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**ENCOURAGING COMPARATIVE EFFECTIVENESS RESEARCH IN THE PRIVATE SECTOR:  
MEMORIAL SLOAN-KETTERING’S MODEL BEHAVIOR**

**By A. Isabel Heine**

**INTRODUCTION**

The concept of a moral hazard is a traditionally economic term that is defined as “excessive expenditure due to eligibility for insurance benefits.”<sup>1</sup> This economic term has found its way into the health care world to mean the additional health care services or treatment that is purchased by individuals once they become insured.<sup>2</sup> For example, an insured individual may spend an extra day in the hospital that is not necessary simply because he/she can due to their insurance coverage.<sup>3</sup> According to economists, the patient consumer’s view of the cost of that extra day at the hospital is zero because their health insurance is paying for it.<sup>4</sup> One can imagine that this was not viewed favorably by the health insurance companies and this economic concept has therefore created a trend towards higher co-payments and deductibles for patients.<sup>5</sup> The rationale behind these increases is that health care consumers will avoid imprudent and pricier health care treatments or services if the co-payment up front is higher.<sup>6</sup> This unfortunately has unintended consequences. The uninsured and underinsured will tend to underuse and forego essential health care services, which may then result in higher morbidity and an increase in preventable hospitalizations and deaths.<sup>7</sup>

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<sup>1</sup> John M. Marshall, *Moral Hazard*, 66 AM. ECON. REV. 880 (1976).

<sup>2</sup> John A. Nyman, *Is ‘Moral Hazard’ Inefficient? The Policy Implications Of A New Theory*, 23(5) HEALTH AFF. 194 (2004).

<sup>3</sup> *Id.*

<sup>4</sup> *Id.*

<sup>5</sup> *Id.*

<sup>6</sup> *Id.*

<sup>7</sup> *Id.*

Health insurance coverage in the United States has increased from 45 percent of the population in 1960 to about 83 percent of the population in 2011.<sup>8</sup> During that same 51-year span, the percentage of United States Gross Domestic Product attributable to personal health care rose from 4.4 percent to more than 15 percent.<sup>9</sup> There is an undeniable relationship between the number of insured Americans and rising health care spending.

But health insurance is not going anywhere and with the implementation of the Patient Protection and Affordable Care Act (PPACA) many more Americans will be insured than ever before. There are cost-containment provisions related to copayments to help curb some of individual health care consumer spending, but one thing that is not being controlled is the costs of services and treatments in general.<sup>10</sup> The concept of the moral hazard as related to health care does not seem to be going anywhere either, so why not remove it? Comparative effectiveness research (CER) has the potential to do this in a sense through its consideration of cost and expansive evidentiary standards. By removing a pricier and otherwise no more effective alternative from a health care consumer's pool of choices, the possibility of increased consumption due to coverage evaporates.

CER is very divisive. Although a lot of federal resources have been dedicated to CER, there are other decisions made by the federal government that demonstrate their ambivalence to the concept. Its opponents refer to it as the rationing of health care and point to programs such as

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<sup>8</sup> Carmen DeNavas-Walt, Bernadette D. Proctor, Jessica C. Smith, *Income, Poverty, and Health Insurance Coverage in the United States: 2010*, UNITED STATES CENSUS Bureau (2011): 60-239, available at <http://www.census.gov/prod/2011pubs/p60-239.pdf>.

<sup>9</sup>Table 1.1 – Personal Health Care (PHC) Expenditures by Source of Funds: Selected Calendar Years 1960-2011, <http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/MedicareMedicaidStatSupp/2012.html>

<sup>10</sup> See, e.g., PPACA § 2705, 124 Stat. 119, codified at 42 U.S.C. § 300gg-4 (for an example of caps and waivers on copayments and other cost-sharing mechanisms).

the Oregon Health Plan as an example of how this type of decisionmaking can fail. Some small institutions continue to press on with the core ideals of CER, encouraging the idea of treating patients based on evidence of the benefits and harms of alternative treatments, which includes the consideration of cost. When the power of CER is harnessed effectively, one hospital's decision to not offer a new drug to their patient population can help influence other providers as well. One particular area of health care worth analyzing due to its tendency of including pricy treatments is cancer care.

After an examination of the current state of cancer care in the United States in Part I, Part II of this piece will address the history and concept of comparative effectiveness research. Opposition to CER will be addressed, with a particular focus on the Oregon Health Plan. In Part III, the story of one hospital, Memorial Sloan-Kettering Cancer Center, will be discussed and their decisionmaking process will be examined to demonstrate how CER can be used. The ramifications of their decision will be evaluated as well. Part IV will introduce the reader to the Accountable Care Organization model and demonstrate how this may in fact be an endorsement of CER-type decisionmaking. Finally, in Part V this piece will conclude that CER is a workable model for health care organizations despite the conflicting messages from our current administration.

## **PART I: THE CURRENT STATE OF CANCER CARE: DATA THAT CANNOT BE IGNORED**

In 2006, the annual cost for cancer care was \$104 billion and is projected to reach \$173 billion by 2020.<sup>11</sup> Much of this rise can be attributed to the dramatic increase in cancer drugs. One example for breast cancer chemotherapy in general showed not only a doubling in use of

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<sup>11</sup> Thomas J. Smith, M.D., and Bruce E. Hillner, M.D., *Bending the Cost Curve in Cancer Care*, 364 NEW ENG. J. MED. 2060 (2011).

chemotherapy, but also a near doubling in the average cost of treatment between 1991 and 2002 (\$8,288 to \$15,974 in 2012 US dollars).<sup>12,13</sup> Across all new cancer drugs, the trend is the same. In 2002, the average cost of a new cancer drug for one month of treatment was about \$4,500 (adjusted to 2012 dollars), whereas 2010 prices demonstrate a median price of \$10,000.<sup>14</sup> Figure 1 demonstrates the monthly costs of cancer drugs at the time of approval by the Food and Drug Administration from 1965 through 2008.<sup>15</sup> Figure 1 does contain outliers but the trend line demonstrates the increasing costs over time. In removing the outliers (Figure 2), the trend is even more pronounced, demonstrating a near exponential rise in the monthly cost of treatment. Additionally, our country's increasing costs in cancer care do not yield better results. Compared to Canada's \$4,500/person annual cost of cancer care, the United States spends \$8,100/person, without demonstrating better results.<sup>16</sup>

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<sup>12</sup> Elena B. Elkin, PhD; Peter B. Bach, MD, MAPP, *Cancer's Next Frontier: Addressing High and Increasing Costs*, 303(11) JAMA 1086 (2010).

<sup>13</sup> Dollar figures adjusted using the Bureau of Labor Statistics CPI Inflation Calculator, *available at* [http://www.bls.gov/data/inflation\\_calculator.htm](http://www.bls.gov/data/inflation_calculator.htm).

<sup>14</sup> Peter B. Bach, Leonard B. Saltz, Robert E. Wittes, *In Cancer Care, Cost Matters*, N.Y. TIMES, Oct. 14, 2012, at A25.

<sup>15</sup> Paul B. Bach, *Limits on Medicare's Ability to Control Rising Spending on Cancer Drugs*, 360 NEW ENG. J. MED. 626 (2009) (supplement to), [http://www.nejm.org/doi/suppl/10.1056/NEJMhpr0807774/suppl\\_file/nejm\\_bach\\_626sa1.pdf](http://www.nejm.org/doi/suppl/10.1056/NEJMhpr0807774/suppl_file/nejm_bach_626sa1.pdf) (data from the supplement was used but graphs are original).

<sup>16</sup> Thomas J. Smith, MD, Rebecca Kirch, JD, *Reducing Cost, Improving Quality Care through Individual Choices: Taking Place at the Table*, ASCO DAILY NEWS (Jun. 5, 2012), <http://chicago2012.asco.org/ASCODailyNews/CostEditorial.aspx>.

Figure 1

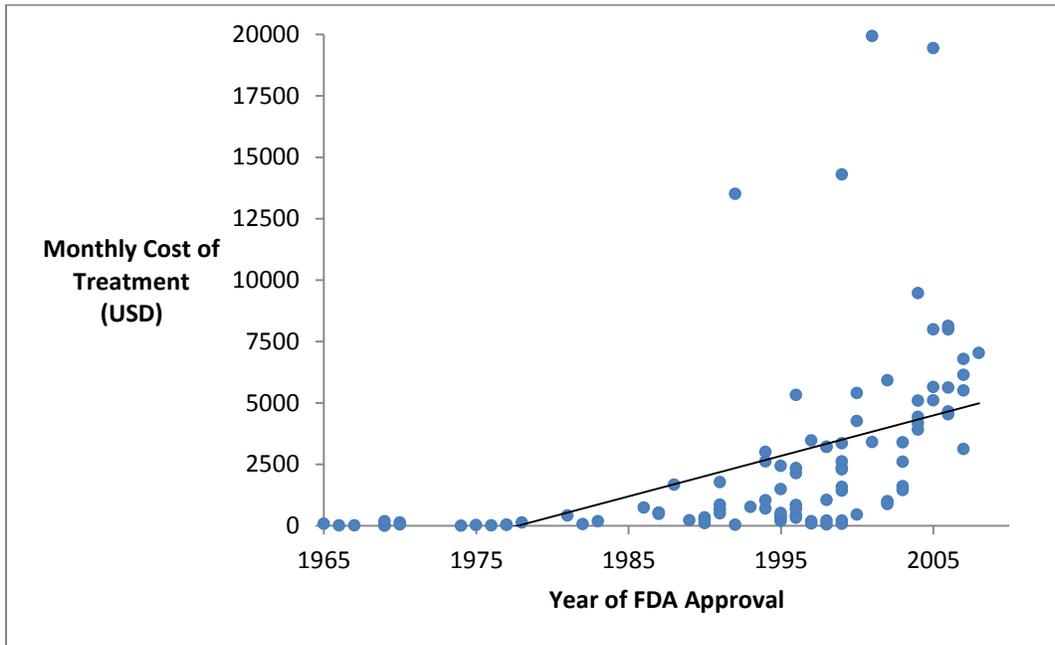
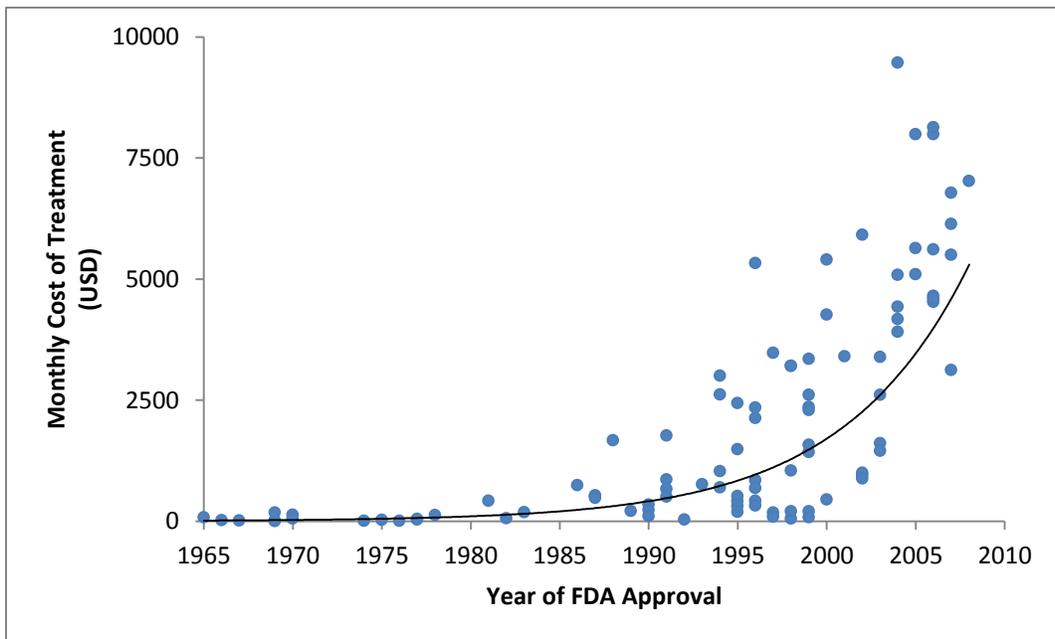


Figure 2



These increasing costs create a burden on the Medicare and Medicaid systems and the insurance industry as well. Average annual health insurance premiums for family coverage have risen 97 percent between 2002 and 2012.<sup>17</sup> The rise in costs has had a staggering effect on the American family as well. A comprehensive survey conducted by the Kaiser Family Foundation in 2006 explored some of the financial effects of cancer on the American household. Fifty-six percent of those surveyed experienced an increase in the past year in the costs of drugs related to their cancer.<sup>18</sup> Twenty-five percent used up all or most of their savings as a result of the financial cost of dealing with their cancer.<sup>19</sup> Eleven percent were unable to pay for basic necessities, like food heat or housing, as a result of the financial cost of dealing with their cancer.<sup>20</sup> Thirteen percent were contacted by a collection agency and 3 percent declared bankruptcy as a result of the financial cost of dealing with their cancer.<sup>21</sup> The numbers are even higher in particular types of cancer. Eight percent of families dealing with lung cancer are bankrupt due to the cost of care.<sup>22</sup> Even patients with private insurance, where one may expect adequate coverage, still suffer out-of-pocket costs of more than \$18,000/year, and 5 percent of those patients have out-of-pocket costs greater than \$35,000/year.<sup>23</sup>

Oncologists are beginning to speak out against the pharmaceutical manufacturers regarding the prices of anti-cancer therapies, calling the pricing unsustainable and often

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<sup>17</sup>Employer Health Benefits: 2012 Summary of Findings, The Kaiser Family Foundation and Health Research & Educational Trust (2012), <http://ehbs.kff.org/pdf/2012/8346.pdf>.

<sup>18</sup> National Survey of Households Affected by Cancer, The USA Today/Kaiser Family Foundation/Harvard School of Public Health, <http://www.kff.org/kaiserpolls/upload/7590.pdf>.

<sup>19</sup> *Id.*

<sup>20</sup> *Id.*

<sup>21</sup> *Id.*

<sup>22</sup> Smith & Kirch, *supra* note 16.

<sup>23</sup> Dana P. Goldman, Geoffrey F. Joyce, Grant Lawless, William H. Crown, Vincent Willey, *Benefit Design And Specialty Drug Use*, 25(5) HEALTH AFF., 1319 (2006), <http://content.healthaffairs.org/content/25/5/1319.full.pdf>.

immoral.<sup>24</sup> Although, little tangible evidence exists to suggest that pharmaceutical companies are reacting to the opposition.

## **PART II: COMPARATIVE EFFECTIVENESS RESEARCH AS A BODY OF WORK: SUPPORT OR AMBIVALENCE FOR THIS TYPE OF DECISIONMAKING?**

One common theme throughout many pieces pointing out these daunting statistics is that the solutions are within the hands of the oncologists themselves, including chemotherapy and other treatment choices.<sup>25</sup> Suggested changes in practice include the recognition that the costs of care are driven by what the physicians do and do not do and that the need for cost-effectiveness analysis and other limits on care must be accepted.<sup>26</sup> This is where comparative effectiveness research fits in nicely.

### *A. The Conflicting History of Comparative Effectiveness Research: Promotion and Restriction*

CER has long been used in the United Kingdom where the National Institute of Clinical Excellence uses a metric known as the Quality Adjusted Life Year (QALY) to determine coverage.<sup>27</sup> A QALY accounts for such factors as the improvement in the quality of life and the side effects a treatment may cause, which lead to such considerations as the level of pain a person is in or their mobility.<sup>28</sup> After determining the QALY measurement of a particular treatment, the treatment is then evaluated to see how much it would cost per QALY, in other words, “the cost of using the drugs to provide a year of the best quality of life available.”<sup>29</sup> Each treatment is considered on an individual basis but generally a treatment will be considered cost

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<sup>24</sup> Andrew Pollack, *Doctors Denounce Cancer Drug Prices of \$100,000 a Year*, N.Y. TIMES, Apr. 26, 2013 at B1.

<sup>25</sup> Sandra M. Swain, *The High Cost of a Cancer Drug: An Oncologist’s View*, N.Y. TIMES, Oct. 20, 2012 at A22.

<sup>26</sup> Smith & Kirch, *supra* note 16.

<sup>27</sup> MEASURING EFFECTIVENESS AND COST EFFECTIVENESS: THE QALY, <http://www.nice.org.uk/newsroom/features/measuringeffectivenessandcosteffectivenesstheqaly.jsp> (last visited on Apr. 29, 2012, 11:27PM).

<sup>28</sup> *Id.*

<sup>29</sup> *Id.*

effective, and therefore covered, if it falls within \$33,000 – \$50,000 per QALY.<sup>30</sup> NICE makes sure to point out that this is not the only measurement used to determine coverage.<sup>31</sup>

There are other suggested comparative effectiveness limitations that use the QALY metric for suggested coverage. One study created a line for cost ineffectiveness by using the \$50,000 cost per life-year-gained as a measure.<sup>32</sup> This number is derived from the decision to use federal funding to pay for dialysis but reflects the 1982 cost.<sup>33</sup> The researchers adjusted the 1982 cost to find a value of \$197,000 per life-year-gained in 2007 dollars and made this the threshold for coverage.<sup>34</sup> The World Health Organization (WHO) has also issued their own comparative effectiveness guidance. WHO's guidance uses a multiple of a country's per capita gross domestic product (GDP): less than or equal to one times the country's GDP is considered very cost effective; one to three times the GDP as simply cost effective; and more than three times the GDP as cost ineffective.<sup>35</sup> The World Bank listed the United States' per capita GDP at \$48,112 in 2011, making our three times threshold \$144,336, or what the maximum cost per QALY would be to label a treatment cost ineffective.<sup>36</sup>

Officially, the Institute of Medicine defines comparative effectiveness research as "... the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care. The purpose of comparative effectiveness research is to assist consumers, clinicians,

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<sup>30</sup> John Donnelly, *Comparative Effectiveness Research*, HEALTH AFF.: HEALTH POLICY BRIEF, [http://healthaffairs.org/healthpolicybriefs/brief\\_pdfs/healthpolicybrief\\_28.pdf](http://healthaffairs.org/healthpolicybriefs/brief_pdfs/healthpolicybrief_28.pdf)

<sup>31</sup> *Id.*

<sup>32</sup> Bruce E. Hillner, Thomas J. Smith, *Efficacy Does Not Necessarily Translate to Cost Effectiveness: A Case Study in the Challenges Associated With 21<sup>st</sup>-Century Cancer Drug Pricing*, 27(13) J. CLINICAL ONCOLOGY 2111 (2009).

<sup>33</sup> *Id.*

<sup>34</sup> *Id.*

<sup>35</sup> Christopher J.L. Murray, David B. Evans, Arna Acharya, Rob M.P.M. Baltussen, *Development of WHO Guidelines on Generalized Cost-Effectiveness Analysis*, 9 HEALTH ECON. 235 (2000).

<sup>36</sup> The World Bank, GDP per capita (current US\$), <http://data.worldbank.org/indicator/NY.GDP.PCAP.CD>

purchasers and policy makers to make informed decisions that will improve health care at both the individual and population levels.”<sup>37</sup> Historically, two big forces led to the prominence of comparative effectiveness research. One was the focus on delivering clinical care based on evidence, which began in the 1980s and led to the creation of the US Preventive Services Taskforce in 1984 and the Cochrane Collaboration in 1993, followed by the evidence-based practice centers of the Agency of Healthcare Research and Quality in 1998.<sup>38</sup> On the other hand was the need to make care more effective while containing costs, with the research being led by the work of John Weinberg and Elliot Fisher on the area of spending and outcomes.<sup>39</sup> One of their more prominent studies demonstrated that high health care spending areas of the country do not have better health outcomes than their counterparts in lower health care spending areas of the country.<sup>40</sup> In 1996, the U.S. Public Health Service suggested evaluating certain drugs and treatments based on how many years of healthy life they produced per dollar, a measure synonymous with CER and in 2003, George W. Bush signed the Medicare Modernization Act into law, authorizing \$50 million to be used towards cost effectiveness research of health care treatments.<sup>41</sup>

The drive for evidence and the drive for cost containment also led to a report from the Congressional Budget Office in 2007.<sup>42</sup> The report included research on the comparative

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<sup>37</sup> *Initial National Priorities for Comparative Effectiveness Research* (2009),

<http://www.iom.edu/Reports/2009/ComparativeEffectivenessResearchPriorities.aspx>

<sup>38</sup> Jodi Segal, MD, MPH, *Comparative Effectiveness Research: Recent Past to Present*,

<http://ictr.johnshopkins.edu/ictr/CER.Segal.pdf>.

<sup>39</sup> *Id.*

<sup>40</sup> Gail R. Wilensky, *The Policies and Politics of Creating a Comparative Clinical Effectiveness Research Center*, 28(4) HEALTH AFF. W79 (2009).

<sup>41</sup> Philip Longman, *The Republican Case for Waste in Health Care*, THE WASHINGTON MONTHLY (Mar./Apr. 2013), [http://www.washingtonmonthly.com/magazine/march\\_april\\_2013/features/the\\_republican\\_case\\_for\\_waste043314.php?page=5](http://www.washingtonmonthly.com/magazine/march_april_2013/features/the_republican_case_for_waste043314.php?page=5)

<sup>42</sup> Research on the Comparative Effectiveness of Medical Treatments, CONGRESSIONAL BUDGET Office (2007), available at <http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/88xx/doc8891/12-18-comparativeeffectiveness.pdf>.

effectiveness of medical treatments, which led to the conclusion that it is possible to constrain health care costs both in the public programs and in the rest of the health system without adversely affecting the health of individuals.<sup>43</sup> The report also pointed out that geographic differences in health care spending do not lead to higher life expectancies or measured improvements in other health outcomes in the more health care costly regions.<sup>44</sup> The report also expressed concern for the fact that patients and their caregivers have limited access to information on which treatments work best for which patients and whether the benefits of pricier treatments warrant the added expense.<sup>45</sup> Additionally the report posited that Medicare spending – and perhaps all health care expenditure in the country – could be cut by 30 percent if the more conservative practice styles used in the lowest spending one-fifth of the country could be adopted nationwide.<sup>46</sup> This report advocated for further research on the comparative effectiveness of medical treatments.

2007 and 2008 saw successive legislation encouraging further cost-effectiveness metrics. The Children’s Health and Medicare Protection (CHAMP) Act bill was created with the purpose of extending Medicaid benefits to low-income children and would have involved the creation of a Center for Comparative Effectiveness Research within the Agency for Healthcare Research and Quality.<sup>47</sup> The bill never made it to the Senate.<sup>48</sup> In the following year, the Comparative Effectiveness Research Act (known as Baucus-Conrad for its two sponsors) was introduced with the purpose of creating the Health Care Comparative Effectiveness Research Institute.<sup>49,50</sup> This

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<sup>43</sup> *Id.*

<sup>44</sup> *Id.*

<sup>45</sup> *Id.*

<sup>46</sup> *Id.*

<sup>47</sup> Stephen Barlas, *Congress Agrees on the Need for Comparativeness Research but Funding Will be a Problem*, 33(10) PHARMACY AND THERAPEUTICS 569 (2008).

<sup>48</sup> *Id.*

<sup>49</sup> *Id.*

institute would use evidence-based research to generate treatment information on how to attain the best clinical outcomes.<sup>51</sup> Both bills used the term comparative clinical effectiveness research and the latter suggested that cost-effectiveness should be explored.<sup>52</sup>

The American Reinvestment and Recovery Act (ARRA) of 2009 had a powerful impact on comparative effectiveness research when it provided for \$1.1 billion for patient-centered health care research.<sup>53</sup> This was followed in 2010 by the Patient Protection and Affordable Care Act (PPACA), which included a section titled Patient-Centered Outcomes Research.<sup>54</sup> In PPACA, comparative effectiveness research is defined as “research evaluating and comparing health outcomes and the clinical effectiveness, risks, and benefits of 2 or more medical treatments, services, and items described.”<sup>55</sup> PPACA also established the Patient-Centered Outcomes Research Institute (PCORI), which notably is an independent non-profit organization and not an agency of the government.<sup>56</sup> PCORI’s mission is to “assist patients, clinicians, purchasers, and policymakers in making informed health decisions by advancing the quality and relevance of evidence concerning the manner in which diseases... can effectively and appropriately be prevented, diagnoses, treated ... through research and evidence synthesis ... the dissemination of research findings...”<sup>57</sup> In December, 2012, PCORI announced it would be

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<sup>50</sup> The Comparative Effectiveness Research Institute was the precursor to the Patient-Centered Outcomes Research Institute (PCORI). Its name was changed due to the controversy over the inference that comparative effectiveness research would be used. Kathryn Nix, *Comparative Effectiveness Research Under Obamacare: A Slippery Slope to Health Care Rationing*, THE HERITAGE FOUNDATION (Apr 12, 2012) <http://www.heritage.org/research/reports/2012/04/comparative-effectiveness-research-under-obamacare-a-slippery-slope-to-health-care-rationing>

<sup>51</sup> *Id.*

<sup>52</sup> Wilensky, *supra* note 40.

<sup>53</sup> RECOVERY.GOV TRACK THE MONEY, <http://www.recovery.gov/Pages/default.aspx> (last visited Apr. 29, 2013).

<sup>54</sup> PPACA § 6301, 124 Stat. 119, codified at 42 U.S.C. § 1320e.

<sup>55</sup> *Id.*

<sup>56</sup> *Id.*

<sup>57</sup> PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE, [www.pcori.org/about-us/](http://www.pcori.org/about-us/) (last visited Apr. 29, 2013).

disbursing more than \$40.7 million worth of funding for its first comparative effectiveness research projects.<sup>58</sup>

Although the history of CER suggests an inclination by our government to further this type of research, PCORI's focus is on patient-centered outcomes research, which does not necessarily equate to CER. Under PPCACA, PCORI is allowed to compare the benefits of various treatments but not compare the costs to benefits of various treatments.<sup>59</sup> Additionally, PPACA states that PCORI "shall not develop or employ **a dollars-per-quality adjusted life year (or similar measure that discounts the value of a life because of an individual's disability)** as a threshold to establish what type of health care is cost effective or recommended."<sup>60</sup> Quality-adjusted life years are at the center of recommendations and guidelines by those that practice comparative effectiveness research. The QALY metric involves quantifying the two things that most people would want from their health care: the most years of quality of life and the least cost for those years.<sup>61</sup> Conducting CER without the use of QALYs or a similar metric seems undoable.

One explanation for this sharp restraint on comparative effectiveness research is the composition of PCORI's Board of Governors. The board consists, although not solely, of pharmaceutical and device manufacturer executives as well as the chair and founder of Friends of Cancer Research, a cancer research think tank and advocacy group whose funding comes from large pharmaceutical companies.<sup>62</sup> It would not be a stretch to say that drug and device

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<sup>58</sup> PCORI Announces Funding for First Comparative Effectiveness Research Projects, <http://www.pcori.org/2012/funding-awards/> (last visited Apr. 29, 2013).

<sup>59</sup> Longman, *supra* note 41

<sup>60</sup> *Supra* note 54.

<sup>61</sup> Longman, *supra* note 41.

<sup>62</sup> *Id.*

manufacturers have a stake in any research that could keep their drugs and devices from consumers by way of federal recommendations for use.

Lastly, the FDA does not consider a drug's cost at the time of the approval decision, only its safety and efficacy, and PPACA prohibits the use of quality-adjusted life years or other cost-effectiveness metrics to be used in determining Medicare coverage or reimbursement as well.<sup>63,64</sup>

#### B. *The Case Against Comparative Effectiveness Research*

Opponents of the use of cost as a measure of a treatment's effectiveness say that the assertion that health care spending can be reduced by foregoing medical technologies and treatment that add little benefit is misguided.<sup>65</sup> They argue that in fact there is evidence that medical innovation is associated with "greater longevity" and that comparative effectiveness research could potentially decrease research and development through its impact on innovation in our society.<sup>66</sup> If forced to conduct comparative effectiveness studies prior to and as a condition for coverage of a new medicine (note: this is currently not required), research and development costs would soar and researchers may just decide to forego the research altogether.<sup>67</sup> One study found that CER has the potential to increase research and development costs by as much as 50 percent in certain phases of the drug development process and would reduce research and development spending by over \$30 million over ten years if required to

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<sup>63</sup> HOW FDA APPROVES DRUGS AND REGULATES THEIR SAFETY AND EFFECTIVENESS (2012), <http://www.fas.org/sgp/crs/misc/R41983.pdf>.

<sup>64</sup> *Supra* note 54.

<sup>65</sup> John Vernon, PhD, Robert Goldberg, PhD, *Shorter Lives, Less Prosperity: The Impact of Comparative Effectiveness Research on Health and Wealth*, CENTER FOR MEDICINE IN THE PUBLIC INTEREST (2009), [http://www.cmpi.org/uploads/File/CER\\_Paper\\_FINAL.pdf](http://www.cmpi.org/uploads/File/CER_Paper_FINAL.pdf).

<sup>66</sup> *Id.*

<sup>67</sup> *Id.*

conduct CER studies during drug development.<sup>68</sup> Additionally, this same study estimated that because research and development and higher life expectancy are correlated, CER could cost this country 81 million life years and \$4 trillion dollars.<sup>69</sup> Furthermore, another recent study that compared the effect of comparative effectiveness research on access to approved anti-cancer treatments in Europe and the United States demonstrated that the process led to delays of over two years and 60 percent fewer medications being made available when effectiveness reviews were in place.<sup>70</sup>

Critics of CER point to the possibility of studies only examining a heterogeneous patient population, meaning that the results of a study will show that one treatment is superior over another **on average**.<sup>71</sup> The treatment may work far better in one group but a study measuring average efficacy would not demonstrate this.<sup>72</sup> One example of this effect can be seen in a case involving panitumumab, a drug used to treat metastatic colorectal cancer.<sup>73</sup> In 2007, it was rejected for coverage in Europe for being similarly as effective as its predecessor chemotherapy that cost far less.<sup>74</sup> A closer look at the data demonstrated that patients with a normal gene type responded far better than patients with a particular mutation in their genes.<sup>75</sup> A CER study that only looked at the average benefits of those receiving the drug would have not captured this very important difference within the patient population.<sup>76</sup> Luckily, this particular difference was discovered and the drug was approved for coverage the following year for those with a normal

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<sup>68</sup> *Id.*

<sup>69</sup> *Id.*

<sup>70</sup> Anne Mason, Michael Drummond, Scott Ramsey, Jonathan Campbell, Dennis Raisch, *Comparison of Anticancer Drug Coverage Decisions in the United States and United Kingdom: Does the Evidence Support the Rhetoric?*, 28(20) J. CLINICAL ONCOLOGY 3234 (2010).

<sup>71</sup> Amitabh Chandra, Anupam B. Jena, Jonathan S. Skinner, *The Pragmatist's Guide to Comparative Effectiveness Research*, 25(2) J. ECON. PERSP. 27 (2011).

<sup>72</sup> *Id.*

<sup>73</sup> *Id.*

<sup>74</sup> *Id.*

<sup>75</sup> *Id.*

<sup>76</sup> *Id.*

gene.<sup>77</sup> Supporters of CER take this concern to heart and note that knowing the average effect is better than having no knowledge at all.<sup>78</sup> Additionally, CER will make information far more accessible to patients and providers alike since more expansive sets of information will allow providers to better tailor treatment to their patients.<sup>79</sup> The finite entry criteria for clinical trials that the drug manufacturers require do not allow for the same sort of extensive objective analysis across many subgroups that CER does.<sup>80</sup> The Institute of Medicine's own recommendation on CER includes research involving very precise subgroups.<sup>81</sup>

Proponents of comparative effectiveness studies suggest that one key element should be left out of the research in the short term, namely cost.<sup>82</sup> Cost is the main factor within CER that creates controversy and including it in future research will increase the likelihood of exposing all such research to political vulnerability.<sup>83</sup> Eliminating the financial factor in CER studies would still lead to valuable conclusions that would be useful to the general health care consumer population.<sup>84</sup> Although, it would still leave the larger problem of an unsustainable health care industry untouched since cost is the real problem being faced.

### *C. The Oregon Health Plan as Not an Example of the Failure of Comparative Effectiveness Research*

The Oregon Health Plan (OHP) is often referred to as the Oregon Experiment because of the bold steps it took to expand Medicaid coverage for Oregonians, specifically those with

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<sup>77</sup> *Id.*

<sup>78</sup> *Id.*

<sup>79</sup> Ellen-Marie Whelan, Sonia Sekhar, *Better Health Through Better Information: Comparative Effectiveness Research Will Help Deliver Better Medical Care*, CENTER FOR AMERICAN PROGRESS (Sept. 29, 2009) <http://www.americanprogress.org/issues/healthcare/news/2009/09/29/6658/better-health-through-better-information/>.

<sup>80</sup> *Id.*

<sup>81</sup> *Id.*

<sup>82</sup> Wilensky, *supra* note 40.

<sup>83</sup> *Id.*

<sup>84</sup> *Id.*

income below the federal poverty line.<sup>85</sup> The Plan is often cited by opponents of cost effectiveness metrics as a failure of this type of decisionmaking because the implementation of rationing was unable to control costs.<sup>86</sup> But this assertion is worthy of further investigation.

The Oregon Medicaid Priority Setting Project was initiated in 1988 by Dr. John Kitzhaber, an emergency room physician turned state senator turned governor, and became the cornerstone of the Oregon Health Plan.<sup>87</sup> The Oregon Health Fund Board described the five main goals of the plan as the following: 1) health care for the uninsured; 2) broad participation by providers; 3) decrease cost shifting and charity care; 4) a basic benefit package of effective services; and 5) a rational process for making decisions on how to allocate resources for health care.<sup>88</sup> The approach was novel; the plan would limit the services covered under the plan in order to increase the number of people covered.<sup>89</sup> The plan unfortunately has encountered some impediments to fulfilling its five stated goals. The desired cost containment never came to fruition and providers began to limit access to Medicaid patients due to a decline in reimbursements.<sup>90</sup> Soon after, plan beneficiaries became subject to premiums and copayments that are in effect to this day.<sup>91</sup>

The list of covered services was created with the goal of reducing costs by eliminating coverage for treatments that were not proven cost-effective.<sup>92</sup> In essence, the plan sought to

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<sup>85</sup> Eric Fruits, PhD, Andrew Hillard, Laura Lewis, *The Oregon Health Plan: A "Bold Experiment" That Failed*, CASCADE POLICY INSTITUTE (2010), [http://cascadepolicy.org/wp-content/uploads/2010/09/Oregon\\_Health\\_Plan\\_-\\_The\\_Bold\\_Experiment\\_That\\_Failed.pdf](http://cascadepolicy.org/wp-content/uploads/2010/09/Oregon_Health_Plan_-_The_Bold_Experiment_That_Failed.pdf)

<sup>86</sup> Linnea Laestadius, *The Oregon Health Plan – From Boom to Bust*, 6 MICH. J. PUB. AFF. 1 (2009), <http://www.mjpa.umich.edu/uploads/2/9/3/2/2932559/oregonhealthplanpdf.pdf>.

<sup>87</sup>Fruits, *supra* note 85.

<sup>88</sup> *Id.*

<sup>89</sup> *Id.*

<sup>90</sup> *Id.*

<sup>91</sup> *Id.*

<sup>92</sup> *Id.*

cover those treatments that provided the biggest “bang-for-your-buck”.<sup>93</sup> The problem, though, became how to make this determination and the word rationing came to the forefront of this project.<sup>94</sup>

The covered services were to be determined by the Oregon Health Services Commission, a group that included providers and consumers or purchasers of health care services.<sup>95</sup> This list would prioritize services deemed cost-effective and would exclude any service or treatment determined to be cost-ineffective.<sup>96</sup> Dr. Kitzhaber viewed this particular aspect of the program as a way to impact physician decisionmaking, which, according to him, controls 70 percent of the health care budget through the effects of their decisions to hospitalize (or not), what procedure to perform, and what drugs to prescribe.<sup>97</sup> The Commission first created a list of 709 diagnoses and their treatments, which were referred to as “condition/treatment pairs”.<sup>98</sup> The list was intended to be purely objective and to be based on a mathematical formula that combined clinical data and outcomes research.<sup>99</sup> Condition/treatment pairs would be moved up or down the list based on this cost-benefit formulary or onto the list in the case of new treatments and procedures.<sup>100</sup> Any additional condition/treatment pairs were to be added based on this formula.<sup>101</sup> Several condition/treatment prioritization lists were proposed and rejected.<sup>102</sup> The list that was eventually put into practice used a ranking system that was not purely based on cost-

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<sup>93</sup> *Id.*

<sup>94</sup> Jonathan Oberlander, Theodore Marmor, Lawrence Jacobs, *Rationing medical care: rhetoric and reality in the Oregon Health Plan*, 164(11) CAN. MED. ASSOC. J. 1583 (2001), <http://www.cmaj.ca/content/164/11/1583.full.pdf>.

<sup>95</sup> Fruits, *supra* note 85.

<sup>96</sup> Oberlander, *supra* note 94.

<sup>97</sup> Fruits, *supra* note 85.

<sup>98</sup> *Id.*

<sup>99</sup> Oberlander, *supra* note 94.

<sup>100</sup> Lawrence Jacobs, Theodore Marmor, Jonathan Oberlander, *Report from the Field: The Oregon health Plan and the Political Paradox of Rationing: What Advocates and Critics Have Claimed and What Oregon Did*, 24(1) J. HEALTH POL. POL'Y & L. 1 (1999), [http://mba.yale.edu/faculty/PDF/marmor\\_oregonjhpl.pdf](http://mba.yale.edu/faculty/PDF/marmor_oregonjhpl.pdf).

<sup>101</sup> *Id.*

<sup>102</sup> Fruits, *supra* note 85.

effectiveness, as originally planned but, but also included many metrics based on subjective judgment.<sup>103</sup> The Commission’s instructions to the clinical advisory panels conducting outcomes research even included instructions such as the following: “It is understood that some outcome data may be subjective in nature. A disease may be bimodal with significantly different outcomes occurring dependent on age of onset or vary according to the extent of the disease at the time of presentation (stage). If this is the case... please think of the average patient that presents with this condition not the extremes.”<sup>104</sup> Additionally, the lack of sound scientific studies that considered the costs and benefits of various treatments was concerning to many participating providers because it was not known how exactly the Commission was to create a list based on objective factors.<sup>105</sup> In fact, the Commission encouraged providers to continue to make “medical decisions ... based on their best clinical judgment,” which led to physicians exercising their judgment and deciding to pursue treatments and services that were not covered by the Plan.<sup>106</sup> Essentially, the Commission was relying on these panels to provide outcomes information based on their clinical judgment – a subjective approach – and not on the formulaic and objective approach that was intended. Cost-effectiveness yielded to other factors, including political pressures, in determining coverage and was essentially abandoned.<sup>107</sup>

The list was not and is not utilized as envisioned. Plan participants receive many services and treatments that were meant to be excluded, whether it is through loopholes in the plan or physicians diagnosing patients with covered diagnoses, when in fact an “uncovered” diagnosis

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<sup>103</sup> *Id.*

<sup>104</sup> U.S. CONGRESS, OFFICE OF TECHNOLOGY ASSESSMENT, EVALUATION OF THE OREGON MEDICAID PROPOSAL, OTA-H-531 (1992).

<sup>105</sup> Jacobs, *supra* note 100.

<sup>106</sup> *Id.*

<sup>107</sup> *Id.* (The OHP gained national media attention in 1987 when Coby Howard, a seven-year-old boy with leukemia, was denied a bone marrow transplant. OHP had cut funding in organ transplants in order to change coverage. This case led to some of the political pressure that led to abandoning the objective-focus of the list.)

may be more appropriate.<sup>108</sup> The program overall has not demonstrated promising results. The percentage of uninsured Oregonians is not significantly different than the percentage of uninsured in the rest of the country.<sup>109</sup> (See Figure 3<sup>110</sup>). Additionally, Oregon’s Medicaid expenditures have tracked the country’s Medicaid expenditures, demonstrating that the plan has not led to the hoped for decrease in spending.<sup>111</sup> (See Figure 4<sup>112</sup>). Regardless of one’s opinion of why the Oregon Health Plan may be a failure or has not met its goals, one thing is clear – neither rationing nor the cost-effectiveness determination for coverage was what led to the lack of success of the great Oregon Experiment. Furthermore, one of the Plan’s uses of cost effectiveness that remains in place has proven quite successful. The Plan’s formulary members compare drugs to create a list of preferred and covered drugs under the plan.<sup>113</sup> A drug is covered if it is determined to be “as effective as any other drug in the class but more cost-effective.”<sup>114</sup> This appears to be the essence of what makes comparative effectiveness research so valuable. The objective determinations based on effectiveness and outcomes research flourish, whereas subjective determinations do not.

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<sup>108</sup> Fruits, *supra* note 85.

<sup>109</sup> *Id.*

<sup>110</sup> *Id.*

<sup>111</sup> *Id.*

<sup>112</sup> *Id.*

<sup>113</sup> Peter J. Neumann, *Using Cost-Effectiveness Analysis to Improve Health Care: Opportunities and Barriers* (Oxford University Press 2004).

<sup>114</sup> *Id.*

Figure 3

Percent of population covered by Medicaid  
Oregon and U.S., 1987–2008

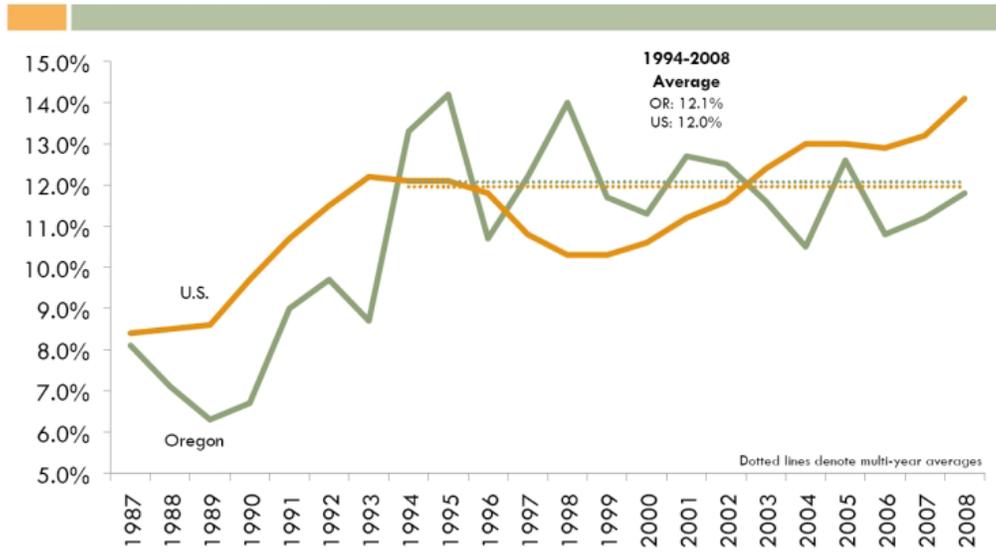
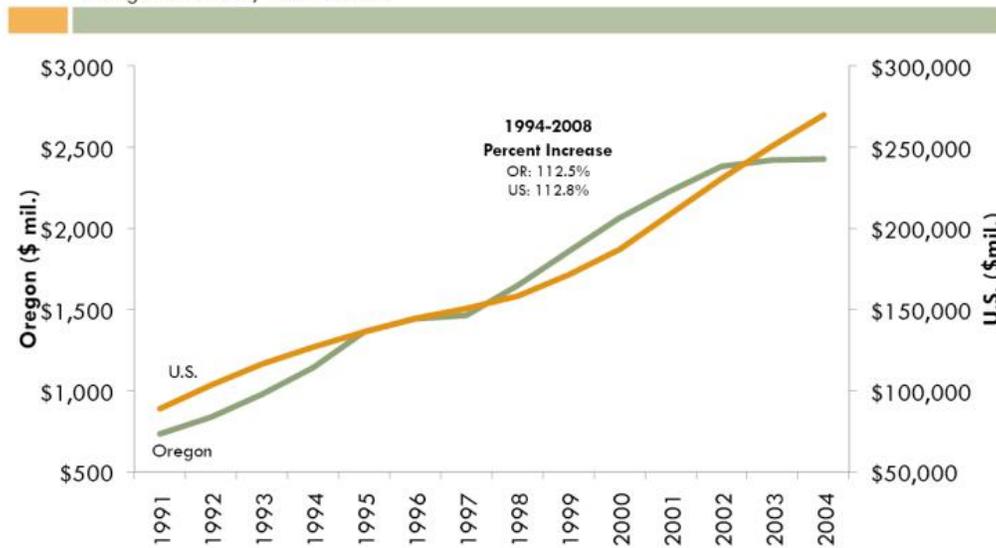


Figure 4

Medicaid expenditures  
Oregon and U.S., 1991–2004



D. Findings

The wavering legislation between congressional proposals pushing for comparative clinical effectiveness research and an institute that is forbidden from using comparative effectiveness metrics

suggests a deep ambivalence towards CER by our government.<sup>115</sup> PCORI almost seems like a consolation prize to proponents of CER. There are valid arguments against the use of CER on the front end of research, where the effect could lead to an increase in research and development costs.<sup>116</sup> The arguments against CER on the back-end, where the decisions of what to offer patients are made, do not seem as strong. As an example, the OHP is often cited as an example of the failure of rationing but a closer look demonstrated that in fact the comparative effectiveness metrics were not carried out as intended. Comparative effectiveness research has not been properly implemented in this country by the government so perhaps it should be implemented voluntarily by the private sector. Memorial Sloan-Kettering Cancer Center is one example of a private institution that made a decision based on the evidence available to them, including cost.

## **PART II: MEMORIAL SLOAN-KETTERING AS AN EXAMPLE OF PRIVATE SECTOR USE OF COMPARATIVE EFFECTIVENESS RESEARCH**

The vehicle was the New York Times. The words were those of three Memorial Sloan-Kettering Cancer Center (MSKCC) oncologists. Dr. Peter Bach, Dr. Leonard Saltz, and Dr. Robert Wittes made the bold decision to author an op-ed piece titled In Cancer Care Cost Matters that appeared in the October 14, 2012, issue of the New York Times.<sup>117</sup> The op-ed detailed MSKCC's decision to exclude Zaltrap<sup>®</sup> (ziv-aflibercept) from the hospital's formulary.<sup>118</sup> The Food and Drug Administration had recently approved Zaltrap (manufactured by Sanofi-Aventis) on August 3, 2012, for use in combination with chemotherapy to treat metastatic colorectal cancer.<sup>119</sup> The MSKCC physicians' decisionmaking followed a comparative effectiveness

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<sup>115</sup> See discussion *supra* Part II.A.

<sup>116</sup> See discussion *supra* Part II.B.

<sup>117</sup> Bach, *supra* note 14

<sup>118</sup> *Id.*

<sup>119</sup> FDA Approves Zaltrap for Metastatic Colorectal Cancer, U.S. FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm314372.htm>.

research framework by using such factors as overall survival benefit, the side effect profile, patient convenience, and the fairly controversial factor of cost.<sup>120,121</sup>

A. *The Memorial Sloan-Kettering Cancer Center Decision*<sup>122</sup>

The MSKCC physicians wanted Zaltrap to work. The Phase I trials were done at MSKCC and unfortunately all evidence showed that the drug in fact did not work as well as the investigators wanted it to. It is a common misconception that Phase I trials do not evaluate efficacy and simply determine safety dosage. The modern and sensible approach is to look for activity in a Phase I trial and if it is not seen, it is highly unlikely that there will be activity in a Phase II trial of the same drug, and therefore a Phase II trial does not pose good cost-effectiveness. During Zaltrap's research and development process, there was another agent known as Avastin that had been approved by the FDA in 2004 for use in patients with metastatic colorectal cancer. MSKCC has been using Avastin since its approval.

As Chair of MSKCC's Pharmacy and Therapeutics Committee, Dr. Saltz began to prepare the necessary paperwork for adding the newly approved Zaltrap to the hospital's formulary. Although not terribly excited about the drug's prospects, the hospital had never not placed a newly FDA-approved drug on the formulary. Dr. Saltz had every reason to believe it would be approved. What followed was an email from a pharmacy administrator that changed the course of this drug, at least within MSKCC. The administrator informed Dr. Saltz that Zaltrap had been priced at over \$11,000 on average for a month of treatment, more than twice

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<sup>120</sup> How are Comparative Effectiveness Reviews Conducted?, AGENCY FOR HEALTHCARE RESEARCH AND QUALITY, <http://effectivehealthcare.ahrq.gov/index.cfm/what-is-comparative-effectiveness-research1/how-are-comparative-effectiveness-reviews-conducted/>.

<sup>121</sup> Bach, *supra* note 14

<sup>122</sup> Interview with Dr. Leonard Saltz in New York, NY (Apr. 1, 2013). (Section IIIA of this piece is sourced from my interview with Dr. Leonard Saltz at Memorial Sloan-Kettering Cancer Center, unless otherwise specified.)

the price of the standard of care, Avastin, which costs about \$5,000 a month. Dr. Saltz approached the entire gastrointestinal oncology service with one simple question – knowing the data and the newly found price, could anyone envision using the drug? Nobody could. The next step was to approach the Pharmacy and Therapeutics Committee with a new message and plenty of data.

“Sanofi-Aventis chose to pretend that Avastin didn’t exist.” MSKCC did everything but that and drew upon the similarities between Zaltrap and Avastin when the Pharmacy and Therapeutics Committee met to discuss Zaltrap. Seen in Figures 5 and 6 are the Overall Survival curves for Zaltrap (Figure 5) and Avastin (Figure 6).<sup>123</sup> The survival curves were virtually identical. Both were compared to the same chemotherapy regimen and both showed an equal overall survival benefit of 1.4 months. This was not entirely surprising since both drugs also work along the same molecular pathway. They are both Vascular Endothelial Growth Factor (VEGF) inhibitors.<sup>124</sup> Both drugs are also used in the same setting – second-line colorectal indication – meaning that the VEGF inhibitors are used after frontline chemotherapy fails in patients with metastatic colorectal cancer. The study that Sanofi-Aventis used when filing for FDA approval became commonly known as the VELOUR trial. Often trials that follow similar molecular pathways require that patients have been treated with the similar drug and that the drug have failed prior to moving on to the new treatment so that the investigators have an idea of the similarity in response rates in what may be, especially in this case, very similar treatments. The study design in this case did not require that patients have frontline Avastin, or another VEGF inhibitor, and about half were naïve to VEGF inhibitors. The side effects profiles of the

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<sup>123</sup> Peter Bach, MD, *The Evolving Landscape of Oncology Cost Containment*, <http://www.cancerprogressbydh.com/wp-content/uploads/2013/03/0845-BachCPBYDH2013.pdf>

<sup>124</sup> Paul Goldberg, MSKCC Bars Zaltrap From Formulary, Triggering Debate Over Drug Pricing, 38(41) THE CANCER LETTER 1 (2012).

drugs were also incredibly similar and perhaps even worse in Zaltrap. Both were required to carry black box warnings indicating that the FDA felt that the drugs carried a significant risk of serious adverse events. The boxed warnings were for gastrointestinal perforation and hemorrhaging. Additionally, Avastin was also slightly more convenient for patients because it takes less time to administer than Zaltrap.<sup>125</sup>

In addition to the clinical data, the MSKCC physicians looked to clinical practice guidelines. The National Comprehensive Cancer Network (NCCN) guidelines suggest that Zaltrap is no better than Avastin in the second-line setting for metastatic colorectal cancer.<sup>126</sup> Furthermore, the NCCN guidelines state that besides being essentially equivalent, they point out that there are no data to suggest that switching a patient to Zaltrap after Avastin has failed, or vice versa, would provide any benefit to the patient.<sup>127</sup>

The one stark difference between Zaltrap and Avastin lay in the financial characteristics of each drug. One month of Avastin treatment costs about \$5,000, while a month of Zaltrap treatment costs over \$11,000.<sup>128</sup> Using comparative effectiveness metrics, the cost of Zaltrap for one year of life-gained is \$585,200.<sup>129</sup> Regardless of one's methodology to determine cost-effectiveness, Zaltrap appeared clearly cost ineffective as compared to what was already available, so MSKCC decided to make it unavailable to its patient population.<sup>130</sup>

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<sup>125</sup> Bach, *supra* note 14.

<sup>126</sup> NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY: COLON CANCER, VERSION 3 (2013), [http://www.nccn.org/professionals/physician\\_gls/pdf/colon.pdf](http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf)

<sup>127</sup> *Id.*

<sup>128</sup> Bach, *supra* note 14.

<sup>129</sup> Bach, *supra* note 123.

<sup>130</sup> See discussion *supra* Part II.A. (Using WHO's guidance: The World Bank listed the United States' per capita GDP at \$48,112 in 2011, making our three times threshold \$144,336. By the WHO standards, Zaltrap (at \$585,200 per QALY) would be considered cost ineffective since its cost for one life-year far exceeds three times threshold. One study created a line for cost ineffectiveness by using the \$50,000 cost per life-year-gained as a measure. This number is derived from the decision to use federal funding to pay for dialysis but reflects the 1982 cost. The

Within a week, the president of the American Society of Clinical Oncology had written a letter to the New York Times editor which was published on October 19, 2012.<sup>131</sup> Dr. Swain spoke encouragingly of MSKCC's decision and seemingly endorsed their action by stating it "reflect[ed] a much-needed willingness to address the elephant in the room: unsustainable costs in cancer care."<sup>132</sup> The CEO of Sanofi-Aventis, Christopher Viebacher, rebuffed the new and controversial concerns that the drug was not appropriately priced and claimed that it was competitively priced to the standard of care – Avastin – based on comparable dosing.<sup>133</sup> He went on to say that "the spirit of the op-ed [was] something [he] would fully subscribe to" and that "we really need to make sure that there is complete access with enough incentive for research."<sup>134</sup>

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researchers adjusted the 1982 cost to find a value of \$197,000 per life-year-gained in 2007 dollars and made this the threshold for coverage. Zaltrap's cost for one life-year-gained far exceeds this limit to coverage that the authors suggest. *See* Hillner, *supra* note 34.)

<sup>131</sup> Swain, *supra* note 25.

<sup>132</sup> *Id.*

<sup>133</sup> Matthew Herper, *Sanofi's CEO On The New York Times' Criticism of Drug Prices And Surviving The Patent Cliff*, FORBES (Oct. 26, 2012), available at <http://www.forbes.com/sites/matthewherper/2012/10/26/sanofis-ceo-on-the-new-york-times-criticism-of-drug-prices-and-surviving-the-patent-cliff/>.

<sup>134</sup> *Id.*

Figure 5

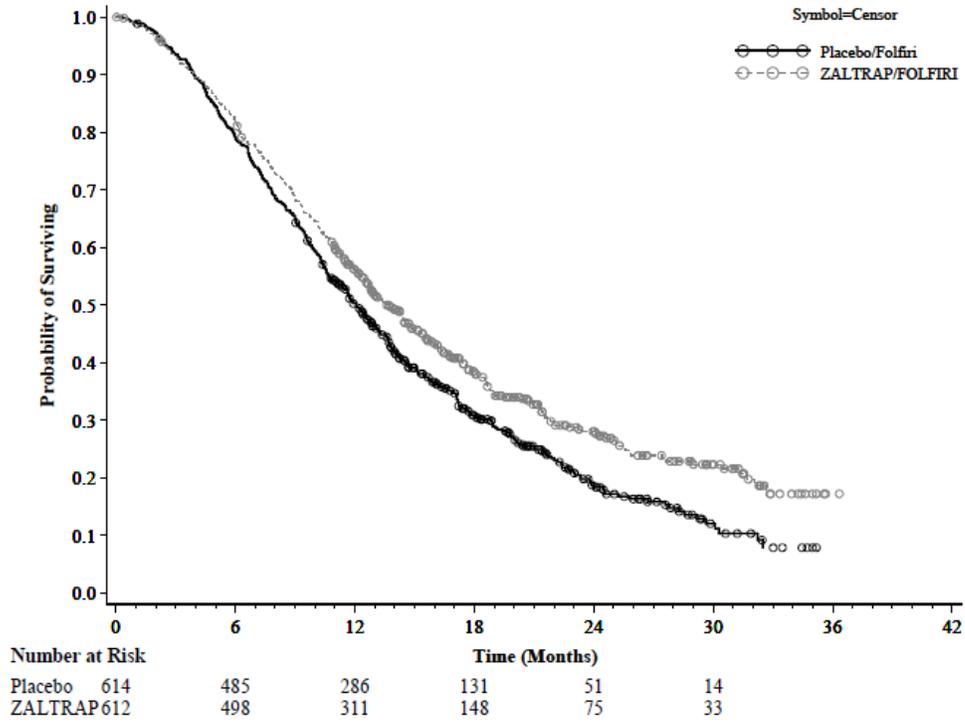
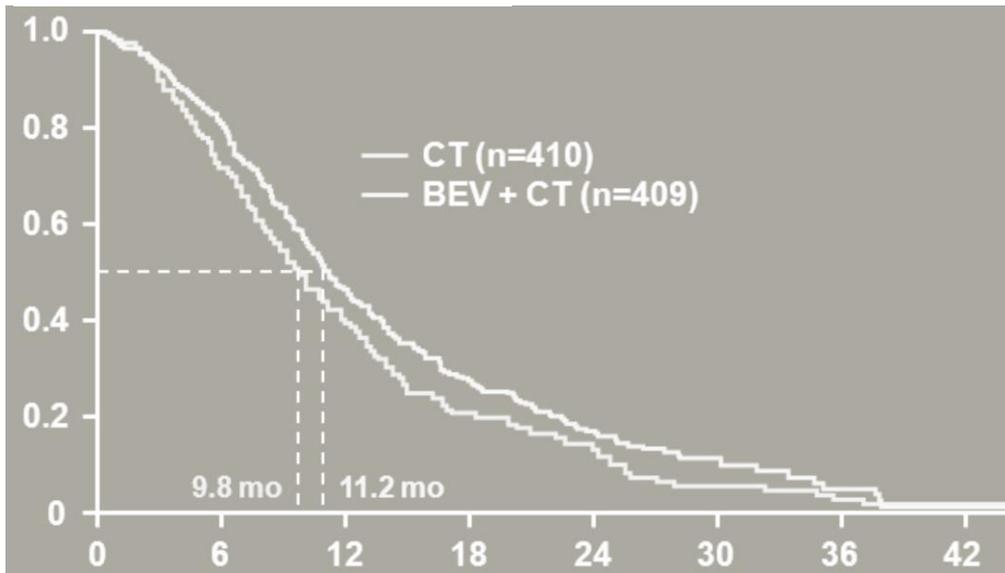


Figure 6



## B. *The Compromising Financial Compromise*

Less than two weeks later, Sanofi-Aventis announced that it was reducing the price of Zaltrap due to “market resistance.”<sup>135</sup> Although, there would be no change in Zaltrap’s official price, Sanofi-Aventis would begin to offer an approximately fifty-percent discount, creating a potentially problematic compromise.<sup>136</sup> Sanofi-Aventis had overtly admitted to setting the price of the drug as what they saw their competition –Genentech’s Avastin – and not on how valuable the drug could be to patients or how well it worked in the clinical trials.<sup>137</sup> Sanofi-Aventis had conducted a marketing study of seventy oncologists which showed that 55 percent of them used Avastin at a dose of 10mg/kg versus the 5mg/kg.<sup>138</sup> Notably, the composition of their sample group consisted mostly of private practitioners.<sup>139</sup> It could be said that the sample group was comprised of physicians who have a financial incentive to use a higher dose because they are paid by the number of milligrams of drug that they use. Although it is not illegal to use 10mg/kg in colorectal cancer patients, and in fact, in every other cancer that Avastin is used for, oncologists use the 10mg/kg dose.<sup>140</sup> Both doses are listed for use on the Avastin label, but the lower dose of Avastin produces equivalent results to its 10mg/kg counterpart and offers the patient a lower risk of side effects.<sup>141</sup> The MSKCC oncologists, and to the best of their knowledge, their colleagues at other academic institutions, all use the 5mg/kg dose of Avastin.<sup>142</sup>

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<sup>135</sup> Andrew Pollack, *Sanofi Halves Price of Cancer Drug Zaltrap After Sloan-Kettering Rejection*, N.Y. TIMES, Nov. 8, 2012, at B3.

<sup>136</sup> *Id.*

<sup>137</sup> Saltz, *supra* note 122.

<sup>138</sup> *Id.*

<sup>139</sup> *Id.*

<sup>140</sup> *Id.*

<sup>141</sup> *Id.*

<sup>142</sup> *Id.*

In addition, all relevant treatment guidelines recommend the 5mg/kg dose.<sup>143</sup> So when Sanofi-Aventis pegged their price for Zaltrap to the 10mg/kg dose of Avastin, it was misguided and this led to a pricing that was essentially twice that of Avastin.

The response came in the form of a 50 percent discount, which can be thought of as a coupon that the hospital or physician would use when purchasing Zaltrap.<sup>144</sup> There was nothing in writing and therefore what has not changed is the official price of the drug as reported to the Centers for Medicare and Medicaid Services (CMS).<sup>145</sup> Changing the published price to 50 percent of the listed price would require that an active step be taken with CMS, which as of now has not been done.<sup>146</sup> Additionally, any reimbursement rates are based on the price set by Sanofi-Aventis.<sup>147</sup> What is potentially very problematic is that if the Medicare reimbursement rates are not adjusted, a scenario would exist where prescribing physicians stand to gain financially from using Zaltrap.<sup>148</sup>

Most academic institutions do not accept the sort of discount that Sanofi-Aventis created, MSKCC included, due to potential incentives in prescribing the drug.<sup>149</sup> A look at Medicare reimbursement practices, for example, demonstrates how a 50 percent discount could create this incentive. A drug's wholesale acquisition cost (WAC) is the manufacturer's published price to

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<sup>143</sup> Goldberg, *supra* note 124. (“Not only the NCCN guidelines say this, but the second-line registry of Avastin use which covers both academic and community centers—the BRITE registry—has fewer than one percent using 10 mg/kg, and 98 percent are using some version of 5 mg/kg every two weeks.”)

<sup>144</sup> Paul Goldberg, *Zaltrap Price Cut In Half Effective Immediately As Sanofi Responds to Criticism From Oncologists*, 38(42) THE CANCER LETTER 1 (2012).

<sup>145</sup> Saltz, *supra* note 122.

<sup>146</sup> *Id.*

<sup>147</sup> *Id.*

<sup>148</sup> *Id.*

<sup>149</sup> *Id.*

wholesale buyers.<sup>150</sup> Medicare's reimbursement price is based on an average WAC for the first two quarters following the drug's launch in combination with the first two quarters' average sales price of the drug, plus six percent.<sup>151</sup> A drug's average sales price (ASP) is defined as the manufacturer's sales of a drug to all purchasers in a calendar quarter divided by the total number of units of the drug sold by the manufacturer in that same quarter, excluding Medicaid rebates and other discounts.<sup>152</sup> Drugs are reimbursed at 80 percent of 106 percent of the Average Sales Price.<sup>153</sup> There would be a potential cost incentive to a doctor to prescribe the drug because it would be sold to them at Sanofi-Aventis' 50 percent discount off WAC but then it would be reimbursed at the 80 percent rate and charged at the wholesale rate to the patients, plus 6 percent.<sup>154</sup> Figure 7 demonstrates the flow of funds for a fictional drug priced at \$1,000 that a provider would purchase using a 50 percent type discount, similar to the Zaltrap discount.<sup>155</sup> The drug's WAC in the first quarter would be \$1,000 (pre-discount). The drug's WAC in the second quarter would be \$500 (post-50 percent discount). The weighted average sales price based on the first two quarters to Medicare beneficiaries would be \$750. The providers pay out \$500 to acquire the drug but take in \$750 (\$600 from Medicare and \$150 from the patient). By statute, Medicare does not possess the ability to immediately bargain for the lower price.<sup>156</sup> On the other hand, insurance companies may be able to, which could lead to copayment savings for those patients insured by private insurance.<sup>157</sup> These renegotiations may lead to decreasing any

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<sup>150</sup> Rena Conti, Ernst Berndt, *Winners and Losers From the Zaltrap Price Discount: Unintended Consequences?*, HEALTH AFF. BLOG (Feb. 20, 2013), <http://healthaffairs.org/blog/2013/02/20/winners-and-losers-from-the-zaltrap-price-discount-unintended-consequences/>.

<sup>151</sup> *Id.*

<sup>152</sup> *Id.*

<sup>153</sup> *Id.*

<sup>154</sup> *Id.*

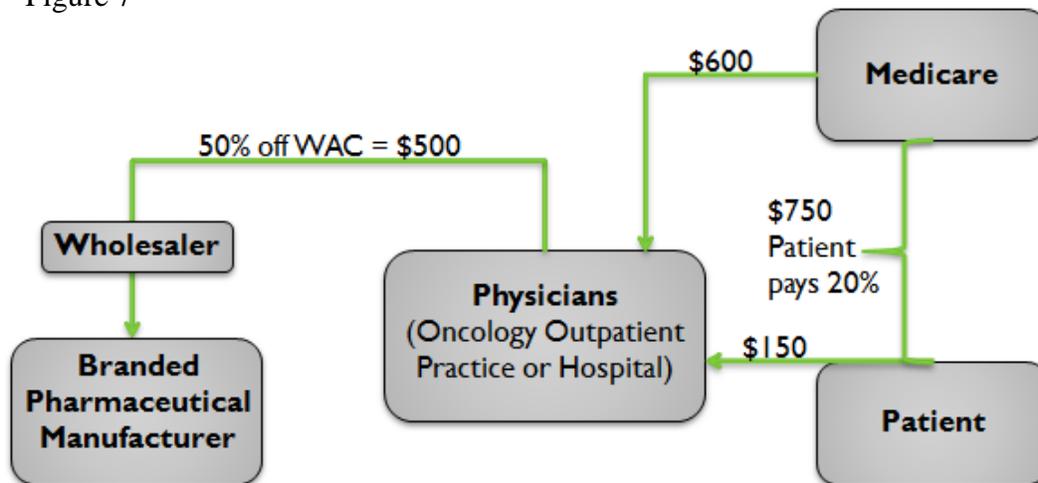
<sup>155</sup> *Id.* (The figure design and numbers were taken from the blog and recreated.)

<sup>156</sup> Bach, *supra* note 15.

<sup>157</sup> *Id.*

possible incentive to treat with this pricey, yet discounted, drug. The unresolved issue regarding Medicare beneficiaries would remain though.

Figure 7



Using an example of a drug whose Wholesale Acquisition Cost = \$1,000.

1<sup>st</sup> quarter: WAC = \$1000 for the 1<sup>st</sup> quarter after launch.

2<sup>nd</sup> quarter: WAC = \$500

3<sup>rd</sup> quarter: weighted ASP after launch = \$750

\$600 paid by Medicare + \$150 paid by the patient (assuming no secondary insurance).

### C. Findings and Recommendations

This decision to exclude Zaltrap from MSKCC’s formulary should be uncontroversial and to date, only Sanofi-Aventis has resisted in praising the decision. Avastin was the readily available, widely used, cheaper, and equally effective alternative. The struggle comes in spreading this type of decisionmaking to other hospitals. Perhaps this was too easy and too perfect of a decision to make. Zaltrap and Avastin mirrored each other with the exception of their cost. Other treatment counterparts do not measure so equally, making the decision much more difficult. At least one other institution, US Oncology, has publicly stated that they also

excluded Zaltrap from their formulary.<sup>158</sup> On the other hand, Ohio State included Zaltrap in its formulary but they had no plans to offer the treatment until the discount was announced.<sup>159</sup>

Perhaps the answer is in the formulary (pharmacy and therapeutics) committee itself. Formulary committee guidelines state that “a formulary system is the ongoing process through which a health care organization establishes policies regarding the use of drugs, therapies, and drug-related products and identifies those that are most medically appropriate **and cost-effective** to best service the health interests of a given patient population.”<sup>160</sup> The cost-effectiveness aspect of formulary inclusion or exclusion does not seem to be taking place if MSKCC’s decision was considered so bold and groundbreaking. Formulary guidelines also state that formulary decisions should be based on evidence-based evaluation, which is defined as “as systematic approach to the evaluation of biomedical literature and application to clinical practice and should be applied to formulary decisionmaking for medication product selection.”<sup>161</sup> Evidence-based decisionmaking with the consideration of cost is at the core of CER. The problem may lie in the final gatekeepers to the pricier drugs – the formulary committee – and the possibility that they are not following their own guidelines.

#### **PART IV: ACCOUNTABLE CARE ORGANIZATIONS AS AN INDIRECT PROMOTION OF COMPARATIVE EFFECTIVENESS RESEARCH**

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<sup>158</sup> Goldberg, *supra* note 144.

<sup>159</sup> *Id.*

<sup>160</sup> American Society of Health-System Pharmacists, *ASHP Guidelines on the Pharmacy and Therapeutics Committee and the Formulary System*, 65 AM. J. HEALTH-SYST. PHARM. 1272 (2008), <http://www.ashp.org/DocLibrary/BestPractices/FormGdlPTCommFormSyst.aspx>.

<sup>161</sup> *Id.*

Elliott Fisher, the Director of the Center for Health Policy Research at Dartmouth Medical School, first coined the term Accountable Care Organization (ACO) in 2006.<sup>162</sup> ACOs were drafted into three healthcare reform bills in 2009 but the pinnacle came in 2010 when the Patient Protection and Affordable Care Act (PPACA) included the concept in its final legislation.<sup>163</sup> Appearing in Section 3022, PPACA authorizes the Centers for Medicare and Medicaid Services to “establish a shared savings program ... that promotes accountability for a patient population and coordinates items and services under parts A and B, and encourages investment in infrastructure and redesigned care processes for high quality and efficient delivery service.”<sup>164</sup> The current Medicare payment method is quite fragmented, paying hospitals and their physicians separately and paying physicians separate fees for the same patients depending on the diagnosis and treatment received (commonly known as fee-for-service).<sup>165</sup> This fragmented method promotes anything but coordination and accountability.<sup>166</sup> An ACO would not do away with the fee-for-service method of payment but would instead create financial incentives through bonuses when providers keep costs low.<sup>167</sup> The providers and hospitals would also have to meet certain quality benchmarks that focus on preventative measures and managing chronic conditions.<sup>168</sup> This is one way that ACOs are held accountable, a key measure of their success. There are process, outcome, and efficiency measurements. A process measurement looks at whether a particular service was provided to a patient consistent with

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<sup>162</sup> Kip Sullivan, *The History and Definition of the “Accountable Care Organization”*, PHYSICIANS FOR A NATIONAL HEALTH PROGRAM (Oct., 2010), <http://pnhpcalifornia.org/2010/10/the-history-and-definition-of-the-%E2%80%9Caccountable-care-organization%E2%80%9D/>

<sup>163</sup> *Id.*

<sup>164</sup> PPACA § 3022(a)(1), 124 Stat. 119, 395, codified at 42 U.S.C. § 1395jjj(a)(1).

<sup>165</sup> Jeff Goldsmith, *Physicians and Hospitals: Can They Cooperate to Control Costs?*, HEALTH AFF. BLOG (Jan. 19, 2007), <http://healthaffairs.org/blog/2007/01/19/physicians-and-hospitals-can-they-cooperate-to-control-costs/>.

<sup>166</sup> *Id.*

<sup>167</sup> Jenny Gold, *FAQ on ACOs: Accountable Care Organizations, Explained*, KAISER HEALTH NETWORK (Oct. 21, 2011), <http://www.kaiserhealthnews.org/Stories/2011/January/13/ACO-accountable-care-organization-FAQ.aspx>.

<sup>168</sup> *Id.*

clinical guidelines.<sup>169</sup> An outcome measurement evaluates how well patients are doing after receiving health care services.<sup>170</sup> An efficiency measurement assesses the cost of care as compared to its quality, i.e., did a provider use a costlier treatment when a less costly alternative was available and would have worked just as well.<sup>171</sup>

Determining how an incentive payment for meeting quality benchmarks and lowering costs involves evaluating four factors: the benchmark against which expenditures will be compared, the minimum savings rate, the sharing or loss rate, and how the benchmark will be updated.<sup>172</sup> Determining the comparator benchmark focuses on establishing the patient population that will be served, whether there will be one or multiple benchmarks based on different patient groups, and how the benchmarks will be adjusted.<sup>173</sup> The minimum savings or loss rate is the percentage above which the ACO would share in savings or pay back any losses.<sup>174</sup> This rate accounts for fluctuations in expenditures in case they occur.<sup>175</sup> CMS has set the minimum rate at 2 percent, meaning if an ACO's rate is set at 2 percent but their expenditures happen to increase by 4 percent in a given year, they would be penalized because they went above the allowable 2 percent loss.<sup>176</sup> Staying within that 2 percent would lead to no penalty.<sup>177</sup> The sharing or loss rate is the rate that the ACO will receive as an incentive

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<sup>169</sup> Kim Bailey, Marc Steinberg, Ingrid VanTuinen, Nancy Magill, *Putting the Accountability in Accountable Care Organizations: Payment and Quality Measurements*, FAMILIES USA (Jan. 2012), <http://familiesusa2.org/assets/pdfs/health-reform/ACOs-Payment-and-Quality-Measurements.pdf>

<sup>170</sup> *Id.*

<sup>171</sup> *Id.*

<sup>172</sup> Kim Bailey, Marc Steinberg, Ingrid VanTuinen, Nancy Magill, *Accountable Care Organizations: Determining Shared Savings or Losses*, FAMILIES USA (Jan. 2012), <http://familiesusa2.org/assets/pdfs/health-reform/ACOs-Shared-Savings-or-Losses.pdf>.

<sup>173</sup> *Id.*

<sup>174</sup> *Id.*

<sup>175</sup> *Id.*

<sup>176</sup> *Id.*

<sup>177</sup> *Id.*

payment.<sup>178</sup> A Medicare Shared Savings Program (MSSP) ACO will use a 50 percent sharing rate (even higher for those ACOs that assume greater risk).<sup>179</sup> The rate is determined by a measure known as a quality score.<sup>180</sup> A quality score takes into account certain factors like patient/caregiver experience, preventative health, and implementation of electronic health records.<sup>181</sup> For example, an ACO that generates \$100,000 in savings over the minimum savings rate and receives a perfect quality score of 100 percent would receive \$50,000 as an incentive payment (50% sharing rate x 100% quality score x \$100,000).<sup>182</sup> A lower quality score, for example 75 percent, would lead to a lower incentive payment (50% sharing rate x 75% quality score x \$100,000 = \$37,500 incentive payment).<sup>183</sup> Lastly, an ACO needs to determine when and how its benchmark will be updated.<sup>184</sup>

The purpose of ironing out the details of an ACO is to demonstrate that its elements very closely align with those of CER. Some have opined that if CER results are to influence the choices of physicians and their patients, the results must be accompanied by economic incentives.<sup>185</sup> It appears that ACOs, through their financial motivations for cost-saving, are this very incentive that has been spoken of. Despite PPACA's prohibition on PCORI using QALYs and similar metrics, an argument can be made that the law may have indirectly and inadvertently encouraged the consideration of cost during the treatment determination process.<sup>186</sup> An ACO cannot save money and thereby partake in the financial incentives without including cost in the

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<sup>178</sup> *Id.*

<sup>179</sup> *Id.*

<sup>180</sup> *Id.*

<sup>181</sup> Guide to Quality Performance Scoring Methods for Accountable Care Organizations, <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/sharedsavingsprogram/Downloads/2012-11-ACO-quality-scoring-supplement.pdf>

<sup>182</sup> Bailey, *supra* note 172.

<sup>183</sup> *Id.*

<sup>184</sup> *Id.*

<sup>185</sup> James Robinson, *Comparative Effectiveness Research: From Clinical Information to Economic Incentives*, 29(10) HEALTH AFF. 1788 (2010).

<sup>186</sup> See discussion *supra* Part II.A.

treatment determination process. It should be noted that cost cannot be the only factor when providers undergo treatment decisionmaking since their quality scores and other benchmarks are based on patient health and satisfaction outcomes. CER also is not entirely based on cost, although its opponents would have you believe this.<sup>187</sup> CER's goal is to generate data that compares the benefits of various treatments, which will undoubtedly include cost, since a patient will benefit from saving money. ACO providers will exclude pricier and no more effective treatments because they will be incentivized to do so, whether it is through meeting their efficiency measurement benchmarks or ensuring that they maintain an adequate share or loss ratio that will lead to savings.

#### **PART IV: CONCLUSION**

In returning to the concept of the moral hazard, CER appears to fit in quite nicely as the vehicle to eliminating the concept of over-consumption by the insured. The OHP was an attempt at removing the costlier, less-effective options from the table but faltered due to outside pressures. The OHP should not be viewed as a failure of CER decisionmaking but as a learning lesson. Their objective formula for inclusion or exclusion to the list does not seem so passé when there is research pointing to the ability of mathematical models to out-perform doctors in predicting patient outcomes.<sup>188</sup>

Memorial Sloan-Kettering took a giant leap at removing an option from the table through their decision to exclude the pricey Zaltrap from their formulary. Their publication of this decision has inspired other oncologists to stand up to big pharmaceutical manufacturers and their

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<sup>187</sup> See discussion *supra* Part II.B.

<sup>188</sup> Mathematical models out-perform doctors in predicting cancer patients' responses to treatment, SCIENCE DAILY (Apr. 19, 2013) [http://www.sciencedaily.com/releases/2013/04/130420110651.htm?utm\\_source=feedly&utm\\_medium=feed&utm\\_campaign=Feed:+sciencedaily+%28ScienceDaily:+Latest+Science+News%29](http://www.sciencedaily.com/releases/2013/04/130420110651.htm?utm_source=feedly&utm_medium=feed&utm_campaign=Feed:+sciencedaily+%28ScienceDaily:+Latest+Science+News%29)

pricing practices but it is unclear how the pharmaceutical companies will respond.<sup>189</sup> Before waiting for the companies to respond, one area worth evaluating are the practices of formulary committees, whose very guidelines dictate the use of cost as an inclusion/exclusion criteria, but this does not seem to be put into practice.

The ramifications of a MSKCC-type decision are still unclear. MSKCC has thus far received only positive feedback regarding their decision but long term legal consequences are still unclear. The pharmaceutical companies may be the party that should be concerned. After a decision to exclude a pricey drug, it would seem that pricing a drug based on your competition does not seem to be the smart move. They are now on notice that not everyone will put up with their decisions. A company's loyalty to its shareholders bottom line may lead them to avoid CER studies at the front-end of their research development process but it should also lead to smarter marketing studies. Could a flawed marketing study, like the one that led to the misguided Zaltrap pricing create actionable grounds for shareholders against the company? At least some consider Zaltrap to be one of the worst drug launches of all time.<sup>190</sup> The resistance to egregious drug-pricing is building and for the time being, the power seems to be on the side of the private sector's use of comparative effectiveness research to do away with the expensive drugs if the pharmaceutical companies refuse to do so.

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<sup>189</sup> Stacy Cowley, *Doctors Blast Ethics of \$100,000 Cancer Drugs*, CNN MONEY (April 25, 2013, 10:55AM) [http://money.cnn.com/2013/04/25/news/economy/cancer-drug-cost/index.html?source=cnn\\_bin](http://money.cnn.com/2013/04/25/news/economy/cancer-drug-cost/index.html?source=cnn_bin)

<sup>190</sup> 10 top drug launch disasters, FIERCEPHARMA, (Nov. 27, 2012) <http://www.fiercebiotech.com/tags/zaltrap>.