed “coverage with evidence development” or CED by Medicare, is likely to falter if it remains a tool used by government. Technology developers should work actively with private payers to develop private market frameworks for this approach that could eventually supplant Medicare – creating a situation where the government relies on the private institutions to set its policy, rather than the private institutions pegging their reimbursement decisions to government conclusions. The fact is that Medicare lacks the clinical support to engage in discussions about real-world use of medical products. There are about 15 doctors inside the office that makes national coverage decisions, and about a dozen in the office that sets reimbursement rates. By contrast, large private insurers employ hundreds of clinicians.<sup>59</sup> Private plans use clinically-trained people to consult with practicing doctors on a case-by-case basis, determining whether a given product or service should be covered in a given circumstance. One metric has smaller plans using a clinician for every 10,000 beneficiaries — a formula that means Medicare would need 4,500 clinicians to keep pace. The private market is uniquely qualified to displace the government agencies when it comes to making assessments about new technologies, yet too often they are unwilling to step out on these decisions, preferring instead to follow the lead of the government agencies.<sup>60</sup>

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<sup>58</sup> Prescribing tools that are likely to be used in the future to penalize patients for off-label use of medicines should instead be used to titrate costs patients are increasingly saddled with according to how beneficial an intended use is and how much evidence supports it.

<sup>59</sup> By one estimate, Aetna has more than 200 physicians on staff, and more than 2,000 clinicians once non-physician providers are counted

<sup>60</sup> JR Holzgraefe. Controlling Health Care Costs Through Commercial Insurance Companies. *Duke Law Journal*, Vol. 1978, No. 2, Symposium on the Antitrust Laws and the Health Services Industry, pp. 728-752

Longer term, legislators should consider folding Medicare’s Part B (which pays for most injected, physician-administered drugs) and Medicare’s new Part D drug benefit into comprehensive contracting with health plans for full health services. This is likely to offer the most efficient approach to managing the drug benefit and ensuring high value use of new technologies. As Patricia Danzon and colleagues noted, writing in *the American Journal of Managed Care*, the advantages of competitive contracting for comprehensive health benefits, rather than contracting only for stand-alone pharmacy benefits (let alone stand-alone Part B drugs) is that comprehensive contracting allows the government to harness the health-benefit expertise of private insurers in an integrated, competitive bidding model. This approach may, over time, maximize value by creating efficiencies and savings in both benefit costs and the delivery of care.<sup>61</sup> Medicare, in particular, would resemble a defined contribution rather than a defined benefit.<sup>62</sup>

Properly regulated private health plans have more experience setting up treatment guidelines and monitoring use, something CMS struggles with given its how remote it sits from the actual delivery of care. This point was driven home by recent news of shortcomings in Medicare’s efforts to better manage care for patients with chronic conditions. Rolling the physician-administered drugs into Part D will also open up these products to more price competition. Right now, Medicare’s approach to contracting for specific services separately—hospitals, physicians, or prescription drugs—is problematic, because of the distorting incentive effects of silo reimbursement. Because products and services are paid separately, it makes it hard to recognize value across the continuum of care. Even if savings from drugs show up in the way of fewer medical procedures, Medicare would neither recognize nor appreciate these benefits under its current structure. By removing the silos associated with the way Medicare currently pays for drugs and services, contracting for comprehensive health benefits may enhance incentives and opportunities for savings in hospital or physician services that are offered by the creation of comprehensive drug coverage.<sup>63</sup> This would likely mean turning over more of these decisions to private plans, presumably through Medicare Advantage programs that offer a comprehensive drug and health benefit within the same plan.

Of course, political leaders and consumer groups often malign any attempt by private insurance plans to make formulary or reimbursement decisions that restrict coverage for some aspect of healthcare delivery, but it is unclear why it’s preferable for these decisions to be made by Medicare. The fact is that patients have far less recourse when decisions about access are made centrally, by Medicare, as opposed to their private health plans, for which they exert some discretion over, not only to change a plan’s administrative judgment on any individual matter, but to change plans entirely. Unlike private plans, Medicare can’t be in the business of weighing individual medical cases, and doesn’t want to be. It sets formulaic rules from Washington. The political drive to move more of these health decisions to Medicare rather than reside them with properly regulated private plans seems more about the political economy of who controls healthcare rather than how we maximize benefit to patients.

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<sup>61</sup> PM Danzon, GR Wilensky, KE Means. Alternative Strategies for Medicare Payment of Outpatient Prescription Drugs—Part B and Beyond. *The American Journal of Managed Care*, March 2005, volume 11:173-180

<sup>62</sup> JK Iglehart. Changing Health Insurance Trends. *New England Journal of Medicine* 2002;347:956-962

<sup>63</sup> PM Danzon, GR Wilensky, KE Means. Alternative Strategies for Medicare Payment of Outpatient Prescription Drugs—Part B and Beyond. *The American Journal of Managed Care*, March 2005, volume 11:173-180

Lowering the growth in medical spending will involve some form of allocation procedure involving administrative judgments. As in all events, the inevitable trade-offs and dilemmas cannot be wished away.<sup>64</sup> The further removed these kinds of clinical considerations are from the actual provision of care, the less accommodating our healthcare system will be to individual preference. The best tool for unlocking value may be policy approaches that expose consumers to a reasonable portion of the cost of their incrementally more expensive healthcare choices. Right now, the current approaches to co-pays, even in consumer-directed plans, fail to align choice with value since they are not tied directly to carefully considered assessments of the benefit that is being delivered. Too often, co-pays have no real attachment to value. It could be different. Private payers employ skilled technology assessment teams to evaluate evidence — yet they don't always make full use of this expertise when it comes to making decisions about price, formulary tiering, and access. Co-pays are driven as much by business deals between drug companies and pharmacy benefit managers as by value. Access is often all-or-nothing — either a plan covers a drug, passing on to patients a fixed percentage of the costs, or it pays for nothing at all. Yet it's rare that the evidence surrounding a novel treatment is based on a body of evidence that presents the same binary choice — swinging between highly useful or useless. Ideally, co-pays should be constructed with more and not fewer “tiers,” with each decision to pass on some of the costs to consumers based on some approximation of the evidence available to substantiate a certain use of a product and its potential benefit or “value” in a particular indication.

Recent history has taught us that a drug targeted to specific molecular processes almost invariably goes on to prove other potential uses. There are many complicated reasons for this but at its simplest form it is a lesson in systems biology: the body is a conservative system, meaning that it uses a discrete number of molecular processes to drive its millions of different functions. So a drug able to intervene in one molecular system in a certain disease state is invariably able to intervene on the same molecular system when it goes awry in other disease processes. Ideally, our approach to paying for new medical products should be flexible, based on the expectation that post market information about new benefits should be used to tailor reimbursement decisions. But policymakers need to make decisions in the moment that impact future opportunities. This clash between the present and the future can thwart comprehensive consideration of benefits. The worst alternative would be a system that “estimates value” to patients early in the life cycle of new technologies, and then uses these measures to make binary and binding decisions about price and access. If we take this approach, a lot of subsequent value creation will be forestalled. Such a system will merely disguise fixed controls on access behind a shroud of clinical language.

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<sup>64</sup> S Gottlieb. Edwards and Organ Transplants. The Wall Street Journal, January 11, 2008. A14