



An Action Plan to Save Lives

ACKNOWLEDGEMENTS

We wish to thank the following, who contributed time and ideas to this project:

- Peter Arno, Ph.D., Professor, Department of Epidemiology & Population Health, Albert Einstein College of Medicine
- David Baltimore, Ph.D., President, California Institute of Technology, and Nobel Laureate, Medicine, 1975
- Gary Becker, Ph.D., Professor of Economics and Sociology, University of Chicago, and Nobel Laureate, Economic Sciences, 1992
- Edward Benz, M.D., President, Dana-Farber Cancer Institute
- Samuel Broder, M.D., Chief Medical Officer, Celera Genomics, and former Director, National Cancer Institute
- Arthur Caplan, Ph.D., Director, Center for Bioethics, University of Pennsylvania
- Stephen Carter, M.D., Consultant, and former head of worldwide clinical development, Bristol-Myers Squibb
- Donald Coffey, Ph.D., Professor of Urology, Oncology and Pharmacology and Molecular Sciences, Johns Hopkins University School of Medicine
- David Cutler, Ph.D., Professor of Economics, Kennedy School of Government, Harvard University
- Michael Davis, Professor of Law, Cleveland-Marshall College of Law, Cleveland State University
- Robert Fogel, Ph.D., Professor of American Institutions, University of Chicago, Graduate School of Business, and Nobel Laureate, Economic Sciences, 1993
- Stuart Holden, M.D., Medical Director, CaP CURE, and Medical Director, Louis Warschaw Prostate Cancer Center, Cedars-Sinai Medical Center
- Leroy Hood, M.D., Ph.D., President, Institute for Systems Biology
- Jeff Leiden, M.D., Ph.D., President and Chief Operating Officer, Pharmaceutical Products Group, Abbott Laboratories
- Christopher Logothetis, M.D., Chair, Genitourinary Medical Oncology, M.D. Anderson Cancer Center
- Mark McClellan, M.D., Ph.D., Commissioner, Food and Drug Administration
- Richard Merkin, M.D., Chief Executive Officer, Heritage Provider Network
- Leslie Michelson, Chief Executive Officer and President, CaP CURE
- Michael Milken, Chairman, Milken Institute
- Joseph Newhouse, Ph.D., Professor of Health Policy and Government, Kennedy School of Government, Harvard University
- Perry Nisen, M.D., Divisional Vice President, Oncology Drug Development, Abbott Laboratories
- Uwe Reinhardt, Ph.D., Professor of Public Policy, Woodrow Wilson School, Princeton University
- Judith Rodin, Ph.D., President, University of Pennsylvania
- Peter Scardino, M.D., Chairman, Department of Urology, Memorial Sloan-Kettering Cancer Center
- Howard Soule, Ph.D., Executive Vice President and Chief Science Officer, CaP CURE
- Kip Viscusi, Ph.D., Professor of Law and Economics, Harvard University
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EXECUTIVE SUMMARY

The Center for Accelerating Medical Solutions (CAMS) is dedicated to shortening the time it takes to find cures, improved treatments and effective prevention of the most deadly and debilitating diseases.

The Center is non-profit, non-partisan and independent of interest groups. As outlined in this report, CAMS will not conduct scientific or clinical medical research. Rather, we will mobilize economists, medical researchers, clinicians, biologists, ethicists, genomics specialists, chemists, physicists, mathematicians, computer scientists, legislative analysts and others to evaluate the entire research process from beginning to end and then publish concrete policy recommendations and provide leadership for their implementation.

The Center's scholars will examine all possibilities and may take stands, consistent with CAMS' mission, on contentious issues. Examples of issues that they might study include:

- Will extending patent lives accelerate science?
- How can the regulatory process be streamlined while protecting patients?
- How can we improve coordination of medical research among academic institutions, for-profit corporations and government agencies?
- The overwhelming majority of the global costs for prescription drugs, medical research and drug development are paid for in the U.S. How can the

international community be encouraged to bear more of this burden?

- What tax policies can most effectively and appropriately stimulate research?
- What are the most effective incentives to encourage participation in clinical trials?
- How can we expand tissue banks and improve both data collection and patient records?
- Should the drug-approval process be modified to require evidence of safety, but not efficacy?
- Would incentives for scientific and medical graduates to pursue research careers lead to faster breakthroughs?
- Would greater access to medical files – with patient approval – accelerate the research process?
- Do we need more interdisciplinary academic programs combining such areas as medicine, engineering, biology and computer science?

We recognize and appreciate the remarkable achievements that medical research has produced in recent years. Yet, despite these advances, cardiovascular disease, cancer, diabetes and other illnesses continue to take a staggering toll in treatment costs, lost productivity, suffering and deaths. More than half-a-million Americans die from cancer each year. More than one million will suffer heart attacks this year, while strokes will hit 600,000. Millions more suffer from debilitating disorders such as Alzheimer's disease and multiple sclerosis.

Why haven't we made more progress against a broad range of diseases? Why, for example, 32 years after the launch of the war on cancer, do we still not have more effective treatments for a disease that kills more than six million people

worldwide every year? Why, given the astonishing improvements in computer processing and other technologies, are too many people suffering from a poor quality of life as a result of intractable illnesses?

The Center for Accelerating Medical Solutions intends to answer those questions – and challenge the notion that the complex machinery driving breakthroughs in medicine must advance at a stately pace. We believe that a rigorous and thorough systems analysis of the entire research process will point to new efficiencies that can accelerate scientific discovery and suggest changes in misplaced priorities, sometimes inefficient regulations, and conflicting incentives that slow progress.

Part of the problem is priorities. We spend only one dollar seeking cures for every \$25 spent on treatment. But the availability of money for research is not the only problem. Indeed, there is ample reason to believe that our inability to create and sustain incentives to keep modern medical technology moving forward as swiftly as possible will doom millions of people who are alive today to premature disability and death.

As Gary Becker, the Nobel prize-winning economist (and CAMS board member) puts it: “The system is riddled with inefficiencies, raising the costs of life-saving treatment and delaying access to desperately ill patients.”

Why the urgency? Because even a year’s acceleration in medical solutions would make a huge difference. For example, finding a breast-cancer cure just one

year earlier would not only prevent half a million deaths worldwide, but save millions of women from painful and disfiguring treatments. Tens of millions of others will die from heart disease or suffer from Alzheimer's, stroke or diabetes. One in two families will be touched by cancer alone unless there are breakthroughs. We believe it's possible to change those kinds of statistics and in so doing, give millions of people longer, fuller lives while strengthening our economy.

With our population aging – the 76 million members of the baby-boom generation are turning 50 at the rate of one every seven seconds – those afflicted by these diseases, and the costs to treat them, are expected to rise dramatically in the decades ahead.

For the first time in history, success in the race to find cures may save those already afflicted as well as those who will be afflicted in the future. The goal of the Center for Accelerating Medical Solutions is to save them sooner.

I. INTRODUCTION

Dedicated efforts by government agencies, academic researchers, pharmaceutical and biotechnology companies, physicians running clinical trials, patient advocate groups, foundations and other charities have yielded some remarkable achievements in recent years. Treatments for many serious diseases have been improved and mortality has been reduced in a number of cases. For example, compared to 30 years ago, far fewer heart attack victims die in the first days and weeks after being stricken.

Thanks to medical research, up to 70 percent of all children with cancer can now be cured. Thanks to the discovery of a “clot-busting” drug, stroke victims now have a 30-percent greater chance to recover if the drug is administered within three hours of the initial stroke. And thanks to better diagnostic techniques and treatments for breast cancer, the lives of many mothers, sisters and daughters have been saved.

The biomedical revolution promises to extend human life spans while relieving human suffering.

Yet, despite a flood of scientific advances, cancer, cardiovascular disease, diabetes and other illnesses continue to take a staggering toll in treatment costs, lost productivity, suffering and deaths.

More than 560,000 Americans die from cancer each year. Some 1.1 million Americans will have heart attacks in 2002, while some 600,000 will suffer a stroke.

Over 17 million have diabetes and another million are diagnosed each year – many of them young adults. Millions more suffer from debilitating disorders such as AIDS, muscular dystrophy, Alzheimer’s disease and multiple sclerosis.

Meanwhile, health-care spending continues to rise. In 2001, it increased faster than in any year since 1991 in the U.S. – to \$1.4 trillion, or 14.1 percent of GDP. That’s one-seventh of the national economy. Translation: \$5,035 spent, on average, by every American.

Why haven’t we made more progress against a broad range of diseases? Why, for example, 32 years after President Nixon declared war on cancer, do we still not have a cure for the disease that kills more than 1,500 Americans *every day*? Why hasn’t the amazing advance of computer power since the invention of the microchip done more to accelerate better treatments and cures?

The Center for Accelerating Medical Solutions intends to answer those questions – and challenge the notion that the complex machinery driving breakthroughs in medicine must advance at a stately pace.

The goal of the Center is to speed things up – to shorten the path to cures, better treatments and effective prevention of our most deadly and disabling diseases – to save lives today. Enough is enough: it’s time to get the job done.

We are certain that a comprehensive systems approach to evaluating the research process at every stage can create new efficiencies and breakthroughs. We believe more can be done to focus and coordinate medical research efforts – and

that a host of new technologies can provide cures for a variety of deadly diseases quickly enough to save millions already diagnosed.

By supporting the Center's efforts, you have an opportunity to be at the creation, to turn the abstract promise of a new era in medicine into a very tangible reality.

II. HOW WE'LL PUT YOUR DOLLARS TO WORK

The Center for Accelerating Medical Solutions plans to mobilize a variety of disciplines – economics, medicine, biology, ethics, genomics, chemistry, physics, law, mathematics, engineering, computer science, journalism, politics – to understand what can be done to win the multi-fronted war on deadly diseases. But it will be more than a think tank: we'll offer concrete proposals and encourage government, non-profits and private industry to adopt them. Our goal, in other words, is to *accelerate medical solutions*.

In some cases, the modifications may require sweeping changes in the way medical research is conducted and regulated. In other cases, we'll focus on particular opportunities, such as the acceleration of specific clinical trials that promise radical new therapies. In either event, we intend to produce actionable recommendations quickly.

Why the urgency? Think about what a difference a year's acceleration in finding medical solutions would make in people's lives. Finding a cure for, say, type

2 diabetes just one year sooner could save hundreds of thousands from blindness, amputation of limbs or premature death. Accelerating a cure for breast cancer by just one year would not only prevent some half a million deaths worldwide, but it would save millions of women from painful and disfiguring treatments.

Why, in this most advanced economy on earth, at a time when the perils of killer diseases are all too obvious, is the effort to accelerate medical solutions necessary? The explosive development of science and engineering in the past few decades has produced a house of bureaucracy – and a Tower of Babel – that has not been comprehensively analyzed to identify redundancies, change structures that have outlived their utility and minimize administrative burdens.

It's not that progress has ground to a halt. Advancing medical science continues to amaze us. But there has never been a systematic effort to beat back the tangle of regulation, misplaced priorities and conflicting incentives that slow progress in an era in which the cure for so many diseases is tantalizingly close.

The funds that the Center will raise will be used neither for medical research nor to reform the delivery of health care. While those tasks are vital, others are working hard on them. What the Center will do is devise ways to increase the efficiency of the sprawling apparatus dedicated to advancing medical solutions. Our goal is to ensure that this crucial sector of our society is functioning as effectively as possible.

III. THE GOOD NEWS

Stories of breakthroughs in heretofore-terminal illnesses offer much reason for hope. Lance Armstrong, the world's greatest cyclist, would probably have died years ago, were it not for advances in medical technology. Thanks to a combination of surgery and chemotherapy, Armstrong was cured of testicular cancer that had already metastasized to his brain – and he went on to win four straight Tour de France races, including his most recent victory in 2002.

The most common childhood leukemia was a virtual death sentence in the 1960s, with just 5 percent of patients living five years. Today, most are cured. AIDS decimated patients in the 1980s and early-'90s, including Rock Hudson, Rudolf Nureyev, Arthur Ashe and Ryan White, who lived brief, agonizing lives after diagnosis. Today, hundreds of thousands of sufferers, like Magic Johnson, who have access to advanced drugs, are keeping the virus at bay.

Less dramatic – but far more significant in terms of lives extended – combinations of drugs, surgery and research-driven changes in living habits have reduced mortality and morbidity from cardiovascular disease. While the incidence of heart attacks remained roughly the same from 1975 to 1995, the percentage of victims who died within 30 days fell from 27 percent to 17 percent. Life expectancy reached a record high in the U.S. of nearly 77 years in 2000. Indeed, much of the four-year increase in average life expectancy in the United States since 1975 – and the parallel delay of disabling morbidity to older ages – can be attributed to success

in coping with heart disease and preventing strokes. America's infant mortality rate reached a record low of 6.9 deaths per 1,000 live births in 2000, and infectious disease rates have declined.

What makes many of these and future breakthroughs possible are tremendous advancements in technology. By one estimate, everything in computing – from memory and information processing speed to reduction in size – has doubled every 18 months for the last 30 years. Today, thousands of PCs, connected through the Internet, are solving computational problems that were far beyond the conceptual horizons of 1980s-style mainframe supercomputers. Exploiting computer databasing techniques that did not exist just five years ago, scientists can create and analyze libraries of cancer genes that may well hold the key to determining what differentiates normal cells from malignant ones. No longer do researchers need to study just one gene or one protein at a time. Technology makes it possible to look at tens of thousands of genes simultaneously and find out how they differ.

In addition, computer technology may lead to improved success rates, shorter development times and lower R&D costs for new drugs. Using on-demand computing in which thousands of computers and applications are joined together, IBM says pharmaceutical companies will be able to cut the time it takes to launch a new drug from more than 10 years to as few as three, while reducing development

costs from as much as \$800 million to \$200 million. Other computer companies are pursuing related initiatives.

We need to make similar progress in understanding the nature of deadly diseases and transforming basic science into technology that every clinician can use.

IV. THE CHALLENGES AHEAD

As welcome as statistics about lives saved from disease are, and as heartwarming as the very human stories behind them, they conceal a bitter irony.

Medical technology is advancing at an incredible pace. The mapping of the human genome promises a cornucopia of treatments. Nanotechnology and advanced materials science offer the prospect of physical repairs to otherwise inaccessible organs. Molecular biology is reaching ever deeper into the mysteries of life that drive the aging process. Cheap, high-speed computers, linked through the Internet, offer computational solutions for seemingly intractable problems.

But the practical, often mundane, building blocks needed for transforming ideas into medical breakthroughs lag far behind.

Part of the problem is money. For example, the federal investment in finding cures for cancer is \$4 billion annually – less than .04 percent of our gross domestic product – or about \$15 for every American. Meanwhile, our nation spends well over \$100 billion every year – much of it by the federal government – for cancer *care*.

While industry, government and non-profits in America spent a total of \$56 billion on health care research in 1999 (the latest year with comprehensive figures), there is good reason to believe that the returns from additional strategic investments would be huge in terms of speeding development of lifesaving treatments, reducing suffering, extending life spans and enhancing productivity.

But the availability of money for research is not the only problem. Indeed, there is ample reason to believe that our inability to create and sustain incentives to keep the machinery of modern medical technology moving at maximum pace will doom millions of people who are alive today to premature disability and death.

As Gary Becker, the Nobel Prize-winning economist, puts it: “The system is riddled with inefficiencies, raising the costs of life-saving treatment and delaying access to desperately ill patients.”

Dr. Christopher Logothetis, an oncologist at the M.D. Anderson Cancer Center in Houston, uses equally blunt language: “The medical research community is now probably more bureaucratic than the Eastern Bloc ever was.”

To understand how this could be, think for a moment about an entirely different enterprise – the petroleum industry. Gasoline doesn't come out of the pump at half the price of bottled water by magic. Likely oil deposits, thousands of feet below ground must be identified using complex seismic technologies. Legal rights to exploit deposits must be acquired and environmental issues resolved. Capital must be raised to drill for oil that may not be there in commercial quantities.

Once oil is found, a transportation infrastructure must be created to get the crude from oil field (or deepwater platform) to refinery. Then the petroleum must be refined, and a dozen different products moved to markets by pipeline, ship, rail and truck, and sold to hundreds of companies that make petrochemicals and tens of thousands of distributors who sell everything from high-octane gasoline for luxury cars to kerosene for B-2 bombers.

Complex? Of course. But efficient enough to bring the cost of petroleum-based fuels within reach of billions of consumers and to make petrochemical-based products ubiquitous.

Now compare the petroleum industry to the still more complex process of generating new medical technologies. Ideas – that most intangible of raw materials – must wend their way from seminar to computer to laboratory to clinical trial to commercial production to hospital to patient, with each stage being second-guessed by regulators, university officials, liability lawyers, corporate managers and physicians with diverse, often-conflicting incentives.

Consider one glaring example. Dr. Stephen Carter, the former head of worldwide clinical development at Bristol-Myers Squibb, and the driving force behind the introduction of the powerful anticancer drug Taxol, notes that no organization in the world – not the National Institutes of Health, not the National Cancer Institute, not the FDA – is keeping track of all of the drugs under development worldwide. Coordinating this effort and knowing what everyone is

working on would undoubtedly accelerate science, he says. He is careful to distinguish between coordination and control, however.

David Baltimore, president of the California Institute of Technology and a winner of the Nobel Prize in medicine, points to the way the system drives ambitious scientists away from important areas of medical development. Science rewards big discoveries in basic research, he notes. At the other end of the pipeline, there are enormous amounts of money to be made in creating new treatments. But in the middle, there is a hole.

“We just don’t attract enough talented people to do translational research,” he laments – far less glamorous work, but equally important to the advancement of medicine.

There are echoes of this problem in the concerns of Dr. Donald Coffey, professor of Urology, Oncology and Pharmacology and Molecular Sciences at Johns Hopkins University School of Medicine. Some of the most productive medical researchers are what he calls “translational” researchers – physicians who spend time in both the lab and hospital wards, and use their hands-on knowledge to generate many of the real breakthroughs in medicine. But the drive to cut overhead in teaching hospitals has enormously increased their workload.

“These doctors have incredible pressures on them,” he argues. “They no longer have time to do their research.”

Professor Becker points to yet another problem. Before 1962, drug companies were obliged to show only that new compounds were safe. Now, they face more stringent controls on safety and, more significant in this context, they must prove that the drugs are effective in treating specific conditions. While there have been modest attempts to streamline the system, the average time for drug development from conception to market has increased from eight years in 1960 to as much as 14 years today.

Even in the best of circumstances, most ideas for new treatments never pan out. And new drugs can cost up to \$800 million to develop. Meanwhile, external factors ranging from stock market volatility to government budget crunches can disrupt the process.

Another issue raised by Dr. Peter Scardino, head of urology at Memorial Sloan-Kettering Cancer Center in New York, is physician resistance to change. He notes, for example, that although many surgical techniques were first developed in the U.S., the latest minimally invasive techniques have developed faster in Europe. “There's an arrogance that comes with success,” says Dr. Scardino. “When surgeons have developed a certain way and are good at it, they don't want to change.” At Sloan-Kettering, his colleague, Dr. Bertrand Guillonnet, a surgeon trained in France, performs minimally invasive laparoscopic prostatectomies that involve far less pain, trauma, cost, hospital days and recovery time than traditional open prostatectomies. Yet most urologic surgeons in the U.S. still focus on the old

method because there have not been enough controlled studies to prove the superiority of newer techniques. Similar resistance to change can be seen in kidney transplants, heart bypass procedures and other surgery. Minimally invasive techniques are being used increasingly, but the rate of change is slow.

V. ISSUES TO EXAMINE

Some of the issues the Center will examine are straightforward: Do the returns on investment in medical research justify greater financial commitment? Some are elusive: How can one reconcile individual researchers' incentives for recognition with the need for teamwork in complex, multifaceted research projects? Some are ethical: When is it acceptable to risk some lives to save others? And, of course, some of the issues simply can't be identified without a long, hard look at the complex mix of factors driving the system.

Here we discuss 10 issues that bear examination by experts in science, medicine, government, economics, law and ethics.

1. The Rate of Return on Research

In 1999, the federal government spent almost \$19 billion on medical research, up from \$13 billion in 1995. Private industry invested almost \$35 billion and non-profits in America invested another \$3 billion. These figures have almost

certainly gone up in the interim. What reason, then, is there to believe that we are investing too little in research?

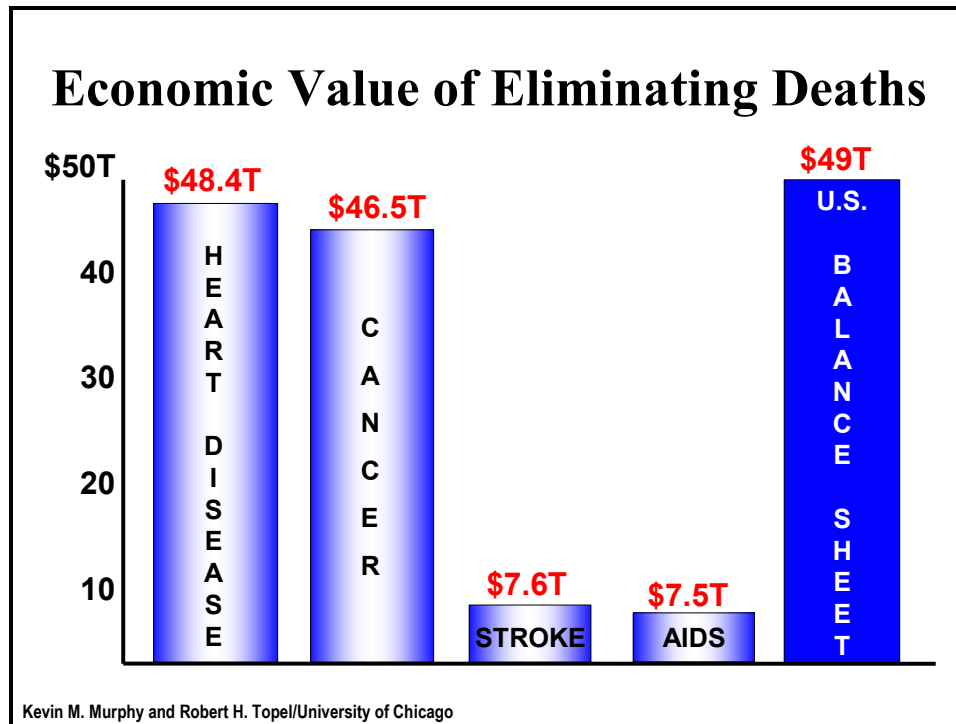
One crude measure is the proportion of National Institutes of Health-approved projects that are actually funded. Dr. Coffey of Johns Hopkins points out that this number has slipped from 40 percent in the early 1970s to just 25 percent today.

Economists view the problem from another perspective, estimating the potential return on more medical research in terms of the value of lives saved. To get from here to there, one must first assign a value to life – a seemingly intractable problem. But economists argue that people implicitly place a finite value on their own lives every day by making choices between buying safety devices and other goods or services – say, by deciding whether to buy carbon monoxide detectors for their houses.

Kip Viscusi, an economist at Harvard University, notes that this indirect method of valuing life, using everything from wage premiums in dangerous occupations to decisions on whether to speed on the highway, generates a surprisingly narrow range of estimates. On average, Americans seem to value their lives between \$3 million and \$7 million.

A number of well-respected economists – notably Kevin Murphy and Robert Topel of the University of Chicago and the Milken Institute – have thus been able to compare the value of life-extending research to the cost. Professors

Murphy and Topel estimate that advances in medicine added \$2.8 trillion per year to GDP – that’s right, *trillion* – between 1970 and 1990. (See figure below for the value of curing selected diseases. The last column, “U.S. Balance Sheet,” refers to all personal financial assets.)



Hence, the likely returns on investment in medical knowledge are so large that vast increases in research budgets would be justified. Indeed, the justifiable increases would probably be so large that the current battles over the division of the research pie – AIDS vs. cancer, etc. – would be moot.

Convincing government, insurance companies or universities to pump more money into the system – if, in fact, that is the answer – will not be easy, however. Researchers chafe at the bean-counter mentality in the managed care industry that

looks with deep suspicion at every technological advance because it may add to treatment costs.

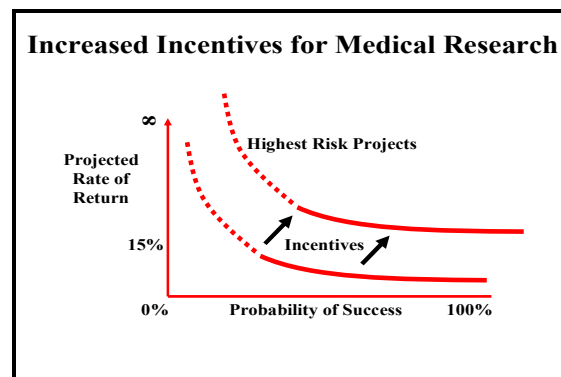
In fact, the jury is still out on whether such advances will increase the overall cost of health care or decrease it. Drugs, which now comprise only one-tenth of the American medical bill, can often substitute for more expensive surgery or for the long-term care of the chronically ill – and may thereby generate net savings. And as Robert Fogel, the Nobel Prize-winning economist, points out, even sharp increases in overall health care costs may simply be evidence of an efficient reallocation of resources in a rich, aging society.

“Public policy should not be aimed at suppressing the demand for health care,” he insists. “Expenditures on health care are driven by demand, which is spurred by income and by advances in biotechnology that make health interventions increasingly more effective.”

His comments parallel those of economists David Cutler and Mark McClellan (now FDA commissioner), who wrote in 2001: “The benefits from just lower infant mortality and better treatment of heart attacks have been sufficiently great that they alone are about equal to the entire cost increase for medical care over time.”

2. Funding High-Risk Research

As any schoolchild knows, the voyages of Christopher Columbus were financed by the Spanish throne. Before stock markets were established to spread risk broadly, governments were typically the source of funds for projects with uncertain outcomes. Today, government's cost of capital remains lower than it is to private industry. And the returns from high-risk medical research often far exceed the gains that could be captured by a patent holder. Hence, we would expect under-investment in high-risk research by the private sector. One way or another, then, it is widely understood that it should be government's job to move the risk-return tradeoff into territory that makes the potential payoff from blue-sky efforts attractive to private investors.



The great inefficiency – indeed, the tragedy – is that government agencies, with mandates to fund basic research, are also inclined to tilt toward lower-risk investments. While government decision-makers are not under the same pressure to generate tangible results as their private counterparts, they are prone to turning to

older, established researchers for direction, and new ideas often get sidetracked in the process.

“A lot of the best investigators use their National Institutes of Health funding to keep their labs going,” explains Judith Rodin, President of the University of Pennsylvania, “and then look for other money to do the things that are more interesting and ambitious.”

Private philanthropy can cover part of the funding shortage for high-risk research – for example, it is a primary mission of CaP CURE, The Prostate Cancer Foundation. But philanthropy can cover only a small part of the shortage. The sums involved demand direct government funding or heavy subsidies for private, for-profit investment. It would be foolish to think that it is easy to fine-tune incentives with respect to risk. But the potential payoff from improving the mix of research projects could be large.

The Center for Accelerating Medical Solutions will evaluate the system of incentives that encourage or discourage researchers from undertaking these high risk/high reward projects.

Dr. Samuel Broder, the former director of the National Cancer Institute and now chief medical officer of Celera Genomics, sees promise in a radical decentralization of responsibility for a portion of government outlays for medical research. “We need to trust individual researchers,” he argues, offering them substantial budgets and minimal second-guessing while they pursue novel approaches.

Dr. Broder is even optimistic that the same committees that now make such conservative choices in what research to fund could be persuaded to revise their thinking. “If you change the mandate, the decision-makers could implement the change,” he says.

The payoff for thinking outside the box can be quite dramatic, Dr. Broder notes. In 1982, Australian physicians Robert Warren and Barry Marshall had the radical insight that most stomach ulcers (and cases of stomach cancer) were probably caused by a common bacterium rather than by stress or diet. Yet it took many years for this insight to filter through the medical establishment and for ulcer therapies to be redirected to antibiotics.

3. Safety and Efficacy Regulation

Virtually everyone favors regulation of medical therapies. But by the same token, few subjects generate so much disagreement in terms of the consequences for both costs and availability of life-extending drugs. The Food and Drug Administration has often been caught in the political winds as it attempts to balance risk against potential reward.

Clinical trials and their review typically take many years, and only a small minority of candidate drugs ever receives approval for marketing. The average number of months to review an application actually rose in the late 1990s, before drifting down by a few months in 2001. But under a program for accelerated review

of critical drugs, the FDA claims it can now turn on a dime. For example, in the case of Gleevec, a drug used to treat a form of leukemia, the time between the day Novartis submitted clinical data on the drug to approval was less than three months.

Another positive sign is new FDA Commissioner McClellan's attempt to speed up the approval process for drugs. In a report, "Improving Innovation in Medical Technology: Beyond 2002," he called for improved communication between his agency and drug applicants, fellowships that would bring in new expertise from the outside, and tapping the expertise of practicing cancer doctors to establish "appropriate endpoints for clinical trial design."

But those looking at the process from the side of the pharmaceutical industry are less sanguine. "I have been involved in the drug-approval process for 35 years," says Dr. Carter, the former Bristol-Myers Squibb researcher and now a consultant. "I would say that it has never been harder to get a drug approved than it is today."

The inherent conservatism of bureaucracies is one problem. But Joseph Newhouse, a health economist at Harvard's Kennedy School of Government, argues that technological changes in the way drugs are developed offer good reason to take a fresh look at the whole testing process.

Advances in genomics, he suggests, may make it possible to approve the use of drugs selectively for groups that are not genetically at risk from side effects. "The

fact that an identifiable 5 percent of patients can't tolerate a drug, shouldn't deprive the other 95 percent of access," he says.

Steve Forbes, the publisher and former presidential candidate, is less circumspect in this criticism of the FDA's compulsion to cling to the status quo: "It's a lethal obstruction to progress," he concludes.

Dr. Jeff Leiden, President and Chief Operating Officer of the Pharmaceutical Products Group at Abbott Laboratories, also suggests that the FDA focus should be on safety, provided that manufacturers make a reasonable case for efficacy. It would be more efficient, he believes, to let doctors develop dosing and combination-therapy regimens in the clinic. This would bring life-saving therapies to the clinic faster and make investments in research-oriented companies more attractive. Gary Becker agrees, noting that elimination or reduction of the efficacy burden would lower the price of drugs for patients.

4. Surrogate Markers

Dr. Carter says the FDA has resisted another innovative approach based on new technology: the use of "surrogate markers" in determining drug efficacy. For example, physicians routinely use PSA scores to identify the presence of (and progress against) prostate malignancies. Accordingly, "every pharmaceutical company developing drugs for prostate cancer makes its decisions about whether to go forward on the basis of the PSA," Dr. Carter says. "But the FDA won't approve

a drug based on PSA response” – it demands direct evidence of increased survival. Thus drugs that would probably help cancer patients languish in review limbo.

Dr. Leiden argues that we need a paradigm shift from current treatments of late-stage disease with highly toxic drugs to drugs that are less harmful to healthy cells and potentially more effective for early intervention and even prevention. FDA policy does not recognize that different processes apply. Under current regulations, a proposed preventative or early-stage treatment must be proven efficacious against late-stage disease.

“When you have a disease that advances slowly in its early stages,” says Dr. Leiden, “clinical trials to prove efficacy take a very long time. By the time you get approval, your patent has almost run out, so there is little economic incentive to test these compounds.”

Dr. Leiden argues there is a desperate need for surrogate markers as proof of efficacy in cancer therapies.

“The acceptance by the regulatory community of some measurable surrogates versus the absolute is really tough,” he says. “So we end up subjecting thousands and thousands of patients to trials when they’re dying, which is not such a great thing.”

Paul A. Bunn, Jr., president of the American Society of Clinical Oncology, says that cancer research should not focus solely on curing the disease, but on

helping those who have it survive longer and live better lives – in other words, treating it as a chronic illness.

“People say, ‘When is cancer going to be cured?’ But that implies that it’s either cure or nothing,” he said in a recent *Wall Street Journal* article. “That isn’t the paradigm. It’s not all or nothing.”

5. Research Coordination

A significant portion of the research effort within the sprawling public-private medical establishment is duplicated because of lack of coordination. While lip service is paid to the issue, major research centers, public and private, as well as key researchers, have substantial incentives to keep their work to themselves.

That is no different than any other enterprise driven largely by technological change: Intel and AMD will surely duplicate efforts in creating the next generation of microprocessors. Yet competition between the two will also speed the process of bringing better microprocessor technology to market. But medical technology is unique, since much of the basic research is publicly funded and since there are often no shareowners to hold managers accountable for wasted effort. By the same token, lives are at stake – a delay of a few years in the development of a new drug can consign tens of thousands to an early grave.

Getting academic scientists and for-profit companies to work more closely could go a long way toward accelerating solutions to medical problems. But the

obstacles are daunting, says Dr. Perry Nisen, head of oncology at Abbott Laboratories. “How do you align the academic basic research enterprise with the applied effort of making stuff you can give to people?” he asks. “Some of it is ego. Some of it is focus. Some of it is a lack of understanding of what it takes to give something to somebody. Some of it is intellectual property. Some of it is money. They are big issues.”

Dr. Leroy Hood, President of the Institute for Systems Biology and a pioneer in the mapping of the human genome, says the complexity of the problems faced by medical researchers demands integrative approaches that are alien to much of the scientific establishment. He notes, for example, that “we know a lot about immunological responses – we’ve been studying them for 30 years.” But we know a lot less than we should because we’ve been “studying them one protein at a time,” thereby losing the insights that come with viewing the immunological system as a whole.

Dr. Carter views the lack of coordination and cooperation between pharmaceutical and biotech companies on the one side, and government, academic and non-profit research entities on the other, as a major stumbling block to finding medical solutions sooner. He cites AIDS as one example of what can happen when the walls between the two sides come down. Here, pharmaceutical companies shared their early test findings, which sped up the development of therapies for the disease – and helped prolong lives and reduce suffering.

Dr. Andrew von Eschenbach, Director of the National Cancer Institute, agrees that coordination is a key to accelerating the pace of innovation. He argues that the nation's health depends not only on dedicated researchers, scientists and physicians, but on leadership that will coordinate their efforts with a strategic view that brings all parties together for a single goal: finding treatments and cures sooner.

But Dr. von Eschenbach stresses that an effective “business plan” must be wrapped around the research. He says the nation's physical and economic health depends on an adequate rate of return on the national investment in public and private biomedical research. This involves more than simply throwing more money at the problem. As important as adequate funding is, it is the strategic application of those funds under inspired and coordinated leadership that will most likely create breakthroughs.

As a political reality, the government will appropriate and spend more money only if there is credible evidence of an adequate rate of return on the investment – in lives saved or productivity enhancements. Part of the mission of the Center for Accelerating Medical Solutions is to develop that evidence.

6. Protecting Intellectual Property

The linchpin to private investment in medical R&D is patent protection. The primary law governing the protection of new drugs is the Hatch-Waxman Act of 1984, complex legislation that extended patent protection beyond 20 years to

account for lags in regulatory review and eased rules for bringing generic versions to market once a patent had expired.

Industry trade associations note that most drugs that do make it to market fail to cover industry development costs. It takes an average of 14.2 years to bring a drug from the lab to market – and only one of five experimental drugs makes it through clinical trials and the FDA approval process, they say. But the patent rules remain controversial.

The whole area of patents is a complex subject that is beyond the scope of this paper, and one that continues to evolve. The broader question here is how to create an optimal patent structure – one that balances tensions between incentives to produce new treatments and accessibility of drugs for those who need them. This question is made even more difficult to answer by political, economic and regulatory uncertainties that dog the industry.

7. Unprofitable Treatments

While the government underwrites a substantial portion of the cost of research in medical therapies, the system still depends heavily on private industry to develop, test and market them. But for a variety of reasons, the market sometimes provides inadequate incentives to develop useful therapies.

The classic examples are “orphan drugs” used to treat rare disorders. In 1983, Congress granted special financial incentives to developers of such drugs.

And research by Frank Lichtenberg of Columbia University suggests that the program, which has yielded some 200 commercialized therapies, is successful. “One additional orphan drug approval is estimated to save an average of 211 lives in the subsequent year,” he concludes.

But compounds that cannot be patented because of their age and general availability may not see the light of day because it doesn’t pay for the industry to test and market them. The federal government has filled the gap in part – for example, by funding long-term studies on the anti-carcinogenic properties of common antioxidants like vitamin E. However, there is considerable disagreement about whether this approach has been pursued with sufficient vigor. And, in a few cases, there is genuine conflict between those who would introduce potential therapies with no commercial value and the holders of patents to competing drugs. In this context, Judith Rodin points to the protracted battle over the approval of lithium – a common compound that costs almost nothing to manufacture – for manic-depressive disorder.

Paradoxically, one may observe the opposite phenomenon – resistance to rigorous testing of new therapeutics on the part of a suspicious public. Dr. Stuart Holden, a Los Angeles-based urologist who is medical director of CaP CURE, points to the irony: “The same people who will casually use anything sold in a health food store,” he laments, “are deeply reluctant to be part of clinical trials for promising experimental drugs.”

8. Price Regulation

In theory, the makers of medical therapies are free to charge whatever the market will bear. And, in simple economic models of drug pricing, sellers maximize long-term profits by charging different prices to different segments of the market with different demand characteristics – much the way airlines charge vacationers willing to stay over Saturday night less than business travelers eager to get home to tuck the kids into bed.

But this market is far from simple. For one thing, the Bayh-Dole Act of 1980, which outlined the rules for patents on research that is partially or wholly underwritten by the federal government, mandates that products must be made available at a “reasonable” price. According to Peter Arno, Ph.D., an epidemiologist at the Albert Einstein College of Medicine in New York, and Michael Davis, a law professor at Cleveland State University, this regulatory power has rarely (if ever) been exercised. But it certainly casts a shadow over pricing policies in an era of tightening medical care budgets.

More significantly, buyers of drugs are organizing to create countervailing market power. Thus, big HMOs and major health care insurers bargain for rates using the threat of refusing to cover the use of specific drugs. And outside the United States, buyers are typically organized as government-mandated monopolies. Prices are thus set through bargaining – a process that leaves uninsured consumers, who have the least bargaining power, stuck with a disproportionate share of the bill.

A 1998 report to Congress estimated that pharmacy prices were 72 percent higher in Maine than in Canada and 102 percent higher than in Mexico. Patricia Danzon, a specialist in health care finance at the University of Pennsylvania, argues that these figures are substantial overestimates of the true price differences. Moreover, she notes that efficiency does not require uniform pricing any more than it would be efficient to leave seats empty on airline flights if marginal travelers couldn't or wouldn't pay full fare.

But the political tensions created by price differences – and the tendency to resolve the issues by narrowing price gaps – create uncertainty and raise the rate of return required by investors in hugely expensive drug-development programs.

Uwe Reinhardt, a health economist at Princeton University, says that government's hand in pricing drugs is here to stay, and that the realistic task for policy is to direct the government's role in ways that speed innovation and spread the cost burden to those who can afford it.

One answer, he says, is for the government to increase the returns on important new drugs by allowing federal programs to pay more for them – and make up the difference by paying much less for close substitutes. “The Japanese and French do this already,” he notes. “Their pricing policies are quite brutal.”

By the same token, American consumers and taxpayers bear a grossly disproportionate share of the cost of developing new therapies. (The total cost of prescriptions in the U.S. in 2001: \$132 billion.) In part that reflects ability to pay –

Africa cannot foot the bill for curing AIDS, malaria or a half dozen other diseases that plague the continent. But Dr. Reinhardt notes that, by virtue of using government as a monopoly buyer, most European countries pay far less for the fruits of modern medical technology than Americans.

“Maybe I’m naïve,” he says, “but wouldn’t it be possible to use diplomatic pressure to get other rich countries to pay their fair share?” That would increase the potential return on new therapies, and thus the amount invested in research.

9. Clinical Trials

Advances in genomics and informatics make it possible to know a lot more about the impact of a drug before it is tested on humans than in the days of largely random searches for therapeutic chemicals. But Dr. Stuart Holden, the Los Angeles urologist who is a researcher in prostate cancer, notes that there is still “no substitute for a careful, well-thought-out clinical trial.” And that is an expensive process: roughly 30 percent of the average cost of developing new therapies is spent on clinical trials.

There may, however, be relatively low-tech ways to reduce these costs sharply. In developing drugs, time is money – the return on a successful drug depends critically on how quickly it can come to market. Yet, on average, clinical studies take about seven years from design to completion. And, according to Dr.

Holden, a good portion of that time is spent finding suitable test subjects willing to participate.

In 2001, 86 percent of all clinical trials failed to meet their enrollment goals – up from 80 percent in 1999 – causing delays of up to a year, according to CenterWatch, a Boston-based group that provides information on clinical research worldwide.

One part of the answer may be to create better electronic databases of trials in progress, trials in the process of recruiting subjects and potential patient-subjects by infirmity, age, gender, location, etc. Another is to educate doctors about opportunities to enroll patients in trials. This should appeal to the profession, Dr. Holden argues, “because access to experimental treatments gives physicians a competitive edge – something they can offer very sick patients.”

Another part of the answer is to change the mindset of insurers in funding the use of promising drugs approved for other uses. “Insurance companies will pay for chemotherapy we know doesn’t work,” he notes ironically, “but won’t pay for drugs that might work.”

Dr. Edward Benz, President of the Dana-Farber Cancer Institute in Boston, agrees that the whole area of clinical trials is in desperate need of help – financial support, more patients and more physician/scientists who can bridge the gap between basic science and drug development. He points to the example of Dr. Barry S. Collier, a physician who worked in a basic science lab for years studying

blood-clotting, while also teaching and working with patients. Connecting his scientific findings with what he saw in his patients led him to discover a new antibody, commonly known as ReoPro, which has become one of the most widely used and effective therapeutic agents in modern cardiology.

“Those kinds of stories are getting rarer and rarer,” says Dr. Benz, “because there are fewer and fewer people who make that connection.”

Dr. Perry Nisen of Abbott Labs agrees that clinical trials is an area where much more is needed. “As low as three percent of cancer patients go into clinical trials, when everybody is still dying,” he says. “That’s pretty sick.”

10. Medical Ethics and the Law

Ethical and legal issues are always near the surface in the battle to accelerate medical solutions. Some are as fresh as yesterday’s headlines: Should it be possible to use fetal tissue to repair failed organs? Should the unexpected death of a subject in a gene therapy trial be cause to slow development in this astonishingly promising field? Is it wrong to allow those in need of organ transplants to offer financial incentives to obtain them?

“Libertarians believe that virtually any voluntary transaction should be permitted,” notes Arthur Caplan, Director of the University of Pennsylvania’s Center for Bioethics. “But that is hardly the consensus.”

Other issues have been simmering for decades. It is one thing to enroll terminally ill patients in experimental drug programs that offer hope, however faint, of helping them. But how much risk should others be asked to bear, and what should constitute informed consent? “In early-stage drug testing to establish safety,” Dr. Caplan points out, “subjects typically have little or nothing to gain.”

If Americans won’t volunteer, is it ethical to pay poor people in other countries to serve as guinea pigs? In Dr. Caplan’s words: “When does payment become exploitation?” Or turn the question around: Do we have the right to impose our ethical views on other cultures, which may choose not to regulate drug testing?

Many people are impatient with abstract considerations of the ethical issues that can interfere with the development of lifesaving treatment. But attempts to short-circuit public discussions of ethics can backfire. Dr. Caplan offers the example of genetically engineered plants, whose development has been slowed to a crawl by adverse publicity and the response of an ill-informed public.

“The failure to attempt consensus on the ethical basis for using new technologies can be disastrous,” he argues.

A far more visible issue at the crossroads of medicine, ethics and the law is the issue of legal liability. Drug makers and physicians argue that Americans’ inclination to use the courts for compensation when treatment fails slows technological progress and drains money from research budgets. “If you force

physicians to practice defensive medicine,” warns Dr. Richard Merkin, Chief Executive Officer of Heritage Provider Network, “before you know it you’ll have bankrupted the system.” President Bush has already weighed in on this side, calling for Congress to limit the amount injured patients can win from doctors as the answer to cutting high malpractice insurance costs. For their part, trial lawyers argue that easy access to courts is vital to redress wrongs and deter reckless behavior on the part of physicians and pharmaceutical companies.

CAMS does not anticipate taking sides on core issues of ethics or partisan politics. But it can play a valuable role in narrowing differences among people of good will by answering some key questions: How much do liability considerations really affect the pace of technological change and the diffusion of new treatments? How much would limitations on access to legal redress – voluntary or involuntary – affect the incentives of those pursuing high-risk treatments for terrible diseases?

The issue promises to heat up this year. President Bush has called on Congress, and the two sides are gearing up for a difficult political fight.

VI. IT’S TIME TO ACT

The need for this effort to find medical solutions sooner is clear. One in two families will be touched by cancer alone, and it is predicted that one out of five babies born in the United States today will someday die from cancer unless there

are breakthroughs. Millions of others will die from heart disease or suffer from Alzheimer's, stroke or diabetes.

With our population aging – the 76 million members of the baby-boom generation are turning 50 at the rate of one every seven seconds – those afflicted by these diseases, and the costs to treat them, are expected to rise dramatically in the decades ahead.

We all have an interest in finding improved treatments and cures. Most of us know someone – a father, sister, child, friend or colleague – who has suffered from or died from one of these diseases. No one is immune.

Make no mistake: We have accomplished a tremendous amount in the past few decades. But much remains to be done. And many answers lie within our grasp.

For the first time in history, success in the race to find cures may save those already afflicted as well as those who will be afflicted in the future. It's possible for us to save many people who are alive today, but who in the past would have died.

The Center for Accelerating Medical Solutions is in a unique position to tackle the issue of accelerating medical solutions. It has the ability to bring together key decision makers from various disciplines. And it offers concrete, attainable goals and plans of action in a non-partisan, non-profit framework.

The choice is ours: We can sit back and wait for cures and treatments in a generation or two, or we can marshal our resources and solve these problems sooner. The clock is ticking.

We all want to leave our children a nation free of war – a world that cherishes the sanctity of a single life. Yet nearly as many American lives will be lost to cancer in the next 12 months as were lost in all the wars of the 20th century. We all want to leave our children with a country free from debt. Yet we are burdening them with massive medical costs associated with an aging population. We want to change that for the better.

Above all, this effort requires leadership, commitment and support – a call to action that will mobilize our brightest minds in an urgent and vital effort. Many doubted that we could reach the moon in a decade when President Kennedy established that goal in 1961. We did it and we did it ahead of schedule because smart people under able leadership broke through bureaucracy and stayed focused on the goal. We need that same drive and focus in the effort to accelerate medical solutions. It's time to act. We urge you to join us.