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# 2015: A Target Date for Eliminating Suffering and Death Due to Cancer

**Reported by Mike Miller**
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*BenchMarks* talked with NCI Director Andrew C. von Eschenbach, M.D., about his recently announced challenge goal of eliminating suffering and death due to cancer by 2015. The following is a transcript of that discussion.

**Q: You have issued a 'challenge goal' to eliminate suffering and death due to cancer by 2015. Why this particular goal, and why now?**

I believe we are at what I call a strategic inflection in biology, which means a point of unprecedented growth in three key areas related to cancer research: knowledge, technology, and resources. The integration of growth in these three sectors provides an opportunity for exponential progress. To achieve this progress, we must set a clear direction and focus our efforts into a cohesive strategy.

The goal of eliminating suffering and death due to cancer provides this focus. It does not mean “curing” cancer but, rather, it means that we will eliminate many cancers and control others, so that people can live with -- not die from -- cancer. We can do this by 2015, but we must reach for it. We owe it to cancer patients around the world -- and their families -- to meet this challenge.

**Q: Why is this goal feasible?**

This is feasible because the intersection of exponential growth in biomedical research and the explosion of enabling technologies has resulted in a “new science” of oncology. This goal is also feasible because the fruits of cancer research since the signing of the National Cancer Act of 1971 have taught us a tremendous amount about cancer and brought us to a turning point.

We are now in the era of molecular oncology. We have more cancer researchers and more financial resources than ever before in the history of medical research. I believe we have an unprecedented opportunity to align our resources, our enabling technologies and our knowledge of cancer to achieve this goal.

And cancer research is not progressing in a vacuum. It contributes to, and benefits from, progress in all of the life sciences.

**Q: Why do you say our knowledge of cancer has expanded exponentially?**

To understand the impact of exponential growth, consider the question: "If you won the lottery, would you prefer to collect one million dollars up front or one penny on day one and then double it every day for just one month?" My advice to you is to take the doubling of the penny for one month. At the end of one week you only have 64 cents and at the end of 2 weeks only $82, but by day 27, you will have over $600,000 and by day 30 over $5 million. If pennies were knowledge, this would be the kind of growth we are witnessing in cancer research, and we are no longer in the first or second week of this process, so we can expect to continue to witness rapid expansion in our knowledge.

One strong indicator of our growth in knowledge is the number of published research papers on cancer. By the time of the signing of the National Cancer Act in 1971, there were about 130,000 research papers on cancer published, but today there are almost 1.5 million papers available.

More important than numbers of publications, however, is the profound new understanding that they have provided us with regard to the normal growth of multicellular organisms and what goes awry in the case of cancer.

We no longer see the cell as a mysterious "black box," but rather as a robust entity bombarded daily at its surface by hormonal and chemical signals, signals from neighboring cells, and nutrients. Our knowledge of intracellular signaling pathways has grown dramatically. We also know that to remain alive and normal, an organism must decode, filter, and respond properly to many molecular conversations, and we continue to learn about normal cellular pathways.

Today we understand cancer as both a genetic disease and a cell signaling failure. Genes that control orderly replication become damaged, allowing the cells to reproduce without restraint. A single cell's progress from normal, to cancer, to metastasis appears to involve a series of interactive processes, each controlled by a gene or set of genes. These altered genes produce defective protein signals, which are, in turn, mishandled by the cell. This understanding of the biology of cancer is enabling us to design interventions to preempt the cancer's progression to uncontrolled growth and spread that is the cause of suffering and death.

**Q: What are some examples of exponential growth in enabling technologies?**

It is instructive to look back at the progress technology has enabled in the past few decades. Shortly after Watson and Crick's discovery in 1953 of the structure of DNA (deoxyribonucleic acid), the 1960s ushered in electron microscopy. Its 100-fold increased magnification enabled researchers to see DNA inside the tiny viruses called phages that infect bacteria. By the end of the decade, the enzyme polymerase, used by these phages to copy DNA, was known. Then, in the

1970s, phages were combined with enzymes like polymerase and ligase to develop technology for replicating DNA in a test tube. This, in turn, enabled development of systems to study the regulation of DNA replication.

Technology in the 1980s emerged from basic research's earlier discoveries of restriction enzymes and reverse transcriptase. Biochemical systems were created that could slice, dice, insert, delete, and mass produce sections of DNA. This recombinant DNA technology enabled bacteria to become factories for the mass production of gene fragments as well as entire genes and their corresponding proteins.

With the discovery of PCR (polymerase chain reaction) and automated gene sequencing in the 1990s, progress in gene-protein discovery accelerated with unprecedented speed. Gene hunts that used to take 10 years to complete could be completed in two to three years by the 1990s. Today, these hunts can be done in a matter of hours or days with the completion of the human genome sequence.

This century finds technology such as gene and protein microarrays, high-throughput assays, robotics, high-resolution NMR (Nuclear Magnetic Resonance), functional imaging, artificial intelligence, supercomputing and, more recently, nanotechnology and iRNAs (interference RNAs), all at the service of today's researchers.

So what are we doing with all these technologies? Such sophisticated technology is being applied to better understand how genes and proteins interact in normal and cancerous cellular networks. These technologies, coupled with new disciplines such as genomics and proteomics, are improving our ability to predict cancer risk and to detect and diagnose cancer earlier. Artificial intelligence and supercomputing already have been harnessed successfully to analyze proteomic patterns for signatures of early-stage ovarian cancer.

New technologies are also making a huge difference in new drug discovery. High through-put robotic screens, combinatorial chemistry, and new probes for functional imaging are changing how molecular targets are identified and validated, and even how new interventions are designed. Also, supercomputing enables bioinformatics to link the work of researchers across disciplines, so that interdisciplinary teams of scientists can rapidly and effectively share information, insights, and accrual onto clinical trials.

These enabling technologies are creating a classic 'chain reaction,' not at all unlike what the world witnessed when scientists first discovered the secrets of the atom. Scientific discovery is fueling further scientific discovery at an ever increasing rate of progress. This explains the exponential trajectory of our progress.

**Q: How has the biomedical revolution changed our understanding of cancer?**

We are able to understand that cancer is a disease process. It has a beginning and a number of further steps that it must achieve if it is to become a lethal threat to a person. We are increasingly able to describe cancer initiation and progression in terms of interactive pathways and processes that lead to cancer deaths. Cancer must stop responding to anti-growth signals from its neighbors, supply its own growth signals, evade self-destruction even though it carries genetic errors, recruit its own blood supply, grow indefinitely, then finally spread and invade other tissues and organs. Only then does it become lethal.

We are now dissecting cancer from a genetic, molecular, and cellular perspective. This is teaching us about the collective processes required for cancer progression and metastasis to occur, which will help us preempt the process by slowing, delaying, or stopping it. The bottom line is that we now know that cancer and its progression are vulnerable.

**Q: What strategy will NCI employ to reach the 2015 goal and how will it work?**

We will focus our efforts and accelerate our progress with what I call the "seamless three-D approach" to cancer research -- the three Ds being discovery, development, and delivery.

Discovery is the process of generating new information about fundamental cancer processes at the genetic, molecular, cellular, person, and population levels. This research allows us to identify the mechanisms responsible for the initiation and progression of cancer in the cell and in the patient.

Development is the process of creating and evaluating tools and interventions that are of value in detecting, diagnosing, predicting, treating, and preventing cancer.

Delivery involves promoting and facilitating the application of cancer interventions to all people who need them. NCI does this in a research context in which monitoring the application yields not only information on effectiveness, but insights into the human biology of cancer and its interaction with the patient. This requires the use of research, technology, training, communication, and education.

The three Ds are major components of our portfolio at NCI, not a strategy *per se*. Rather, our overarching strategy is to create a greater degree of seamlessness between these three components than has existed in the past. This enhanced seamlessness will dramatically accelerate the pace by which the fruits of discovery are harvested for the benefit of cancer patients and the public at large.

This strategy continues NCI's historical emphasis on investigator-initiated basic research as the engine that drives the entire biomedical research enterprise. We are absolutely committed to that course. The "seamless three-D" strategy also builds on this strength by speeding translation of investigator-initiated discovery into the development of new interventions and by accelerating the rate at which proven interventions are put into widespread clinical and public health practice.

Beyond reducing the lag time from bench to bedside, the strategy will also offer important dividends to the basic research community. Investing in initiatives that create greater seamlessness between the three Ds will yield new tools and new platforms for collaboration that will enable members of the basic research community to test their ideas quickly and move worthy science forward faster and better than ever before.

Implementation of this strategy is a work in progress, and will undoubtedly be revised continuously until the challenge goal has been accomplished. One example of the strategy, however, is our current effort to bridge the gap that sometimes exists between development and delivery by forming an historic partnership with the FDA to accelerate approval of drugs and devices. This partnership is emblematic of our new approach.

**Q. What other initiatives is NCI putting in place to meet this goal?**

Along with several key ongoing initiatives, such as molecular imaging and proteomics, we are developing new initiatives and priorities in seven key areas: molecular epidemiology; integrative cancer biology; strategic development of cancer interventions, including the FDA partnership which I previously mentioned; early detection, prevention and prediction; an integrated clinical trials system; overcoming health disparities; and bioinformatics (see article below).

We will adapt and refine these as we go, but the basic strategy in all of these initiatives is for NCI to use its resources to remove barriers that currently inhibit progress broadly across the discovery-development-delivery continuum. Whether re-engineering the clinical trials system to safely accelerate progress of new interventions through the pipeline, or using bioinformatics to link people and data together, or partnering with the FDA, we have an opportunity to accelerate progress throughout the field of cancer research by eliminating the bottlenecks. We think of this as creating an "enabling culture" that will accelerate progress both within and between the discovery, development, and delivery components of our portfolio.

**Q: What is bioinformatics, and why do you believe it holds promise?**

Bioinformatics is a discipline that uses information technology to create tools needed to collect, share, and analyze biomedical data. With the surge in the amount of biomedical data that we are now collecting, the ability to share and

analyze this data efficiently and effectively is key to making rapid progress against cancer. For example, in a single experiment, an investigator can produce thousands of pieces of data about genes or proteins expressed in a particular tumor. These parts and pieces of research data are often disconnected databases that are difficult for colleagues to access. Similarly, there is often a data disconnect between clinical trials on the very same agent.

We are working to integrate diverse databases and tools, enabling data sharing across the broadest research community possible, encouraging collaboration and multi-disciplinary research, and ultimately speeding delivery of an end product to the public. Our bioinformatics initiative -- by enhancing data sharing -- will go a long way toward creating that enabling culture I spoke of a moment ago.

**Q: What drugs are in the pipeline that might help accelerate the goal?**

At the end of 2002, there were 100 new cancer drugs in the Phase III stage of clinical trials testing. But given that only a handful of drugs receive FDA (Food and Drug Administration) approval every year, it is obvious we need to do what we can to improve the process. That is why we're working jointly with the FDA on building a partnership in several areas of cancer research. The NCI-FDA proteomics program already has developed a promising screening tool for ovarian cancer and more recently has developed a technique to evaluate drug efficacy.

But let's be clear. There is not going to be one single intervention that cures all cancers. Instead, we are looking for combinations of agents or therapies that work together to shut down cancer at vulnerable points in the progression process.

**Q: What will be done to reduce the suffering of cancer patients?**

Allow me to answer this question at two different levels. First, we have renewed our focus on symptom management and palliative care. Our Community Clinical Oncology Program (CCOP) supports some 60 clinical trials investigating such symptoms as cognitive dysfunction, fatigue, hot flashes, pain, and nausea and vomiting. But much remains to be done in the palliative care field. We need to develop less debilitating treatments, and we are exploring more effective ways to support patients and their families during treatment and in the post-treatment phase.

Second, and perhaps more importantly, by slowing the progression of cancer and turning it into a manageable disease, the burden of cancer, and the suffering that it causes, will be reduced. When we can prevent cancer from progressing to its later and more virulent stages, we likewise will prevent much of the suffering that accompanies those later stages.

**Q: Could we completely eliminate cancer by 2015?**

Given the complexity of the myriad diseases that we call cancer, it is unlikely that we will progress that far, that fast. But the point I wish to make is that a cure isn't necessary to eliminate the worst aspects of the cancer experience -- suffering and premature death. I do believe that by 2015, we can both eliminate some cancers as well as bring other cancers under control as chronic, manageable diseases, much like people today live with diabetes and heart disease. And one day, we may even eliminate cancer, but not in the foreseeable future. What is foreseeable is to expand our ability to preempt the suffering and death caused by cancer. That's why we have issued this challenge goal -- to focus ourselves on reducing the burden of cancer in the foreseeable future.

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**NCI Initiatives Take Aim at 2015**

*Reported by Sarah Schroeder*

A focus on the following initiatives will move the work of NCI through the process of discovery, development, and delivery toward the goal of eliminating suffering and death from cancer by 2015.

**Molecular Epidemiology: Understanding the Causes of Cancer**
NCI will expand the understanding of cancer causes and progression by promoting relationships between basic, clinical, and population sciences. This initiative will develop strategies and technologies that promote a multi-disciplinary approach to identifying risk factors and underlying mechanisms, studying the interaction of genetic and environmental determinants of cancer risk, and shaping the design of preventive interventions.

**Integrative Cancer Biology**
This initiative aims to understand cancer as a complex system and involves developing bioinformatics and computational biology as equal partners in cancer biology. It will build on our understanding of the molecular signatures of the cancer cell by facilitating research in the areas of intracellular networks, cell-cell interactions, tumor microenvironment, and macroenvironment.

**Strategic Development of Cancer Interventions**
The NCI will optimize the drug development process by validating new cancer targets for prevention, detection, and treatment. This will involve a seamless continuum and a working partnership which includes the NCI, academic medical centers, the private sector, and the FDA.

**Early Detection, Prevention, Prediction**
Trans-disciplinary research units will address obesity, fitness, and cancer risk. In addition, clinical trials will be aimed at the prevention of breast, colorectal, and prostate cancer as well as lung cancer in former smokers. Through work with FDA, NCI will evaluate surrogate biomarker endpoints (markers of clinical benefit) on a case-by-case basis, leading to consideration of how best to use biomarkers to add efficiency to clinical trial design. The drug approval process also will be reviewed to assure an evidence-based, time-saving process.

**Integrated Clinical Trials System**
By 2015, we will have in place an integrated clinical trials system that addresses a wide range of clinically relevant questions. This system will produce an array of effective treatment interventions and screening and prevention strategies. We will be able to evaluate a number of factors that influence outcome in diverse groups of cancer patients, thereby providing a new understanding of apparent racial and ethnic disparities. The system will be widely accessible to cancer patients and populations at risk from cancer and will include a broad investigator community.

**Overcoming Health Disparities**
Medically underserved populations suffer from a disconnect between discovery and delivery that may contribute to health disparities. NCI will strive to bridge this gap through public education, targeted research to define who is at risk and the causes of disparities, and shaping health policy for equal access to cancer diagnosis and treatment.

**Bioinformatics**
Bioinformatics will integrate data from multiple fields of research to help reach the 2015 goal. It makes information accessible broadly throughout the cancer research community, and beyond to allied disciplines in cancer research. As part of this initiative, NCI will undertake several tasks: establishing a biomedical informatics infrastructure in partnership with the cancer research community; closing the circle in bench-to-bedside research; empowering participants in clinical research; and establishing a network of information technology partners.

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