

# **The Ethics of Comparative Effectiveness Research and the Establishment of the Patient Centered Outcomes Research Institute**

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In March of 2010 President Obama signed the Affordable Care Act (ACA) into law, overhauling the nation's health care system. This massive legislation included the establishment of the Patient Centered Outcomes Research Institute (PCORI).<sup>1</sup> PCORI is a non-profit that aims to assist patients, clinicians, purchasers, and policy makers in making health care decisions.<sup>2</sup> PCORI will fund research that identifies which treatments will lead to the best health outcomes.<sup>3</sup> This research will compare existing treatments in order to give patients and clinicians valuable information about comparative effectiveness as they make health care choices.<sup>4</sup> The PCORI mission statement commits the organization to high integrity research that is "guided by patients, caregivers, and the broader healthcare community."<sup>5</sup>

PCORI is a new entity, but the concept of comparative effectiveness research is not as novel.<sup>6</sup> There have been calls for comparative effectiveness research in the past and major studies focused on this front.<sup>7</sup> Comparative effectiveness research faces several criticisms and PCORI presents new challenges as well. This paper will discuss ethical criticisms of comparative effectiveness research and discuss whether the PCORI can withstand the objections. First this paper will introduce PCORI and explain its structure and goals. Then this paper will discuss some of the major ethical objections to comparative effectiveness research. Next it will discuss how PCORI has responded to some of those criticisms and explain the value of comparative effectiveness research. Finally, this paper will conclude that while the ethical criticisms of

comparative effectiveness research are valid, they are not strong enough to overcome the potential benefits of PCORI.

## **I. WHAT IS PCORI?**

The Patient-Centered Outcomes Research Institute (PCORI) is authorized by Congress to conduct research and develop data to help patients and their physicians make informed decisions about treatment options.<sup>8</sup> Patient centered research:

- Assesses the benefits and harms of preventive, diagnostic, therapeutic, palliative, or health delivery system interventions to inform decision making, highlighting comparisons and outcomes that matter to people;
- Is inclusive of an individual's preferences, autonomy and needs, focusing on outcomes that people notice and care about such as survival, function, symptoms, and health related quality of life;
- Incorporates a wide variety of settings and diversity of participants to address individual differences and barriers to implementation and dissemination; and
- Investigates (or may investigate) optimizing outcomes while addressing burden to individuals, availability of services, technology, and personnel, and other stakeholder perspectives.<sup>9</sup>

PCORI is funded through the Patient Centered Outcomes Research Trust Fund receiving money from different funding streams that will change over time.<sup>10</sup> PCORI will be funded just through 2019.<sup>11</sup> It is overseen by a board of governors appointed by the Government Accountability Office.<sup>12</sup> PCORI is currently led by Executive Director Joe Selby, a former director of research at Kaiser Permanente.<sup>13</sup> PCORI will award contracts for peer-reviewed research.<sup>14</sup> In addition, PCORI will make research findings publicly available within 90 days, broadly disseminate research findings, provide public comment on major actions, and create a database of resources to make sure that the findings and analysis of PCORI funded research are available and widespread. This will make it easier for patients to use to make informed health care decisions.<sup>15</sup>

The PCORI agenda does not identify priority conditions or interventions, but calls for studies that are broad in range.<sup>16</sup> Proposed studies must align with 9 criteria that are specified in the ACA that emphasize consideration of the burden of illness, the current level of uncertainty faced by patients and clinicians, and the potential of the proposed research to reduce uncertainty.<sup>17</sup>

The PCORI Board approved its first 50 Pilot Projects Program funding awards, totaling \$30 million over two years, to investigators in 24 states and the District of Columbia.<sup>18</sup> Some of these projects will address a range of questions concerning methods for engaging patients in various aspects of the research and dissemination process. The projects are collecting preliminary data that can be used to advance patient-centered outcomes research.<sup>19</sup> A project in Minnesota was given one of these grants to study imaging and diagnostic treatments for low back pain and abdominal pain. They are developing a computerized algorithm to look through medical records to find out about patient imaging and then speak to the patients about their experiences with imaging.<sup>20</sup> The project will be looking into whether the outcomes are the same when there is sophisticated imaging and when there is not, to discuss how the imaging influenced the outcome.<sup>21</sup>

Another pilot project at Florida Atlantic University is studying the various patient decision aids used in acute transfer decision making for nursing home residents.<sup>22</sup> They will interview nursing home residents, their families, primary care providers, nurses and social workers about their experiences and the literature and decision aids that they use to find out what is helpful and what is not. The University research team will use this information to develop a better decision aid to help caregivers, residents, and their families in making these difficult decisions.<sup>23</sup>

## **II. CRITICISM OF COMPARATIVE EFFECTIVENESS RESEARCH AND PCORI**

Comparative Effectiveness Research and PCORI face several criticisms. First, many argue that they have an unacceptable effect on the practice of medicine. In addition, critics suggest that comparative effectiveness research is a waste of resources because the data created is not valuable.

### **A. PCORI'S EFFECT ON THE PRACTICE OF MEDICINE**

PCORI and the prospect of comparative effectiveness research has been attacked for its potential effects on the practice of medicine. Many fear that comparative effectiveness research will reduce patient choices of treatments and therapies diminishing autonomy. In addition, some argue that PCORI may hinder the emergence of the much touted personalized medicine because it studies larger populations and may draw sweeping conclusions.

#### **1. PCORI Impairs Patient Choice**

Critics of comparative effectiveness research argue that adhering to these research findings would inhibit individual choice. They suggest that individuals would only be able to receive treatments that the government has chosen for them.<sup>24</sup> After the government made new recommendations on PSA tests for prostate cancer and changing the frequency of breast cancer screenings there was serious public dissent.<sup>25</sup> Government interference in practice of medicine is a threat that many feel is imminent. Critics contend that the cost control imperative on the government might be so great that expensive interventions would be disfavored as not cost-effective. This may lead to denial of important treatments and a diminishing of patient choice in their care.<sup>26</sup>

Often this stems from a fear of rationing. Rationing of medicine was a big part of the outcry over “death panels” in the debate over health reform in 2009.<sup>27</sup> On January 23 2009, Republican Representative from Georgia Tom Price sent out an “alert” through the Republican Study Committee, warning that the comparative effectiveness legislation would create “a permanent government rationing board prescribing care instead of doctors and patients.”<sup>28</sup> He wrote that the true intent of the legislation was “to enable the government to ration care.”<sup>29</sup> These critics argue that comparative effectiveness research is not about informing choices, but taking away options.<sup>30</sup> The risk they cite is that the conclusion data will be flawed but still used to restrict coverage decisions including and especially by Medicare and CMS.<sup>31</sup>

Respect for person’s autonomy has become an important part of both research and clinical practice.<sup>32</sup> In addition, a trusting doctor- patient relationship has been recognized as an integral part of quality of care.<sup>33</sup> When the government gets in between doctors and patients, people are concerned that their quality of care will suffer as their autonomy is diminished by fewer choices.

## **2. PCORI Inhibits the Emergence of Individualized Medicine**

Comparative effectiveness research is also subject to criticism because it may inhibit the prospect of personalized medicine.<sup>34</sup> Since the mapping of the genome, researchers have envisioned a world of individualized medicine where treatments and diagnostic tests are designed specifically for a patient based on their individual characteristics and genetics.<sup>35</sup> Population- based studies that focus on average effects might fail to detect benefits for special populations.<sup>36</sup> Critics of PCORI argue that comparative effectiveness research will hinder the advancement in the field of personalized medicine to the detriment of patients’ quality of care.

In most studies and in clinical practice there are people who respond poorly to the treatment that works for the majority of the population and people that respond better to the less favored treatment. Critics suggest that comparative effectiveness research will make it harder for those outlier patients to receive the treatment they need because the less favored drug or device will be phased out as unprofitable or not valuable if a PCORI study deems it less effective. Personalized medicine as an emerging area of research and clinical practice suggests that people are not homogenous and treatments should be tailored to the individual. PCORI may limit this developing area and effect quality of care and patient autonomy.

## **B. QUESTIONING THE VALUE OF PCORI**

In addition to questioning the effects of PCORI on the doctor patient relationship, critics also attack the value of comparative effectiveness research in general. They criticize that it is hard to change clinical practice with data and the information gathered will have little influence on patient or physician choices. Critics suggest that comparative effectiveness research will divert funds away from innovation and away from research surrounding rare illnesses to favor the study of popular or more widespread diseases.

### **1. PCORI Won't Change Clinical Practice**

Critics of PCORI point out that comparative effectiveness research is not of great value because even with good data it is difficult to change clinical practices.<sup>37</sup> Physicians and patients are stuck in their ways and these studies will have little effect in medicine. These critics cite an example in the ALLHAT Study which did not yield much change in physician practice. The ALLHAT study compared antihypertensive and lipid lowering treatments and found that one diuretic was superior to other antihypertensive medications. Yet, there were only very small

effects on the use of this drug following the study despite widespread dissemination of the results.<sup>38</sup> This could be the same fate for PCORI research and the resulting data would have little effect on clinical practice and quality of care. If the resulting data from comparative effectiveness research is incapable of changing clinical practice, then this type of research is not valuable and a waste of research funds that could be used elsewhere.

## **2. PCORI Will Stifle Research in Other Research Areas**

An increase in comparative effectiveness research may stifle research in other areas by decreasing their funding or diverting attention. PCORI by design studies treatments that already exist. This means that this research funding will be used to compare treatments already being used in clinical settings. There are many illnesses that have no cures or treatments. Spending more money to compare effectiveness of existing therapies may stifle innovation by decreasing funding to those frontier projects. Other research areas that may suffer are those that aim to find a better treatment than those that already exist or research that studies the basics of disease. While some may suggest that this research is simply adding funding to the field, not taking away from other projects, the budget constraints on the federal government are immense and placing funding in one area likely effects funding in other areas. PCORI considers burden of illness in its allocation of funding,<sup>39</sup> and so, rare diseases may not receive as much attention as more widespread diseases like vascular disease or diabetes.

PCORI's funding of certain research at the expense of others brings to light questions of what kind of research is most worthy and how that ought to be determined. Should funding allocation be based on how common the disease is? How terrible or dangerous the results are? Which is more terrible, a slow degeneration from Alzheimer's Disease, which effects 4 million

people,<sup>40</sup> or imminent death from Creutzfeldt- Jakob Disease effecting only about 200 people in the United States per year?<sup>41</sup> It is questionable whether these issues can be addressed by a small board choosing which research projects should be funded by PCORI. Does comparative effectiveness research have any value in the face of these important questions?

### **III. RESPONSES TO THE ETHICAL CHALLENGES TO COMPARATIVE EFFECTIVENESS RESEARCH AND PCORI**

The criticisms to PCORI and comparative effectiveness research are worth noting, but there are also important considerations in response to those criticisms. This section will discuss those responses and explain how PCORI can adapt to them.

#### **A. PCORI'S EFFECT ON THE PRACTICE OF MEDICINE WILL BE A POSITIVE ONE**

Critics fear that PCORI will get between a doctor and their patient. To critics this is assumed to be a bad thing. PCORI's research will affect the practice of medicine by providing better information to doctors and patients on treatment options and this will create a positive effect on patient outcomes. In addition, PCORI will not inhibit the growing area of individualized medicine.

##### **1. Fear of Rationing is Not a Strong Criticism of PCORI and PCORI Will Enhance Patient Choice**

PCORI responded to the criticism of comparative effectiveness research as rationing by including in the legislation that cost- effectiveness will not be a factor in comparing treatments.<sup>42</sup> In addition, the health secretary cannot use results from PCORI research to determine or deny coverage or reimbursement for healthcare services.<sup>43</sup> Concerns that cost effectiveness will still



affect treatment options despite these prohibitions may be understandable as cost effectiveness may be inherent to the work. Yet, this is a benefit of PCORI rather than rationing we should be afraid of. This is because a better treatment decision at the forefront of facing disease or disability will lead to better outcomes and hopefully fewer issues that require further care. Improving quality of care leads to lower healthcare costs in the aggregate and for each individual patient.<sup>44</sup>

The idea that PCORI will ration care or diminish patient choice is too narrow a view. There is an inherent downside of established or stagnant rules in treatment. Studies will develop data on average effect of the treatment which will not catch those outlier patients that respond differently.<sup>45</sup> Yet, having data on average effect is superior to what we have now which is no knowledge on comparative effectiveness.<sup>46</sup> In addition, PCORI will not be a gateway to rationing because offering a myriad of treatments without knowledge of their comparative value will lead to greater financial pressures to ration care by cutting insurance coverage in both the private and public sectors.<sup>47</sup> Cost may be a factor in PCORI research, but quality of care is the driver of this cost effectiveness and to rely on a system without any comparative knowledge is to invite higher healthcare costs.

## **2. PCORI is Patient Centered and will not Inhibit the Prospect of Individualized Medicine**

Rather than hinder individualized medicine, PCORI will provide important information towards that goal. It will give patients and physicians unique information on what works that they can use to create the best treatment plan with the best available knowledge.<sup>48</sup> Dr. Selby, the executive director, has stated that the continued engaging of clinicians and patients will keep PCORI's research agenda focused on practical questions and on the possibility that treatment

effects may be different across different patient populations.<sup>49</sup> Individualized medicine will not be hindered by this legislation, it will be enhanced.

The goal of PCORI is to be patient centered. PCORI aims to fund research that will “assist patients, clinicians, purchasers, and policy makers in making informed health decisions by advancing the quality and relevance of evidence...”<sup>50</sup> PCORI will certainly change the way doctors and patients discuss treatment options, but it will change that interaction for the better. Treatment decisions will be with more and better information on a patient’s options so a patient can chose their own best treatment plan.

## **B. PCORI IS VALUABLE**

Critics question the value of comparative effectiveness research. They suggest that PCORI will come up with results that clinicians and patients will ignore. They also argue that this research that focuses on treatments we already have is not as important as research that searches for new cures. These criticisms are important to note, but PCORI is a valuable research endeavor and the potential benefits could make great changes in clinical practice for the improvement of patient care.

### **1. PCORI Will Change Clinical Practice with Proper Dissemination**

Continuing medical education has become an important part of state licensing requirements for clinicians. Recertification and licensing requirements keep providers from relying solely on what they have always done and compels providers to keep up with medical knowledge as it expands. With proper dissemination features PCORI can make sure that clinical practice does respond to the data generated in comparative studies.

Communication is a major goal of PCORI. One board member, Harlan Krumholz, stated that PCORI is about gaining knowledge but also investing in “practitioners and patients understanding that knowledge.”<sup>51</sup> The executive director of PCORI has argued that PCORI will be a test of the value of involving patients and practitioners in the research process. It remains to be seen whether PCORI will reduce clinical uncertainty and speed adoption of useful findings on effectiveness, but the law was set up to be accountable for widespread dissemination of results.<sup>52</sup>

The PCORI trust fund reserves 16% for comparative effectiveness research dissemination and training through the Agency for Healthcare Research and Quality. The board and the director understand the importance of this part of comparative effectiveness research and the law faces this criticism with a plan to counter the dismissal amongst practicing physicians of emerging research.<sup>53</sup> In addition, the targets of this information will go beyond the physician to include the patient and community in this post- trial conversation. PCORI recognizes that new evidence will not likely be adopted unless barriers that restrict acting on the new information are removed.<sup>54</sup>

## **2. PCORI’s Agenda Will Benefit Many, but Not at the Expense of Few**

Comparative effectiveness research under the guiding board of PCORI could have broad and lasting effects improving patients’ care experiences, decision making, and health outcomes.<sup>55</sup> Utilitarianism suggests that the right thing to do, is that which will do the most benefit for the largest number of people.<sup>56</sup> PCORI’s focus on research that addresses those diseases that are a particular burden to society follows this mantra. It is important to note though, that PCORI will also focus on areas of uncertainty, which would not exclude those rare diseases that are not as large a burden on society. The current PCORI research agenda does not identify any particular

conditions or interventions for study, rather the agenda calls for studies across a broad range of decisions that patients face.<sup>57</sup>

Critics claim that comparative effectiveness research is not as important as discovering a new vaccine, new surgery, or the emerging technologies in nanomedicine or stem cells. They suggest that PCORI will take money away from new horizons medicine and will simply chew on old information. Comparative effectiveness research studies therapies that are already used when there is still much to discover and a lot of illness that has no established treatment. Yet, just developing new drugs or treatments does not guarantee that these therapies are good. The goal of medicine is not always a new technique, drug, procedure or, operation, it is to treat patients successfully. We are looking for outcomes. Is the goal of treating diabetes to reduce blood glucose or to improve quality of life? Determining what quality of life means is important to the practice of medicine, and PCORI's inclusion of patients perspective reflects the growing need of information on what people see as a good or favorable outcome from their experiences with medicine.

All research funding faces the issue of what type of research is most worthy. Should we look for new therapies when there are existing ones? Are there diseases that need more attention than others? Should we focus on the more prolonged debilitating illnesses or those that bring imminent death? Comparative effectiveness research faces criticism, just as all research does, but it also has proven value. It answers questions that require attention and PCORI aims to improve outcomes through informing patient choices. The goal of health care to improve quality of life is also the goal of PCORI.

### **3. There Will Still Be Innovation**

Comparative effectiveness work will not be replacing rigorous randomized control trials or damaging innovative research.<sup>58</sup> The market for innovation in healthcare will not disappear or diminish because of expanded evidence on effectiveness. Drug and device manufacturers and academic researchers striving towards innovation will continue to have work because the value of new therapies will not go away. Rather, PCORI and the research it funds will develop another area of research that focuses on patient outcomes and improving quality of care by developing data to help clinicians, policy makers and patients chose the best treatment option.

#### **4. Examples of Comparative Effectiveness Studies with Value**

There is hope that the findings from comparative effectiveness research will develop helpful information that will allow clinicians to make evidence-based decisions, will involve patient's perspectives and preferences, will improve quality of care and eventually help control the cost of health care.<sup>59</sup> A comparative effectiveness theme issue from the Journal of the American Medical Association published five studies that compared available treatments illustrating the importance of PCORI and comparative effectiveness data. The articles addressed common and serious health questions that have alternative options with clinical and sometimes financial consequences.<sup>60</sup>

While the ALLHAT study was not widely accepted, there are several examples of comparative effectiveness research radically changing medicine and drastically improving patient outcomes. The ACCORD (Action to Control Cardiovascular Risk in Diabetes) study was a clinical trial of adults with established type 2 diabetes at high risk of cardiovascular disease.<sup>61</sup> The study tested three treatment approaches to determine the best ways to decrease the high rate of major cardiovascular disease events including heart attack, stroke or death.<sup>62</sup> The three

approaches they tested were “intensive lowering of blood sugar levels compared to a more standard blood sugar treatment; intensive lowering of blood pressure compared to standard blood pressure treatment; and treatment of multiple blood lipids with two drugs—a fibrate plus a statin – compared to one drug, a statin alone.”<sup>63</sup> In looking to these strategies of intensive control did not reduce the incidence of major cardiovascular events. In fact, it was increasing the risk of death.<sup>64</sup> These methods of treatment which had been widespread were actually harming patients, and the ACCORD comparative effectiveness study proved it.

## **5. PCORI is the Only Reputable Funding for This Important Research**

PCORI is also important because if the government is not doing this research, it will not be done. Private industry will not likely participate in valid comparative effectiveness trials because it could potentially result in losing money. Their conflict of interest would affect the the data as they are unlikely to publish a negative trial. If the insurance industry designed the research it would be focused on cost effectiveness to save money. It is possible that special interest groups like the American Diabetes Association (ADA) would do some comparative effectiveness work, but they too often have strong alliances with the pharmaceutical industry. The ADA receives a lot of funding from Lilly, the major manufacturer in the U.S. of diabetes treatments.<sup>65</sup>

The government has designed PCORI to do something that is not limited by the above organization’s burdens. It will not be driven solely by the bottom line or cost saving, but will be driven by the goal of better outcomes. This seems to be the only entity with the capacity to do comparative effectiveness research ethically. Having better evidence rather than no evidence is

much preferred when making clinical and policy decisions and the federal government is the only reputable funding available for this important work.

## CONCLUSION

Medicine is replete with tradition, opinion, assumptions, guesswork, incomplete knowledge and uncontrolled experimentation.<sup>66</sup> Despite the expensive health-care system in the U.S., there is very little and sometimes no evidence that widely used treatments and procedures actually work better than various alternatives.<sup>67</sup> Comparative effectiveness research aims to dispel the fog that surrounds the practice of medicine to allow clinicians and patients to make decisions based on evidence. This is valuable because it will lead to greater patient autonomy, and better outcomes for patient and population health. The criticisms of comparative effectiveness research are worth discussing but PCORI responded by removing the element of cost, and making the research patient centered. PCORI has only been guaranteed funding until 2019 and has great pressure to create valuable data quickly. There is potential for comparative effectiveness research to make a real difference in improving quality of care, but it remains to be seen if PCORI can accomplish those goals.

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<sup>1</sup> Sarah Kliff, *PCORI: Funny Acronym, Serious Work*, WASHINGTON POST, Jan. 18, 2012.

<sup>2</sup> Carolyn Clancy & Francis S. Collins, Patient- Centered Outcomes Research Institute: The Intersection of Science and Health Care, 2:37 *Science Translational Medicine*, 23 Jun. 2010.

<sup>3</sup> Sarah Kliff, *PCORI: Funny Acronym, Serious Work*, WASHINGTON POST, Jan. 18, 2012.

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

<sup>5</sup> Joe Selby *et al.*, *The Patient Centered Outcomes Research Institute (PCORI) National Priorities for Research and Initial Research Agenda*, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Apr. 18, 2012.

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<sup>6</sup> Alexander K. Ommaya & Joel Kupersmith, *Challenges Facing the US Patient- Centered Outcomes Research Institute*, 306 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 756, 756 Aug. 17, 2011.

<sup>7</sup> Alexander K. Ommaya & Joel Kupersmith, *Challenges Facing the US Patient- Centered Outcomes Research Institute*, 306 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 756, 756 Aug. 17, 2011. The ALLHAT study compared three antihypertensive medications and while all three lowered blood pressure, one did so more than the others.

<sup>8</sup> *PCORI: About Us*, <http://www.pcori.org/about/>.

<sup>9</sup> *PCORI: What We Do*, <http://www.pcori.org/what-we-do/pcor/>.

<sup>10</sup> *PCORI: How We're Funded*, <http://www.pcori.org/how-were-funded/>

<sup>11</sup> *Id.*

<sup>12</sup> Sarah Kliff, *PCORI: Funny Acronym, Serious Work*, WASHINGTON POST, Jan. 18, 2012.

<sup>13</sup> *Id.*

<sup>14</sup> Carolyn Clancy & Francis S. Collins, Patient- Centered Outcomes Research Institute: The Intersection of Science and Health Care, 2:37 Science Translational Medicine, 23 Jun. 2010.

<sup>15</sup> *Id.*

<sup>16</sup> Joe Selby *et al.*, *The Patient Centered Outcomes Research Institute (PCORI) National Priorities for Research and Initial Research Agenda*, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Apr. 18, 2012.

<sup>17</sup> *Id.*

<sup>18</sup> *PCORI: Funding Opportunities*, <http://www.pcori.org/funding-opportunities/>.

<sup>19</sup> *PCORI: Pilot Projects*, <http://www.pcori.org/pilot-projects/>.

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

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

<sup>22</sup> *Id.*

<sup>23</sup> *Id.*

<sup>24</sup> Douglas Kamerow, PCORI: Odd Name, Important Job, Potential Trouble, 342 British Medical Journal, Oct., 2011.

<sup>25</sup> Sarah Kliff, *PCORI: Funny Acronym, Serious Work*, WASHINGTON POST, Jan. 18, 2012.

<sup>26</sup> Eugene C. Rich *et al.*, *The Implications of Comparative Effectiveness Research for Academic Medicine*, 86 ACADEMIC MEDICINE, June 2011.

<sup>27</sup> See Douglas Kamerow, PCORI: Odd Name, Important Job, Potential Trouble, 342 British Medical Journal, Oct., 2011 and Sarah Kliff, *PCORI: Funny Acronym, Serious Work*, WASHINGTON POST, Jan. 18, 2012.

<sup>28</sup> Jerry Avorn, *Debate About Funding Comparative Effectiveness Research*, 360 N. Eng. J. Med. 1927, 1928 May 7, 2009.

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

<sup>30</sup> The Pro Diabetes Board (editorial), Wall Street Journal Mar. 18, 2011, <http://online.wsj.com/article/SB10001424052748704662604576202883913468422.html>.

<sup>31</sup> Jerry Avorn, *Debate About Funding Comparative Effectiveness Research*, 360 N. Eng. J. Med. 1927, 1928 May 7, 2009.



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- <sup>32</sup> *The Belmont Report*, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, Apr. 18, 1979, available at <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>.
- <sup>33</sup> See George J. Annas, *HIPAA Regulations— A New Era of Medical- Record Privacy?* 348 NEW ENG. J. MED. 1486, 1486 (Apr. 10, 2003) (arguing that the public policy rational for protection of privacy is that patients will be less likely to disclose details necessary for proper medical care if they do not trust their physicians to keep the information secret, and HIPAA is a way to ensure these principles in the electronic age).
- <sup>34</sup> Eugene C. Rich *et al.*, *The Implications of Comparative Effectiveness Research for Academic Medicine*, 86 ACADEMIC MEDICINE, June 2011.
- <sup>35</sup> Margaret A. Hamburg & Francis S. Collins, *The Path to Personalized Medicine*, 363 New Eng. J. Med. 301 July 22, 2010.
- <sup>36</sup> Eugene C. Rich *et al.*, *The Implications of Comparative Effectiveness Research for Academic Medicine*, 86 ACADEMIC MEDICINE, June 2011.
- <sup>37</sup> Alexander K. Ommaya & Joel Kupersmith, *Challenges Facing the US Patient- Centered Outcomes Research Institute*, 306 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, 756, 756 Aug. 17, 2011.
- <sup>38</sup> See Stafford RS *et al.* Impact of the ALLHAT/JNC7 Dissemination Project on Thiazide- Type Diuretic Use. 170 Arch. Intern. Med. 851, 2010.
- <sup>39</sup> Joe Selby *et al.*, *The Patient Centered Outcomes Research Institute (PCORI) National Priorities for Research and Initial Research Agenda*, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Apr. 18, 2012.
- <sup>40</sup> DJ Iverson, *Practice Parameter Update: Evaluation and Management of Driving Risk in Dementia: Report of the Quality Standards Subcommittee of the American Academy of Neurology*, 74 NEUROLOGY 1316-1324, 2010.
- <sup>41</sup> National Institute of Neurological Disorders and Stroke, National Institutes of Health, *Creutzfeldt- Jakob Disease Fact Sheet*, May 16, 2012.
- <sup>42</sup> Robert H. Brook, *Can the Patient- Centered Outcomes Research Institute Become Relevant to Controlling Medical Costs and Improving Value?* 306 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 2020, 2020 Nov. 9, 2011.
- <sup>43</sup> Douglas Kamerow, PCORI: Odd Name, Important Job, Potential Trouble, 342 British Medical Journal, Oct., 2011.
- <sup>44</sup> Jerry Avorn, *Debate About Funding Comparative Effectiveness Research*, 360 N. Eng. J. Med. 1927, 1928 May 7, 2009.
- <sup>45</sup> Amitabh Chandra, *The Pragmatists Guide to Comparative Effectiveness Research*, 25 J. Econ. Perspect. 2011.
- <sup>46</sup> *Id.*
- <sup>47</sup> *Id.*
- <sup>48</sup> Joe Selby *et al.*, *The Patient Centered Outcomes Research Institute (PCORI) National Priorities for Research and Initial Research Agenda*, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Apr. 18, 2012.
- <sup>49</sup> *Id.*
- <sup>50</sup> *Id.*
- <sup>51</sup> Sarah Kliff, *PCORI: Funny Acronym, Serious Work*, WASHINGTON POST, Jan. 18, 2012.

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<sup>52</sup> Joe Selby *et al.*, *The Patient Centered Outcomes Research Institute (PCORI) National Priorities for Research and Initial Research Agenda*, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Apr. 18, 2012.

<sup>53</sup> Carolyn Clancy & Francis S. Collins, *Patient- Centered Outcomes Research Institute: The Intersection of Science and Health Care*, 2 SCIENCE TRANSLATIONAL MEDICINE, 23 Jun., 2010.

<sup>54</sup> Joe Selby *et al.*, *The Patient Centered Outcomes Research Institute (PCORI) National Priorities for Research and Initial Research Agenda*, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Apr. 18, 2012.

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

<sup>56</sup> *See Consequentialism*, Stanford Encyclopedia of Philosophy, available at <http://plato.stanford.edu/entries/consequentialism/>.

<sup>57</sup> Joe Selby *et al.*, *The Patient Centered Outcomes Research Institute (PCORI) National Priorities for Research and Initial Research Agenda*, JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Apr. 18, 2012.

<sup>58</sup> Robert M. Golub, *Comparative Effectiveness Research Relative Successes*, 307 Journal of the American Medical Association, 1643, 1643 Apr. 18, 2012.

<sup>59</sup> Robert M. Golub, *Comparative Effectiveness Research Relative Successes*, 307 Journal of the American Medical Association, 1643, 1643 Apr. 18, 2012.

<sup>60</sup> *Id.*

<sup>61</sup> *See ACCORD Questions and Answers*, National Heart Lung and Blood Institute, Mar. 15, 2010 [http://www.nhlbi.nih.gov/health/prof/heart/other/accord/q\\_a.htm#trial](http://www.nhlbi.nih.gov/health/prof/heart/other/accord/q_a.htm#trial).

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

<sup>63</sup> *Id.*

<sup>64</sup> Harlan M. Krumholz & Thomas H. Lee, *Redefining Quality- Implications of Recent Clinical Trials*, 358 N. ENG. J. MED. 2537, 2538 June 12, 2008.

<sup>65</sup> *See eg.*, Sarah Bradley, *Lilly Diabetes and the American Diabetes Association partner to send 88 children with diabetes to American Diabetes Association Diabetes Camps in 2011*, American Diabetes Association, March 18, 2011 available at <http://www.diabetes.org/for-media/2011/lilly-diabetes-camperships-2011.html>.

<sup>66</sup> John Carey, *Medical Guesswork*, Bloomberg BusinessWeek Magazine, May 28, 2006.

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