

# The Anticipated and Unintended Consequences of the Patient Protection and Affordable Care Act on Cancer Research

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**Abstract:** Continued research is critical to build upon past improvements in mortality and morbidity from cancer. Provisions in the Patient Protection and Affordable Care Act (PPACA) of 2010 address health research that affect cancer research in many positive and some potentially negative ways. The impact of PPACA on cancer research must be viewed in the context of the federal economic situation and the ongoing reform of the American clinical trial system. Major components of PPACA affect cancer research including requiring insurance coverage of standard care provided as part of clinical trials, establishment and funding of the Patient Centered Outcomes Research Institute focused on comparative effectiveness research, and establishment of the Cures Acceleration Network to foster rapid translation of basic research to the bedside. This article reviews these programs, their strengths, and our concerns regarding their potential shortfalls and areas needed to support cancer research on which PPACA is silent.

**Key Words:** Health care reform, Patient Protection and Affordable Care Act, health policy, cancer research

(*Cancer J* 2010;16: 606–613)

Cancer is one of the leading causes of illness and death in the United States. Overall, it is expected that there will be 1.5 million new cancer cases in the United States in 2010 exclusive of in situ cancer and squamous cell skin cancers.<sup>1</sup> It is further estimated that 570,000 will die each year from cancer. Cancer is only second to heart disease as the leading cause of death and accounts for the death of 1 of every 4 Americans. However, these sobering statistics are actually increasingly bright compared with even a decade ago. Overall, the American Cancer Society estimates that the 5-year survival rate has improved from 50% to 68% in the last decade. The mortality rates for many cancer types have seen a clear and sustained drop over the last 2 decades. This includes colon and rectal cancer, stomach cancer, breast and uterus cancer in women, and lung and prostate cancer in men. These hopeful trends are the combined effect of advances in cancer detection and screening,

public awareness and openness, and improved local and systemic treatments. If these hopeful trends are to continue, we believe it is critically important that health care reform encourage and even accelerate the rate of progress in cancer research. In its current form, the Patient Protection and Affordable Care Act (PPACA) passed by Congress gives us reason for both hope and for concern as to whether such progress will be continued.<sup>2</sup>

Improvements in cancer detection, screening, and treatment have been hard won through decades of work by scores of dedicated researchers addressing key questions in the basic principles of cancer biology (and deriving new diagnostic and treatment approaches therefrom), basic technologies of imaging, and rigorous clinical research. Beyond direct clinical research, many key advances in treatment emanate from studies of basic scientific principles. Two clear examples for which Nobel Prizes were awarded are the development of the mathematical and physics principles for construction of cross-sectional images with computed tomography and the discovery of the molecular techniques for polymerase chain reaction for amplification of genetic material, advances that revolutionized diagnostic capabilities and our understanding of cancer genetics.

Making continued progress in reducing cancer mortality will require (1) continued strategic investment in early detection, screening, and prevention; (2) ongoing investment in basic research; (3) funding for training the upcoming generations of cancer researchers; (4) incentives to speed up and simplify both academic and industry pursuit of translational research that moves laboratory discoveries to produce effective new treatments; (5) funding to support cutting edge clinical trial research; and (6) policies that ensure that all patients have affordable access to clinical trials.

This article provides an overview of key provisions in the 2010 PPACA that affect cancer research, as well as related other critical issues likely to affect the progress of cancer research. In addition, we address our concerns regarding some of the provisions and directions of research mandated by the PPACA as well as the potential negative impact that the continuing federal economic crisis may have on the funding for cancer research and on our ability to maintain the environment for training researchers and conducting cancer research.

As of this writing, there is some chance that the PPACA or individual items in PPACA may be altered or reversed by a new Congress or that key aspects of PPACA may be overturned in the courts. Perhaps the most critical issue is whether the contained mandate for all individuals to purchase health insurance will survive a challenge from several states including Virginia and Florida, although the constitutionality of the individual mandate was upheld in early October 2010.<sup>3</sup> As political and legal challenges are debated, however, key provisions of the legislation are already being enacted including extending coverage for young adults up to age 26 years on their parents' policies, formation of high-risk pools needed to provide coverage for people with

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Dr Zwelling is supported by a Robert Wood Johnson Health Policy Fellowship and by a University of Texas Chancellor's Health Fellowship from the University of Texas Executive Vice Chancellor for Health Affairs, Dr Kenneth Shine, and by the Center for Comparative Effectiveness Research on Cancer in Texas, a multiuniversity consortium funded by the Cancer Prevention and Research Institute of Texas (grant RP101207).

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ISSN: 1528-9117

preexisting conditions, and payment for “donut-hole” drug costs for seniors. Given this background, readers need to recognize that the observations we make apply to the PPACA as passed by Congress in March 2010 and that ensuing changes to that legislation could alter provisions related to cancer research.

### Sources of Funding for Cancer Research

Cancer research is funded through a variety of mechanisms. Sponsors may have different stakes in the outcome of the research. Federal agencies support research as part of their mission from Congress to better the health of the American people as do some specialized nonprofit charitable organizations (e.g., the American Cancer Society). The pharmaceutical and biotechnology industries support research, both within and outside their walls, with an eye toward creating useful and profitable drugs and devices through regulatory approval of their products as “safe and effective.” In addition, providers and health care institutions routinely subsidize clinical trials because sponsor support (grants, contracts) for study-related expenses often does not cover the full cost of study participation.

Given that industry is a major source of funding for clinical research, changes in the current business climate and restrictions on relations with academic researchers that may have arisen in response to instances of conflicts of interest<sup>4,5</sup> may also retard the speed of cancer research. Furthermore, a potential and unanticipated effect of PPACA is that it could result in decreased corporate earnings and thereby lead to restrictions in research and development spending, although this would be difficult to quantify.

Another essential component of our cancer research mechanism is the need for training of sufficient numbers of new clinical and basic research scientists. Although not directly addressed in PPACA, potential future workforce shortages in oncology specialties could be exacerbated as a result of expanded coverage, and critical reductions in young people entering academic careers may have significant deleterious effects on progress in cancer research.<sup>6,7</sup>

### Overview of the Impact of PPACA on Cancer Research

The PPACA carries a number of provisions that promise positive impact on research and some that could conceivably have a negative impact. There are also certain areas where reforms needed to ensure conduct of ongoing research have, in our opinion, been omitted. Although PPACA addresses coverage costs for clinical trials and provides significant funding for comparative effectiveness research (CER), most of the provisions do not specifically address cancer research. Each of the following major provisions below that may be expected to be of significant benefit for oncology research and on clinical oncology practice is reviewed.

- Mandated coverage for clinical trials (PPACA section 2709)
- Establishment of a Patient-Centered Outcomes Research Institute (PCORI) devoted to the field of CER (identifying best treatments using “real world” data) (PPACA section 6301)
- Implementation of the Cures Acceleration Network (CAN) to speed translation of particularly promising basic scientific knowledge into effective therapies (PPACA section 10409)
- Elevating the status of the National Center on Minority Health and Health Disparities to status of a national institute on minority health and health disparities [PPACA section 1701A(c)]
- Enhancing data collection infrastructure (PPACA section 3101)

- Mandating development of a national education campaign in breast health for young women and health professionals and to conduct breast cancer prevention research in younger women (PPACA section 10413)
- A defined pathway for the approval of follow-on biologics including those used in cancer patients (section 7001–7003)

### Clinical Trials Research and PPACA

The scope of clinical cancer research ranges from population cancer surveillance, studies of cancer incidence, and disparities in cancer care to primary testing of new drugs and procedures. Cancer clinical trials test new drugs and treatments in a stepwise fashion from dose finding and toxicity testing (phase I) to preliminary studies of efficacy (phase II) and on to controlled (randomized) evaluations of new therapies versus current standard care (phase III). Phase IV postmarketing trials, which are sometimes conducted to examine such things as previously unrecognized adverse effects, efficacy questions and drug interactions may rely on retrospective examination of large data sets and, in fact, utilize methods used in CER. However, in many cases, phase IV trials may not be completed. They are not widely favored by the pharmaceutical industry as they provide only downside risk for their newly approved products. This is particularly concerning when approval was gained using the accelerated Food and Drug Administration (FDA) process, which is supposed to be followed by a postapproval trial, but often is not, with few consequences to the delinquent sponsor, although this may be improving.<sup>8</sup>

Clinical trials may be conducted by a single institution or investigator or by groups of institutions. Large phase III trials usually require multiple institutions that sometimes collaborate through several National Cancer Institute (NCI)–funded cooperative cancer groups. This system has provided enormous value to Americans, providing clear improvements in cancer treatment outcomes, and survival. However, the clinical trial system is hampered by inefficiencies and limited access to trials for some cancer patients. The current system is slow in developing, implementing, and completing clinical trials. It is estimated that it may take as long as 10 to 15 years for a new drug to enter routine practice through this system. A recent report for the Institute of Medicine (IOM) highlighted these issues and made far-reaching recommendations for revamping the clinical trial system in oncology.<sup>9</sup> The IOM specifically suggested that (a) the system receive a higher fraction of the NCI research budget; (b) the speed and efficiency of design, launch, and conduct of clinical trials be improved; (c) there be more rapid use of scientific innovations; and (d) that means be applied to foster greater participation by both patients and physicians.

Far too many trials are never finished, which is unquestionably a major waste of both opportunity and financial resources. In addition to the issues identified by the IOM report, the research community bears responsibility in improving clinical trial research. It needs to ensure that every trial is asking a question of vital importance, that no trial goes unfinished, and that the results of all trials are reported. Unfinished trials represent the suspension of the fiduciary trust between investigators and the human subjects who had already been entered on the trial. Except in the circumstance where new evidence makes continuance potentially harmful to future enrolled subjects, failure to complete trials may be considered unethical.

Unfortunately, many factors conspire to make clinical trials difficult to conduct and complete. The regulatory system is cumbersome, and the consent process is often burdensome when patients are asked to review and sign detailed consent forms up

to 20 pages in length. Another factor contributing to slow accrual is that medicine remains a fee-for-service system, whereas the performance of clinical research is costly and time consuming for physicians. This means that practitioners are minimally incentivized to do clinical research. Furthermore, the academic centers that serve as the organizing structures for many trials primarily reward and promote faculty based on individual achievement and not team efforts such as clinical trial development and participation. In addition, patients may be able to gain access to new agents and treatments outside a trial setting before these new drugs are completely evaluated. Sometimes other new agents that show greater promise than the one under evaluation may become available before trials of the first agent are complete. Nonetheless, an unfinished trial is equivalent to breaking a contract between the investigators of the unfinished trial and the human subjects who consented to participate knowing they were part of an effort to generate generalizable information.

It should be remembered that the existing clinical trial system was developed to address the serious limitations of such methods as retrospective record review and the limitations posed by not having appropriate control groups. As research organizations prepare to take advantage of the major funding for CER to be made available through PPACA, it is important that we also be fully cognizant of its limitations and exercise caution about not entering a journey “back to the past.” It might also be argued that progress might best be made by fundamentally rebuilding our current trials system to address its conspicuous deficits.

Another factor limiting clinical trial research is the concern that trial participation adds to care costs. This has led some payers to restrict access to clinical trials for their subscribers because of the not wholly unreasonable stance that they are not mandated to cover the added costs of clinical research. Whereas some states mandate coverage for trials by payers subject to state insurance regulations, other states do not have such mandates.<sup>10</sup> In recent years, there has been an increase in the number of employers that are establishing self-insured coverage for employees rather than purchasing commercial health insurance. These self-insured plans are currently exempt from state regulations and are regulated by the federal Employee Retirement Income Security Act (ERISA) that does not mandate coverage for clinical trial participation. In what seems to be an increasing trend, some self-insured plans have denied payment for any treatment provided to a patient who is on a clinical trial, even when the major component of treatment would otherwise be considered standard care and all costs related to the investigational component of the study are reimbursed by the sponsor. Some plans have gone so far as to deny coverage for current necessary care because of past participation in a trial. Such plans have even denied coverage for pediatric cancer patients on the grounds that essentially all pediatric cancer treatment is conducted on an intergroup protocol. Needless to say, practices such as these are having a dampening effect on the ability to conduct clinical research.

The PPACA addresses clinical trial access on 2 fronts. First, providing health coverage to the many Americans who are currently uninsured and underinsured is a primary tenet of the PPACA. The means by which reform legislation effects this change is addressed elsewhere in the monograph and is not further reviewed here. However, it is critical to recognize that certain racial, ethnic, and socioeconomic groups and the elderly have been underrepresented in clinical trials because of access issues. Generalization of findings of clinical trials has been limited by these disparities. Increasing coverage for these groups coupled with open access to and payment for care on clinical

trials is needed to address these problems, and PPACA would seem to ameliorate them.

Second, the PPACA specifically requires that payers allow subscribers to participate in clinical trials. The legislation stipulates that payers must cover all standard treatment costs that are incurred during conduct of the clinical trial. The legislation specifically states (section 2709) that a group health plan or health insurance issuer

- (1) “...may not deny the individual participation in a clinical trial referred to in subsection (b).”<sup>2</sup>
- (2) “may not deny (or limit or impose additional conditions on) the coverage of routine patient costs for items and services furnished in connection with participation in the trial and ...may not discriminate against the individual on the basis of the individual’s participation in such trial.”
- (3) Must cover “...routine care costs including all items and services consistent with the coverage provided in the plan that is typically covered for a qualified individual who is not enrolled in a clinical trial.”

Excluded from this coverage are costs for the specific investigational item, device, or service and those costs incurred solely to collect data and satisfy analytic needs and any service that is “clearly inconsistent with widely accepted and established standards of care for a particular diagnosis.” The legislation continues that the plan may compel the patient to use a network participating provider for the trial, but the trial costs must be covered even if the approved clinical trial is conducted outside the state of the patient’s residence.

The legislation defines an “approved clinical trial” as “a phase I, phase II, phase III, or phase IV clinical trial that is conducted in relation to the prevention, detection, or treatment of cancer or other life-threatening disease or condition...” [PPACA section 2709(d)]. These may include federally funded trials, other studies conducted under a FDA investigational new drug application, or a drug trial that is exempt from having an investigational new drug application. Studies must be reviewed and approved by peer review.

With passage of PPACA, Congress and the President have assured the public that “if they like their current health plan, they can keep it.” That seemingly sensible promise has created serious ambiguity regarding the mandate to cover clinical trials by those plans that are currently exempt from the trial mandate, especially plans operating under ERISA regulations.<sup>11</sup> If plans that currently do not cover trials are recognized as being “grandfathered” and allowed to maintain current coverage provisions, patients covered by such plans may be denied coverage for trial-related expense well beyond the 2014 implementation date for the mandate. A number of cancer centers are already experiencing denials by ERISA-regulated plans that formerly provided coverage for trials. Coupled with the increasing prevalence of self-insured plans, this could represent a significant loophole in coverage for trials. Considerable attention is being focused on this conundrum by consultants and responsible agencies.

### Comparative Effectiveness Research

It has been proposed that as much as half of what doctors do is either ineffective or not cost-effective and that some form of research that compares the outcomes, cost, and value of alternative diagnostics and treatments would lead to more efficient medical practice and fewer expenditures on ineffective care. Such research is called CER. The IOM published its initial priorities for CER in June 2009.<sup>12</sup> The IOM defined CER as “the generation and synthesis of evidence that compares

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 CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels.<sup>12</sup> The Federal Coordinating Council's report published the same day as the IOM report emphasized that CER must gain its insights using subjects representative of the "real world," rather than using the carefully selected eligibility criteria (e.g., certain age limitations and the absence of comorbid conditions) usually applied to patients enrolled in clinical trials that measure efficacy, not effectiveness.<sup>13</sup>

Comparative effectiveness research is performed using a variety of methods including review of existing data, published and unpublished, using meta-analysis; retrospective analysis of medical records; prospective nonexperimental reviews of the literature or medical records; and the more traditional method of clinical comparison, the clinical trial.<sup>14</sup> Clearly, each of these forms of research has its own advantages. The retrospective methods are less costly and time consuming to perform and can take advantage of large databases drawn from unselected patients. Prospective trials, particularly randomized clinical trials (RCTs), have the least ambiguity and apply the power of biostatistics and statistical significance to determine the criteria of success or failure prior to the research's initiation. However, RCTs are costly and take time and expertise to be performed well, and many RCTs are not completed owing to poor accrual, leaving important questions unanswered.

Comparative effectiveness research was initially supported with more than \$1 billion in the American Recovery and Reinvestment Act of 2009. Subsequently, CER became a critical part of the PPACA. Title VI, subtitle D, section 6301: "establishes a private, nonprofit entity (PCORI) governed by a public-private sector board appointed by the Comptroller General to identify priorities for and provide for the conduct of CER." The PCORI will replace the Federal Coordinating Council for CER that was created by the American Recovery and Reinvestment Act legislation. The PCORI will be provided sufficient funds through a federally funded Patient-Centered Outcomes Research Trust Fund. The funds will equal in the first year \$1 multiplied by the average number of beneficiaries eligible for Part A or enrolled under Part B and will increase in fiscal year 2014–2019 to \$2 per beneficiary. The funds shall be awarded through contracts through other federal agencies and directly with academic and private entities.

The PCORI will report to the secretary of the US Health and Human Services (HHS) with oversight from a board of governors and a methodology committee. The board of governors has 21 members, with 19 appointed by the Government Accountability Office plus the director of the Agency for Healthcare Research and Quality and the director of the National Institutes of Health (NIH) or their designees. The PPACA stipulates that members of the board of governors must include representatives of academia, advocacy groups, and the medical manufacturing industry. The Government Accountability Office announced its selection of board members in September 2010. The selections included several respected authorities in health services research and medicine, although only one, Dr Ellen Sigal, seems to have a specific focus in oncology.

A key provision of the PPACA CER mandate is the restriction from use of the results of CER by public or private payers to mandate practice guidelines or coverage decisions based on age, disability, terminal illness, or an individual's quality-of-life preferences. Specifically, the results of this work may not overrule coverage determinations made by the secretary

of HHS. Section 1182(c)<sup>1</sup> that states, "The secretary shall not use evidence or findings from comparative clinical effectiveness research conducted under section 1181 in determining coverage, reimbursement, or incentive programs under title XVIII in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill." In addition, it states in section 1182(d)<sup>3</sup> that "The Patient-Centered Outcomes Research Institute... 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" or "...as a threshold to determine coverage, reimbursement, or incentive programs under title XVIII." For determining Medicare coverage policies, the legislative language in the PPACA specifically limits the use of CER for these purposes unless the determinations are subject to broad, transparent review and considerations of impact on subpopulations.

This provision was the result of political dialogue over the perception that CER could be used as a means of withholding care that might prolong life, leading to the description of "death squads," "death committees" or "death panels."<sup>15</sup> This inflammatory language stemmed from misconstrued opposition to reasonable proposals to provide physician reimbursement for discussing end-of-life care decisions with their patients, nothing more. Unfortunately, these restrictions may specifically limit the value of findings of CER and the impact of the PCORI.

Comparative effectiveness research is a cornerstone of the Obama administration's plan to reduce health care costs and "bend the cost curve" (reducing the rate of health care inflation to that in the general economy and below its current higher rate of increase).<sup>16</sup> If used as originally intended, providers and payers could utilize CER to reduce expenditures by eliminating very costly or ineffective medical procedures and treatments. This use implies "rationing" of care to some people, but in reality represents appropriate utilization based on science and patient need rather than our current de facto system of rationing care based on personal financial capability and what individual insurance coverage allows or disallows.

The restrictions subsequently applied on the use of CER mean that the original intent of CER—its use to make crucial decisions about coverage, access, and therapeutic choices or its major purpose, cost control—cannot be fulfilled. This seems like a "Catch-22"<sup>17</sup>—an intent of the PPACA is to control costs without impacting quality, and we need CER to bend the cost curve—but PPACA makes it extremely difficult to apply the results in this way.

Overall, CER provides the opportunity to examine care on large populations not traditionally included in clinical trials. However, there are many methodological pitfalls and concerns that must be addressed if we are to depend on CER to make advances in cancer care. It would be a tragedy if CER distracts the oncology community and diverts funding from research into the basic biology of cancer and the translation of those findings into meaningful new treatments. Comparative effectiveness research may provide more rapid short-term findings that yield value in improving cancer care or reducing unnecessary expenditures. However, it is basic scientific discoveries that will provide the long-term permanent improvements in cancer prevention and treatment that fundamentally reduce the impact of cancer on society.

Given this background on CER, how might the related provisions of PPACA affect cancer research positively and negatively?

### Strengths of CER

- It provides an influx of additional monies for this cancer research.
- CER provides the promise of using large data sets to define effectiveness of treatment options that have been differentially implemented in varied practice settings, especially as they relate to off-label use of drugs and devices.
- CER may provide data to improve care for types of cancer where incidence is very low, making it impractical to conduct a randomized trial of current treatments in a realistic time frame. In such instances, CER, utilizing data from cases systematically recorded in relational databases, may provide the best available means for assessment of treatment efficacy and toxicity. The recent CER study of lymphoma subtypes using the National Comprehensive Cancer Network non-Hodgkin lymphoma database is a relevant example.<sup>18</sup>
- Many of the therapies commonly utilized in cancer treatment have never been subjected to a formal trial or FDA approval in the particular setting where they are used. This off-label use of drugs and biologics has been the subject of considerable controversy in recent years, and in some instances, insurance coverage for such agents has been denied. With systematic data collection, CER studies might provide convincing evidence of efficacy—or lack there of—in settings where prospective trials might never be practical.

### Weaknesses of CER

- If funds for CER are gleaned from funds that otherwise might go to more traditional forms of biomedical research, particularly from the NCI, this could adversely affect research into new more effective cancer therapies.
- CER relies on real-world data from which findings will be confounded by the inability to account for differences in patient populations related to factors such as biological tumor characteristics, patient characteristics (e.g., comorbid conditions), and health systems issues (e.g., access to care and appropriateness of care).
- CER using existing databases will inherently be evaluating treatment administered in the past using historical care standards. Comparative effectiveness research examines the effectiveness in large groups of seemingly similar cases in an era where oncology is increasingly basing treatment on very granular understanding of the individual cancer—so-called personalized medicine. Findings in a number of cancer types demonstrate that the treatment for patients who seem to have the same demographic and socioeconomic characteristics and to have similar diseases (e.g., hormone receptor-positive breast cancer) really differs dramatically in the likely responsiveness to treatment and may have genetic differences in metabolism of drugs that impact effectiveness. As conceived to date, CER cannot account for these differences so that relying on past care to compare effectiveness could have the paradoxical effect of stifling innovation and research in new approaches.<sup>19</sup>

### Unanswered Questions and Concerns Regarding Application of CER

- Will CER be utilized to gain FDA approval for newer therapies that may be more effective (not a current requirement for new drugs) or less expensive than currently approved agents? This could raise the bar at the FDA, which currently asks only that new drugs be safe and effective, but not better or cheaper.
- Will there be issues regarding third-party payer reimbursement for patients treated in practices participating in pro-

spective data collection for CER? Currently, the routine care costs associated with any clinical trial are to be covered by Medicare, and soon (2014) this will apply to all insurers [PPACA, title X, section 10103(c)]. It will be important for these provisions to apply to CER as well as prospective clinical trials.

- Will cost be considered in CER, and will an equally effective but more costly treatment no longer be covered by third-party payers just as some brand name drugs are not covered today?
- Will HIPAA be amended to facilitate CER and other forms of database research obviating the need for investigators to gain consent and authorization from patient-years after their treatment?<sup>20</sup>

To use CER in the modern health care system may require some major societal shifts if CER is to change practice and payment.

- CER, like all research, must be conducted in accord with accepted principles of human subject research with appropriate protection of research subjects and individual privacy and in compliance with applicable research and privacy regulations. The extent to which CER may be conducted on existing and/or new data with and without individual consent will need to be fully addressed, as will the use of any data collected specifically for the purposes of prospective CER.
- A precept of CER is that it will be conducted by leveraging disparate existing data sets collected in the normal course of providing care. Data sources may include cancer registries (governmental and private), medical records (especially electronic records), and administrative data such as payer claims. The extent to which the data sets may be used and which personally identified information collected for other purposes may be used for CER is unclear. In addition, PCORI must define how it may incorporate data from proprietary sources such as federally funded clinical trials and pharmaceutical industry-sponsored trials where the data are the property of the sponsoring company.
- The PCORI will need to work with other federal agencies and private organizations developing electronic systems for recording medical record data to standardize the reporting of treatment and outcomes. Existing systems use disparate standards and data elements and do not provide medical data in a searchable form. Having such standardized information and data system interoperability would greatly assist the performance of CER.
- The PCORI must develop means to communicate the results of CER that are comprehensible to the medical professional and to the public. Comparative effectiveness research may indicate that, in some circumstances, it is appropriate to withhold certain services. Experience suggests that it will be difficult to communicate the benefits of withholding care to the public.

### Cures Acceleration Network

The PPACA provides new support for accelerated translation of high-value science into effective new therapeutic agents by establishing the CAN within the office of the director of the NIH (section 10409). The purpose is to identify key advances in basic research and speed their translation to the bedside. The CAN will accomplish this work by awarding grants and contracts to qualified entities, reducing barriers to development of clinical trials, and facilitating communication and review of new therapies by the FDA.

A 24-member board that includes basic and clinical researchers, individuals from industry, experts in bioinformatics

and regulatory issues, and professionals in venture capital and equity investing will direct the CAN. Under the direction of the CAN Review Board, the NIH director will make awards to “accelerate the development of high-need cures” and “reduce the barriers between laboratory discoveries and clinical trials for new therapies” and “facilitate review in the FDA for the high-need cures funded by the CAN.” The CAN will make 3 types of awards: (a) Cures Acceleration Partnership Awards for which up to \$15 million may be awarded per project. Eligible entities include research institutions and industry. As a condition of award, the funded entity must contribute \$1 in nonfederal funds for every \$3 awarded by the NIH unless waived by the director; (b) Cures Acceleration Grant Awards of up to \$15 million per grant for the first year, and (c) Cures Acceleration Flexible Research Awards for projects the director of the NIH determines cannot be performed through other grant or contract mechanisms. A total of \$500 million is appropriated in fiscal year 2010 for CAN. The CAN provides substantial flexibility to the director to move aggressively in promising areas of translational research beyond the realm of traditional grants and contracts.

### Health Care Disparities

Historically, there have been disparities in the treatment of cancer and application of research efforts based on race and ethnicity and socioeconomic status. Efforts to understand and address the causes of such disparities are required. The efforts have been previously coordinated by the existing National Center on Minority Health and Health Disparities. Under the PPACA, this office will be elevated to the status of National Institute on Minority Health and Health Disparities (section 1707A). The director of the institute will be responsible for coordinating NIH research on disparities and “plan, coordinate, review, and evaluate research and other activities conducted or supported by the institutes and centers of the NIH.”

### Breast Cancer Education and Research in Younger Women

Specific language in PPACA (section 10413) addresses breast cancer research in young women. This expands HR 1740, the Breast Education and Awareness Requires Learning Young Act of 2009, and requires the secretary of the US HHS to develop a campaign to educate young women and health care professionals about breast cancer and breast cancer risk among women younger than 40 years. Furthermore, it stipulates the conduct of prevention research and research in new screening tests for breast cancer in younger women.

### Data Collection Infrastructure

Research in quality care delivery and efforts to improve community-wide quality of care are a national priority. The PPACA legislation addresses this area of research as well as the need to develop quality measures for purposes of evaluating health care delivery, public reporting of quality findings, and for provider accountability and reimbursement. Toward this end, the legislation requires the President to convene a work group to foster collaborative and cooperative efforts between agencies to develop strategies to improve health care quality. Termed the Interagency Working Group on Health Care Quality, this group must report annually to congressional committees on efforts to coordinate quality improvement goals, avoid duplication of effort, and coordinate public and private efforts.

A key component of the legislation is support for collecting and analyzing data to evaluate care and apply quality metrics. The legislation stipulates support for enhancing the data infra-

structure and for enhancing the aggregation and integration of data from multiple sources. It also stipulates in section 3101 that federally supported health care or public health programs must collect and report data on race, ethnicity, primary language, and disability at the smallest possible geographic level. It further stipulates that the secretary ensure that there are national standards for data management and interoperability.

The act does not specifically address data acquisition in cancer. However, when established, these national data acquisition standards could have major implications for cancer research. Oncology has the most robust existing data infrastructure of any chronic disease discipline through the system of federal, state, and private cancer registries. Many groups are working to improve the completeness, timeliness, efficiency of data collection, and utility of these oncology data systems through enhancing electronic data capture and linkage of administrative and care data. Should these provisions of the PPACA be implemented, they could foster and speed these efforts toward establishment of a more comprehensive cancer data system in the U.S.

### Follow-On Biologics

The PPACA provides a clear pathway for generic biological agents that could both protect the initial inventor with sufficient market exclusivity (12 years for the reference drug and 1 additional year for the first follow-on biologic) to incentivize new product development and also allow less expensive versions of costly large molecules to be brought to market. This is a necessary provision as biological drugs, unlike small-molecule drug entities, are not regulated under the Federal Food, Drug, and Cosmetics Act, but under the Public Health Service Act. The latter had not been amended to identify a pathway for the approval of generic forms of biological products, defined as “a virus, therapeutic serum, toxin, antitoxin, vaccine blood component, or derivative.” Thus, biologics were not addressed in the Hatch-Waxman Act of 1984 that gave birth to the generic drug industry.<sup>21–23</sup>

It should be noted that some studies indicate that the high cost of developing follow-on biologics may prevent these new drugs from seriously lowering health care costs to the degree generic, small-molecule drugs have.<sup>24</sup>

Additionally, the idea that these provisions will somehow short circuit the need to test generic biologics in rigorous clinical trials is naive. The complexity of potentially therapeutic macromolecules extracted from living systems and the likelihood that subtle chemical differences between the initial and follow-on biologics (e.g., posttranslational and epigenetic modifications like methylation) could have significant effects on activity and toxicity of generics. Oncologists will likely reserve use of these follow-on products until the generics have been demonstrated to possess equivalent clinical activity to the primary reference biologic.<sup>25</sup>

## DISCUSSION

The PPACA and any implications for cancer research must be viewed in the broader context of how it fits into the overall federal budget and the mushrooming federal deficit. The Congressional Budget Office scored PPACA as a means of reducing federal expenditures over the next 20 years based on specific projected cost savings in redundant treatment and administrative services. However, common sense indicates that the provision of health insurance for 32,000,000 more people inevitably could lead to greater, not reduced, spending. A critical overriding question is what federal programs will fall victim to budget cuts that seem inevitable. Budget-cutting pressures may well be

directed toward PPACA or provisions therein or on the traditional federal agencies that fund cancer research. The ultimate costs of the PPACA program implementation will certainly perturb overall health care expenditures and require some degree of rebalancing of priorities and potentially the priority given to cancer research. There is recent documentation of a vast difference in per capita Medicare expenses in otherwise similar cities<sup>26</sup> attributed to excessive variation in patterns in medical treatment ([www.dartmouthatlas.org](http://www.dartmouthatlas.org)). Credible estimates are that as much as half of what doctors do is either ineffective or not cost-effective.<sup>27</sup> Given this economic context, we view it unfortunate that PPACA did not embrace more explicit strategies for reduction of unnecessary utilization and expense in the American health care system.

Although we strongly support efforts to better translate promising new discoveries into trials, ensure that diverse populations are properly represented in trials, ensure access and coverage for clinical trials, learn more about patterns of care and efficacy through proposed CER initiatives, build comprehensive data systems, learn more about prevention of breast cancer in young women, and hasten the development of less costly versions of antineoplastic biologic agents, we also believe that there is great opportunity to better apply current medical knowledge at the bedside today. We have learned a great deal about cancer prevention and treatment in the past half century. The field of oncology has developed more comprehensive guidelines for cancer diagnosis and treatment than any other field of medicine. Given our current understanding of cancer, we know a great deal about what works best for patients. Beyond demonstration projects with Medical Homes and Accountable Care Organizations, we would like to have seen more emphasis on changing incentives and systems to encourage use of guidelines based on current evidence and systems to encourage reduction of care that we already know to be both ineffective and cost-ineffective.

Another concern is that PPACA lacks content in other areas that could aid cancer research. This includes amending the HIPAA law to allow data sharing for CER, incentivizing commercialization of academic discoveries, clarifying conflict of interest rules, and truly elucidating what the national cancer program is, what its strategic plan is, and who will direct it.

We are also concerned that projected shortages of physicians in oncology disciplines will constrain the available pool of clinician scientists to mount high-priority trials and deliver cancer care needed by a growing populace and some 32 million newly insured Americans.<sup>6,7</sup> The PPACA does not address the need for additional specialists, the increasingly imbalanced system for funding graduate medical training, or the need for a health workforce planning mechanism that is coupled with both the resources and the authority to effectively address both shortages and maldistribution of health workforce. However, we are somewhat encouraged that PPACA includes creation of a National Health Care Workforce Commission that will be charged with analyzing current shortages and recommending solutions (section 5101).

Although PPACA may well enhance our ability to conduct important comparative effectiveness studies, it is critical that we recognize that although such studies can supplement knowledge gained through formal clinical trials, it will not supplant the need for such trials. Although PPACA carries the promise of increasing access to clinical trials because of its important mandate for insurance carriers to provide coverage for standard care trial costs, we still need to address the urgent business of correcting the numerous deficiencies with the current clinical trials system. As was the case with the original Medicare legislation, PPACA will, in all likelihood, undergo numerous modifications over

ensuing years. It is critical that informed cancer experts be involved with those adjustments. We can ill afford to leave that responsibility just to those who crafted the original legislation.

Finally, we believe that there is a compelling need to develop a serious educational dialogue about health care with the American people. Going forward, we must avoid the use of language such as “death panels” and develop broad understanding that we are rationing health care now, but irrationally; as medical professionals, we have an obligation to contribute to a civil discourse on the value of CER and the need for acceptance of results of well-designed clinical studies by our professional colleagues and by the public. This kind of discussion has yet to take place.

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