Improving Health:
Is Biomedicine Up To the Task?

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The Clinical Research Roundtable has worked exceptionally well over the past four years to bring coherence and direction to the complex clinical research enterprise. I hope to do no harm today! I am reminded of the aphorism that the difference between an optimist and a pessimist is that the optimist thinks this is the best of all possible words --- and the pessimist thinks the optimist is right.

I was asked to speak as an outsider - as someone with no stake in any piece of the clinical research complex. Well - no formal stake, that is, except that of a person who has on occasion been a patient in clinical trials and who is here today because of clinical research that has been transformed into the diagnostic devices, the drugs and surgeries that keep saving my life.

The title of my talk is "Improving Health: Is Biomedicine Up to the Task?" We hope it is, but the answer to this question lies in the kind of clinical research infrastructure we maintain and build.

First, it is important to acknowledge, as Don Peck did in a recent *Atlantic Monthly* article[1], that heart disease, HIV and breast cancer death rates are all down, as are those of chronic disabilities. Life expectancy is up and various medical interventions are prolonging and enhancing quality of life or staving off aging. So, while we seem to be in good health as a nation, I want to talk today about what it will take to maintain this positive trajectory over the next 10 years.

One powerful trend that may derail the decreasing mortality rate is the growing extent to which people today are on their own in making decisions about health and health care. This means that while we have more options about preventing and treating diseases than ever before, most of us have to struggle to figure out the best choices for *ourselves* and our families.

Half of us in this room – maybe 7 out of 10 – are already living with a chronic condition of some sort. And most of us spend most of our time far from the oversight of our own health professionals, relying instead on a family member, or ourselves to make important health decisions.

As more people have more health decisions to make, many lack health insurance or are underinsured. And those of us who are accustomed to receiving health insurance through our workplace are in for a big surprise over the next couple of years. [2]

A recent survey found that 73 percent of employers are planning to offer Health Savings Accounts to employees over the next two years.

This move is usually accompanied by implementation of a high deductible catastrophic health insurance plan that means most of us will be making unfamiliar judgments about various services from various doctors and various hospitals – on our own.

Even when you do have insurance – even when you are a health professional – you will find that the health care delivery is fragmented and uncoordinated and that you are bombarded with advertising promising to make you potent, hairy or continent.
The result is we all wind up acting as our own diagnosticians and medical historians as we piece together care that works for ourselves, our kids and our parents.

We are left even further on our own by the systematic dismantling of science-based public health protections by Congress and the administration. In recent months, the Bush administration and the Republican Congress have

- overturned ergonomics regulations in the workplace
- refused to raise taxes on cigarettes
- ignored the rising urban asthma rates when considering revisions to the Clean Air Act and
- continued to insist, all evidence to the contrary, that condom distribution promotes promiscuity.

Apparently even public health is now a matter of personal responsibility.

In short, the success of biomedicine in improving health depends increasingly on the most fragile link between scientific knowledge and outcomes: individuals' actions. While biomedical research is producing innovations that might improve health, our risk of preventable illness is growing due to a confusing welter of choices that we are unprepared to make.

The missed opportunities that result from depending on individual behavior to connect knowledge and practice will only be multiplied by two larger trends - demographics and technology.

The first trend - demographics - is as predictable as the return of the cicadas in 2021. These facts are deeply familiar to you:

- In five years, the 78-million Baby Boomers will begin to retire, peaking in 2015. The 45 million born into the following generation won't be nearly enough to replace them, much less to fill the 22 million white collar jobs expected to be created by then.

- The racial and ethnic makeup of the country also will change significantly: Whites as a share of the total population will decline from the current 74 percent to about 65 percent by 2015, which means a broadening of language and cultural diversity in America.

- The recent report by the IOM on health literacy found that poor understanding of health information is clustered in those groups that are expected to increase in size in the next 10 years - minorities, the elderly and the chronically ill.[3]

The second trend - technology – will change the map of biomedicine at precisely the same time individuals are less able to navigate it.

- Personalized medicine will tailor interventions to fit each individual's unique genetic make-up.

- The management of chronic conditions will be greatly enhanced with the use of in-home monitoring devices, 24/7 electronic contact with health care advisers to prompt medication compliance.

- Advances in cardiovascular care will mean treatment in less costly settings. Better, longer-lasting artificial joints will mean more independence for older people, and premature babies will be kept alive through advances in prenatal steroids and high-frequency oscillatory ventilators.

That's the great news. The less great news is that each of these innovations will require people to weigh the benefits and costs and examine the short- and long-term consequences in order to make decisions reflecting their values, preferences and resources. And then they will have to participate in their increasingly complex medical care. Given what we currently know about people's willingness and abilities to comply with complex medical regimens, this is not going to be a slam dunk.

If you put all this together, what you get is a picture that looks like this: Decentralized medical authority with you at the center of decision-making in a country that will soon include a very large group of old people, the majority of whom are white and who have chronic or disabling conditions. They - or we -- will be cared for by a younger population that is largely nonwhite or foreign born, with less income and whose taxes will pay for the older generation's care.

So we need to ask ourselves what we need to do differently today in order to address the health needs of *this* population in 2014 and what the clinical research enterprise must do to make sure that happens.

These questions, however, assume a close relationship between biomedical research and public health imperatives that really is not operational in the United States today. As you well know, public health imperatives do not drive the public or private research agendas except in the most general manner.

Which brings me to a second set of observations:

When I was asked to look at the clinical research infrastructure as an outsider, I asked myself what if I could create from scratch a research system that would actually improve health.

What would be so incredibly obvious that outsiders like me would be completely baffled if it didn't already exist?

My outsider's eyes envision an integrated way of analyzing the root causes of ill health and the creation of multiple, robust lines of research focused on achieving the desired goals. That is, we need a system driven by what we know and what we know we want to achieve.

Imagine what would have happened if we had devoted efforts exclusively to working out all the basic mechanisms of how polio caused paralysis, but we had no vaccine, no way to effectively deliver it or no rehabilitation services? What if there were no treatment centers for those who got the disease and needed to be sustained? No rehabilitation services to help people return to optimal functioning?

Of course we need to value and support research at every level of this enterprise, from molecular biology to effective physical therapy.

So, for example, we'd look at the mounting threat of obesity: what causes it? Based on the answers, what kind of research would we fund?

We are not going to beat obesity with a pill. Even people who withstand the horrors of gastric bypass surgery regain weight – because even though their food intake volume is drastically cut – most of them increasingly elect to eat small amounts of calorie-rich food.

And we are not going to beat cancer with basic science. Of course, I recognize that there are rare exceptions to this – the Gleevecs of the world. But the big picture is that preclinical models approximate human disorders too crudely, NIH study sections resist recommending innovative proposals and we continue to kid ourselves about the role behavior plays in cancer prevention and treatment.

We have lobbied ourselves into believing basic science can do an end run around human behavior. We continue to believe this at our peril. The fact is that the major contributions to improved health over that last 30 years have been seat belts, air bags, bike helmets and smoking cessation.

In a system driven by what we know and what we want to achieve, there is no doubt about the importance of basic science.

But basic science generates *knowledge* - it does not generate *health*. We have to stop asking it to.

Basic science is where we make progress in accumulating biological information. We need equally robust translational, clinical and behavioral studies. These are where we make health progress. And they need to be aimed at achieving positive changes in the health status of the nation.

Let's look at obesity.

Given the recent blitz of public and scientific attention to the obesity epidemic, one would think this thick blanket of fat suddenly descended upon the United States at the dawn of the 21st Century, prompting Surgeon General's reports, a wave of worthless diets and the crash of the carbohydrate industry.

Someone should ask the CDC how long it has been forecasting this epidemic.

Allen Spiegel, director of NIDDK and cochairman of the Obesity Research Task Force at the National Institutes of Health, said, "Not to disparage anyone, but this has been a backwater of science for many years."[4] I say maybe some disparagement IS in order. Note that NIH will spend 12 times more on studies of cancer than obesity this year.

Why is NIH late to recognize the size and urgency of obesity as a health problem and why now, after three years, is it still having trouble programming money and researchers to work on it? Well, because NIH has no mandate to use a formal, rational method to set priorities that directly address public health imperatives.

The lack of direction of publicly funded health research has been argued and re-argued over the years.

Congress has done so repeatedly - notoriously when Rep Ernest Istook, in 1996, recommended a "body count" allocation of research dollars5 suggesting that NIH funding should be related proportionally to deaths due to various diseases.

Advocacy groups have taken another tack. The Parkinson's Action Network, for example, proposed in 1998 to allocate research funds by disease prevalence.[6]

In Planning for Serendipity, the Progressive Policy Institute's proposal for research priority-setting,[7] decision scientist Tammy Tengs wrote that the NIH mission should be to "produce the greatest possible reduction in the future burden of disease and injury." She goes on to speculate about which strategic allocation of funds could accomplish this while simultaneously taking advantage of scientific opportunities for breakthroughs and incremental findings to reduce the size of the burden.

In 1998, Leon Rosenberg chaired an IOM Committee on NIH Priority-Setting Process which produced a report[8] recommending that NIH have better procedures in place to allow the public to makes its views known. (That led to the office of public liaison). But another recommendation received less eagerly was that NIH work more diligently to gain knowledge about the burden on illness within the United States, since NIH needs a database for setting priorities in making funding decisions.

And ethicist Daniel Callahan, in his recent book, *What Price Better Health: The Hazards of the Research* Imperative, wrote: "While research advocacy and its politics have played a central role

in the allocation of research money, some higher standards can be envisioned. Medical research ought also to reflect some vision, some long-range picture of what a society desires in the name of greater biological knowledge and improved health."[9]

Even the Clinical Research Roundtable obliquely addresses this issue in its proposal for the Cooperative for Healthcare Improvement Research, which recognizes the need for research to accomplish specific aims.10
And this is only a small sample of recent calls for accountability of publicly funded biomedical research to address public health needs.

As I mentioned before, the aim of basic research is not to contribute to health gains but rather to increase knowledge about human biology. And the current NIH Roadmap will eliminate redundancies, streamline research and produce information that ultimately will be useful to clinical research.

But it is pretty clear that the current laissez faire method of allocating clinical research dollars primarily to investigator-initiated research grants does not produce knowledge that will adequately address the new and burdensome health imperatives that will inexorably develop over the coming decade. And the obesity example is only the most obvious one this week.

Given the impending health challenges ahead, I think it is time to once again seek innovative ways to square the public's investment in health research with the population's health needs.

The trick is how to shape publicly funded clinical research to respond to current and future health threats in a highly political environment with many public, private and non-profit stakeholders vying for resources. This will take leadership from all the stakeholders that make up the clinical research enterprise.

But aligning the clinical research enterprise with actual health needs is only one strategy to use scarce public resources more wisely. Another is to improve the effectiveness of the clinical research enterprise itself.

To my knowledge, we rarely systematically subject the way we fund, conduct, train for, or communicate clinical research to the scrutiny of its own methodological and analytical tools. Could it be that a perfect system of supporting and conducting research to achieve optimal benefit has evolved on its own? That would be a first.

If we can agree that it is not perfect, why would we resist investing in the systematic investigation of what kinds of training, grant mechanisms, public-private partnerships would help us do it better? It is ironic that such a bastion of scientific knowledge as the U.S. Department of Education is using scientific methods to evaluate different means of producing student outcomes, while the clinical research establishment is satisfied with the status quo and is generally resistant to any such scrutiny.

Well, I say - let no *scientist* be left behind! Especially not when the NIH budget is less than half that of the Education Department. Let's apply the scientific method to the question of how to improve the scientific method!

- Do we know, for example, what works and what does not in training researchers to cross disciplinary boundaries?
- What is the best composition of study sections to ensure flexibility in funding innovation?
- Do we know the career trajectory for M.D.-Ph.D.s?
- What do we know about the relative effectiveness of RFAs, Program Announcements and RFPs in addressing different levels of research questions?

It seems that most changes in the federal biomedical research enterprise take place in response to problems or criticism that something isn't working and that the solutions are chosen by their face validity. It is interesting that scientists, who are trained to reject face validity out of hand, are so willing to depend on common sense alone to ensure the best outcomes.

Clinical researchers lag behind even their clinician colleagues in systematically scrutinizing their own performance.

This is not to minimize efforts that are under way to apply scientific methods to improving the application of knowledge in at least part of the clinical research establishment: AHRQ Director Carolyn Clancy, who you are hearing from later, talks about improving the health care delivery system as a *scientific* challenge.

She said in a speech to the annual meeting of Research!America last year, "We have always assumed that if we produce knowledge the health care delivery system will pick it up. As scientists, if we don't stand up for delivering what we have discovered, health care delivery is a failure."[11]

So, for example, we are seeing development and evaluation of electronic medical records, exam-room and bedside decision-support and real-time home monitoring. As they become more efficient, they will become part of the fabric of measuring which care is delivered and connecting it to clinical outcomes – with the aim of ensuring that evidence-based medicine is more the norm than the exception.

How far back into the clinical research enterprise do you think we can push the use of science-based methods to help us figure out what is working and what is not? It is responsible. It is possible. It is being done in other parts of the health system. How can we make this more of a priority in clinical research and whose responsibility is it to do so?

And this leads me to the critical question for a meeting of this kind in a place like this: What is the unique role of the government in improving and maintaining the clinical research infrastructure?

In these times it is particularly important to determine where commercial interests succeed, where they fail, and, correspondingly, where government must assume responsibility.

As I talk with to leaders in the voluntary sector, in professional societies, in health plans, and in the advocacy groups, I find there is real confusion among the different stakeholders about who is carrying what ball down which field. This confusion leads to redundancy of effort in some cases, absence of activity in others and a general sense that competition rules the day.

I'm talking here about the public sector's role in a larger sense: what are those things that are falling through the cracks? It is not the responsibility of government to translate the products of clinical research into health care practice and policy. That we leave to the private sector. But there are clear gaps where commercial and professional interests have neither the incentive nor means to fill. Spelling out those gaps, to me seems to be part and parcel of figuring out the parameters of the task at hand - improving the infrastructure of clinical research.

The members of the Clinical Research Roundtable described some of these elements in the paper authored by Sung and the members of the Clinical Research Roundtable last year in JAMA.[12] The article precisely identified some investment that should be made to build the research capacity for what you identified as the second translational barrier – translation of new knowledge into clinical practice and health decision-making.

It called for more support for information technologies, of AHRQ, of training M.D.-Ph.D.s and of the nation's 79 general clinical research centers. This paper was exquisitely clear about whose responsibility it is to build and support these clinical research capacities.

Actually, since the Clinical Research Roundtable was so successful in identifying the gaps in capacity -- and since all stakeholders are represented here, I wonder if *you* could come up with a consensus about what is not getting done that must be done to contribute toward the upward trajectory of health in this nation. And then name whose responsibility it is to do that and how it is going to get done. Or say, "No one can do this; it is too controversial."

Clinical research infrastructure on the public side seems hamstrung by lack of clear definition of role – a mandate so broad and inexplicit that it can't say no to anything, but can't really say yes either for fear of stepping on the private sector's toes. At the most recent AHRQ National Advisory Council meeting, I participated in a discussion about the development of electronic medical records in which the notion of the role of the government ranged from creator to arbiter to evaluator to pitchman for good examples. Should the government develop standards for electronic medical records? Conduct research on their use? Should it be the source of information for public about EMRs or should it set standards and provide or enable quality ratings? Where is commercial competition standing in the way of progress?

The question we all have to answer – and which the Clinical Research Roundtable has been working on in a thoughtful, thorough way over the past four year's is how can we use limited public research funds in the wisest, most strategic way to amplify the work of the for-profit and non-profit sectors to improve the health of Americans?

I started out today asking whether biomedicine is up to the task of improving health. And frankly, as I heard myself talk, I became pessimistic.

Because the health challenges we can anticipate - the demographic, social and technological trends – cannot be overcome by simply doing more of the same things: you can't just put more money into existing activities and institutions and expect you will produce a better outcome.

I have suggested three broad approaches to improving the clinical research infrastructure.

1. Agreeing on a way to measure the burden of disease in America and devising formal rational plans to anticipate and mobilize the clinical research enterprise to address that burden.

2. Launching a strategic and comprehensive evaluation and quality improvement effort to increase the effectiveness of the clinical research enterprise in producing interventions to prevent, treat and manage disease.

3. Coming to a clear agreement of where the private and non-profit sectors do not operate well - where progress is halted or retarded because it is in no one's institutional interest to act. That delineates the job of the government. Then look for the things that the government can't do because they are too controversial. And identify a new solution.

Now these three recommendations are pretty idealistic. They violate some of the most powerful taboos of the scientific tradition.

But unless these things are done in some form or another, chances of continuing that positive health trajectory are dim, given what we know about the future.

No one sector or group represented on the Clinical Research Roundtable can do any of these things alone. The rest of you would have it for lunch.

The genius and the burden of the Roundtable is that everyone is represented. Genius because your endorsement of an idea or direction – should you put real muscle behind it – is absolutely unstoppable. And burden because there are not that many things you agree upon sufficiently to do be willing to really pony up.

The description for the Cooperative for Healthcare Improvement Research that we will discuss over the course of this meeting gives me great hope that that participants in the CRR will continue to interact to produce some greater goods. But if it is to make a difference, the approaches I've identified to improve the clinical research infrastructure today apply equally to

the development of a smaller entity – this cooperative. You need a plan, a way to set priorities about what you take on. You need to have confidence that the methods you use are best suited to answer the problems you choose to address. And you need to take on responsibilities that such an organization can uniquely perform - not what the private sector or voluntary sectors do and not what the government should do.

It is a fundamentally American trait to view the future with optimism: that we can do more and do it better. And flexibility and optimism are what we need right now.

Investing in clinical research is an investment in hope – hope for a cure for one's self, a relative or a friend -- and for future generations. If health research doesn't produce better health, the public's faith in science will falter.

Given the problems biomedicine will be expected to solve in the next 10 years, and the investments and priorities in clinical research we are making today, the answer to our question is that biomedicine will not be up to the task of actually improving health.

But this doesn't have to happen.

We are fortunate that we have notice of these potential failures: we can see now where we will fall short then. We have time to adjust, to re-balance. We can build on existing efforts to use evidence as the basis of decision-making for clinicians and extend it to refining the ways in which we set priorities and fund research for the future.

This means applying the tools of scientific analysis to the operation of the entire clinical research enterprise. It means being willing to do things differently, adapting to shifting demands and contingencies. And it means building the capacity of health systems and professionals to absorb new information and practices.

It's my hope that you who have vision, flexibility and the authority will take the lead in ensuring that clinical research lives up to its promise of improving health.

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